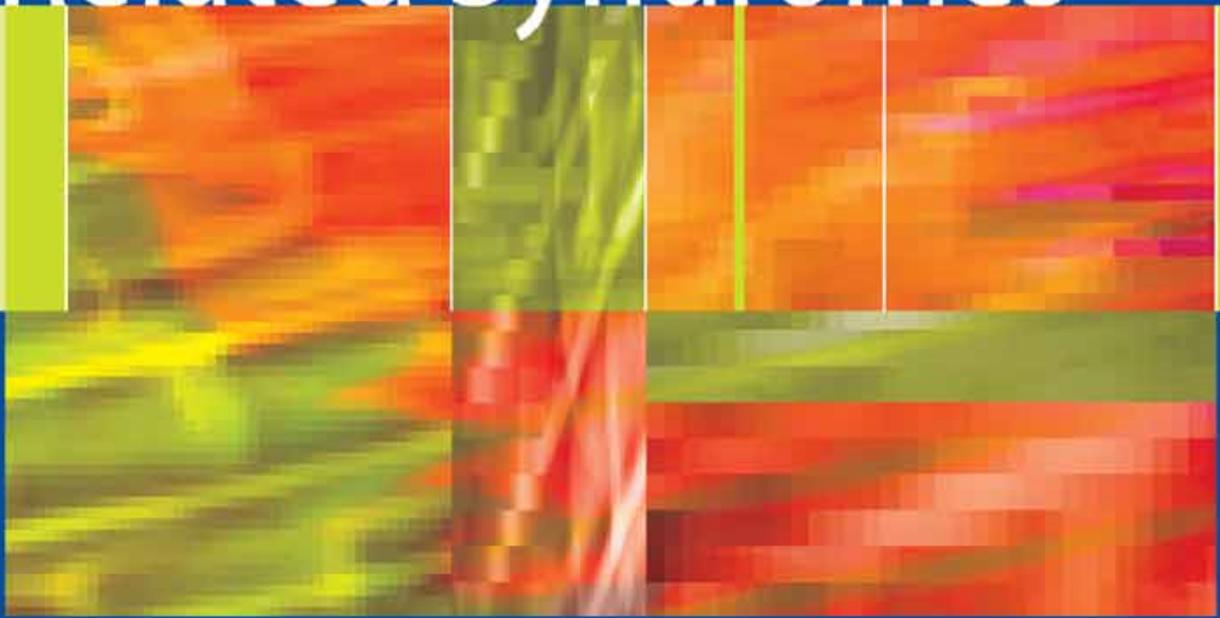


Ragavendra R. Baliga  
Christoph A. Nienaber  
Eric M. Isselbacher  
Kim A. Eagle *Editors*

# Aortic Dissection and Related Syndromes



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# **AORTIC DISSECTION AND RELATED SYNDROMES**

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# AORTIC DISSECTION AND RELATED SYNDROMES

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# Preface

Aortic dissection affects approximately two out of every 10,000 individuals. Despite its common occurrence and potential to be fatal, up-to-date references have been difficult to locate. To meet this need, the editors have assembled an international group of authors with substantial experience in this field and in the International Registry of Aortic Dissection (IRAD) to contribute to this book.

The book has been divided into sections to make it user-friendly: Section I, Epidemiology, Pathophysiology, and Clinical features; Section II, Imaging Methods; Section III, Initial Treatment; Section IV, Subsequent Follow-up and Treatment; Section V, Evaluation and Management of Special Subsets; and Section VI, Future Frontiers. Each of the book's 18 chapters provides a succinct overview of the current clinical literature and incorporates several figures to illustrate the text.

We hope that this state-of-the-art publication will enhance understanding of aortic dissection and stimulate research in the area of acute aortic syndromes.

Sincerely,  
The Editors



SECTION I:  
EPIDEMIOLOGY, PATHOPHYSIOLOGY,  
AND CLINICAL FEATURES

# 1

## **EPIDEMIOLOGY OF THORACIC AORTIC ANEURYSMS, AORTIC DISSECTION, INTRAMURAL HEMATOMA, AND PENETRATING ATHEROSCLEROTIC ULCERS**

Eric M. Isselbacher

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### **THORACIC AORTIC ANEURYSMS**

Anatomically the thoracic aorta is divided into a several distinct segments (Figure 1.1). The ascending aorta extends from the left ventricle (at the aortic annulus) and rises in the anterior mediastinum to the innominate artery. The base of the ascending aorta is referred to as the *aortic root*. The root is the widest aortic segment and is comprised of three coronary sinuses, which bulge outward, and serves as the support structure for the aortic valve cusps. The portion of the ascending aorta above the root is narrower and tubular in shape. Distal to the ascending aorta is the aortic arch, which moves posteriorly and to the left in the superior mediastinum, extending from the innominate artery to the ostium of the left subclavian artery. Thereafter, the descending aorta courses posteriorly, adjacent to the vertebral column, and continues to the level of the diaphragm, after which it becomes the abdominal aorta.

The true incidence of thoracic aortic aneurysms is difficult to determine, as many go undiagnosed. However, in a Mayo Clinic sampling from 1980–1994, the incidence in Olmstead County, Minnesota, was 10.4 per 100,000 person years<sup>1</sup>. This was significantly higher than the incidence in the same

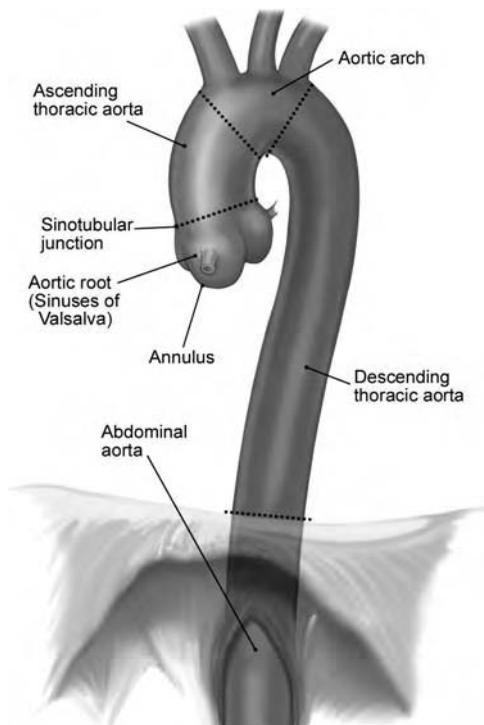


Figure 1.1. Thoracic aortic anatomy. © Massachusetts General Hospital Thoracic Aortic Center. Used with permission.

population prior to 1980 but may have reflected advances in diagnostic imaging techniques. Thoracic aortic aneurysms are classified according to the segment of aorta involved—either ascending, arch, or descending thoracic aortic aneurysms. Aneurysms of the descending thoracic aorta that extend below the diaphragm are known as *thoracoabdominal aortic aneurysms*. The anatomical distinctions are important because the etiology, natural history, and treatment of thoracic aneurysms differ for each of these segments. Based on the most current data, approximately 60% of thoracic aneurysms involve the ascending aorta, 10% involve the arch, 40% involve the descending aorta, and 10% involve the thoracoabdominal aorta<sup>2</sup>.

Thoracic aortic aneurysms most often result from cystic medial degeneration, which appears histologically as smooth muscle cell drop-out and elastic fiber degeneration, resulting in the presence in the media of cystic spaces filled with mucoid materia. The histologic changes occur most frequently in the ascending aorta but in some cases may involve the entire aorta. The medial degeneration results in a weakening of the aortic wall, which in turn leads to progressive aortic dilatation and eventually an aneurysm.

## CYSTIC MEDIAL DEGENERATION

### Hypertension

Cystic medial degeneration is known to occur to some extent with aging, but this process is accelerated by hypertension<sup>3</sup>. Hypertension leads to intimal thickening, degradation of the extracellular matrix, loss of elastic fibers, and smooth muscle cell necrosis. As a consequence, the aortic wall becomes stiff and progressively dilates. Thus, advanced age and hypertension are, collectively, important risk factors for the development of thoracic aortic aneurysms.

### Marfan Syndrome

On the other hand, when cystic medial degeneration occurs at younger ages, it is classically associated with recognized connective tissue disorders, such as Marfan syndrome (see Chapter 2) or, less commonly, Ehlers–Danlos syndrome (see Chapter 2) or Turner syndrome. Among those with Marfan syndrome, thoracic aortic aneurysms predominantly involve the aortic root in a pattern known as *annuloaortic ectasia*. Penetrance is variable, and in some with Marfan syndrome the aortic root is significantly aneurysmal by the teenage years, whereas others have much slower progression of disease, and still others have minimal or no aortic dilatation.

### Bicuspid Aortic Valve

Other congenital conditions can predispose to thoracic aortic aneurysms. It is now well recognized that those with a congenital bicuspid aortic valve have a significantly increased risk of aortic dilatation, aneurysm, and dissection. Echocardiographic studies of young people with normally functioning (neither stenotic nor regurgitant) bicuspid aortic valves have shown that about 50% have dilatation of the ascending aorta<sup>4</sup>. In the majority of cases the dilatation involves the tubular portion of the ascending aorta, whereas in a minority it involves primarily the aortic root (annuloaortic ectasia). A number of studies have identified cystic medial degeneration as the culprit. In one series, of those with bicuspid aortic valve undergoing aortic valve replacement surgery, 75% had biopsy proven cystic medial degeneration, compared with a rate of 14% among those with tricuspid aortic valves undergoing similar surgery<sup>5</sup>. One possible mechanism for the association of cystic medial degeneration and bicuspid aortic valve is that inadequate production of fibrillin-1 during embryogenesis results in both the bicuspid aortic valve and a weakened aortic wall<sup>6</sup>. No single gene responsible for bicuspid aortic valve has yet been identified, and it may well be genetically heterogeneous.

## Familial Thoracic Aortic Aneurysm Syndrome

Cystic medial degeneration has also been found as the cause of thoracic aortic aneurysms among many of those with neither an overt connective tissue disorder nor a bicuspid aortic valve. Moreover, while such cases of thoracic aortic aneurysms may be sporadic, they are often familial in nature and have now been termed the *familial thoracic aortic aneurysm syndrome*.

In an analysis using a large database of patients with thoracic aortic aneurysms, the Yale group found that at least 19% of patients without Marfan syndrome had a family history of a thoracic aortic aneurysm<sup>7</sup>. Moreover, they found that those with familial syndromes presented at a mean age of 57 years, which was significantly younger than the sporadic cases, who presented at a mean age of 64 years. Most pedigrees have suggested an autosomal dominant mode of inheritance, but some have suggested a recessive mode and possibly X-linked inheritance as well<sup>7</sup>. In a study of 158 patients referred for surgical repair of thoracic aortic aneurysms or dissections, Biddinger et al. found that first-degree relatives of probands had a higher risk (RR 1.8 for fathers and sisters, RR 10.9 for brothers) of thoracic aortic aneurysms or sudden death compared with controls<sup>8</sup>.

The genetics of the familial thoracic aortic aneurysm syndrome are being actively investigated. Milewicz et al. have identified a mutation on 3p24.2-25 that can cause both isolated and familial thoracic aortic aneurysms<sup>9</sup>. Aortic histopathology of these families reveals cystic medial degeneration. There appears to be dominant inheritance, yet there is marked variability in the expression and penetrance of the disorder, such that some inherit and pass on the gene but show no manifestation. More recently, two studies of familial thoracic aortic aneurysm syndromes have mapped mutations to at least two different chromosomal loci, whereas other families mapped to neither of these—suggesting at least a third locus<sup>10,11</sup>. The genetics may be rather complex; indeed, the fact that there is such variable expression and penetrance suggests that this may be a polygenic condition.

## Atherosclerosis

Atherosclerosis is infrequently the cause of ascending thoracic aortic aneurysms and, when it is, tends to be associated with diffuse aortic atherosclerosis. Aneurysms of the aortic arch are most often contiguous with aneurysms of the ascending or descending thoracic aorta. Arch aneurysms may be due to atherosclerotic disease but are often due to cystic medial degeneration and syphilis or other infections. Conversely, atherosclerosis is the predominant etiology of aneurysms of the descending thoracic aorta. These aneurysms tend to originate just distal to the origin of the left subclavian artery and may be either fusiform or saccular. The pathogenesis of such atherosclerotic aneurysms in

the descending thoracic aorta may resemble that of abdominal aneurysms but has not been extensively examined.

## **Syphilis**

Whereas syphilis was once the most common cause of ascending thoracic aortic aneurysms, accounting for up to 80% of cases, in the current era of aggressive antibiotic treatment of the disease it is now rarely the cause. The latent period from initial spirochetal infection to aortic complications is most commonly 10–25 years (range 5 to 40 years). During the secondary phase of the disease, spirochetes directly infect the aortic media, with the ascending aorta most often affected. The infection and attendant inflammatory response destroys the muscular and elastic medial elements, leading to weakening of the aortic wall and progressive aneurysmal dilatation.

## **Vasculitis**

Takayasu's arteritis typically causes obliterative lesions of the aorta, producing signs and symptoms of vascular insufficiency, but less often can produce aortic aneurysms. Takayasu's arteritis primarily affects young the young, typically those 10–30 years old, with females affected in 90% of the cases. It occurs most often in Asian populations. On the other hand, giant cell arteritis tends to affect an older population, especially those over the age of 55, but again with females affected far more often than males. In most cases, giant cell arteritis presents with signs and symptoms of temporal arteritis. When the aorta is affected, it may result in thoracic aortic aneurysms, most often involving the arch or descending aorta.

## **Other Causes**

Infectious aneurysms may result from a primary infection of the aortic wall causing aortic dilatation with the formation of fusiform or saccular aneurysms. Thoracic aortic aneurysms can also result from aortic trauma (see Chapter 2) or aortic dissection (see below).

## **Natural History**

The natural history of thoracic aortic aneurysms is affected by the size and location of the aneurysm. The best data presently available on the natural history of thoracic aortic aneurysms come from a longitudinal report by Davies et al. from the Yale group in which 304 patients with thoracic aortic aneurysms at least 3.5 cm in size were followed for a mean of more than 31 months<sup>12</sup>. The mean rate of growth for all thoracic aortic aneurysms was 0.1 cm per year. However, the rate of growth was significantly greater for aneurysms of

the descending aorta (0.19 cm per year) than for those of the ascending aorta (0.07 cm per year). In addition, dissected thoracic aneurysms grew significantly more rapidly (0.14 cm per year) than did nondissected ones (0.09 cm per year). Not surprisingly, those with Marfan syndrome also had more rapid aneurysm growth.

In this same study population, the mean rate of aortic rupture or dissection was 2% per year for thoracic aortic aneurysms less than 5 cm in diameter, 3% per year for aneurysms 5.0–5.9 cm, and 7% per year for aneurysms 6.0 cm or larger. In a multivariate logistic regression analysis of the predictors of dissection or rupture, the relative risk of an aneurysm diameter of 5.0–5.9 cm was 2.5, an aneurysm diameter of 6.0 cm or larger was 5.2, Marfan syndrome was 3.7, and female gender was 2.9. Other natural history studies that focused on thoracic and thoracoabdominal aneurysms have found that the odds of rupture are increased by chronic obstructive pulmonary disease (RR 3.6), advanced age (RR 2.6 per decade), and aneurysm-related pain (RR 2.3)<sup>13</sup>.

Thoracic aortic aneurysm size is an important predictor of rate of growth. Dapunt et al. monitored 67 patients with thoracic aortic aneurysms and found that aneurysms that were 5.0 cm or smaller grew more slowly than did those larger than 5.0 cm, and the only independent predictor of rapid expansion (>0.5 cm per year) was an initial aortic diameter greater than 5.0 cm<sup>14</sup>. Nevertheless, even when controlling for initial aneurysm size, substantial variation was still seen in individual aneurysm growth rates, thus making such mean growth rates of little value in predicting aneurysm growth for a given patient.

## AORTIC DISSECTION

The true incidence of acute aortic dissection is difficult to determine, as many cases may go undiagnosed, but its documented incidence is approximately 2.9 per 100,000 per year, with at least 7,000 cases per year in the United States<sup>15</sup>. A healthy aorta with an intact medial layer rarely dissects. Alternatively, those in whom the integrity of the media is compromised are at risk for aortic dissection. Therefore, any disease process or condition that damages the elastic or muscular components of the media predisposes the aorta to dissection. Indeed, cystic medial degeneration, as discussed above, is a major predisposing factor in aortic dissection.

The peak incidence of aortic dissection is in the sixth and seventh decades of life, with a mean age of 62 years among more than a thousand subjects in the International Registry of Acute Aortic Dissection (IRAD)<sup>16</sup>. Overall, men are affected twice as often as women (68% vs. 32%) and are affected at younger ages as well, with male patients having a mean age of 60 years and female patients a mean age of 67. However, as shown in Figure 1.2 the male predominance is most striking at young ages, with males outnumbering females 4:1

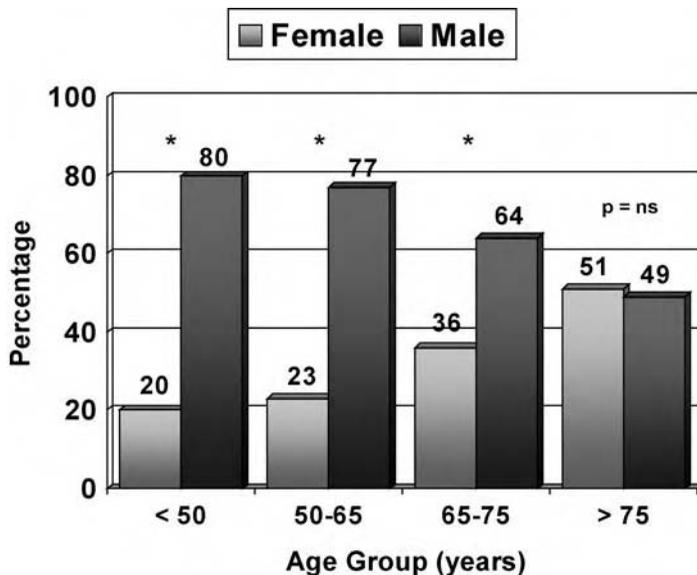


Figure 1.2. Proportion of males vs. females per age group in IRAD; \*  $p < 0.001$ . Adapted with permission from reference 16.

at ages less than 50. With increasing age, however, the difference lessens, and among those older than 75, males and females are equally represented.

Table 1.1 summarizes the contribution of recognized risk factors on the incidence of aortic dissection among the IRAD population. About three-quarters of patients had a history of hypertension. Only 14% had a known thoracic aortic aneurysm. Many more patients likely had a preexisting aneurysm that had simply gone undetected prior to the aorta's dissection. Bicuspid aortic accounted for 3.4% of aortic dissection cases, which was not much less than the 5% attributable to Marfan syndrome. As is the case with ascending thoracic aortic aneurysms, the risk of aortic dissection appears to be independent of the severity of the bicuspid valve stenosis. Much less commonly, aorta dissection results from other congenital cardiovascular abnormalities, including coarctation of the aorta and Turner syndrome.

The risk factors for and presentation of aortic dissection differ between younger and older patient populations. In IRAD, 7% of patients were younger than 40 years old. The differences between the two age groups are summarized in Table 1.2. Not surprisingly, Marfan syndrome was the major risk factor among younger patients, accounting for 50% of cases<sup>17</sup>. Conversely, this can be reframed to highlight the fact that 50% of young patients did not have underlying Marfan syndrome as a predisposing risk factor for aortic dissection.

*Table 1.1.* Known risk factors for aortic dissection from IRAD

Advanced age (mean)	62 years
Male gender	68%
History of hypertension	72%
Prior aortic dissection	5%
Known aortic aneurysm	14%
Marfan syndrome	5%
Bicuspid aortic valve	3%
Peripartum period of pregnancy	0.2%
Cocaine	0.5%
Cardiac catheterization/surgery	5%
Prior cardiac surgery	22%

*Table 1.2.* Comparison of younger vs. older patients with aortic dissection

Feature	Age < 40 (%)	Age $\geq$ 40 (%)
Marfan syndrome	50	2
Bicuspid aortic valve	9	3
History of hypertension	34	72
Hypertension on presentation	25	45

*Source:* Adapted with permission from reference 17.

Moreover, hypertension was much less common as a risk factor among young patients, and only 25% of young patients were hypertensive on presentation.

A number of reports have identified cocaine abuse as a risk factor for aortic dissection, typically among young, black, hypertensive men. However, cocaine likely accounts for less than 1% of cases of aortic dissection, and the mechanisms by which it causes dissection remain speculative<sup>18</sup>.

For decades, there has been recognition that there exists an unexplained relationship between pregnancy and aortic dissection, typically occurring in the third trimester or in the early postpartum period. In IRAD, only 0.2% of all aortic dissection cases were associated with pregnancy, which might suggest at first that it is a relatively minor contributor<sup>16</sup>. However, given that 93% of patients in IRAD were  $\geq$ 40 years old and the majority of patients were men, only a small minority could even have had pregnancy as a risk factor. Alternatively, if one considered only a cohort of those IRAD patients who were female and under the age of 40, one would find that 12% were associated with pregnancy, implying that there is some causal association. However, it is quite likely that pregnancy is a precipitant of aortic dissection among women

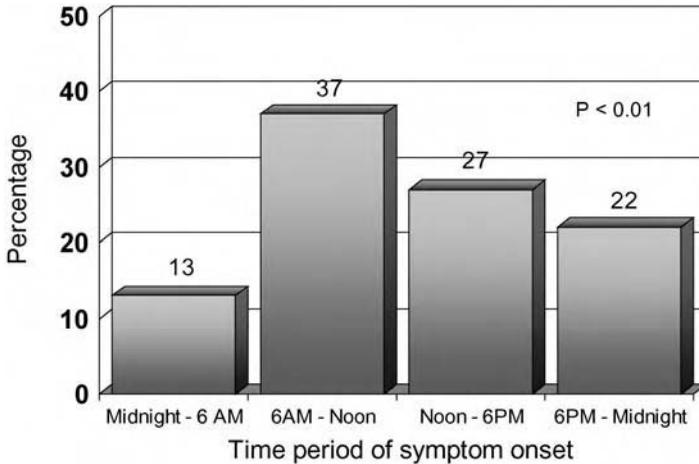


Figure 1.3. Frequency of dissection symptom onset during four periods of the day. Adapted from reference 20.

otherwise at risk (due to some underlying cystic medial degeneration), rather than the primary cause of aortic pathology.

Trauma can also cause aortic dissection. Blunt trauma and deceleration injuries tend to cause localized tears, hematomas, or frank aortic transection but only rarely cause classic aortic dissection. More commonly, iatrogenic trauma is associated with true aortic dissection and accounts for 5% of cases in IRAD<sup>19</sup>. Both the manipulation of catheters and wires within the aorta and the insertion of intraaortic balloon pumps may puncture the aortic intima induce aortic dissection. In addition, cardiac surgery also entails a very small risk (0.12–0.16%) of acute aortic dissection, which is usually discovered and repaired intraoperatively. Aortic dissection appears to occur more often as a late complication of cardiac surgery, typically occurring months to years after the procedure; in fact, 22% of those with acute aortic dissection have a history of prior cardiac surgery, 9% had preexisting aortic disease (prior thoracoabdominal aortic aneurysm or dissection repair), and 5% had prior aortic valve replacement. The association of dissection with aortic valve replacement may reflect the fact that many of those having undergone aortic valve surgery did so because of an underlying dysfunctional bicuspid aortic valve and thus would likely have had underlying cystic medial degeneration as well. It could then be the congenital cystic medial degeneration rather than the cardiac surgery itself that predisposed this group to late aortic dissection. Nevertheless, 6% of those with aortic dissection had only a CABG as their surgical procedure.

Data from IRAD indicate that there are chronobiological patterns of acute aortic dissection<sup>20</sup>. There is diurnal variation in the onset of aortic dissection (see Figure 1.3), with dissection occurring most often in the early daytime

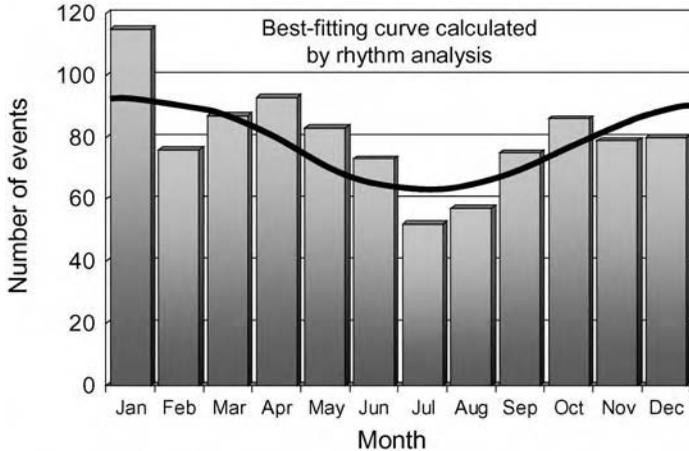


Figure 1.4. Seasonal variation in the onset of aortic dissection. Adapted from reference 20.

hours of 6 a.m. until noon and least often during the nighttime hours of midnight to 6 a.m. This circadian pattern was similar for all subgroups examined, suggesting that there are likely common triggers. Of interest is the fact that this pattern is similar to that seen with the onset of acute coronary syndromes. There is also a seasonal variation in the incidence of aortic dissection, with significantly higher rates of aortic dissection in the winter months, whereas event rates were lowest in the summer months (Figure 1.4).

## INTRAMURAL HEMATOMA

Intramural hematoma is a variant of classic aortic dissection. It results from hemorrhage that occurs in and is contained within the medial layer of the aortic wall, rather from a primary tear in the intima. Consequently, there is no communication between the hematoma and the aortic lumen. Nevertheless, the clinical signs and symptoms associated with intramural hematoma resemble those seen in classic aortic dissection. The distinction is therefore made on the basis of the findings of imaging studies, in which anywhere from 5% to 17% of apparent aortic dissection cases are diagnosed as intramural hematoma.

In the IRAD experience, of 1,010 patients presenting with apparent acute aortic dissection, 58 (5.7%) met the strict criterion of acute intramural hematoma<sup>21</sup>. Table 1.3 summarizes some of the demographics of the two groups in this study. As shown, those diagnosed with intramural hematoma were significantly older on average than those with classic aortic dissection ( $61.7 \pm 14.3$  vs.  $68.7 \pm 10.4$ ;  $p < 0.001$ ). There was no significant difference in the history of hypertension between the groups. Although it did not reach

*Table 1.3.* Demographics, history, and location of aortic involvement among patients with aortic dissection vs. intramural hematoma

Variable	Classic aortic dissection, % ( <i>n</i> = 952)	Intramural hematoma, % ( <i>n</i> = 58)	<i>p</i>
Age, years (mean ± SD)	61.7 ± 14.3	68.7 ± 10.4	<0.001
Gender:			
Female	30.9	39.7	0.16
Male	69.1	60.3	
White	85.9	98.1	0.17
Hypertension	71.1	77.6	0.29
Marfan syndrome	5.4	0.0	0.11
Type:			
A	64.7	39.7	<0.001
B	35.3	60.3	

Source: Adapted with permission from reference 21.

*Table 1.4.* Demographics of population with penetrating atherosclerotic ulcer

Age (mean)	71–77 years
History of hypertension	85%
Smoking	72%
Known coronary artery disease	61%
Thoracic or abdominal aortic aneurysm	38–53%
Peripheral arterial disease	17%
Prior stroke	12%
Chronic renal insufficiency	31%

Source: Adapted from references 22–24.

statistical significance, there was a trend toward a lesser proportion of Marfan syndrome patients among those with intramural hematoma compared with classic aortic dissection (5.4% vs. 0%;  $p = 0.11$ ). The anatomic location of aortic involvement was significantly different between the groups, with aortic dissection presenting twice as often as type A than type B, whereas intramural hematoma presented more often as type B.

## PENETRATING ATHEROSCLEROTIC ULCER

Penetrating atherosclerotic ulcers are atherosclerotic lesions of the aorta that penetrate the internal elastic lamina and allow hematoma formation within

the media of the aortic wall. The large majority of such ulcerations occur in the descending thoracic aorta, but less often they may occur in the arch or, rarely, in the ascending aorta. The ulcers may progress to form aortic pseudoaneurysms or, less often, lead to transmural aortic rupture. Table 1.4 summarizes the collective demographics from three series of patients with of intramural hematoma. Those in whom penetrating atherosclerotic ulcers develop tend to be elderly and are on average about a decade older than those who present with typical aortic dissection. Most have a history of hypertension and smoking. They tend to have severe and extensive atherosclerosis; the majority have evidence of other atherosclerotic cardiovascular disease and as many as half also have a history of a preexisting abdominal or thoracic aortic aneurysm.

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# 2

## **PATHOPHYSIOLOGY OF ACUTE AORTIC SYNDROMES**

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Cardiovascular disease is the leading cause of death in most Western societies and is increasing steadily in many developed countries. Aortic diseases constitute an emerging share of this burden. New diagnostic imaging modalities, longer life expectancy in general, longer exposure to elevated blood pressure, and the proliferation of modern noninvasive imaging modalities have all contributed to the growing awareness of acute and chronic aortic syndromes. Despite recent progress in recognition of both the epidemiological problem and diagnostic and therapeutic advances, cardiology and the medical community in general are far from comfortable in understanding the spectrum of aortic syndromes and defining an optimal pathway to manage aortic diseases<sup>1–13</sup>. This chapter reviews the etiology of aortic wall disease, natural history, and the pathophysiology of the complexity of acute aortic syndromes.

### **ETIOLOGY OF AORTIC DISSECTION**

All mechanisms weakening the aorta's media layers via micro apoplexy of the vessel wall lead to higher wall stress, which can induce aortic dilatation

and aneurysm formation, eventually resulting in intramural hemorrhage, aortic dissection, or rupture (Table 2.1). Thus, besides the chronic trauma resulting from arterial hypertension (which represents the major reason and mechanism for stress to the aortic wall), three inherited connective tissue disorders are currently known to affect the arterial walls as well—the Marfan’s syndrome, Ehlers–Danlos syndrome, and familial forms of thoracic aneurysm and dissection.

*Table 2.1.* Risk conditions for aortic dissection

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Long-standing conditions
<ul style="list-style-type: none"> <li>● Long-standing arterial hypertension</li> <li>● Smoking</li> <li>● Dyslipidemia</li> <li>● Cocaine (crack) use</li> </ul>
Connective tissue disorders
<ul style="list-style-type: none"> <li>● Hereditary fibrillinopathies <ul style="list-style-type: none"> <li>○ Marfan’s syndrome (MFS)</li> <li>○ Ehlers–Danlos syndrome (EDS)</li> </ul> </li> <li>● Hereditary vascular diseases <ul style="list-style-type: none"> <li>○ Bicuspid aortic valve</li> <li>○ Coarctation</li> </ul> </li> <li>● Vascular inflammation <ul style="list-style-type: none"> <li>○ Giant cell arteritis</li> <li>○ Takayasu arteritis</li> <li>○ Behcet’s disease</li> <li>○ Syphilis</li> <li>○ Ormond’s disease</li> </ul> </li> </ul>
Deceleration trauma
<ul style="list-style-type: none"> <li>● Motor vehicle accidents</li> <li>● Downhill ski injuries</li> <li>● Fall from height</li> </ul>
Iatrogenic factors
<ul style="list-style-type: none"> <li>● Catheter/instrument intervention</li> <li>● Valvular/aortic surgery <ul style="list-style-type: none"> <li>○ Side or cross clamping/aortotomy</li> <li>○ Graft anastomosis</li> <li>○ Patch aortoplasty</li> <li>○ Cannulation site</li> <li>○ Aortic wall fragility</li> </ul> </li> </ul>

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## ACQUIRED CONDITIONS (HYPERTENSION)

Chronic hypertension affects the arterial wall composition causing intimal thickening, fibrosis and calcification, and extracellular fatty acid deposition. In parallel, the extracellular matrix undergoes accelerated degradation, apoptosis, and elastolysis with hyalinization of collagen. Both mechanisms may eventually lead to intimal disruption, most often at the edges of plaques as seen in coronary plaque. Intimal thickening increases, which further compromises nutrient and oxygen supply to the arterial wall. Adventitial fibrosis may obstruct vessels feeding the arterial wall as well as small intramural vasa vasorum. Both result in necrosis of smooth muscle cells and fibrosis of elastic structures of the vessel wall leading to stiffness and vulnerability to pulsatile forces, creating a substrate for aneurysms and dissections<sup>14–18</sup>. In addition to chronic hypertension, smoking, dyslipidemia, and potentially the use of crack cocaine are modulating risk factors.

Inflammatory diseases can destroy the medial layers of the aortic wall and lead to weakening, expansion, and dissection of the aortic wall; autoimmune processes may affect vasa vasorum and promote nutrient deficiency of aortic wall layers.

Iatrogenic aortic dissection is usually associated with invasive retrograde catheter interventions or occur during or late, after valve or aortic surgery<sup>18–21</sup>. Given the morbidity and mortality of iatrogenic aortic dissection, careful assessment is strongly encouraged in patients with unexplained hemodynamic instability or malperfusion syndromes following invasive vascular procedures or aortic surgery (Table 2.2).

Pregnancy-related dissection, although one of the most dramatic scenarios in medicine, is an extremely rare event as long as the patient is not affected by any form of connective tissue disease. The putative association of acute dis-

Table 2.2. Etiology of iatrogenic aortic dissection in IRAD<sup>a</sup>

Cause	Type A	Type B
Cardiac surgery	18 (69%)	1 (12%)
Coronary angiography/intervention	7 (27%)	7 (87%)
Renal angioplasty	1 (4%)	—
Complication	Iatrogenic	Spontaneous
Myocardial ischemia	36% <sup>a</sup>	5%
Myocardial infarction	15% <sup>a</sup>	3%
Limb ischemia	14%	8%
Mortality (30 days)	35%	24%

Source: Adapted from reference 33.  $p \leq 0.001$ .

<sup>a</sup> International Registry of Aortic Dissection.

section in pregnancy in otherwise healthy women may be largely an artifact of selective reporting. Pregnancy is a common condition and may coincidentally occur in women with concomitant existence of other risk factors such as long-standing or pregnancy-associated hypertension and Marfan's syndrome. Preliminary data from IRAD show that even in women, Marfan's syndrome-related dissection occurs primarily outside the setting of pregnancy, supporting the notion that pregnancy in Marfan's syndrome is not typically associated with aortic tears, unless root size exceeds 40 mm.

## MARFAN'S SYNDROME

Among hereditary diseases Marfan's syndrome (MFS) is the most prevalent connective tissue disorder with an estimated incidence of 1 per 7,000 and an autosomal dominant inheritance with variable penetrance. More than 100 mutations on the fibrillin-1 (FBN-1) gene have been identified encoding for a defective fibrillin in the extracellular matrix, which may affect the ocular, cardiovascular, skeletal, and pulmonary systems, as well as skin and dura mater. The diagnosis of the Marfan syndrome is currently based on revised clinical criteria of the *Gent nosology*<sup>9</sup>. The Gent criteria pay particular attention to genetic information like Marfan's syndrome in kindreds of an unequivocally affected individual. Moreover, both skeletal and cardiovascular features are major (diagnostic) criteria, and Marfan's is said to be present when  $\geq$  four of eight typical manifestations are present. Considering, however, borderline manifestations (such as the MASS phenotype) or subtle phenotypic features (*forme fruste*), the molecular analysis of suspected Marfan's syndrome and the delineation of criteria for differentiating other inherited conditions (genotypes) from a Marfan phenotype are of keen interest<sup>22-28</sup>.

The clinical variety of the Marfan's syndrome is only partially explained by the number of mutations on the fibrillin-1 (FBN-1) gene but is likely to be due to variable penetrance. Genetic heterogeneity and the involvement of a second gene (MFS2, Marfan syndrome type 2) may further add to the broad spectrum of symptoms<sup>28</sup>.

A common denominator of all phenotypic forms of aortic wall disease is the dedifferentiation of vascular smooth muscle cells not only with classic progression of atherosclerosis and aneurysm formation but also from enhanced elastolysis of aortic wall components<sup>29</sup>—as shown in a fibrillin-q-deficient animal model<sup>30</sup>. Moreover, enhanced expression of metalloproteinases in vascular smooth muscle cells of the Marfan aorta may promote both fragmentation of medial elastic layers and elastolysis, thus initiating an activated phenotype of smooth muscle cells<sup>31</sup>. In parallel, expression of peroxisome proliferator-activated receptor- $\gamma$  (PPAR- $\gamma$ ) is upregulated in smooth muscle cells of Mar-

fan's aorta and with cystic medial degeneration and correlates with clinical severity. Also, vascular smooth muscle cell apoptosis is likely to be related to progression of aortic dilatation. Thus, PPAR- $\gamma$  expression might reflect the pathogenesis of cystic medial degeneration and disease progression in the aorta of Marfan's and non-Marfan's without any vascular inflammatory response<sup>32</sup>.

## **EHLERS–DANLOS SYNDROME**

Ehlers–Danlos syndrome (EDS) is a heterogeneous group of hereditary connective tissue disorders characterized by articular hypermobility, skin hyperextensibility, and tissue fragility. Eleven types of EDS have been characterized; the true prevalence of EDS is unknown. An aggregate incidence of 1 per 5,000 births is often cited with no racial or ethnic predisposition. Aortic involvement is seen primarily in autosomal dominant EDS type IV<sup>33</sup>.

## **ANNULOAORTIC ECTASIA AND FAMILIAL AORTIC DISSECTION**

More than five mutations in the FBN-1 gene have now been identified in patients presenting with either sporadic or familial forms of thoracic aortic aneurysms and dissection<sup>34,35</sup>. Histological examination of the aortic wall reveals elastolysis or loss of elastic fibres, deposits of mucopolysaccharide-like materials, and cystic medial degeneration similar to Marfan's syndrome. However, no abnormalities of types I and III collagen or of fibrillin or any specific fibrilopathy were found in fibroblast cultures.

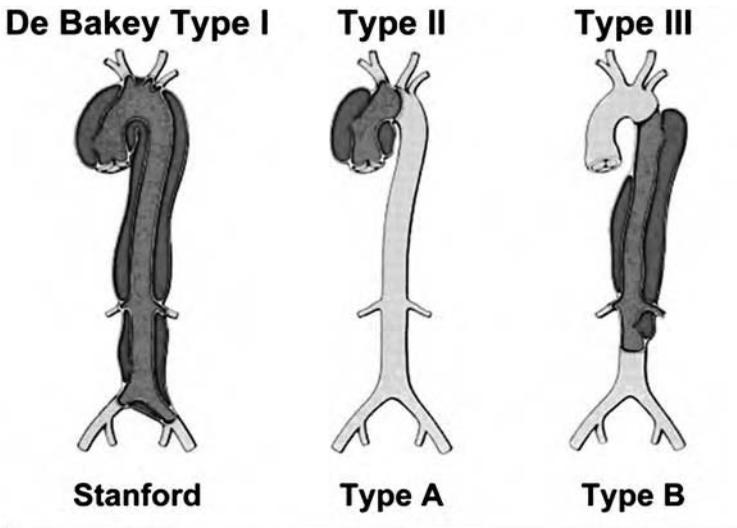
## **ABDOMINAL AORTIC ANEURYSMS AND DISSECTION**

Careful examination of family pedigrees often reveals both involvement of the abdominal aorta and disease in proximal aortic segments or other features suggestive of Marfan's or Ehlers–Danlos syndrome. Differentiation of familial forms of abdominal aortic aneurysm/dissection from thoracic aortic aneurysms/dissection with an abdominal component is difficult considering that only one mutation within the COL3A1 gene is known<sup>35</sup>. In fact, many candidate genes encoding for collagens, fibrillins, fibrillins, microfibril-associated glycoproteins, matrix metalloproteinases, and their inhibitors have been investigated, but no mutation has been identified. Similar pathogenetic processes have been described with coarctation<sup>14</sup> and with the bicuspid aortic valve architecture<sup>15</sup>.

## STAGING AND CLASSIFICATION OF ACUTE AORTIC SYNDROME

### STAGING OF AORTIC DISSECTION

The Stanford classification of aortic dissection distinguishes between type A and type B (Figure 2.1)<sup>36,37</sup>. Type A means the dissection involves the ascending aorta; a type B dissection does not involve the ascending aorta. This distinction or description is applied in similar fashion to all acute aortic syndromes, including all variants of dissection such as intramural hematoma and penetrating aortic ulcerations. The De Bakey classification subdivides the dissection process in type I dissection involving the entire aorta, type II dissec-



#### De Bakey

- Type I** Originates in the ascending aorta, propagates at least to the aortic arch and often beyond it distally.
- Type II** Originates in and as confined to the ascending aorta.
- Type III** Originates in the descending aorta and extends distally down the aorta or, rarely retrograde into the aortic arch and ascending aorta.

#### Stanford

- Type A** All dissections involving the ascending aorta, regardless of the site of origin.
- Type B** All dissections not involving the ascending aorta.

Figure 2.1. Most common classification systems of thoracic aortic dissection (e.g., the Stanford and DeBakey classification).

tion involving only the ascending aorta, and a type III dissection sparing the ascending aorta and the arch. Various attempts to further subdivide both classification systems have not been established in the medical community<sup>38,39</sup>, although the arch region deserves integration into a modern classification system<sup>40</sup>. Recent observational evidence highlights the importance of precursors of typical aortic dissection such as intramural hematoma, penetrating aortic ulcers, or localized intimal tears as variants of a wall dissecting process<sup>41–46</sup>, and suggests a need to utilize the identical staging and classification system for all variants of aortic dissection.

### Classic Aortic Dissection

Typical acute aortic dissection is characterized by the rapid development of an intimal flap separating the true and false lumen<sup>47–49</sup>. In the majority of cases (~90%) intimal tears are identified as sites of communication between true and false lumen<sup>49,50</sup>. The dissection can spread from diseased segments of the aortic wall in an antegrade or retrograde fashion, involving side branches and causing complications such as malperfusion syndrome by dynamic or static obstruction (from coronaries to iliac arteries), tamponade or aortic insufficiency<sup>48,50–52</sup>. The arbitrary classification of acute, subacute, or chronic dissection does not appear helpful for didactic or for differential therapeutic considerations but may be used to describe the individual situation and time span of survival of a given patient. From a pathophysiological point of view, progression of dissection is difficult to predict once a patient with dissection has survived the initial two weeks after its inception, although false lumen expansion is likely to develop over time. Several clinical features may be used to estimate late risk, including spontaneous false lumen thrombosis, evidence of persistent communication, patent false channel, and others<sup>39,47,53</sup>.

### Intramural Hematoma

Acute aortic intramural hematoma is considered a precursor of classic dissection, originating from ruptured vasa vasorum in medial wall layers that may provoke a secondary tear and communication with the aortic lumen<sup>45,46</sup>. This process may be initiated by an *aortic wall infarction* or *microapoplexy* of the vessel wall. Similar to classic dissection, intramural hematoma may extend along the aorta, may progress or regress, and may eventually reabsorb<sup>43–45,54–56</sup>. The prevalence of intramural hemorrhage and hematoma in patients with suspected aortic dissection, as observed by various modern imaging techniques, seems to be in the range of 10–30%<sup>42,45–56</sup>. Intramural hematoma can lead to acute aortic dissection in 28–47% of the patients and is associated with aortic rupture in 21–47%. Regression of intramural hematoma

is seen in about 10% of patients. Involvement of the ascending aorta or proximal type A IMH is generally considered an indication for expeditious surgery due to the inherent risk of rupture, tamponade, or compression of coronary ostia<sup>42,43,45-59</sup>. Distal intramural hematoma may warrant watchful waiting and potentially elective or emergent interventional stent-graft placement<sup>60</sup> (Figure 2.2).

### **PLAQUE RUPTURE/PENETRATING ATHEROSCLEROTIC ULCER (PAU)**

Ulceration of atherosclerotic aortic plaques can lead to aortic dissection or perforation<sup>61-65</sup>. Noninvasive imaging of aortic ulceration has been improved by tomographic scanning and has shed light on its pathophysiology and etiology. The ulcers seem predominantly to affect the descending thoracic aorta, as well as the abdominal aorta, in localized fashion; branch vessel compromise is rare. However, ulcers may penetrate intimal borders, often appearing in nipplelike projection with an adjacent hematoma<sup>62,65</sup>. Symptomatic ulcers and those with signs of deep erosion are more likely to rupture than others.

### **DECELERATION AND BLUNT TRAUMA**

Traumatic aortic rupture is an infrequent but not rare event. Trauma represents the leading cause of death of individuals in the United States under the age of 40, with aortic rupture trailing only head trauma as the most frequent cause of death. Deceleration trauma from automobile accidents, fall from height, blast injuries, or injuries during downhill skiing or equestrian accidents appear to be the primary mechanism. In a demographic analysis of 144 patients with aortic rupture, 83% were involved in motor vehicle crashes, 4.9% in motorcycle accidents, and 9.1% in sports activities and falls from height.

The aortic region subjected to the greatest strain with vertical or horizontal deceleration trauma is the isthmus at the insertion of the ligamentum arteriosum. Trauma may result in intimal hemorrhage with or without laceration, partial or complete laceration with periaortic hemorrhage, and possibly formation of false aneurysm. Although highly lethal, even complete aortic transection may be survived occasionally in the presence of hematoma containing the ruptured site.

The diagnosis of aortic trauma is to be suspected in association with any high-impact deceleration trauma. Depending on the level of consciousness, patients may describe severe back and chest pain typically associated with aortic dissection. However, individuals suffering major trauma may be ventilated or sedated, eliminating the ability to describe any symptoms. A high level of suspicion in patients without pain but with severe dyspnea and/or hemodynamic

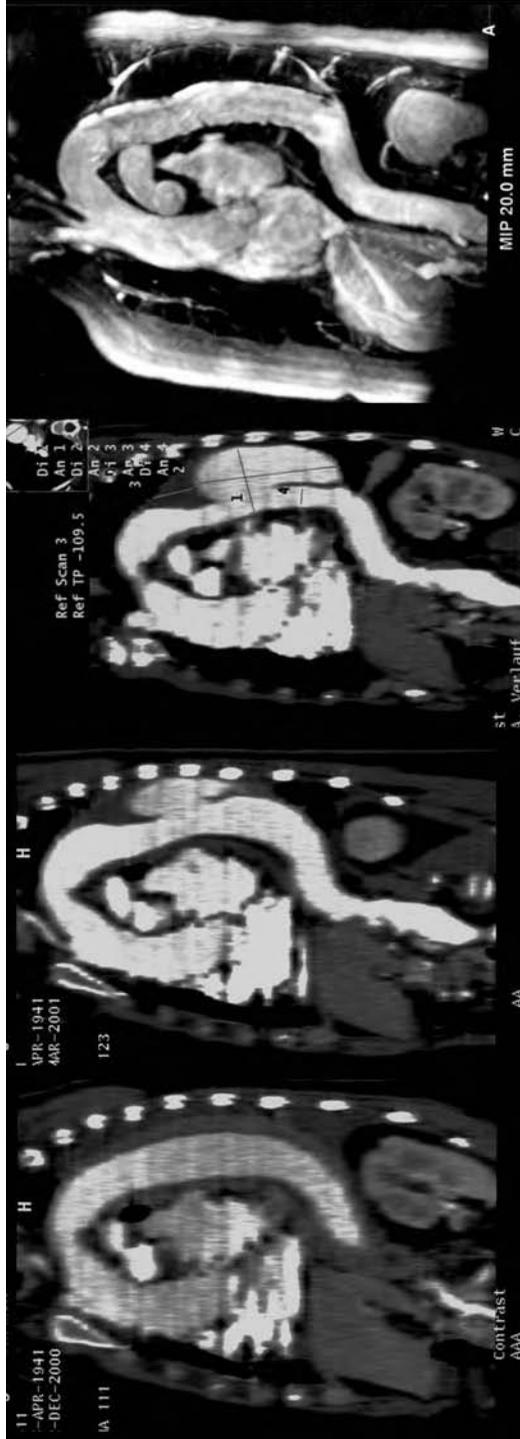


Figure 2.2. Evolutions of acute intramural hematoma of the descending aorta (left) to growing local dissection and formation of an aneurysm on spiral contrast-enhanced CAT scans within 4 months; reconstruction of the dissected aorta and exclusion of aneurysm after interventional stent-graft placement.

instability and low blood pressure after blunt or deceleration trauma should trigger a diagnostic reflex to search for aortic injuries.

## NATURAL HISTORY

Natural history of acute aortic syndrome is best outlined prognostically by differentiating patients into those with involvement of the ascending aorta (type A) versus individuals with acute pathology confined to the distal arch and the descending aorta (type B). This distinction is notable for the differing risk factors for development of dissection and also for the critical proximal branch vessels and anatomic details affecting patient outcomes acutely and chronically by virtue of malperfusion syndrome, syncope, tamponade, or shock<sup>8,13,48,66,67</sup>.

### TYPE A (PROXIMAL) DISSECTION

Acute aortic dissection of the ascending aorta is highly lethal, with mortality ranging between 1–2% per hour early after symptom onset<sup>3,49</sup>. Symptoms such as instantaneous onset of severe chest (85%) or back (46%) pain are characteristic presenting symptoms, however; abdominal pain (22%), syncope (13%), and stroke (6%) are common<sup>3,11–13,66,67</sup> but not always present. Some patients may have lost consciousness or are severely hypotensive from shock, making a reliable history impossible. Contained rupture into the pericardium (pericardial tamponade), involvement of one or more coronary arteries causing acute myocardial ischemia/infarction, or dissection compromising cerebral perfusion carries a particularly high risk<sup>48,51,53</sup>. Additionally, aortic valve disruption leading to acute congestive heart failure, extensive aortic involvement as manifested by multiple pulse deficits and/or renal failure, and advanced age also correlate with increased risk<sup>8,11,13,66,68</sup> (Figures 2.3A, 2.3B). Other less appreciated risk scenarios for type A dissection include prior cardiac and valvular surgery (15%)<sup>3,18,34</sup> and iatrogenic dissection occurring during cardiac surgery or cardiac catheterization (5%). Iatrogenic aortic dissection carries a mortality of 35%, which is even higher than noniatrogenic (24%)<sup>19</sup>.

Acute type A dissection is always a surgical emergency. Medical management alone is associated with a mortality of nearly 20% by 24 hours, 30% by 48 hours after presentation, 40% by day 7, and 50% by one month. Even with surgical repair, mortality rates are 10% by 24 hours, 13% by 7 days, and nearly 20% by 30 days, as recently documented in the largest registry of aortic dissection (Figure 2.4). Aortic rupture, stroke, visceral ischemia, and cardiac tamponade or circulatory failure are the most common causes of death<sup>8,13,66,69</sup>.

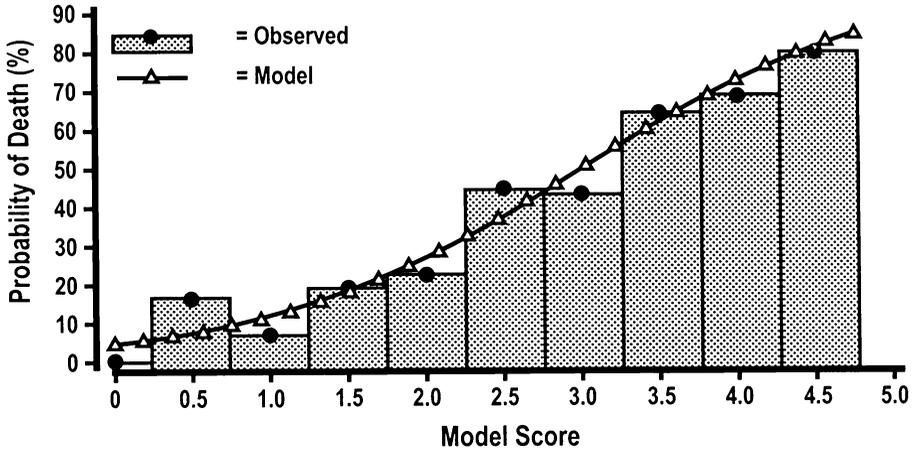


Figure 2.3A. Observed versus predicted mortality for acute type A aortic dissection based on a risk score; each risk factor was statistically extracted from retrospective analysis in IRAD and then prospectively confirmed. Both predicted and observed mortality rates in IRAD increase with increasing number and weight of risk factors. Adapted from reference 66.

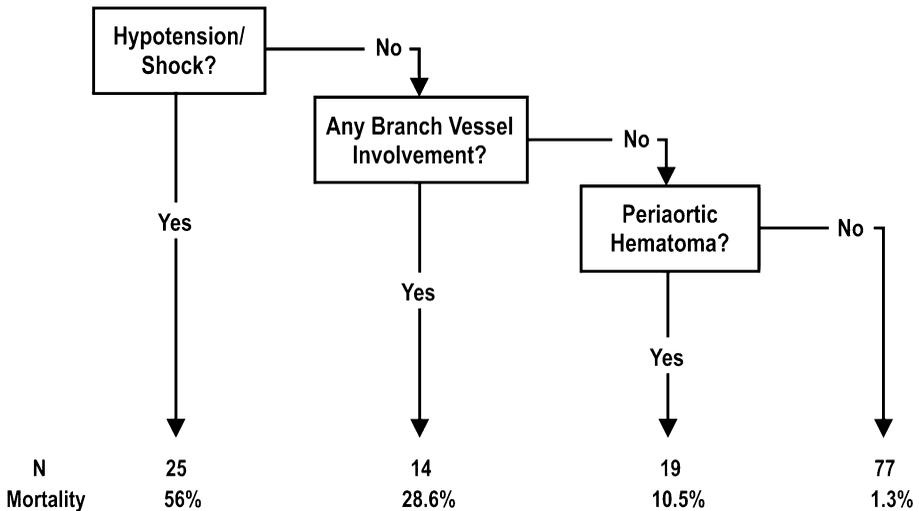


Figure 2.3B. Simple risk prediction scheme for type B dissection. The associated symptoms relate to the individual risk of death and may be used to select a given patient for emergent interventional therapy.

Present surgical techniques target the ascending aortic tear primarily with replacement or repair of the aortic root and the aortic valve apparatus (if necessary). Meanwhile, elimination of the remaining false lumen and potential remodeling of the dissected descending aorta currently play a secondary role.

Replacement or repair of the ascending aorta does not consistently eliminate flow and pressure from the distal false channel. Fewer than 10% of operated type A dissections develop postoperative false lumen obliteration with time<sup>52</sup>.

## TYPE B (DISTAL) DISSECTION

Acute aortic dissection affecting the descending aorta is less lethal in the acute phase than type A dissection but is not strikingly different with respect to clinical presentation. Instantaneous onset of severe back (64%) or chest (63%) pain are frequently reported symptoms, as is sudden abdominal pain (43%). Stroke is less common (21%), and presentation with an ischemic leg or peripheral ischemic neuropathy is encountered on occasion<sup>2-4,8,13,66,68,69</sup>.

Patients with uncomplicated type B dissection have a 30-day mortality of 10%<sup>3</sup> (Figure 2.4). Conversely, those who develop an ischemic leg, renal failure, visceral ischemia, or contained rupture often require urgent aortic repair; their mortality is 20% by day 2 and 25% by one month. Not surprisingly, advanced age, rupture, shock, and malperfusion are the most important indepen-

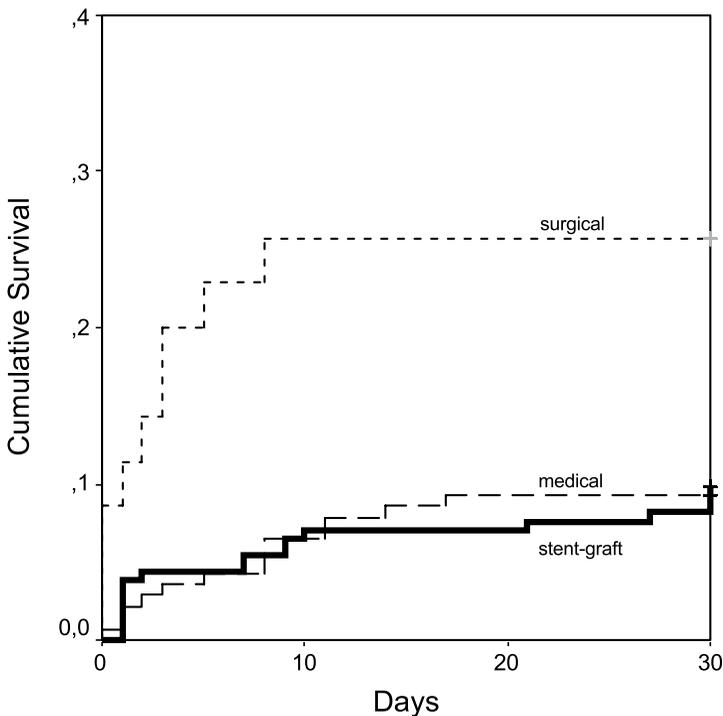


Figure 2.4. 30-day mortality in 464 patients from IRAD stratified by medical and surgical treatment in both type A and type B aortic dissection. Adapted from reference 3.

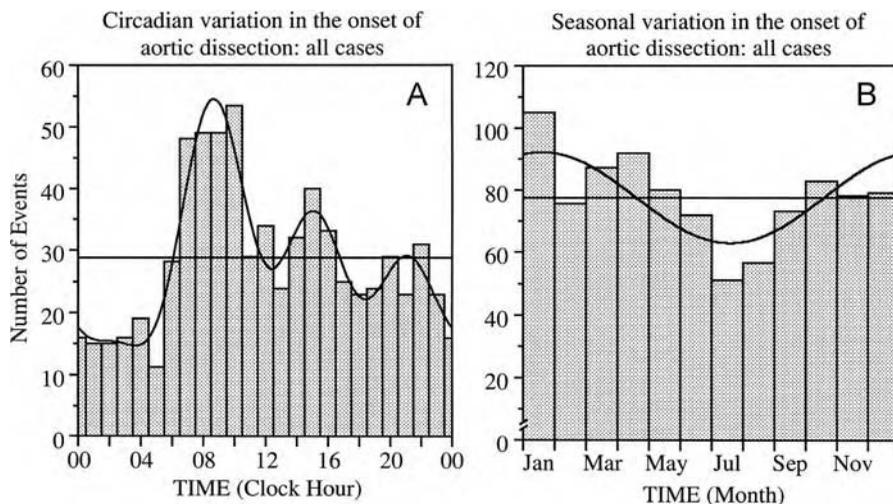


Figure 2.5. (A) Histogram of circadian variation in onset of acute aortic dissection showing total events per hour with superimposed best-fitting curve. (B) Histogram of seasonal variation in onset of aortic dissection showing total number of events each month with superimposed best-fitting curve. Adapted from reference 72.

dent predictors of early mortality<sup>11,13,66</sup>. Chronic use of crack cocaine appears to predispose patients to acute aortic dissection, with preferred manifestation in the descending aorta<sup>70,71</sup>. Similar to acute myocardial infarction and other cardiovascular conditions, acute aortic dissection follows a chronobiological pattern and exhibits significant circadian and seasonal variations, with onset of dissection preferentially in the morning between 6 and 10 a.m. and in the early afternoon; moreover, the risk of dissection is higher in the cold season (winter and spring) than in the summer<sup>72</sup> (Figure 2.5). These observations may have implications for tailoring treatment strategies, such as antihypertensive drugs, to vulnerable periods.

## INTRAMURAL HEMATOMA

The natural history of acute intramural hematoma continues to be debated. The cardiac and surgical community have recommended that acute intramural hematoma of the ascending aorta should be managed surgically because of an unacceptably high mortality with medical treatment<sup>41–43,45,46,54,56,73</sup>. Studies in Asian patients from Japan and Korea have argued that wall hematoma is reflecting a more benign condition in which aggressive medical therapy and serial imaging may allow watchful waiting and avoid surgery in some patients<sup>57,59,74</sup>. The reasons for this disparity may either relate to a genetic variant of the aortic disease in Caucasian patients or be explained by criti-

cal semantic differences. Acute intramural hematoma, when first diagnosed, may be a classic subtle aortic dissection, which may escape diagnosis on initial imaging but may eventually show on subsequent imaging or re-review of initial studies. A second scenario is progression of IMH to classic aortic dissection between an initial diagnostic study and an interim follow-up image (Figure 2.2). Not uncommonly in type B intramural hematoma, the findings remain unchanged over time or even reveal evidence of reposition and reabsorption. For acute aortic dissection or intramural hematoma involving the ascending aorta, extent and location of aortic involvement and time from onset of symptoms are critically related to outcome<sup>44–46,56,75</sup>. For a patient presenting within a few hours of symptom onset with an unequivocal acute hematoma in the ascending aorta extending toward the coronary ostia or the aortic valve, watchful waiting is by far more hazardous than surgical repair. Conversely, in a patient seen beyond 48 hours of symptom onset with a limited IMH near the arch or distally, watchful waiting and medical therapy is an appropriate approach in the light of currently available data. Given these uncertainties, until further studies provide more predictive data, many experts recommend definitive aortic repair for acute IMH of the ascending aorta similar to type A dissection and a less aggressive attitude toward hematoma in the descending aorta similar to the accepted strategy in type B aortic dissection.

## **BLUNT AORTIC TRAUMA**

Traumatic lesions of the aorta are considered highly lethal with respect to natural history. According to Parmley's landmark analysis, 85% of all high-impact traumatic aortic lesions lead to death from free rupture on the scene, and only those surviving the first hour have a chance, with 70% surviving the next 6 hours, 50% the next 24 hours, and 10% the next 4 months, if no appropriate therapy is initiated. This impressive mortality underlies the concept of early surgical intervention, which is associated with an operative mortality between 15 and 50%, despite progress in cardiac and aortic surgery as well as anesthesiology. At present, the modern concept of controlled hypotension and delayed (subacute) deployment of customized stent grafts may be more promising. Initial experience with a staged interventional approach appears to be associated with an improved prognosis.

## **THE CLINICAL PICTURE**

### **TRIGGERS OF DISSECTION**

Aortic dissection and its variants originate at the site of the intimal tear in >95% of cases. Primary rupture of the inner aortic lining or rupture of

the vasa vasorum (of the aortic wall) with initial intramural bleeding and secondary rupture are the two initiating mechanisms of acute aortic syndrome. The trigger to the initiating lesion, however, is any kind of specific trauma, which may be due to blunt macrotrauma or deceleration injury or repetitive “chronic” microtrauma of pulsatile aortic flow, especially in the presence of chronic hypertension. Moreover, hypertension itself induces high vessel rigidity, rendering the less elastic aorta to higher wall stress and more susceptibility to the pulsatile systolic pressure. Along with a slow but progressive negative remodeling of the aortic wall and in conjunction with accelerated atherosclerosis, a continuous decomposition, deterioration, and subsequent loss of both collagen and elastin in the medial layer seem to be a predisposing process preceding acute aortic syndromes.

Thus, any disease process undermining the integrity of the elastic and muscular components of the media may trigger aortic dissection, such as cystic media necrosis. Focal cystic media necrosis is found in long-standing hypertension, with advanced age, and in several hereditary connective tissue disorders, most frequently in Marfan and Ehlers–Danlos syndromes, predisposing to acute aortic syndrome at young age. The peak incidence of acute aortic syndrome, however, is between ages 55 and 75, with a clear male preponderance. In patients younger than 40 years, sex distribution is equal, probably due to the occurrence of aortic dissection in women during late pregnancy.

Among predisposing factors and besides connective tissue disorders, untreated arterial hypertension is encountered in 80% of acute aortic syndromes. Hypertension may not just weaken the aortic media layer but accelerate sclerosis of the vasa vasorum or the nutrient intramural vessels. The triggering role of hypertension is supported by observational evidence that coarctation predisposes to acute aortic syndrome as do other scenarios, such as congenital bicuspid or unicommissural aortic valves or acquired aortic valve disease (especially late after aortic valve replacement surgery at the site of previous aortotomy). Acute aortic syndromes have also been found associated with Turner and Noonan’s syndrome and with giant cell arteriitis. Similarly, some association with the use of crack or cocaine has been postulated in young male individuals probably via episodes of highly elevated blood pressure. Conversely, in young females, especially with Marfan syndrome, the elevated risk for dissection may be triggered by increased blood volume pressure and cardiac output in the third trimester. With the typically dilated aortic root, such patients are at particularly high risk of full dissection, and in some cases the diagnosis of Marfan’s was discovered when a tall slim woman presented with peripartum acute aortic syndrome.

Iatrogenic lesions, either as localized tear, intramural hematoma, or partial disruption, usually after intraarterial catheterization or with intraaortic balloon

pumping, may result from direct mechanical forces and may be seen in otherwise healthy aortas.

## CLINICAL PRESENTATION

The challenge in managing acute aortic syndrome, especially dissection, is an appropriate clinical suspicion and action in pursuing rapid diagnosis and therapy<sup>60,76</sup>.

Typical features of dissection are the acute onset of chest and/or back pain of blunt, severe, and sometimes radiating and migrating nature. A history of or signs of chronic hypertension are common if obvious signs of connective tissue disorders are absent. Clinical manifestations of acute aortic dissection are often dominated by the anatomicopathological characteristics of specific malperfusion syndrome from dissection-related sidebranch obstruction. Up to 20% of patients with acute aortic dissection may present with syncope without a history of typical pain or neurological findings<sup>4,10–13,60,76</sup>. Cardiac tamponade may result in hypotension and syncope<sup>2,62</sup>. Syncope may also result from severe pain, obstruction of cerebral vessels, or activation of aortic baroreceptors. After an initial dominance of chest or back pain, cardiac failure may become the main symptom and is usually related to severe aortic regurgitation<sup>2,60,62</sup>. Cerebrovascular manifestations and limb ischemia with pulse deficits are caused by involvement of a sidebranch orifice into the dissection or obliteration of the true lumen by an expanding false lumen<sup>61,66</sup>. Paraplegia may emerge if too many pairs of intercostal arteries are separated from the aortic true lumen.

Recurrent abdominal pain, elevation of acute phase proteins, and increase of lactate dehydrogenase are indicators of involvement of either the celiac trunk observed in about 8% or the mesenteric artery in 8–13%. Involvement of the renal arteries may result in oliguria or anuria<sup>76,77</sup>. Further propagation of the dissection will usually result in repetitive bouts of acute pain often along with a deteriorating clinical picture<sup>3</sup>. Dissection from trauma, after valve replacement or from iatrogenic causes, is usually obvious; however, dissection after aortic (valve) surgery is less frequent and easily overlooked<sup>63,78</sup>.

## SIGNS AND SYMPTOMS

Pulse deficits on physical examination are important clues and an ominous sign heralding complications and poor outcome (Figure 3.1). The International Registry of Aortic Dissection (IRAD) reported pulse deficits in fewer than 20% of patients; pulse phenomena, however, may be transient including neurological symptoms, such as loss of consciousness or ischemic paresis<sup>3,68</sup>.

Table 2.3. In-hospital complications and mortality in type A dissection

In-hospital complications	Pulse deficits(s) present (%)	Pulse deficit(s) absent (%)	<i>p</i> -value
Mortality	41.1	24.7	<0.0001
All neurological deficits	35.1	11.2	<0.0001
Coma/altered consciousness	26.8	9.1	<0.0001
Myocardial ischemia/infarction	8.9	11.1	0.47
Mesenteric ischemia/infarction	4.8	3.0	0.34
Acute renal failure	10.3	4.6	0.009
Hypotension	34.5	22.4	0.006
Cardiac tamponade	20.1	15.5	0.21
Limb ischemia	28.8	2.1	<0.0001

Source: Adapted from reference 68.

Table 2.4. Predictors of subsequent reoperations after surgery for type A dissection

	Hazard ratio	95% CI	<i>p</i>
Arch involvement	3.6	0.84–15.1	0.09
Marfan's syndrome	2.7	1.1–6.6	0.03
Pulse deficit	2.3	1.1–4.5	0.02
Male gender	2.1	0.96–4.8	0.07
Coronary disease	1.9	0.99–3.8	0.06

Source: Adapted from reference 84.

A diastolic murmur indicative of aortic regurgitation is seen in 40–50% of patients with proximal dissection. Signs of pericardial involvement, jugular venous distension, or a paradoxical pulse should alert caregivers to pursue rapid diagnostic confirmation. Shock may be a presenting sign from tamponade, coronary compression, acute aortic valve incompetence, or loss of blood and imminent exsanguination<sup>3,60,66</sup>.

Up to 30% of patients later found to have aortic dissection are initially suspected to have other conditions, such as acute coronary syndromes, nondissecting aneurysms, pericarditis, pulmonary embolism, aortic stenosis, or even cholecystitis<sup>3,4,8,78</sup>. Consequently, the acute aortic dissection should always be considered in patients presenting with unexplained syncope, chest pain, back pain, abdominal pain, stroke, acute onset of congestive heart failure, pulse differentials, or malperfusion syndrome of extremities or viscera (Table 2.3).

In absence of currently useful specific biomarkers for aortic dissection, interpretation of elevated cardiac biomarkers may be even more complex in a scenario of the aortic dissection compromising the coronary ostia.

Table 2.5. Considerations for surgical, medical, and interventional therapy in aortic dissection

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Surgery
<ul style="list-style-type: none"><li>• Treatment of choice in acute type A dissection</li><li>• Acute type B dissection complicated by the following:<ul style="list-style-type: none"><li>◦ Retrograde extension into the ascending aorta</li><li>◦ Dissection in Marfan's syndrome</li><li>◦ Rupture or impending rupture (e.g., saccular aneurysm formation (stent grafts?))</li><li>◦ Progression with compromise of vital organs (stenting?)</li></ul></li></ul>
Medical therapy
<ul style="list-style-type: none"><li>• Treatment of choice in uncomplicated type B dissection</li><li>• Stable, isolated arch dissection</li><li>• Stable type B dissection (chronic, <math>\geq 2</math> weeks of onset)</li></ul>
Interventional therapy
<ul style="list-style-type: none"><li>• Stent grafts to seal entry to false lumen and to enlarge compressed true lumen:<ul style="list-style-type: none"><li>◦ Unstable type B dissection</li><li>◦ Malperfusion syndrome (proximal aortic stent graft and/or distal fenestration/stenting of branch arteries)</li><li>◦ Stable type B dissection (under study)</li></ul></li></ul>

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## INITIAL DIAGNOSTIC STEPS AND DECISIONS

A routine chest X-ray is abnormal in 60–90% of cases of suspected aortic dissection. However, acute dissection (especially type A) can present with a normal chest film and this may distract physicians from pursuing further imaging<sup>3,8,76</sup>. ECG analysis may also be misleading since it may be normal in dissection or very abnormal when ascending dissection causes coronary compromise. Bedside specific biomarkers are not yet in clinical use, although biochemical diagnosis of aortic dissection may become feasible based on studies examining the concentrations of smooth muscle myosin heavy chain<sup>80</sup> or soluble elastin compounds in the early hours of aortic dissection<sup>79</sup>. In suspected aortic syndromes, swift noninvasive diagnostic imaging is advised to differentiate conditions requiring immediate action (involvement of the ascending aorta) from less dramatic conditions<sup>5–7</sup>. Visualization of an intimal flap separating two lumina identifies dissection. If the false lumen is completely thrombosed, central displacement of the intimal flap, calcification, or separation of intimal layers signals chronic dissection rather than mural thrombosis.

In the International Registry of Aortic Dissection, the first diagnostic test used was transthoracic echocardiography (TTE) and transoesophageal

echocardiography (TEE) in 33%, computed tomography (CT) in 61%, magnetic resonance imaging (MRI) in 2%, and angiography in 4%, reflecting the current use of diagnostic resources<sup>3,80</sup>. In 56%, TTE/TEE were used as secondary techniques; in 18%, CT; in 9%, MRI; and in 17%, angiography. An average of 1.8 methods were utilized to diagnose aortic dissection. CT was used in 40%, MR in 30%, and angiography in 21% of those cases where three methods were chosen. Preferred use, availability, and access in the emergency setting may impact on the choice of imaging method since overall accuracy for the parameters are similar<sup>5,7</sup>. Moreover, a high index of suspicion for the problem is more important than the type of test used. If acute aortic dissection is suspected, patients should be transferred to a center with interventional and surgical back up. Each institution should establish pathways for diagnosis, early treatment, and eventual transfer to definitive care.

## DETAILING DISSECTION

The extent (beginning and end points) of a dissection is described by taking wall thickness and the intimal flap into consideration. Antegrade, retrograde, or delayed flow is identified in the false lumen by Doppler ultrasound, cinetomographic imaging (using CT or MR technology) or by motion of the flap synchronized to heart beat. With diminishing false lumen flow, thrombus formation may take place heralded by spontaneous contrast<sup>6,81,82</sup>. Conversely, noncommunicating aortic dissections cannot always be differentiated from intramural hematomas; an acute symptomatology may speak for intramural hematoma, potentially progressing to full dissection with typical appearance<sup>41,42,46,59</sup>.

In the presence of false lumen flow, the exact location of entries may be instrumental to choosing potential treatment options. New imaging techniques even allow differentiation of antegrade from retrograde dissection. Retrograde dissection with involvement of the ascending aorta and presence of a tear at the aortic isthmus is found in up to 20% of type A (type I) and constitutes an indication for surgery even when initially identified as type B (type III) dissection<sup>38</sup>.

Plaque ulceration following plaque rupture is typically visualized by TEE, CT, or MRI<sup>46,62-65</sup>. In the case of multiple lesions, each lesion has to be carefully checked for signs of penetration or rupture, evidenced by fluid extravasation into the pericardium, pleural space, or mediastinum, which often heralds the risk of sudden death from exsanguination<sup>56,74</sup>. The presence of pericardial fluid around the aortic root is a sign of ongoing penetration or imminent perforation regardless of dissection or intramural hematoma. Fluid within the pleural space can be detected by echocardiography, CT, and MRI. The pres-

ence of blood in a pleural space is associated with a mortality greater than 50%<sup>3,4</sup>.

Even more challenging is the interpretation of myocardial ischemia or infarction resulting from a dissection flap or from diastolic collapse of the true lumen. Transesophageal echocardiography can generally visualize the ostium and proximal part of both coronary arteries. Multislice CT and MRI can now visualize the proximal third of all coronary arteries. Coronary angiography adds little to the decision making process and should generally be avoided in type A dissection. However, in stable patients, particularly in type B (type III) dissection, coronary angiography via the right radial or brachial artery may add to vascular staging in the chronic phase of the disease<sup>82</sup>. Contrast-enhanced CT (in spiral and multislice technique) and transesophageal ultrasound as an extension of conventional echocardiography are key imaging tools for decision making in the emergency setting with excellent accuracy. Diagnostic pitfalls currently are less of a problem than delays in the diagnostic pathway. Modern imaging techniques can reliably identify variants of dissection such as intramural hematoma, plaque ulceration, or traumatic aortic injury<sup>7,46,52</sup>.

## CONCLUSIONS

Considering both the aging patient population in Western societies with prolonged survival despite hypertension and the better diagnostic strategies available to more patients, cardiology and the cardiovascular community face an increasing incidence of acute and chronic aortic problems that desperately need to be stratified using both early biomarkers of an inflammatory and dissecting process and functional imaging of the aortic wall. At this pivotal point in time, an elevated level of awareness in clinical cardiology and the availability of modern imaging technology should trigger interest in diagnosing and treating the complex of acute aortic syndromes similar to previous efforts in acute coronary syndromes. Cardiologists should improve diagnostic pathways and vascular staging in acute and chronic aortic diseases, form regional referral networks and allocation systems, and utilize uniform follow-up programs. Moreover, precise definitions of pathology using clear semantics should be integrated into prospective registries of aortic diseases by a multidisciplinary team of physicians in an attempt to validate previous retrospective observations and to make the best use of evolving diagnostic and therapeutic strategies. Finally, cardiologists are in need of credible prognostic models that can support decisions for individual patient care independent of investigators, at different times, and in worldwide locations.

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# 3

## **AORTIC DISSECTION: CLINICAL PRESENTATION**

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More ink than blood has been split on the subject of aortic dissections, beginning with the first well-documented case of aortic dissection—George II of England, who died while straining on the commode. Morgagni first described aortic dissection more than 200 years ago. The advent and adoption of modern cardiac surgical procedures have dramatically altered the outcome what was once a uniformly fatal disease. Dramatic advances in imaging the aorta and the heart have facilitated the early diagnosis of aortic dissections. Here we go through the clinical presentation of aortic dissection, by way of history, clinical examination, physical findings, and laboratory investigations.

## CLINICAL FEATURES

Aortic dissection is a catastrophic disease if not recognized early and treated promptly (Table 3.1). Aortic dissection is the most common catastrophe of the aorta, two to three times more common than rupture of the abdominal aorta. When left untreated, about 33% of patients die within the first 24 hours, and 50% die within 48 hours. The two-week mortality rate approaches 75% in patients with undiagnosed ascending aortic dissection. Untreated, aortic dissection has a mortality rate of over 1% per hour.

The diagnosis of aortic dissection is easily missed due to its variable clinical presentation, which mimics the involvement of various organ systems. At present, over 2,000 cases of aortic dissection are diagnosed annually in the United States. Advanced age, with its increased risk of both hypertension and degenerative vascular changes, portends an increased risk for aortic dissection. As the population over 60 years of age continues to grow, more patients potentially will be at risk for this disease. Men have aortic dissection more often than women do. The male-to-female ratio ranges from 2:1 to 5:1. The peak age of occurrence of proximal dissection is age 55. Distal dissection occurs most often at age 70 (see Table 3.1). High blood pressure is the most common factor predisposing the aorta to dissection. It's implicated in 62–78% of cases (see Table 3.1).

Aortic diseases are also predisposing factors (Table 2.1). These diseases include

- Aortic dilation
- Aortic aneurysm
- Congenital aortic valve abnormalities (such as bicuspid aortic valve)
- Coarctation of the aorta
- Marfan syndrome
- Ehlers–Danlos syndrome
- Iatrogenic (cardiac surgery, coronary intervention, renal angiography) (Table 3.2).

The manifestations of aortic dissection may be protean and can mimic a variety of conditions: “spontaneous tear of the arterial coats is associated with atrocious pain, with symptoms, indeed, in the case of the aorta, of angina pectoris and many instances have been mistaken for it” (William Osler, 1910).

## PRESENTING SYMPTOMS AND SIGNS

Chest pain is the most common presenting complaint in patients with an aortic dissection (72.7% of patients with type A aortic dissection) (Table 3.3).

Table 3.1. Demography and history of patients with acute aortic dissection\*

Category	No. † (%)	Type A, No. (%) (n = 289)	Type B, No. (%) (n = 175)	P Value, Type A vs. B
<b>Demographics:</b>				
Age, mean(SD), yr	63.1 (14.0)	61.2 (14.1)	66.3 (13.2)	<0.001
Male sex	303 (65.3)	182 (63.0)	121 (69.1)	0.18
Referred from primary site to IRAD center	280 (60.3)	177 (61.2)	103 (58.9)	0.61
Ethnicity (n = 407):				0.51
White	337 (82.8)	205 (84.4)	132 (80.5)	
Asian	55 (13.5)	31 (12.8)	24 (14.6)	
Black	7 (1.7)	2 (0.8)	5 (3.0)	
Other	8 (2.0)	5 (2.0)	3 (1.9)	
<b>Patient history:</b>				
Marfan syndrome	22/449 (4.9)	19 (6.7)	3 (1.8)	0.02
Hypertension	326/452 (72.1)	194 (69.3)	132 (76.7)	0.08
Atherosclerosis	140/452 (31.0)	69 (24.4)	71 (42)	<0.001
Known aortic aneurysm	73/453 (16.1)	35 (12.4)	238 (2.2)	0.006
Prior aortic dissection	29/453 (6.4)	11 (3.9)	18 (10.6)	0.005
Diabetes mellitus	23/451 (5.1)	12 (4.3)	11 (6.6)	0.29
Prior cardiac surgery:‡	83 (17.9)	46 (15.9)	37 (21.1)	0.16
Aortic valve replacement	24/444 (5.4)	16 (5.8)	8 (4.8)	0.66
Aortic aneurysm and/or dissection	43/444 (9.7)	20 (7.2)	23 (14)	0.02
Coronary artery bypass graft surgery	19/442 (4.3)	14 (5)	5 (3.0)	0.32
Mitral valve surgery	3/444 (0.7)	1 (0.3)	2 (0.1)	NA
Iatrogenic:	20 (4.3)	14 (4.8)	6 (3.4)	0.47
Caterization/PTCA	10/454 (2.2)	5 (1.7)	5 (2.8)	NA
Cardiac surgery	10/454 (2.2)	9 (3.1)	1 (0.6)	NA

\* IRAD Indicates The International Registry of Acute Aortic Dissection; PTCA, percutaneous transluminal coronary angioplasty; NA, not applicable; type A dissections involve the ascending aorta and type B dissections occur distal to the left subclavian artery.

† Denominator of reported responses is given if different than stated in the column heading.

‡ Prior cardiac surgery includes aortic valve surgery, coronary artery bypass graft surgery, aortic aneurysm and/or dissection, mitral valve surgery, or other aortic surgery.

Source: From reference 6.

Thoracic aortic dissection should be considered in the differential diagnosis of all patients presenting with chest pain. The pain usually is described as “ripping” or “tearing”. This description is not universal, and some patients may present with only mild pain, often mistaken for musculoskeletal conditions, located in the thorax, groin, or back. The pain of aortic dissection typically is distinguished from the pain of acute myocardial infarction (AMI) by its abrupt onset: 84.8% of patients recall having abrupt onset. Aortic dissection should be considered strongly in all patients complaining of acute, sudden, and severe

Table 3.2. Etiology of iatrogenic aortic dissection in IRAD

Cause	Type A	Type B
Cardiac surgery	18 (69%)	1 (12%)
Coronarography/intervention	7 (27%)	7 (87%)
Renal angioplasty	1 (4%)	...
Complication	Iatrogenic	Spontaneous
Myocardial ischemia	36%*	5%
Myocardial infarction	15%*	3%
Limb ischemia	14%	8%
Mortality (30 days)	35%	24%

\*  $p \leq 0.001$ .

Source: From reference 14.

chest pain that is maximal at onset. The truly sudden onset of chest pain is seen in few other conditions. This is thought to be due to acute stretching of the aortic wall. The nervi vascularis (bundles of nerve fibers found in the aortic adventitia) are involved in the production of pain.

The description of the pain may indicate where the dissection arises. Anterior chest pain and chest pain that mimics AMI usually are associated with anterior arch or aortic root dissection (71% for type A vs. 44% for type B), whereas patients with type B dissection more often had back (63.8% of type B vs. 46.6% type A) and abdominal pain (42.7% type B vs. 21.6% with type A). This is caused by the dissection interrupting flow to the coronary arteries, resulting in myocardial ischemia. Pain that is described in the neck or jaw indicates that the dissection involves the aortic arch and extends into the great vessels of the arch. Tearing or ripping pain that is felt in the intrascapular area may indicate that the dissection involves the descending aorta. The pain typically changes as the dissection evolves.

Aortic dissection is painless in about 10% of patients. Painless dissection is more common in those with neurologic complications from the dissection and those with Marfan syndrome.

Presenting signs and symptoms in acute thoracic aortic dissection include the following:

- Anterior chest pain: ascending aortic dissection
- Neck or jaw pain: aortic arch dissection
- Interscapular tearing or ripping pain: descending aortic dissection
- Myocardial infarction

Neurological features include the following:

Table 3.3. Presenting symptoms and signs in patients with acute aortic dissection ( $n = 464$ )\*

Category	Present, no. reported (%)	Type A, no. (%)	Type B, no. (%)	<i>P</i> value, type A vs. B
Presenting symptoms:				
Any pain reported:	443/464 (95.5)	271 (93.8)	172 (98.3)	0.02
Abrupt onset	379/447 (84.8)	234 (85.4)	145 (83.8)	0.85
Chest pain	331/455 (72.7)	221 (78.9)	110 (62.9)	<0.001
Anterior chest pain	262/430 (60.9)	191 (71.0)	71 (44.1)	<0.001
Posterior chest pain	149/415 (35.9)	85 (32.8)	64 (41)	0.09
Back pain	240/451 (53.2)	129 (46.6)	111 (63.8)	<0.001
Abdominal pain	133/449 (29.6)	60 (21.6)	73 (42.7)	<0.001
Severity of pain: severe or worst ever	346/382 (90.6)	211 (90.1)	135 (90)	NA
Quality of pain: sharp	174/270 (64.4)	103 (62)	71 (68.3)	NA
Quality of pain: tearing or ripping	135/267 (50.6)	78 (49.4)	57 (52.3)	NA
Radiating	127/449 (28.3)	75 (27.2)	52 (30.1)	0.51
Migrating	74/446 (16.6)	41 (14.9)	33 (19.3)	0.22
Syncope	42/447 (9.4)	35 (12.7)	7 (4.1)	0.002
Physical examination findings:				
Hemodynamics ( $n = 451$ ) <sup>†</sup> :				
Hypertensive (SBP $\geq$ 150 mm Hg)	221 (49.0)	99 (35.7)	122 (70.1)	<0.001
Normotensive (SBP 100–149 mm Hg)	156 (34.6)	110 (39.7)	46 (26.4)	<0.001
Hypotensive (SBP < 100 mm Hg)	36 (8.0)	32 (11.6)	4 (2.3)	<0.001
Shock or tamponade (SBP $\leq$ 80 mm Hg)	38 (8.4)	36 (13.0)	2 (1.5)	<0.001
Auscultated murmur of aortic insufficiency	137/434 (31.6)	117 (44)	20 (12)	<0.001
Pulse deficit	69/457 (15.1)	53 (18.7)	16 (9.2)	0.006
Cerebrovascular accident	21/447 (4.7)	17 (6.1)	4 (2.3)	0.07
Congestive heart failure	29/440 (6.6)	24 (8.8)	5 (3.0)	0.02

\* SBP indicates systolic blood pressure; NA, not applicable. For definitions of type A and B dissections, see footnote to Table 3.1.

<sup>†</sup> Systolic blood pressure is reported for 277 patients with type A and 174 patients with type B acute aortic dissection, respectively.

Source: From reference 6.

- Syncope: Up to 20% may have syncope without chest pain or neurologic deficits. Syncope and hypotension may also be a result of cardiac tamponade. Syncope may also result from severe pain, obstruction of cerebral vessels, or activation of aortic baroreceptors.

- Cerebrovascular accident (CVA) symptoms
- Altered mental status
- Limb paresthesias, pain, or weakness
- Hemiparesis or hemiplegia
- Horner syndrome

Other features include the following:

- Dyspnea may be caused by congestive heart failure or tracheal or bronchial compression. Dyspnea and hemoptysis if dissection ruptures into the pleura
- Dysphagia from compression of the esophagus may be present
- Orthopnea and signs of cardiac failure are usually associated with acute aortic regurgitation and is seen 8.8% of proximal dissections
- Anxiety and premonitions of death
- Recurrent abdominal pain suggests involvement of either the celiac trunk (seen in ~8%) or the mesenteric artery (in 8–13%)
- Flank pain, oliguria, or anuria suggests involvement of renal arteries
- Paraplegia may occur when too many pairs of intercostal arteries are separated from the lumen of the aorta

## PHYSICAL EXAMINATION

A pulse deficit on clinical examination was found in <20% of patients in the IRAD registry and is a poor prognostic sign (Figure 3.1). Pulse deficit was noted more often in patients with type A dissection ( $p = 0.006$ ).

Blood pressure may increase or decrease:

- Hypertension is more often an initial presentation in type B aortic dissection (70.1% vs. 35.7% in type A,  $p < 0.001$ ).
- Hypertension may result from a catecholamine surge or underlying essential hypertension. This is a common concomitant finding.
- Hypotension is an ominous finding and should suggest the likelihood of rupture or a leak. Hypotension may be the result of excessive vagal tone, cardiac tamponade, or hypovolemia from rupture of the dissection. Only 4 out of 289 patients with type A aortic dissection in the IRAD registry had an initial systolic blood pressure less than 100 mm Hg.

Neurologic deficits are a presenting sign in up to 20% of cases:

- The most common neurologic findings are syncope and altered mental status.
- Syncope is part of the early course of aortic dissection and may be the result of increased vagal tone, hypovolemia, or dysrhythmia. Syncope was

a presenting feature of 12.7% of patients with type A aortic dissection and 4.1% of patients with type B dissection.

- Other causes of syncope or altered mental status include CVAs from compromised blood flow to the brain or spinal cord and ischemia from interruption of blood flow to the spinal arteries.
- Peripheral nerve ischemia can present with numbness and tingling in the extremities. There may be motor symptoms, such as localized weakness of muscles or muscle groups.
- Hoarseness from recurrent laryngeal nerve compression has also been described.
- Horner syndrome is caused by interruption in the cervical sympathetic ganglia and presents with ptosis, miosis, and anhidrosis.

Other signs include the following:

- Superior vena cava syndrome caused by compression of the superior vena cava from a large distorted aorta may occur.
- Findings suggestive of cardiac tamponade (such as muffled heart sounds, hypotension, pulsus paradoxus, jugular venous distension, and Kussmaul sign) must be recognized quickly. These are all ominous and portend a poor prognosis unless intervened on immediately.
- Other diagnostic clues include a new diastolic murmur (seen in 40–50% of patients with proximal dissection), asymmetrical pulses, and asymmetrical blood pressure measurements. Pay careful attention to carotid,

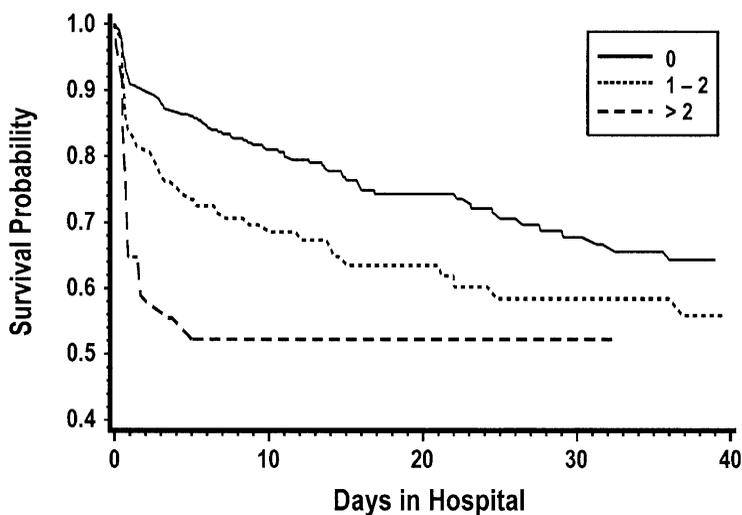


Figure 3.1. Kaplan–Meier survival curves from patients with and without pulse deficits; logrank for curves of patients with 1, 2, or 3 or more pulse deficits differ from patients with no pulse deficits ( $p < 0.03$  and  $0.004$ ). *Source:* From reference 14.

brachial, and femoral pulses on initial exam and look for progression of bruits or development of bruits on reexamination. It is essential to check for pulses bilaterally to help localize the location of the initial tear. Physical findings of a hemothorax may be found if the dissection ruptures into the pleura. However, it is common to find a concomitant left pleural effusion.

## SPECIAL CIRCUMSTANCES

### CLINICAL PROFILES OF TYPE A AND TYPE B DISSECTIONS

Another specific feature of acute aortic dissection in terms of presentation and prognosis is the location of the intimal tear and the site of dissection. The Stanford classification describe two types (Figure 2.1):

- Type A: affects the ascending aorta and/or aortic arch and beyond, and
- Type B: affects the descending aorta beyond the left subclavian artery.

Type A dissections (AAD) tend to present more acutely with hemodynamic compromise, either from rupture, tamponade, myocardial ischemia, or neurological dysfunction due to involvement of branch vessels or the aortic arch. The location of the pain is also different, with type A dissections causing more anterior pain and pain resembling angina, and type B dissections (ABAD) often presenting with interscapular pain or back pain.

Type A dissections often progress quickly and give this whole raft of diagnoses a bad name. This is why time is of the essence in managing these patients emergently and effecting urgent surgical repair. Type B dissections can often be managed medically because of less end-organ dysfunction associated with the condition and because the risk of rupture is lower (Table 3.4). The 30-day mortality risk with uncomplicated type B dissections is 10%. The mode of presentation in both types may be remarkably similar, however, and the diagnosis is best made by good-quality imaging performed promptly.

### Women

Women were less likely to have AAD (32.1% in one study); however, they tended to be significantly older than men ( $p < 0.008$ ) and were more likely to have altered mental status or coma than men. Pulse deficit, however, was less common. Women were more likely to have features of rupture (such as periaortic hematoma) and pleural or pericardial effusion on diagnostic imaging. Also more common in women are in-hospital complications of tamponade and hypotension. Women with AAD (after adjusting for hypertension and age) were more likely to die than men (OR, 1.4,  $p < 0.04$ ) and were found to be predominantly in age group 66 to 75 years. AAD in women was associated with a

Table 3.4. Clinical presentation, signs, EKG, and chest radiography in type B aortic dissection

Variable	Overall	Survived	Died	P-value
Clinical presentations and signs:				
Chest/Back pain (%)	328 (86.3)	298 (89.2)	30 (65.2)	<0.0001
Abrupt onset of pain (%)	332 (89.2)	298 (91.1)	34 (75.6)	0.002
Migrating pain (%)	90 (24.7)	86 (26.6)	4 (9.8)	0.02
Spinal Cord ischemia (%)	10 (2.7)	9 (2.8)	1 (2.2)	1.00
Ischemic peripheral neuropathy (%)	8 (2.2)	7 (2.2)	1 (2.2)	1.00
Hypotension/shock (%)	13 (3.4)	5 (1.5)	8 (16.7)	<0.0001
Hypertension (%)	260 (69.1)	235 (71.4)	26 (52.1)	0.007
Any pulse deficit (%)	73 (21.1)	61 (20.0)	12 (29.3)	0.17
Diagnostic imaging results:				
Chest radiograph (%):	360 (93.8)	315 (93.8)	45 (93.8)	1.00
Normal (%)	74 (20.6)	65 (20.6)	9 (20.0)	1.00
Wildened mediastinum (%)	202 (56.4)	170 (54.1)	32 (72.7)	0.02
Abnormal aortic contour (%)	171 (49.4)	159 (52.0)	12 (30.0)	0.009
Periaortic hematoma (%)	72 (19.2)	53 (16.8)	19 (45.2)	<0.0001
Electrocardiogram (%):	369 (96.1)	324 (96.4)	45 (93.8)	0.37
Normal (%)	113 (30.6)	101 (31.2)	12 (26.7)	0.54
Findings on diagnostic imaging:				
Aorta diameter $\geq 6$ cm**	44 (15.9)	22 (9.5)	12 (27.3)	0.001
Intramural hematoma (%) <sup>*†</sup>	60 (18.0)	55 (18.4)	5 (14.7)	0.60
False lumen closure status:				
Patent	158	138 (87.3)	20 (12.7)	0.71*
Partially thrombosed	107	94 (87.9)	13 (12.1)	
Completely thrombosed	48	44 (91.7)	4 (8.3)	

\* P-value for chi-square test for survival by lumen closure status.

† Intramural hematoma of the aorta as defined in references 18 and 25.

\*\* 108 patients are missing.

Source: From reference 16.

higher surgical mortality of 32% vs. 22% compared to men despite similar delay, surgical technique, and hemodynamics. Moreover, surgical outcome was worse in women than men ( $p < 0.013$ ).

## Elderly

About a third of the patients with AAD were elderly (aged >70 years), whereas over 40% of patients with ABAD were age >70 years. Hypertension, atherosclerosis, and iatrogenic dissection were more common in AAD, whereas Marfan's syndrome was the most common association in younger patients. Age at presentation often affects the clinical profile and outcome following AAD: elderly patients (>70 years) were less likely to have typical symptoms such as abrupt onset of chest pain and back pain. Although hy-

potension was more common (46% vs. 32%,  $p < 0.002$ ) in the elderly, other signs that were less likely to occur—including focal neurological deficits (18% vs. 26%,  $p < 0.04$ ), aortic regurgitant murmurs, or pulse deficits—were less common in older patients. Consequently, older patients were managed later in the course of the disease, often due to delayed diagnosis. This combined with end-organ dysfunction, advanced age, and surgical reluctance (fewer elderly patients were managed surgically than younger patients (64% vs. 86%,  $p < 0.0001$ ), led to a significantly higher in-hospital mortality in older patients (43% vs. 28%,  $p < 0.0006$ ). Logistic regression analysis showed that age  $> 70$  years as an independent predictor of hospital mortality in AAD (odds ratio 1.7, 95% confidence interval 1.1–2.8;  $p < 0.03$ ).

Elderly patients with ABAD were more likely to have hypertension, diabetes, history of prior aortic aneurysm, and arteriosclerosis, whereas Marfan's syndrome and cocaine abuse were less common. The in-hospital complication of hypotension/shock was more common among elderly ABAD, whereas inadequate perfusion of a major visceral organ was less frequent in this cohort. In-hospital death was higher in the elderly ABAD compared with the younger patients (16% vs. 10%,  $p = 0.07$ ). These investigators found that elderly patients with hypotension/shock had the highest risk of mortality (56%). Other predictors of mortality in AAD include involvement of any branch vessel (28.6%) and presence of periaortic hematoma (10.5%). The mortality rate in elderly patients without any of these three risk factors was extremely low (1.3%).

## Connective

Patients may have a history of connective disorders in the family, such as Marfan's syndrome, Ehler's Danlos syndrome, or a history of abdominal aortic aneurysms. Diseases such as Marfan's syndrome may often cause dissection with decreased intensity of symptoms such as pain because of the abnormal nature of the vascular collagen. A high index of suspicion needs to be maintained in patients with these conditions.

## Prior Cardiac Surgery

Patients who have undergone prior cardiac surgery (PCS) or invasive cardiac procedures are also at increased risk of aortic dissection. The incidence of acute aortic dissection is 0.03–0.1% after major cardiac surgery, and this incidence is highest for patients undergoing aortic valve replacement (AVR) (0.5–1.0%). Other conditions predisposing to subsequent dissection include congenitally deformed aortic valve, root aneurysms, redissection, and overlooked annuloaortic ectasia. Symptoms and signs in patients that have undergone cardiac surgery may be confused with those of incisional pain or a post-

cardiotomy pericarditic syndrome. These iatrogenic dissections are associated with a higher mortality<sup>14</sup>. In one study of patients with type A aortic dissection, a history of PCS was present in 100 of 617 patients. AAD patients with PCS were more likely to be older ( $p < 0.014$ ) and male ( $p < 0.02$ ) and to have a history of previous aortic dissection ( $p < 0.001$ ) or aneurysms ( $p < 0.001$ ). Chest pain is less likely to be the presenting symptom in AAD patients with PCS patients ( $p < 0.001$ ). PCS patients were also less likely to have cardiac tamponade ( $p < 0.007$ ). AAD patients with PCS were less likely to undergo surgical repair ( $p < 0.001$ ). PCS did not adversely impact in-hospital mortality (odds ratio [OR], 1.46; 95% confidence interval [CI], 0.81 to 2.63), but a trend for increased mortality was seen in patients with previous aortic valve replacement (AVR) (OR, 2.31; 95% CI, 0.98 to 5.43). PCS patients who were at increased mortality were those 70 years or older, previous AVR, shock, and renal failure.

### **Chronobiological Pattern (Figure 2.5)**

Finally, the presentation of acute aortic dissection does follow a definite chronobiological pattern similar to myocardial infarction. There is significant seasonal/monthly variation. The onset of dissection is most common between 6 and 10 a.m. and in the early afternoon. There is also a higher risk of dissection in the cold months of winter and early spring than in summer. Seasonal/monthly variations were observed only among patients aged  $<70$  years, those with type B AAD, and those without hypertension or diabetes.

## **INITIAL DIAGNOSTIC TESTS: EKG, CHEST X-RAY, BIOMARKERS**

The initial chest X-ray may be abnormal in 60–90% of cases and is often the essential first step in making the diagnosis (Figure 3.2; Table 3.5). A widened mediastinum occurs in 62.6% of type A dissection and 56% of type B dissection. An abnormal aortic contour occurs in 45–55% of cases (46.6% type A and 53% type B patients). Other abnormalities include abnormal cardiac contour, displacement/calcification of aorta, and pleural effusion.

The ECG examination is normal in less than a third of the patients. Non-specific ST-segment or T-wave changes occurs in about 42% of patients with type A or type B dissection. Left ventricular hypertrophy occurred in 25% of type A and 32.2% of type B patients. Coronary compromise from an acute ascending dissection may cause ECG features of ischemia.

There is promising news on the development of quick bedside tests that may prove confirmatory in the setting of acute aortic dissection, such as soluble elastin compounds and smooth muscle myosin heavy chain<sup>15</sup>. The bedside

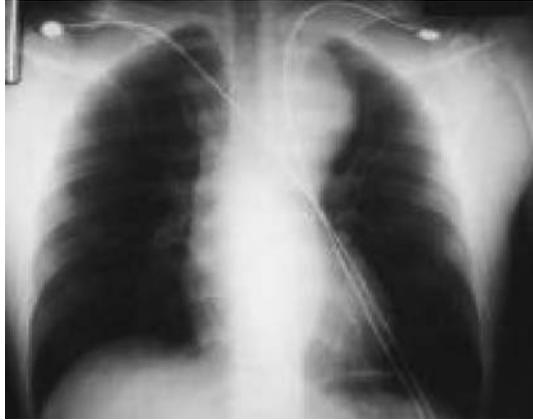


Figure 3.2. Chest—X ray of thoracic aortic dissection showing widened aortic arch.

Table 3.5. Chest radiography and electrocardiography in acute aortic dissection\*

Category	Present, no. reported (%)	Type A, no. (%)	Type B, no. (%)	<i>P</i> value, type A vs. B
Radiography findings ( <i>n</i> = 427):	427 (100)	256 (88.6)	171 (97.7)	
No abnormalities noted	53 (12.4)	26 (11.3)	27 (15.8)	0.08
Absence of widened mediastinum or abnormal aortic contour	91 (21.3)	44 (17.2)	47 (27.5)	0.01
Widened mediastinum	263 (61.6)	169 (62.6)	94 (56)	0.17
Abnormal aortic contour	212 (49.6)	124 (46.6)	88 (53)	0.20
Abnormal cardiac contour	110 (25.8)	69 (26.9)	41 (24.0)	0.49
Displacement/calcification of aorta	60 (14.1)	29 (11.3)	31 (18.1)	0.05
Pleural effusion	82 (19.2)	46 (17.3)	36 (21.8)	0.24
Electrocardiogram findings ( <i>n</i> = 444):				
No abnormalities noted	139 (31.3)	85 (30.8)	54 (32.1)	0.76
Nonspecific ST-segment or T-wave changes	184 (41.4)	116 (42.6)	68 (42.8)	0.98
Left ventricular hypertrophy	116 (26.1)	67 (25)	49 (32.2)	0.11
Ischemia	67 (15.1)	47 (17.3)	20 (13.2)	0.27
Myocardial infarction, old Q waves	34 (7.7)	19 (7.1)	15 (9.9)	0.30
Myocardial infarction, new Q waves or ST segments	14 (3.2)	13 (4.8)	1 (0.7)	0.02
Initial modality ( <i>n</i> = 453):				
Computed tomography	277 (61.1)	145 (50.2)	132 (75.4)	<0.001
Echocardiogram (TEE and/or TTE)	148 (32.7)	122 (42.2)	26 (14.9)	<0.001
Aortography	20 (4.4)	12 (4.2)	8 (4.6)	0.92
Magnetic resonance imaging	8 (1.8)	2 (0.7)	6 (3.4)	0.36
Images performed per patient, mean (SD)	1.83 (0.82)	1.64 (0.69)	2.15 (0.91)	<0.001

\* TEE indicates transesophageal echocardiography; TTE, transthoracic echocardiography. For definitions of type A and B dissections, see footnote to Table 3.1.

Source: From reference 6.

test with the greatest potential for diagnosing acute aortic dissection is an assay of circulating smooth muscle myosin heavy chain protein, a protein that is released from damaged aortic medial smooth muscle. Circulating smooth muscle myosin heavy chain protein is elevated within a few hours after acute aortic dissection. When patients with proximal dissection present within 3 hours of symptom, the sensitivity of this test approaches 91% with a specificity of 98%. Additional biochemical markers that are under investigation, include acute-phase reactants such as the white blood cell count, C-reactive protein, fibrinogen, and D-dimer. The confirmatory tests in this setting would be imaging using either one or a combination of CT scanning, transesophageal echocardiography, or magnetic resonance imaging.

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SECTION II:  
IMAGING METHODS

# 4

## **ROLE OF ECHOCARDIOGRAPHY IN THE DIAGNOSIS OF AORTIC DISSECTION**

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Aortic dissection is a catastrophic medical emergency if not recognized early and treated promptly. There is no survival study of untreated dissection to assess the natural history. Nevertheless, the prognosis has been shown to be poor

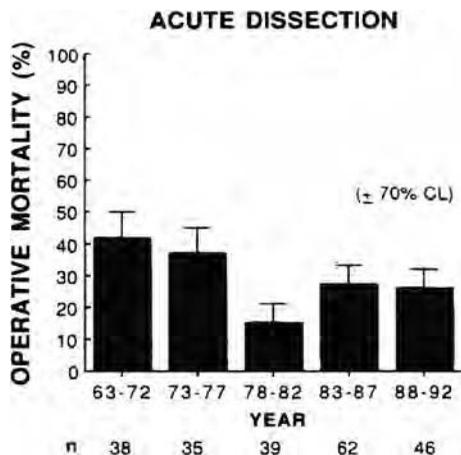


Figure 4.1. This bar graph demonstrates the Stanford surgical mortality for aortic dissection from 1963 to 1992. There is a small but no significant improvement over the past 30 years despite significant improvement in surgical techniques. Reprinted with permission, from reference 2.

for untreated aortic dissection<sup>1</sup>. Advances in the diagnosis of aortic dissection along with early medical and surgical treatments have had a significant impact on the outcome. However, this has plateaued over the last two decades (Figure 4.1)<sup>2</sup>. Advances in the imaging technology have allowed improved diagnosis of this entity<sup>3-8</sup>. However, the myriad presentations of this disease<sup>9,10</sup> and the spectrum of pathology with atypical features on the imaging modality<sup>11</sup> have often delayed its recognition. Unless a high index of suspicion exists, the diagnosis may not be made early enough to avoid the catastrophic natural history.

Understanding the anatomy of the aorta and pathogenesis of dissection is crucial for proper diagnosis regardless of the diagnostic modality.

## ANATOMY

The aortic wall consists of an innermost layer the *intima* (consisting of endothelial cells), middle layer the *media* (consisting of elastic collagen fibers and smooth muscle fibers), and an outer layer the *adventitia* (consisting of fibrous connective tissue with blood vessels). The aortic intima is separated from the media by internal elastic membrane and the media from adventitia by the external elastic membrane.



Figure 4.2A. Autopsy specimen of the heart with the entire thoracic aorta demonstrates a ruptured ascending aortic dissection. Note that the white tubular marker demonstrates the site of the intimal tear (entry site) just below the origin of innominate artery as well as the rupture of the false lumen (dark with clotted blood) in to the mediastinum. The false lumen extends proximally to the aortic annulus and distally to the origin of the left subclavian artery. This demonstrates the importance of looking for the primary entry site.

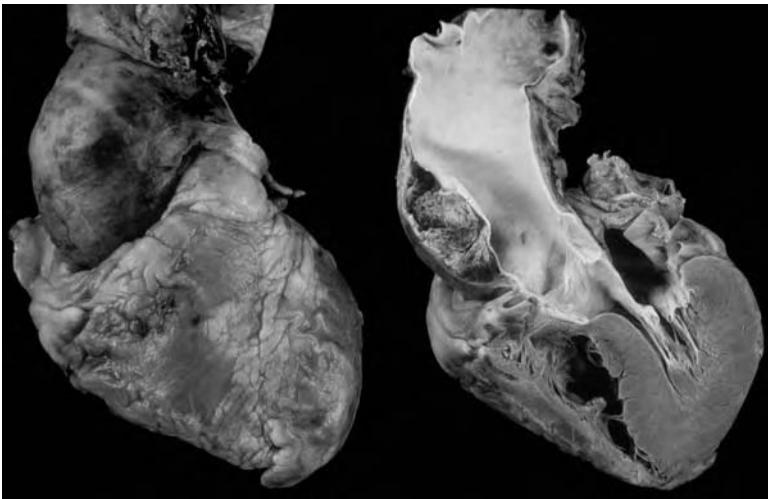


Figure 4.2B. Gross specimen and the sectioned specimen demonstrating dissecting aneurysm with blood clot in the media resulting from hemorrhage (intramural hematoma).

## DEFINITION

*Aortic dissection* is defined as “splitting” of the aortic wall. Classic aortic dissection occurs when the intimal disruption is caused by forces on the aortic wall related to pulsatile blood flow (Figure 4.2A). Dissection may also occur from within the aortic wall by hemorrhage within the media from the vasa vasorum (Figure 4.2B). This splitting involves and occurs within the media. The propulsion of blood creates a false channel within the media usually between the inner two-thirds and the outer third. This false lumen is separated from the true lumen by the avulsed layer of intima plus media. The term *intimal flap* commonly used is comprised of intima and part of the media.

The term *dissecting aneurysm* is defined as a fusiform enlargement of the false channel from the dilatation of the outer wall of the false lumen (Figure 4.3) or a preexisting fusiform aneurysm of other etiology with superimposed dissection.

## CLASSIFICATION

Aortic dissection was originally classified by DeBakey et al.<sup>12</sup> based on the site of intimal tear and the extent of dissection. The Stanford classification proposed by Daily et al. five years later is based on the presence or absence



Figure 4.3. Autopsy specimen demonstrating a dissecting aneurysm that has ruptured into the pericardial sac (red arrow). Note the clotted blood in the aneurysmal false lumen and pericardial sac.

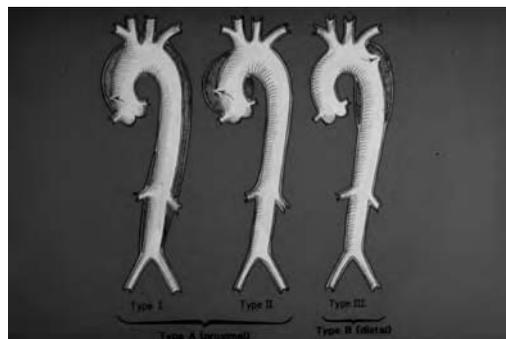


Figure 4.4. Cartoon demonstrating the commonly used classification of aortic dissection. Texas classification proposed by DeBakey classifies dissection based on the entry site while Stanford classification proposed by Daily classifies based on involvement of ascending aorta.

of ascending aortic involvement irrespective of the entry site<sup>13</sup> (Figure 4.4). The later classification is widely used because of its clinical value. Patients with involvement of the ascending aorta have a poor outcome unless operated emergently<sup>14–16</sup>. Aortic dissection is further classified as acute or chronic based on symptom duration of less than or greater than 2 weeks<sup>17</sup>.

## DIAGNOSTIC CHARACTERISTICS

The presentation of aortic dissection is quite variable; hence understanding of pathological presentation is essential for prompt diagnosis. Commonly observed morphologies from autopsy, surgical, and imaging studies have demonstrated the following spectrum of findings:

- Intimal avulsion, tear alone without hematoma
- Intimal tear with a localized false aneurysm with thrombus
- Highly mobile intimal flap with a true lumen and a false lumen with blood flow within them
- Immobile intimal flap separating the true lumen from the false lumen each with varying degrees of thrombosis of the false lumen
- True lumen, intimal flap, and aneurysmal enlargement of the false lumen with no or minimal thrombus.

In addition to the above spectrum of pathology seen in classic dissection, recent developments in the imaging modalities have identified two pathologic variants of aortic dissection, intramural hematoma (Figure 4.2B) and penetrating aortic ulcer (Figures 4.5A, 4.5B). Hence, the morphology of these two entities should be kept in mind.

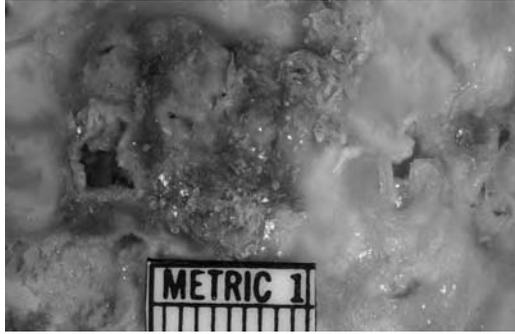


Figure 4.5A. Gross aortic specimen demonstrating significant atherosclerosis of the intimal surface with ulcers.

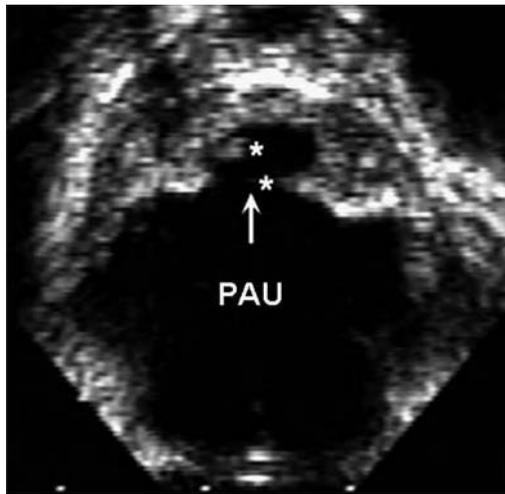


Figure 4.5B. Transesophageal echo (TEE) cross sectional image of descending thoracic aorta demonstrating a penetrating aortic ulcer (arrow) and the asterisks point to the overlying mobile debris.

## WHAT CONSTITUTES AN IDEAL ECHO EXAM FOR THE DIAGNOSIS OF DISSECTION?

Patients suspected of aortic dissection should undergo TTE followed by TEE depending on the findings of TTE as well as the urgency of the clinical condition. TTE and TEE should be used in a complementary manner. TEE is semi-invasive and requires sedation and may cause elevation of systemic pressure from retching and gagging. Therefore, all clinically important data should be obtained by TTE; the TEE exam can be focused only to confirm

and assess the extent of dissection along with the morphological features of dissection that impact management.

## **TRANSTHORACIC ECHO EXAM (TTE) SHOULD BE FOCUSED TO ANSWER THE FOLLOWING**

- **Is the ascending aorta involved?** Look for dilatation, double lumen, thickness of the aortic wall, intimal flap and its movement, thrombus, and variation in the color flow pattern. Use high left parasternal as well as right parasternal windows.
- **Does the intimal flap and false lumen extend into the arch?** Look for subtle differential flow acceleration in the arch, unusual soft tissue echoes between the aorta, and the pulmonary artery or left atrium. Use supra sternal and right supra clavicular windows.
- **Is the aortic root involved?** Identify aortic valve morphology and mobility, sinuses of Valsalva and aortic tubular morphology, and with Doppler color flow, regurgitation.
- **Are the coronary arteries involved?** Assess left ventricular regional wall motion.
- **Is the dissection ruptured or leaking?** Look for pericardial effusion or thrombus, left pleural effusion and rarely widening of the oblique sinus with soft tissue echoes indicating hematoma, compression of right pulmonary artery, compression of the superior vena cava. Use multiple windows including left and right lower sternal border, supra clavicular and subcostal windows.
- **Are neck vessels involved in dissection?** Look for origin of innominate, left carotid, and left subclavian arteries from true or false lumen. This may be necessary in patients presenting with neurological symptoms and chest pain.

## **TRANSESOPHAGEAL ECHO EXAM (TEE) SHOULD BE FOCUSED TO ANSWER THE FOLLOWING**

- **Is there a dissection or dissecting aneurysm?** If there is aneurysmal enlargement, surgical attention is even more urgent, since the chances of rupture are greater. Look for true aortic lumen size, false lumen size, flow characteristics and thrombus in the false lumen, and morphology of the outer boundary of the false lumen. More often, aneurysmal dilatation of the false lumen precludes optimal assessment of the outer boundary even with multiplane imaging. This is true even if there is no dilatation of the distal portion of the ascending aorta.

- **Does the dissection involve the intra pericardial portion of the ascending aorta?** Look for morphology of the intrapericardial aorta from the anulus to the level of the right pulmonary artery crossing in detail since rupture of this portion of the aorta often results in rapid death from tamponade. Care needs to be exerted to look at the aortic wall thickness and periaortic morphology when the typical double barrel appearance of aortic dissection is not present to exclude intramural hematoma or retrograde extension of an arch dissection.
- **Is the aortic root architecture disturbed?** Look for aortic valve morphology and mobility, aortic sinuses thickness and geometry, asymmetric thickening of the aortic sinus or aortic valve prolapse, severity of aortic regurgitation, and relationship of the intimal flap to coronary ostia. Severe aortic regurgitation may be the only sign and may preclude optimal assessment of the root in a rare dissection involving the aortic sinus. The intimal flap may disrupt the aortic commissure or even prolapse into the left ventricle causing aortic insufficiency. All these have impact on the surgery.
- **Is it a true dissection or intramural hematoma, or penetrating ulcer?** Look for thickness of the aortic wall, transducer to anterior aortic wall thickness, site of intimal tear, intimal flap, mobility of the flap, identify true and false lumen, morphology and flow characteristics of the false lumen, atherosclerotic debris, and/or ulcer crater.
- **Is the dissection leaking?** Look for pericardial effusion, distortion of the aortic and main pulmonary artery geometry, hazy echoes in the posterior trigone and transverse pericardial sinus. Increased flow velocity or color flow turbulence in the distal main pulmonary artery indicates compression of the vessel from hematoma.

## AORTIC DISSECTION DIAGNOSIS

Diagnosis of dissection depends on demonstration of the double barrel appearance of aorta with the intimal flap, separating the true and false lumens (Figures 4.6 and 4.7).

### INTIMAL FLAP

It is easily recognized as a linear echo of varying thickness. It is usually thin <2 mm in acute dissections and thick >4 mm due to neo intima formation on the false lumen side, in chronic dissections. When there is uncertainty as to which is the true and which is the false lumen, intimal flap mobility as assessed by M-mode echo can be helpful. The movement of the intimal flap depends on the extent of separation and the blood flow dynamics in the true

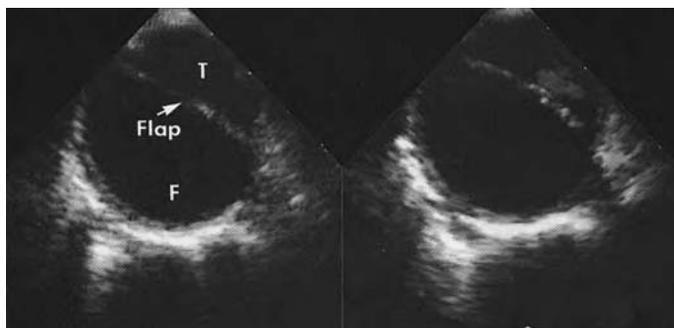
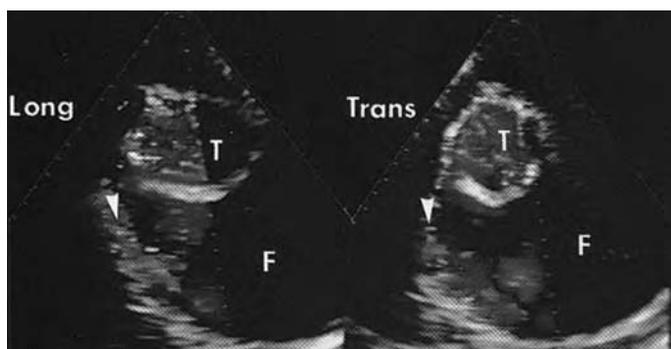
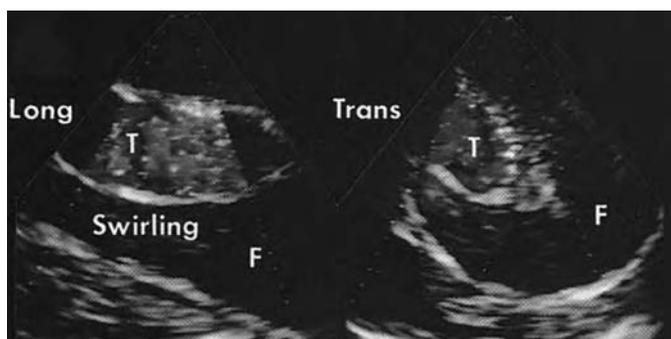


Figure 4.6. TEE short axis image of an aortic dissection. Note the large false lumen (F), small true lumen (T), intimal flap (arrow). Color flow demonstrates flow in the true lumen. Reprinted from *J. Invasive Cardiol.* 1 (1989), 328–338 with permission from HMP Communications.



(a)



(b)

Figure 4.7. TEE images of an aortic dissection demonstrating the usefulness of multiple views. F = false lumen, T = true lumen. Arrow head pointing to the communication demonstrated by color Doppler. Reprinted from *J. Invasive Cardiol.* 1 (1989), 328–338 with permission from HMP Communications.

and false lumen and thrombus formation. A tear in the intima with out avulsion from the underlying layers will be seen as abrupt discontinuity of the surface. However, the tear may not be obvious in an aorta with atherosclerosis. Image optimization by using edge enhancement and imaging with multiple frequency may be necessary for recognition and differentiating classic dissection from atherosclerotic ulcer. A highly mobile undulating flap indicates free flow between the true and false lumen, reentry into the true lumen, and minimal or no thrombosis of the false lumen. Intimal flap moves toward the false lumen in early to midsystole and toward the true lumen in late systole to early diastole. This is because the major flow is still in the true lumen. Limited systolic mobility of the intimal flap generally indicates that the false lumen is more of a blind pouch or column with no reentrant tear or thrombosis of the false lumen distally. On the other hand, movement of the flap toward the true lumen in early to midsystole and no movement in diastole generally indicate compromised true lumen distally and the major flow is via false lumen. Movement of the flap parallel to the aortic wall is generally seen when the false lumen is thrombosed or when there is a retrograde extension of the dissection either from the arch or from the proximal descending aorta to the ascending aorta. Parallel movement may also be seen with reverberation artifacts. Small intimal tears can be missed easily unless multiple views and multiple windows are used. Similarly meticulous incremental views of the aorta should be obtained using a multiplane transducer, imaging the entire segment from short axis to long axis so that all portions are seen. The diagnosis may be missed even with a multiplane transducer in cases involving only a small segment of the distal ascending aorta obstructed by the left main stem bronchus. In dissecting aneurysm with a small intimal avulsion and severely enlarged false lumen<sup>11</sup>, the dissection may be missed and mistaken for an aneurysm alone.

## **TRUE LUMEN**

The true lumen is easily recognized in the ascending aorta, but in the descending thoracic aorta at times it may be difficult. It is usually smaller in size and blood flow demonstrates increased velocity by pulsed Doppler and turbulent flow by color flow Doppler. Outward movement of the intimal flap during early systole can be used to identify the true lumen. It may be difficult to recognize the true lumen when there is poor runoff downstream from peripheral vascular disease resulting in low velocity flow in the true lumen. Again, as mentioned above, meticulous incremental examination of the aorta from the root to the diaphragm should be carried out using a multiplane TEE transducer. Care should be taken to image all walls of the aorta. Use of ultrasound contrast may aid in the correct identification of the true lumen as long as there is differential flow between true and false lumen.

## **FALSE LUMEN**

It is generally large and has slow swirling spontaneous echo contrast. This is due to poor run off from the false lumen. Again morphology and mobility features of the intimal flap as described above are used to identify the false lumen. Often some degree of thrombus is seen in the false lumen. Doppler flow features at the entry site can also identify the true and false lumen. Recognition of the false lumen becomes very important in the arch as well as in the abdominal aorta because of blood supply to the branches. This has enormous impact on surgical management and the need for subsequent percutaneous intervention. An ultrasound contrast agent can be used to help identify the true and false lumen. Contrast washout time is delayed in the false lumen.

## **ENTRY SITE OF INTIMA**

Identifying the entry site is very important. It identifies those at risk for rupture and in need of emergent surgery: 70% of the primary tears in ascending aortic and arch dissection are located in the ascending aorta, of which 86% are within the first 4 cm of the ascending aorta and another 10% within the next 4 cm. Most of the external rupture occurs at the site of the initial tear and hence recognition of the site of the intimal tear has an impact on the surgical approach. Intrapericardial rupture occurred in 70% of cases when the dissection began in the ascending aorta, 35% in cases where it began in the arch and 12% in those where the dissection began from the descending thoracic aorta<sup>17</sup>. Both pulsed and color flow Doppler have characteristic patterns at the entry site that allow correct recognition of the true and false lumens. The site of the entry tear in the distal ascending and proximal arch has surgical implications. Repairing the intra pericardial ascending aorta without addressing the primary entry site in the distal proximal or arch of the aorta will only prevent potential sudden death from rupture into the pericardial sac but does not eliminate the complications resulting from continued blood flow into the false lumen.

## **INTRAMURAL HEMATOMA**

Intramural hematoma (Figure 4.8) results from hemorrhage into the media from vasa vasorum or from a rupture of an atherosclerotic plaque<sup>18,19</sup>. This creates a layer of blood clot of varying thickness and varying consistency between the intima and adventitia. The systolic and diastolic force of blood on the vessel wall propels this clot to a varying degree. It can rupture in to the lumen of the aorta or outside through the adventitia. This could lead to either development of a classic dissection or penetrating ulcer by disrupting the internal elastic membrane or a rupture into the pericardial or pleural cavities by disrupting the external elastic membrane.

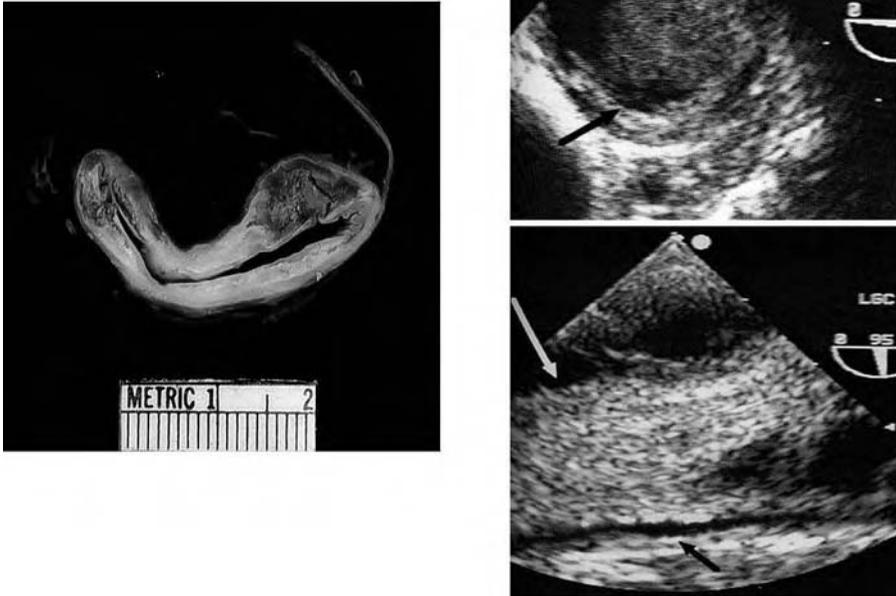


Figure 4.8. Composite picture demonstrates morphological and TEE short and long axis images of the aorta in a case of intramural hematoma. Note that the true lumen is completely obliterated slit-like appearance (black arrows) by the hematoma (white arrows) in the TEE images. Reprinted with permission.

## PENETRATING AORTIC ULCER

Penetrating aortic ulcer (Figure 4.5A, 4.5B) results from erosion/rupture of an atherosclerotic plaque through the internal elastic membrane into the media. This penetration into the media may create a localized intra medial dissection resulting in localized intramural hematoma of varying thickness, or it may penetrate beyond the external elastic membrane into adventitia resulting in a pseudoaneurysm or rupture<sup>20</sup>.

## TRANSTHORACIC ECHOCARDIOGRAPHY

Two-dimensional echocardiography is a useful imaging tool in the initial evaluation of patients suspected of aortic dissection<sup>21-23</sup> for both confirming the diagnosis as well as excluding other conditions in patients presenting with similar clinical picture. Although several diagnostic criteria exist (Table 4.1), the hallmark of aortic dissection is the detection of *undulating linear echoes of*

Table 4.1. Echo features that aid in the diagnosis of dissection

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**Transthoracic echo:**

- Linear echo with undulating motion (intimal flap)
- Aortic root dilatation >42 mm
- Widening of aortic walls:
  - Anterior 16–21 mm
  - Posterior 10–13 mm

**Transesophageal echo:**

- Linear undulating echo (intimal flap)
  - Small true lumen
  - Large false lumen
  - Accentuated color flow Doppler in true lumen
  - Spontaneous echo (swirling) and thrombus in the false lumen
  - Communications demonstrated by color flow Doppler
- 

*an intimal flap*. When seen in multiple views, this finding increases the predictive accuracy of the diagnosis<sup>24</sup>. Several studies have shown that high-quality imaging can be obtained in many patients with aortic dissection and with the use of multiple windows including right parasternal, left parasternal, and paraspinale, the thoracic aorta can be imaged in its entirety. High left parasternal and right parasternal windows allow imaging of the aortic root and ascending aorta. Supra sternal and right supra clavicular windows permit imaging of the distal ascending aorta, arch of aorta including the neck vessels, and proximal descending thoracic aorta. The distal portion of the descending thoracic aorta can be visualized from modified apical and from the subcostal windows. However, the major limitation is inconsistent image quality of the ascending aorta and aortic arch and suboptimal imaging of the descending thoracic aorta, more so in patients with obesity, chest deformity, and emphysema<sup>23</sup>. The major issue is correctly differentiating the intimal flap from scanning artifacts that result from a calcified aortic root, catheter from the right ventricular outflow tract, and fluid in the transverse pericardial sinus<sup>25</sup>. The sensitivity and specificity for TTE is 75% and 90%, respectively<sup>21,23,26</sup> when adequate images are obtained. However, its sensitivity is 78–100% in the ascending aortic dissection but only 31–50% in descending thoracic aortic dissection<sup>27</sup>. None-the-less, in descending thoracic aortic dissection, using all available windows has provided reliable diagnostic accuracy<sup>28</sup>. TTE in addition to identifying the intimal flap also provides important information pertaining to involvement of the aortic root, coronary arteries as well as impending rupture by demonstrating aortic regurgitation and its mechanism, regional wall motion, and pericardial effusion respectively. This information is essential for the timing of surgery. In

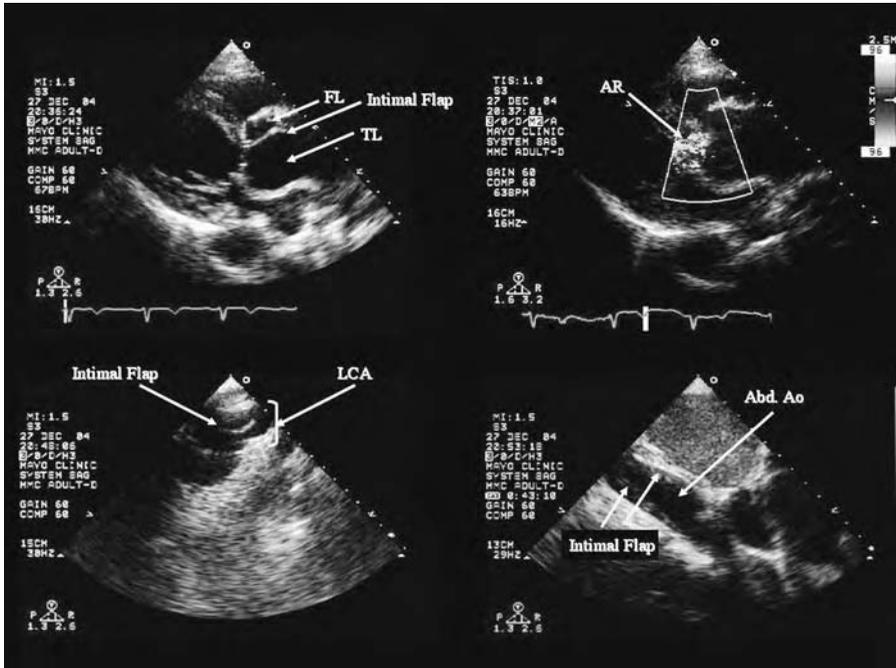


Figure 4.9. This composite TTE images demonstrates the comprehensive assessment of the type A dissection. Note the intimal flap extends from the aortic root to the abdominal aorta. TL = true lumen, FL = false lumen, AR = aortic regurgitation, LCA = left carotid artery, and Abd. Ao = abdominal aorta.

unstable patients, the information from TTE may be sufficient to allow immediate transfer to the operating room where TEE can be used intra operatively to further refine the findings. Figure 4.9 demonstrates the ability of comprehensive assessment of Type A aortic dissection by TTE.

## TRANSESOPHAGEAL ECHOCARDIOGRAPHY

Transesophageal echocardiography (TEE) can image the entire thoracic aorta except for a small portion of the distal ascending aorta near the proximal arch<sup>29</sup>. It overcomes the limitations encountered by TTE. Being close to the aorta from the esophagus provides high-resolution images from higher-frequency TEE endoscopes. Furthermore, availability of multiplane imaging permits improved incremental assessment of the aorta from the root to the descending thoracic aorta. This has overcome the diagnostic limitations posed by single plane transverse imaging by monoplane TEE and has improved the diagnostic accuracy as well as provided insight into the false negative tests<sup>27,30</sup>.

## **TEE EXAM TECHNIQUE FOR AORTIC DISSECTION**

### **PATIENT PREPARATION**

The TEE utilizes the standard protocol used for upper gastroenterologic endoscopy<sup>29</sup>. There is, however, some modification of this protocol in patients with suspected aortic dissection. For elective TEE, it is recommended that the patient be fasting for at least 6–8 hours prior to the procedure. In patients with suspected aortic dissection, the period of fasting may be less. Although, the use of agents that promote gastric emptying can be used, it does not ensure optimal gastric emptying in these critically ill patients. When the fasting interval is short, the procedure should be performed with extra caution, being careful to protect the airway and suction apparatus at hand.

As patients with suspected aortic dissection are generally in significant pain, sedation and maintenance of a low blood pressure are important in their management. The TEE procedure has the potential to produce patient discomfort, which can be avoided by good topical anesthesia of the pharynx and appropriate titration of intravenous sedation depending on the needs of the individual patient. Even before the TEE procedure begins, it is imperative to control blood pressure by appropriate intravenous antihypertensive agents in all patients who are not hypotensive.

### **TOMOGRAPHIC VIEWS OF ANATOMY**

The esophagus courses through the chest from the pharynx to the stomach with a slight rotation (Figure 4.10A). In the superior mediastinum, it lies between the vertebral column and the trachea, slightly to the left of the midline. As it courses through the mediastinum, it comes in contact with the aortic arch lying behind and to the right. In the posterior mediastinum, it lies on the right side of the descending aorta. Progressing downward through the chest, the esophagus moves anterior to the descending aorta. This varying relation of the esophagus to the descending aorta in the chest means that the only reliable reference landmark for TEE is the depth of the probe from the incisors. This imprecise registration of depth is a relative disadvantage of TEE compared with computed tomographic scanning, magnetic resonance imaging, and angiography.

### **AORTIC ROOT AND ASCENDING AORTA**

In a patient with suspected aortic dissection, the aortic root and ascending aorta should be imaged first because involvement of the ascending aorta makes the patient a potential surgical candidate.

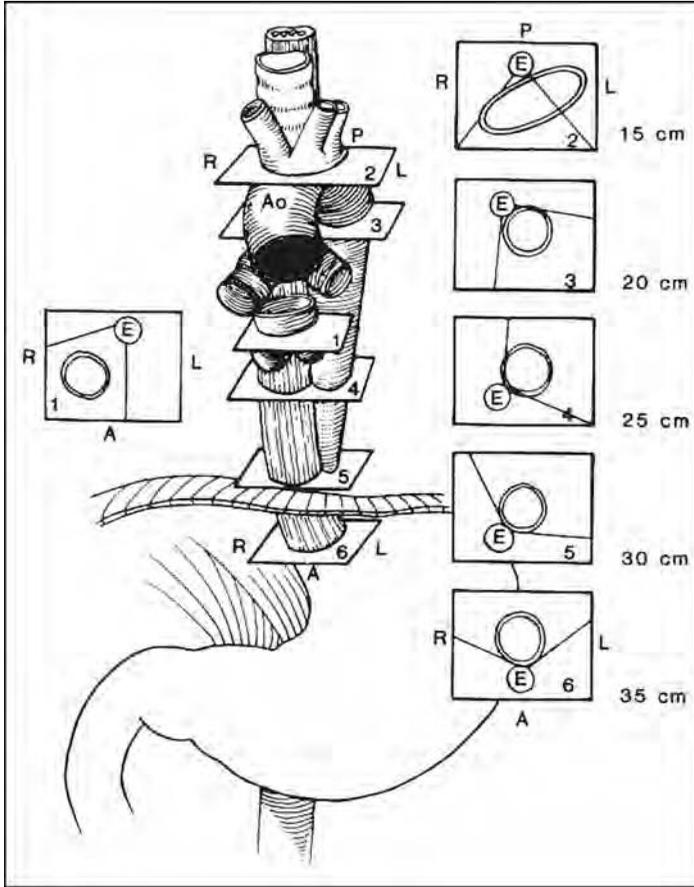


Figure 4.10A. Schematic diagram demonstrating the relationship of esophagus to the aorta. Reprinted with permission from reference 29.

To visualize the aortic root the probe is advanced to approximately 30 cm from the incisors where the aortic valve can usually be identified (Figure 4.10B). The probe is then carefully withdrawn to the bifurcation of the pulmonary artery to visualize the proximal ascending aorta (Figure 4.10B). Optimal imaging of the ascending aorta can be obtained from the aortic valve to the pulmonary artery bifurcation. Careful incremental rotation of the imaging plane from 0 degree to 135 degrees is essential at each level to avoid missing a localized abnormality or erroneously interpreting an artifact as an intimal flap. The distal ascending aorta near the proximal arch cannot be adequately imaged because of the interposition of the left main stem bronchus between the ascending aorta and the esophagus. However, in the majority of cases, one may be able to image if not all then some portion of this aorta by careful probe

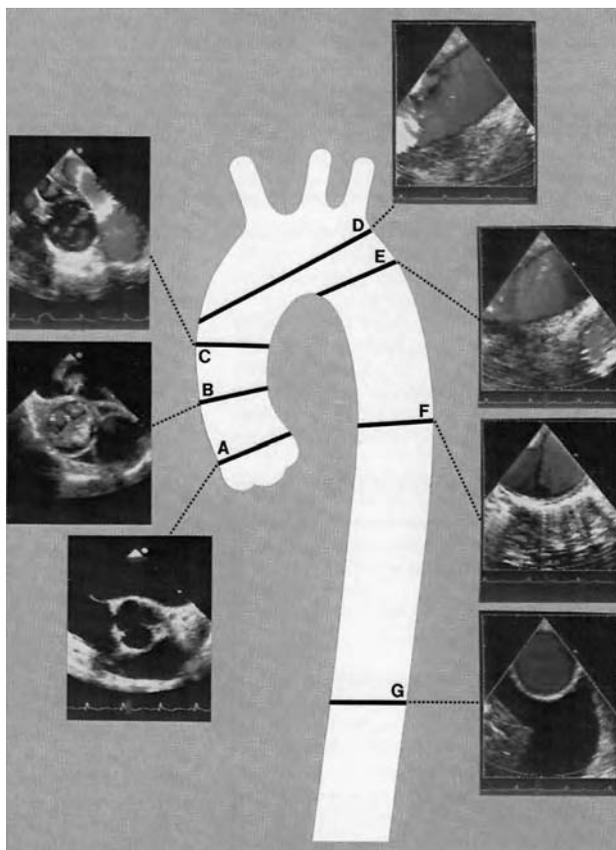


Figure 4.10B. This figure demonstrates the various tomographic sections of the aorta from the anulus to the level of diaphragm. Reprinted from *J. Invasive Cardiol.* 1 (1989), 328–338 with permission from HMP Communications.

manipulation in addition to incremental imaging from cross sectional to longitudinal views. Figures 4.11A, 4.11B, and 4.12 demonstrate type A aortic dissection. Classic intimal tear in the distal aortic arch of type B dissection is shown in Figure 4.13.

## AORTIC ARCH

The aortic arch is usually seen in its long axis as the probe is gently withdrawn from the pulmonary artery bifurcation to about 18–20 cm from the incisors and slowly rotating the probe to the left. Cross sections of the aortic arch including the origin of the neck vessels can be obtained in the majority of patients by careful manipulation of the probe tip controls and incremental imaging from 0 to 45, 60, and 90 degrees. Care needs to be taken at this level

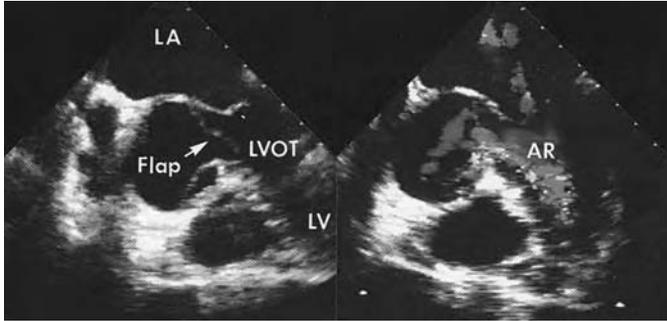


Figure 4.11A. Demonstrates the mechanism of aortic regurgitation in a type A aortic dissection. Note that intimal flap prolapse into the LVOT interferes with the coaptation of the aortic cusps leading to regurgitation. Reprinted from *J. Invasive Cardiol.* 1 (1989), 328–338 with permission from HMP Communications.

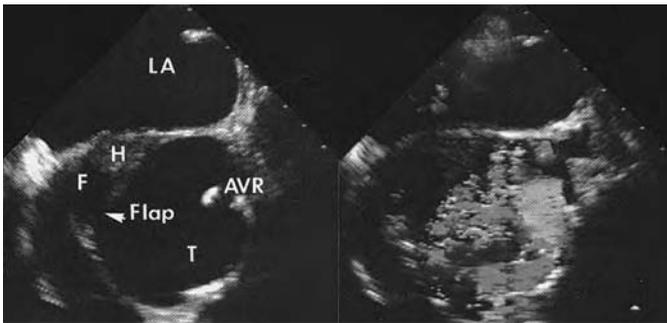


Figure 4.11B. Demonstrates a localized dissection of the posterior aortic root in a patient with aortic valve replacement. Reprinted from *J. Invasive Cardiol.* 1 (1989), 328–338 with permission from HMP Communications.

since the probe tip is in the very proximal esophagus and can be easily pulled out accidentally. In addition, it is important to realize that excessive probe manipulation at this level can result in pain and discomfort for the patient.

## DESCENDING THORACIC AORTA

The descending thoracic aorta is easily imaged from the level of the arch to the diaphragm (Figures 4.10A, 4.10B). The probe is initially advanced into the stomach at about 50 cm and then progressively withdrawn in approximately 2-cm increments. In patients with an ectatic, tortuous, or aneurysmal aorta, the image planes may be oblique, and therefore use of a multiplane TEE probe is essential for thorough examination. TEE appearance of a type III dissection is shown in (Figures 4.7 and 4.13).

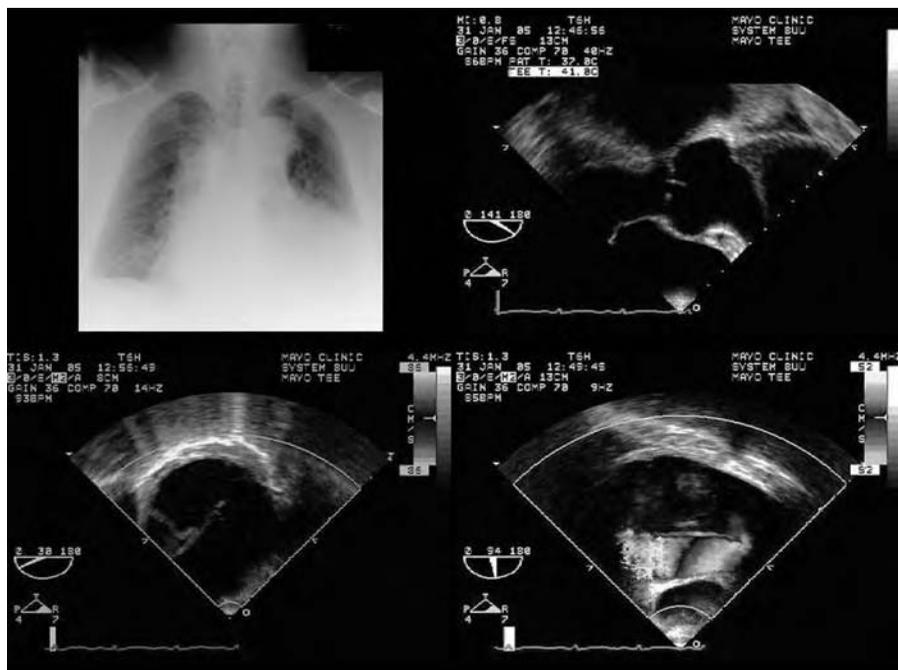


Figure 4.12. This composite figure demonstrates the complex morphology of the true and false lumen at different parts of the aorta. It also shows widened mediastinum on the CXR of this patient with a type A dissection.

The morphology of the individual segments of the aorta should be assessed carefully for an increase in aortic wall thickness, to identify the intimal flap and entry site. Similarly, identifying the morphological features of true and false lumen, extent of thrombus and flow dynamics at each level is essential.

Once the aorta has been fully examined, attention should be diverted to the cardiac structures to assess the morphology of the aortic valve, presence of aortic regurgitation, left ventricular function, presence of wall motion abnormalities, other valvular pathology, and the presence and size of pericardial and pleural effusions. It is important to know that one should spend time gathering these data only in cases where TTE was not performed.

## PITFALLS

The operator should be familiar with several pitfalls in the evaluation of possible aortic dissection:

- Artifacts mimicking intimal flaps are common in the ascending aorta<sup>25,27</sup>. They are either side lobe or reverberation artifacts. A side lobe is a curvi-



Figure 4.13. This long axis TEE view of the distal arch demonstrates the intimal flap and the entry site. Reprinted with permission.

linear echo along a sector arc and is not undulating. Side lobe artifacts are commonly caused by calcification of the aortic root, aortic valve, and sinotubular junction. A reverberation artifact is the duplication of a linear echo signal along the path of the ultrasound beam. Reverberation artifacts commonly originate from the left atrial wall, right pulmonary artery, and/or Swan–Ganz catheter. At times, fatty infiltration of the crista terminalis of the superior vena cava or an infusion catheter in the SVC can also produce side lobe artifacts. Appelbe et al. have demonstrated from a retrospective review that linear artifacts are more frequent when the aortic diameter is larger than the left atrium<sup>31</sup>. These artifacts can be easily recognized by using M-mode to assess their movement and color flow Doppler to assess the flow characteristics on either side of the linear echo. M-mode echo demonstrates the artifact to have the same motion as the structure from which it is originating. At times the primary structure's echo is not as obvious as its reverberation artifact. Color flow Doppler demonstrates normal homogeneous color on both sides of the curvilinear echo without communicating jets. Careful echo image parameter and frequency adjustments are necessary to avoid side lobe and reverberation artifacts from simulating an intimal flap. Recognizing the artifacts is es-

sential for correct diagnosis of dissection. Sensitivity and specificity are significantly impacted by appropriately recognizing such artifacts<sup>32</sup>.

- A limited arc of imaging due to the probe being very close to the anterior aortic wall may not permit thorough evaluation of a dilated tortuous descending thoracic aorta and may pose problems in differentiating a thrombus in an ectatic aorta from a thrombosed false lumen. Furthermore, it may not be possible to image the entire aortic segment.
- It is very difficult to optimally measure the true level of the imaging plane, and hence one should use the distance marks on the echo scope from the level of the incisors as well as relation to the cardiac structures themselves. For instance, by rotation of the probe from the position in the descending aortic rightward, one can determine the level of the aortic finding at the level of the left atrium or left ventricle, etc.

## ADVANTAGES OF TEE IN AORTIC DISSECTION

The major advantage of TEE as the optimal screening test is its *ease of application at the bedside, which allows immediate and accurate diagnosis* for the potential emergent surgical intervention. A TEE can generally be done within 10–15 minutes with very little preparation compared with angiography, computed tomographic scanning, and magnetic imaging, which may require 30 minutes to one hour to organize and perform, time that may be life threatening. Aortography and coronary arteriography can then be performed if there is a need to delineate the blood supply of vital organs or the coronary arteries or if the TEE is inconclusive especially if a penetrating ulcer is a consideration.

TEE has been used very successfully because of the high-quality imaging of the thoracic aorta. It provides a dynamic assessment of the intimal flap and of the presence and extent of luminal thrombus and an assessment of sites of communications. Erbel and the European Cooperative Study Group for Echocardiography<sup>4</sup> published a multicenter study showing the diagnostic accuracy in 164 consecutive patients with suspected aortic dissection. The sensitivity and specificity were 99% and 98%, respectively, for TEE compared with 83% and 100%, respectively, for computed tomographic scanning, and 88% and 94%, respectively, for aortic angiography. Experienced operators in this study used only the monoplane TEE probe.

Hashimoto et al.<sup>33</sup> have utilized the next generation biplane transesophageal probe and demonstrated that the intimal flap and entry site can be recognized in 100% of cases. Ballal et al.<sup>5</sup> have shown the superior diagnostic yield with TEE for the diagnosis of the aortic dissection. However, their study was limited because of the use of aortography to exclude the diagnosis of dissection. Bansal et al.<sup>30</sup> have shown the limitations of aortography and the improved

diagnosis of dissection by TEE. A thrombosed false lumen, noncommunicating dissection and equal flow in both the true and false lumen and intramural hematoma were all missed by aortography and correctly diagnosed by TEE. Keren et al.<sup>34</sup> have shown that biplane and multiplane imaging provided better visualization of the arch and ascending aorta permitting highly reliable diagnosis of dissection with a sensitivity and specificity of 98% and 95%, respectively. The specificity for type A and type B dissection was 97% and 99%, respectively. However, it did not improve on the high degree of sensitivity, specificity, and accuracy reported by other investigators using monoplane TEE<sup>4,5,30,32,33</sup>.

Nienaber et al.<sup>35</sup> and Moore et al.<sup>36</sup> have demonstrated a lower specificity for the diagnosis of dissection by TEE. The sensitivity for the diagnosis of dissection was 97.7% and specificity was 76.9% in Nienaber's study. The authors, however, conceded that there is a learning curve for differentiating artifacts, and this can adversely affect the specificity of the TEE<sup>37</sup>. Moore et al.<sup>36</sup> have also shown that overall specificity for the diagnosis of dissection by TEE was 88% and was slightly better for type A, compared with type B dissection (90% versus 80%). That study too may suffer from learning curve errors. It is important to know the technical limitations of TEE and their impact on diagnosis. Svenson et al.<sup>11</sup> demonstrated that in 5% of their patients the dissection was not recognized despite multiple noninvasive imaging modalities and required aortography. These missed diagnoses were due to an inability to completely image an eccentric aortic aneurysm with a small intimal tear (but no flap) which was located in the far field.

Movsowitz et al.<sup>38</sup> have demonstrated the additional benefit of using TEE to identify who might require aortic valve replacement or repair by assessing the mechanism of aortic regurgitation prior to surgery. They demonstrated that 16 of 22 patients with moderate to severe regurgitation had normal valve leaflets and the valve could be repaired in 15 patients.

TEE also has an important role in the follow-up of patients with aortic dissection. Mohr-Kahaly et al.<sup>39</sup> followed 18 patients with aortic dissection by serial TEE performed in the outpatient setting. The TEE study showed the structure of the dissection, the surgical repair, and blood flow dynamics in the true and false lumen. It showed the evolution of the dissection in many patients; 25% having complications of either extension of the dissection (5%), dilatation of the aorta (11%), or aortic regurgitation (17%). In addition, in two patients, TEE documented healing of the dissection and obliteration of the false lumen with time. This study shows the potential application of TEE to follow up these patients for disease progression, healing, or the need for surgical intervention as an alternative to the more often used CT scan.

Thus, in a patient suspected of dissection both TTE and TEE provide reliable complementary information essential for clinical decision making. This

information can be obtained within 10 to 15 minutes either at the bedside or in the emergency room. However, one should be aware of the pitfalls. When the diagnosis is elusive one should not hesitate to use other equally sensitive and specific diagnostic modalities such as spiral computed tomography or even MRI if the clinical condition permits.

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# 5

## CT EVALUATION OF AORTIC DISSECTION

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Computed tomography (CT) is used to evaluate the aorta, specifically aortic dissection, in the following clinical circumstances:

- Diagnosis of acute dissection in patients with the acute onset of chest or back pain or neurologic deficit<sup>1</sup>,
- Follow-up of known medically treated type B dissection, and
- Surveillance after surgical repair or percutaneous intervention.

Worldwide, CT is the most frequently used initial imaging examination for patients with suspected aortic dissection<sup>1</sup>. The first role of CT in the acute setting is to establish the diagnosis of dissection and to determine the type of dissection. This is important, as type A dissection involving the ascending aorta requires surgical repair, while a type B dissection starting distal to the left subclavian artery is usually managed conservatively unless there is continued chest pain or inability to control hypertension. CT also identifies signs of aortic rupture, such as extraluminal contrast extravasation and pericardial or retroperitoneal fluid. Information obtained from CT about the dissection itself includes determining the extent and configuration of the dissection, identifying

aortic branch vessel involvement, identifying the true and false lumens, localizing intimal tears and fenestrations in the intimal flap, and providing accurate measurements of the aorta. Furthermore, CT is used to distinguish between classic aortic dissection and atypical forms of dissection, such as penetrating atherosclerotic ulcers and intramural hematomas.

In this chapter, we review the technical factors that are important for obtaining high-quality imaging of the thoracic aorta and aortic dissection and the technical and interpretative pitfalls that may be encountered in this setting. The accuracy of CT for diagnosing and evaluating aortic dissection and the imaging findings of classic and atypical forms of dissection also are detailed.

## **TECHNIQUE**

With the advent of rapid helical CT scanners, particularly multidetector CT scanners of four rows or more, CT angiography has replaced catheter angiography for the diagnostic evaluation of the thoracic aorta. MDCT imaging of 16 rows and greater also permits isotropic imaging in the *z*-axis, thereby generating equal resolution in any plane within the helical three-dimensional data sets, improving the quality of multiplanar and three-dimensional reconstructions and virtual angiography or fly-through imaging. Lastly, ECG gating can be used with 16-row and greater MDCT, reducing cardiovascular motion artifacts and evaluating the coronary arteries. Imaging is usually performed both before and during intravenous contrast administration. Details of the protocols that may be used are given in Table 5.1.

Evaluation of the thoracic aorta in the setting of aortic dissection usually begins with nonintravenous contrast-enhanced images to identify acute hematoma in the aortic wall, as well as fluid in the mediastinum, pleural space, pericardium, or retroperitoneum. This is particularly useful when there are any acute symptoms, whether in the evaluation of a newly suspected dissection or in patients with a known dissection or previously repaired dissection. Acute hematoma is easily identified on noncontrast enhanced images as it is higher in attenuation when compared to muscle and blood in the aortic lumen. In addition, nonintravenous contrast-enhanced images facilitate detection of aortic calcification; localization of the calcification is useful for distinguishing the true and false lumens. The noncontrast enhanced series is performed in helical mode, with coverage of the entire aorta and the pelvic arteries to the level of the groin. A slice thickness of 5–7.5 mm is sufficient to detect acute hemorrhage and aortic calcification. Thinner slices are not needed for these images and would unnecessarily increase the radiation dose to the patient.

Intravenous contrast-enhanced helical CT imaging is then performed from the top of the thorax through the groin for evaluation of the entire thoracoab-

Table 5.1. CT acquisition parameters for contrast CT of the aorta on single slice and multislice helical CT

	Single-slice CT	4-row MDCT	8-row MDCT	16-row MDCT	16-row MDCT gated	64-row MDCT gated
Pitch	2:1	(0.75-1.5):1	1.375:1	1.375:1	0.22-0.26	0.2-0.26
Slice thickness (mm)	3	2.5	2.5	2.5	Chest: 1.25 mm, A/P: 2.5 mm	Chest: 1.25 mm, A/P: 2.5 mm
Reconstruction interval (mm)	3	1.25	1.25	1.25	1.25	1.25 mm
Table speed (mm)/rotation	6	15	27	27.5	Chest: 8.8-10.4 A/P: 27.5	Chest: 22.8-29.6 A/P: 55
Gantry rotation time (s)	1.0	0.8	0.8	0.5	0.5	0.35-0.4
Detector size (mm)	1	1.25	1.25	0.625/1.25	0.625/1.25	0.625
Coverage per rotation (mm)	1	5	10	20	20	40
FOV (cm)	28	25	25	25	25	25
Gating	No	No	No	No	Yes	Yes
KV	120	120	120	120	120	120
MA	230-270	380	400	400	550-650	650-750
Scan timing	24-28 seconds	Automated bolus detection (SmartPrep™) with ROI in descending aorta	Automated bolus detection (SmartPrep™) with ROI in descending aorta	Automated bolus detection (SmartPrep™) with ROI in descending aorta	Automated bolus detection (SmartPrep™) with ROI in descending aorta	Time delay between injection and scan is determined by test bolus

Abbreviations: MDCT = multidetector CT; FOV = field of view; KV = kilovolt; MA = milliampere × seconds; ROI = region of interest; if automated bolus detection is used, the scan is automatically started when contrast appears within the region of interest.

dominal aorta and branch vessels into which the dissection may extend or occlude. Even with fast helical CT scanning that reduces scan times considerably, thereby reducing patient motion generated artifacts, there are areas of the thoracic aorta that may be compromised due to cardiovascular motion. In particular, there is considerable motion at the aortic root and ascending aorta. For the thoracic aorta, ECG gating may be used to obtain motion-free imaging of the aortic root and thoracic aorta, improving evaluation of the dissection flap due to reduction of motion artifact and also allowing visualization of the coronary arteries<sup>2-4</sup>. In addition to providing higher-quality axial images, ECG gating improves the quality of multiplanar and three-dimensional reconstructed images.

Iodinated contrast material is administered with a power injector through a 20 gauge or larger venous cannula, usually located in an antecubital vein. The time delay between injection of contrast material and start of the scan is optimized to obtain maximum concentration of contrast within the aorta. This is achieved either with a timing bolus or with automated bolus detection; automated bolus detection is used for nongated studies. A timing bolus is used for all gated studies, with 15–20 ml of contrast material injected at a rate of 4–5 ml/s, followed by 20 ml saline, with serial imaging through the aortic root to determine peak arterial enhancement.

For the contrast enhanced series, 80–120 ml of nonionic contrast material is injected at a rate of 4–6 ml/s, followed by 50 ml saline. The amount of contrast material depends on scanner generation and may be reduced with higher scanner speed. Injection into the right arm is preferred to avoid streak artifact caused by concentrated contrast material in the innominate vein, which may obscure the proximal aspects of the great vessels. Specific parameters for the contrast enhanced series using single slice or multidetector helical CT are listed in Table 5.1. In selected patients, a delayed scan of the aorta is performed (see below).

Although assessment of cardiac pathology may not be needed in every patient, it might be useful in selected patients, particularly patients with type A dissection or chest pain. To facilitate evaluation of aortic valve, coronary arteries, and cardiac morphology and function, image data obtained with retrospective cardiac gating is postprocessed to reconstruct an additional series with temporal resolution at 5% increments of the cardiac cycle. Coverage for this series of image reconstructions is from the aortic root to the apex of the heart, at a slice thickness of 1.25 mm or less. Note that this is not an additional image acquisition that would require additional radiation exposure; this is a reconstruction of the dataset already acquired with intravenous contrast to evaluate the thoracic aorta.

Images are reviewed on a computer workstation, which allows generation of multiplanar reformatted images (MPR). This is necessary due to the large

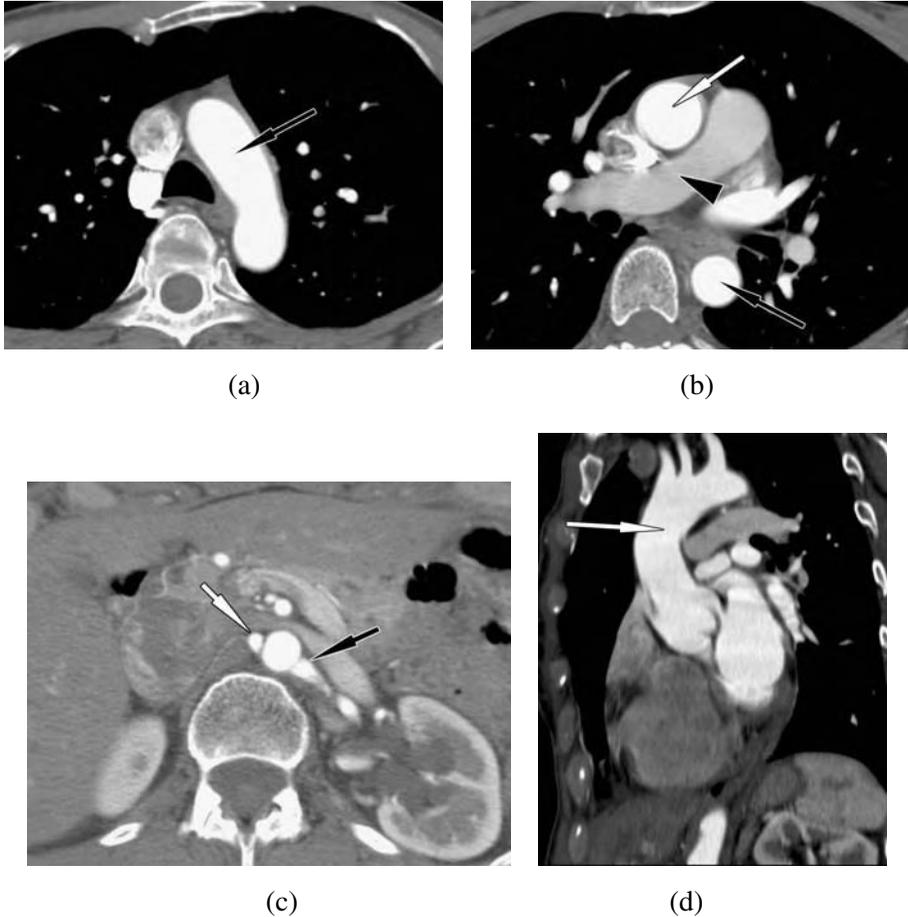


Figure 5.1. Intravenous, contrast-enhanced CT examination of a normal aorta with a 16-row multidetector CT; no ECG gating was used: (a) axial image of the aortic arch (black arrow); (b) axial image of ascending (white arrow) and descending aorta (black arrow) at the level of the right pulmonary artery (black arrowhead); (c) abdominal aorta at the level of the renal artery origins (right renal artery indicated by white and left renal artery indicated by black arrow); (d–f) multiplanar reformatted images of ascending aorta and aortic arch (white arrow in d), descending aorta (black arrow in e), and abdominal aorta with renal artery origins (arrows in f indicate renal arteries) (note stair step artifact through the aortic root on this non-ECG gated examination).

amount of thin-section images generated. The MPR images are sometimes helpful to better delineate the extent of the dissection flap and are either better than or as helpful as 3D reformatted images<sup>5</sup>. Figure 5.1 illustrates an intravenous contrast-enhanced CT examination of a normal aorta obtained on a 16 row multidetector CT scanner, without ECG gating.

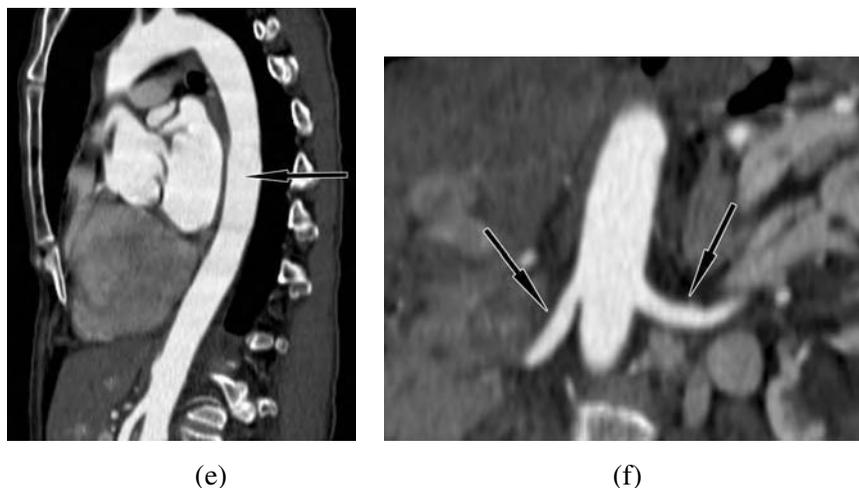


Figure 5.1. (Continued)

## LIMITATIONS AND PITFALLS OF CT FOR AORTIC DISSECTION

Limitations are inherent in any imaging technique and cannot be avoided. Recognizing the limitations and pitfalls, whether they are related to the technology itself or technical failure, imaging artifacts or interpretive pitfalls is important to avoiding them and rendering an accurate diagnosis and evaluation of the aorta.

### LIMITATIONS

The most important limitations of CT affect the diagnosis of type A dissection:

- CT is currently not the method of choice for evaluation of coronary artery involvement. Note that recent advances in 16- and 64-row ECG-gated CT make this possible.
- Aortic insufficiency, another common complication of type A dissection, cannot be diagnosed with CT.

### TECHNICAL FAILURES

Technical failures may result in insufficient enhancement of the aorta and can lead to false negative diagnoses or difficulty in evaluating aortic branch vessel compromise. Probably the most important technical pitfall is the incorrect timing of the image acquisition relative to the intravenous contrast bo-

lus. While automated bolus detection and timing bolus techniques have nearly completely eliminated this, it may still occur with automated bolus detection if the region of interest (ROI) is erroneously placed in the false lumen or the patient moves between placement of the ROI in the aortic root and acquisition of images. Visual check and, if needed, manual stopping and starting of the scan acquisition may help avoid this pitfall.

## **STREAK ARTIFACT**

Streak artifact can mimic or obscure dissection of the aorta. Streak artifact is commonly caused by nondiluted contrast in the brachiocephalic vein or superior vena cava (SVC) (Figure 5.2), metallic foreign bodies (Figure 5.2), and cardiac motion<sup>3,6,7</sup> (Figure 5.3a–b). Evaluations of the ascending aorta and great vessels off the aortic arch are the most frequently affected (Figure 5.3a–b). Contrast injection into the right arm followed by saline flush reduces the concentration of contrast in the SVC and avoids contrast within the left brachiocephalic vein, thereby reducing streak artifact<sup>8</sup>. Cardiac gating<sup>3,4</sup> as well as a 180 degree linear-interpolation algorithm<sup>9–11</sup> are used to reduce cardiac motion artifact. Streak artifacts can be differentiated from dissection flaps by recognizing that the low attenuation band extends outside the confines of the aortic lumen or by recognizing parallel bands on opposite sides of the aortic lumen in the case of aortic motion (Figure 5.3a). Multiplanar reformatted images may be helpful to differentiate between dissection and streak artifact in difficult cases<sup>12</sup>.

## **INTERPRETATIVE PITFALLS**

Several interpretative errors can be made on CT when evaluating for aortic dissection. Generally, these may be related to periaortic structures and aortic branch vessel origins, relative high attenuation of the aortic wall in patients with anemia, atherosclerotic disease, atypical dissection and prior surgical repair of the aorta.

### **Periaortic Structures and Aortic Branch Vessel Origins**

Structures immediately adjacent to the aorta (for example, the anterosuperior pericardial recess or the left brachiocephalic vein) can mimic a double lumen and may be confused with dissection (Figure 5.4). The same applies to aortic branch vessel origins, which can simulate the presence of an intimal flap<sup>7</sup>. Familiarity with the anatomy and, in difficult cases, image review in multiple planes can aid in avoiding these pitfalls.

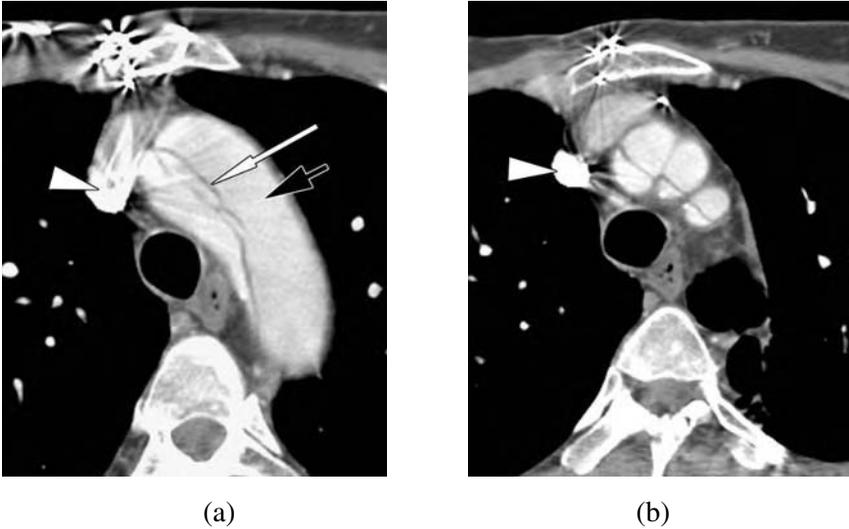


Figure 5.2. Axial contrast-enhanced CT images of classic type A dissection in a patient with prior sternotomy: (a) shows dissection flap in the aortic arch (long white arrow) (the false lumen is indicated by the short black arrow); (b) shows extension of the dissection flap into the brachiocephalic arteries (the flap does not occlude those branches, and perfusion is not impaired); streak artifact from metallic sternotomy wires and concentrated contrast in the superior vena cava (white arrowhead) is also demonstrated.

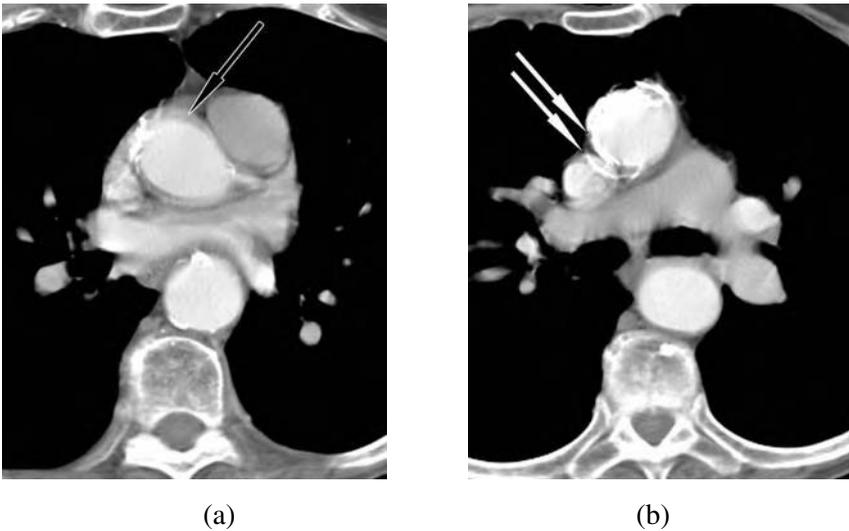


Figure 5.3. Axial contrast-enhanced CT images of motion artifact simulating dissection of the ascending aorta: (a) black arrow indicates apparent peripheral low attenuation rim in the ascending aorta mimicking dissection; (b) white arrows indicate apparent double contour of calcifications in the ascending aorta, mimicking chronic dissection with calcified false lumen.

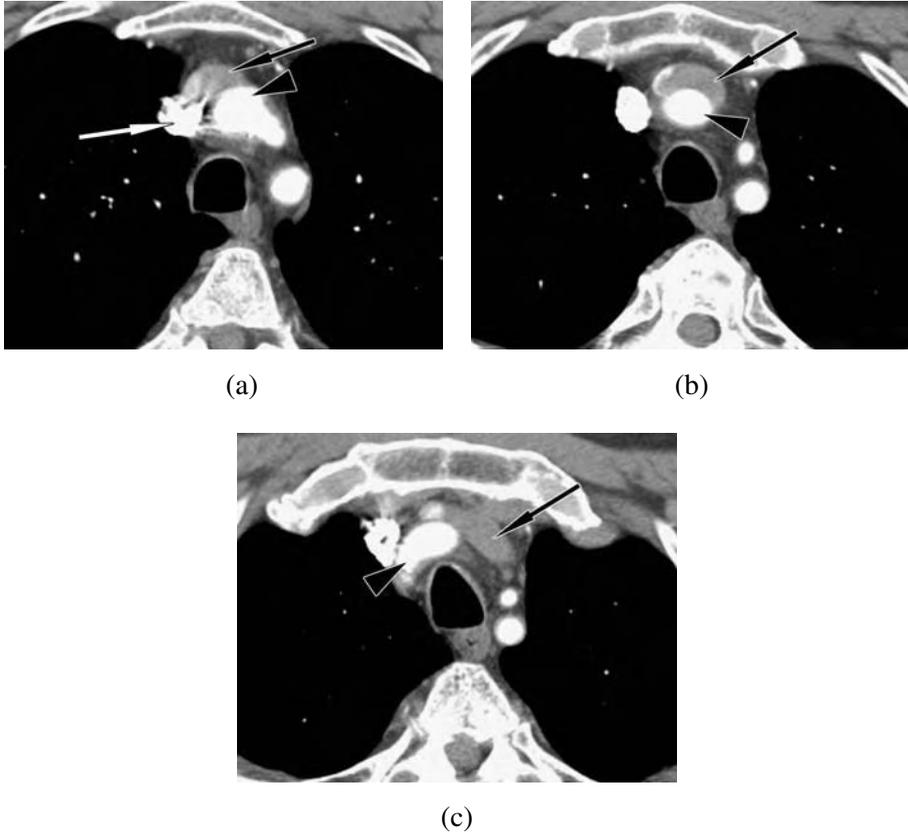


Figure 5.4. Axial contrast-enhanced CT images of left brachiocephalic vein simulating dissection of the brachiocephalic artery: (a) shows junction of left brachiocephalic vein (black arrow) and SVC (white arrow) (black arrowhead indicates origin of brachiocephalic artery from the aortic arch); (b) image superior to (a) shows left brachiocephalic vein (black arrow) adjacent to brachiocephalic artery (black arrowhead), simulating dissection; (c) image superior to (b) shows left brachiocephalic vein (black arrow) coursing anterior to brachiocephalic artery (black arrowhead).

### Atypical Dissection: Importance of Window Settings

In the acute setting, identification of intramural hematoma (IMH) is based on the appearance of a high attenuation rim or crescent along the curvature of the aortic wall on nonintravenous contrast enhanced CT images. Although described to be present on CT in 100% of patients with acute intramural hemorrhage<sup>13,14</sup>, this finding may be subtle and may not be appreciated on standard mediastinal window settings. Narrow window settings are essential to appreciate the often subtle attenuation difference between acute intramural hematoma and the perfused lumen of the aorta<sup>15</sup> (Figure 5.5a–b).

Lastly, the high attenuation of a thrombus may be completely missed on the contrast-enhanced images, as the relative difference in attenuation of the acute hematoma is hard to recognize in the presence of intravenous contrast.

### **Relative High Attenuation of the Aortic Wall in Patients with Anemia**

The attenuation of blood is related to the hematocrit and is decreased in patients with anemia<sup>16–18</sup>. Whereas attenuation of the normal aortic wall and blood is similar on noncontrast enhanced CT images of patients with normal hematocrit, in patients with anemia the aortic wall becomes visible secondary to its relatively higher attenuation compared to the decreased attenuation of intraluminal blood. This appearance might be confused with the high attenuation of acute intramural hematoma (IMH). Absence of the typical crescent shape of IMH and absence of displaced intima calcifications usually helps to distinguish anemia from hematoma.

### **Atherosclerotic Disease and Atypical Dissection**

On contrast-enhanced CT, IMH has the appearance of a nonenhancing low attenuation rim or crescent, which can be difficult to distinguish from atherosclerotic intraluminal thrombus (Figure 5.5c–f). Three imaging characteristics are useful to differentiate between IMH and intraluminal thrombus:

First, the false lumen of acute IMH shows high attenuation on unenhanced CT; intraluminal thrombus does not. However, this imaging criterion becomes unreliable in subacute and chronic intramural hematoma because the attenuation of IMH decreases over time and the initial high attenuation of the aortic wall is commonly absent in the subacute and chronic stage. In a study by Yamada et al.<sup>14</sup>, high attenuation of the aortic wall on unenhanced CT was observed in all eight patients evaluated in the acute stage of intramural hematoma but in none of the four patients evaluated while in the subacute stage<sup>14</sup>.

Second, most aortic calcifications are intima calcifications. Thus, calcifications within a thrombus detached from the aortic wall suggest IMH (Figure 5.5b) and calcifications at the outside of a thrombus suggest intraluminal thrombus (Figure 5.6). However, differentiation between atherosclerotic intraluminal thrombus and intramural hematoma on the basis of aortic calcification alone can be problematic because chronic intraluminal thrombus can calcify over time and mimic detached intima calcification (Figure 5.7). Furthermore, intima calcifications may not be present, particularly in the younger age group<sup>19</sup>. In the acute setting, this diagnostic dilemma can be solved by review of the unenhanced CT images, which demonstrate the high attenuation of acute intramural hematoma (Figure 5.5a–b) or the low attenuation of intraluminal thrombus (Figure 5.6a).

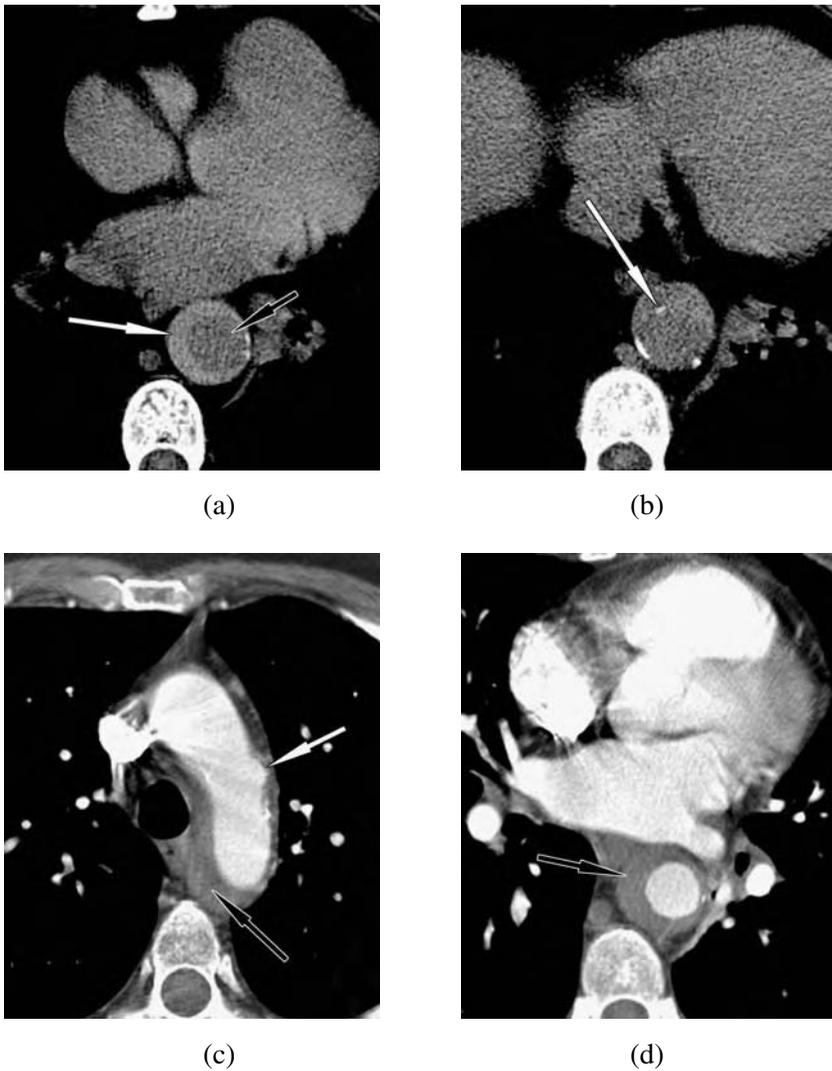


Figure 5.5. CT examination of type B intramural hematoma (IMH): (a) unenhanced axial image shows higher attenuation of acute intramural hematoma (white arrow), compared to low attenuation of the perfused true lumen of the aorta (black arrow); (b) unenhanced axial image inferior to (a) shows displaced intima calcification (white arrow); (c) axial contrast-enhanced image of the aortic arch shows low attenuation of the intramural hematoma (black arrow), compared to the contrast filled true lumen of the aorta; a focal contrast outpouching of the true lumen (white arrow) suggests intimal tear or ulceration; (d–e) axial contrast enhanced images at the same level as (a) and (b) demonstrate intramural hematoma of the descending thoracic aorta (black arrow); (f) maximum intensity projection reformatted image nicely demonstrates the extent of the intramural thrombus (black arrows), however, does not add additional diagnostic information.

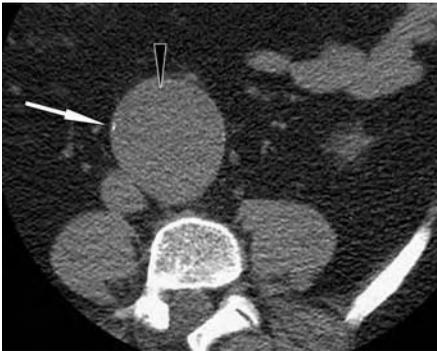


(e)

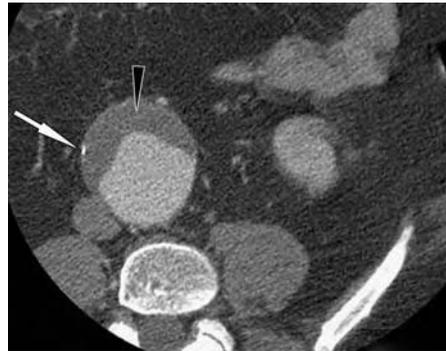


(f)

Figure 5.5. (Continued)



(a)



(b)

Figure 5.6. Axial CT images of atherosclerotic intraluminal thrombus in abdominal aortic aneurysm demonstrate intima calcification at the outside of the thrombus (white arrow): (a) unenhanced image shows low attenuation of the intraluminal thrombus (black arrowhead), which cannot be distinguished from the perfused lumen of the aorta; (b) contrast enhanced image delineates the intraluminal thrombus (black arrowhead), which shows low attenuation compared to the contrast enhanced lumen of the aorta. This example of intraluminal thrombus is relatively smoothly demarcated and could be confused with IMH on the contrast enhanced scan; however, low attenuation on the unenhanced scan excludes acute IMH.

Lastly, IMH is usually smoothly margined and crescent shaped (Figure 5.5), as opposed to the often jagged appearance of intraluminal thrombus (Figure 5.8). However, this imaging criterion is not always helpful, as demon-

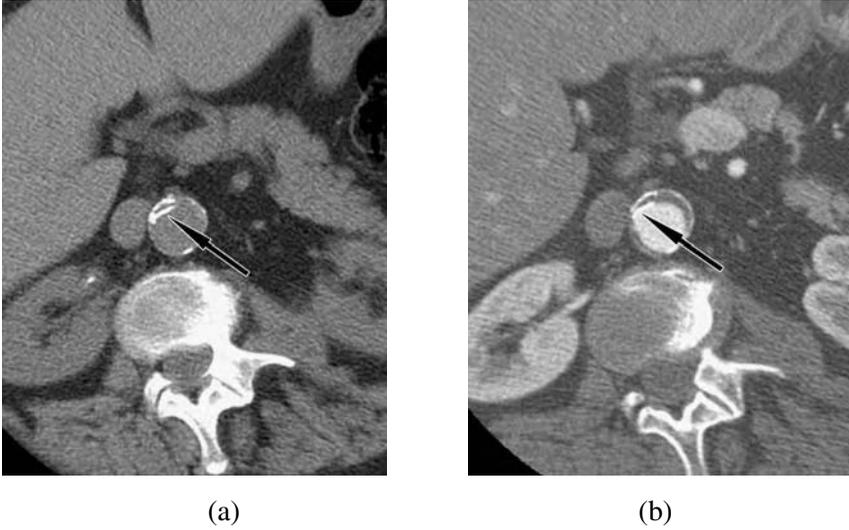


Figure 5.7. Axial CT images of calcified intraluminal thrombus simulating detached intima calcification (black arrow): (a) unenhanced image; (b) contrast enhanced image; note isoattenuation of intraluminal thrombus compared to the perfused lumen of the aorta on the unenhanced image.

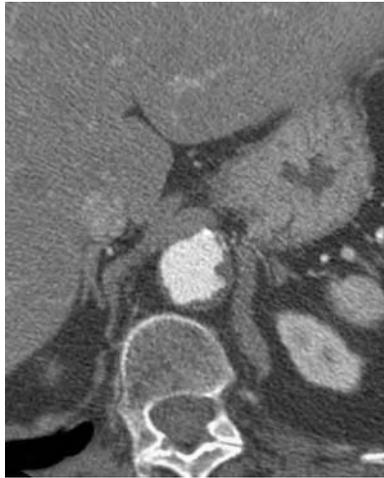


Figure 5.8. Axial contrast-enhanced CT image of atherosclerotic intraluminal thrombus in a different patient demonstrates the more typical jagged appearance.

strated by the relatively smooth appearance of intraluminal thrombus in an abdominal aneurysm in the example in Figure 5.6.

## **Differentiation Between Periaortic Hematoma of Aortic Rupture and Atypical Dissection**

Another potential pitfall is differentiating between periaortic hematoma and atypical dissection, as shown by Quint et al.<sup>20</sup>, who reported a thrombosed false lumen of the ascending aorta simulating mediastinal hematoma.

## **Intimo-intimal Intussusception**

Dissection of the ascending aorta may be missed in the case of an intimo-intimal intussusception, a rare complication of type A dissection, with only a few cases reported in the literature. Intimo-intimal intussusception is caused by a circumferential intimal tear of the proximal ascending aorta, with subsequent prolapse of the torn intima into the true lumen, creating the appearance of a windsock. Because the entire intima is torn off, the ascending aorta can appear normal on CT images, and the only sign of dissection may be a curvilinear filling defect within the true lumen of the aortic arch, corresponding to the prolapsed intima. Intimo-intimal intussusception is a serious complication, since the prolapsed intima may occlude the origins of the aortic arch vessels. The prolapsed intima may be continuous with a dissection flap in the descending aorta<sup>21–26</sup>.

## **Prior Surgical Repair of the Aorta**

The appearance of an aortic graft may simulate a dissection flap, particularly if the graft is bended or kinked. Kinks of aortic grafts are most commonly observed near the proximal or distal anastomoses and multiplanar reformatted images are often helpful for identifying them. However, knowledge of the surgical history is of utmost importance for the correct interpretation of CT images in patients with prior aortic repair. Two-stage repair of the thoracic aorta with the so-called elephant trunk procedure<sup>27</sup> creates a complex appearance on CT images that can mimic atypical dissection<sup>28</sup>. An example of a thoracic aorta after elephant trunk procedure is shown in Figure 5.9.

## **DIAGNOSTIC ACCURACY**

The accuracy of CT for detection of aortic dissection and classification as either type A or type B has been evaluated for single-slice CT, yielding a specificity between 94% and 100%<sup>5,13,29,30</sup> and a sensitivity from 93% to 100%<sup>1,5,29,30</sup>. Moore et al. evaluated the patient records of 628 patients enrolled in the International Registry of Acute Aortic Dissection (IRAD) between 1996 and 1999, 618 of whom had imaging studies performed<sup>1</sup>. In this study, CT was more sensitive than transesophageal echocardiography (TEE)

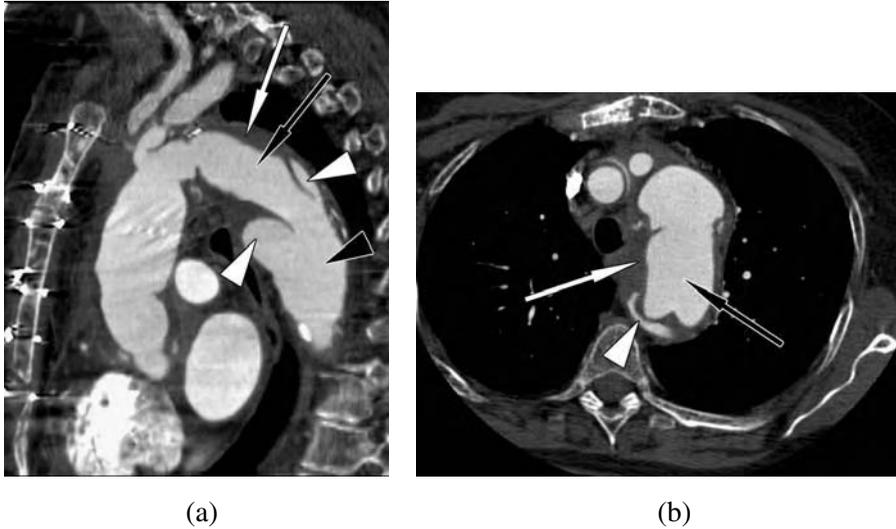


Figure 5.9. Multiplanar reformatted contrast-enhanced CT images after replacement of the ascending thoracic aorta and aortic arch with a graft that extends into the descending thoracic aorta using elephant trunk technique: (a) sagittal oblique reformatted image; (b) axial reformatted image at the level of the graft of the aortic arch and proximal descending thoracic aorta. The graft is indicated by the thin black arrow. There is a partially thrombosed aneurysm of the proximal descending thoracic aorta surrounding the graft (thin white arrow). There is retrograde flow of contrast into the aneurysm (white arrowhead); the descending thoracic aorta distal to the graft is indicated by the black arrowhead. The appearance is entirely due to the presence of the graft within the aneurysm of the descending thoracic aorta, and there is no dissection.

but less sensitive than MR imaging for the detection of aortic dissection: Overall sensitivities were 88% (TEE), 93% (CT), 100% (MRI), and 87% (conventional angiography). For type A dissection, sensitivities were 90% (TEE), 93% (CT), 100% (MRI), and 87% (conventional angiography). For type B dissection, sensitivities were 80% (TEE), 93% (CT), 100% (MRI), and 89% (conventional angiography). Excluding cases of intramural hematoma (IMH), overall sensitivity was 87% for TEE, 93% for CT, 100% for MRI, and 88% for conventional angiography. Currently, there is no published research that evaluates the accuracy of multidetector CT for evaluation of aortic dissection.

## CLASSIC DISSECTION

Classic dissection is characterized by intimal rupture and communication between true and false lumens. The typical appearance on CT is the presence of two perfused and contrast-enhanced lumina separated by a thin low attenuation band representing the detached intima (Figure 5.10). Displaced intima calcifications located between true and false lumen may be present in

cases with atherosclerotic disease (Figure 5.11). Attenuation of the false lumen is dependent on timing of the image acquisition and is often lower than that of the true lumen secondary to slow flow (Figures 5.10 and 5.11). Delayed images demonstrating delayed contrast enhancement of the false lumen are helpful to differentiate between slow flow and thrombus. Atypical appearances of the dissection flap in otherwise classic dissection include complex dissection, where the dissection flap is separated with more than one false lumen present<sup>12</sup> (Figure 5.12), and circular configuration of the dissection flap, where the true lumen is visualized in the center of the aorta and surrounded by the false lumen<sup>12</sup>. The false lumen of classic dissection may partially or completely thrombose, mimicking the appearance of an IMH.

## LOCALIZATION OF INTIMAL TEARS

Localization of intimal tears is important for endograft placement because the goal of the endograft is to occlude the communication between the true and the false lumen. The reported sensitivity of single slice helical CT for the detection of intimal tears varies between 82% and 93%<sup>13,31</sup>. Quint et al. evaluated 52 patients with aortic dissection—26 patients using single slice and 26 patients using multidetector helical CT<sup>32</sup>. All patients showed at least one intimal tear, with a total of 129 intimal tears identified in the 52 patients. The images obtained with multidetector helical CT were superior to images obtained with single slice helical CT to demonstrate intimal tears. The CT appearance of intimal tears is illustrated in Figures 5.10b–c and 5.13a–b.

## IDENTIFICATION OF TRUE AND FALSE LUMEN

Identification of true and false lumen is an important prerequisite for percutaneous treatment of dissection. In most cases of type B dissection, the true lumen is easily identified by its continuity with the nondissected ascending aorta. However, in type A dissection and in cases where the aorta is incompletely imaged, identification of true versus false lumen may not be straightforward. The following imaging criteria are helpful to distinguish between true and false lumen<sup>33–35</sup>.

- *The beak sign*: This is defined as acute angle between the dissection flap and the outer aortic wall, and indicates the location of the false lumen (Figure 5.14). This sign has been reported to be 100% accurate for identification of the false lumen in both acute and chronic aortic dissection<sup>33</sup>.
- *Cobwebs*: These are thin, linear low attenuation filling defects attached to the aortic wall, and are only seen in the false lumen (Figure 5.15), as shown by LePage et al.<sup>33</sup>. In this study, cobwebs were 100% specific for identification of the false lumen. Unfortunately, cobwebs were observed



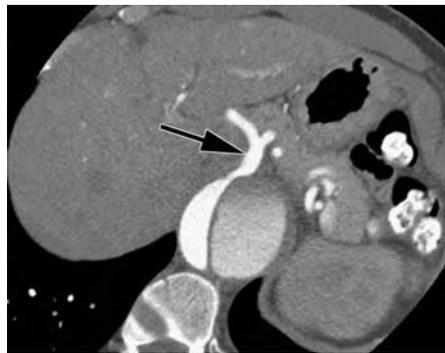
(a)



(b)



(c)



(d)

Figure 5.10. Contrast-enhanced CT examination of type B classic dissection, multiplanar reformatted images: (a) sagittal reformatted image of the descending aorta shows dissection flap (black arrow) starting just distal to the left subclavian artery (white arrow) (the false lumen is indicated by the thin black arrow; note dilation of the descending aorta and lower attenuation of the false lumen due to slow flow and early image acquisition); (b) sagittal reformatted image of the descending aorta shows tear of the dissection flap (black arrow); (c) axial reformatted image shows same tear of the dissection flap (the end of the dissection flap is indicated by the thin black arrow; status postsurgery to the ascending aorta (large black arrow), as indicated by surgical clips; trace left pleural effusion (white arrowhead); (d) axial oblique reformatted image shows origin of celiac artery (black arrow) from true lumen; (e) axial oblique reformatted image shows origin of right renal artery (black arrow) from true and left renal artery (thin black arrow) from false lumen (note again lower attenuation of the false lumen and delayed enhancement of the left kidney (arrowhead) due to slow flow in the false lumen and early image acquisition; incidental low attenuation hepatic lesions are also noted).

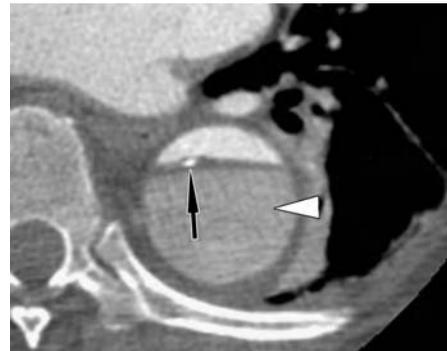


(e)

Figure 5.10. (Continued)



(a)



(b)

Figure 5.11. Axial CT images of the descending aorta show classic dissection and displaced intima calcifications within the dissection flap (black arrow): (a) unenhanced image; (b) contrast-enhanced image (the false lumen is indicated by the white arrowhead; note again the lower attenuation of the false lumen on the contrast-enhanced image due to slow flow and early image acquisition; the false lumen is larger than the true lumen).

in only 9% of the scans reviewed, limiting the usefulness of this sign due to its low prevalence.

- *Wrapping*: If one lumen wraps around the other at the level of the aortic arch, the inner lumen is always the true and the outer lumen is always the false lumen<sup>33</sup>.
- *Lumen size*: The false lumen is usually larger than the true lumen in classic dissection (Figures 5.10 and 5.11). In the study of LePage et al.<sup>33</sup>, at one quarter of the distance along the dissected length of the aorta, the larger lumen was the false lumen in 85% of the acute cases and 83% of

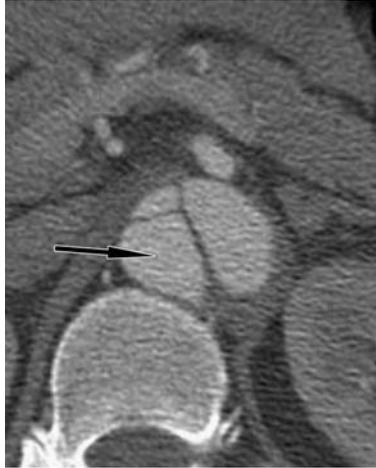


Figure 5.12. Axial contrast-enhanced CT image of complex dissection flap with two false lumens visualized. The arrow indicates the true lumen.

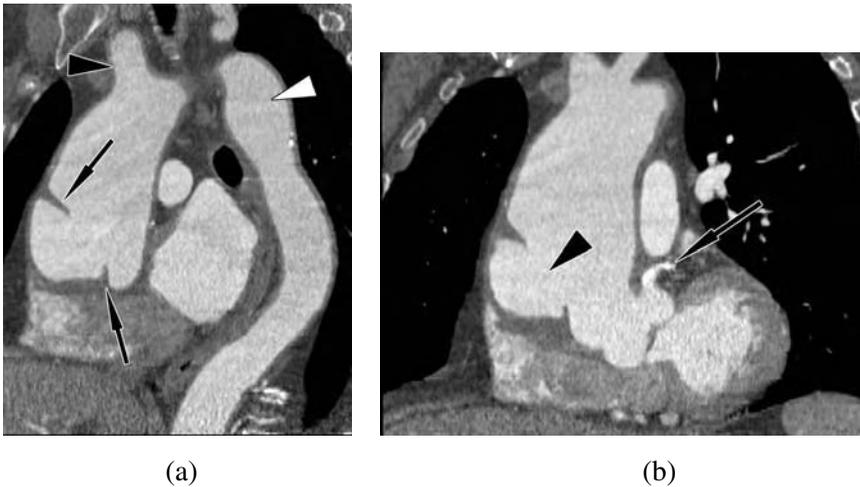


Figure 5.13. Multiplanar reformatted contrast-enhanced CT images of type A dissection: (a) demonstrates a localized dissection flap in the ascending aorta (black arrows); the brachiocephalic artery (black arrowhead) is not involved; the white arrowhead indicates the descending thoracic aorta; (b) shows the origin of the left coronary artery, which is calcified but not involved by the dissection; there is a large tear in the dissection flap (black arrowhead).

the chronic cases. At one half of the distance along the dissected length of the aorta, the larger lumen was the false lumen in 94% of acute cases and in 96% of chronic cases.

- *Outer wall calcification*: This indicates the true lumen in acute dissection (Figure 5.16). However, this sign is unreliable in chronic dissection, where calcification of the outer wall of the false lumen is occasionally observed (Figure 5.17). Outer wall calcification has been shown to be 60% sensitive and 100% specific for identification of the true lumen in acute aortic dissection. On the other hand, outer wall calcification of the false lumen has been observed in 17% of chronic cases<sup>33</sup>.
- *Thrombosis*: A thrombosed lumen is usually the false lumen. This sign, however, is of limited value in patients with aneurysm, where intraluminal thrombus may be present in the true lumen as well. In the study of LePage et al., thrombosis in the false lumen was observed in 46% of cases with acute dissection and 83% of cases with chronic dissection. On the other hand, intraluminal thrombus in the true lumen was observed in 6% of the cases with acute dissection and 4% of the cases with chronic dissection.
- *Direction*: Blood flow direction is from true to false lumen at the level of intimal tears, with the ends of the flaps pointing toward the false lumen in acute dissection. LePage et al. observed the dissection flap curved toward the false lumen at one quarter of the distance along the dissected length of the aorta in 56%, flat dissection flap in 38%, and the dissection flap curved toward the true lumen in 6% of cases with acute dissection. For chronic dissection, the dissection flap was flat in 75% and curved toward the false lumen in 25% of cases. In a study of Kapoor et al., the free edges of the dissection flap were pointing toward the false lumen in all five patients with acute aortic dissection in which an intimal tear was visualized<sup>35</sup>.

On most exams, attenuation of the false lumen will be lower than that of the true lumen, due to early image acquisition (Figures 5.10, 5.11, 5.17). However, attenuation of the lumina is not a reliable sign to distinguish between true and false lumen. Although flow is faster in the true lumen than in the false lumen, attenuation of the false lumen may be less, equal or higher than that of the true lumen, dependent on timing of the image acquisition<sup>36</sup>.

## ASSESSMENT OF THE CORONARY ARTERIES

In patients with type A dissection, assessment of the coronary arteries is important. As mentioned above, published research about CT evaluation of aortic dissection is currently limited to single slice CT, an insufficient technique for evaluation of the coronaries. However, multidetector CT with cardiac gating is now widely available and has shown to be accurate and reliable for evaluation of coronary artery stenoses<sup>37-41</sup>. Recent case reports demonstrate the potential of multidetector CT for assessment of the coronary arteries in type A

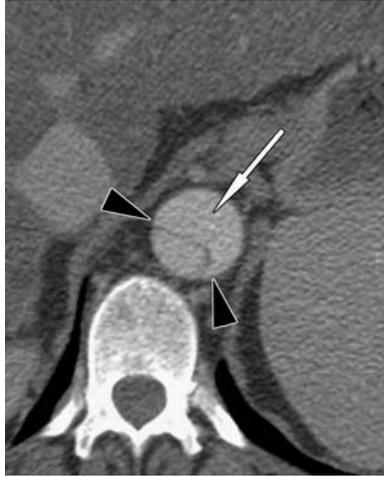


Figure 5.14. Axial contrast-enhanced CT image of classic dissection. The white arrow indicates the false lumen. Note the acute angle between the dissection flap and the outer aortic wall of the false lumen (black arrowheads).



Figure 5.15. Axial contrast-enhanced CT image of classic dissection demonstrates cobwebs in the false lumen (black arrow).

dissection<sup>42,43</sup>. However, TEE and not CT is currently the method of choice for evaluation of the proximal coronary arteries. This may soon change with the proliferation of 16 and greater row MDCT scanners. Figure 5.13 shows images of type A dissection, demonstrating accurate delineation of the dissection flap as well as the origins of the aortic arch vessels and the left main coronary artery.



Figure 5.16. Axial contrast-enhanced CT image of classic dissection demonstrates calcification of the dissection flap and the outer wall of the true lumen (black arrows).



Figure 5.17. Axial CT images of chronic classic dissection demonstrates calcification of the dissection flap and the outer wall of the false lumen (black arrows in (a) and (b): (a) unenhanced image; (b) contrast-enhanced image (note low attenuation of the false lumen on the contrast-enhanced image due to slow flow and early image acquisition).

## EVALUATING THE DIAMETER OF THE DISSECTED AORTA

The dissected aorta has the tendency to enlarge, and aortic dilatation may be present upon initial presentation or develop on subsequent follow up examinations. Sueyoshi et al. evaluated the growth rate of classic type B aortic dissection<sup>44</sup>. This study included 62 patients with spontaneous aortic dissection and excluded cases with traumatic dissection and Marfan syndrome; 81% of patients in this study had a history of hypertension. Growth rate was  $2.2 \pm 6.9$  mm per year for the aortic arch,  $2.2 \pm 10.1$  mm per year for the descending thoracic aorta,  $1.0 \pm 5.8$  mm per year for the suprarenal abdominal

aorta, and  $1.0 \pm 2.2$  mm per year for the infrarenal abdominal aorta. Mean growth rate of the iliac arteries was  $-0.4 \pm 4.7$  mm per year.

Aneurysmal dilatation of the dissected aorta increases the risk of complications, particularly the risk of aortic rupture<sup>45,46</sup>. As outlined above, an expanding false lumen may cause compression of the true lumen with subsequent ischemic complications. Thus, the aortic diameter and its increase or decrease on subsequent follow-up examinations is an important risk factor considered in the decision whether to perform surgery<sup>47-50</sup>.

Although measurement of the aortic diameter on contrast-enhanced CT images seems to be a straightforward task, there is relatively high interobserver variability<sup>51-53</sup>. Furthermore, measurements on axial images may result in overestimation of the aortic diameter, particularly if the aorta is tortuous and what appears to be a measurement across the aortic lumen is really an oblique measurement. Multiplanar reformatted images allow for measurements perpendicular to the blood flow and improve interobserver agreement, as shown by Sprouse et al.<sup>52</sup> Furthermore, consistency of repeated measurements will be further improved by software that automatically determines the centerline of the aorta using 3D data (Advanced Vessel Analysis™, GE Healthcare Technologies, Waukesha, Wisconsin, USA). However, although measurements on multiplanar reformatted images are more accurate, Dillavou et al. found a high correlation between the short axis diameters measured on axial CT slices and those measured perpendicular to the blood flow on multiplanar reformatted images and postulate that short axis measurements on axial slices are sufficient in most clinical situations<sup>54</sup>.

Independent of how the aortic diameter is measured, it is important to keep in mind the substantial interobserver variability and never compare with reported measurements without comparing the actual images when assessing aortic growth on follow-up examinations.

## ISCHEMIC COMPLICATIONS

On CT, the finding of a filiform true lumen and a large false lumen suggests one of the most dreaded complications of aortic dissection—namely, compression of the true lumen by an expanded false lumen<sup>55-58</sup> (Figure 5.18). Compression may be static or dynamic, depending on whether the expanded false lumen is thrombosed or perfused. Branch vessel occlusion, occlusion of the distal aorta, and subsequent ischemia are the consequences. Accordingly, impairment of branch vessel perfusion can be static, dynamic, or both<sup>59-61</sup>. Static impairment has to be assumed if

- The dissection flap extends into the branch vessel with subsequent narrowing or occlusion of the branch (Figure 5.19),
- The branch vessel originates from a thrombosed false lumen, or



Figure 5.18. Axial contrast-enhanced CT images of a thrombosed false lumen (intramural hematoma), which compresses the true lumen at the level of the renal artery origins: (a) perfusion of the right renal artery (arrow) from the true lumen is maintained; (b) left renal artery origin is compressed (arrow), (note delayed enhancement of the left kidney consistent with impaired perfusion).

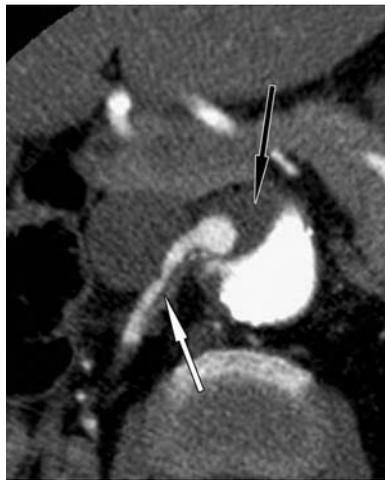


Figure 5.19. Axial contrast-enhanced CT image of aortic dissection with largely thrombosed false lumen (black arrow) and extension of the dissection into the right renal artery. The white arrow indicates the dissection flap in the right renal artery. There was diminished perfusion of the right kidney (not shown).

- The true lumen is compressed by an expanded and thrombosed false lumen (Figure 5.18b).

Dynamic impairment of branch vessel perfusion can occur if the dissection flap is located close to the origin of the branch vessel and covers its origin



Figure 5.20. Axial contrast-enhanced image of traumatic type B dissection with rupture in patient with motor vehicle accident. Black arrow indicates dissection flap in the descending thoracic aorta. High attenuation of the mediastinum is consistent with hemo-mediastinum (white arrow). Black arrowhead indicates high attenuation pleural fluid consistent with hemothorax. White arrowhead indicates chest tube.

like a curtain<sup>59</sup>. This may be the case if the true lumen is compressed by an expanded but perfused false lumen.

## AORTIC RUPTURE

Rupture is a serious complication of aortic dissection and not infrequent. Roseborough et al. retrospectively evaluated the outcome of 119 patients with type B dissection, 22 of which were treated by surgery and 97 of which were treated medically<sup>62</sup>. There was aortic rupture in six patients upon initial presentation. Of the medically treated group, there were two delayed ruptures of the descending thoracic aorta several days after admission. Data about the accuracy of helical CT for identifying aortic rupture are derived mostly from patients with aortic trauma<sup>63–65</sup>. According to the data, helical CT is highly accurate for diagnosing aortic rupture, with a sensitivity of 100% and a specificity of 83–99.7%<sup>64,65</sup>. Signs for aortic rupture on CT are

- Aortic wall defects<sup>63,65</sup>,
- Hyperattenuating or heterogeneous periaortic fluid collections in mediastinum or retroperitoneum<sup>12,63,65–67</sup> (Figure 5.20),
- Hyperattenuating or heterogeneous pleural fluid collection (hemothorax)<sup>12,66,67</sup> (Figure 5.20),
- Hyperattenuating or heterogeneous pericardial fluid collection (hemo-pericardium)<sup>12,66,67</sup>,
- Pseudoaneurysm<sup>65</sup>, and
- Contrast extravasation<sup>12,66,67</sup>.

The CT signs of hemopericardium may be subtle. In type A dissection, enlargement of the anterosuperior pericardial recess suggests rupture into the pericardium, even if the circumferential pericardial thickness is normal<sup>13</sup>.

## ATYPICAL VARIANTS OF AORTIC DISSECTION

Recently, specific variants of aortic dissection have been recognized as separate entities—namely, intramural hematoma without appreciable intimal tear (IMH) and intramural hematoma with penetrating atherosclerotic ulcer (PAU). As opposed to classic dissection, intramural hematoma is characterized by complete thrombosis of the false lumen (by the presence of thrombosed blood within the aortic wall); no contrast is seen in the false lumen. The typical imaging findings of acute intramural hematoma—namely, high attenuation of the aortic wall on unenhanced CT corresponding to a nonenhancing rim or crescent on intravenous contrast-enhanced CT—have been described above (Figure 5.5). Intramural hematoma may occur with penetrating ulcer (PAU) or without appreciable intimal disruption (IMH).

Unfortunately, there is considerable controversy in the literature regarding the definition of both IMH and PAU. The confusion can to some extent be explained by the fact that the disease concept of both IMH and PAU has been developed based on the recognition of specific imaging criteria that distinguish those entities from classic dissection. Since most patients with those atypical forms of dissection do not undergo resection of their aorta, there is lack of sufficient histopathologic correlation. However, the most significant cause of confusion is probably variable use of the term *intramural hematoma* by different authors: this term is used to describe thrombosed blood within the aortic wall regardless of its cause (including secondary thrombosed false lumen of classic dissection, intramural hematoma without appreciable intimal disruption (IMH), and intramural hematoma with penetrating ulcer (PAU)) and also can be restricted to intramural hematoma without appreciable intimal disruption (IMH). As a consequence, definitions of those entities in the literature vary. This discrepancy particularly affects outcome studies, which need to be read with caution, due to usually imaging-based patient selection.

Despite these limitations, atypical forms of dissection that meet the specific imaging criteria of IMH or PAU are regarded and treated differently from classic dissection and thus need to be distinguished.

### INTRAMURAL HEMATOMA WITHOUT APPRECIABLE INTIMAL DISRUPTION (IMH)

First described by Yamada in 1988<sup>14</sup>, intramural hematoma without appreciable intimal disruption (IMH) is thought to be caused by hemorrhage into

the aortic wall from ruptured vasa vasorum as opposed to classic dissection, which is thought to be caused by an intimal tear. However, as denoted above, the concept about the etiology of IMH has not been sufficiently validated. Unfortunately, CT does not allow for direct visualization of the intima if the false lumen is thrombosed and the absence of visible ulceration or contrast within the false lumen does not necessarily exclude the presence of intimal rupture<sup>13,20,68</sup>. As a matter of fact, IMH may disappear over time<sup>14</sup>, or may progress to open dissection, aneurysm, or rupture<sup>69–74</sup>. To date, the pathophysiology of intramural hematoma without appreciable intimal disruption is still controversial and beyond the scope of this chapter. In the acute setting, the diagnosis of IMH is made if there is fresh intramural hemorrhage, as indicated by a high-attenuation false lumen on unenhanced CT images, with no evidence of perfusion of the false lumen on contrast-enhanced images, and in the absence of any evidence for an intimal defect (absence of any focal contrast outpouchings of the perfused aortic lumen into the false lumen).

### **PENETRATING ATHEROSCLEROTIC ULCER (PAU)**

Penetrating atherosclerotic ulcer (PAU) was first described in 1986 by Stanson et al.<sup>75</sup> as a localized defect of intima and media caused by atherosclerotic plaque that has ruptured through the intima with subsequent hematoma formation within the media of the aortic wall. Penetrating ulcer with associated intramural hematoma is regarded as a variant of aortic dissection, however, as an entity distinctly different from classic (“open”) dissection and also from intramural hematoma due to ruptured vasa vasorum (IMH)<sup>20,76–80</sup>. Differences are as below:

- As opposed to classic dissection, there is usually no reentry tear in acute penetrating ulcer and the false lumen will be thrombosed rather than perfused<sup>20,76</sup>.
- The intimal defect in case of PAU is an atherosclerotic ulcer and not a simple intimal tear<sup>20</sup>.
- As opposed to intramural hematoma due to ruptured vasa vasorum where the intima is thought to be intact, penetrating ulcer (PAU) implies an intimal defect.

On CT, a focal contrast outpouching representing the ulceration with adjacent intramural hematoma is regarded the most specific imaging appearance of PAU<sup>20,76–79</sup>. The intramural hematoma is most commonly focal and contained by medial fibrosis that is present with extensive intimal atherosclerosis. Less commonly, the intramural hematoma of a PAU extends along a long segment of the aortic wall, both proximal and distal to the ulceration. Unfortunately, there

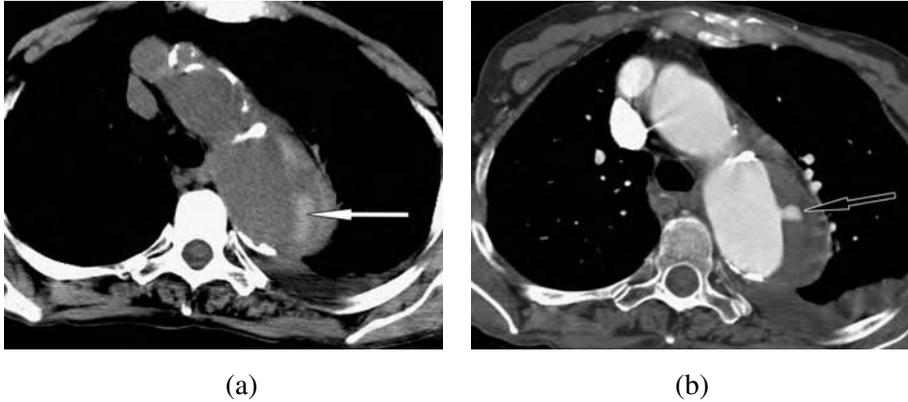


Figure 5.21. Axial CT images of penetrating atherosclerotic ulcer with acute intramural hematoma in the aortic arch: (a) unenhanced image shows high attenuation intramural hematoma (white arrow); (b) contrast-enhanced image shows focal contrast outpouching of the true lumen, consistent with penetrating ulcer (black arrow).

are only small case series that correlate the CT imaging characteristics of penetrating atherosclerotic ulcer with histopathologic conformation<sup>20,76</sup>. Kazerooni et al. retrospectively evaluated 16 cases with a CT diagnosis of PAU; surgical verification was available in seven patients<sup>76</sup>. In all but one case, the ulceration was located in the thoracic aorta. The seven patients with surgical verification had the following CT findings:

- Focal contrast outpouching representing the ulcer (7/7) (Figure 5.21),
- Adjacent intramural hematoma (7/7) (Figure 5.21),
- Displaced intima calcifications (6/7),
- Thickened, enhancing aortic wall (5/7),
- Pleural effusion (2/7),
- Mediastinal fluid collection (3/7), and
- Pseudoaneurysm (1/7).

Quint et al.<sup>20</sup> reported 49 patients with surgically proven thoracic aortic disease, including six patients with PAU. In this series, only four of six penetrating ulcers had both ulceration and intramural hematoma on CT. In two cases, CT demonstrated only the intramural hematoma but not the ulceration. There was one false positive CT diagnosis of PAU; however, at surgery there was a dissection with thrombosed false lumen and a simple tear in the dissection flap, with no atherosclerotic ulceration.

Unfortunately, there is considerable controversy regarding the definition of penetrating ulcer (PAU), and some authors regard the presence of intramural hematoma as one of several possible complications but not an obligate finding<sup>80</sup>. For example, atherosclerotic ulcers have been observed to penetrate

the aortic wall with subsequent contained or frank aortic rupture but no intramural hematoma: Batt et al. evaluated eight patients with surgically proven PAU of the abdominal aorta<sup>80</sup>. None of the patients in this series had associated intramural hematoma, but all eight patients had complications, either contained pseudoaneurysm ( $n = 5$ ) or periaortic hematoma ( $n = 3$ ). The authors speculated that intramural hematoma might be more frequent in thoracic than in abdominal PAU.

It adds to the confusion that in clinical practice, the term *penetrating ulcer* is often used as a descriptive term for any observed ulcerlike aortic lesion, even if there are no associated findings like intramural hematoma or pseudoaneurysm and regardless whether patients are symptomatic. Unfortunately, imaging methods including CT do not allow for direct visualization of the intima except in classic dissection.

Furthermore, the only CT evidence that an observed ulcerlike lesion of the aorta has penetrated the intima is the observation of either adjacent intramural hematoma or signs of even deeper penetration—namely, pseudoaneurysm or periaortic fluid. Thus, the CT finding of an ulcerlike lesion of the aorta without adjacent intramural hematoma might be due to irregular intraluminal thrombus, rather than to a true penetrating ulcer.

To evaluate the significance of the CT finding of an “ulcerlike aortic lesion” regardless whether this constitutes true penetrating ulcer or not, Quint et al. retrospectively evaluated the CT scans of 38 patients in whom such a lesion was observed<sup>78</sup>. At the time of the initial scan, 22 patients presented with acute symptoms, and 16 patients were asymptomatic. The overall number of lesions included in this series was 56, 50 of which were located in the thoracic aorta. Of 49 lesions with available clinical follow-up, 37 remained clinically stable; 6 of these showed progression on CT. Two lesions were associated with recurrent chest/back pain but were stable on follow up CT. Eight lesions were treated surgically because the patients were either symptomatic or because an aneurysm had developed at the site of the ulcer. Two lesions occurred in patients who died shortly after the initial scan. The only CT feature predictive for clinical outcome on the initial scan was lack of pleural effusion. Presence of intramural hematoma on the initial scan was observed in 22 lesions but was not predictive for clinical outcome. Ulcerlike lesions that progressed on follow up imaging developed into fusiform, saccular, or combined aneurysms.

As a conclusion, although the disease concept of penetrating ulcer (PAU) remains controversial, the CT finding of a focal contrast outpouching of the aortic lumen with associated intramural hematoma is regarded as consistent with the diagnosis of PAU and subsequent dissection of blood into the media. For patient management, the diagnosis of PAU makes an important difference compared to the diagnosis of “simple” intramural hematoma without appreciable intimal disruption (IMH) because of different treatment implications:

As opposed to IMH, PAU may be amenable to endovascular repair. Thus, in all patients with acute intramural hematoma, it is important to search for any focal contrast outpouchings of the true lumen and not to miss the penetrating ulcer that would potentially be amenable to endovascular treatment.

## **COST-BENEFIT ISSUES**

CT is less invasive than angiography, less operator dependent than transesophageal echocardiography, and takes significant less time than MR imaging. CT is readily available and provides a rapid and highly accurate diagnosis for patients with suspected aortic dissection. As opposed to MR imaging, monitoring of high-risk and severely ill patients is easily accomplished in the CT suite. Important alternative diagnoses (for example, pulmonary embolism or ruptured aneurysm) and potential complications (like cardiac tamponade or hemothorax) are evaluated simultaneously.

The drawbacks of CT are radiation exposure and use of iodinated contrast material. Radiation risk is certainly negligible in the case of elderly patients who undergo CT for suspected aortic dissection. However, younger patients undergoing unlimited follow-up examinations may experience significant radiation exposure, and MR imaging should be preferred in this patient population.

The most important risks inherent to iodinated contrast administration are allergic reaction and injury to the kidneys. Patients with a history of prior allergic reaction to iodinated contrast material, asthma or other allergies are at increased risk. The decision to perform contrast enhanced CT is dependent on the severity of the prior reaction and feasibility of appropriate antiallergic premedication. Patients with elevated creatinine, diabetes mellitus, renal transplant, multiple myeloma, nephrotoxic medication, and severe chronic heart failure are at risk for renal failure after contrast injection. Hydration, reduced dose of contrast material, and use of isoosmolar contrast agents are options to reduce nephrotoxicity in this vulnerable patient population. However, alternative methods, particularly MR imaging, should be considered if available and no contraindications exist.

## **CONCLUSION**

CT is widely available, is noninvasive, and provides a rapid and highly accurate diagnosis for patients with suspected aortic dissection. CT is also performed for surveillance of patients with chronic dissection and to follow up on patients after surgery or endovascular repair. Current limitations affect particularly patients with type A dissection, as aortic insufficiency cannot be eval-

uated. Rapid advances in MDCT make evaluation of coronary artery involvement possible. Drawbacks of CT are radiation exposure and the risks inherent to iodinated contrast material; MR evaluation is preferred for young patients undergoing serial evaluation of known aortic pathology.

## ACKNOWLEDGEMENTS

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# 6

## ROLE OF MRI IN THE DIAGNOSIS OF AORTIC DISSECTION

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MR imaging is increasingly becoming a first-line investigation for the evaluation of diseases of the aorta<sup>1</sup>. Advantages of MRI include avoidance of ionizing radiation and the use of contrast agents, which are not nephrotoxic. Over the last years, major technological advances resulted in significant increases in acquisition speed.

Due to its large field of view MRI is well suited to visualize the thoracic and abdominal aorta. Additionally, many functional questions can be addressed that are important in patients with aortic disease such as regional and global ventricular function, the status of the heart valves, the condition of the pericardium and the presence of coronary artery disease. This chapter discusses the role of MRI in the work-up of patients with suspected aortic dissection. We also address the role of MRI in patients with other forms of acute aortic syndromes.

### TECHNICAL CONSIDERATIONS

#### SPIN ECHO

With the use of spin-echo imaging rapidly flowing blood produces no signal, whereas slowly moving blood produces an increased intraluminal signal. Therefore, this type of sequences is often referred to as *black blood*. On spin-echo sequences, the intimal flap is a linear structure of intermediate signal intensity dividing the aortic lumen into two channels, both of which exhibit a

flow void. In black blood sequences, increases in intraluminal signal intensity can be caused by stagnant, retrograde, or turbulent blood flow or by poor ECG gating<sup>2</sup>. We use the HASTE sequence (half Fourier acquisition single shot fast spin echo) in patients with aortic syndromes to provide black blood MR images. The HASTE sequence is a very fast sequence, which only acquires half the usual number of lines in k-space. Transverse slices with a slice thickness of 6 mm covering the entire thorax and abdomen can thus be performed in a few seconds. The spatial resolution is, however, not as good as with the commonly used gradient-echo sequences.

Black blood techniques alone may be inadequate for the diagnosis of supraaortic branch vessel involvement<sup>3-5</sup>.

## **GRADIENT ECHO**

The intimal flap on gradient-echo sequences is visualized as a low-intensity linear structure dividing the aortic lumen into two channels, both of which exhibit high signal intensity if they contain flowing blood. Because gradient-echo sequences are flow sensitive, they are very useful to distinguish between slow flow and thrombus.

Cine gradient-echo imaging for the evaluation of aortic disease has been described first by Sonnabend in 1991<sup>6</sup>. Today, the standard gradient-echo pulse sequence is steady-state free precession (SSFP, TrueFISP) sequence<sup>7</sup>. SSFP produces high signal from blood and a good contrast to soft tissue without contrast material. In the case of aortic regurgitation, turbulence of flow leads to signal loss projecting from the aortic valve into the high-intensity blood pool in the left ventricle during diastole. With SSFP cine acquisition, it is possible to diagnose aortic regurgitation with high confidence. In a retrospective study, Pereles and coworkers examined the diagnostic accuracy of the SSFP portion alone of their comprehensive imaging protocol in patients with suspected aortic syndromes<sup>8</sup>. The comprehensive imaging protocol included transverse nonenhanced and contrast-enhanced gradient-echo T1-weighted fat-saturated two-dimensional acquisitions, sagittal oblique and coronal contrast-enhanced time-resolved MR angiography of the chest, contrast-enhanced high-spatial-resolution 3D MR angiography, transverse and coronal single-shot SSFP imaging of the chest and four breath-hold cine SSFP acquisitions. In 29 examinations, the SSFP portion alone was sufficient to diagnose the presence or absence of dissection or aneurysm of the aorta. The entire time required for this part of the protocol was less than 4 minutes. However, SSFP sequences are susceptible to magnetic field inhomogeneities and pulsatile flow, both of which may cause artifacts. Artifacts can occur in patients with sternotomy wires or surgical clips. Nevertheless, even in patients with a history of prior aortic graft repair SSFP yields diagnostic images in most cases<sup>8</sup>.

In patients who cannot hold their breath, real-time SSFP without ECG-triggering represents a reasonable alternative. Despite lower spatial and temporal resolution, diagnostic images of the aorta and aortic valve can usually be obtained<sup>9</sup>.

## CONTRAST-ENHANCED 3D ANGIOGRAPHY

Gadolinium-enhanced 3D MR angiography minimizes the influence of cardiac output and altered flow dynamics that might otherwise degrade techniques dependent on inflow of blood. Advantages are a rapid acquisition time without the need for ECG triggering and breath holding. The images are often more easily communicated to a surgical team. In a retrospective study, contrast-

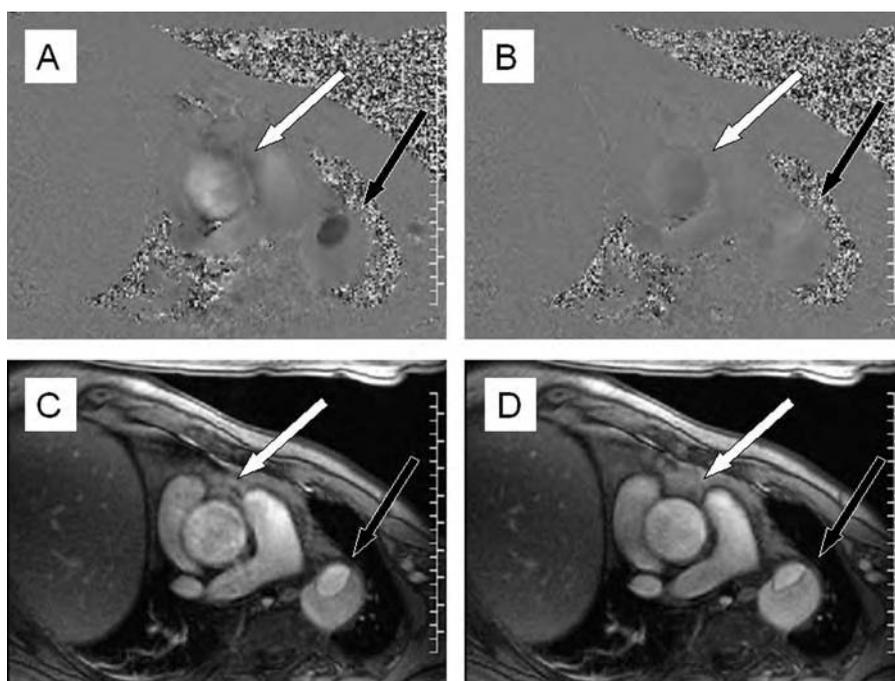


Figure 6.1. Phase contrast sequences in MRI in a patient with severe aortic regurgitation and a type B aortic dissection. Transverse plane. A: Phase contrast in systole. The ascending aorta shows high signal intensity with fast flow toward the head (white arrow). The true lumen in the descending aorta is dark, meaning fast flow in the opposite direction (black arrow). The false lumen of the descending aorta is encoded gray similar to the surrounding structures, indicating slow flow or no flow. B: Phase contrast in diastole. The ascending aorta is now slightly dark, indicating flow towards the left ventricle, caused by aortic regurgitation. C: The corresponding magnitude image to panel A, showing the anatomic structures at the same time. D corresponds to panel B.

enhanced MR angiography was superior to black blood imaging (spin-echo, T2 weighted, and T1 weighted) for visualizing the intimal flap in the thoracic aorta as well as supraaortic branch vessels and yielded better overall image quality<sup>10</sup>. However, intramural hematoma may be missed and the aortic wall is not depicted<sup>11</sup>. Aortic insufficiency can only be detected by cine-MRI. Therefore, 3D angiography cannot be the exclusive modality for imaging acute aortic syndromes.

## **PHASE CONTRAST**

Quantitative information about blood flow is obtained from modified gradient-echo sequences. On phase-contrast images the velocity is encoded as gray value of a pixel. Phase-contrast is useful to distinguish between the true and the false lumen and between fast flow, slow flow and areas of no flow (Figure 6.1).

## **CONTRAST-ENHANCED INVERSION RECOVERY SEQUENCE**

We use an inversion recovery sequence after application of gadolinium for the MR-angiography. With the help of this sequence thrombi can be detected with high accuracy<sup>12</sup>.

## **UTILITY OF MRI IN ACUTE AORTIC SYNDROMES**

### **DIAGNOSTIC CRITERIA OF AORTIC DISSECTION**

As with echocardiography and CT, the main criterion used to diagnose aortic dissection by MRI is the presence of a double lumen of the aorta with a visible intimal flap. This feature can be visualized with all pulse sequences commonly used for the examination of the aorta. With cine sequences the movement of the intimal flap can be seen. Differentiation of the true and false lumen is possible with the help of the movement of the intimal flap in systole and diastole (Figure 6.2).

A number of indirect signs are suggestive but not diagnostic of a dissection, including widening of the aorta, thickening of the aortic wall, thrombosis of a false lumen, or spiraling of a thrombosed false lumen. Entry sites appear as interruptions of the dissecting membrane often associated with turbulent flow extending from the true into the false lumen. The origin of the supraaortic arteries and the abdominal aortic branches from either the true lumen or the false lumen can usually be determined by using MR angiography<sup>13</sup>.

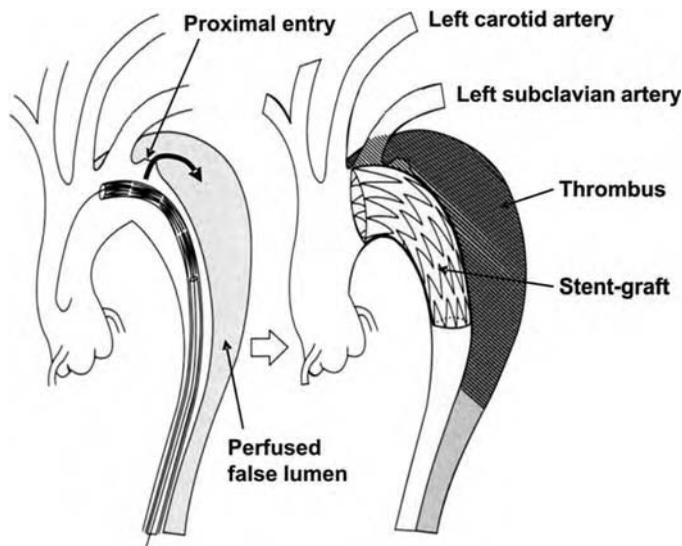


Figure 6.2. Concept of interventional reconstruction of the dissected aorta with sealing of the proximal entries, depressurization of the false lumen and initiation of false lumen thrombosis.

## SENSITIVITY AND SPECIFICITY OF MRI IN AORTIC DISSECTION

In a retrospective analysis of 54 cases with known or excluded aortic dissection, spin-echo MR images obtained with a 0.35 Tesla scanner identified 22 of 23 cases with dissection and all 33 cases without dissection correctly<sup>14</sup>. In 1992, Nienaber and coworkers compared the diagnostic value of TEE and MRI in 53 patients with suspected dissection of the thoracic aorta<sup>15</sup>. TEE was performed with a monoplane probe, whereas MRI was performed with a 1.5 T scanner and ECG-gated spin-echo pulse sequences. Three patients were ventilated at the time of MRI. Both MRI and TEE detected all 31 patients with aortic dissection. In 7 of the 22 patients without dissection, TEE yielded false-positive results, resulting in a specificity of 68.2%, whereas MRI identified all true-negative cases correctly. For identifying the site of entry, the sensitivity was 85% and specificity 100% for MRI. In 43% of the patient's gradient-echo cine sequences were performed for the assessment of aortic insufficiency. The sensitivity for identifying aortic insufficiency in comparison to angiography was 85%, the specificity 100%.

In 1993, Nienaber and coworkers reported their extended experience of using TEE and MRI in 110 patients with suspected aortic dissection. In addition, they provided a comparison to CT and TTE<sup>16</sup>. Conventional single slice CT and monoplanar TEE were used in this study. Not every patient underwent all four imaging studies: all patients underwent TTE, 70 patients underwent TEE,

*Table 6.1.* Sensitivity, specificity, and accuracy of MRI in acute aortic syndromes in prospective trials

Author and year	Sensitivity in %	Specificity in %	Accuracy in %
Nienaber 1993	98.3	97.8	98.0
Sommer 1996	100.0	94.0	98.0

79 patients underwent CT, and 105 patients underwent MRI. The sensitivity of MRI for detecting aortic dissection was 98.3%; the specificity was 97.8%. This resulted in an accuracy of MRI of 98.0 %, higher than the accuracy of CT with 91.1%, TEE with 90.0%, and TTE with 69.8%. The suboptimal accuracy of CT can be explained as conventional CT, which was state of the art at that time, was used in the study. As the scanning time per slice was much longer than with the spiral CTs in use today, blurring of fast moving dissecting membrane was possible resulting in a reduced sensitivity.

The authors concluded: “A noninvasive diagnostic strategy using MRI in all hemodynamically stable patients and TEE in patients who are too unstable to be moved should be considered the optimal approach to detecting dissection of the thoracic aorta. Comprehensive and detailed evaluation can thus be reduced to a single noninvasive diagnostic test in the investigation of suspected dissection of the thoracic aorta”.

In 1996, Sommer et al. portrayed a somewhat different picture in their prospective study in patients with clinically suspected aortic dissection<sup>5</sup>. Forty-nine patients underwent spiral CT, multiplanar TEE, and MRI. MRI was performed with a 0.5 T scanner using ECG-triggered, T1-weighted, spin-echo sequences with respiratory gating. In some cases, additional cine gradient-echo sequences were used to differentiate between slow flow, intraluminal thrombus, and intramural hematoma. Imaging results were confirmed at autopsy, intraoperative exploration, angiography, and follow-up. Sensitivity was 100% for all techniques. Specificity was 94% for MRI, 100% for spiral CT, and 94% for multiplanar TEE.

Thus, TEE, state-of-the-art CT, and MRI all have an excellent accuracy for the detection of aortic dissection in the hand of an experienced operator. The use of these techniques in patients with suspected dissection of the aorta thus depends on local experience and availability (Table 6.1).

## **ADDITIONAL FEATURES IMPORTANT IN PATIENTS WITH SUSPECTED AORTIC DISSECTION**

Besides the presence or absence of an intimal flap, other features are important to assess the differential diagnosis, surgical strategy, and prognosis of the patient (Figure 6.3). These features include detection of entry and reentry,

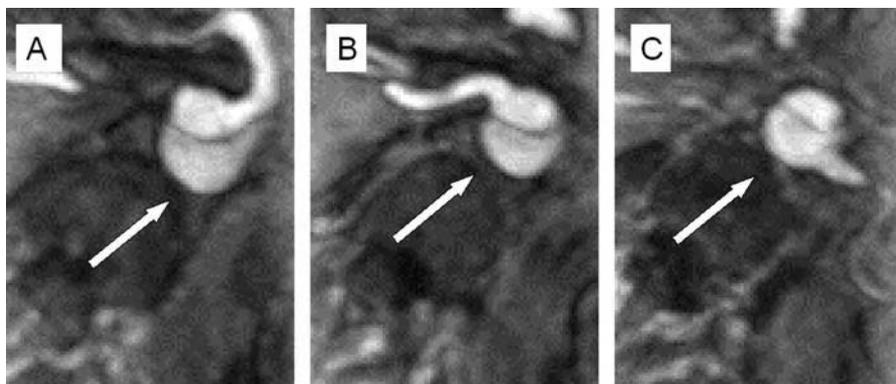


Figure 6.3. MRI images of the main abdominal aortic branches in a patient with type B dissection. White arrows: false lumen. A: Celiac trunc, originating from the true lumen. B: Right renal artery, originating from the true lumen. C: Left renal artery, originating from the false lumen.

*Table 6.2.* Comparison of the main imaging modalities with regard to important features beside presence of aortic dissection in acute aortic syndromes. 0 = no information, + = little information, ++ = moderate information, +++ = good information. Modified from reference 18.

	TTE/TEE	CT	MRI	Angiography
Tear localization	+++ <sup>a</sup>	—	++	+
Aortic regurgitation	+++	—	++	+++
Pericardial effusion	+++	++	+++	—
Mediastinal hematoma	++	+++	+++	—
Side branch involvement	+	++	++	+++
Coronary ostial involvement	++	—	+	+++
Coronary artery disease	—	+ <sup>b</sup>	—	+++
X-ray exposure	—	++	—	+++
Patient comfort	+	++	+	—
Follow-up studies	++	++	+++	—
Intraoperative availability	+++	—	—	—
Ventricular function	+++	—	+++	+++
Myocardial scar	++	—	+++	—

<sup>a</sup> No information below diaphragm.

<sup>b</sup> CT of the coronary arteries is possible but time consuming, usually not performed in unstable patients.

presence and degree of aortic regurgitation, involvement of the aortic branches, especially the supraaortic branches, pericardial effusion, stenosis of the coronary arteries, and function of the left and right ventricles. In cases without an obvious flap, the most important feature to characterize aortic pathology is the configuration of the aortic wall including wall thickening caused by intramural

hematoma or atheroma and the presence of ulcerations. If an aortic pathology can be excluded, the main differential diagnosis in patients with thoracic pain usually is an acute coronary syndrome. A technique that would be able to verify or exclude this differential diagnosis in one examination would be clinically very useful. As demonstrated in Table 6.2, MRI seems to be the most versatile technique to provide such information<sup>17</sup>.

### INTRAMURAL HEMATOMA

The typical features of intramural hematoma (IMH) are a crescentic or circular local aortic wall thickening without a visible intimal tear or flap (Fig-

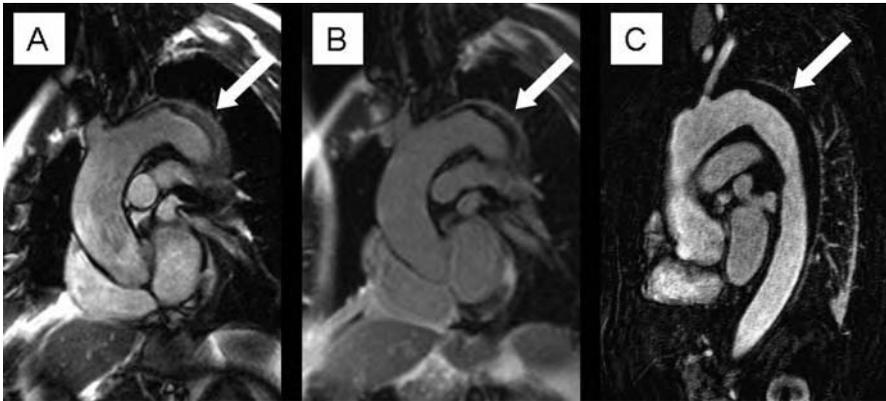


Figure 6.4. Intramural hematoma of the descending aorta (arrow). Panel A: SSFP cine. Panel B: late enhancement sequence. Panel C: MR angiography.

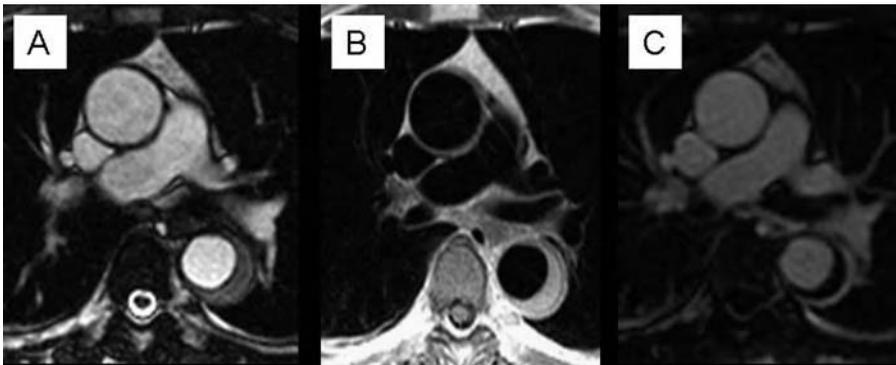


Figure 6.5. Transverse CMR-images of an intramural hematoma of the descending aorta, same patient as in Figure 6.4. Panel A: SSFP cine. Panel B: HASTE. Panel C: late enhancement sequence.

ures 6.4 and 6.5)<sup>19</sup>. Murray et al. performed serial examinations in 22 patients with intramural hematoma (IMH) to analyze the time course of different findings<sup>20</sup>. The MRI examination consisted of T1-weighted “dark-blood” spin-echo sequences and cine “bright-blood” gradient-echo sequences. The presence of blood flow within the thickened portion of the aortic wall was examined with the use of a dynamic phase-contrast sequence. There were moderately strong correlations between days after symptom onset and signal intensity of hematoma on spin-echo sequences. The signal intensity of the hematoma changed from intermediate to high after about seven days on spin-echo sequences and on gradient-echo sequences. MRI was useful in monitoring the course of the illness, which resulted in some patients in resolution of the IMH, whereas others experienced recurrent bleeding and dissection. Hematoma site was the only finding on MRI that correlated with the course of the illness, with patients with a hematoma in the ascending aorta having a worse prognosis than patients with hematoma of the descending aorta.

Atheromatose mural plaques can lead to penetrating atherosclerotic ulcers (PAU). These ulcers may finally penetrate the elastic lamina and result in an adjacent IMH<sup>21</sup>. The combination of PAU with IMH is observed preferentially in the descending aorta.

## **PENETRATING AORTIC ULCER**

A penetrating atherosclerotic ulcer of the aorta is characterized by ulceration that penetrates through the elastic lamina and into the media and is associated with a variable amount of hematoma within the aortic wall<sup>22</sup>. With MRI, the two main features of penetrating atherosclerotic ulcer can be demonstrated: the ulcerlike lesion, which is a contrast-filled outpouching that extends beyond the level of intima, and an intramural hemorrhage that dissects focally around the ulcer (Figures 6.6 and 6.7)<sup>23</sup>. Ulcer crater can be visualized on SSFP sequences on MRI with the same high signal intensity as free-flowing blood in the aorta (Figure 6.6A–B). Intramural hematoma has intermediate image intensity on SSFP images. On contrast-enhanced 3D angiography the ulcer is visualized as an outpouching that fills with contrast (Figure 6.6D)<sup>24</sup>.

## **FOLLOW-UP**

The value of MRI in the follow-up of patients with surgically corrected or conservatively treated aortic dissection has been well established. The long-term prognosis of patients with aortic dissection is determined by the development of complications. Rupture of the aorta after development of a secondary aneurysm is the most common cause of late death. Other causes are the development of severe aortic insufficiency or malfunction of a prosthetic valve<sup>18</sup>.

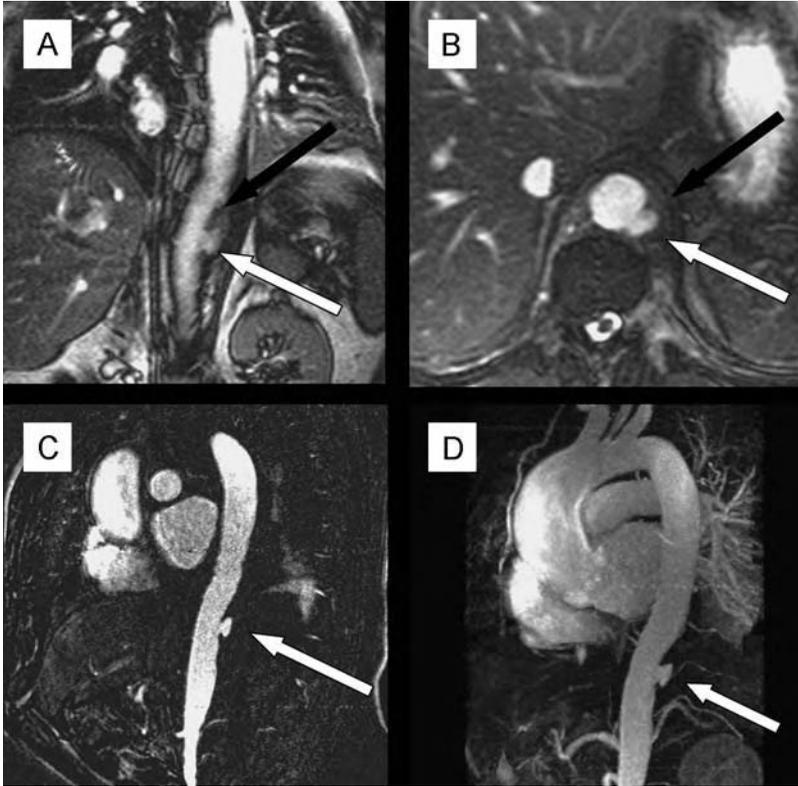


Figure 6.6. Images of a patient with a penetrating aortic ulcer in the descending aorta. The patient presented with abdominal pain and fever. Blood cultures grew salmonella species. White arrows: penetrating ulcer. Black arrows: surrounding hematoma. A: MRI image, SSFP sequence, oblique coronal plane. B: MRI image, SSFP sequence, transverse plane. C: Oblique sagittal MRI image, contrast-enhanced. D: Oblique sagittal MRI image, contrast-enhanced 3D reconstruction, maximal intensity projection (MIP) reconstruction.

Therefore, regular follow-up examinations are necessary, and the Task Force on Aortic dissection of the European Society of Cardiology recommended MRI as the best tool to provide serial information in operated and conservatively treated patients<sup>18</sup>. MRI provides a comprehensive evaluation of the entire aorta with all important aspects of the disease. Assessment of progressive thrombosis and residual flow in the false lumen is possible<sup>25</sup>. Serial exact and highly reproducible documentation of aortic diameter perpendicular to aortic lumen can be accomplished. Incompetent aortic valves can be identified by cine imaging. Phase-contrast flow measurements allow the quantification of aortic regurgitation. As compared to serial echocardiography (usually TEE), it is much more convenient and accurate to compare serial MRI examinations

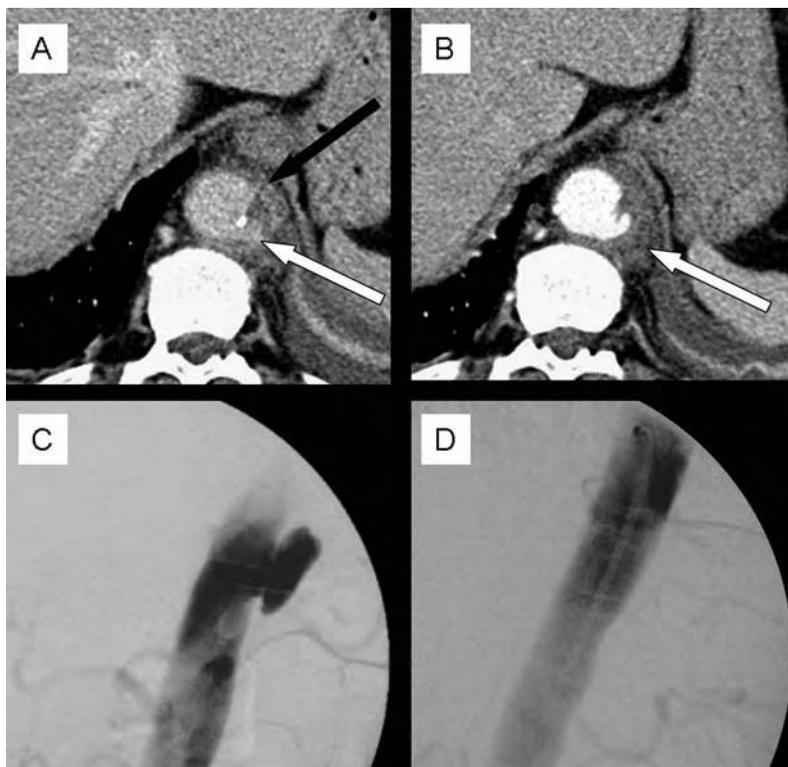


Figure 6.7. Images of the same patient as in Figure 6.6. A: CT image, transverse plane. White arrows: ulcer. Black arrow: calcification adjacent to the ulceration. B: CT image, transverse plane postcontrast. C: Angiography. D: Angiography after implantation of an endoprosthesis. C and D courtesy of H. Schumacher, MD, University of Heidelberg, Department of Vascular Surgery.

as they provide a complete 3D set of aortic anatomy and related structures facilitating quantitative comparisons.

Detailed knowledge of surgical technique and its anatomical consequences are essential for accurately evaluating postoperative imaging. Abnormal soft tissue is occasionally demonstrated outside a graft or anastomosis. The anatomical relationships can usually be explained once surgical details are known<sup>26</sup>. Late complications following surgery for aortic dissection are frequently related to the anastomosis or the aortic arch and its side branches. MRI is better suited to depict the anastomoses (Figures 6.8 and 6.9) and neck vessels<sup>27</sup> and may thus be preferable to TTE/TEE for serial evaluation of post-surgical patients with type I dissection.

MRI also lacks the disadvantages of CT such as radiation and nephrotoxic contrast material.

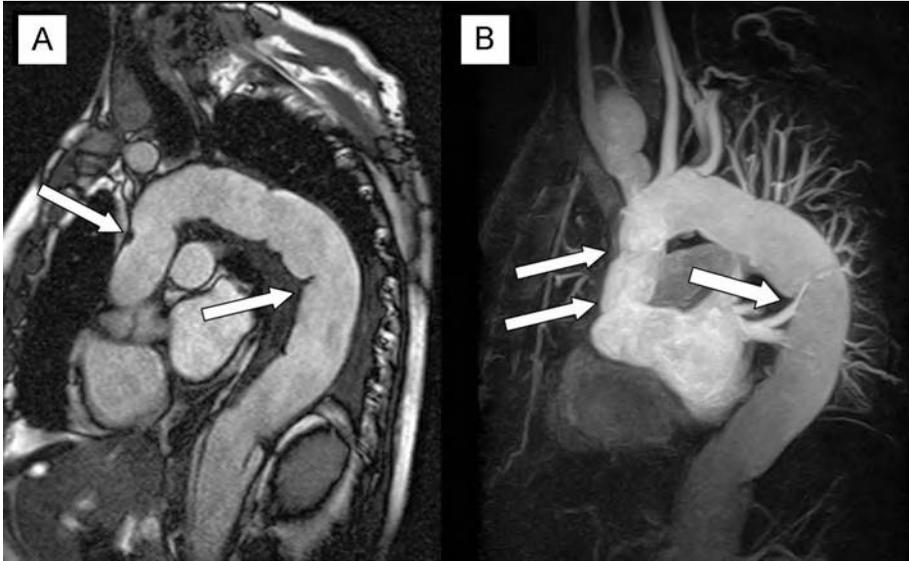


Figure 6.8. MRI images of a patient with multiple aortic operations. The patient had a type A aortic dissection. A hemiarch was implanted. A few years the descending aorta dilated and was replaced. The right subclavian artery is dilated. A: SSFP sequence, sagittal oblique plane shows the anastomoses in the ascending and in the descending aorta (white arrows). B: Surface reconstruction of a contrast-enhanced 3D angiography. Anastomoses in the ascending and in the descending aorta (white arrows).

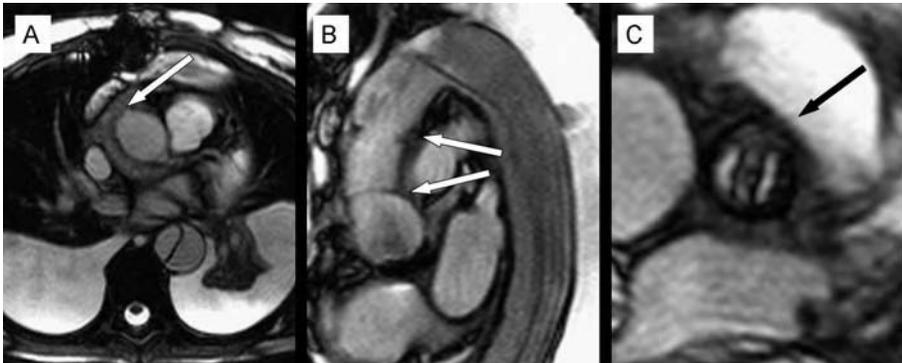


Figure 6.9. MRI images of a patient 5 days after an operation for type A aortic dissection with aortic valve replacement and conduit. A: Transverse plane. Around the ascending aorta a circular structure can be seen. This represents periaortic hematoma (white arrow). B: Sagittal oblique plane shows the two anastomoses in the ascending aorta (white arrows) and the remaining dissection in the descending aorta. C: Bileaflet aortic valve opens normally in systole (black arrow).

## **MRI PROTOCOL**

The elements of the standard imaging protocol used at the Robert-Bosch Hospital are shown in Table 6.3. Continuous monitoring of blood pressure and ECG is performed. Special infusion systems are used if continuous intravenous medication is given. If imaging in a mechanically ventilated patient is necessary, a ventilator with special tubing is in place.

As a first step, transverse, coronal, and sagittal 2D localizer images are acquired using an ultrafast breath hold echo-planar CMR technique. Echo planar imaging is followed by transverse steady state free precession (SSFP) gradient echo cine imaging starting at the renal arteries and then moving cranial in 10 mm steps (6 mm slice, 4 mm gap) up to the carotid arteries. In addition, half Fourier black blood still frame spin echo imaging (HASTE) is performed in the exact same imaging planes as the previous cine images in one breathhold (Figure 6.10). Based on the transverse data, oblique parasagittal SSFP cine as well as HASTE images are acquired allowing the evaluation of the ascending aorta, the aortic arch and the descending aorta (“candy cane projection”) (Figure 6.11). If necessary, cine as well as HASTE imaging can be repeated in an additional plane (e.g., to evaluate an intimal flap or entry). A three-chamber view is taken to assess the presence and severity of aortic regurgitation and to assess the function of the left ventricle in the long axis. At the end of an examination a three-dimensional gadolinium-enhanced MR angiography is performed. The sequence used is a gradient-echo pulse-sequence with severe T1-weighting. The acquisition is performed in a single breathhold without ECG-triggering. Accurate bolus timing is accomplished by using a test bolus. The three-dimensional dataset can be displayed in every possible plane. Slices in the oblique sagittal plane are shown in Figure 6.12. The surface of the vessels can be reconstructed as a maximal intensity projection (MIP) image in a three-dimensional dataset and displayed as a figure, which can be turned in every direction, as shown in Figure 6.13.

Large entries can be seen on 3D images. However, identification of small additional entries and reentries may require the use of flow-sensitive pulse sequences.

If questions about the extravasation of blood remain an inversion recovery sequence is performed. In addition to this basic protocol, phase contrast flow mapping gradient echo CMR can be performed in any plane to differentiate between intramural hematoma and false lumen as well as to evaluate flow in a true and/or false lumen respectively.

The combination of different sequences results in a high sensitivity and specificity and facilitates the assessment of all important features of acute aortic syndromes.

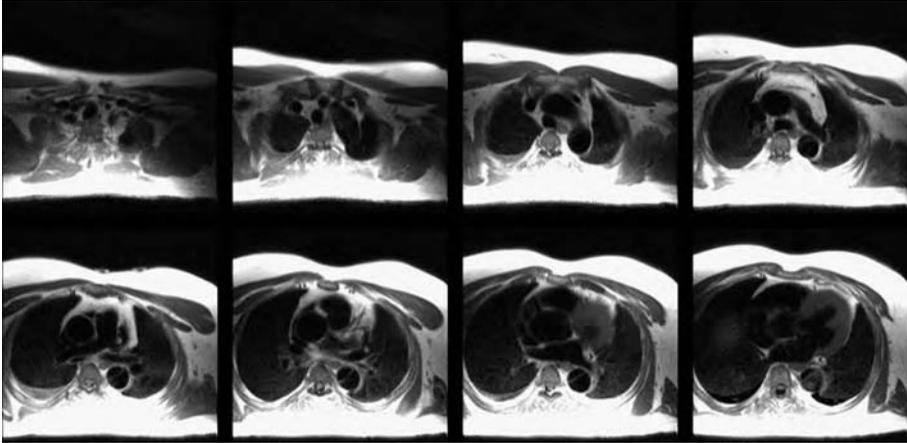


Figure 6.10. Transverse T2-weighted HASTE sequence in a patient with type A aortic dissection. Blood is visualized as black (black-blood technique). All images are taken in a single breathhold, gated. The intimal flap is clearly delineated.



Figure 6.11. Oblique sagittal view. Patient with chronic type B aortic dissection. SSFP sequence.



Figure 6.12. MRI 3D angiography in a patient with type B aortic dissection. Oblique sagittal view, parallel slices, slice thickness 1.2 mm. The entry and reentry sites can be clearly delineated (arrows).

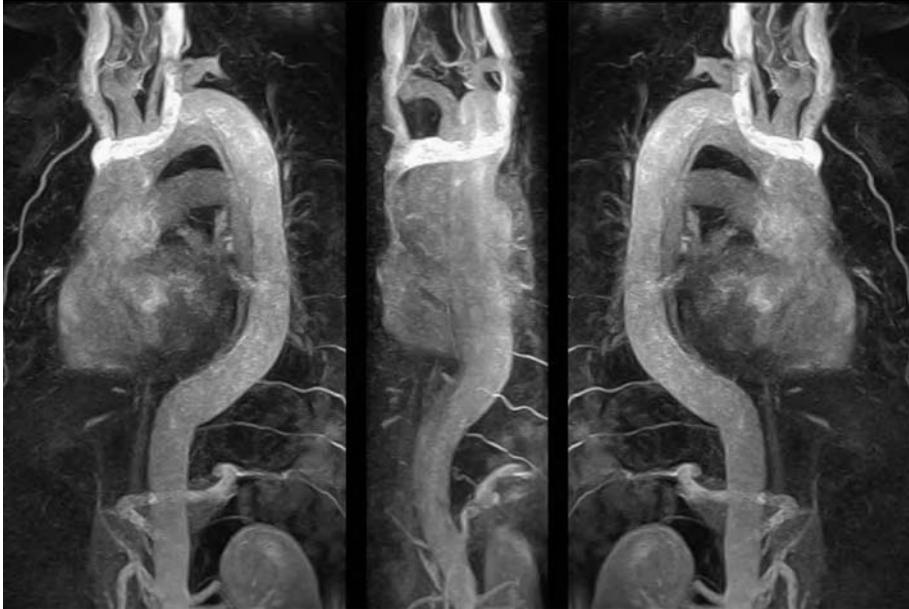


Figure 6.13. Surface reconstruction of a MRI 3D-angiography in a patient with type B aortic dissection.

In our experience, an examination with the basic sequences in not-ventilated patients takes about 25 min, depending on the number of sequences. It takes about 5 minutes to put the patient in the scanner and prepare him for the examination. The basic sequences (scout, transverse HASTE, transverse SSFP, SSFP in the oblique sagittal view, SSFP in the three-chamber view) take about 15 minutes. In patients with an acute syndrome, at this point it has to be decided if to proceed to the operation theater or if further information is needed. If it is decided to perform a full protocol with phase contrast sequences, angiography and inversion recovery sequences additional may be necessary.

## LIMITATIONS AND PITFALLS

### CONTRAINDICATIONS

MRI is contraindicated in patients with cardiac pacemakers, implanted cardioverter defibrillators, retained pacemaker leads, and other electronic implants. The performance of MRI is also contraindicated in many patients with cerebrovascular clips. However, other metallic implants such as hip prostheses, prosthetic heart valves, coronary stents, and sternal sutures are not contraindications<sup>1</sup>.

Table 6.3. MRI protocol at the Robert–Bosch–Krankenhaus Stuttgart

Sequence	Plane
Scout: echo planar (EPI) sequence	Transverse
SSFP cine gradient-echo, T1 weighted	Transverse, 6 mm slice thickness, 4 mm gap, distance 10 mm, one breathhold for one cine
Haste still frame (half Fourier spin echo) spin-echo	Transverse, 6 mm slice thickness, 4 mm gap, distance 10 mm, one breathhold for all slices
True FISP cine gradient-echo, T1 weighted	Oblique sagittal, aortic arch, aortic valve and descending aorta should be included, if possible; parallel planes to each side in 2 mm distances
True FISP cine gradient-echo, T1 weighted	Three-chamber view to assess aortic regurgitation
Phase contrast imaging optional	Transverse, if differentiation between slow-flow and thrombus is necessary and result of other sequences is equivocal
Echo planar imaging	Test bolus: transverse in the plane of the aortic valve, one image per second for 60 s after gadolinium bolus
FISP angio sequence (SSFP) gradient-echo, T1 weighted	Application of gadolinium; imaging delayed according to the results of the test bolus
Inversion recovery	Transverse, candy cane, according to the point of our interest to image thrombus

## NEPHROTOXICITY

Major morbidity in patients of aortic dissection is caused by secondary renal failure. The renal impairment may be related to the patient's underlying vascular disease or the damage caused by aortic surgical repair with cross-clamping. However, take-off of one or both renal arteries from a poorly perfused false lumen will also result in renal failure. Iodinated contrast material that many patients receive at CT scans or arteriography before aortic repair may worsen renal impairment. The nephrotoxicity of gadolinium based contrast agents is much less than that of iodinated contrast agents. However, a few cases of acute renal failure following the application of gadolinium-based contrast material in patients with underlying chronic insufficiency have been described<sup>28</sup>.

## RISK

To our knowledge, there are no cases in the literature of death during MRI in patients with acute aortic syndromes. Defibrillators and other metallic devices cannot be used in the room of the scanner. In case of an emergency, for

extended life support with intubation the patient has to be taken out of the scanner and has to be transferred to the next room, which takes about 90 s.

## **ARTIFACTS**

Artifacts that mimic aortic dissection may occur in a substantial percentage of thoracic MRI examinations. In a retrospective study published in 1990 by Solomon and coworkers, 53 thoracic MR examinations were reviewed<sup>2</sup>. In 19% of the examinations, artifacts occurred that required the use of images from other planes or sequences to distinguish them from a dissection. Motion artifacts were the most common artifacts encountered. Causes of misinterpretation included the left brachiocephalic vein, the superior pericardial recess, motion artifacts, and others. The authors stressed the importance of knowledge of the normal anatomy and the use of axial images in all cases with the addition of images in other planes as needed.

With the advent of faster and better sequences, since that time the number of artifacts has declined. However, in our experience, the value of MRI in the imaging of acute aortic syndromes still is dependent on the experience and the knowledge of the operator.

## **CURRENT PRACTICE IN PATIENTS WITH AORTIC DISSECTION**

### **IRAD REGISTRY**

In the IRAD registry, CMR was performed as primary or secondary procedure in 19% of all patients, much less than CT (75%) or transesophageal echocardiography (72%)<sup>29</sup>. MRI was the first imaging study only in 1%. CT was performed first in 63%, TEE was performed first in 58%, and aortography was performed first in 4% of all patients. Among the patients with a second imaging study, MRI was performed in 10%. The sensitivity of MRI in this series was 100% (CT 93%, TEE 88%, and aortography 87%). In 66% of the patients, two or more imaging studies were performed. This shows that in many cases the information gathered in the first imaging study was not felt to be sufficient to proceed to surgery, even though time plays a vital role in aortic dissection.

### **AVAILABILITY AND COST**

The main obstacle for a larger role of MRI in the diagnostic work-up of acute aortic syndromes is the limited availability. As compared to CT and TEE,

MRI scanners equipped for cardiac imaging are present only in a small percentage of hospitals. Especially scanners with 24 h availability are only infrequently available. There is a lack of experienced radiologists and cardiologists able to perform and read an examination. In most countries, the cost of a MRI examination is higher than the cost of CT scan or a TEE.

## **THE FUTURE**

A period of a rapid increase of the number MRI scanners and cardiovascular magnetic resonance examinations is anticipated. The first scanners with a magnetic field strength of 3.0 Tesla are being introduced. This will decrease imaging time and may improve image quality<sup>30</sup>. The era of coronary artery imaging by CMR is far closer than it was a few years ago<sup>30</sup>. The value of MRI as a routine first-line diagnostic modality in patients with aortic syndromes remains to be elucidated.

## **SUMMARY**

MRI has the ability to exclude or confirm an aortic dissection with a very high sensitivity and specificity. All variants of acute aortic syndromes (such as intramural hematoma and penetrating aortic ulcer) can be visualized. All important clinical questions such as the extension of the dissection in the abdominal aorta, the aortic branches, insufficiency of the aortic valve, and fluid in the pericardial sac can be answered. Important additional information like the function of the left ventricle can be obtained. Unlike aortography and CT, MRI does not depend on nephrotoxic contrast media. However, the poor availability of MRI, long imaging times, and problems with monitoring of vital signs in the scanner currently restrict the use of MRI to a secondary procedure when important questions remain after imaging with other modalities. In the future, as a result of better availability, technical improvements, and shorter imaging time, MRI may become the first-line imaging modality in acute aortic syndromes.

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SECTION III:  
INITIAL TREATMENT

# 7

## **MEDICAL THERAPY AND ACUTE SURVEILLANCE**

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### **IMMEDIATE MEDICAL MANAGEMENT**

Without appropriate treatment, aortic dissection has a high early mortality in the range of 1–2% per hour<sup>1</sup>. The dissection flap per se does not result in mortality, but it is when the dissection flap produces branch vessel compromise or severe aortic insufficiency, or the dissected aorta ruptures that patients suffer significant morbidity or death. Consequently, the purpose of therapy for aortic dissection is to prevent progression of the dissection process and reduce the likelihood of aortic rupture or end-organ/limb ischemia. For type A aortic dissection, surgical aortic repair is required to prevent aortic rupture, but medical therapy is still essential to protect the patient while awaiting surgery. For uncomplicated type B aortic dissection, medical therapy—rather than surgery—is the treatment of choice.

### **REDUCTION OF $dp/dt$ AND TREATMENT OF HYPERTENSION**

The primary objectives of pharmacological therapy are the reduction of the rate of rise of systolic aortic pressure due to left ventricular ejection of blood ( $dp/dt$ ) and the lowering of the systolic blood pressure. Such medical therapy is accepted as the initial treatment for virtually all patients in whom aortic dissection is suspected, even before a definitive diagnosis is made, and should be continued thereafter once the diagnosis is confirmed. All patients

with acute aortic dissection should be managed in an acute care setting for intensive medical therapy, hemodynamic monitoring, and cardiac telemetry. When dissection is suspected, patients should be monitored with an automatic blood pressure cuff if hemodynamically stable. However, if patients are unstable or after dissection is confirmed, a radial arterial line should be placed for continuous accurate blood pressure monitoring. It is essential at the outset to measure blood pressures in both arms, as there is a blood pressure differential in 15% of cases. Should a blood pressure differential exist, one must make certain to monitor and treat the higher of the two pressures, as this more accurately reflects the actual aortic pressure. Therefore, the arterial line should be placed on whichever side has the higher pressure.

The therapeutic goal is a reduction of systolic blood pressure to 100 to 110 mm Hg and the heart rate to 50–60 beats per minute or the lowest level commensurate with adequate vital organ (cardiac, cerebral, renal) perfusion. In otherwise healthy patients, a systolic blood pressure of 100 mm Hg is well tolerated and thus a reasonable goal, but in older patients with atherosclerotic vascular disease it may be necessary to maintain a systolic blood pressure in the range of 120–130 mm Hg, or greater. One should monitor mental status, cardiac symptoms, and urine output on a frequent basis to see that the organ perfusion is adequate. Also, all caregivers should be familiar with the hemodynamic targets and notify the physician if those targets cannot be maintained.

Beta-blocking agents are the mainstay of pharmacologic therapy given their ability to reduce  $dp/dt$ . In the acute setting, intravenous agents are preferred, given their rapid onset and one's ability to titrate doses to achieve the desired effect. Therapy should be administered initially in incremental doses until satisfactory beta blockade is achieved, usually indicated by a reduction in heart rate to 50–70 beats/min. However, sometimes the starting blood pressure is too low to allow sufficient doses of beta blockers to achieve this target heart rate.

Intravenous propranolol is widely used in treating acute aortic dissection because it is relatively short acting and can be administered in either bolus fashion or as a continuous infusion. One should begin with a propranolol dose of 1 mg intravenously every 3–5 min until the desired effect is achieved, and then additional doses should be given intravenously every 3–6 hours or administered as a continuous intravenously infusion. Another commonly used beta blocker in this setting is labetalol, which acts as both an alpha- and beta-adrenergic receptor blocker. It is especially useful among patients with aortic dissection who have marked hypertension on presentation, as it will serve to significantly lower arterial pressure as well as to reduce  $dp/dt$ . The initial dose of labetalol is 20 mg intravenously, followed by repeated doses of 40–80 mg every 10–15 min until the heart rate and blood pressure have been controlled or a maximum total dose of 300 mg has been reached. Patients should then be

started on a continuous intravenous infusion starting at 2 mg/min and titrating up to 5–10 mg/min.

Esmolol is an ultra-short-acting beta blocker, and because the infusion can be abruptly discontinued if necessary, it is especially useful in patients starting with relatively normal blood pressures in whom one still wants to achieve a reduction in  $dp/dt$ . Esmolol may also be preferable when there is uncertainty about the safety and tolerance of beta blockers, such as in patients with a history of obstructive pulmonary disease who may be at risk for bronchospasm. However, esmolol is not a very potent beta blocker, so once the safety of therapy has been established, it may be preferable to switch over to a more effective but cardioselective beta blocker, such as intravenous metoprolol. Esmolol is administered as a 0.5 mg/kg intravenous bolus followed by continuous infusion at 50  $\mu\text{g}/\text{kg}/\text{min}$  and titrated up to 200  $\mu\text{g}/\text{kg}/\text{min}$ .

Beta blockers are the first line of medical therapy but are often insufficient to adequately control the hypertension that may accompany acute aortic dissection. The preferred second line agent to add in this setting is the intravenous vasodilator sodium nitroprusside. It is infused at an initial rate of 20  $\mu\text{g}/\text{min}$ , which is then titrated progressively upward to a dose as high as 800  $\mu\text{g}/\text{min}$ , as required to achieve and maintain the desired blood pressure response. Although nitroprusside is extremely effective, it should also be recognized that when used alone it can actually cause an increase in  $dp/dt$ , which could be detrimental in the setting of acute aortic dissection. Therefore, it is essential that one initiate therapy with a beta blocker prior to administering nitroprusside. For those patients with acute or chronic renal insufficiency, the intravenous vasodilator fenoldopam may be preferable to sodium nitroprusside<sup>2</sup>.

When contraindications exist to the use of beta blockers (e.g., sinus bradycardia, atrioventricular block, congestive heart failure, or bronchospasm), one should consider the use of other agents to reduce arterial pressure and  $dp/dt$ . Calcium channel antagonists may be used safely among those with bronchospasm. Diltiazem and verapamil have vasodilator and negative inotropic effects, and both can be administered intravenously, so they are well suited for the treatment of aortic dissection. Nifedipine has little effect on heart rate or conduction, so it may be ideal for the patient who has bradycardia or heart block. Nifedipine also has the advantage that it can be administered via the sublingual route, permitting rapid initiation of therapy while intravenous access is established and other medications are being prepared. Conversely, an important limitation of nifedipine is that it has little effect in reducing  $dp/dt$ .

On occasion, acute hypertension may result when a dissection flap compromises one of the renal arteries, thereby causing the release of large amounts of renin. In this situation, the most efficacious antihypertensive may be the intravenous angiotensin-converting enzyme (ACE) inhibitor enalaprilat, which is

administered initially in doses of 0.625 mg every 4–6 hours and the dose then titrated upward.

Finally, the majority of patients with acute aortic dissection have significant pain, and the pain itself may exacerbate hypertension and tachycardia. Often reducing arterial pressure will relieve the presenting pain, likely due to a decrease in the tension on the dissected aortic tissue. However, when pain persists it should be treated promptly with intravenous morphine sulfate. In some instances a patient's fear and anxiety may predominate in the acute setting, in which case intravenous anxiolytics may be helpful.

## HYPOTENSION

Although hypertension is common among those with acute aortic dissection, 12% of those with type A aortic dissection present with hypotension (systolic blood pressure 81–99 mm Hg) and another 13% present in shock (systolic blood pressure  $\leq 80$  mm Hg)<sup>3</sup>. Hemodynamic embarrassment is most often the result of cardiac tamponade or aortic rupture, although in some instances it may result from severe aortic insufficiency. Also, when the measured arterial pressure is low but the patient nevertheless looks relatively well, one must make certain to exclude the possibility of *pseudohypotension*, which occurs when arterial pressure is being measured in an extremity whose circulation is selectively compromised by the dissection. If hypotension is present and thought to be a consequence cardiac tamponade or aortic rupture, rapid volume expansion should be administered. If the refractory hypotension persists, vasopressors may be required to maintain organ perfusion, in which case norepinephrine (Levophed) or phenylephrine (neo-synephrine) are preferred. Dopamine should be avoided given that it may increase  $dp/dt$ .

Cardiac tamponade (due to rupture of the ascending aorta) is a feared complication, occurring in 19% of those presenting with type A aortic dissection<sup>4</sup>. Patients with cardiac tamponade may present with hypotension, shock, or pulseless electrical activity. Pericardiocentesis is commonly attempted in this setting in an effort to stabilize such patients while awaiting more definitive surgical repair. In those with profound shock or pulseless electrical activity, this approach is warranted given the lack of options. However, among those with hypotension rather than shock, pericardiocentesis may be harmful rather than beneficial because it may precipitate hemodynamic collapse and death rather than stabilize the patient as intended. In one retrospective series of seven patients who were relatively stable despite the presence of cardiac tamponade (six hypotensive, one normotensive), three of four who underwent successful pericardiocentesis died suddenly between 5–40 min after the procedure due to acute pulseless electrical activity<sup>5</sup>. In contrast, none of the three patients managed medically without pericardiocentesis died prior to surgery. It may be that

because pericardiocentesis results in an increase in intraaortic pressure and a decrease in intrapericardial pressure, a closed communication between the dissected aorta and pericardial space reopens, leading to recurrent hemorrhage and fulminant cardiac tamponade.

Therefore, when a patient with acute aortic dissection complicated by cardiac tamponade is relatively stable, the risks of pericardiocentesis probably outweigh the benefits, and every effort should be made to proceed as urgently as possible to the operating room for direct surgical repair of the aorta with intraoperative drainage of the hemopericardium. However, when patients have pulseless electrical activity or marked hypotension, an attempt to resuscitate the patient with pericardiocentesis is warranted and may indeed be successful. A prudent strategy in such cases is to aspirate only enough pericardial fluid to raise blood pressure to the lowest acceptable level<sup>5</sup>.

## **SUBACUTE MEDICAL MANAGEMENT AND SURVEILLANCE**

Type A aortic dissection should be managed with urgent aortic repair, whereas type B aortic dissection is generally managed medically in the absence of complications. Thus the majority of patients who are managed medically will have type B acute aortic dissection. Nevertheless, in some instances patients with type A aortic dissection have contraindications to surgery (progressive cancer, end-stage COPD, subacute stroke), in which case medical therapy is indicated as an alternative.

Patients should be admitted to a cardiac intensive care unit for ongoing medical therapy and hemodynamic monitoring. The initial pharmacologic therapy described above is continued through the initial intensive care unit stay. However, even on the first hospital day, oral medications can be started and the doses titrated upward, with the goal of gradually transitioning from the intravenous medications to all oral ones over a period several days. Beta blockers are again the mainstay of therapy, but the majority of patients will require the addition of several oral antihypertensive medications before they can fully wean off the intravenous ones. Typically, an angiotensin converting enzyme inhibitor is added next, followed by a calcium-channel antagonist and/or a thiazide diuretic. Alpha blockers or other vasodilators may also be required. Most patients will require two to five different oral medications to achieve stable blood pressure and heart rate targets.

In addition to pharmacologic therapy of  $dp/dt$  and hypertension, patients need to be closely monitored for any evidence extension of the aortic dissection process or the development of any new complications of the existing dissection. Among those with type B aortic dissection, retrograde extension

could result in involvement of the ascending aorta, thus transforming it into an acute type A aortic dissection that would require urgent aortic repair. Evidence of retrograde extension includes the onset of new chest or neck pain, the onset of hypotension or shock, a new blood pressure differential between the two arms, the appearance of a new diastolic murmur of aortic insufficiency or a pericardial rub, or new electrocardiographic evidence of pericarditis or acute myocardial infarction. Complications of the existing type B aortic dissection that would merit consideration of aortic repair include compromise of arterial flow to vital organs or extremities, leaking or rupture of dissected aorta, or a rapidly expanding aortic aneurysm.

Frank mesenteric ischemia may present as abdominal pain out of proportion to findings on physical examination, progressing to bloody diarrhea, acidosis, and hypotension. However, in its early stages the presentation of mesenteric ischemia may be more subtle, with symptoms of postprandial abdominal pain (“abdominal angina”) or perhaps just nausea or anorexia. Because bowel infarction may occur before the symptoms and signs of mesenteric ischemia are fully manifest, it is essential that all care providers be aware of and vigilant for the earliest warning symptoms so that intervention can be performed in a timely fashion<sup>6</sup>. Renal ischemia or infarction may present with flank pain (renal infarction) but more often is manifest only by acute renal insufficiency and a drop in urine output. Lower extremity arterial compromise may result in a cold, pulseless, and/or painful limb. Therefore, patients with acute aortic dissection should be monitored for renal function and urine output and should have femoral and pedal pulses checked on a daily basis.

In the past, it was advocated that recurrent pain was an indication for surgical repair of a type B aortic dissection. However, most no longer believe this to be the case. In a retrospective study by Januzzi et al. of 53 patients with acute type B aortic dissection, 34 (64%) had one or more episodes of recurrent pain<sup>7</sup>. Repeat imaging studies were performed in 31 of these 34 patients (91%), and there was no change in the mean aortic diameter compared with presentation, nor was there any radiographic evidence of extension of the dissection, impending or active rupture, or branch arterial compromise. Among the 34 patients with recurrent pain, there was only one death and one who required surgery, whereas among the 19 patients without recurrent pain, there were three deaths and two others who required surgery. Therefore, recurrent pain predicted neither radiographic complications nor adverse outcomes and, thus, in and of itself, appears not to be an indication for surgical intervention.

A significant proportion of patients with type B aortic dissection develop severe or refractory hypertension during their stay in the intensive care unit, even if they did not have such significant hypertension on presentation. Many care providers assume that worsening hypertension is likely a manifestation of acute renal artery compromise and order a renal artery MRA or CTA. However,

typically there is no objective evidence of renal ischemia. In another retrospective study by Januzzi et al.<sup>8</sup> of 53 patients with acute type B aortic dissection, 34 (64%) had what was termed refractory hypertension, which was defined as a requirement for four or more concurrent adequately dosed antihypertensive agents to achieve an arterial pressure of  $\leq 140/80$  mm Hg. When compared with the 19 study patients who did not have refractory hypertension, those with refractory hypertension had no greater incidence of renal artery compromise; in fact, if anything, there was a trend toward a lower incidence of renal artery compromise among the refractory hypertension group (12% vs. 32%;  $p = 0.06$ ). There was no difference between the two groups in the frequency of acute renal failure or adverse events (death, vascular surgery, extension of dissection, or aneurysm expansion). Therefore, in the absence of compelling evidence of renal ischemia, such as rise in creatinine or a decline in urine output, one should manage the refractory hypertension with appropriate medications, but routine imaging of the renal arteries is not necessary.

## PREDISCHARGE MANAGEMENT

Once patients are on an oral regimen of appropriate medications, and both the heart rate and blood pressure are optimally controlled, patients can be transferred out the intensive care unit to a step-down floor. There they should be monitored for several more days to see that they remain stable and symptom free as they are mobilized. Prior to discharge a follow-up imaging study—typically a CT angiogram—of the aorta should be performed to ensure that no unsuspected complications have arisen and to serve as the baseline study for future comparison. Patients should be carefully educated about symptoms that should prompt medical attention, and after discharge patients should be followed by physicians with expertise in the management of aortic dissection.

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# 8

## ENDOVASCULAR THERAPY IN AORTIC PATHOLOGY

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The interventional management of aortic dissection and the use of stent grafts evolved slowly in anticipation of the risk of paraplegia from spinal artery occlusion. This complication occurs in up to 18% after surgery initiating the search for alternative therapeutic strategies such as endovascular procedures. Today, after rapid technical improvement, a large number of aortic dissection patients have been successfully treated by percutaneous stent-graft placement covering the entry tear in the descending aorta and even in the aortic arch, and studies have demonstrated that closure of the entry tear is essential to reconstruct the true lumen and reduce total aortic diameter. Entry tear closure promotes both thrombus formation in the false lumen and remodeling of the en-

tire aorta<sup>1-4</sup>. Thus, in aortic dissection there appears to be a role for stent-graft placement in the treatment of static or dynamic obstruction of aortic branch arteries.

## PRINCIPLE OF ENDOLUMINAL STENT GRAFT IN AORTIC DISEASE

The most effective method for excluding an enlarging and aneurysmal dilated false lumen is the sealing of the proximal entry tear with a customized stent graft; the absence of a distal reentry tear is desirable but not a prerequisite. Besides dissection, however, focal *true (or false) aneurysm* of the descending thoracic aorta represents another potential target for endovascular repair instead of open surgical repair.

*Penetrating aortic ulcers*, often originating from a localized intramural hematoma of the aorta, may also benefit from stent-graft patching, both in emergency and elective scenarios (as in posttraumatic aortic lesions such as incomplete aortic rupture after deceleration trauma).

*Partial or complete rupture* almost always occurs as a result of deceleration trauma (as in a car accident or a fall from a height). Emergent or preferably delayed (but timely) endovascular management by stabilization of the disrupted aorta with stent graft has proven beneficial, with amazing reconstruction of the thoracic aorta by virtue of the inner lining by the endoprosthesis that can prevent enlargement, aneurysm formation, and eventual rupture but also allowed self-healing of the transected aortic tissues.

Conventional treatment of type A (type I, II) dissection consists of surgical reconstruction of the ascending aorta with restoration of antegrade flow into the true lumen. Currently, interventional endovascular strategies have no clinical application in this population except to relieve critical malperfusion prior to surgery by performance of distal fenestration in type B (type III) dissection with ischemic complications. Various scenarios of true lumen compression with resultant malperfusion syndrome are amenable to endovascular management. Typical examples include dynamic malperfusion caused by intima invagination, static collapse of the aortic true lumen, dynamic or static occlusion of one or more vital side branches, or an enlarging false aneurysm due to patent proximal entry tear. Aims of treatment include reconstruction of the thoracic aortic segment by containing the entry tear, initiating thrombosis of the false lumen, remodeling the entire aorta and reestablishing sidebranch flow (Figure 8.1).

With surgical repair of the dissected thoracic aorta, approximately 90% of peripheral pulse deficits can be reversed at the expense, however, of a high mortality; patients with mesenteric or renal ischemia do even worse. Mortality

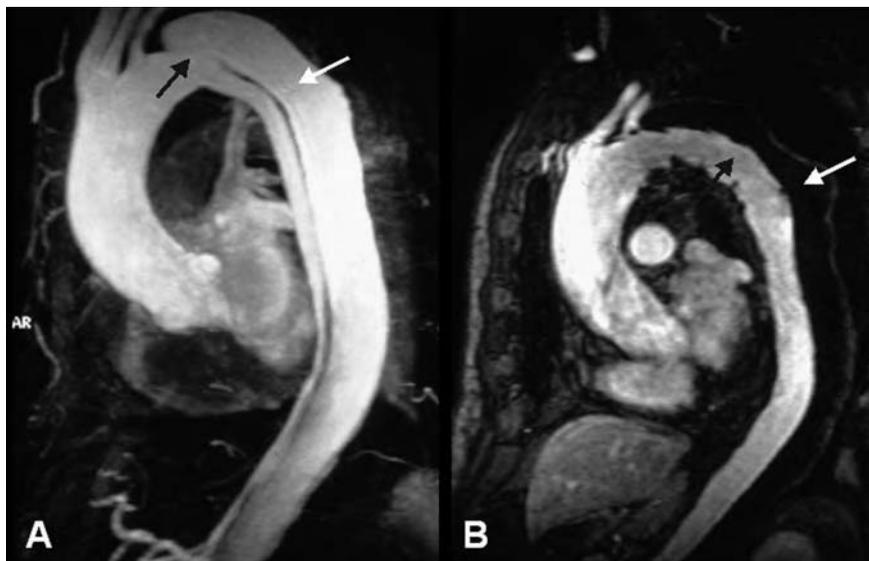


Figure 8.1.

of patients with renal ischemia is 50–70% and as high as 87% in mesenteric ischemia<sup>5–7</sup>. The surgical mortality rates in patients with peripheral vascular ischemic complications are similar to those with mesenteric ischemia, with an 89% in-hospital mortality rate<sup>8–11</sup>. Operative mortality of surgical fenestration varies from 21% to 61%, and thus percutaneous interventional management using endovascular balloon fenestration of a dissecting aortic membrane to treat mesenteric ischemia has emerged as a niche indication in such complicated cases of malperfusion<sup>10–12</sup>.

The interventional management of aortic dissection and the use of stent grafts evolved slowly in anticipation of the risk of paraplegia from spinal artery occlusion. This complication occurs in up to 18% after surgery<sup>11–14</sup>.

## INDICATIONS FOR STENT PLACEMENT AND FENESTRATION

The exact role of percutaneous fenestration and stent placement in the treatment of *aortic dissection* continues to evolve. In dissection, there appears to be a role for stent-graft placement in the treatment of static or dynamic obstruction of aortic branch arteries because static obstruction of a branch can be overcome by placing endovascular stents across the vessel origin, and dynamic obstruction may benefit from stents in the aortic true lumen with or without

additional balloon fenestration. In classic aortic dissection, successful fenestration leaves true and false lumen pressure unchanged. Sometimes bare stents must be deployed in the true lumen to buttress the flap in a stable position remote from branch artery origins<sup>7</sup>. In chronic dissection where fenestration of a fibrosed dissecting membrane may result in collapse of the connection between true and false lumen, a stent may be necessary to keep the fenestration open. A rare use of fenestration is to create a reentry tear for the dead-end false lumen back into the true lumen with the aim to supply blood to branches fed exclusively from the false lumen or jointly from the false and true lumen—a concept, however, that lacks any clinical proof. Conversely, fenestration may in fact increase long-term risk of aortic rupture because a large reentry tear promotes flow in the false lumen and provides the basis for aneurysmal expansion of the false lumen. There is also a risk of peripheral embolism from a patent but partly thrombosed false lumen<sup>7,8</sup>.

The most effective method to exclude an enlarging and aneurysmal dilated false lumen is the sealing of the proximal entry tear with a customized stent graft; the absence of a distal reentry tear is desirable but not a prerequisite. Adjunctive treatment by fenestration and/or ostial bare stents may help establish flow to compromised aortic branches. Compression of the true aortic lumen cranial to the main abdominal branches with distal malperfusion may also be corrected by stent grafts that enlarge the compressed true lumen and improve blood flow<sup>2,3,10,12</sup>. Depressurization and shrinking of the false lumen is the most beneficial result to be gained, ideally followed by thrombosis and remodeling of the entire aorta and in rare occasions even in retrograde type A dissection<sup>14</sup>. Similar to previously accepted indications for surgery in type B dissection, scenarios such as intractable pain with a descending dissection, a rapidly expanding false lumen diameter, or extraaortic blood collection as a sign of imminent rupture or distal malperfusion syndrome are accepted indications for emergent stent graft placement<sup>16–19</sup>. Dissection of a chronically aneurysmal aorta may still be considered a surgical emergency. However, late onset of complications such as malperfusion of vital aortic side branches warrants endovascular stent grafting of an occlusive lamella (or fenestration) to improve distal true lumen flow. After an unsuccessful attempt, surgery may still be required. At present, surgical repair failed to prove superiority over interventional treatment even in uncomplicated cases; in complicated cases the concept of endovascular treatment is currently replacing surgical interventions in advanced aortic centers<sup>1–3,17–20</sup> (Figure 8.2).

Besides dissection, however, focal *true (or false) aneurysm* of the descending thoracic aorta represents another potential indication for endovascular repair instead of open surgical repair. A number of studies have documented

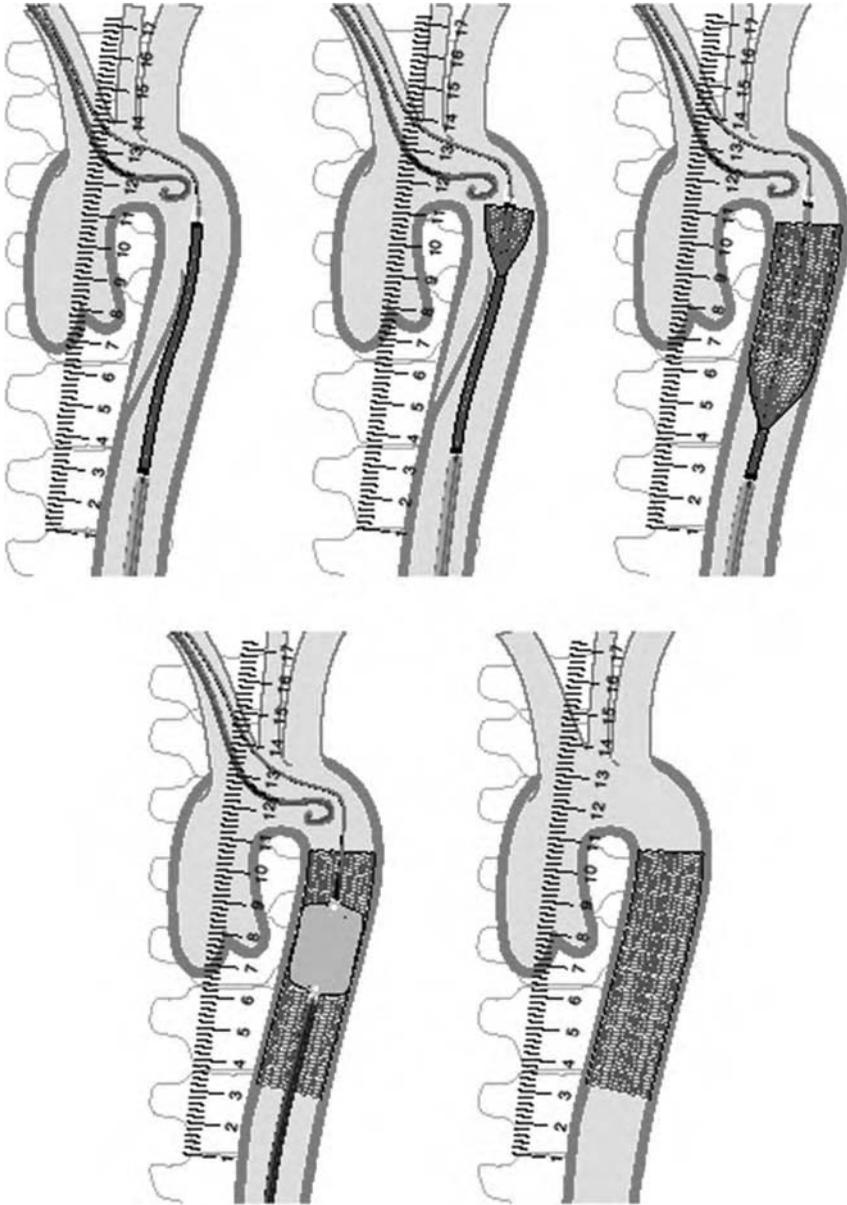


Figure 8.2.

not only feasibility and safety but also favorable short- and midterm outcomes especially in patients with multiple comorbid conditions subjected to elective stent-graft treatment for circumscribed thoracic aneurysms that otherwise would be considered for surgical therapy based on pathoanatomical



Figure 8.3.

cal features<sup>21–23</sup>. With the most recent technical refinements of endovascular devices, previous shortcomings of homemade stent-grafts are likely to be overcome<sup>24</sup>. Treatment of descending thoracic aneurysms—if anatomically suitable—by endovascular stent grafting is the primary management consideration today<sup>25</sup>.

*Penetrating aortic ulcers*, often originating from a localized intramural hematoma of the aorta, may become an attractive indication for stent-graft patching, both in emergency and elective scenarios. However, few reports to date have documented successful sealing of ulcers by use of commercial stent grafts in an endovascular approach. While aortic ulcers may only occasionally progress so rapidly to generate a medical emergency, traumatic aortic rupture or partial or even complete transection of the descending thoracic aorta is always a truly emergent life-threatening condition.

*Partial or complete rupture* almost always occurs as a result of deceleration trauma as in a car accident or fall from a significant height. The aorta most frequently ruptures at the fixation points and may be contained by nothing more than the adventitia. Emergent or better delayed (but timely) endovascular management by stabilization of the disrupted aorta with a suitable stent graft has proven feasible, with resultant reconstruction of the thoracic aorta by virtue of the inner lining by the endoprosthesis that prevented enlargement, aneurysm formation and eventual rupture, but also promoted self healing of the transected aortic tissues<sup>26</sup> (Figure 8.3).

## **TECHNIQUE OF PERCUTANEOUS BALLOON FENESTRATION**

The technical goal in percutaneous balloon fenestration is to create a tear in the dissection flap between the true and false lumen. Fenestration is performed from the smaller (usually the true lumen) into the larger or false lumen. Most commonly a Roesch-Uchida, Brockenborough, or Colopinto needle is used for fenestration at locations close to compromised side branch arteries. After the needle and a stiff wire are advanced from the true into the false lumen at the desired location, a balloon catheter of 12–15 mm diameter and 20–40 mm length is used to create a transverse tear. If intravascular ultrasound (IVUS) is not available, a pulmonary balloon catheter can be used as a targeting object for piercing the dissecting membrane with the needle<sup>15</sup>.

## **TECHNIQUE OF AORTIC STENT GRAFT PLACEMENT**

Aortic stent grafts are primarily used to correct compression of the supplying true lumen cranial to major aortic branches and to increase distal aortic and branch arterial flow. Moreover, proximal communications should be sealed whenever possible to depressurize the false lumen and induce thrombosis, fibrosis transformation, and subsequent remodeling of the aorta. Stent-graft placement across the origin of the celiac, superior mesenteric, and renal arteries is strongly discouraged due to concerns that it will induce end-organ ischemia and thus has not been studied extensively.

Based on the measurements obtained during angiography (IVUS, TEE, CT, or MRI), customized stent grafts should be used in covering up to 18 cm of dissected aorta and particularly the major tear. The procedure is best performed in the catheterization laboratory with the patient under general anesthesia. The femoral artery is the most popular access site and can usually accommodate a 24 F stent-graft system. Using the Seldinger technique a 260 cm stiff wire is placed over a pigtail catheter that has been navigated with a soft wire in the true lumen under both fluoroscopic and transesophageal ultrasound guidance. Carefully advanced over the stiff wire the launching of the stent graft is performed with blood pressure briefly lowered to 50–60 mm Hg by infusing sodium nitroprusside. In the moment of stent expansion, aortic pressure transiently increases, and the system may dislodge without lowering blood pressure. After deployment, short inflation of a latex balloon may be used for improved apposition of the stent struts to the aortic wall to seal proximal thoracic communications and to promote eventual reconstruction and remodeling of the aorta. Both Doppler ultrasound and contrast fluoroscopy are most

Table 8.1. Considerations for surgical, medical, and interventional therapy in aortic dissection

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<p>Surgery</p> <ul style="list-style-type: none"> <li>● Treatment of choice in acute type A dissection</li> <li>● Acute type B dissection complicated by the following:           <ul style="list-style-type: none"> <li>○ Retrograde extension into the ascending aorta</li> <li>○ Dissection in Marfan's syndrome</li> <li>○ Rupture or impending rupture (historically classic indication)</li> <li>○ Progression with compromise of vital organs</li> </ul> </li> </ul>
<p>Medical therapy</p> <ul style="list-style-type: none"> <li>● Treatment of choice in uncomplicated type B dissection</li> <li>● Stable, isolated arch dissection</li> <li>● Stable type B dissection (chronic, <math>\geq 2</math> weeks of onset)</li> </ul>
<p>Interventional therapy</p> <ul style="list-style-type: none"> <li>● Stent grafts to seal entry to false lumen of aortic dissection and to enlarge compressed true lumen           <ul style="list-style-type: none"> <li>○ Unstable type B dissection</li> <li>○ Malperfusion syndrome (proximal aortic stent-graft and/or distal fenestration/stenting of branch arteries)</li> <li>○ Stable type B dissection (under study)</li> </ul> </li> <li>● Stent grafts to exclude thoracic aortic aneurysm (<math>\geq 5</math> cm)</li> <li>● Stent grafts to cover perforating aortic ulcers (especially deep, progressive ulcers)</li> <li>● Stent grafts to reconstruct the thoracic aorta after traumatic injury</li> <li>● Stent graft placement as an emergency treatment of evolving or imminent aortic rupture</li> </ul>

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instrumental for documenting the immediate result or initiating adjunctive maneuvers. For thoracic aortic aneurysms or ulcers, the navigation of wires and instruments is markedly easier, but meticulous imaging with ultrasound and fluoroscopy is equally important.

A dissection that propagates into a branch artery and causes static obstruction is treated by ostial branch vessel stents. A stent is usually inserted when a significant gradient between the branch artery and the supplying aortic lumen exists. It is important that the aortic true luminal cross section and true lumen pressures are reassessed after flow restoration in large arteries, as stenting of arterial branch stenoses can result in significant reorientation of the dissection flap with subsequent changes in the pressure of the supplying aortic lumen. Precise stent placement is crucial and minimal stent shortening appears advantageous<sup>27</sup>. A summary of treatment options is listed in Table 8.1.

Table 8.2. Patient characteristics reported in meta-analysis<sup>29</sup>

	Data available (n)	Number of events or cases (n)	
Total numbers of studies included	39	—	
Total number of patients reported	1007	—	
Number of patients with aortic dissection	609	—	60.5%
Patient age (years)	442	—	61.0%
Male gender	240	182	75.8 ± 2.6%
Acute dissection	427	248	58.1 ± 1.8%
Presenting with rupture	491	79	16.1 ± 1.2%

Table 8.3. In-hospital data of meta-analysis<sup>29</sup>

	Data available (n)	Number of events (n)	
Procedure success	551	541	98.2 ± 0.5%
Surgical conversion	609	7	2.3 ± 0.6%
Adjunctive endovascular procedures	324	5	1.5 ± 0.6%
Overall complications	449	61	13.6 ± 1.5%
Major complications	449	50	11.2 ± 1.4%
Minor complications	449	11	2.4 ± 0.7%
Procedure-related complications	429	29	6.8 ± 1.2%
Retrograde type A-aortic dissection	429	8	1.9 ± 0.6%
Access complications	429	10	2.3 ± 0.7%
Neurologic complications	518	15	2.9 ± 0.7%
Stroke	518	10	1.9 ± 0.6%
Paraplegia	609	5	0.8 ± 0.4%
In-hospital mortality	524	27	5.2 ± 0.9%
In-hospital mortality, procedure related	397	9	2.3 ± 0.7%
In-hospital mortality, nonprocedure related	397	16	4.0 ± 0.9%

## RESULTS OF INTERVENTIONAL THERAPY

With both fenestration maneuvers and bare stents in side branches, compromised arterial flow can be restored in more than 90% (range 92–100%) of vessels obstructed by aortic dissection. The average 30-day mortality rate is 10% (range 0–25%), and additional surgical revascularization is rarely needed. Most patients remain asymptomatic over a mean follow-up time of about one year. Fatalities are rarely related to the interventional procedure, but death may occur as a result of nonreversible ischemic changes, progression of the dissection, or complications of additional reconstructive surgical procedures on

the thoracic aorta<sup>1-3,17,20,27</sup>. Potential problems may arise from unpredictable hemodynamic alterations in the true and false lumen after fenestration and side branch stenting. These alterations can result in loss of previously well perfused arteries, as well as in loss of initially salvaged sidebranches. Affected arteries can also be managed by endovascular techniques such as additional stent procedures.

Recent reports suggest that percutaneous stent-graft placement in the dissected aorta may be safer and produce better results than surgery for type B dissection. Paraplegia may occur after use of multiple stent grafts but is extremely rare, especially when the stented segment does not exceed 16 cm. Results of short-term follow-up are excellent with a 1-year survival rates of >90%; intimal tears are readapted, and aortic diameters generally decrease with complete thrombosis of the false lumen. This suggests that stent placement may facilitate healing of the dissection, sometimes of the entire aorta, including abdominal segments. However, late leakages have been reported, highlighting the need for stringent follow-up. In some patients, follow-up has revealed tears that had initially been overlooked, requiring additional stents. Some individuals may develop a systemic inflammatory reaction after stent implantation. This may present as an elevated C-reactive protein in concert with fever. Both signs may disappear spontaneously or with transient nonsteroidal treatment as aortic remodeling progresses.

Both acute and midterm results of stent-graft therapy for patients with thoracic aortic aneurysms, ulcers, and traumatic aortic lesion are encouraging, since patients in these scenarios are likely to die from their conditions and comorbidities rather than from deterioration of their aortic lesion. While the endovascular maneuvers usually ensure complete occlusion of the aneurysmal sac or ulcer, such patients are usually older with various comorbidities that may limit life expectancy<sup>24,25</sup>. However, better patient selection, avoidance of endoleak, and further technical refinement will improve outcomes even for those patients that would never be accepted for open surgical repair.

## COMPLICATIONS OF INTERVENTIONAL THERAPY

In view of the fact that the postprocedural mortality rate seems largely dependent on the severity and duration of ischemia before the interventional procedures (e.g., in one report half of the 30-day mortalities were due to irreversible damage sustained before the endovascular treatment) timely percutaneous stent treatment seems highly desirable<sup>28</sup>, this notion is confirmed by a meta-analysis on endovascular treatment (with stent grafts) in patients with type B aortic dissection that feasibility and high technical success rate at the expense of only a limited procedure-related complication and death rate as

summarized in Table 8.2<sup>29</sup>. Considering the excess mortality of acute type A dissection with malperfusion of peripheral branches, percutaneous intervention for relief of malperfusion has been suggested before surgical repair—a concept, however, that requires further study.

## LONG-TERM FOLLOW-UP AND TREATMENT

The long-term approach to patients with successful initial treatment of acute aortic dissection or aneurysm begins with an appreciation that such patients have a systemic illness that variably predisposes their entire aorta and potentially its larger branches to dissection, aneurysm, and rupture. Systemic hypertension, advanced age, aortic size, and presence of a patent false lumen are all factors that identify higher risk, as does the entire spectrum of the Marfan's syndrome. However, all patients merit extremely aggressive medical therapy, follow-up visits, and serial imaging. It has been estimated that nearly a third of patients surviving initial treatment for acute dissection will experience dissection extension, aortic rupture, or require surgery for aortic aneurysm formation within 5 years of presentation. Furthermore, this risk is substantial in the first few months after initial therapy.

Treatment with effective beta blockade is the cornerstone of medical therapy. By lowering both blood pressure and contractility, beta blockers have been shown to retard aortic expansion in Marfan's syndrome<sup>30</sup> and that associated with chronic abdominal aortic aneurysms<sup>31</sup>. Observational studies suggest similar unique benefits in aortic dissection when compared to other antihypertensive agents; guidelines recommend progressive uptitration of dosage to achieve a blood pressure <135/80 in usual patients and <130/80 in those with Marfan's syndrome<sup>31–33</sup>.

Serial imaging of the aorta is an essential component of long-term treatment and follow-up of patients with aortic aneurysm (before and after surgery or stent-graft placement) in Marfan's disease and in all cases of chronic dissection. Choice of imaging modality is dependent on institutional availability and expertise, extent of aortic involvement, and age of the patient. Previous recommendations suggest follow-up imaging and examination at 1, 3, 6, 9, and 12 months following discharge and annually thereafter<sup>34,35</sup>. This aggressive strategy underlines the observation that both hypertension and aortic expansion/dissection are common and not easily predicted in the first months following hospital discharge. Further, imaging is not confined simply to the region of initial involvement since both dissection and aneurysm formation may occur any where along the entire length of the aorta.

Development of an ascending aortic diameter of 4.5–5.0 cm is an indication for surgical repair in patients with Marfan's syndrome. For others, aorta's exceeding 5.5–6 cm warrant repair, as does distal aortic expansion to >6.0 cm in

all types of patients. As with nondissecting aneurysms, rate of growth and size of the aorta are both important factors to consider when it comes to prophylactic vascular surgery. An ascending aortic aneurysm of 5.0 cm may merit urgent repair in a young patient with Marfan's syndrome<sup>36</sup>. Conversely, an aneurysm of 5.0 cm for 3 years in an elderly person with well controlled blood pressure is unlikely to rupture.

Patients who have been treated with surgery and/or endovascular stent grafting warrant follow-up similar to those whose initial treatment was limited to medical treatment. Aortic expansion, dissection, and rupture both at the surgical suture site and at a distance are common in survivors of type A dissection. Meticulous attention to blood pressure control and serial imaging are just as relevant to operative survivors as for patients in early stages of aortic pathology.

## CONCLUSIONS

Considering the aging patient population in Western societies, prolonged survival despite hypertension, and the improved diagnostic strategies available to more patients, the cardiovascular community faces an increasing incidence of acute and chronic aortic problems (such as dissection, aneurysm, intramural hematoma, ulcerations, and traumatic lesions) that desperately need to be stratified using both early biomarkers of an inflammatory and dissecting process and functional imaging of the aortic wall. At this pivotal point in time, an elevated level of awareness in clinical cardiology and the availability of modern imaging technology should trigger the interest in diagnosing and treating the complex of acute aortic syndromes similar to previous efforts in acute coronary syndromes. Cardiologists should improve diagnostic pathways and vascular staging in acute and chronic aortic diseases, form regional referral networks and allocation systems, and utilize uniform follow-up programs. Moreover, precise definitions of pathology using clear semantics should be integrated into prospective registries of aortic diseases by a multidisciplinary team of physicians in an attempt to validate previous retrospective observations and to make the best use of evolving diagnostic and endovascular treatment strategies. Finally, cardiologists are in need of credible prognostic models that can support decisions for individual patient care independent of investigators, at different times, and in worldwide locations.

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# 9

## **CARDIOVASCULAR SURGERY IN THE INITIAL TREATMENT OF AORTIC DISSECTION AND ACUTE AORTIC SYNDROMES**

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### **THE ACUTE AORTIC SYNDROMES CONSIDERED FOR SURGERY**

This chapter describes our present knowledge of surgical treatment options and outcomes in acute dissections and intramural hematomas. However, there is another large group of patients with acute aortic syndromes—patients with ruptured aortic aneurysms. When patients with this dramatic condition present

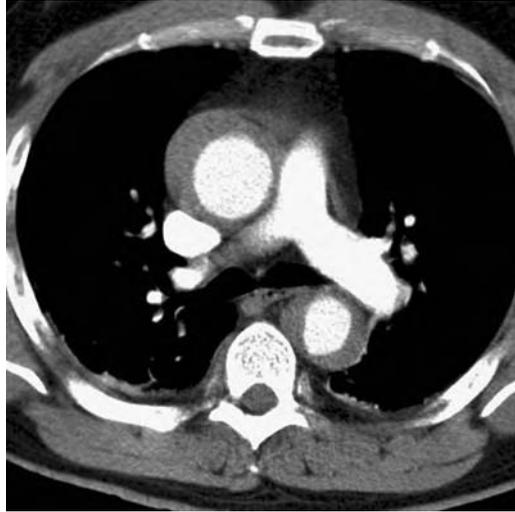


Figure 9.1. A 60-year-old man was admitted with a clinical presentation of aortic dissection. The CT scan on admittance showed an extensive intramural hematoma affecting both the ascending and descending aorta. At surgery, a primary tear was located in an almost completely fragmented arch demanding an arch resection.

with a ruptured thoracic aorta, the patients are mainly older<sup>1</sup>, have multiple comorbidities, and have often been deemed inoperable for elective surgery<sup>2</sup>. Many of them have been evaluated for stent grafting but, due to their often very extensive disease, have also been found not to be candidates for stent-graft placements. Thus, the acute aortic syndrome in these patients is the end stage of a degenerative disease that often has been observed for years ahead of the acute episode.

Acute thoracic aortic syndromes often considered for surgery, however, are the classic dissections, their modern variant intramural hematomas, and penetrating aortic ulcers. Until recently, some uncertainties have been connected to the preferred treatment of intramural hematomas (IMH) and penetrating aortic ulcers (PAU). However, in a reasonably large series of patients with IMHs, Nienaber and coworkers<sup>3</sup>, found the prognosis for patients with this disease affecting the ascending aorta to be particularly dismal, mimicking the natural history of classic aortic dissections affecting the first part of the aorta. Four out of five patients in the Eppendorf series with an IMH affecting the ascending aorta succumbed on medical treatment alone, while all seven patients treated surgically did survive. Thus, an IMH affecting the ascending aorta should be addressed as a classic dissection, and patients should have prompt surgical treatment addressing the ascending aorta and in some cases the arch<sup>4</sup> (Figure 9.1).

There has been some confusion when describing the morphologies and pathophysiology differentiating the IMHs and penetrating aortic ulcers (PAU), and much is still to be learned about the dynamics of these vascular wall traumas in the aorta. An IMH is thought to occur on the basis of rupture and bleeding originating in the small vessels within the aortic wall (*vasa vasorum*). A penetrating atherosclerotic ulcer (PAU), on the other hand, will progress from the aortic lumen with a small rupture when penetrating the elastic lamina from the atherosclerotic intimal side of the aortic wall. The first mechanism has been proposed to occur most frequently in the ascending aorta presenting as an IMH, and the primary bleed in a PAU has been found to have its predilection in the descending aorta. The PAU mechanism of an aortic dissection probably represents a particular dismal dissection in the descending aorta demanding aggressive treatment<sup>5</sup>.

When considering surgical treatment for these patients, there are a few simple rules of thumb to guide the surgeon in his or her decision making. An intramural hematoma or classic dissection of the ascending aorta should be treated surgically unless the patient is beyond salvage or has a dismal short-term prognosis from other diseases. All the other variants of this disease have to be assessed individually in the present era, considering conservative medical treatment, stent grafting, and surgery. There are few undisputable guidelines in these relatively rare and often lethal acute vascular catastrophes, and local resources and therapy traditions have to be relied upon and developed further.

## **THE HISTORY OF SURGICAL TREATMENT OF ACUTE AORTIC DISSECTIONS**

The first surgical procedure done for an acute type A aortic dissection is somewhat difficult to reconstruct from the literature but was most probably done by Norman Shumway at Stanford University Medical Center in the early 1960s. This set off a surge of attempts to save these severely ill patients<sup>6–10</sup>, and surgery soon became accepted as the means of treating dissections involving the ascending aorta. It became apparent that the most favorable surgical technique was to implant a short graft between the aortic valve and the innominate artery<sup>11,12</sup>. The pioneering work done by Shumway and his team at Stanford resulted in this institution having its name on the most widespread classification of aortic dissection—Stanford type A involving the ascending aorta and type B confined to the descending aorta<sup>12</sup>. This classification, as simple as can be, is a treatment-related classification as type A mandate surgery, while type B has mostly been addressed conservatively with antihypertensive medication. A major motivation for establishing this classification was based

on the initial futile attempts to surgically repair the dissected descending aorta and the reasonably good results from treating these patients conservatively<sup>13</sup>.

The first clinical application of a stent graft in the treatment of an acute aortic dissection was done at Stanford University Medical Center by Michael D. Dake and D. Craig Miller in October 1996<sup>14</sup>. The patient had an acute type B dissection with concomitant intestinal malperfusion due to true lumen collapse in the proximal descending thoracic aorta. He was treated successfully with a home-made stent graft covering the entry site just beyond the takeoff of the left subclavian artery. Due to brisk retrograde filling of the false lumen from a large reentry fenestration where the celiac axis had been sheared off, "paving" of the descending thoracic aortic true lumen with multiple uncovered stents was also performed. This patient is still alive; the bulk of the false lumen throughout the descending aorta clotted, fibrosed, and subsequently disappeared over the years. The reentry tear at the celiac axis continues to fill the false lumen in the suprarenal abdominal aorta (DC Miller, personal communication).

The introduction of stent grafting of severely diseased aortas has opened up the now widespread search for less invasive treatments to improve on the dismal results following acute surgery of the descending aorta and reducing the morbidity related to surgical treatment in general. As stent grafting has now been introduced in clinical practice throughout the world<sup>15,16</sup>, the choice of an initial treatment strategy for patients with aortic dissections has become more diversified, and treatment algorithms are constantly changing. Particularly for dissections of the descending aorta, the treatment options are several, including antihypertensive medication alone, fenestration of the intimal flap, stent grafting, small surgical procedures as creating surgical fenestrations of the occluding membrane or transecting the aorta, and large reconstructive aortic procedures.

## **THE ROLE OF SURGICAL TREATMENT IN THE PRESENT ERA**

The indication for surgery in acute type A aortic dissection is now undisputed for all patients who are not in a completely unrescuable medical condition. The timing of the surgery is also of paramount importance to avoid early mortality. It is obvious from the survival curves in patients with an acute type A aortic dissection (i.e., an approximately 50% death rate within 48 hours) that early operation is mandatory to avoid dreaded and often lethal complications from a proximally destroyed aorta. However, in the IRAD experience, the patients operated in the earliest hours after arriving at an IRAD center, had higher mortality than patients operated after a longer in-hospital observation period<sup>17</sup>. Also, the average time from onset of symptoms until surgery

was more than three days. These somewhat surprising observations may have several explanations. First, it demonstrates that even in tertiary referral centers some patients with acute aortic dissections are waiting out the odd hours of the night, most probably waiting for a definitive clinical and radiological diagnosis. Second, the most deranged patients in the IRAD experience were operated immediately with an average waiting time between diagnosis and surgery of 3.5 hours while stable patients were kept waiting somewhat longer. This makes way for a selection bias in the comparison of waiting times. Patients who died while waiting have not yet been analyzed in the IRAD data. These patients have to be added to the group of late-surgery patients to get the true mortality from the late-operation strategy. It can be concluded, however, that series with many patients with long observation periods after the acute clinical event probably represents a considerable selection bias. The rule of thumb is to do the operation at first opportunity if the resources are there at all.

For patients with acute type B dissections, the treatment priorities, and thus the role for surgery are less obvious. Patients with uncomplicated acute type B dissections have traditionally been treated conservatively with focus on antihypertensive medication, due to the dismal initial surgical experience in acute type B patients<sup>12,13</sup>. However, outstanding results, even with zero surgical mortality<sup>18,19</sup>, have been presented in recent years. Thus, a case for early surgery has been made from these institutions. The rationale for such early surgery is defended with in the hope to avoid late adverse outcomes due to downstream aortic pathology. Data supporting such a treatment algorithm is still lacking after 40 years, however, and the majority of these patients are still been treated conservatively.

Whether or not patients with uncomplicated acute type B dissections should have a stent-graft placement covering the intimal tear is the obvious question in the current era. The aim of such a treatment would be to promote thrombosis of the false lumen and avoid the downstream pathology that might develop after the acute episode. This question requires a randomized trial, and indeed such trials are in progress. However, it is to be expected that the answers from such trials will demand years of follow-up, and the experience from coronary stenting has taught us that improvements in technology will make such studies almost obsolete very soon after publication.

The emerging role of stent grafting skews the indication for surgery. There is still a lack of firmly designed studies, but given the option and extensive morbidity and mortality after surgery for the highest-risk cases, these syndromes most probably will benefit from the use of stent grafts. This particularly holds true for patients with ischemic complications and end-organ dysfunction. Such a therapeutic tradition indeed is emerging.

## **THE TRICKS OF THE TRADE: USEFUL ADJUNCTS TO SURGICAL TECHNIQUES**

Handling these patients has taught us some useful strategies in the practical conduct of surgical procedures. First, the surgeon should take advantage of the images available to him or her. By carefully analyzing the CT images in almost 70% of the IRAD patients, the state of the distal aorta can be assessed. In a case of a DeBakey type II dissection (i.e., a dissection confined to the ascending aorta) the femoral artery could most probably be safely cannulated with minimal danger of organ malperfusion and no anticipated need for antegrade cerebral perfusion or an extensive arch procedure. The sound surgical principal of making things “as simple as possible” certainly holds true for these severely ill patients. Furthermore, the state of the innominate artery should be carefully assessed in case the axillary artery is chosen for cannulation. Also, the state of the arch and organ perfusion can be assessed and taken into consideration when planning the surgery. Dissection extending into the neck vessels is a particularly ominous sign and combined with clinical evidence of cerebral malperfusion indicates that the surgeon must be prepared for alternative strategies for intraoperative cerebral perfusion and including a total arch repair extending into the neck vessels.

Transesophageal echocardiography has become an indispensable part of the surgical handling of patients with acute aortic syndromes. It is by far the simplest and best method of assessing the pericardium, myocardium, and aortic valve preoperatively and should also be used throughout the surgical procedure. TEE can be used to evaluate the placement of cannulas—for example, the sometimes difficult placement of a venous femoral cannula from the left femoral vein crossing into the inferior caval vein and then extending to the right atrium. Also, when commencing cardiopulmonary bypass, TEE should be used to assess the state of perfusion in the different compartments of the aorta and whether or not the true lumen is been perfused. Should there be any signs of malperfusion, TEE can be further used to assess the alternative perfusion strategy chosen in such an acute situation.

Several techniques of cannulation should be available to the surgeon. In unstable redo cases particularly, the patients should be connected to the bypass circuit prior to sternotomy. If peripheral venous cannulation is chosen, the right femoral vein is an easier and more direct access to the right atrium than the left femoral vein. The axillary artery, particularly on the right side, has gained increasing popularity among surgeons for several reasons. First, it is a peripheral artery and therefore can be used for cannulation before sternotomy. Second, perfusion through the right axillary is often a secure access to the true lumen and therefore a means of avoiding malperfusion. Lastly, perfusion

through the axillary is an easy way to secure a selective antegrade cerebral perfusion if an arch procedure is to be undertaken during the procedure. Perfusion of the axillary artery concomitant with clamping of the innominate and subclavian artery gives direct access of blood flow to the right carotid and therefore a secure perfusion of the Circle of Willis. If this perfusion leads to a stream of blood coming from the orifice of the left carotid, the circulus of Willis is intact, and this perfusion should be an adequate antegrade perfusion of the brain, particularly if the carotid and left subclavian arteries are clamped with an atraumatic clip to increase the pressure in the cerebral perfusion. Should there be no flow coming from the left carotid, this could be a sign of a non-functioning Circle of Willis. In such a case, a single arterial line perfusing the carotid will allow antegrade perfusion of the left part of the brain.

The extensive use of the right axillary artery for antegrade perfusion has challenged the use of deep hypothermic circulatory arrest (DHCA). Since Griep developed the technique of DHCA<sup>20</sup>, this has been used extensively as an adjunct for brain protection during arch surgery. However, selective antegrade perfusion through the right axillary artery can be done during arch reconstructions without interfering with surgery, and the demand for the extra protection from temperatures in the range 15–18°C is therefore not as necessary. Several surgeons have therefore started to do these extensive procedures in the 20°C temperature range instead of DHCA, and a new routine of perfusion will therefore probably be instituted widely as more experience is gathered using this perfusion.

In cases of extensively damaged aortas leading to malperfusion during CPB from the first-choice artery (e.g., the femoral or axillary), a useful alternative can be to introduce the cannula through the left ventricular apex. Guided by TEE, these cannulas can be brought through the aortic valve and into the true lumen of the aorta. However, when perfusing the artery through such a cannula, the aortic valve will be rendered insufficient, and the surgeon will have to make sure that the left ventricle will not be overinflated or volume loaded through retrograde perfusion. A bimanual compression of the ventricle will counteract such a damaging impact.

Many experienced surgeons will not clamp the aorta during the cooling period. The rationale for this self-imposed restriction in using the cooling time to reconstruct the root is to avoid undue pressure on the false lumen by clamping the ascending aorta. Clamping can increase the pressure and subsequently lead to more extensive damage of the aorta through more entry-reentries, malperfusion, or in the worse of cases an induced rupture.

A sound principle when reconstructing the ascending aorta has been to do a small procedure and sparing the valve and root, if at all possible. However, emerging evidence<sup>17,21,22</sup> indicates that a composite graft or complete recon-

struction of the aortic root do not increase mortality or morbidity. A valve sparing procedure has also been done extensively with good immediate results<sup>23</sup>.

To what extent the arch should be replaced during the initial operation is a long-standing controversy<sup>22,24</sup>. This is more than anything a surgical “art” question and should be governed more by the demand to have a live extubated patient the day after surgery than to avoid a possible reoperation in years to come.

## STATISTICAL UNCERTAINTIES IN TREATMENT DOCUMENTATION

A population of nonsurgically treated patients with acute Stanford type A dissections would probably have a 90-day mortality in the order of 70–90%. Data from IRAD<sup>25</sup> show that the in-hospital mortality among 87 patients with a Stanford type A dissection treated medically was 58% (47 patients). This dismal natural history is dramatically altered by surgical treatment, and the in-hospital mortality among the 208 patients in the initial IRAD experience with acute Stanford type A dissection treated surgically was 26% (54 patients). This is a therapeutic “slam-bang” effect that does not need more than a few consecutive series to prove its superior merit<sup>26</sup>. Furthermore, this clear treatment advantage translates into the undisputed logic of treating patients in extremely deranged clinical settings and also treating patients in the advanced age groups.

However, due to the acuity, life-threatening nature, relative rarity, and the treatment difficulties related to this serious disease, the best methods to evaluate treatment outcomes (randomized trials and rigorously matched cohort or case-control observational studies) are hard, if not impossible, to conduct. When treatment trends and traditions evolve, clinicians have to trust the logical superiority of evolving technology more than statistically high-powered studies. This is commented by Jean Bachel in an editorial on surgical treatment of acute dissections stating that “surgery is not a science, it is a technological structure managed, performed and developed daily by technicians”<sup>27</sup>. The craft of cardiovascular surgery certainly has a scientific foundation, but the application of this trade is managed on a daily basis by technicians developing their craft through knowledge, experience, and the challenge of a complicated surgical disease.

To demonstrate the level of evidence base for treatment choices in the surgical management of acute aortic dissection, we did a review of the studies documenting surgical treatment recommendations in acute aortic dissection<sup>26</sup>. We chose three central questions as clinical examples illustrating the scientific basis for therapeutic tradition. These questions were whether an open distal anastomosis was superior to clamping the aorta and selectively do the arch in

circulatory arrest (Table 9.1), whether a persistent false lumen would influence long-term outcome (Table 9.2), and whether surgical or medical treatment in the initial phase of an acute Stanford type B dissection was to be preferred (Table 9.3).

The most relevant literature addressing the question of whether or not an open-distal anastomosis is preferable is referenced in Table 9.1. These studies are uniformly underpowered, and most represent retrospective patient series using historical controls. Therefore, the studies give a description of this treatment alternative that can be characterized as “logical, relatively safe but it can not be the whole answer to the suboptimal results of surgical treatment”. Are such studies therefore unnecessary and of little interest to the practicing cardiovascular surgeon? Certainly not; they are describing the treatment effects of what some of the most influential and experienced surgeons can achieve in the present era. Maybe the most important message to be learned from these reports is that the demand for randomized trials and high powered studies is not necessary or productive for diseases like aortic dissection. The words of E. Stanley Crawford hold true more than 20 years after they were written: “Ideally, a randomized trial should be conducted to determine the indications for including the arch in all replacement operations for acute DeBakey type I aortic dissections. However, because of the variability that can be expected among patients with acute dissections involving the ascending aorta, a large group of patients would be required, and a very long-term follow-up would be necessary to determine the probability of freedom from an unfavorable outcome events. Such a study will probably not be done”<sup>24</sup>.

The second illustrative question in our survey was whether a persistent false lumen would influence long-term outcome after the initial dissection. A persistent false lumen is viewed as a bad sign for all clinicians involved in the follow-up of patients with aortic dissection and leads to a sharpened indication for more aggressive conservative treatment and maybe earlier surgery in the chronic phase. Surprisingly, the documentation for this concept is almost lacking. Since our study, some more evidence favoring the perception of a persistent false lumen as an ominous sign<sup>41</sup> has emerged, but still this documentation is rather inadequate. However, this is an example of a question that is possible to answer in large registries, and hopefully registries like the IRAD can be of help to put this concept into the right perspective.

Lastly, we reviewed studies comparing the outcome from treating acute B dissections medically or surgically. This is a question that lends itself to a randomized design, but by tradition, the mainstream treatment of acute B dissections has been conservative. However, as the groups at New York University and Stanford have challenged the conservative treatment tradition, we need to look more carefully at the documentation available today. As demonstrated in

Table 9.1. Effect of an open distal technique<sup>a</sup> on surgical outcome

Study	Design	Patients	Results	Comments
Baylor College of Medicine (Crawford, 1992) <sup>24</sup>	Retrospective series. Multivariable risk-factor analysis. Open distal not entered in analysis (circulatory arrest serves as substitute).	<i>N</i> = 82 (1968–1992). Routine HCA and open anastomosis used from 1981.	Circulatory arrest not significant factor in predicting surgical outcome.	Continuing improvement of results during the period with no direct evidence of benefit of open-distal technique. Multiple factors altered during the period.
University of Philadelphia (Bavaria, 1996) <sup>29</sup>	Retrospective case-control design (historical controls). Comparing selective HCA <sup>b</sup> (group 1) with routine open distal technique (group 2).	<i>N</i> = 41 (group 1) (1987–1995), <i>N</i> = 19 (group 2) (1993–1995).	60-day mortality: group 1, 29% (12/41), group 2, 5% (1/19), <i>p</i> = 0.04. CVA: group 1, 6% (10/38), group 2, 0% (0/19), <i>p</i> = 0.02.	Selection criteria unclear. Multiple alterations in protocol concomitant with open distal (use of retrograde cerebral perfusion, EEG, TEE, drug alterations, more use of composite grafts).
Kobe University (Yamashita, 1997) <sup>30</sup>	Retrospective case-control design (historical controls). Comparing cross-clamped ascending repair (group 1) with routine open distal technique (group 2).	<i>N</i> = 27 (group 1) (1986–1991), <i>N</i> = 16 (group 2) (1991–1996).	Operative mortality: group 1, 19% (5/27), group 2, 19% (3/16). Persistent false lumen: group 1, 50% (9/18), group 2, 13% (2/13), <i>p</i> < 0.05.	Unequal graft techniques between groups. Most persistent false lumens found in patients operated with ring grafts (16/18 ring grafts used in group 1). Short follow-up in group 2. Effect on long-term survival uncertain.

Table 9.1. (Continued)

Study	Design	Patients	Results	Comments
University of Bern <sup>31</sup> (Nguyen, 1999)	Retrospective case-control design (historical controls). Comparing cross-clamped ascending repair (group 1) with routine open distal without (group 2) or with (group 3) use of glue.	N = 20 (group 1), N = 16 (group 2), N = 18 (group 3)	Operative mortality: group 1, 13% (3/23), group 2, 15% (3/20), group 3, 18% (4/22). Long term distal aneurysm: group 1, 20% (4/20), group 2, 13% (2/16), group 3, 11% (2/18), $p < 0.05$ (1 vs. 3).	No information on exact year of operation or whether the follow-up time was different in the three groups (probable difference, deducted from discussion). No details of aneurysmal development (diameter, rupture, survival effect).
University of Toronto (David, 1999) <sup>32</sup>	Retrospective case-control design (historical controls). Comparing selective HCA (group 1) with routine open distal technique (group 2).	N = 55 (group 1), N = 54 (group 2). (1979–1996, time period separating the two groups not given)	Operative mortality: group 1, 20% (11/55), group 2, 9% (5/54), $p = 0.1$ Strokes: group 1, 15% (8/55), group 2, 4% (2/54), $p = 0.05$ . A non-significant tendency toward less persistent false lumens and longer survival was observed in group 2.	Time point discriminating the two groups and detailed operative protocols (including other potentially altered factors) not given.

Table 9.1. (Continued)

Study	Design	Patients	Results	Comments
Stanford University (Lai, 2002) <sup>22</sup>	Retrospective case-control design (historical controls). Subgroup analysis using propensity scoring. Comparing profound hypothermic circulatory arrest (PHCA, group 1) with patients were no PHCA was used (group 2).	$N = 121$ (group 1), $N = 186$ (group 2) (1967–1999). Subgroup propensity: $N = 113$ , PHCA $N = 39$ , no PHCA.	Survival overall: 30-day, $81 \pm 2\%$ , 1-year, $74 \pm 3\%$ , 5-year, $63 \pm 3\%$ . No difference between PHCA and no-PHCA in any groups.	Long time period with concomitant time-related changes in surgical methods (historical controls). Large series of patient with careful statistical approach, but unequal and small numbers in propensity-matched groups.

*Source:* Table includes studies found in the literature where this has been addressed as a separate issue. Tables 9.1, 9.2, and 9.3 are reproduced from Myrnel et al. (2004) Eur. J. Cardioth. Surg. 25, 236–242, with permission from Elsevier.

<sup>a</sup> Open distal technique: the use of routinely hypothermic circulatory arrest and construction of the distal anastomosis without aortic clamp.

<sup>b</sup> Selective HCA (hypothermic circulatory arrest), HCA used when intimal tear extended to arch (20 of 41 patients in group 1). CVA = cerebrovascular accident, EEG = electro-encephalogram, TEE = transesophageal echocardiogram.

Table 9.2. Effect of a persistent false lumen on surgical outcome (rupture, reoperation, and death)

Study	Design	Patients	Results	Comments
Mount Sinai Medical Center (Ergin, 1994) <sup>33</sup>	Retrospective case-control design. Comparing survival in patients with persistent (group 1) and occluded (group 2) false lumen after surgery for acute type A dissection.	$N = 18$ (group 1), $N = 20$ (group 2) (1986–1992). Subgroup of acute type A dissections with observed preoperative distal false aortic lumen.	5-year survival: group 1, 76%, group 2, 95%, ns. 5-year event-free: <sup>a</sup> group 1, 63%, group 2, 84%, ns.	Two different surgical techniques were used—25 suture anastomosis and 13 intraluminal grafts. Persistent false lumen was observed in 30% of the intraluminal grafts (4/13) and 56% of suture (14/25).
Southampton General Hospital (Barron, 1997) <sup>34</sup>	Retrospective case-control design. Comparing aortic diameter in patients with (group 1) or without (group 2) persisting false lumen after surgery for acute type A.	$N = 29$ (group 1), $N = 11$ (group 2). 20 years subgroup of all patients (40/87) with surgically treated acute type A dissection eligible for follow up MRI.	Diameter of the aorta, at hiatus: group 1, 4.4 cm, group 2, 3.4 cm. $p < 0.02$ . In abdomen: group 1, 4.4 cm, group 2, 3.3 cm, $p < 0.01$ .	Complete follow-up of patients eligible for MRI. No difference in the diameter in the ascending aorta and arch.

Table 9.2. (Continued)

Study	Design	Patients	Results	Comments
National Cardiovascular Center, Osaka (Okita, 1999) <sup>36</sup>	Retrospective case-control design. Comparing aortic diameter, persistent false lumen, and aortic events in surgically treated acute type B dissections with the anastomosis to the true lumen (group 1) or both lumens (group 2).	$N = 67$ (group 1), $N = 19$ (group 2). 1978–1998 subgroup analysis of surviving patients (86/119) after surgical treatment of acute type B dissections.	Time-related increase in aortic diameter (hiatus): group 1, 4.5 mm, group 2, 10.1 mm, $p = 0.04$ . Persistent false lumen: group 1, ~25%, group 2, ~95%, $p < 0.001$ . No difference in aortic related events.	Selection and eligibility criteria for different treatment choices not defined.
Mount Sinai Medical Center (Juvonen, 1999) <sup>37</sup>	Retrospective patient series. Risk-factor analysis for rupture in patients with medically treated acute type B dissection.	$N = 50$ subgroup of acute type B dissections (50/120) with at least 2 follow-up CT scans.	Persistent false lumen not a risk factor for rupture.	Highly selected subgroup of patients in an environment of aggressive prophylactic surgery.
University Hospital Jean-Minjoz (Bernard, 2001) <sup>35</sup>	Retrospective patient series. Risk-factor analysis for late death.	$N = 109$ . 1984–1996 average follow-up: $57 \pm 43$ months both acute types A and B dissection in a follow-up study using different (echo, CT, and MRI) imaging techniques.	Persistent false lumen relative risk factor for late death (RR-3.2, 95% CI: 1.17–8.8).	Not stated whether the group of patients is consecutive. Unclear number lost to follow-up. Medical treatment criteria and success in follow-up unknown (i.e., hypertension).

<sup>a</sup> Event-free survival is without rupture, reoperation, or death.

Table 9.3. Comparison between medical and surgical treatment of acute type B dissections

Study	Design	Patients	Results	Comments
Duke University Medical Center and Stanford University Medical Center (Glower, 1990) <sup>38</sup>	Retrospective case-control design. Comparison of long-term outcome in selected surgically (group 1) and medically (group 2) treated type B dissections (both acute and chronic).	$N = 23$ (group 1), $N = 33$ (group 2). 1975–1988 subgroup of good risk patients (55/136).	5-year survival: group 1, 80%, group 2, 87%. 10-year survival: group 2, 50%, group 1, 32%, ns. No difference within other subgroups with more general organ disease.	No randomization. Selection at the discretion of the surgeon.
Mount Sinai Medical Center (Schor, 1996) <sup>39</sup>	Retrospective case-control design. Comparison of long term outcome in selected surgically (group 1) and medically (group 2) treated acute type B dissections.	$N = 17$ (group 1), $N = 48$ (group 2). 1985–1995 most of the patients (65/68) during the study period.	1-year survival: group 1, 93%, group 2, 90%. 5-year survival: group 1, 68%, group 2, 87%, ns.	No randomization. Selection at the discretion of the surgeon.
University of Berne (Gysi, 1997) <sup>40</sup>	Retrospective case-control design. Comparison of long term outcome in selected surgically (group 1) and medically (group 2) treated acute type B dissections.	$N = 38$ (group 1), $N = 187$ (group 2). 1980–1995 all patients.	5-year survival: group 1, 85%, group 2, 76%. 10-year survival: group 1, 67%, group 2, 50% $P < 0.001$ .	No randomization. Selection at the discretion of the surgeon. Unequal group size in the comparison.
Stanford University (Umana, 2002) <sup>19</sup>	Retrospective case-control design. Subgroup analysis using propensity scoring. Comparing long-term outcome in selected surgically (group 1) and medically treated patients (group 2) with acute type B dissections.	$N = 67$ (group 1), $N = 122$ (group 2). 1963–1999 subgroup propensity: $N = 31$ , surgical, $N = 111$ , medical.	Survival overall: 1 year, 71%, 5 years, 60%, 10 years, 35%, 15 years, 17%. No difference in survival, freedom from reoperation or freedom from aortic complications overall or in propensity matched groups.	No randomization. Large time span. Small number of surgical patients eligible for propensity matching.

Table 9.3, the scientific basis for choosing one over the other is almost nonexistent. This also makes a conceptual background when the introduction of stent grafting is emerging.

## WHY DOES SURGICAL MORTALITY REMAIN HIGH?

Surgical treatment of acute aortic dissections remains a tour de force, and the operative mortality still remains in the level of 20% and upward in many centers, including very experienced institutions<sup>17,22</sup>. Why has the early mortality not shown the same overall positive trend as other cardiovascular procedures in high-risk patients (such as ischemic mitral valve surgery)? Two case reports from the IRAD experience may illustrate the complexity and challenges involved when treating these patients.

### CASE 1

A 72-year-old woman was admitted to a community hospital with back pain radiating into the chest. On admittance, her blood pressure was 220/110 mm Hg, and the ECG was remarkable for a 2 mm ST-elevation in leads V1 to V3. The patient was thought to have unstable coronary disease and treated with nitroglycerine and low molecular weight heparin (LMWH). After initiation of this treatment, the patient became hypotensive with loss of sensibility and motion in her legs and with no palpable pulses in her groins. A CT scan was obtained (Figure 9.2). The CT scan and patient was transferred to the IRAD center and the patient was brought directly to the OR. A strategy of direct surgery was chosen with the intention to relieve the compromised circulation in the descending aorta and treat the life-threatening affection of the ascending aorta.

At the initiation of anesthesia, the patient became abruptly in deep shock with no arterial pressure measurable. She was given heparin directly, her femoral vessels cannulated, and her chest opened. A large accumulation of blood was found in the right pleural cavity. Extracorporeal circulation was initiated, and her blood volume replenished. On surgery, both the left and non-coronary aortic leaflets were found to be destroyed, and the aortic root was replaced with a Medtronic Freestyle 23 mm graft. The ascending aorta and hemiarch was replaced by a 24 mm Vascutec Gelweave graft. The patient was transferred to the ICU in stable condition.

The following day, the sedation was stopped to wake the patient for extubation. However, the patient did not regain consciousness and died on day 2 after surgery. An autopsy revealed a large infarct in her right hemisphere and a dissection of the brachiocephalic trunk extending into the right carotid artery.

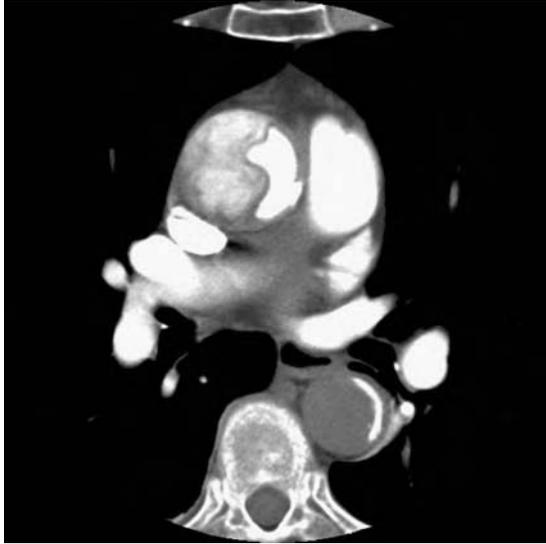


Figure 9.2. An acute Stanford type A dissection in a 72-year-old woman with loss of sensibility in her legs and no pulses in the femoral arteries. Note the relatively large false lumen in the ascending aorta and an almost compressed true lumen in the descending aorta.

### Comment

This patient illustrates several problems when treating patients with acute aortic dissections. Her rupture illustrates a narrow-escape situation and thus the demand for expeditious treatment of these patients. The patients who are late for treatment and thus a large part of patients in tertiary referral centers represent patients with a natural selection toward good-risk cases as many of the most stable patients will be operated late. The most dramatic clinical presentation in this patient was the malperfusion of her lower body. However, by looking at her CT, the very fragile and large ascending aorta is obvious. The route of rupture was from the posterior part of the arch along the intercostals space to the right pleural cavity. Finally, there was no indication of a defect in the brachiocephalic trunk leading to the lethal dissection of the precerebral vessels when looking into the arch vessels during surgery. Thus, despite a technical successful repair in a dramatically unstable patient, the patient succumbed to a not-detected malperfusion of her brain.

### CASE 2

A 62-year-old man was admitted to a community hospital after experiencing acute pain in his jaw and head. He also had a near syncope but did not faint. At admission, his blood pressure was 97/39 mm Hg, and his pulse regular with



Figure 9.3. An acute Stanford type A dissection in a 62-year-old man. Note the completely destroyed intima and perfusion of the false lumen with no protective thrombus leading to an early rupture.

a rate of 58. An ECG revealed a 2 mm ST-elevation in leads II, III, aVF, and V<sub>2-4</sub>. Blood tests revealed a small increase in the myocardial markers CK-MB and Troponin-T. The condition was diagnosed to be an acute coronary syndrome, and LMWH, clopidogrel, and nitroglycerine were administered. The patient was transferred to the IRAD unit for a coronary arteriography. On admission, the blood pressure was 115/63, and a clear diastolic aortic murmur was observed. An echocardiogram in the ER was diagnostic for a Stanford type A dissection. A CT scan was obtained while an OR was prepared (Figure 9.3), but the patient suddenly collapsed and was resuscitated while taken by the emergency team to the OR. He was immediately connected to a CPB circulation trough cannulation in the groin, and the sternum was opened. A very large cardiac tamponade was relieved when opening of the pericardium was performed, with all four chambers compressed.

The operation was from this point uneventful, and the ascending aorta was replaced by a supracoronary graft while the root was conserved. However, the patient did not recover consciousness, and a CT scan demonstrated diffuse cerebral damage compatible with global hypotension. He died after two days, and an autopsy revealed diffuse cerebral damage.

### Comment

In this patient, the tamponade and following complete circulatory collapse due to a high-pressure accumulation of blood in the pericardium probably pre-

vented an effective resuscitation before the institution of cardiopulmonary bypass. Thus, despite a technically successful procedure, the preoperative treatment was inadequate as a means of securing cerebral perfusion.

## THE WAY AHEAD: WILL BETTER IMAGING AND PRECISE DIAGNOSTICS ALLOW FOR ACCURATE AND MINIMALLY TRAUMATIC TREATMENT?

The single most important goal when handling patients who need surgical treatment for aortic dissection is to get the patients through the initial stabilization and subsequent surgical procedure alive. The experiences documented in IRAD point to a series of negative predictors related to mortality for both acute type A and acute type B aortic dissection (Table 9.4).

It is apparent from these data that the patient with an unstable circulation in tamponade or hypovolemic shock belongs to the approximately 25% of type A dissections and 8% of type B dissections that succumb during their index stay in the present era<sup>25</sup>. How can the treatment of these patients be altered to reduce their immediate mortality?

Based on a single series with an operative mortality of 6.3%, Westaby<sup>44</sup>, and Bechet<sup>45</sup> in an accompanying editorial, call for a refined and simplified surgical approach. However, an overwhelming amount of data indicates that a hospital mortality of well over 10% is more the rule than the exception even in very experienced centers<sup>17</sup>. It is also important to realize that although the surgical mortality has declined for almost all cardiac surgical procedures, this is not the case for aortic dissections despite refinement for all technical aspects of surgery. Does an improvement demand a completely altered surgical approach to this condition?

In our opinion, refining our surgical technique will not be enough to save these extremely ill patients in complete circulatory compromise. Even in the most experienced centers, the treatment of these patients is a formidable task,

*Table 9.4.* Negative predictors related to surgery for acute aortic dissection, the IRAD experience (OR; odds ratio)

Acute type A (Mehta, 2002) <sup>42</sup>		Acute type B (Suzuki, 2003) <sup>43</sup>	
Kidney failure	OR 4.77	Hypotension/shock	OR 23.8
Hypotension/shock/tamponade	OR 2.97	Lack of chest/back pain	OR 3.5
Abrupt onset of pain	OR 2.60	Brachial vessel involvement	OR 2.9
Any pulse deficit	OR 2.30		
Abnormal ECG	OR 1.77		
Age over 70 years	OR 1.70		



Figure 9.4. The scan is from a 58-year-old man with an acute type B dissection. As shown, the left kidney has no perfusion, and the left renal artery comes off the false lumen. Also, the perfusion of the right kidney is marginal due to the scant perfusion of the right renal artery. The right kidney was saved by auto transplantation.

and adding a surgical trauma to their extreme situation will probably be disastrous to many patients in the future. A possible alternative approach would be to treat these patients in a modern radiology/OR suite with two primary aims: to rapidly determine the major pathological aortic segment using precise and rapid imaging techniques and attack this pathology using percutaneous techniques aimed at the defects only in an attempt to do a rescue procedure alone. Such an approach will depend heavily on physicians with precise clinical understanding of these patients who also can master the diagnostics and intervention radiology techniques to rapidly reverse an almost lost situation.

What can be done in the radiology or interventional surgery suite with these patients? First and foremost, they demand a team with determined anesthesiologists, cardiologists, radiologists, surgeons, or physicians with particular skills in handling these complex patients. Important points to address will be to close the sites of entry and/or rupture with covered stent grafts concomitant with ongoing resuscitation and handling of an acute tamponade or occluded coronary arteries. Probably the most challenging will be to rapidly address cerebral, spinal, and renal malperfusions. Figure 9.4 illustrates the use of such combined procedures. This 58-year-old man presented with gross malperfusion of his kidneys and an almost occluded true lumen from an expanding false lumen. A stent graft was immediately placed over the primary entry site to expand the

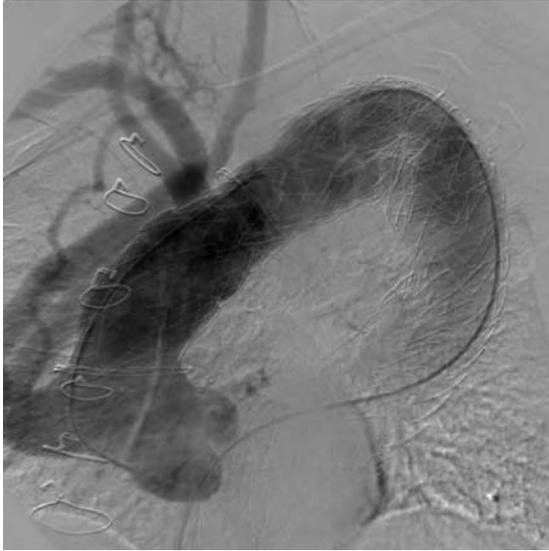


Figure 9.5. Complete debranching of the aortic arch covered by stent graft for arch aneurism and intrathoracic bypass between ascending aorta, innominate artery, and left common carotid artery.

true lumen and therefore improve the intestinal perfusion. The left kidney was reperfused by fenestration but was permanently damaged from long-standing complete ischemia. In the ensuing weeks, the function of the right kidney was marginal, and after 3 weeks, the kidney was auto transplanted into the pelvis with subsequent normalization of kidney function.

Treating a destroyed aortic valve with percutaneous techniques will also be a demanding task. However, it can be envisioned in a foreseeable future.

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SECTION IV:  
SUBSEQUENT FOLLOW-UP AND  
TREATMENT

# 10

## LONG-TERM MEDICAL THERAPY IN AORTIC DISSECTION

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The long-term approach to patients with successful initial treatment of acute aortic dissection is based on the understanding that such patients have a systemic illness that predisposes their entire aorta and potentially its larger branches to dissection, aneurysm, and rupture and that assiduous long-term follow-up for these patients is crucial. Systemic hypertension, advanced age, baseline aortic size, and presence of a patent false lumen are all factors that identify higher risk, as does the entire spectrum of the Marfan's syndrome<sup>1,2</sup>. All patients merit extremely aggressive medical therapy, follow-up visits, and serial imaging. Data suggest that nearly a third of patients surviving initial treatment for acute dissection will experience dissection extension or aortic rupture or will require surgery for aortic aneurysm formation within five years of presentation<sup>2</sup>. Furthermore, this risk is highest in the first few months after initial therapy. The cornerstones of optimal long-term therapy include adequate beta-blockade and additional therapies to achieve optimal blood pressure control and lipid-lowering therapy.

## OPTIMAL BLOOD PRESSURE CONTROL

### BETA BLOCKADE

Treatment with effective beta blockade is an important component of medical therapy. Beta blockers lower blood pressure and decrease  $dp/dt$  and have been shown to retard aortic expansion associated with Marfan's syndrome<sup>1</sup> and that associated with chronic abdominal aortic aneurysms<sup>3</sup>. In a cohort of patients with the Marfan syndrome, Shores et al.<sup>1</sup> demonstrated that the mean slope of the regression line for the aortic-root dimensions, which reflect the rate of dilatation, was significantly lower in the beta-blocker group than in the control group (0.023 vs. 0.084 per year,  $p < 0.001$ ) (Figures 10.1 and 10.2). Current guidelines recommend progressive increase of dosage of these agents to achieve a blood pressure  $< 135/80$  mm Hg in usual patients and  $< 130/80$  mm Hg in those with Marfan's syndrome<sup>4-6</sup>. It seems reasonable, however, to extend aggressive blood pressure goals to most patients, unless a specific contraindication exists (such as visceral malperfusion).

Given the clear benefits of beta blockers in Marfan patients, it is reasonable to impute that chronic beta blockade would be beneficial for long-term aneurysm management in non-Marfan patients. While short-acting preparations are useful for titration of doses, once-daily beta-blocker preparations ensure compliance and tend to minimize side effects and are thus preferred over shorter-acting beta blocker agents.

### CALCIUM CHANNEL BLOCKADE

Although no data exist for the use of calcium antagonists for the long-term management of aortic dissection, these agents remain a reasonable alternative for those patients who are beta-blocker intolerant. In addition, those calcium channel antagonists with negative inotropic or negative chronotropic effects (verapamil, diltiazem) may be reasonable for treatment of those patients in whom a suboptimal response to beta blockade (such as tachycardia despite attainment of maximal doses) is observed. Due to their vasodilating effects, shorter-acting dihydropyridine calcium channel blocker agents should not be used in the absence of beta blockade, due to the risk of reflex tachycardia, with concomitant increase in  $dP/dT$ . Longer-acting agents such as amlodipine are reasonable due to the reduced risk of reflex tachycardia, but these agents should be used only after adequate beta blockade has been established.

### OTHER AGENTS

No data exist for the use of other vasodilator agents (such as angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, diuretics, or

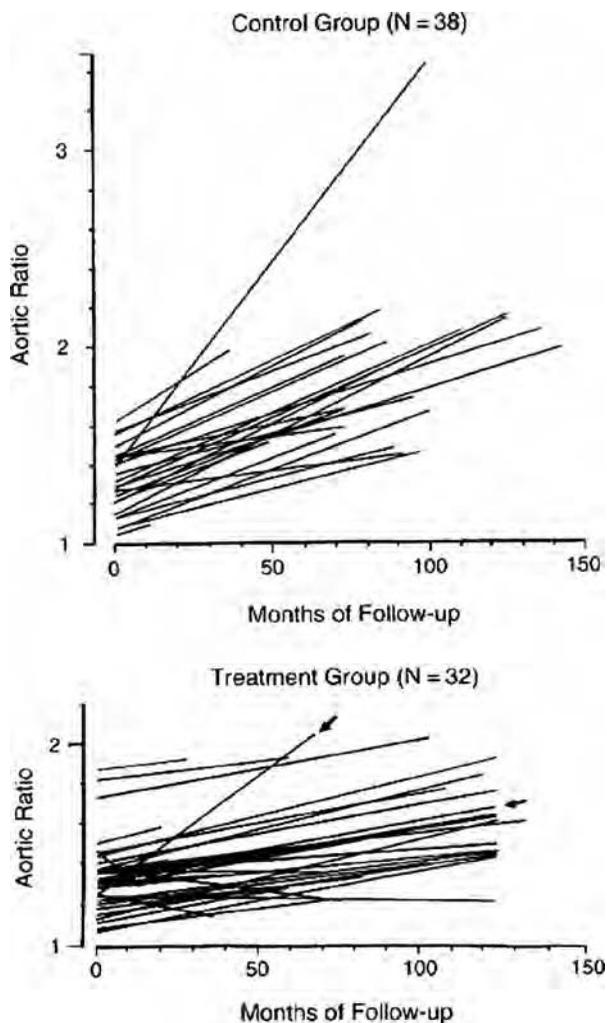


Figure 10.1. Changes in the aortic ratio in the beta-blocker group and the control group. The aortic ratio is the ratio of the diameter of the aorta measured in a patient to the diameter expected in a subject with the same body-surface area and age. The ratio in each patient is presented here as a fitted regression line: the data points are not shown, but the length of each line indicates the length of follow-up. One patient in the control group had an exceptional aortic ratio ( $>3.4$ ) at 100 months. Two patients in the beta-blocker group (arrows) did not comply with propranolol therapy. Adapted from Shores et al.<sup>1</sup>

alpha blockers) in the setting of chronic aortic disease. Logic would dictate that such agents would be of benefit for their antihypertensive effects, but only in the presence of good heart rate control with a beta blocker (preferred) or calcium blocker.

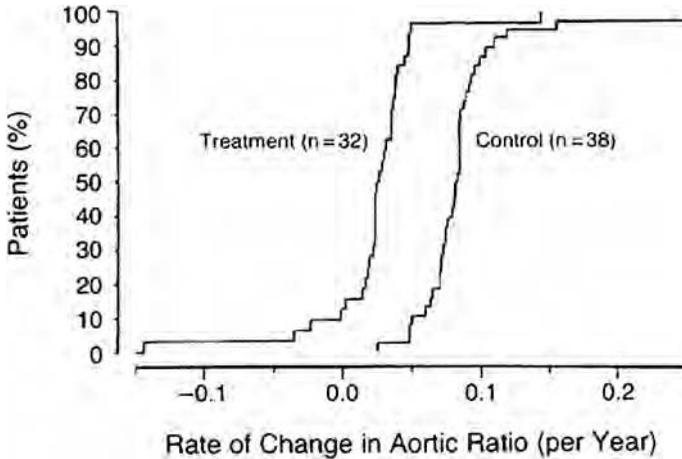


Figure 10.2. Empirical distribution functions of the rate of change in the aortic ratio, according to study group. The height of each curve at any point shows the proportion of patients with values at or below the value given on the  $x$  axis. There is little overlap between the beta-blocker treated and control groups. Adapted from Shores et al.<sup>1</sup>

### Lipid-Lowering Therapy

Kertai et al. assessed the potential long-term beneficial effects of statin use after successful abdominal aortic surgery and demonstrated that long-term statin use is associated with reduced all-cause and cardiovascular mortality irrespective of clinical risk factors and beta-blocker use<sup>7</sup>. After adjusting for clinical risk factors and beta-blocker use, the association between statin use and reduced all-cause (hazard ratio [HR] = 0.4; 95% confidence interval [CI]: 0.3 to 0.6;  $p < 0.001$ ) and cardiovascular (HR = 0.3; 95% CI: 0.2 to 0.6;  $p < 0.001$ ) mortality was robust and highly significant<sup>7</sup>. Mechanistically, statins can directly modulate the biology of the aorta and suppress MMP-9 production in the aortic wall by inhibiting the activation of neutrophils and macrophages. It is probable that such therapy can be useful for the prevention or treatment of aortic aneurysms<sup>8</sup>. At this point in time, it is reasonable to optimally control lipid levels with statins in patients with aortic aneurysms and dissections with a currently recommended target LDL of  $<70$  mg/dl<sup>9</sup>. This is particularly true of the patient with intramural hematoma, consequent to penetrating atherosclerotic ulceration, a syndrome related to classic aortic dissection, whose etiology is dependent on unstable atherosclerosis of the aorta.

### Serial Imaging

Imaging of the aorta is an important component of long-term treatment and follow-up of patients with aortic aneurysm (before and after surgery or stent-

graft placement) in Marfan's disease and in all cases of chronic dissection. Choice of imaging modality is dependent on institutional availability, expertise, as well as extent of aortic involvement and possibly the age of the patient. Generally speaking, unless a contraindication exists (such as elevated serum creatinine), contrast-enhanced computerized tomography (CT) appears to be the method of choice in most centers. A very reasonable alternative would be magnetic resonance imaging (MRI), as it affords comparable sensitivity and specificity as CT scanning. Neither CT scanning or MRI afford functional images of the cardiac structures. Thus, in the presence of significant valvular regurgitation due to aneurysm formation, transesophageal echocardiography is reasonable but difficult to recommend on a routine basis.

Recommendations are for follow-up imaging and examination at 1, 3, 6, 9, and 12 months after discharge and annually thereafter<sup>6,10</sup>. This aggressive strategy is based on the fact that both hypertension and aortic expansion/dissection are common and not easily predicted in the first months after hospital discharge, despite apparent stability. Imaging should not be limited/confined simply to the region of initial involvement because both dissection and aneurysm formation may occur anywhere along the entire length of the aorta. Of particular concern are patients with patent false channels of the aorta. Since the aortic wall is only buttressed by the adventitia in regions of a false channel, this portion of the aorta is weak and prone to expansion and rupture.

Development of an ascending aortic diameter of 5–5.5 cm is an indication for surgical repair in patients with Marfan's syndrome. For others, aortas exceeding 5.5–6 cm warrant repair, as does distal aortic expansion to  $\geq 6.0$  cm in all types of patients. As with nondissecting aneurysms, rate of growth and size of the aorta are important factors to consider when it comes to prophylactic vascular surgery. An ascending aortic aneurysm of 5.0 cm may merit urgent repair in a young patient with Marfan's syndrome but an aneurysm of 5.0 cm for 3 years in an elderly person with well-controlled blood pressure is unlikely to rupture and may not require repair<sup>11</sup>. Patients who have been treated with surgery and/or endovascular stent grafting warrant similar follow-up to those whose initial strategy was limited to medical treatment. Aortic expansion, dissection, and rupture both at the surgical suture site and at a distance are common in survivors of type A or B dissection. Meticulous attention to blood pressure control and serial imaging are just as relevant to operative survivors as for patients in early stages of aortic pathology.

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# 11

## **ACUTE AORTIC SYNDROMES: SURVEILLANCE WITH IMAGING**

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Acute aortic dissection (AAD) is an uncommon but catastrophic cardiovascular emergency, with an early mortality as high as 1% per hour if untreated<sup>1</sup>. However, with a prompt diagnosis and appropriate medical and/or surgical management, early survival can be significantly improved to 70–90%<sup>2</sup>. Even with successful “definitive” in-hospital treatment of aortic dissections, patients remain at considerable risk for late dissection, as well as for aortic aneurysm formation and rupture<sup>3,4</sup>. Thus, serial follow-up visits and imaging studies are mandatory to prevent life-threatening complications. This comprehensive chapter underlines the necessity of surveillance with imaging of patients who have experienced successful initial treatment of AD and focuses on diagnostic performance and the practical utility of each imaging modality.

## LONG-TERM COMPLICATIONS AND FOLLOW-UP

Although the dissection of the aorta is an acute event, long-term survivors of aortic dissection are also predisposed to late complications, by other factors, including the underlying chronic disease of the aortic wall media, systemic hypertension, advanced age, rate of growth and size of aorta, presence of patent false lumen, and the entire spectrum of Marfan’s syndrome—even after a successful and appropriate medical or surgical management<sup>3–15</sup>. Regardless of the type of dissection (proximal vs. distal, acute vs. chronic) and treatment (surgical vs. medical), at 10 years 15–30% of patients require new surgery for threatening conditions, including aortic expansion leading to re-dissection and rupture, progressive aortic regurgitation requiring aortic valve replacement, organ malperfusion with the risk of dysfunction, and irreversible ischemia<sup>3,5,7,9,16–18</sup>. In particular, enlarging saccular aneurysms, reported to develop in as many as 14–29% of patients with distal dissections, are at high risk of rupture and require prompt surgical repair<sup>3</sup>. Because the risk of aortic lesions is substantial in the first few months after initial therapy, surveillance of the aorta should start during initial hospitalization, with more frequent early follow-up at 1, 3, 6, 9, and 12 months after discharge and annually thereafter, depending also on the size and rate of the increase of the aorta’s diameter<sup>5,18</sup>.

Thus, all patients, regardless of the initial therapeutic strategy implemented (surgical and/or endovascular stent grafting and/or medical) merit extremely close follow-up visits by a specialized team, including (1) long-term medical therapy with beta blockers to lower blood pressure, wall stress, and  $dP/dt$  and (2) serial imaging to detect potential complications in early stages<sup>5,18,19</sup>.

## IMAGING MODALITIES

The ideal tool for the follow-up of aortic diseases should be harmless, be easily repeatable, and offer the possibility of evaluating the morphology (including shape, presence of internal flap and communications sites between true and false lumen in the presence of a dissection, external and internal diameters, and wall irregularities) and the functional status (such as the measurement of inner flows). Furthermore, it is clinically relevant to detect the involvement of the main branches (such as supra-aortic vessels in the thorax and the celiac trunk, renal arteries, and mesenteric arteries) in the abdomen.

The different imaging modalities—namely, transesophageal echocardiography (TEE), magnetic resonance imaging (MRI), and computed tomography (CT)—employed in the diagnosis and subsequent follow-up of patients with aortic dissection are described below, with subsequent considerations regarding their advantages and disadvantages, accuracy, and practical utility.

### TRANSESOPHAGEAL ECHOCARDIOGRAPHY

Transesophageal echocardiography (TEE) is a reliable, accurate, and convenient diagnostic tool for expeditiously evaluating patients with known or suspected AAD<sup>2,18–20</sup> in the emergency room or even in the operating theater. In addition to its high accuracy, it has distinct advantages as it is readily accessible, is relatively noninvasive, and requires no intravenous contrast agents or ionizing radiations<sup>18–27</sup>. Furthermore, it can be performed quickly and at bedside for unstable patients, provides a host of information about aortic anatomy and cardiac function, and may identify alternate cardiovascular pathology, whose symptoms may mimic AAD<sup>27–31</sup>. TEE may also provide important prognostic information, above and beyond clinical risk factors—such as old age ( $\geq 70$  years), pulse deficit, kidney failure, hypotension or shock, abrupt onset of chest pain, and abnormal ECG—that are found to be associated with in-hospital death<sup>32–35</sup>. With regard to this, in our previous work we have reported that in-hospital mortality rates were directly proportional to the number of vessels showing pulse deficits. Hence, the bigger the number of major vessels involved, the higher the mortality<sup>35</sup>. Fluid extravasation into pericardium, pleural space, and/or mediastinum detected by TEE may be a sign of an ongoing penetration and impending rupture. Thus, it has to be considered as an *adverse prognostic indicator*<sup>15,18</sup>. In particular, cardiac tamponade is one of the most common causes of hypotension and death in acute proximal aortic dissection, and every effort should be made to transfer the patient to the operating room for an urgent surgical repair of the aortic tear, with evacuation of the pericardial hematoma<sup>2,18,32,36,37</sup>. On the other hand, the presence of a dissection flap confined to the ascending aorta or a complete thrombosis

of false lumen appears to be a *protective prognostic indicator*, being less frequent in patients who die<sup>14,15,18</sup>. In fact, false lumen thrombosis may induce low flow and low pressure in the false lumen and consequent lower wall stress on the outer aortic wall<sup>14,15,18</sup>.

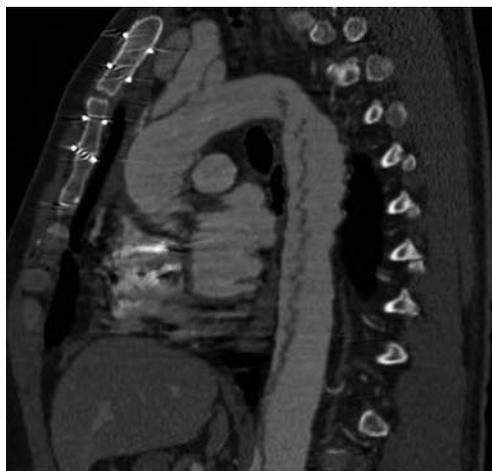
TEE has also been employed for the long-term imaging surveillance of patients with AAD<sup>38–47</sup>. After the initial therapeutic management, a reevaluation with TTE/TEE may be needed to assess the global and segmental functions of the left ventricular wall to detect early signs of progressive aortic dilatation and/or aortic insufficiency, fluid extravasation into pericardium, pleural space, and/or mediastinum, thrombus formation, spontaneous echocardiographic contrast in the false lumen, residual entry, and reentry tears<sup>18,38</sup>. In subsequent follow-ups, MRI or CT scan should be preferred to obtain a more complete anatomical visualization of the aorta and its branches (in particular, the distal part of the ascending aorta, the anterior portion of the aortic arch, and the distal aorta) and to demonstrate a potential involvement of the surrounding tissue<sup>18,20,38</sup>.

Thus, in the light of its accuracy, safety, speed, and convenience, TEE has indeed become the procedure of choice in many hospitals in patients with known or suspected AAD, while it is considered to be less suited than CT and MRI for long-term imaging monitoring of patients with aortic dissection, where a complete and detailed map of the entire aorta and its branches is necessary.

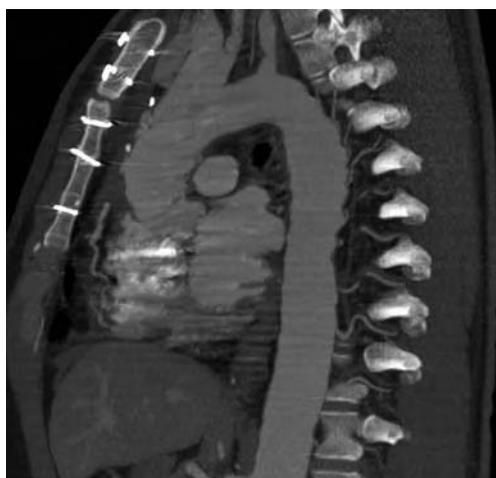
## COMPUTED TOMOGRAPHY

Helical computed tomography (CT) is an highly accurate and most frequently selected imaging technique (sensitivity and specificity of nearly 100%) for the diagnosis of AAD<sup>22–26,48,49</sup>. It has also been proven to be useful to identify atypical forms of AAD, such as intramural hematoma and atherosclerotic ulcers<sup>50,51</sup>.

It has important advantages. It is fast and noninvasive, easy to perform, almost always well-accepted by the patient, and not operator-dependent<sup>52</sup>. It allows three-dimensional visualization of the entire aorta and its branches with a single breath-hold and a single bolus injection (Figures 11.1 and 11.2), and it provides the detection of life-threatening complications such as side branch involvement and fluid extravasation into pericardium, pleural space, and/or mediastinum (Figure 11.3)<sup>53,54</sup>. However, it requires the use of an intravenous contrast agent and presents limitations related to the diagnosis of aortic insufficiency, tear localization, as well as detections of intimal tears and subtle aortic dissection<sup>15–19,23,55</sup>. Pitfalls and artefacts should also be taken into account during the interpretations of CT. Cardiac motion artefacts are more



(a)



(b)

Figure 11.1. Postprocessing of native CT images is required for the evaluation of aortic dissection. Multiplanar reformation (MPR) represents the best reconstruction modality to demonstrate the course of the intimal flap throughout the thoracic aorta ((a), sagittal view), whereas the maximum intensity projection (MIP) does not seem to be able to clearly visualize the intimal flap and does not differentiate the true and the false lumen ((b), sagittal view).

evident at the level of the proximal ascending aorta<sup>56–58</sup>. They consist of localized duplication and pseudo-thickening of the aortic wall and are located mainly in the left antero-lateral and right postero-lateral positions and limited to only few contiguous scans. They can be distinguished from intimal flaps



Figure 11.2. On unenhanced CT scans, the diagnosis of aortic dissection can be indicated by the identification of intimal calcifications displaced toward the aortic lumen, such as in this image (axial scan) at the level of the aortic arch (arrows).

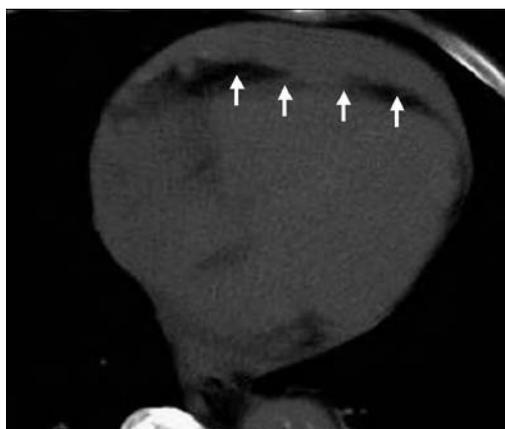


Figure 11.3. Unenhanced CT images are important to identify complications of aortic dissection, such as pericardial effusion (arrows, axial scan), that can be slightly hyperdense, indicating the presence of hemopericardium.

because of their position and shape and by careful analysis of contiguous images. Moreover, the use of cardiac gating can help reducing the cardiac motion artefacts<sup>59,60</sup>. Cardiac gating is limited by reduced volume coverage, limiting the study to the thoracic aorta alone, which is not sufficient when an AAD is suspected. The streak artefacts are hypodense straight lines (Figures 11.4 and 11.5) extending beyond the confines of the aorta and are visible in only a few axial sections caused by the aliasing of markedly attenuating materials,



Figure 11.4. On the arterial phase, the diagnosis of an aortic dissection is based on the identification of the intimal flap that is visible as a thin hypodense band within the opacified aortic lumen, such as in this example (axial scan) of Stanford type A aortic dissection, involving the origin of the ascending aorta (arrow). Pericardial effusion can also be clearly appreciated.

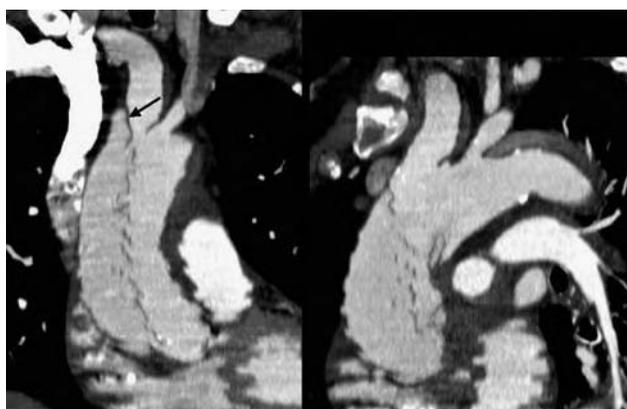


Figure 11.5. The relationship between the intimal flap and the supraaortic vessels can be clearly delineated by MPR reconstruction (coronal and sagittal view). In this example of type A dissection, the origin of the brachiocephalic trunk is involved by the intimal flap (arrow), whereas the left carotid and subclavian arteries are not involved.

cardiac motion, and sharp contrast interfaces, such as the concentration of contrast material within the left brachio-cephalic venous trunk when the bolus is injected into the left arm<sup>61</sup>.

CT is also a useful imaging tool for serial follow-up of patients with AAD, being capable of detecting any increase in aortic diameter, development of false or true lumen aneurysms (Figures 11.6–11.10), organ malperfusion, and leakages at anastomoses or stent sites (Figures 11.10–11.14)<sup>62</sup>. Furthermore,



Figure 11.6. The false lumen can be identified through the “beak sign”, represented by an acute angle between the dissection flap and the outer wall of the aorta at the level of the false lumen (arrow, axial scan).

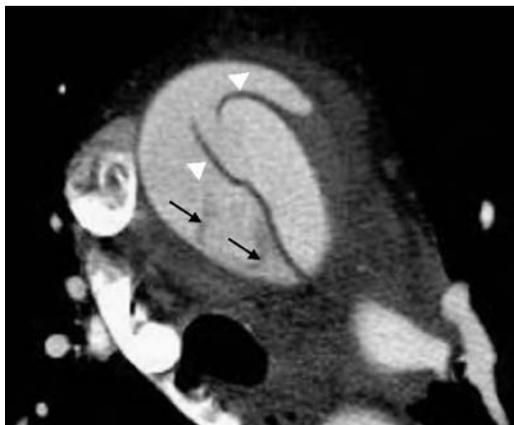


Figure 11.7. Another sign that may allow the identification of the false lumen is the “cobweb sign”; the cobwebs appear as fine, hypodense linear areas within the false lumen, attached to the aortic wall (arrows, axial scan). The intimal tears are also clearly delineated within the ascending aorta (arrowheads).

it may monitor healing or progression of intramural hematoma to a saccular or fusiform aneurysm (Figure 11.13)<sup>63</sup>. Finally, helical CT scanning is very useful in identifying static or dynamic obstruction of abdominal branch vessels associated with increased mortality and morbidity rates in AAD patients (Figure 11.11)<sup>64,65</sup>.



Figure 11.8. The false lumen can be completely thrombosed. In this case, the presence of displaced intimal calcifications (arrow, axial scan) can help differentiating the dissection from an aortic aneurysm or partial thrombosis.

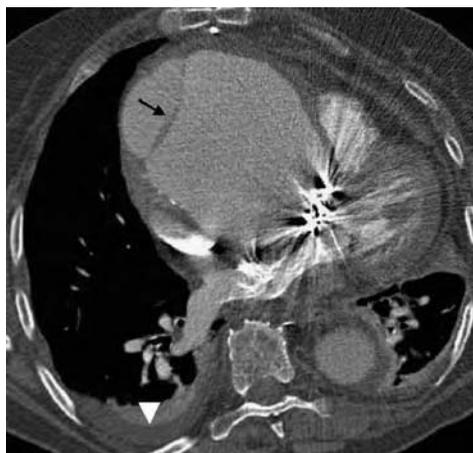


Figure 11.9. Aortic rupture can occur after dissection. In this example, a dissected and dilated ascending aorta can be clearly appreciated. The opacified lumen appears irregular and highly dilated, indicating an impending rupture. The intimal flap can be clearly visualized (arrow). Moreover, pericardial and pleural effusion (arrowhead) are appreciated as complications of the dissection.



Figure 11.10. The involvement of aortic branches in the dissection has to be analyzed carefully starting from the supraaortic vessels, whose involvement can cause neurologic complications. Intimal tears can be appreciated on the axial scan (arrows) at the level of the brachiocephalic trunk and left carotid arteries.

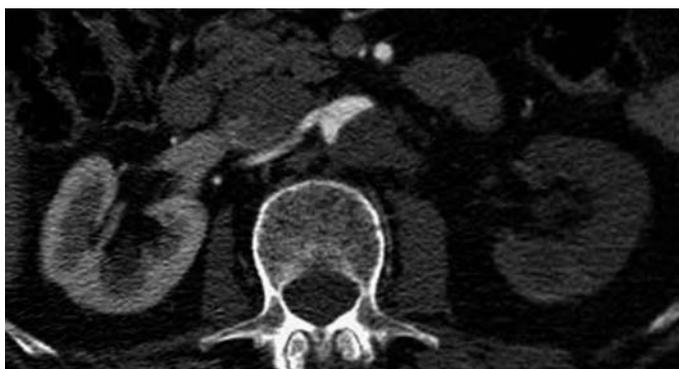


Figure 11.11. Also the splanchnic arteries need to be carefully visualized. In this axial scan, the left renal artery is included in the false lumen that is completely thrombosed, and therefore the renal artery is completely occluded, causing the acute ischemia of the left kidney.

## MAGNETIC RESONANCE IMAGING

In the last decade, MRI has reached a level of development that allows it to be considered the most powerful tool in the diagnostic process of aortic diseases. Images obtained in a modern MRI scanner, in fact, give morphologic and functional information with high diagnostic accuracy of thoracic and abdominal aorta, as well as of its main branches. The combination of the different kinds of images obtainable leads to a comprehensive evaluation of histopathol-

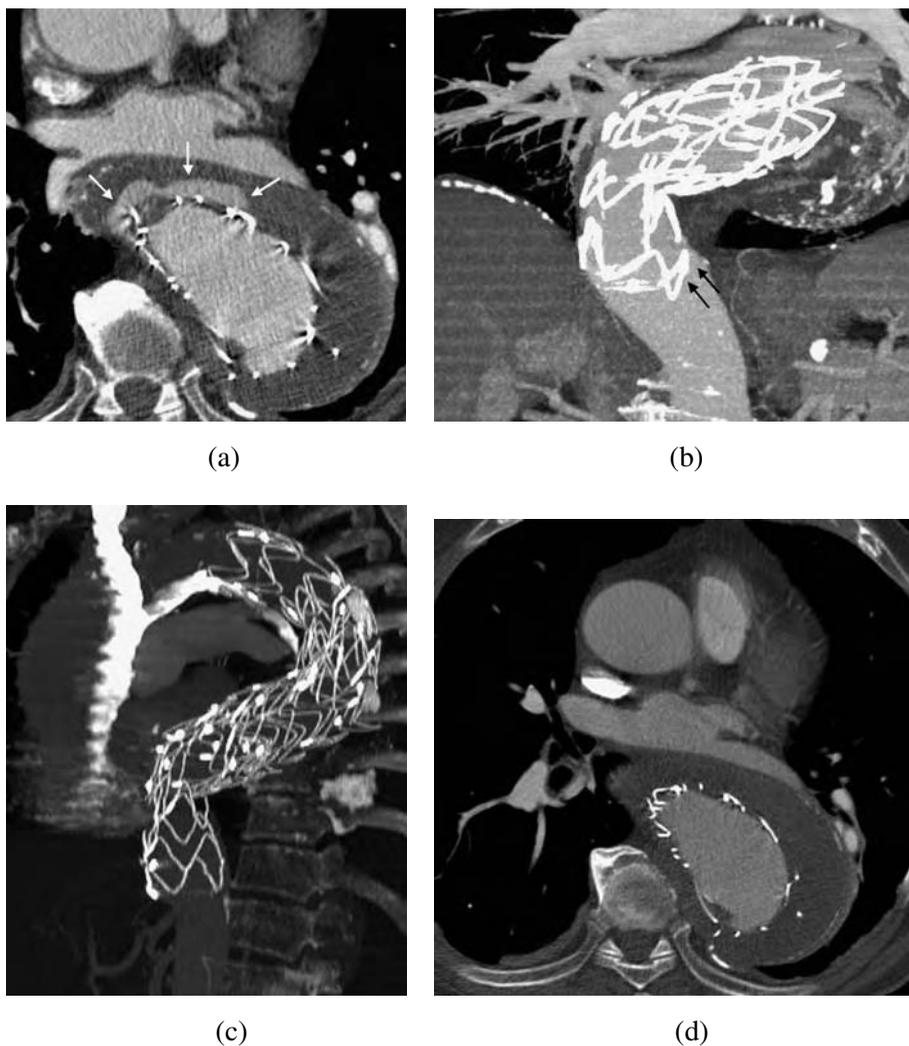


Figure 11.12. CT is very helpful in the follow-up of aortic dissections treated by endovascular techniques. In this example, an endoleak can be visualized after the deployment of a stent graft in the descending aorta, represented by contrast enhancement within the thrombosed sac and outside the graft lumen ((a), axial scan, arrows). The endoleak is caused by the incomplete anchorage of the stent graft at the level of the distal neck ((b), MIP reconstruction on coronal plane, arrows). Therefore, an extended cuff is positioned percutaneously at the distal level. CT control performed after 1 month shows the adequate fixation of the stent graft and of the cuff to the aortic wall ((c), MIP reconstruction on sagittal plane); the endoleak is no longer visualized ((d), axial scan).

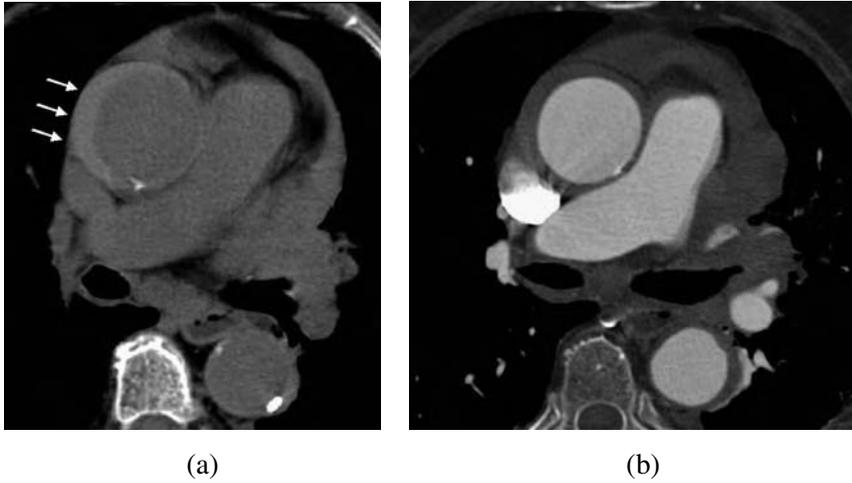


Figure 11.13. Intramural hematoma (IMH) is diagnosed on the unenhanced CT scans on the basis of the identification of a crescent-shaped area of attenuation in the aortic wall, corresponding to the hematoma, such as in this example of type A IMH ((a), axial scan, arrows). This area does not show contrast enhancement after contrast material injection ((b), axial scan), and no intimal tears are visualized. Therefore, the unenhanced scans are required for the diagnosis.

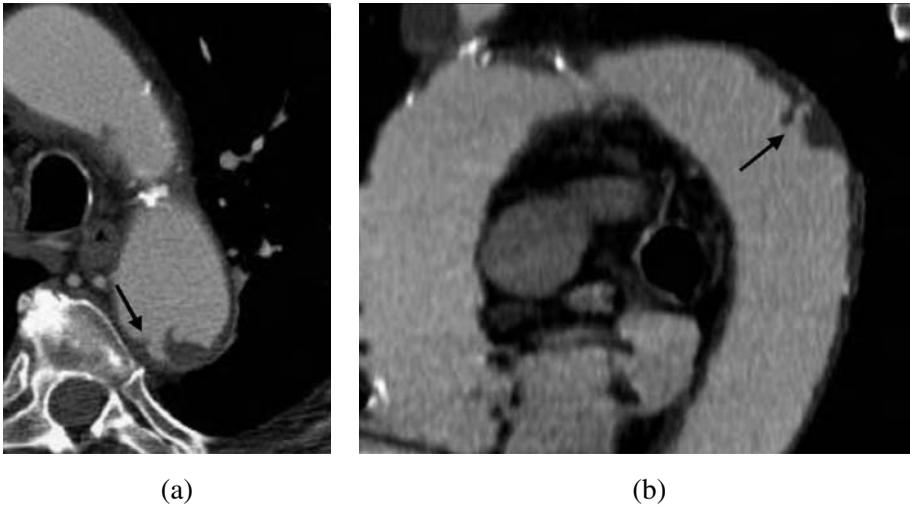


Figure 11.14. The penetrating atherosclerotic plaque of the thoracic aorta is visualized as an ulcerlike area of contrast enhancement outside the aortic lumen ((a), axial scan, arrow). The corresponding aortic wall can be thickened ((b), MPR reconstruction in sagittal plane, arrow).

ogy of the wall, status of the lumen, flow, and functional properties of the vessel. For these reasons, MRI has been proposed for the evaluation of acute

aortic diseases, such as aortic dissection, intramural hematoma, as well as for chronic diseases such as aneurism and inflammatory diseases<sup>69–73</sup>.

MRI has several advantages (such as the use of nonionizing radiations, and the use of nonnephrotoxic contrast agents) and, similar to CT, it has the capability of producing two- and three-dimensional images with a panoramic field of view. Spatial resolution is lower than both TEE and CT; however, it remains high enough to allow an excellent diagnostic accuracy, higher than TEE and superimposeable to CT<sup>18,66–69</sup>. Beyond the crude anatomical information, MRI allows a finer depiction of histopathologic components of the vessel wall, such as the presence of edema, fat, and hemorrhage. A great advantage of MRI is the possibility of quantitatively evaluating the flow inside the vessel and, eventually, in the presence of a dissection, of evaluating the relative flow in both the true and the false lumen. Finally, similar to TEE, MRI easily offers the possibility of evaluating the morphology and functionality of the aortic valve and the presence of valvular, perivalvular regurgitation, which has relevant clinical and therapeutical implications.

With respect to the other techniques, MRI has some disadvantages, such as the reduced availability of scanners and higher cost. It also is more demanding both for the operator and the patient: claustrophobia affects 5% of patients, and patients have to be clinically and hemodynamically stable. However, in specialized centers the availability of qualified personnel who are able to manage unstable patients inside the scanner and of vital-signs monitors, which can be used inside the magnet room, reduces the number of patients who cannot be studied with MRI, if clinically indicated<sup>66</sup>.

### **Magnetic Resonance Imaging in the Follow-Up of Aortic Dissection**

MRI offers different techniques for obtaining images of the aorta and its main branches<sup>5,19,66,74–81</sup>. Static spin echo (SE) “black-blood” images are useful to study the characteristics of the vessel wall, such as the presence of thrombotic material inside the lumen, as well as the presence of perivascular hemorrhage. With advanced equipment it is possible to obtain slices 3–8 mm thick and with high in-plane spatial resolution (1.4 mm). In SE “black-blood” images, the slow flow, as usually found inside the false lumen, can show a bright signal giving an indirect marker of function. T2 weighted images often show an unsatisfactory signal-to-noise ratio (SNR), being prone to flow and motion artefacts. However, the most recent fast SE T2, obtained with synchronization with patient breathing, can be useful to describe the wall characteristics, such as intramural hemorrhage or inflammatory tissue.

Dynamic “white-blood” images, such as fast spoiled gradient echo (SPGR) or the ultrafast *steady-state free precession* (SSFP), offer the possibility of visualizing both the wall and the flowing blood with high temporal resolution (usually the R-R interval is divided into 30 phases). Dynamic images are

very useful for identifying the presence of intimal flap and turbulent flow, the latter being easy to see as it induces inhomogeneity of the signal, which appears darker than the surrounding laminar flow. This makes it easier to identify the communication sites between the true and the false lumen. Because of the sharp contrast between the different tissues, such as the vessel wall and the surrounding anatomical structures, these images are ideal for a precise measurement of diameters. Measurements of vessel diameters have a relevant clinical meaning in aortic pathologies, because the external dimension of the vessel is one of the main prognostic findings with direct therapeutical implications<sup>18,19,26</sup>. One of the advantages of MRI, with respect to the other imaging modalities, remains the possibility of obtaining images in whichever spatial plane without limitations. Furthermore, when using fixed anatomical landmarks, such as bones or joints, the measurements in the same patient become highly reproducible.

Generally, at first, sagittal images are obtained to see the longitudinal profile of the vessel (Figure 11.15(a), (b)) and to drive the following axial/coronal images in short axis of the vessel (Figure 11.16). The latter, if obtained in planes orthogonal to the local major axes of the vessel, is the more suitable approach for measuring the diameters. In the case of aortic dissection, either the global external diameters or the inner diameters of both the true and the false lumens are of clinical relevance.

MRI also offers the possibility of obtaining quantitative measurement of flow in absolute flow (ml/min). This can be achieved by *phase contrast* (PC) images. This possibility is very useful in measuring the differential flow in the false and true lumen, whose values have relevant prognostic implications (Figure 11.17(a), (b)).

Besides these morphologic and functional images, *magnetic resonance angiography* (MRA) leads to a three-dimensional depiction of the lumen, with results that are superimposable to those obtained by invasive angiography. MRA can be performed both without and with the injection of paramagnetic contrast agent.

The first approach to be introduced with significant clinical results was the *time-of-flight* (TOF) *technique*. In this case, while stationary  $H^1$  nuclei are saturated by repetitive radio frequency pulses, the moving  $H^1$  nuclei are magnetized. This process results in 2D or 3D images.

The three-dimensional approach is preferable, as it gives a better spatial resolution; however, it can only be performed in high field scanners ( $> 1$  Tesla). This technique has several disadvantages, such as a possible shading effect, which can strongly reduce the effectiveness of the method (Figure 11.18).

However, today the most frequently used technique for visualizing vessels is the 3D-MRA with contrast injection—*contrast-enhanced magnetic resonance angiography* (CEMRA). With this technique, the arrival of a bolus of contrast

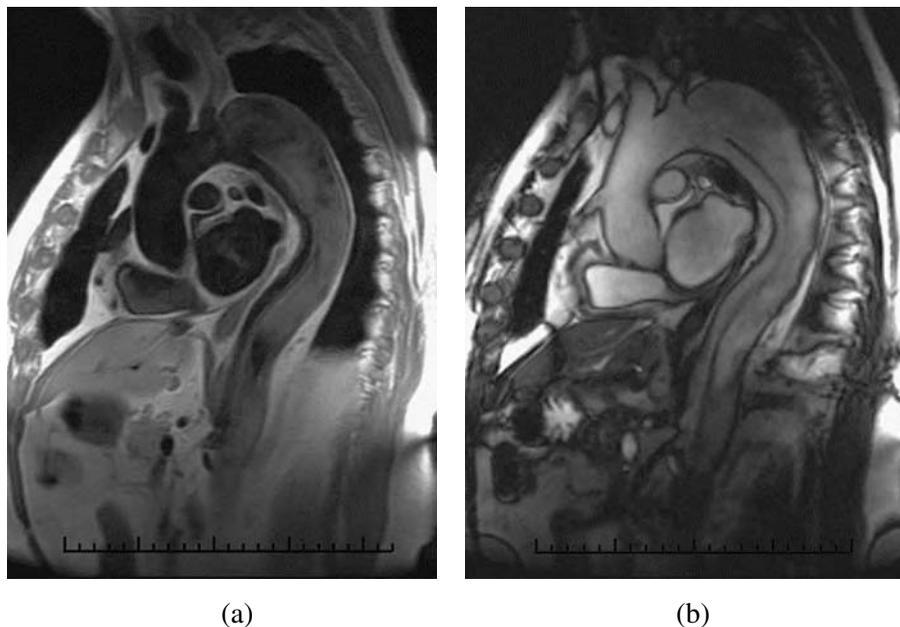


Figure 11.15. Images in SE T1 “black blood” (a) and in steady-state free precession (SSFP) “white blood” (b) in parasagittal plane of thoracic aorta in a patient with type B aortic dissection. In the “black blood” image, the false lumen appears slightly hyperintense due to slow flow. In the “white blood” image, the communication site is easily recognized.

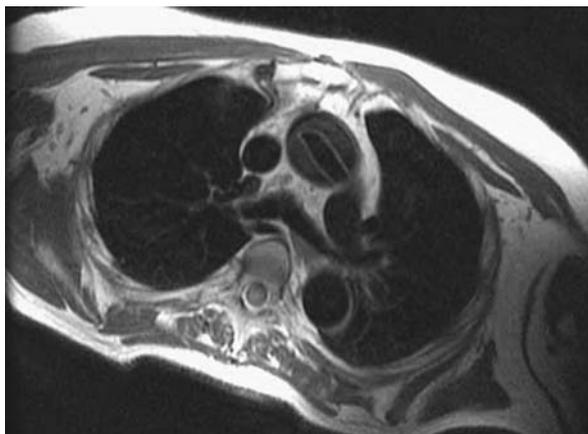
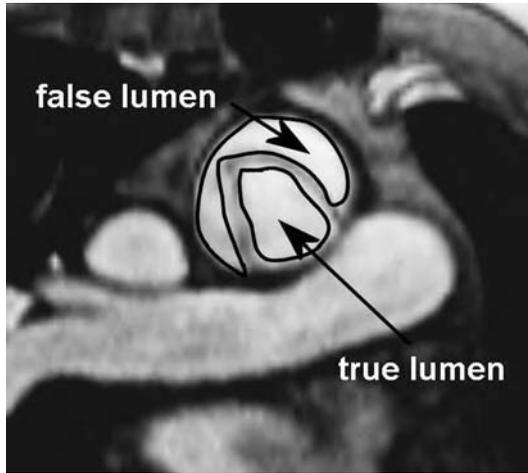
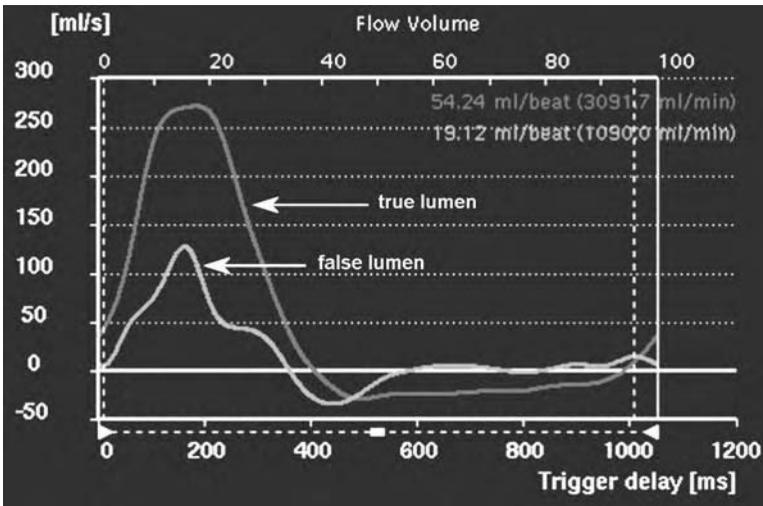


Figure 11.16. Image in SE T1 “black blood” in a patient with type A aortic dissection in short axis plane of the vessel. The intimal flap is evident in ascending aorta.

agent inside the vessel strongly shortens the T1 of the flowing blood, inducing a strong increase of contrast-to-noise ratio. With this sequence, while the



(a)



(b)

Figure 11.17. (a) Figure of the short axis of the ascending aorta in a patient with type A aortic dissection. (b) Flow measurement of true and false lumen by the phase contrast method.

presence of contrast induces a marked increase of signal within the vessel, the signal deriving from the stationary tissue is practically null. The acquisition itself is performed with a three-dimensional approach, and the result is a luminogram of the vessel (Figure 11.19a–e). There are several advantages to using this technique, such as a lower sensitivity to turbulences and to local slowing of flow. The major technical problem arises from the necessity of es-



Figure 11.18. Image by three-dimensional TOF of thoracic aorta. The shades effect is evident on the vessel profile, reducing the diagnostic accuracy.

establishing a synchronism between the arrival of the contrast agent (when the effect on T1 of the highest) and the start of the acquisition. Practically, the operator has to decide the delay (in seconds) between the start of the contrast injection and the start of the acquisition signal. To reach this goal, there are several different approaches. The most often used are (1) the so-called best guess, where the expected time of circulation is presumed; (2) the monitoring system adopting detection algorithms, capable of online processing of the signal intensity within a defined volume positioned inside the targeted vessel and automatically starting the acquisition of the signal at the arrival of the contrast agent; and (3) the fluoroscopic imaging, where the operator is asked to visually monitor the vessel while ultrafast images (less than 100 ms) are continuously acquired, until the arrival of the contrast agent and then starting the signal acquisition. The latter seems to be the more efficient when the necessary expertise is reached inside the MRI Lab<sup>66,69-71</sup>.

With modern equipment, the simple acquisition of 3D CEMRA takes no more than 10 min. Only if the examination is made complex by the acquisition of adjunctive images (such as the fast SE for morphology or PC images to calculate the flow inside the vessel), an extra 10 min are needed.

An MRI examination for the follow-up of an aortic dissection should be a comprehensive morphologic evaluation of the lumen, the vascular wall, and

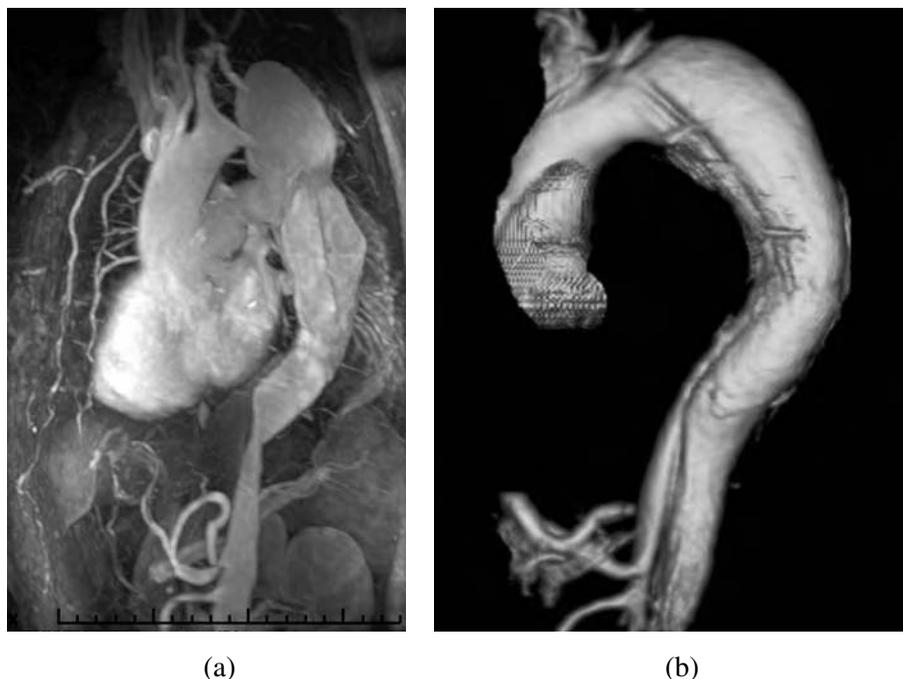
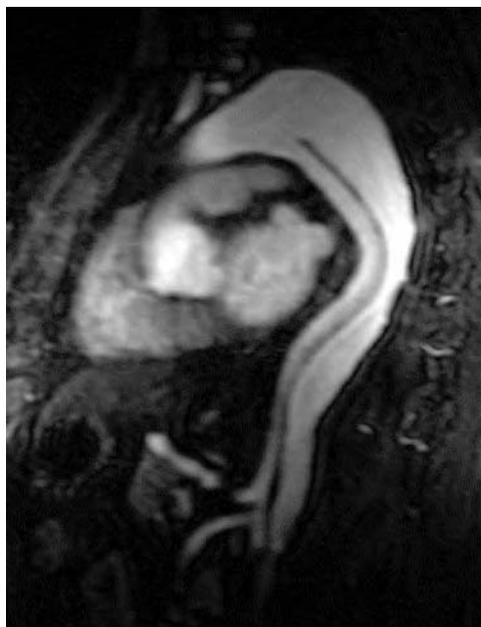


Figure 11.19. Three-dimensional CEMRA of type B aortic dissection. (a) The original maximum intensity projection. (b) The same case after volume rendering filtering. (c) The same case, analysis of the single partition to evidence the connection site between false and true lumen. (d) Multiplanar volumetric reconstruction, the involvement of right renal artery is evident. (e) The same case, the multistation acquisition procedure allows to follow the dissection along the whole vessel to the iliac arteries.

the perivascular findings (Figure 11.20). The presence of complications (such as intramural bleeding), the measurement of flow in the true and false lumen, and the comparative evaluation of results with those already available from previous studies have to be reported.

The identification of connection sites (proximal and distal) is not always possible, but it necessary to underline that in 13% of cases the intimal rupture is not even detectable at autopsy. In 65% of cases, dissection starts in the ascending aorta, in 20% in the descending aorta, in 10% at the arc level, and in 5% in the abdominal aorta. However, the disease has a dynamic evolution either spontaneously or following the therapy. Massive thrombotic phenomena can take place within the lumen mainly if excluded by the surgical intervention, and in some cases proximal and distal extension of the dissective process can be observed.

The incidence of valve regurgitation in type A aortic dissection is variable, ranging from 16% to 67% in published series. MRI can easily assess the in-



(c)



(e)



(d)

Figure 11.19. (Continued)

involvement of the valve and the worsening of an already existing regurgitation on a native valve. Usually, the presence of a valvular prosthesis does not reduce the possibility of the MRI examination; however, the presence of a valve with metallic components can significantly reduce the image quality (Figure 11.21).

Cerebral ischemia has been reported in 3–5% of cases due to involvement of supraortic vessels or embolism. CEMRA images of the thoracic aorta are always comprehensive for the origin and proximal segments of supraortic vessels. Eventually, an ad hoc study can be planned if it is necessary to evaluate the entire course of the vessels.

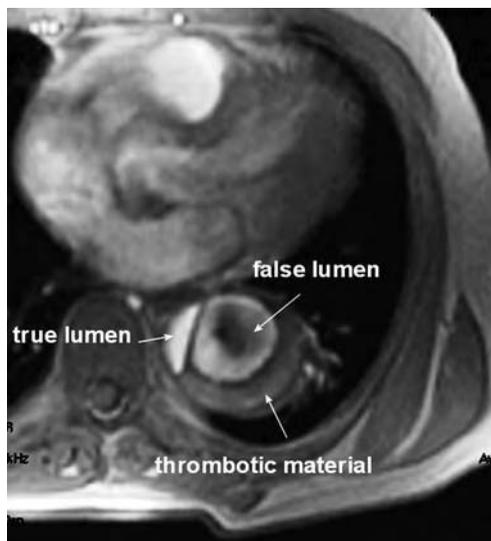


Figure 11.20. Image in gradient echo in short axis of the thoracic aorta. The true lumen and the thrombotic material partially filling the false lumen are evident.



Figure 11.21. Image in 3D CEMRA in a patient with aortic prosthesis MRI compatible (nitinol).

Myocardial infarction due to the involvement of a coronary artery (1–2%) and ischemic lesions of spinal medulla due to involvement of spinal arteries are rare events<sup>21,69</sup> that require a specific diagnostic approach, where MRI may play a role both in the acute phase and in the follow-up. In fact, it has been shown that MRA can identify the spinal arteries and, in particular, the artery of Adamkiewicz, helping the surgical plan of patients who are candidates for descending aorta repair. However, data on this issue are limited to small cohorts of patients, and the task is sometimes hindered by the wide anatomical variability of the spinal vessels and in particular of the artery of Adamkiewicz<sup>82</sup>.

### **Magnetic Resonance Imaging in Intramural Hematoma and Penetrating Ulcer of Aortic Wall**

MRI is an ideal tool for the diagnosis of intramural hematoma as well as for visualizing the presence of accompanying plaques. Often an intramural hematoma looks like a half moon, less frequently surrounding the complete circumference of the vessel (Figure 11.22). Furthermore, it is well known that in MRI metabolites of hemoglobin (oxihemoglobin, deoxihemoglobin, metahemoglobin, hemosiderin) have different magnetic properties. This allows the differentiation between acute bleeding (less than 7 days) when deoxihemoglobin is prevalent and recent bleeding (8 days) where metahemoglobin is the main determinant of signal. In chronic hematoma (>three months), hemosiderin can be detected. Similarly to other chronic pathologies of the aorta, the dimensions of the vessel are a major determinant of prognosis. MRI is an excellent technique for describing morphology, age, and complications (such as changes on the time). The excellent possibilities together with the lack of contraindications make MRI the first methodology of choice for the intramural hematoma follow-up<sup>5,18,19,26,69,81,87–93</sup>.

In regard to the penetrating ulcer of the aortic wall, invasive angiography is the preferred technique for diagnostic purposes; reliable results can also be achieved by CT and MRI. CT has the advantage of visualizing the calcified plaque and any superficial interruptions or dislodgement of the plaque. MRI offers the possibility of identifying the presence of penetrating ulcers despite small dimensions and the presence or absence of an intramural bleeding. With CEMRA, a plus in the profile of the vessel can be appreciated (Figure 11.23(a), (b))<sup>5,18,26,83,94,95</sup>.

Finally, if the patient has been treated by positioning an endovascular prosthesis, the aim of the MRI study is to verify the position of the endovascular device, the relationship with the main arterial branches, and the presence of periprostheses leak. If the material of the prosthesis is MRI compatible, MRI has an high degree of reproducibility and can be suggested as a first-choice diagnostic procedure<sup>18,19,26,69,83–85</sup>.



Figure 11.22. Three-dimensional CEMRA of thoracic aorta in a patient with aortic hematoma.



(a)



(b)

Figure 11.23. (a) Three-dimensional CEMRA of thoracic aorta in a patient with penetrating ulcer of the thoracic aorta. (b) The analysis of partitions allows an accurate definition of the ulcer.

*Table 11.1.* Late complications of aortic dissection and follow-up evaluation

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Late complications:

- Progressive aortic insufficiency
- Aneurysm formation and rupture
- Recurrent dissection or progression of dissection
- Leakages at anastomoses/stent sites
- Malperfusion

Patients at particularly high risk:

- Those with Marfan syndrome—very high risk of recurrent dissection or of aneurysm formation with rupture
- Those with a patent false lumen—increased incidence of late complications and death

Follow-up evaluation:

- Regular outpatients visits and imaging controls at 1, 3, 6, and 12 months and thereafter every year
  - Optimal BP control <135/80 mm Hg with beta blockers
  - First choice is MRI, second choice CT, and third TEE
- 

*Source:* Modified from references 18 and 96.

## CONCLUSIONS

Patients with aortic dissection demand careful clinical and imaging long-term monitoring by specialized physicians to detect early signs of progression of the disease or aneurysm formation and to achieve excellent blood pressure control. Among all imaging modalities, MRI, although not widely available, appears to be the technique of choice. In fact, it is completely noninvasive, provides excellent anatomical details essential to detect interval changes and potential complications, and avoids exposure to ionizing radiation or nephrotoxic contrast agents used for CT.

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SECTION V:  
EVALUATION AND MANAGEMENT OF  
SPECIAL SUBSETS

# 12

## **OPERATION FOR ACUTE AORTIC DISSECTION IN THE OCTOGENARIAN PATIENT**

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Acute aortic dissection is a lethal disease. Based on classic studies from the 1950s, ascending aortic dissection has a mortality rate that increases on an hourly basis, and is fatal in over 90% of patients at one month if untreated<sup>1</sup>. However, recent reports on mortality with maximal antihypertensive therapy reveal improvements with medical therapy. Survival in patients who survive the initial event and present to the hospital has been reported as high as 70% at two years<sup>2</sup>.

With the aging of the population, the proportion of patients presenting with acute aortic dissection in older age groups is increasing. In these patients, co-morbid conditions exist more frequently, including both other cardiovascular diseases and other pathologic conditions. As a result, operative therapy in older age groups is challenging not only from a technical standpoint but also in post-operative management. This report examines the unique aspects to consider when contemplating operative therapy for acute aortic dissection in patients entering their eighth decade of life.

### **PATHOPHYSIOLOGICAL CHANGES WITH AGE**

Aging is associated with myriad changes in organ system function<sup>3</sup>. The end result is a decrease in functional reserve capacity, which can lead to adverse outcomes following any operative procedure. Furthermore, should com-

plications occur with an operation, residual organ function is often challenged to maintain homeostasis.

Cardiac changes of aging include ventricular hypertrophy (especially in the dissection patient population where hypertension is prevalent) and coronary artery disease. There is a concomitant reduction in ventricular compliance and a decrease in response to catecholamines resulting in a predisposition to congestive heart failure during the postoperative period when intravascular fluid shifts are present. Pulmonary function is also often impaired, with reduced chest wall compliance and decreased muscle mass decreasing pulmonary mechanics and functional reserve. There is age-related loss of pulmonary elastic recoil, which can increase residual capacity and thereby diminish gas exchange. Renal cortical atrophy and reduction in renal blood flow are age-related as well, and all contribute to impaired fluid balance in the postoperative period. These alterations also make the kidney more susceptible to dysfunction if marginal cardiac output and hypotension occur. Finally, cerebral atrophy as well as deficiencies in neurotransmitters may predispose the older patient to periods of postoperative delirium.

## **CARDIAC SURGERY IN OCTOGENARIANS**

A number of studies have focused on cardiac surgery outcomes in octogenarians<sup>4-6</sup>. The range of operative mortality is 10% or higher in many series. These studies have often demonstrated a higher proportion of females in their study groups, likely as a result of higher life expectancies seen in women. Three recent studies warrant further mention.

Rady et al. retrospectively evaluated 783 patients undergoing any type of cardiac surgical procedure<sup>4</sup>. This cohort included 96 patients who were octogenarians. This group had a higher prevalence of pulmonary hypertension, cerebrovascular disease, congestive heart failure, and valvular disease. Operative procedures were more complicated, with multiple procedures more common in this group. The results were notable for age identified as an independent predictor—either death or discharge to a nursing facility (53% in octogenarians vs. 14% in younger patients). Coincident with this was a significant increase in the hospital charges, which led the authors to question the cost-effectiveness of offering operative therapy for octogenarians.

Collart et al. reviewed a group of 213 patients undergoing valvular surgery, with special emphasis on both operative and long-term mortality<sup>5</sup>. The mean age of their study population was 83 years, and the majority (74%) underwent aortic valve replacement. Operative mortality was 8.8%, and the only multivariate preoperative predictor of death was a reduced ejection fraction.

Emergent status, accounting for 11.2% of patients, did not fall out as an important predictor of mortality. The five-year survival in the entire group was 56%, similar to the general population at the same age.

Finally, a study by Bridges et al. utilized the Society of Thoracic Surgeons National Database to review the results of cardiac surgery in almost 60,000 patients aged 80 years and older from 1997 to 2000<sup>6</sup>. In this report, 30-day mortality varied from 7% to 12%, depending on the operative procedure. This was in contrast to the 2–7% mortality for patients younger than 80 years. They concluded that coronary bypass grafting could be performed in older patients with careful patient selection.

## **RESULTS OF MAJOR THORACIC AORTIC RECONSTRUCTION IN ELDERLY PATIENTS**

In contrast to elective coronary bypass grafting or cardiac valvular procedures, reconstruction of the thoracic aorta often entails prolonged cardiopulmonary bypass and deep hypothermic circulatory arrest. These adjunctive modalities have been associated with several significant postoperative complications, including death, stroke, renal failure, and excessive hemorrhagic complications. To put the results of aortic resection for acute dissection in perspective, it is worthwhile to examine the results of thoracic aortic resection in the elective setting in octogenarians.

The landmark study by Svensson et al. showed that increased age was associated with an increased risk of death following use of deep hypothermic circulatory arrest<sup>7</sup>. A more recent report from Okita et al. reviewing their experience with 261 patients over 70 years of age showed that the higher the age, the greater the rate of mortality<sup>8</sup>. The mortality of elective thoracic aortic resection in patients over 75 years of age was 27.2%.

## **SURGERY FOR ACUTE TYPE A AORTIC DISSECTION IN ELDERLY PATIENTS**

Reports of surgery for acute type A dissection in octogenarians have yielded conflicting results. In a 30-year review of therapy of aortic dissections (both acute and chronic and both type A and B), Fann and colleagues from Stanford showed a positive linear relationship between age and operative mortality<sup>9</sup>. In multivariate analysis, older age emerged as an independently associated variable. Operative mortality for patients over 70 years averaged over 40%. In addition, older age as well as previous operation were identified as multivariate predictors of late mortality as well.

A more recent report by Kawahito et al. described their experience with 23 patients over age 75 and contrasted this to 86 patients younger than 75 years in their study<sup>10</sup>. They did not find any difference in hospital mortality or survival at one, three, or five years. The operative mortality in their study was 13% in the older group and 10.5% in the younger group ( $p = 0.71$ ). The majority of early deaths in the older patients occurred from rupture of the false lumen in the arch aorta after ascending aortic replacement. In contrast, major causes of early mortality in the younger group included heart failure, visceral ischemia, or intraoperative hemorrhage. They concluded that operation for acute type A dissection can be performed in patients over age 75 with acceptable mortality.

Another study by Neri and colleagues yielded much different results<sup>11</sup>. They evaluated their experience of operative therapy in octogenarians and found in-hospital mortality was 83%. Follow-up on the four survivors showed that none was able to function independently, and mortality for the entire cohort at six months was 100%. Statistical analysis showed that age over 80 years was the most important independent risk factor associated with mortality. This led the authors to question whether older patients should be operated upon, given the dismal outcome seen in their study. In a response to this study, Griep and Hagl reviewed their own experience with 14 patients and found only 21% sustained an adverse outcome<sup>12</sup>. They suggested a more patient-specific approach to deciding whether surgery is contraindicated in advanced age, primarily because their study population had significantly less comorbidity than that group described by Neri et al.

The International Registry of Acute Aortic Dissection (IRAD) was formed to gather data on all patients presenting with acute dissection at multiple international sites. Two recent reports from this consortium add valuable information to the current understanding of operative therapy of acute dissection. The study by Mehta et al. had 34 octogenarians (6% of the study population)<sup>13</sup>. In-hospital mortality for this age group exceeded 45%, whereas those patients managed medically displayed similar mortality rates. Age over 70 years was identified as an independent predictor of mortality.

Another study from the IRAD group describing contemporary results of surgery also showed that overall in-hospital mortality was 25.1% in 526 patients but that age was an important factor in determining mortality<sup>14</sup>.

## **INTERVENTION IN ACUTE TYPE B DISSECTION**

Descending thoracic and thoracoabdominal dissection is traditionally treated with medical therapy at most centers. Operation is generally reserved for those patients in whom complications occur, including rupture, refractory pain, uncontrollable hypertension, and rapid expansion of the false lumen.

In-hospital mortality using this approach has ranged between 10–15%. Age as well as comorbid conditions and presence of other complications such as shock or visceral/renal ischemia have portended a worse prognosis. Again, reports from the IRAD group<sup>9</sup> as well as the Stanford group<sup>15</sup> discuss age as an important variable. Unfortunately, the octogenarian population is not well studied for this entity, and the data are too limited from which to draw a conclusion.

Seminal reports from Dake et al. and Nienaber et al. on the utility of thoracic aortic endograft therapy for acute dissections may be of some importance<sup>16,17</sup>. Open surgery for acute type B dissection has carried with it a significant mortality rate (30–40%), and minimally invasive approaches such as endoluminal therapy have been associated with much lower operative mortality rates (0–16%). In these procedures, the entry tear as well as varying lengths of thoracic aorta are covered with stent grafts, and in doing so, the false lumen is obliterated in a majority of cases. In patients presenting with end-organ malperfusion, the obliteration of the false lumen has restores flow into visceral branches via the true lumen. The long-term results of this approach will be further evaluated in upcoming trials.

## CONCLUSIONS

Surgery for acute dissection in octogenarians is a formidable task, from both operative and postoperative perspectives. The humbling results suggest that an aggressive posture at identifying those patients at risk (such as those with aneurysms or uncontrolled hypertension) would be the most prudent option. Operative therapy can then be performed in the elective setting but only after careful selection of appropriate candidates. In those octogenarians presenting with acute aortic dissection, even with thoughtful and careful selection of candidates deemed appropriate for operation, the long-term outlook for functional recovery is uncertain, and the role of operation questionable.

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# 13

## GENETIC DISORDERS ASSOCIATED WITH AORTIC DISSECTION

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Heritable disorders of connective tissue are an established cause of aortic disease. Genetic defects in matrix protein synthesis can lead to a critical reduction in tensile strength and predispose to aneurysm formation and dissection. Cystic medial degeneration is the common histopathologic expression of a number of such disorders, including Marfan and Ehlers–Danlos syndromes. Several other familial forms of thoracic aortic disease have been reported, and many other are suspected. In this chapter, we review the major features of the connective tissue disorders and their links with aortic dissection.

### MARFAN SYNDROME

#### INTRODUCTION

Marfan syndrome occurs with a frequency of 2–3/10,000 persons and is transmitted in an autosomal dominant pattern with variable penetrance. Approximately 25% of cases occur sporadically as de-novo genetic mutations<sup>1,2</sup>.

The disorder involves chiefly the skeletal, ocular, and cardiovascular systems, but pulmonary, cutaneous, and dural structures can also be affected. Aortic disease confers the principal mortality risk and has been responsible for the large majority of the premature loss of life seen in this disorder. The survival of patients with Marfan syndrome has improved significantly over the last few decades, due in part to better cardiovascular imaging, prophylactic beta-blockade<sup>3</sup>, and the expanding indications for elective aortic root replacement in at-risk individuals<sup>4</sup>. The average life span of patients with untreated Marfan syndrome was 32 years in 1972<sup>5</sup>. Median life expectancy was reported at 41 years in 1993 and 61 years in 1996<sup>6,7</sup>. The majority of premature deaths are attributable to aortic dissection/rupture and heart failure owing to severe aortic regurgitation.

## HISTORY

Marfan syndrome has been recognized for over one hundred years. It is interesting to review the landmark events that have shaped our recognition, understanding, and treatment of this challenging disorder.

- In 1896, Antoine Bernard Jacques Marfan, a renowned professor of pediatrics in Paris, described a syndrome of markedly long and thin extremities in a five-and-a-half-year-old child. His original description noted the presence of the skeletal abnormalities typical of the disorder but did not include recognition of its cardiovascular manifestations. The term that he gave to the disorder was *dolichostenomelia*, in recognition of the strikingly long extremities<sup>8</sup>.
- In 1902, Achard contributed the term *arachnodactyly*, meaning “spider legs”, to describe the long, thin extremities<sup>9</sup>.
- The first association of Marfan syndrome with cardiac abnormalities was reported in 1912<sup>10</sup>. The patient died at two and a half months of age. The postmortem observations included mitral leaflet degeneration and a patent foramen ovale. The next several decades focused attention on the associated cardiac abnormalities, in the early belief that congenital heart disease was a prominent feature of the disorder.
- In 1918, Bronson described the first association with Marfan syndrome with a vascular event, a ruptured aortic aneurysm in a child<sup>11</sup>.
- In 1931, Weve established that Marfan syndrome was an inherited disorder, transmitted in autosomal dominant fashion<sup>12</sup>.
- In 1943, Helen Taussig of John Hopkins University was the first to emphasize aortic involvement in Marfan syndrome<sup>13</sup>. Her report established aortic pathology as the principal cause of premature death in patients with this syndrome.

- In the early 1960s, Gordon suggested that Abraham Lincoln had Marfan syndrome<sup>14</sup>. In 1964, Schwartz proposed the *Lincoln-Brooks sign*—the prominent rocking motion of Lincoln’s left foreleg in the photograph taken of him by Brooks<sup>15</sup>. The motion of the leg may have been caused by the diastolic run-off associated with aortic regurgitation, a common complication of aortic root disease in Marfan syndrome.
- In 1972, Murdoch reported the principal causes of death in patients with Marfan syndrome and documented the markedly reduced life expectancy seen in this disorder. He also emphasized the excess hazard imposed by pregnancy<sup>5</sup>.
- In 1958, Sjoerdsma documented an increased excretion of urinary hydroxyproline in Marfan syndrome patients<sup>16</sup>. This observation led initially to the theory that the disorder was related to an abnormality of collagen metabolism. It was not until 1986 that Sakai identified fibrillin, which was subsequently found to be the principal matrix tissue protein involved in Marfan syndrome<sup>17</sup>.
- In 1968, Bentall and de Bono described a surgical technique to replace the aortic root with a composite valve-graft conduit<sup>18</sup>. Their technique was later modified by Gott and colleagues at Johns Hopkins Hospital and has become the foundation for operative repair of aortic root pathology in patients with Marfan syndrome<sup>19</sup>. Yacoub and David later proposed different methods for aortic root repair with preservation of the valve leaflets<sup>20,21</sup>.
- In 1994, Shores et al. demonstrated in a randomized trial that beta blockade in young patients with Marfan syndrome can reduce the rate of aortic root enlargement and the risk of dissection<sup>3</sup>.
- The 1990s witnessed the rapid growth and refinement of transesophageal echocardiography, CT angiography, and MR angiography. These techniques have impacted significantly on the noninvasive assessment of patients with Marfan syndrome and suspected aortic disease.
- In 2006, Habashi and colleagues showed that the AT-1 receptor blocker, losartan, reduced TGF beta signaling and aortic aneurysm development in a mouse model of Marfan syndrome<sup>22</sup>.

## ETIOLOGY

Marfan syndrome is caused by mutations in the gene (FBN1) encoding fibrillin-1, the major constituent of microfibrils<sup>23</sup>. The elastic fibers of the aortic media are composed of microfibrils and tropoelastin. Over 100 mutations of this very large gene (65 exons) on chromosome 15 (15q21.1) have been reported<sup>24</sup>. Finding a single mutation is quite challenging, and genetic testing is not widely available for routine clinical use. The mutations in FBN1

can affect microfibril formation by interfering with fibrillin-1 synthesis, secretion, or incorporation into the extracellular matrix<sup>25</sup>. Mutations of the FBN1 gene have also been identified in several overlapping syndromes, such as the MASS phenotype (mitral valve, aorta, skin, skeletal) and various familial (non-Marfan) aortic aneurysm disorders<sup>26–28</sup>. The sheer number of potential FBN1 mutations may explain in part the heterogeneity of clinical expression, ranging from the classic phenotypic appearance to a variety of incomplete or “form fruste” presentations. In a minority of cases of Marfan syndrome, a mutation in the FBN1 gene cannot be identified.

Inactivating mutations in the TGF-beta receptor 2 (TGFR2), which also show dominant inheritance and variable penetrance, have been linked to the Marfan syndrome phenotype in some patients<sup>29</sup>. Mutations in other candidate genes may also be operative (e.g., the Marfan syndrome 2 or MFS2 gene)<sup>30</sup>. Enhanced expression of tissue metalloproteinases 2 and 9 in vascular smooth muscle cells (VSMCs) from Marfan syndrome patients with thoracic aortic aneurysms has also been reported<sup>31</sup>. In addition, the qualitative severity of cystic medial degeneration seen in Marfan syndrome patients with annulo-aortic ectasia may be related in part to the upregulation of PPAR- $\gamma$  in vascular smooth muscle cells (VSMCs)<sup>32</sup>. The interrelationships among fibrillin defects, enhanced elastolysis, and VSMC apoptosis remain under active investigation.

## **CLINICAL FEATURES AND DIAGNOSIS**

The major and minor clinical features of Marfan syndrome are listed in Table 13.1. The disorder is recognized chiefly on the basis of the skeletal, ocular, and cardiovascular findings. The major cardiovascular manifestations include dilatation of the aortic root and mitral valve prolapse. Revised criteria according to the 1996 Gent nosology have been formulated to distinguish Marfan syndrome from overlapping connective tissue disorders<sup>2</sup>. Criteria for establishing a diagnosis of Marfan syndrome in the absence of a family history include a major manifestation from two systems and involvement of a third system with either a major or minor manifestation. Criteria for diagnosis with a verified family history can include both genetic information and involvement of at least two systems, one of which should be major.

## **AORTIC DISEASE IN MARFAN SYNDROME**

Dilatation of the root and ascending aorta affects the majority of adult patients with Marfan syndrome. Aortic root dilatation is noted in 50% of children and as many as 60–80% of adults with Marfan syndrome<sup>33</sup>. Involvement of

*Table 13.1.* Dilatation or dissection of the descending thoracic or abdominal aorta below the age of 50

System	Major criteria	Minor criteria
Skeletal system	Presence of at least four of the following manifestations: <ul style="list-style-type: none"> <li>* Pectus carinatum</li> <li>* Pectus excavatum requiring surgery</li> <li>* Reduced upper to lower segment ratio or arm span to height ratio greater than 1.05</li> <li>* Wrist and thumb signs</li> <li>* Scoliosis &gt;20d or spondylolisthesis</li> <li>* Reduced extensions at the elbows (&lt;170d)</li> <li>* Medial displacement of the medial malleolus causing pes planus</li> <li>* Protrusio acetabulae of any degree (ascertained on radiographs)</li> </ul>	<ul style="list-style-type: none"> <li>* Pectus excavatum of moderate severity</li> <li>* Joint hypermobility</li> <li>* Highly arched palate with crowding of teeth</li> <li>* Facial appearance (dolichocephaly, malar hypoplasia, enophthalmos, retrognathia, down-slating palpebral fissures)</li> </ul>
Ocular system	<ul style="list-style-type: none"> <li>* Ectopia lentis (dislocated lens)</li> </ul>	<ul style="list-style-type: none"> <li>* Abnormally flat cornea (as measured by keratometry)</li> <li>* Increased axial length of globe (as measured by ultrasound)</li> </ul>
Cardiovascular system	<ul style="list-style-type: none"> <li>* Dilatation of the ascending aorta with or without aortic regurgitation and involving at least the sinuses of Valsalva, or</li> <li>* Dissection of the ascending aorta</li> </ul>	<ul style="list-style-type: none"> <li>* Mitral valve prolapse with or without mitral valve regurgitation</li> <li>* Dilatation of the main pulmonary artery, in the absence of valvular or peripheral pulmonic stenosis or any other obvious cause, below the age of 40</li> <li>* Calcification of the mitral annulus below the age of 40</li> <li>* Dilatation or dissection of the descending thoracic or abdominal aorta below the age of 50</li> </ul>
Pulmonary system	None	<ul style="list-style-type: none"> <li>* Spontaneous pneumothorax</li> <li>* Apical blebs (ascertained by chest radiography)</li> </ul>

Table 13.1. (Continued)

System	Major criteria	Minor criteria
Skin and integument	None	* Stretch marks not associated with marked weight changes, pregnancy, or repetitive stress * Recurrent incisional hernias
Dura	* Lumbosacral dural ectasia by CT or MRI	None
Family/genetic history	* Having a parent, child, or sibling who meets these diagnostic criteria independently * Presence of a mutation in FBN1 known to cause the Marfan syndrome * Presence of a haplotype around FBN1, inherited by descent, known to be associated with unequivocally diagnosed Marfan syndrome in the family	None

Source: From reference 18.

other aortic segments is less common. Typically, the sinuses are effaced. Aortic regurgitation develops as a function of either the enlarging root/annulus diameter or associated prolapse of the thinned and stretched valve leaflets. *Annuloaortic ectasia* is an older patho-anatomic term used to describe dilatation confined to the root and sinuses, most often with aortic valve regurgitation. The rate of continued aneurysmal growth in any individual patient is difficult to predict, but application of the LaPlace principle is appropriate. Despite its dilation, the aorta is actually stiffer and less compliant than normal, a characteristic that increases further with age<sup>34</sup>. Central pulse pressure, as can be estimated from the carotid pulse pressure, is a major determinant of ascending aortic diameter change<sup>35</sup>.

Although the risk of spontaneous dissection generally increases with increasing aortic diameter, the process can and does occur unpredictably at any aortic size. Pregnancy confers an even higher risk, as does a family history of dissection or rupture<sup>36</sup>. In an unselected adult Marfan patient population reported by Hirata and colleagues, the aortic root and annular dimensions were significantly larger ( $4.1 \pm 0.8$  cm vs.  $3.2 \pm 0.3$  cm,  $p < 0.01$  and  $2.9 \pm 0.4$  cm vs.  $2.3 \pm 0.3$  cm,  $p < 0.01$ ) than normal controls<sup>37</sup>. In another series of 113 patients with Marfan syndrome followed over four years, 80% had dilatation

of the aortic root<sup>38</sup>. The dilatation was localized to the sinuses in 28% of patients and extended beyond the sinotubular ridge in 51% of patients. Aortic complications occurred in 0 of 23 patients with normal (initial) size, in 6% (2 of 32) of patients with localized dilatation, and in 33% (19 of 58) of patients with generalized dilatation of the root. The extent of aortic root dilatation was the only independent predictor of subsequent aortic complications, including dissection.

The overall prevalence of Marfan syndrome among patients entered prospectively in the International Registry of Aortic Dissection (IRAD) registry was low ( $\sim 5\%$ )<sup>39</sup>. Patients with Marfan syndrome, compared with those without Marfan syndrome, were younger and had a higher prevalence of previously known aortic pathology (aneurysm/dissection) or prior aortic or aortic valve surgery. Symptoms associated with the dissection process were similar between the two groups, although it is recognized that Marfan syndrome patients may sometimes present with atypical features. In the IRAD registry, Marfan patients presented far more often with type A than type B dissection and had larger aortic diameters with a higher prevalence of aortic regurgitation but a lower prevalence of intramural hematoma formation. The hospital mortality rate among patients with Marfan syndrome was comparable to the rate among non-Marfan patients, in the range of 20–25%. Thrombosis of the false lumen occurs less commonly among patients with Marfan syndrome, even after successful surgical repair<sup>40</sup>. These patients are at higher risk for redissection and false lumen aneurysm formation, for which repeat surgery or endovascular grafting is frequently necessary.

A heightened clinical index of suspicion for aortic dissection is appropriate when evaluating patients with Marfan syndrome who report chest or back discomfort. The principles of diagnosis and management of acute aortic dissection are otherwise generally the same for patients with and without Marfan syndrome, including the rapid performance of noninvasive imaging, the indications for surgery, and the use of stabilizing pharmacologic agents to reduce heart rate, blood pressure, and its rate of rise ( $dP/dT$ ). Whereas uncomplicated acute type B dissection in patients without Marfan syndrome is usually managed conservatively, some authorities have argued for primary surgical or endovascular stent graft repair in acute type B patients with Marfan syndrome<sup>41</sup>.

## **SURGERY FOR AORTIC DISEASE IN MARFAN SYNDROME**

Elective repair of aortic root aneurysms in patients with Marfan syndrome, to prevent the complications of dissection and rupture, has contributed to the observed improvement in survival. The size criteria for elective repair of an aortic root aneurysm have varied somewhat among the surgical series reported

to date, though in most centers of expertise operation is currently advocated for a maximal aortic diameter of  $\geq 5.0$  cm for all Marfan patients, a diameter  $\geq 4.5$  cm for Marfan patients with a family history of dissection or rupture, and  $\geq 4.0$  cm for young women with Marfan syndrome who contemplate pregnancy<sup>42</sup>.

There are differing opinions regarding the optimal type of aortic root surgery in patients with Marfan syndrome. The eventual approach needs to be tailored to the specific patho-anatomic features and urgency of any individual case. Yacoub (remodeling technique) and David (reimplantation technique) have championed the performance of valve sparing procedures<sup>19,20</sup>. In the Toronto (David) experience, the five-year survival of patients who underwent aortic valve sparing root reconstruction was significantly better than that of patients who underwent composite (valve-graft) root replacement (100% vs.  $88 \pm 6\%$ ,  $p = 0.04$ )<sup>43</sup>. At other centers, composite aortic root replacement has been the preferred technique. Baumgartner reviewed the John Hopkins experience with aortic root surgery in 231 Marfan patients: 218 of the 231 patients underwent composite root repair, 11 underwent homograft root replacement, and two underwent an aortic valve sparing procedure. The overall 30-day mortality was 0.9%, and actual survival was 88% at 5 years, 81% at 10 years, and 75% at 20 years. Baumgartner recommended elective resection of aneurysms of the aortic root in Marfan patients when the diameter approached 5.5 cm<sup>44</sup>. Gott published outcomes data from 10 highly experienced surgical centers for 675 patients with Marfan syndrome who underwent composite root replacement. Thirty-day mortality was 1.5% in patients undergoing elective repair, 2.6% among patients undergoing urgent repair (within seven days of surgical consultation), and 11.7% among patients undergoing emergency repair (within 24 hours of surgical consultation and usually for dissection or threatened rupture). This multicenter experience led to the recommendation for elective surgery in Marfan patients once the aortic root diameter reaches 5.5–6.0 cm<sup>4</sup>. This size recommendation has since been lowered to 5.0 cm, as the results of such complex surgery have continued to improve with advances in anesthetic, surgical, and medical techniques<sup>45</sup>.

Surgery on the acutely dissected aorta in a patient with Marfan syndrome is made technically difficult by the inherently weak and friable nature of the tissues that characterizes the disorder. To reduce late postoperative complications, efforts are maximized to resect or exclude any residual, damaged aortic tissue. Small coronary “buttons” are used to lessen the chance of true or false aneurysm formation at their sites of attachment to the graft, and the sinuses of Valsalva are excluded with valve sparing techniques to reduce the risk of progressive root enlargement and the need for future reoperation. Resection of the segment of the aorta where the cross clamp has been applied has been recom-

mended. Some surgical centers avoid aortic cannulation and perfuse through the groin or axillary vessels<sup>46</sup>.

There are several potential long-term complications following initially successful surgery. Residual patency of the false lumen, which occurs in up to 85% of repaired type A dissections, portends an increased risk of late false aneurysm formation, reoperation, and death<sup>47</sup>. Rapid dilatation of the aorta may occur postoperatively, with one report of 15 cm growth over two years<sup>46</sup>. Residual and progressive disease in the aortic segments left following the initial repair, as well as aortic disease distal to the site of the index surgery, are common indications for reoperation. Carrel et al. observed a 20.5% aortic reoperation rate over five years among 71 Marfan patients who had undergone initial surgical repair. No deaths were reported with reoperation, but two patients developed acute type B dissections and three patients died, including two from aortic rupture, within two years of the second surgery<sup>48</sup>.

Surgical techniques have continued to evolve to address the increasing challenge of performing second and sometimes third aortic operations on patients following initial root replacement surgery. The type of incision will depend on the segment of aorta targeted for repair. Descending thoracic aortic pathology can be approached via a left thoracotomy. Use of circulatory support is standard, and precautions are needed to protect the spinal cord and brain. Operation to replace the arch requires a period of deep hypothermic circulatory arrest. In the series reported by Detter et al., 11 of 33 Marfan patients required 22 reoperations over 15 years of follow-up<sup>49</sup>. Extensive aortic reconstruction (i.e., surgery to replace more than two segments of the aorta) is required for a substantial number of patients with Marfan syndrome. Niinami reported a 26% rate of extensive aortic reconstruction among patients with Marfan syndrome. Surgical procedures included composite aortic root and valve replacement (88%), aortic arch reconstruction (58%), graft replacement of the descending aorta (23%), and graft replacement of the thoraco-abdominal aorta (62%). Twelve percent of patients underwent replacement of the entire aorta, and 81% of patients required multiple operations. The 30-day survival rate was 89%, and the nine-year survival rate was 82%<sup>50</sup>. Finkbohner documented an increased likelihood of reoperation among patients who are hypertensive or continue to smoke following initial surgery<sup>6</sup>. In general, the rate of reoperation following dissection is significantly higher for patients with Marfan syndrome compared with the rate for patients without Marfan syndrome.

## **MEDICAL TREATMENT, EXERCISE, SCREENING, AND SURVEILLANCE**

Negatively inotropic doses (mean 212 mg/day) of propranolol have been shown to reduce the rate of aortic enlargement in patients with Marfan

syndrome<sup>21</sup>. Beta blockade is the cornerstone of medical therapy for the disorder and should be provided to all patients. Rate slowing, nondihydropyridine calcium channel blockers can be substituted for patients intolerant of beta blockers. The dose of either class of agents should be targeted to maintain a sub-maximal exercise heart rate less than 110 beats per minute. Unfortunately, there is no guarantee that medical therapy will prevent aortic complications in all patients. Based on the work of Habashi et al., there is great expectation that antagonists of TGF beta signaling, such as angiotensin receptor blockers, will help prevent or reduce several cardiovascular manifestations of Marfan syndrome<sup>22</sup>. Antibiotic prophylaxis is indicated for either aortic or mitral valve regurgitation. Patients with Marfan syndrome are counseled to avoid strenuous activity or intense competition of any sort and are prohibited from contact sports. Modest, recreational activities (such as bowling, golf, skating, brisk walking, or doubles tennis) are permissible<sup>51</sup>. Echocardiographic screening to assess the dimensions of the aortic root is appropriate for all first-degree relatives of affected patients. The aortic root should also be carefully assessed in young patients with mitral valve prolapse and suggestive, phenotypic features, such as any of the major skeletal manifestations. If the aortic root and first several centimeters of the ascending aorta cannot be adequately visualized with echocardiography, CT or MR angiography is indicated. Longitudinal surveillance imaging, to track the rate of growth of the aorta, is mandatory. Annual studies are obtained until the maximal dimension nears 4.5 cm, at which point studies are obtained every six months. Surveillance is equally important after initial surgical repair of dissection or aneurysm.

## **PREGNANCY**

Pregnancy in a woman with Marfan syndrome is associated with two major risks: spontaneous aortic dissection or rupture and transmission of the disorder to the fetus. In most but certainly not all cases of aortic dissection in pregnant women with Marfan syndrome, important aortic root dilatation has been present. In the Murgatroyd series, the mean aortic root diameter in women with Marfan syndrome who developed aortic dissection was  $5.1 \pm 0.3$  cm, compared with  $3.7 \pm 1.3$  cm in women without dissection<sup>52</sup>. Preconceptual identification of aortic root dilatation allows for institution of prophylactic beta blockade throughout pregnancy and during labor and delivery. The use of beta blockers during pregnancy confers a small risk of fetal bradycardia, intrauterine growth retardation, and hyperbilirubinemia. Cardioselective agents, such as metoprolol and atenolol, are preferred, though propranolol is excreted to a lesser extent in breast milk and may be substituted postpartum.

Pregnancy is considered contraindicated when the diameter of the root exceeds 4.0 cm<sup>53</sup>. Elective surgical repair should be undertaken prior to concep-

tion. Some authorities have advocated therapeutic abortion for Marfan patients first discovered to have root aneurysms ( $>4.0$  cm) during pregnancy<sup>54</sup>. Nevertheless, pregnancy can be safely brought to term in the majority of women with Marfan syndrome who do not have significant aortic root involvement. Acute aortic dissection usually occurs during the latter stages of pregnancy or in the early puerperium and can be successfully managed in many instances with survival of both mother and fetus. Exceptional cases of aortic dissection in the first trimester, or shortly after conception, have been reported<sup>55</sup>. A multidisciplinary approach, with input from high-risk obstetrics, neonatology, cardiology, cardiac surgery, and anesthesia, is needed.

The basis for the increased risk of aortic dissection in pregnant women with Marfan syndrome is not well understood. Purported mechanisms include the altered volume state and hemodynamics of pregnancy, labor, and delivery, as well as the effects of pregnancy-related hormones (estrogen, relaxin) on connective tissue tensile strength<sup>56</sup>.

Preconceptual evaluation of women with Marfan syndrome is optimal, though the clinician is often first confronted with an established pregnancy. Echocardiography and, if needed, CT or MR angiography should be performed to document aortic size, as well as the presence of aortic or mitral valve disease. Preconceptual counseling should stress that there is a 50% chance for transmission to the fetus, that the manifestation of the disorder may be more severe in the offspring than in the mother, that fetal diagnosis may be possible, and that an event-free pregnancy cannot be guaranteed.

A woman with Marfan syndrome and no or minimal ( $<4.0$  cm) aortic root dilatation should receive prophylactic beta blockade throughout pregnancy and during labor and delivery. Continuation of the beta blocker for at least the first several weeks postpartum is reasonable; longer-term use should reflect management guidelines for the nonpregnant woman. Cesarean section is reserved for obstetrical indications; epidural anesthesia and vacuum or forceps assistance are recommended. With greater degrees of aortic dilatation ( $>4.0$  cm), serial echocardiographic studies should be obtained during pregnancy to determine whether there has been any further enlargement. More intensive medical therapy, elective Caesarian section, and even therapeutic abortion should be considered as indicated. Aortic root surgery during pregnancy has been reported, though maternal and fetal risks are extraordinarily high<sup>57-59</sup>.

When acute aortic dissection is suspected, transesophageal echocardiography (TEE) is the preferred imaging modality, though circumstances may dictate that CT angiography be performed with shielding. MR imaging for suspected acute dissection is not widely available. Intravenous beta blockers are the cornerstone of medical therapy. Vasodilator therapy is more problematic, given the potential for fetal harm. Hydralazine can be considered but only after

adequate heart rate lowering with beta blockade has been achieved. Nitropruside should be avoided to prevent fetal thiocyanate toxicity. Labetalol, which combines both beta- and alpha-lowering properties, is an effective and safe alternative. Acute type A dissection is an indication for emergency surgery. A mature fetus can be delivered by Cesarean section before aortic surgery and cardiopulmonary bypass. There is an increased risk of maternal and fetal loss. With stable type B dissection, conservative management is pursued and the fetus delivered via Caesarian section at a later date when mature. Endovascular stent grafting (with shielding) at the time of presentation may play a role for more immediate and definitive aortic repair in this circumstance.

## **EHLERS–DANLOS SYNDROME**

The Ehlers–Danlos syndrome comprises a heterogeneous group of clinical disorders that share in common fragility or hyperextensibility of skin and joint hypermobility. The syndrome was first described in 1892 by Tschernogobow but bears the names of two dermatologists, Ehlers (Dutch) and Danlos (French), who published their clinical observations at the turn of the twentieth century<sup>60–62</sup>. It affects approximately 1 in 5,000 persons and is transmitted in autosomal dominant fashion, though spontaneous mutations may account for as many as 50% of reported cases<sup>63</sup>. Only Ehlers–Danlos type IV, the vascular type, is associated with premature death from spontaneous rupture of large arteries, bowel, or uterus<sup>64</sup>. Arterial aneurysms and dissection are less common than rupture. The major aortic branch vessels and the large arteries of the limbs are most susceptible. The syndrome results from mutations in the gene (COL3A1) encoding type III procollagen, which is located on chromosome 2q31<sup>65</sup>. Diagnosis is challenging but can be suspected on clinical grounds, especially when taking into account the family history and pedigree analysis. The four clinical criteria for diagnosis include easy bruisability, thin skin with visible veins, characteristic facial features, and ruptured arteries or viscera<sup>65</sup>. Genetic testing is not routinely available. As is the case for FBN1, the COL3A1 gene is very large, and numerous mutations are possible, with variable clinical expression<sup>66</sup>. Confirmatory biochemical testing relies on measurement of procollagen production from cultured fibroblasts obtained via skin biopsy from patients suspected of having the disorder<sup>67</sup>. Pepin and colleagues reported the clinical outcomes and genetic features of 220 index patients and 199 affected relatives with vascular type Ehlers–Danlos syndrome<sup>68</sup>. The underlying COL3A1 mutation was identified in 135 of the 220 index patients. Twenty-five percent of the index patients had a first complication by age 20, and more than 80% of index patients had at least one complication by age 40.

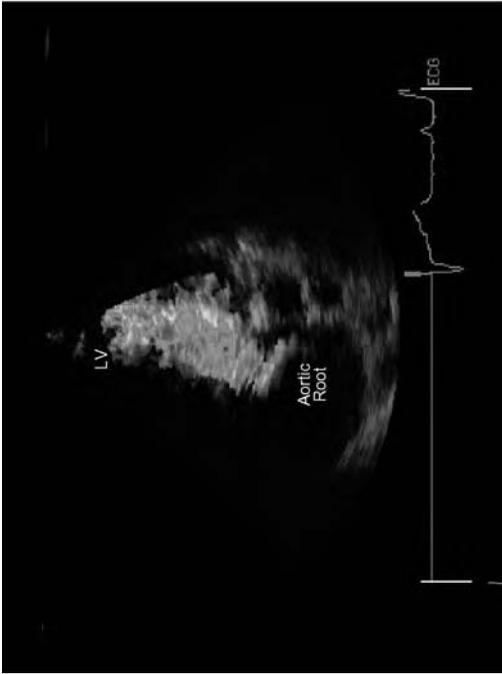
Median survival for the total cohort was 48 years. Arterial rupture was by far the leading cause of premature death, accounting for 103 of 131 total deaths. Pregnancy was associated with an excess risk of death owing to vascular or uterine rupture, either during confinement or in the early postpartum period.<sup>68</sup>

There is no proven medical therapy for this disorder. Because arterial rupture occurs more commonly in the absence of antecedent aneurysm formation, prophylactic surgery is not routinely indicated. Vascular surgery to repair aneurysmal or ruptured vessels is fraught with difficulty, owing to the extremely fragile nature of the tissues. Surgery is usually avoided if the aneurysm (or false aneurysm in the case of a contained rupture) is not deemed an immediate threat.

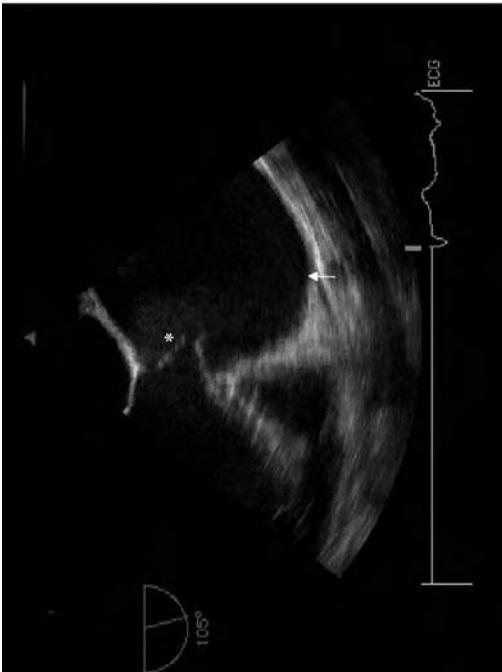
## **HISTORICAL NOTE**

Smith and Worthington suggested that the Italian violinist Nicolo Paganini may have had Ehlers–Danlos syndrome<sup>69</sup>. This hypothesis was offered as an explanation for the violinist's extraordinary talent. Bennati, who had treated Paganini, published his initial observations in 1831<sup>70</sup>:

Paganini is pale and thin, and of medium height. Although he is only 47 years old, his leanness and lack of teeth, which causes his mouth to be drawn in and leaves his chin more salient, give his countenance the expression of more advanced age. At first glance, his bulky head, which is supported by a long slender neck, offers a rather marked disproportion with his fragile limbs. . . . His chest is narrow and rounded; his left side being slightly less ample than the right side and slightly depressed in the superior part. Breathing is equal and easy, though the right side distends more than the left. . . . Let one but remark the manner in which he grasps and places his violin, or the position in which he sometimes places his arm, and then tell me of an artist who can imitate him. For example, who else, to produce certain effects, would be able to cross his elbows almost one on top of the other before his chest? . . . Where else, except in Paganini would we find that natural arrangement which prodigiously facilitates his playing: the left shoulder being more than an inch higher than the other—which, when he stands with his arms hanging down, makes the right seem much longer than the left? And the extensibility of the capsular ligaments of both shoulders, the slackness of the ligaments which connect the wrists to the forearm, the carpals to the metacarpals and the phalanges—who else will have these and thus have ability to do what he does? . . . His hand is not of disproportionate size, but, he doubles its reach by the extensibility achieved in all the parts. For example, he can impart to the first phalanges of the fingers of his left hand . . . an extraordinary flexing motion which, without the hand moving, bears them in a direction lateral to their natural flexion—and this with ease, precision, and speed. . . . Nature must have bestowed upon him the organic disposition which practice perfected.

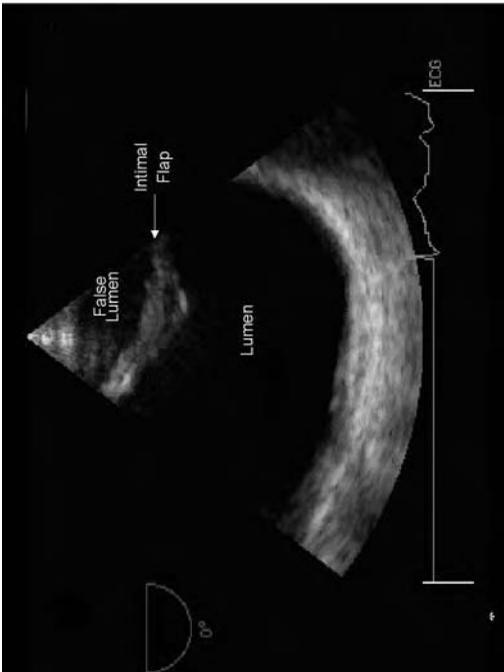


(b)

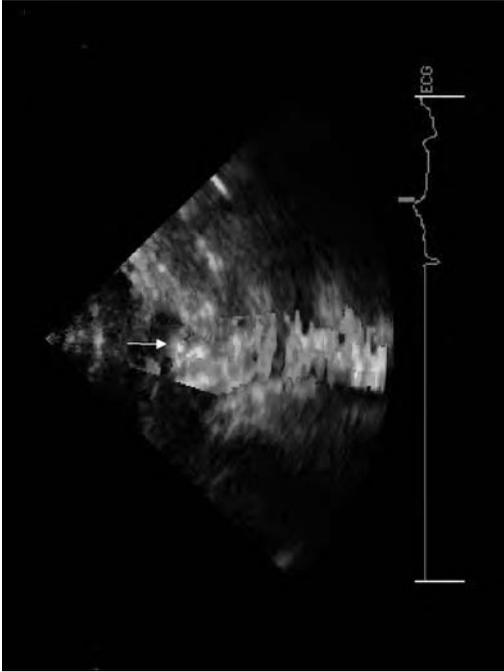


(a)

Figure 13.1. 27-year-old male with dyspnea and previously unrecognized Marfan syndrome. No history of chest pain. The patient underwent emergency composite replacement of the aortic root and ascending aorta, and arch. His postoperative course was uneventful. (a) TEE View: The aortic root and ascending aorta are severely dilated (9.1 cm). There is complete effacement of the sinotubular junction. The aortic valve leaflets are “tented” due to root dilation and traction on the upper aspect of the cusps. No intimal flap is seen in this plane at this level of the aorta. (b) Transthoracic apical view with color Doppler. There is severe aortic regurgitation, due to dilation of the aortic root.



(c)

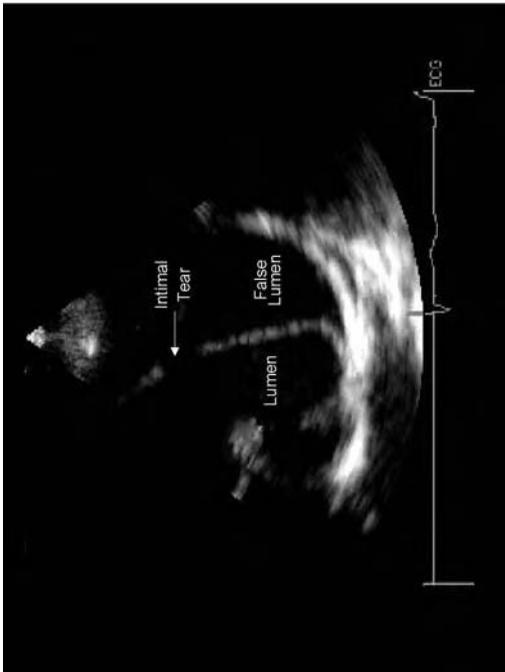


(d)

Figure 13.1. (Continued) (c) The aorta is still dilated at the level of the arch. An intimal flap is present along the posterior wall of the arch (arrows). (d) The responsible tear was in the distal arch and can be seen on this transthoracic view as a (PISA) proximal isovelocity surface area (arrows).

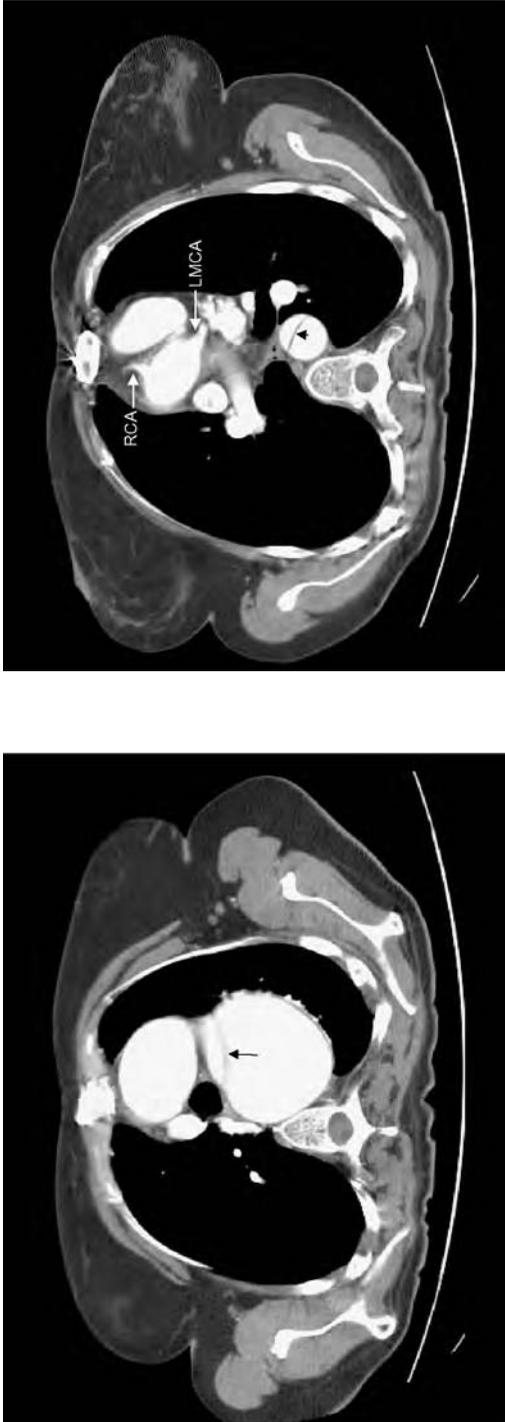


(a)



(b)

Figure 13.2. 19-year-old male who developed severe chest pain while playing basketball. The pain lasted for 20 hours before he sought medical attention. He had numerous Marfanoid features. The patient underwent emergency composite replacement of the root, ascending aorta, and arch. His postoperative course was uneventful. (a) Trans thoracic echo, short axis at the aortic root level. The aortic root is severely dilated and there is an intimal flap (arrows). A tear in the intimal flap can be seen (arrowheads). (b) Trans thoracic echo, suprasternal approach. The intimal flap is readily visible (arrows).



(a)

(b)

Figure 13.3. 38-year-old woman with Marfan syndrome, who five years previously had an elective valve sparing repair of the root and ascending aorta. Postoperative CT scans were performed yearly. Her blood pressure was always low/normal on chronic beta blockade. Postoperatively, she developed moderate (3+) aortic regurgitation due to dilation of the sinuses of Valsalva. The patient was hesitant to undergo repeat surgery. (a) CT scan with moderate contrast at the level of the distal aortic arch. There is an intimal flap in the severely dilated, proximal descending thoracic aorta, which was not clinically suspected. (b) CT scan with contrast at the level of the aortic root. Note the origins of the left and right coronary arteries (arrows). The descending thoracic aorta is of normal caliber at this level, though the intimal flap remains obvious (arrowheads). This cut does not demonstrate the root pathology responsible for her postoperative aortic regurgitation, though it was felt due to continued dilatation of a cuff of native tissue left at the time of her initial repair.

## **OTHER GENETIC DISORDERS ASSOCIATED WITH AORTIC DISSECTION**

Aortic aneurysms and/or dissection have been reported with several other genetic disorders. Familial thoracic aortic aneurysm disease has been mapped to genetic loci, including 5q13-14 and 11q23.2-q24, that are not associated with abnormalities of fibrillin-1 or collagen metabolism<sup>71,72</sup>. Reported patterns of inheritance have included autosomal dominant, autosomal recessive, and sex-linked. More than five mutations in the FBN1 gene have been identified in patients with familial or spontaneous thoracic aortic aneurysm and dissection, with histopathologic changes characteristic of cystic medial degeneration, yet no demonstrable abnormalities of collagen or fibrillin metabolism in fibroblast culture<sup>73</sup>. Familial abdominal aortic aneurysm disease is often accompanied by thoracic involvement, but specific candidate genes have not been identified.

Patients with bicuspid aortic valve (BAV) disease often demonstrate ascending aortic enlargement, which is out of proportion to the associated hemodynamic change imposed by the valve lesion itself. Cystic medial degeneration, of the type seen in fibrillin-1 deficient mice and in patients with Marfan syndrome, underlies this dilatation and predisposes to dissection and/or aneurysm formation<sup>74</sup>. Similar changes have been described in patients with aortic coarctation, independent of an association with BAV disease<sup>75</sup>. Aortic dissection has also been reported in patients with Noonan's syndrome<sup>76</sup>, Turner's syndrome<sup>77</sup>, polycystic kidney disease<sup>78</sup>, cutis laxa<sup>79</sup>, and osteogenesis imperfecta<sup>80</sup>.

## **SUMMARY**

- Marfan syndrome is the most common heritable disorder of connective tissue and is associated with premature death to aortic dissection/rupture or heart failure from aortic regurgitation.
- It is caused by mutations in the gene (FBN1) encoding fibrillin-1. Other gene defects have been reported (MFS2, TFGR2). It is transmitted in autosomal dominant fashion with variable penetrance.
- Clinical diagnosis derives from an appreciation of the major features of the disease, chiefly those involving the skeleton, eyes, and cardiovascular system. Aortic root dilatation occurs in up to 60–80% of adult patients.
- Prophylactic beta-blockade, restriction of activities, and antibiotic prophylaxis (when indicated) are the foundations of medical therapy. Surveillance imaging of the aorta, with or without surgery, is a critical feature of longitudinal follow-up.

- Prophylactic aortic root repair/replacement surgery, to prevent dissection and rupture, is indicated for a maximal diameter >5.0 cm, for a diameter >4.5 cm in patients with a family history of dissection or rupture, and >4.0 cm for women contemplating pregnancy.
- The prevalence of Marfan syndrome among patients with aortic dissection is low. Marfan patients generally present at a relatively young age, with type A dissection, and incur a 20–25% hospital mortality risk. The risk of aortic reoperation following initial dissection repair is higher among patients with Marfan syndrome.
- Pregnancy is particularly hazardous for women with Marfan syndrome.
- Ehlers–Danlos syndrome type IV (vascular type) is associated with premature death due to spontaneous vascular and/or visceral organ rupture. Aortic dissection is less common. The syndrome is due to mutations in the gene (COL3A1) encoding type III procollagen.
- Several other genetic disorders have been associated with aortic diseases. It is anticipated that future research will uncover additional candidate genes and elucidate genotype–phenotype relationships.

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# 14

## **AORTIC INTRAMURAL HEMATOMA: DIAGNOSIS, TREATMENT, AND EVOLUTION**

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Aortic intramural hematoma has been considered a precursor of overt aortic dissection<sup>1,2</sup>; however, the pathophysiologic mechanism, evolution, and prognosis are rather different from those of classical dissection. Advances in imaging techniques have facilitated diagnosis and have aided understanding of the natural history of this entity, practically unknown 10 years ago. Aortic intramural hematoma (IMH) is an entity included in the acute aortic syndrome (AAS) together with aortic dissection and penetrating aortic ulcer<sup>3</sup>. While, in classical aortic dissection, flow communication occurs through a primary intimal tear and blood propagation creates a false lumen, in intramural hematoma hemorrhage occurs within the aortic wall in the absence of intimal disruption<sup>4,5</sup>.

### **ETIOPATHOGENESIS**

Krukenberg, in 1920<sup>6</sup>, first proposed that rupture of the vasavosorum initiated the process of aortic dissection. Gore<sup>1</sup> championed this view in the 1950s and suggested that underlying media degeneration predisposed the vasavosorum toward hemorrhage and IMH. Rupture of the vasavosorum has been related to the atherosclerotic process and systemic hypertension. Other authors have proposed intimal fracture of an atherosclerotic plaque as the primary event, which then allows propagation of blood into the aortic media. Moreover, penetrating atheromatous ulcers were also discussed as a requisite for some intramural bleeding. In such a chronic setting, however, the hematoma is

confined to the area adjacent to an atherosclerotic ulcer<sup>7,8</sup>. The strong relationship between intramural hemorrhage and the atherosclerotic process explains why IMH is located in the descending aorta in 60–80% of cases<sup>9–12</sup>. Intramural hematoma can also be provoked by a thoracic traumatic contusion<sup>13</sup> or by percutaneous catheter manipulation, as in angioplasty (insertion of a balloon pump or catheter ablation on the left side). In these cases, the hemorrhage of the media is generated secondary to an intimedial localized injury, and the false channel (intramural hematoma) would not be decompressed by a reentry tear; therefore, there would be no possibility of detecting flow within the aortic wall<sup>7,14,15</sup>. In this chapter, we consider only spontaneous intramural hematoma.

## PREVALENCE AND RISK FACTORS

The prevalence of IMH in AAS ranges from 5% to 27%<sup>2,10–14,16–18</sup>. This great disparity in the reported incidence is justified by various factors, such as the referral rate of patients from community hospitals and the sensitivity of imaging techniques used by each hospital to diagnose small intramural hematomas. In 1982, an autopsy study noted that 13% of patients with a diagnosis of aortic dissection had IMH<sup>19</sup>. Asian groups reported a higher incidence than the IRAD series—28.9% vs. 5.7%<sup>16–18,20,21</sup>. A possible explanation could be that the diagnosis of intramural hematoma is suspected more frequently in Asian than in Western hospitals. However, this low incidence of IMH in the IRAD series may be due to the fact that IRAD centers are referral centers and some mild IMH may have gone underdiagnosed in primary centers<sup>22</sup>. Patients with IMH are older than those with classical dissection ( $69 \pm 10$  years vs.  $62 \pm 14$  years). Risk factors such as hypertension or hypercholesterolemia tend to be more frequent in IMH, and aortic valve disease and Marfan syndrome more frequent in classical dissection<sup>21</sup>.

## CLINICAL PRESENTATION

IMH is difficult to distinguish from classical dissection on purely clinical grounds. Abrupt onset of severe chest or back pain is the most common presenting symptom of IMH. Pain is rated as worst ever in 40% of cases and is located frequently in the back. Migration of pain is similar to that of dissection (16%) but uncommonly reaches the legs (2% vs. 11%)<sup>21</sup>.

Compared with classical dissection, patients with intramural hematoma seldom have aortic insufficiency, pulse deficits, or lower-limb ischemia. In initial paraclinic examinations, patients with IMH more frequently have a normal

ECG (46% vs. 30%) and a similar tendency to have no abnormalities on initial chest X-ray (23% vs. 15%)<sup>21</sup>.

## DIAGNOSIS

By definition, IMH has neither an intimal flap nor intraluminal flow. Conventional aortography, which is useful for detecting double-channel aorta in classical dissection, failed to identify this disease entity owing to absence of communication between the aortic lumen and the hematoma<sup>23</sup>. Thanks to advances in noninvasive imaging modalities—such as computed tomography (CT)<sup>24</sup>, cardiovascular magnetic resonance (CMR)<sup>2,24</sup>, and transesophageal echocardiography (TEE)<sup>25</sup>—the diagnosis can be correctly made (Figure 14.1). However, to establish the diagnosis requires longer and more imaging tests than classical dissection<sup>21</sup>. One of the IRAD lessons is the low incidence (approximately 6%)<sup>21</sup>, of IMH diagnosed in nontraumatic acute aortic syndromes. This figure is clearly lower than that reported in other series published from a single center and may reflect the degree to which the diagnosis was sought among patients with abnormal but nondiagnostic initial imaging studies.

## IMAGING TECHNIQUE FINDINGS

Computed tomography shows a high attenuation area, usually crescentic or circular, along the aorta wall without intimal flap before contrast injection, which fails to enhance after injection of contrast medium<sup>24</sup> (Figure 14.2). Crescentic aortic wall thickening without intimal flap is very easily detected by magnetic resonance imaging; the signal intensity of the thickened aorta is secondary to methemoglobin formation within the hematoma, resulting in increased signal intensity on T1-weighted images in subacute IMH<sup>2</sup> (Figure 14.1).

Transesophageal echocardiography is also useful to demonstrate thickening of the aortic wall<sup>25</sup> (Figure 14.1), although it offers no signals to identify acute versus chronic hematoma, and a differential diagnosis among other entities that also present thickening of the aorta wall (such as severe atherosclerosis of the intima or aortitis) should be made.

As normal aorta wall thickness is less than 3–4 mm by any imaging modality, aortic wall thickness more than 5 mm with typical clinical symptoms suggesting acute aortic syndrome suffices for diagnosis of intramural hematoma<sup>26</sup>.

Although studies that compare the diagnostic sensitivity and specificity of imaging techniques do not exist, their diagnostic accuracy does not appear to be so different, and imaging modality selection in the acute phase depends on

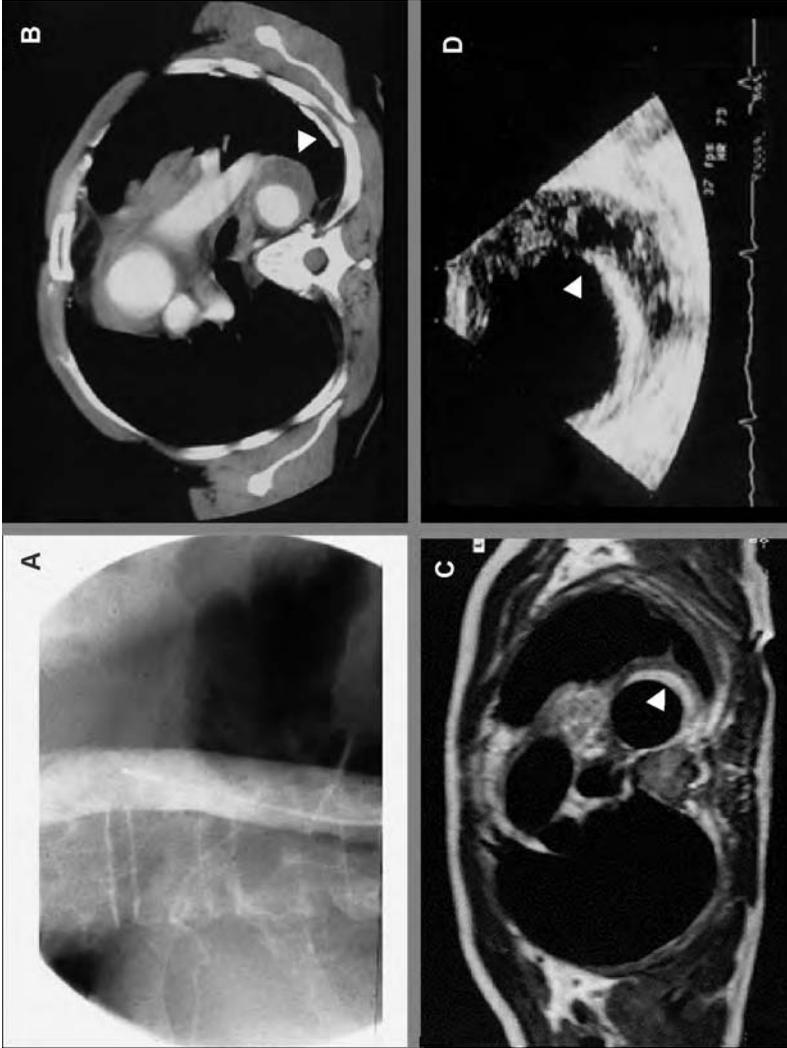


Figure 14.1. IMH in descending aorta by four imaging techniques. A. Aortography revealed no abnormalities. B. CT showed an IMH in proximal descending aorta and paraortic hematoma. C. CMR disclosed a hyperintense signal identifying the hematoma. D. TEE showed the same IMH with echolucent areas.



Figure 14.2. CT reveals a high attenuation signal in ascending aorta (arrows) corresponding to an ascending aorta IMH.

many variables, including clinical situation, physician preference, and availability of experts.

TEE is superior to any other technique for assessing the intima and demonstrating small communications with the Doppler technique (Figure 14.3). One characteristic finding is the presence of echolucent areas or echo-free space within the thickened aorta wall<sup>27</sup>. By CT with contrast enhancement, it is possible to demonstrate, in selected patients, a small communication through an intimal micro-tear, but this is exceptional in the acute phase. However, the wide field of vision of CT and MRI is important to correctly define the global extension of IMH and periaortic bleeding. A high presence of fluid extravasation, pericardial and pleural effusion, and mediastinal hemorrhage is a frequent finding in IMH<sup>12,16,17</sup>.

## DIFFERENTIAL DIAGNOSIS

IMH is quite easily differentiated from classical aortic dissection; intimal tear or flap is absent, and there is no evidence of direct flow communication. However, the diagnosis can be very difficult when the false lumen of dissection is totally thrombosed. In this case, only identification of an entry tear, during surgery or necropsy, permits correct differentiation. On the other hand, only complete chronologic imaging technique findings can permit a correct differential diagnosis between aortic dissection with total thrombus of the proximal



Figure 14.3. Punctiform intimal rupture in a descending aorta IMH.

or distal part versus an intramural hematoma that evolves to classical dissection in one of the segments.

One of the challenging differential diagnoses of intramural hematoma is with aortic wall thickening caused by atherosclerotic changes or with aneurysmal dilatation with mural thrombi<sup>25</sup>. In distinguishing IMH from other aortic conditions, identification of the intima and careful observation of the inner surface of the thickened aortic wall are helpful. Usually, the inner margin of IMH is smooth, and aortic thickening occurs beneath the bright echo-dense intima, whereas an irregular margin caused by thickening above the intima with dilated aorta is commonly observed in patients with aneurysmal dilatation and mural thrombi. In this respect, the presence of intimal calcium can often be used to distinguish intramural hematoma from intraluminal thrombus<sup>26</sup>.

## STRATEGY

Diagnosis of IMH is not always easy. IRAD results showed that in more than 50% of cases two or three imaging techniques were performed in the acute phase<sup>21</sup>. The challenge to early diagnosis of intramural hematoma is considerable. Given the dynamic evolution of IMH and its difficult diagnosis when small, multiple diagnostic imaging tests were needed to confirm its presence (Figure 14.4). In the IRAD series, 7 of 58 IMH were not diagnosed in the first study; however, as acute aortic syndrome was strongly suspected clinically, a second imaging technique was performed and revealed an intramural hematoma. On the other hand, 16% of cases demonstrated signs of classical

dissection on second testing, while other consecutive tests showed the persistence of intramural hematoma<sup>21</sup>. It is advisable when symptoms are clear and there is no alternative cause of the pain to repeat the study 48–72 hours later. In these cases of small intramural hematoma thickness, CT but mainly MRI are more sensitive. The delay in IMH patients' arrival at IRAD centers may also explain the low incidence of IMH in the IRAD series owing to the evolution of some IMH to CLD. Many patients have a combination of IMH and CLD and were excluded from the analysis. On the other hand, depending on the exact time after the onset of symptoms when an imaging “snapshot” is performed, the appearance may be interpreted differently from an impression made from images obtained only hours before or after<sup>27</sup>.

## EARLY EVOLUTION, COMPLICATIONS, AND RISK STRATIFICATION

Prospective studies revealed evidence that IMH evolves to reabsorption or progression to either classical dissection, contained rupture, or formation of an aneurysm within 30 days of hospital admission<sup>28–33</sup>. Acute mortality in the overall published series of more than 500 cases has been considered to be between 15–20%<sup>10,32</sup>, 34% in type A, and 14% in type B<sup>32</sup>. In our series, IMH mortality in the first three months of evolution was 19%<sup>12</sup>. Predictive IMH mortality factors were basically ascending aorta involvement and maximum aortic diameter. Patients with ascending aorta involvement showed 50% mortality and 12% when only the descending aorta or arch were involved. Patients mortality with aortic diameter over 50 mm was 50% and only 2% in those with diameter less than 50 mm<sup>12</sup>.

### TYPE A

Significant controversy exists over natural evolution of type A IMH. The mortality rate of the medically treated groups in European and American series is very high, while in the Asian series it is very low<sup>10–12,17,18,32–34</sup>. A European multicenter study<sup>32</sup> of 66 IMH showed a global mortality rate of 20%. In this study, a high incidence of type A IMH (58%) was observed. Surgery was indicated in 84% of type A cases, and early mortality was 8% with swift surgery versus 55% without surgery. These results suggest that the short-term prognosis is poor in IMH involving the ascending aorta, and surgical repair should be considered. The high risk of “wait and see” in type A IMH, however, is reflected in 55% early mortality with medical treatment compared to 8% with surgical repair ( $P = 0.004$ ). However, the study was retrospective, and the reasons from four different centers for choosing medical treatment

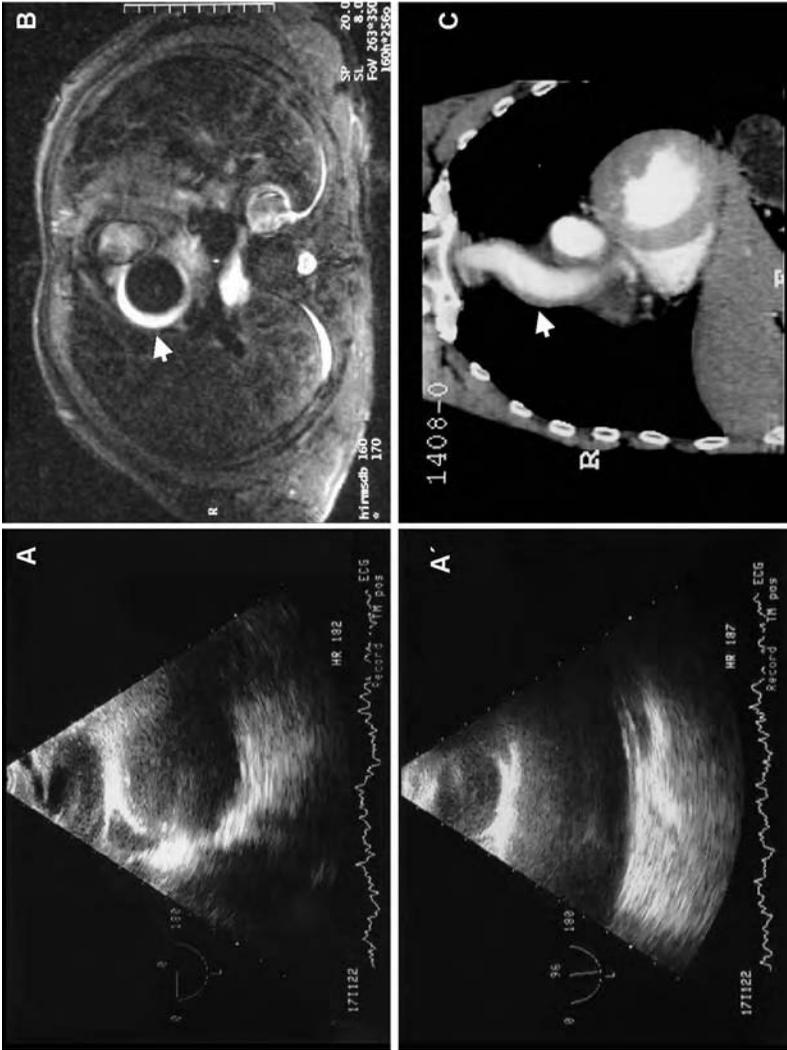


Figure 14.4. In left images, TEE in transverse (A) and longitudinal (A') views show minimal thickening of the ascending aorta wall, which was not diagnosed as abnormal. B. CMR performed 72 hours latter shows hyperintense signal in ascending aorta wall diagnosed as type A IMH. C. CT performed the same day as CMR discloses a small thickening of the aorta wall. The diagnosis of INH was only considered definitive in the CMR study.

were not described. In the IRAD series, IMH of the ascending aorta carried an in-hospital mortality of 39%, a value not statistically different from the 30% in type A dissection. Mortality was a function of the presumed site of the origin for IMH; the more proximal the IMH, the greater mortality observed<sup>21</sup>.

Studies from Japanese and Korean groups showed that medically treated patients with IMH have low mortality, regardless of whether they are type A or B<sup>10,16–18,20</sup>. In Korean patients with type A IMH treated medically, only 1 out of 18 died, but 4 patients required pericardiocentesis or surgery for proximal dissection<sup>35</sup>. There are some reasons to justify these discrepancies: most Western studies are multicenter, and in them IMH comprises less than 10% of AAS<sup>21,32</sup>. Therefore, it is possible that most cases included represent the most complicated spectrum. On the other hand, most Asian reports are based on serial observations from a single center experience, and the relative incidence of IMH in AAS is 30%<sup>16–18,20</sup>. Based on these reasons, it seems that rather than a geographical or racial difference, the discrepancies in the results might be explained by a different severity in the IMH spectrum assessed.

Some studies have shown IMH reabsorption to be related to smaller aortic diameter<sup>5,16,24,30</sup>. In 22 patients with type A IMH, Kaji et al.<sup>34</sup> showed that the group in which IMH regressed had a significantly smaller aortic diameter than the group in which IMH progressed or evolved to dissection or aortic rupture ( $47 \pm 3$  vs.  $55 \pm 6$  mm), which suggested an optimum cutoff value of 50 mm, identical to that obtained in our series<sup>12</sup> (Figure 14.5). Ide et al.<sup>36</sup> observed that evolution to classical dissection was seen only in IMH with aorta diameter  $>50$  mm. However, 54% of cases with aortic diameters  $<50$  mm eventually progressed to dissection or rupture, challenging the Asian experience that IMH in a normal-size aorta precludes complications.

## TYPE B

There is a paucity of information regarding the evolution of type B IMH and maximum aortic diameter. In a recent study, Sueyoshi et al.<sup>37</sup> reported that in the follow-up of 35 type B IMH, maximum aortic diameter over 40 mm predicted IMH progression. Although normal descending aorta diameter is smaller than that of the ascending aorta, the lower risk of descending aorta rupture could justify 50 mm being an adequate cutoff value for both type A and type B. A possible explanation for the prognostic value of maximum aortic diameter in short-term IMH evolution is that when intramural bleeding weakens the aorta wall, the greater stress on the wall of the dilated aorta implies a greater risk of rupture than that of the nondilated aorta.

Ganaha et al.<sup>31</sup> suggested the presence of penetrating atherosclerotic ulcer in acute phase as the factor predicting IMH progression, with maximum aortic diameter lacking prognostic value. The high incidence of aortic ulcers

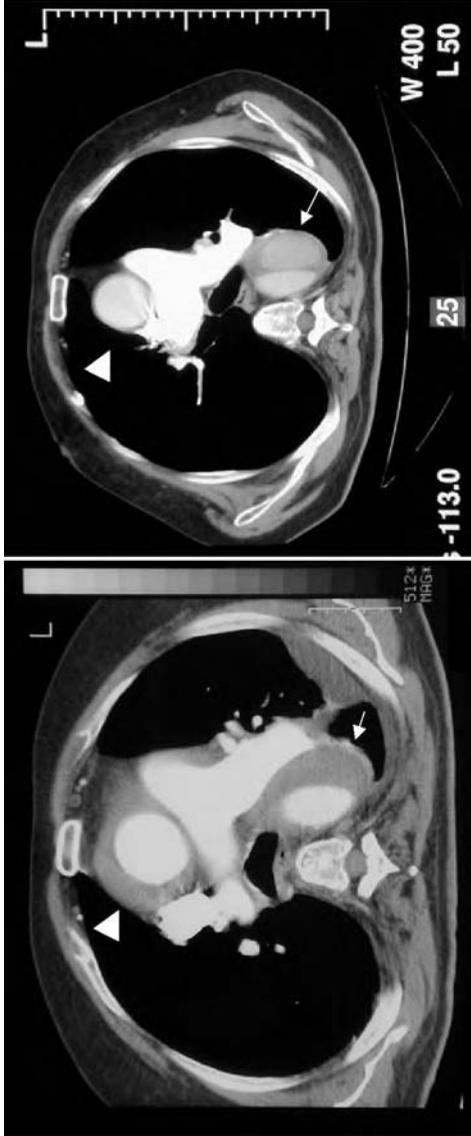


Figure 14.5. CT study showed a type A IMH, which evolved at six months to type B dissection with total reabsorption of ascending aorta IMH (arrowhead).



Figure 14.6. TEE visualized a localized dissection in the descending aorta (arrow) at one month of evolution of IMH. Arrow shows a short intimal flap.

(52%) in this retrospective series could be explained by the inclusion of IMH cases in a subacute or chronic phase with ulcerlike images due to localized dissections during IMH evolution. Thus, these localized dissections would constitute a complication rather than a prognostic variable in an acute phase. In our series<sup>33</sup>, TEE showed localized dissections with ulcerlike images in the study conducted prior to discharge in 28% of patients (Figure 14.6). TEE is the technique of choice for differentiating penetrating atherosclerotic ulcers from ulcerlike images (Figure 14.7). Although some focal dissection evolved to pseudoaneurysm formation, most remain stable without enlargement and others disappear.

Several published series showed that periaortic bleeding is more frequent in IMH than in classical dissection<sup>12,16,17</sup>. Although this bleeding is not necessarily the equivalent of aortic rupture, and most IMH tend to reabsorb without complications (Figure 14.8)<sup>12</sup>, the mortality of our patients with these complications was high (35–43%), particularly in the subgroup of patients who presented anemia on biochemical analysis (47%). However, progressive accumulation of a large amount of pleural effusion is not in itself an indication for surgical treatment.

Risk stratification based on clinical and diagnostic imaging findings in patients with IMH is very useful<sup>38</sup>. Some of the current predictive factors of disease progression proposed for patients with IMH include persistent and recurrent pain despite aggressive medical treatment<sup>31</sup>, difficult blood pressure control<sup>32</sup>, ascending aorta involvement<sup>12</sup>, maximum aortic diameter 50 mm or more on initial CT scan<sup>34</sup>, progressive maximal aortic wall thickness

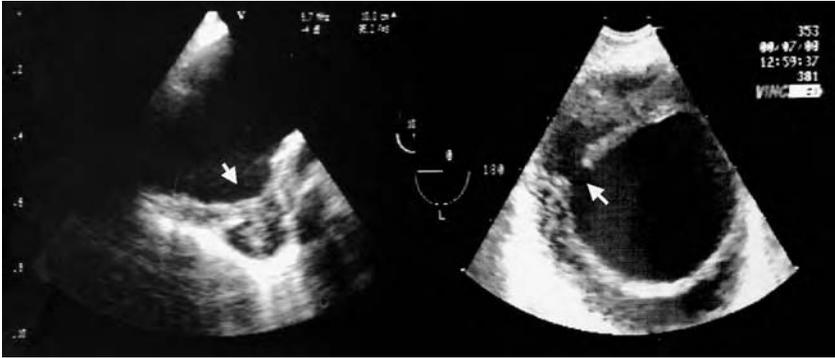


Figure 14.7. Differential diagnosis of aortic ulcers by TEE. In the left image, a penetrating aortic ulcer with thrombosis within is observed. In the right image, the ulcer is secondary to a localized dissection from a IMH.

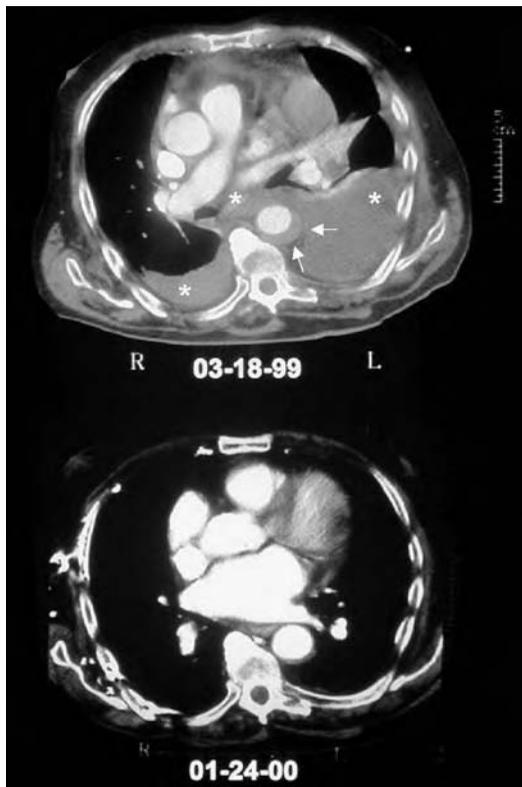


Figure 14.8. Type B IMH (arrows) with hemothorax and hemomediastinum (asterisks), which evolve to total regression of IMH, periaortic hemorrhage, and hemothorax, at eight months of follow-up.

(>11 mm)<sup>35</sup>, enlarging aortic diameter<sup>32</sup>, repetitive pleural effusion<sup>31</sup>, and presence of an associated penetrating ulcer or ulcerlike projection in the involved segment<sup>31</sup>.

## ACUTE TREATMENT

Patients with acute IMH should be admitted to an intensive care or monitoring unit and undergo immediate diagnostic evaluation. Pain and blood pressure control to a target systolic pressure of 110 mm Hg can be achieved by using morphine sulphate and intravenous beta blockers or in combination with vasodilating drugs. In normotensive or hypotensive patients, careful evaluation for blood loss, pericardial effusion or heart failure is mandatory<sup>39</sup>. Although percutaneous pericardiocentesis as a temporizing step has often failed in aortic dissection, the mechanism of extraaortic accumulation from IMH is not necessarily the same, and some reports proved the benefit of pericardiocentesis in medically treated patients<sup>34</sup>.

### TYPE A

Therapeutic management in the acute phase should be similar to that of aortic dissection. Although type A IMH has a worse prognosis than type B, evolution of ascending aorta hematoma can have better short-term evolution than ascending aorta dissection. On the other hand, some subgroups of type A IMH, particularly with nonaortic dilatation (<50 mm) and thickness <11 mm, may evolve to total reabsorption with medical treatment<sup>34,35</sup>. Although emergency surgery is an established standard treatment option for patients with type A classical dissection, initial medical treatment and timed surgery with frequent imaging follow-up can be a rational option for patients with uncomplicated type A IMH<sup>35</sup>. This strategy is based on the fact that development of complications such as dissection and death can be predicted by hematoma thickness and aortic diameter. However, the approach of considering immediate surgical treatment is right to a great extent as asymptomatic progression to dissection is relatively common in the subacute phase and frequently unforeseeable. Pericardial effusion or tamponade are more frequent in IMH than in classical dissection.

Although pericardiocentesis and medical strategy has been considered a good option<sup>35</sup>, surgical therapy is more suitable. No studies have assessed the risk/benefit ratio of emergent surgery versus elective surgery in noncomplicated type A IMH. Optimal assistential conditions and the best surgical team should be balanced with the possible risk of the patient. As IMH patients tend to be older than those who have dissection, comorbidity is not exceptional.

Therefore, it is fundamental that the therapeutic management be individualized. For a patient presenting within a few hours of symptom onset with an unequivocal acute hematoma in ascending aorta extending toward the coronary ostia or aortic valve, watchful waiting is far more hazardous than surgical repair. Conversely, in a patient seen beyond 48 hours of symptom onset with a limited IMH near the arch or distally, watchful waiting and medical therapy is an appropriate approach considering currently available data<sup>28</sup>.

## **TYPE B**

Acute IMH involving the descending aorta has an in-hospital mortality risk of less than 10%, similar to that seen with descending or type B aortic dissection. Literature supports the use of medical therapy as the initial treatment for this condition. Acute IMH confined to the arch remains a controversial issue. In the IRAD series, most of the patients were managed medically without mortality<sup>21</sup>. If complications arise, such as periaortic hematoma, localized dissection, or rapid aneurysm formation, a close imaging technique follow-up should be made. Surgical treatment would have the same indications as type B aortic dissection. Nowadays, endovascular therapy can be considered, particularly in ulcer formation with rapid expansion. However, a recent report shows that the device can cause erosion of the intima in the acute phase<sup>40</sup>. Therefore, it is advisable to implant the stent with the ends placed over the healthy aorta. While definitive results of endovascular therapy in the acute phase of IMH have not been reported, indications in acute phase should be restrictive. Whenever clinical and hemodynamic evolution is stable, treatment of morphologic complications (such as pseudoaneurysm or aneurysm formation) should be considered after regression of the intramural hemorrhage.

An imaging technique, if possible CMR, should be repeated before hospital discharge, to compare it with that performed at one to three months of follow-up. During this period, the hematoma has a very dynamic evolution, and it is important to maintain strict control of blood pressure and repeat imaging techniques if any symptom could be related to the hematoma.

## **LONG-TERM EVOLUTION, COMPLICATIONS, AND RISK STRATIFICATION**

### **TYPE A**

There is little information on the long-term evolution of type A IMH. Kaji et al.<sup>18</sup> reported that 13 of 30 (43%) of type A IMH developed classical dissection or showed an increase of hematoma size during follow-up (Figure 14.9). These patients underwent graft replacement of the ascending aorta (mean 37

days, range 7–94 days after onset). Operative mortality rate was 8%. Considering the relatively low mortality rate in type A IMH patients and the fact that 43% of patients required surgery in this study, it might seem advisable to operate immediately on all patients with type A IMH. It is likely that supportive medical therapy be a reasonable option as the initial modalities and surgical backup are always available. In this series, 17 patients (57%) were discharged without surgery. Among them, hematoma size significantly decreased from  $9 \pm 3$  mm to  $1 \pm 3$  mm and maximum aortic diameter from  $48 \pm 5$  mm to  $45 \pm 6$ . Complete resolution of IMH in the ascending aorta occurred in 12 patients (40%). Actuarial five-year survival of these patients was 90%. In a recent study by Moizumi et al.<sup>41</sup>, 11 of 41 type A IMH (27%) underwent surgery in acute phase and 9 (22%) during follow-up. The estimated freedom from IMH-related events at five years was  $54 \pm 11\%$ .

However, little data exist on clinical predictors for the development of aortic dissection in type A IMH. Initial maximum diameter  $>50$  mm and hematoma thickness  $>11$  mm<sup>34,35</sup> appear to be the best indexes for predicting adverse clinical outcome in stable patients with type A IMH. However, these variables are not prospectively tested. Therefore, clinical and imaging technique follow-up should be done until the IMH is reabsorbed completely, every six months during the first three years, and annually thereafter.

## TYPE B

Long-term prognosis of patients with type B IMH is better than in patients with aortic dissection. However, survival at five years reported in different series ranges from 43% to 90%, depending on the population characteristics<sup>32,33,42</sup>. Several studies have shown important dynamic changes in IMH during evolution, mainly during the six first months<sup>31,33,37</sup>. Regression occurred within six months in 30% of cases, progression to dissection was observed in 40%, with classical dissection in 12% and focal dissection in 28%, and 30% reabsorbed with aortic dilatation<sup>33</sup>. In our series<sup>33</sup>, 50 patients with IMH were followed by clinical and imaging techniques for  $45 \pm 31$  months. At the end of follow-up, the IMH had reabsorbed completely in 34% (Figure 14.10), progressed to classical dissection in 12% (Figure 14.11), evolved to fusiform aneurysm in 22% (Figure 14.12), evolved to saccular aneurysm in 8% (Figure 14.13), and evolved to pseudoaneurysm in 24% (Figure 14.14). Therefore, the most frequent morphological long-term evolution of IMH is to aortic aneurysm or pseudoaneurysm formation (54% of cases).

Maximum aortic diameter in the acute phase is the variable of greatest prognostic yield for IMH regression, showing smaller maximum aortic diameter than in the group that evolved to aortic aneurysm or dissection.

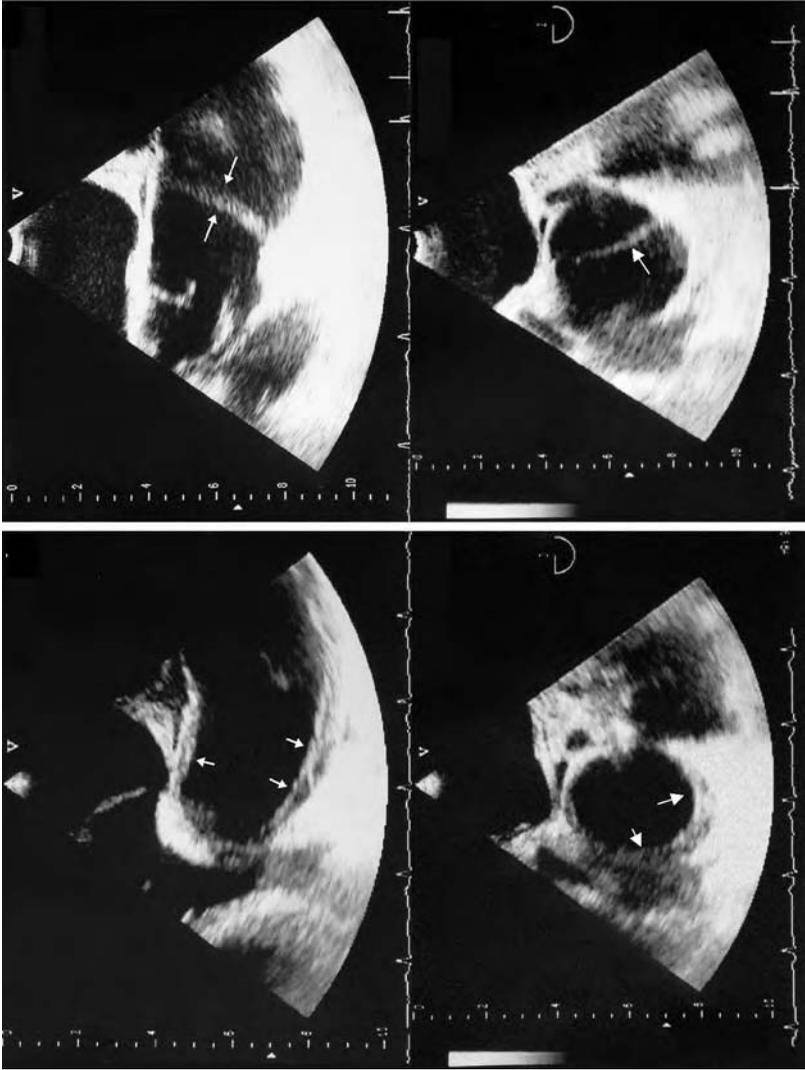


Figure 14.9. Follow-up of type A IMH by TEE. At four months of follow-up, a type A dissection is observed. In left images arrows show intramural hematoma, and in right images arrows show intimal flap.

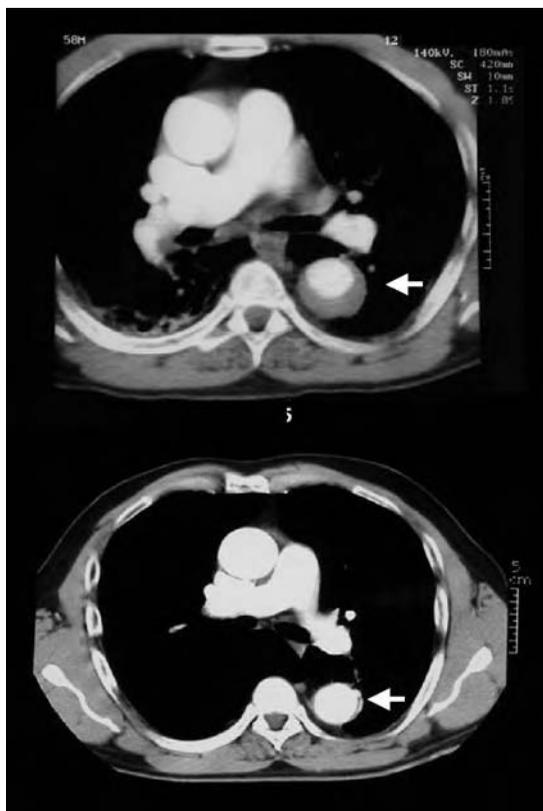


Figure 14.10. Type B IMH, which evolved with a total reabsorption at six months.

It has been reported that IMH with PAU or penetrating atherosclerotic ulcer was associated with a progressive disease course<sup>32</sup>. Sueyoshi et al.<sup>37</sup> reported that 12 of 17 projections progressed to complications such as enlargement or evolution to classical dissection. Ganaha et al.<sup>31</sup> reported that IMH with PAU was significantly associated with a progressive disease course and concluded that it was important to make a clear distinction between IMH with or without PAU. Kaji et al.<sup>40</sup> showed that older age and appearance of an ulcerlike projection are predictive for progression with type B IMH. Literature results seem to confirm that one of the important complications of IMH is the localized dissection which is identified as an ulcerlike image<sup>43</sup> (Figure 14.15). However, little is known about the long-term evolution of this complication.

Other variables (such as echolucency and IMH extension) predict progression to aortic dissection. Song et al.<sup>27</sup> found no prognostic significance between echo-free space detected in IMH and progression to dissection. In that

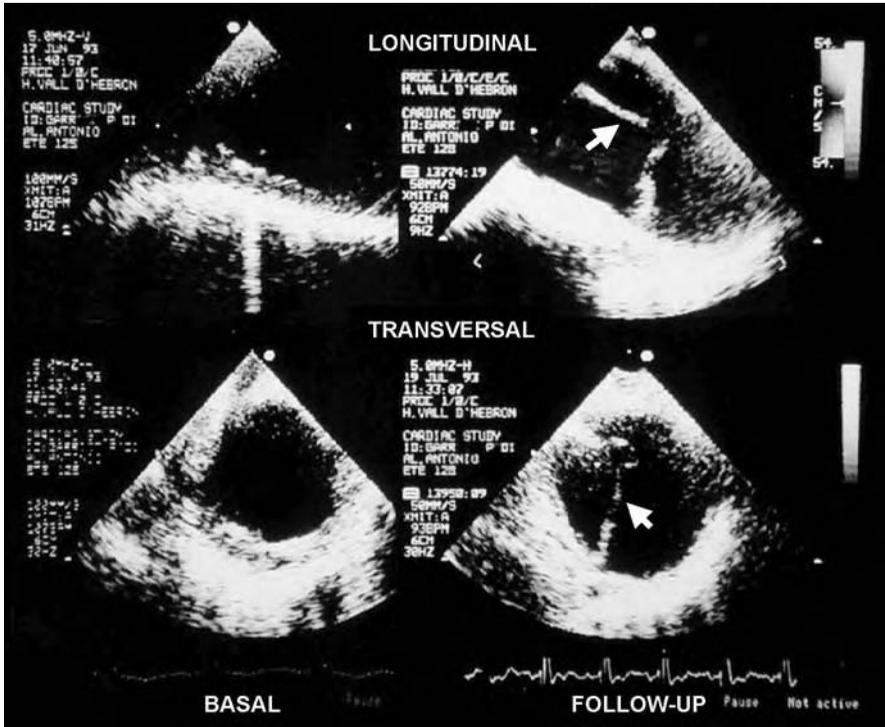


Figure 14.11. TEE shows a type A IMH, which evolved to classical dissection at one month of follow-up (arrows).

study, only TEE was performed during a short follow-up period, and some localized dissections therefore may have gone unnoticed.

Long-term evolution to fusiform aneurysm is related to greater aortic diameter in the acute phase because structural weakness of the media and mechanical stress may favor fusiform dilatation<sup>44</sup>. On the other hand, patients evolving to fusiform or saccular aneurysm had higher frequency of atherosclerotic disease and ulcerated plaque in the aorta, which points to the atherosclerotic process as a leading cause of aneurysm formation. These findings suggest that IMH might be involved in the pathogenesis of chronic aneurysm. In patients with aortic atherosclerosis, some aorta wall hemorrhages may be symptomatic and be diagnosed as IMH within acute aortic syndrome, whereas others might be asymptomatic with silent progression to aortic aneurysm. In our follow-up studies, five asymptomatic aortic rebleeding were found, and all cases evolved to aneurysm formation. Moizumi et al.<sup>41</sup> showed that thickness at two to four weeks after admission (cutoff value > 16 mm) was the only predictor of IMH-related events because of enlargement of the ulcerlike images or classical type B dissection. On the other hand, the maximum aortic diameter on admission

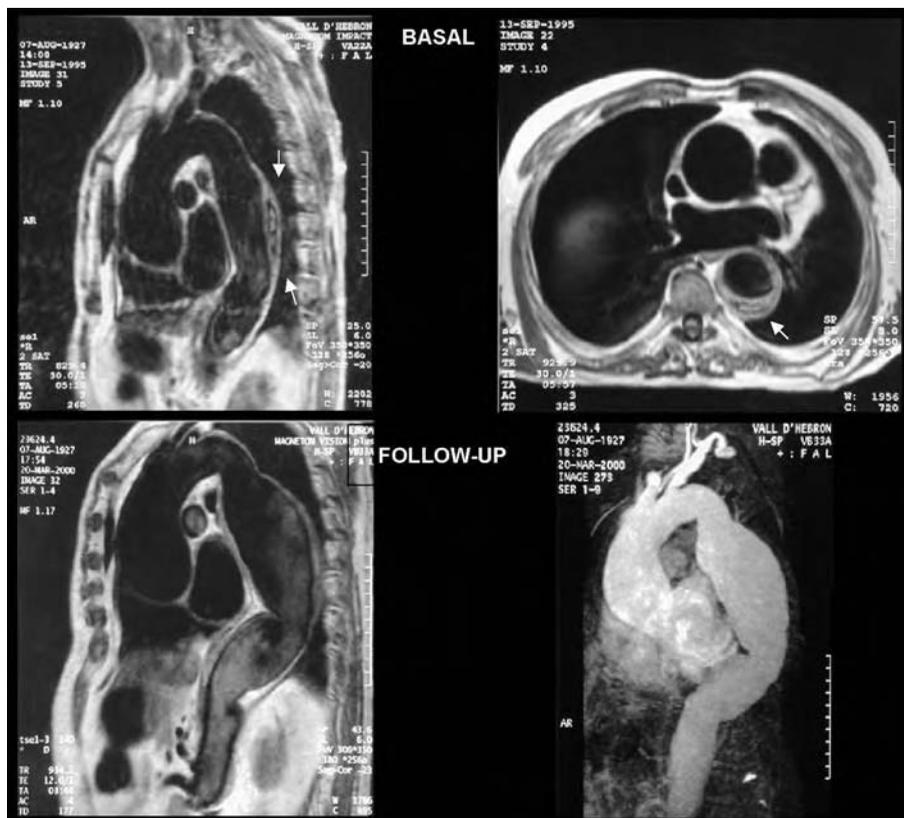


Figure 14.12. IMH diagnosed by CMR: sagittal view (left) and transverse view (right). Marked dilatation of the aorta forming a fusiform aneurysm at five years.

and two to four weeks later (cutoff value  $>53$  mm) was also a significantly correlated variable for IMH-related events because of progressive aortic dilatation or rupture.

## CHRONIC PHASE TREATMENT

The long-term management of patients with successful initial treatment of IMH begins with aggressive antihypertensive therapy. Treatment with effective beta adrenergic blocking agents protects the aorta by reducing both systolic pressure and  $dP/dt$ . Progressive up-titration of dosage is advisable to achieve a blood pressure  $<135/80$  mmHg. IMH should be treated with beta blockers<sup>32,39</sup> and closely followed up with imaging techniques, until complication-free absorption of the hematoma is observed and individualized thereafter. Serial imaging of the aorta is an essential component of long-term

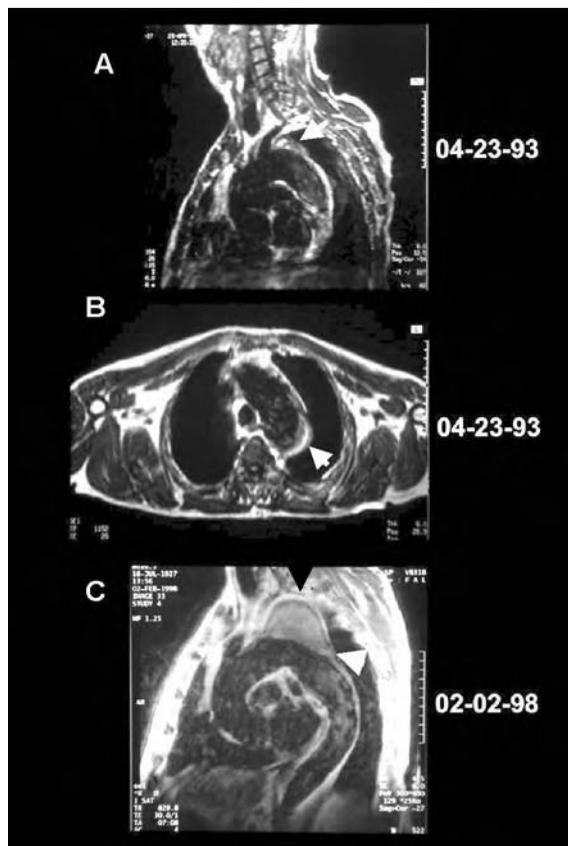


Figure 14.13. IMH secondary to penetrating atherosclerotic ulcer. The upper images show the hyperintensity signal of the subacute IMH. At five years of follow-up, a saccular aneurysm was observed with an increasing diameter from 38 mm to 105 mm.

treatment. Choice of imaging modality is dependent on institutional availability and expertise, as well as the extent of aortic involvement and complications. Recommendations suggest follow-up imaging and examination at 1, 3, 6, and 12 months after discharge and annually thereafter.

The subgroup of patients with aortic dilatation or with localized dissection (ulcerlike images) should be followed up and treated more aggressively if progressive aortic dilatation is observed<sup>27</sup>. Indications for surgical intervention could be (1) maximum diameter of the affected aorta >60 mm, (2) rapid enlargement of the affected aorta, (3) rapid enlargement of an ulcerlike lesion, and (4) rupture of the affected aorta. Although surgical intervention is recommended in this setting, conventional open repair requiring graft interposition is associated with high morbidity and mortality rates, especially in patients of advanced age or with comorbidity. Endovascular placement of the stent grafts



Figure 14.14. Type B IMH evolving with two pseudoaneurysm formations from two localized dissections (asterisks).

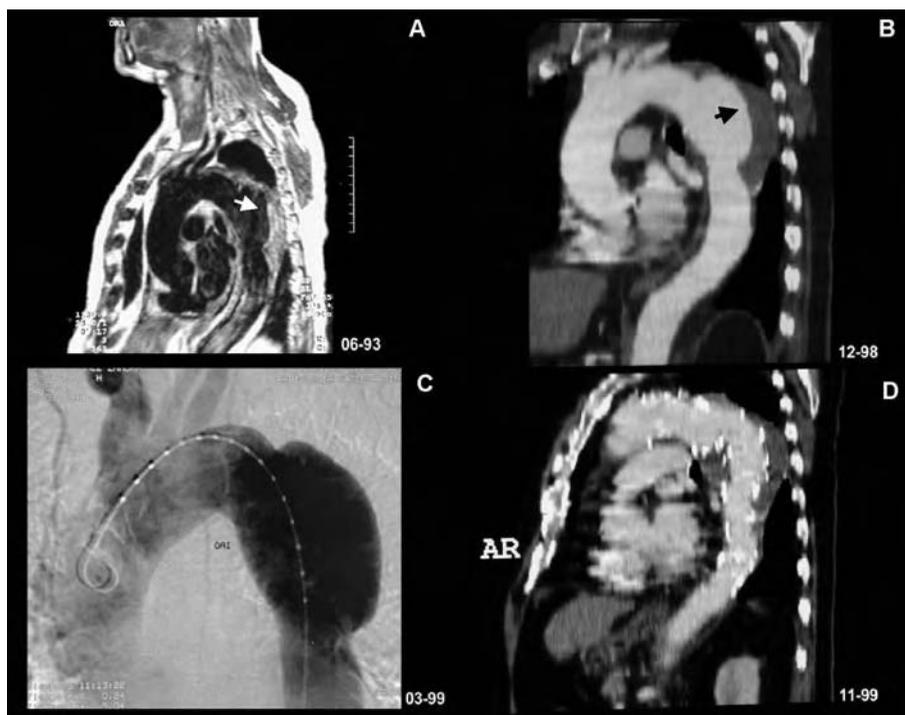


Figure 14.15. Type B IMH with progressive dilatation in descending aorta (A–B). Endovascular treatment was performed at one year (C–D).

to cover the ulcer and part of the IMH has been recently investigated with promising initial results, including a lack of early pseudoaneurysms formation in the treated aortic segment<sup>27</sup>; however, this remains to be confirmed by results from large clinical series.

## CONCLUSIONS

Aortic intramural hematoma (IMH) is an entity included in acute aortic syndrome in which hemorrhage occurs in the media of the aortic wall in the absence of intimal tear. The diagnosis is difficult and requires a high clinical index of suspicion. Its incidence ranges between 15–30% of acute aortic syndromes. Clinical presentation may be identical to that of classical dissection. IMH affects patients with more atherosclerotic risk factors and is located in the descending aorta in 60–70% of cases. Imaging techniques have similar diagnostic accuracy. MRI and CT give additional chronologic and periaortic information. Given the dynamic progressive evolution, a combination of imaging modalities may be useful to confirm the diagnosis. Short-term mortality depends essentially on IMH location and is higher when the ascending rather than descending aorta is involved. Clinical and hemodynamic evolution, together with maximum aortic diameter and thickness of the hematoma are variables to be considered in acute therapeutic management. Although emergency surgery is not always required in noncomplicated type A IMH, surgical management in the first week is advisable in most cases. The most frequent morphologic long-term evolution is to aneurysm or pseudoaneurysm formation. Regression without aortic dilatation is fairly common, essentially in patients with normal aortic size; on the other hand, progression to classical aortic dissection is less frequent. Aggressive antihypertensive treatment appears to be a safe strategy; however, frequent follow-up imaging evaluation is required, and a low threshold for intervention should be maintained if symptoms recur or if the aorta enlarges significantly.

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# 15

## EVALUATION AND MANAGEMENT OF TRAUMATIC AORTIC LESIONS

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### DEMOGRAPHY AND MECHANISM

Traumatic aortic rupture (TAR) is a lesion extending from the intima to the adventitia, occurring as a result of trauma. The first annotation of TAR was in 1557 by Vesalius, who described a patient with an aortic rupture after a fall from a horse. In 1923, Dshanelidze in Russia reported the first successful repair of TAR in a penetrating lesion of ascending aorta, followed in the 1950s by the surgical report of Passaro and Pace<sup>1</sup>. The era of high-speed motor vehicles has brought with it an increased incidence of TAR. Between 1936 and 1942, in a cohort of 7,000 autopsies, Strassman<sup>2</sup> found only 51 patients with traumatic aortic rupture secondary to vehicular collision, whereas several recent investigations have shown that TAR occurs in 10–30% of adults sustaining fatal blunt trauma; it therefore represents one of the most common causes of death at the scene of vehicular accidents<sup>3–6</sup>.

Trauma is the third leading cause of death in the United States and the leading cause of death in individuals under the age of 40. Among lethal traumatic lesions, aortic rupture is secondary only to head trauma: one quarter of deaths resulting from motor vehicle accidents are associated with TAR, accounting for 8,000 victims per year in the US<sup>3</sup>. The lesion may be generated by many different types of sudden-deceleration injury, including car and motorcycle collisions, falls from a height, blast injuries, airplane and train crashes, and skiing and equestrian accidents. The increasing rate of traffic accidents during the last few decades has resulted in motor vehicle accidents becoming the

most frequent cause, accounting for more than 90% in the recent series. The mandatory use of a seat belt, first introduced in the 1970s in Finland and progressively throughout the world, has partially modified the characteristics of the trauma impact that leads to aortic rupture. Changes in epidemiology were reported by Duhaylongsod et al.<sup>7</sup> in a review of their own experiences with 108 patients and of the surgical literature between 1970 and 1990. More sophisticated prehospital care and the proliferation of rapid transport for patients have resulted in an average increase in the number of patients treated. Significantly, despite improvements in transport and treatment, overall mortality was unchanged.

Other significant trends in the last decade are an increasing number of motorcycle accidents, the average patient age increasing from 34 to 38 years, and a lower incidence of rupture of the ascending aorta in seat-belt wearers in comparison with unbelted victims of the 1960s<sup>8</sup>. Although frontal collision is the most common mechanism causing traumatic injury of the aorta, broadside impact accounts for 20–40% of cases in recent studies. The shearing forces in lateral collision seem to produce most frequently a partial laceration involving the lesser curvature of the distal part of the aortic arch, just above the isthmus<sup>9</sup>. Air bags and seatbelts do not protect against this type of impact. Such injuries can be expected to gain prominence in road traffic injury statistics<sup>3</sup>, since the frequency of lethal injuries in head-on collisions is lowered by the mandatory use of restraints, which protect the victim from thoracic and head lesions but not from the mechanism producing aortic rupture.

The most common cause of traumatic aortic rupture is the force generated by rapid deceleration of the body in either the vertical or horizontal plane—that set up between the various portions of the aorta depending on their structure, location, and attachments. The region subjected to the greatest strain is put upon the isthmus, where the relatively mobile thoracic aorta joins the fixed arch and the insertion of the ligamentum arteriosus. Aortic ruptures occur at this site in 80% of the pathological series and in 90–95% of the clinical series<sup>2,4,5,10</sup>. The ascending aorta may be involved in the proximity of the innominate artery or in its proximal segment immediately superior to the aortic valve. Because of the high immediate mortality of traumatic rupture of the ascending aorta, this location has been reported in the 10–20% of the autopsy series versus 5% of the surgical cases<sup>2,6,10</sup>. Other less common locations are distal segments of the descending aorta (12%) or the abdominal infrarenal segment (4.7%). Multiple sites of aortic tears are found in some reports<sup>10</sup>.

Different theories have been advanced to explain the mechanism of aortic injury. The most widely accepted theory is that aortic rupture results from unequal rates of deceleration in different portions of the aorta at points of fixation. Another hypothesis considers a major role in bending stress by chest compression: a direct impact produces flexion of the aortic arch upon hilar

structures acting as fulcrum<sup>11,12</sup>. Occasionally, direct shearing forces are responsible for aortic tears, such as when there is a fraction dislocation of the spine. Abdominal aortic lesions must also include direct injury. Parmley et al. noted that 29 out of 34 patients had spinal fractures associated with an abdominal aorta injury<sup>10</sup>. The tensile strength of the aorta, however, exceeds the gravitational forces generated in trauma. Thus, an additional force such as a sudden increase in hydrostatic pressure, acting with “water hammer” effect, has been postulated. Considering the different causes and types of impact that produce the aortic lesion, it is reasonable to propose that not only one mechanism but a combination of many is involved in its determination.

## **PATHOLOGY**

According to the Parmley et al. study<sup>10</sup> on 296 aortic injuries (275 isolated and 19 multiple), the lesion may be classified as follows: (1) intimal hemorrhage, (2) intimal hemorrhage with laceration, (3) medial laceration, (4) complete laceration of the aorta, (5) false aneurysm formation, and (6) periaortic haemorrhage. This review, up to now the widest pathological series reported in the literature, considered 171 cases of isolated aortic ruptures and 104 associated with cardiac injury. Areas of intimal hemorrhage were noted at autopsy in patients who died of other fatal lesions. The endothelial layer may be intact or the hemorrhage may be associated with circumscribed laceration of the endothelial and internal elastic lamina of the intima. It is probable that lesions of this type occurred frequently but were not recognized. Recent reports indicate that intimal hemorrhage with or without partial intimal laceration tends to heal spontaneously. The laceration may be extended into the tunica media. Due to the effect of the systolic shock wave, blood lifts up the upper edge of the intimomedial lesion, separates the media, and expands in the subadventitial space. At histology, the internal elastic lamina is interrupted, thereby exposing the media, which is dissociated by the hemorrhage. The tear is transverse in 80–90% of patients and involves all or part of the aortic circumference. In a minority of cases, ragged, spiral, or longitudinal ruptures may occur. No particular site in the circumference of the aorta seems to be predisposed to laceration even if ruptures involving only part of the aortic circumference were often posterior. Periaortic hemorrhage occurred independently of the type of lesion. When the lesion involves intimal and medial layers, a false aneurysm formation occurs. The aneurysm is fusiform in the case of a circumferential lesion involving the entire wall on the transversal plane, while in a partial lesion in which only a portion of the wall is lacerated, it appears as localized diverticulum. Soon after the injury, the pouch of the aneurysm contains a thrombus consisting of fibrin and enmeshed red blood cells. It follows fibroblastic proliferation and early vascularization in the aortic wall. After two to

three weeks, the thrombus becomes organized, and the wall of the pouch lined with endothelial cells. Complete rupture of the aorta including the adventitia and the periadventitial connective tissue leads to immediate death. However, mediastinal hematoma may permit temporary survival. In the Parnley et al. report, nine of 38 patients who survived temporarily had complete transection, their survival being dependent on the hematoma contained in periaortic and mediastinal tissues.

## CLINICAL PRESENTATION

Despite the severe nature of the injury, the clinical signs are ambiguously meager. No evidence of chest trauma has been reported in a high percentage of cases<sup>13</sup> because the forces not dissipated by fracturing bones become absorbed by the other structures within the chest. Moreover, the signs of aortic rupture are not specific, and when head, facial, orthopedic, and visceral lesions coexist, their own clinical features keep the attention of the physician. Chest pain and dyspnea are the prominent symptoms presented by victims of aortic trauma. The pain is often localized in the back or midscapular or may be retrosternal, and it is reported in 20–76% of cases<sup>7,14</sup>. Loss of consciousness and hypotension are also frequent, as generally reported in polytraumatized patients, while generalized hypertension is reported in 17% of the Duhayalongsod review. Systolic blood pressure <90 mm Hg despite adequate fluid resuscitation is considered to be a sign of hemodynamic instability and associated with higher mortality<sup>4</sup>.

Less frequently encountered symptoms include dysphagia (due to esophageal compression) and hoarseness. Symptoms of upper extremity ischemia and paraplegia (due to impaired blood flow beyond aortic transection) are reported in 6–31% of cases. However, a small number of patients (6%) have paraplegia without flow reduction. Difference in pulse amplitude between upper and lower extremities, attributed to compression of the aortic lumen by a periaortic hematoma, accounted for 23%<sup>7</sup> to 37%<sup>15</sup> of cases on physical examination. If the torn intima and media form a flap, which acts as a ball valve, partial aortic obstruction occurs, with upper extremity hypertension reported as *acute coarctation syndrome* or *pseudocoarctation*<sup>16</sup>. The hypertension may also be secondary to stretching or stimulation of the cardiac plexus that is located in the area of the isthmus. This mechanism could also account for the postoperative hypertension that is seen in one third of cases. Signs of impending rupture are difficult to determine despite an attempt being made to identify them in several clinical series<sup>17–21</sup>. Hypotension < 90 mm Hg despite an adequate fluid volume resuscitation and free exsanguination into the pleural space (often reproducing despite thoracotomy) are considered to be signs of forthcoming

free aortic rupture<sup>4</sup>. Careful attention must also be paid to manifestations of expanding aneurysm, such as vocal cord palsy or tracheal and superior vena cava compression.

Associated lesions are present in almost all patients with TAR and often predominant in the clinical presentation<sup>3</sup>. In particular, fractures involving the bony thorax and long bones are far more common, occurring in more than half the patients<sup>7</sup>, followed in frequency by fractures to the pelvis and spine. Head injuries have an average incidence of 20% in the literature review with sporadic higher incidence in some series<sup>22</sup>. Spleen and liver injuries predominate among the abdominal lesions. As a result of blunt thoracic trauma, 36% of pulmonary contusions are reported<sup>13</sup>; pulmonary contusion results in edema and interstitial hemorrhage of lung parenchyma, potentially progressing into respiratory insufficiency. Cardiac contusion caused by compression of the heart between the sternum and the vertebral column is associated with TAR in nearly 20% of cases, frequently if the ascending aorta is involved. Finally, negative physical examination is reported in 5–14% of cases<sup>7</sup>.

## **NATURAL HISTORY**

It is conventional to consider traumatic aortic rupture to be a highly lethal injury as far as its natural history is concerned. This concept is primarily based on the 1958 historical study by Parmley and associates<sup>10</sup>, who reported autopsy findings in 296 nonpenetrating TAR. This article has been referred in every subsequent report on this topic and influenced the general opinion over the next 40 years. Remarkably, Parmley's analysis estimated that 85% of the victims died on the scene from free aortic rupture; of those who survived at least for one hour, 30% died within six hours, 49% within 24 hours, and 90% within four months. The impressive negative natural history of TAR victims gave rise to the statement that this lesion requires immediate surgical repair, with absolute priority over any other associated injury. The critical combination of a cardiovascular intervention in a severely injured patient led to an operative mortality of 15–50%, representing the highest rates in vascular surgery.

Despite progress in cardiac surgery and anesthesiology during the last few years, the peri- and postoperative mortality in TAR have not altered perceptibly. This finding has stimulated the need for new strategies along with a critical review of Parmley's data. As underlined by Pate in several editorials and reports, the Armed Forces Institute of Pathology series of the 1950s is a cohort, which probably does not apply to the current clinical reality. Only 45% of aortic lesions are at the aortic isthmus, the prevailing localization in clinical

observations. A clear relation between free aorta rupture and death is not reported, and also not reported is how much the other potentially fatal injuries, occurring in more than half of the patients, actually contribute to death. Moreover, despite the relatively high percentages reported, of the 24 cases with a lesion at the aortic isthmus that survived for more than one hour after trauma, only one patient died in six hours, and three others in 24 hours; the precise cause of death was not defined for these patients. The more current autopsy series is that of Williams<sup>22</sup>, reporting 90 TAR out of 530 motor vehicle fatalities, 75.5% at the aortic isthmus. While 44% died immediately, four patients died within 24 hours, and only one after 24 hours. Although the leading causes of death have not yet been specified in this autopsy series, it is reported that one-third to two-thirds of victims died of something other than aortic rupture.

Because of the complexity of polytraumatized patients, conclusions brought forth from autopsy series cannot strictly apply to the surgical setting. The natural history of TAR has to be reconsidered following the study of Pate and coworkers in 1995<sup>23</sup>. The authors analyzed 15 years of English-language literature and their experiences with 112 patients in their search for evidence of the risk of aortic free hemorrhage in patients affected by acute TAR in the interval between diagnosis and delayed surgical repair. Of the 492 patients in reports specifying the cause of death, 22 (4.5%) died of aortic rupture, mostly presenting with hemodynamic instability and actively bleeding into the pleural space on arrival (class IA). In patients in whom the pseudoaneurysm or hematoma is contained within the mediastinum and who do not present with signs of hemodynamic instability or exsanguination into the pleural space (class IB), free rupture appears to be uncommon. In support of this finding, 46 of their 112 patients were managed under a formal protocol (consisting of antihypertensive therapy and limited fluid administration) and delay of aortic repair after treatment of associated lesions constituting a life-threatening emergency. Only two (4.3%) developed fatal rupture of the hematoma before aortic surgery within four hours of arrival. In both cases, the antihypertensive treatment had been inadvertently stopped, and hypertension (160 and 180 mm Hg) was documented prior to aortic rupture. In the entire group of 101 patients operated on at 12 hours to six months after trauma, there were 11 operative deaths (10.9%), including two desperate cases in which the repair was not completed. This study pointed out that the time of surgical repair of TAR in a polytraumatized patient should be considered and balanced along with other severe injuries, without a fixed priority. Moreover, irrespective of any other acute pathological aortic condition, a pharmacological control of blood pressure, acting to reduce wall stress, is mandatory in these patients.

## **INFREQUENT LOCATIONS OF TRAUMATIC AORTIC LESION**

Laceration of the ascending aorta represents the 5% of aortic injuries in the clinical series, while at autopsy they are found in 20% of cases<sup>24</sup>. Death is usually secondary to severe associated cardiac injury, as aortic valve tears, myocardial contusion, and coronary artery damage occur in 80% of cases of traumatic lesion of the ascending aorta. The point of anatomic fixation in the ascending aorta is constituted by the pericardial attachment. Compression and displacement of the heart between the sternum and the spine places greatest stress on the supra-avalvular aorta and mobile ascending aortic portion. Torsion forces are involved in determining injuries of the proximal great vessels, the innominate artery being the most frequently injured. Because tensile strength in the ascending aorta is greater than in the isthmus, the forces that may determine a tear in the ascending aorta would be expected to be greater than usually encountered in car deceleration impact. This type of lesion is frequently found in pedestrians hit by motor vehicles, ejected passengers, and victims of severe falls.

Posttraumatic aortic valve regurgitation secondary to valve cusp damage has been reported<sup>25</sup>, often associated with sternal and rib fractures. It seems that there is a latent period during which regurgitation develops, which allows operation to be deferred until the patient's condition stabilizes. Because of the protection of its retroperitoneal location, abdominal aortic lesion is a relatively rare occurrence. A review of the English-language literature<sup>26</sup> since 1950 reported 46 cases of abdominal aortic lesions, the incidence being one twentieth that of thoracic aortic rupture. The infrarenal portion is the most frequent location, while the suprarenal portion is very rare. Atherosclerotic disease has been implicated in this lesion, being present in 44% of cases. Neurological symptoms were seen in 70% of patients, due to ischemic peripheral neuropathy or to occlusion of the artery of Adamkiewicz. A decreased peripheral pulse has been reported in 96% of cases. The lesion, an intimal/medial tear, may lead to either false aneurysm formation or to intraperitoneal rupture. In some cases, thrombosis occurs with acute arterial insufficiency. The overall mortality reported in literature for abdominal aortic trauma, due to aortic rupture or severe associated lesions, is 28%.

## **DIAGNOSIS**

### **CHEST RADIOGRAPHY**

As a high percentage of blunt chest trauma patients with aortic rupture do not present with indicative clinical signs, the routine chest radiograph becomes

an essential tool for identifying subjects with suspected aortic injury. Various radiological signs have been considered as indicators of TAR, but there is a great difference in the diagnostic importance of such signs in the various studies. In older studies, emphasis has been placed on *mediastinal widening* as the principal finding on chest radiograph<sup>27,28</sup>. There are many problems in interpreting chest radiographs of acutely polytraumatized patients. A widened mediastinum can be due to causes other than aortic rupture, including bleeding from small mediastinal vessels (arteries or veins), excessive mediastinal fat, thymic tissue, adjacent lung contusion, and dilated vessels. In addition, with the patient supine the superior mediastinal shadow is physiologically wider as a result of an increase in systemic blood volume and of poor inspiration. This experience confirmed by subsequent studies has shown that mediastinal widening, evaluated either subjectively or quantitatively, is a sensitive but relatively nonspecific sign of TAR.

In patients with blunt chest trauma, an irregular, enlarged, or *indistinct aortic outline* can be caused either by periaortic/mediastinal hemorrhage or by an enlarging aneurysm, which is located primarily at the level of the isthmus. Loss of aortic knob and obscuration of the descending aorta outline have shown in many studies to have a good sensitivity (53–100%) but a low specificity (21–63%) for the diagnosis of TAR<sup>29–33</sup>. False positives can also occur in the case of obscuration of aortic silhouette by lung infiltrates or contusions.

The *opacification of the clear space between the aorta and the left pulmonary artery* is a potential indicator of TAR. A study on 205 chest films taken on admission of patients with suspected aortic rupture<sup>33</sup> demonstrated that it has a high negative predictive value (83–86%).

*Deviations of the trachea* reflect the presence of central mediastinal blood, fluid, masses, or aneurysms of the isthmus or descending aorta. Blunt chest trauma can produce hematoma of the anterior or posterior mediastinum originating from injuries of the sternum, ribs, vertebrae, and their associated vessels. This hematoma can cause a widened mediastinum, but they are not anatomically positioned to cause deviation of the trachea and esophagus.

Mediastinal hemorrhage with *widening of either the left or right paraspinous stripe* may occur as a result of major arterial injuries but can also be caused by venous bleeding and vertebral and/or ribs fractures. Therefore, in the evaluation of these features, the radiologist should be aware of the possibility of false positives due to injuries not related to aortic rupture.

In blunt chest trauma, the *left main stem bronchus* may be *depressed* and also *displaced* to the right by a mediastinal hematoma or by an aneurysm at the isthmus. Mirvis et al.<sup>33</sup> showed a high specificity of this finding but also reported a very poor sensitivity (4% on the supine view and 1% on the erect view) related in part to problems in accurately visualizing bronchi on underexposed radiographs.



Figure 15.1. Chest X-ray. Mediastinal widening ( $>10$  cm), with enlargement of the paratracheal stripe. The apical cup sign is visible at the left apex due to hemorrhage of the epi-aortic vessels. A slight deviation of trachea to the right and inferior displacement of left mainstem bronchus are also present.

*Apical cup* hemorrhage from an aortic tear dissecting along the left subclavian artery can extend into the extrapleural space over the apex of the lung, especially the left lung, producing a soft-tissue density. In general, this sign has shown a sensitivity of 9–63% and a specificity of 75–96% for this sign<sup>29,32,34</sup>.

There is wide agreement in the literature on the fact that no single radiographic sign or combination of signs has sufficient sensitivity and specificity to confirm or exclude the presence of TAR. As Mirvis et al. have pointed out<sup>33</sup>, most of the signs described previously are more valuable by their absence as indicators of normality than by their presence as indicators of aortic rupture. In the identification of a normal chest film, the true erect view has shown a higher negative predictive value (98%) than the supine view (96%). The same authors found that the observation of a normal aortic arch and descending aorta, a clear aortopulmonary window, and absence of a tracheal shift or widened left paraspinal line has a 91–92% negative predictive value for TAR. Therefore, chest radiograph on admission remains the essential screening test for identifying traumatized patients in whom an aortic tear is strongly suspected (Figure 15.1) and who thus require further imaging investigations.

## COMPUTED TOMOGRAPHY

Over the past few years, several studies have evaluated the role of CT in the diagnosis of TAR yielding controversial results. Before the introduction of helical CT in clinical practice, CT diagnosis of aortic rupture relied primar-

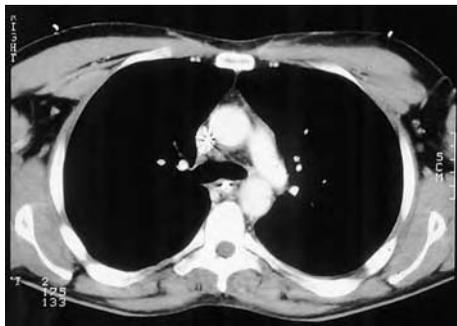


Figure 15.2. CT scan of a traumatic aortic rupture. An intimal tear is clearly visualized within the lumen of the isthmic aorta. No pleural effusion or periaortic hematoma is visible.

ily on the detection of mediastinal hematoma as an indirect sign rather than on the detection of direct signs of aortic injury. In most trauma centers, the next diagnostic step included the performance of aortography to confirm or exclude the aortic origin of the mediastinal bleeding; if hematoma was not present, aortography was not carried out. As pointed out by Raptopoulos in a commentary<sup>35</sup>, the characteristics of mediastinal hematoma on CT scans have not been described in detail in the majority of reports. Brooks et al.<sup>36</sup> describe the CT appearance of a mediastinal hematoma as the presence of material of soft tissue attenuation or slightly higher in the mediastinum. In interpreting the mediastinum for the detection of hemorrhage, false positive findings may occur as a result of thymic tissue, periaortic atelectasis of the left lower lobe, volume averaging of the pulmonary artery with mediastinal fat, and left medial pleural effusion. The hematoma secondary to aortic rupture is mostly periaortic and may extend along the descending aorta. In blunt chest trauma patients, a mediastinal hemorrhage may be present for other reasons such as bleeding from small mediastinal vessels (arteries or veins) often in association with fractures of the thoracic cage. Furthermore, if the adventitia is intact, aortic rupture may occur without hemorrhage (Figure 15.2).

For these reasons, the interpretation of a positive CT scan based only on the presence of mediastinal hematoma results in a large number of negative aortograms and a resulting low specificity. To increase the specificity of CT, direct signs of aortic rupture must be considered. These signs include aortic pseudoaneurysm, an abrupt change in the aortic contour, intimal tear, intramural hematoma, extravasation of contrast material from the aorta (Figure 15.3), diminished caliber of the descending aorta (pseudocoarctation), and double aortic lumen<sup>37</sup>. Problems in the evaluation of these direct findings may arise from artefacts due to respiratory and voluntary movement of the traumatized patients, from cardiovascular motion, and from streak artefacts caused

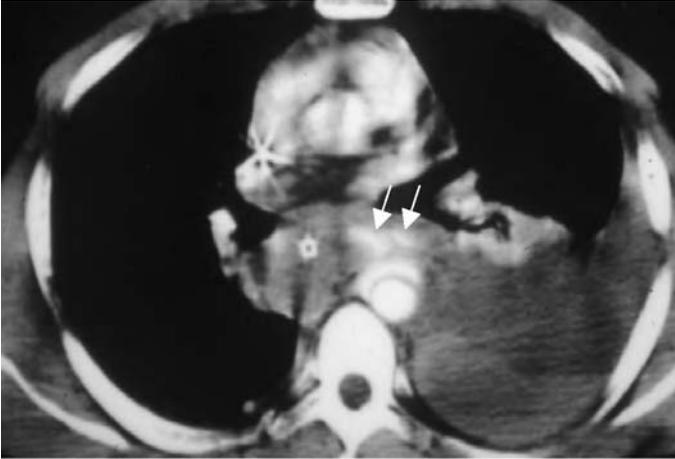


Figure 15.3. CT scan of a traumatic aortic injury with signs of impending rupture. Note contrast media extravasation outside the adventitial wall (arrows). A wide pleural hemorrhagic effusion is also visible.

by nasogastric tubes, external leads, and other devices; presence of effusion in the upper pericardial recess can mimic a double lumen.

In a large study including 104 patients who underwent both CT and aortography, Miller et al.<sup>38</sup> reported a CT sensitivity and a specificity of 55% and 65%, respectively, with five missed major thoracic arterial injuries. Two of these false negative CT scans were due to aortic rupture and the other three were found to be branch injuries.

With conventional CT, the detection of subtle aortic injuries still represents a problem since a small intimal tear that extends on the axial plane may be obscured by volume averaging with the normal aortic lumen. The advent of helical CT overcomes most of these limitations, and it is particularly useful in critically injured patients with suspected associated neurological, visceral, or retroperitoneal lesions, some of which may be more critical than an aortic injury. Helical scanning has the great advantage of providing a better direct evaluation of the aorta with an acquisition time of about 25–30 seconds for the evaluation of the thoracic aorta. Gavant et al.<sup>39</sup> used helical CT exclusively to screen 1,518 patients with nontrivial blunt chest trauma, 127 of whom presented abnormal findings at CT and underwent aortography. Helical CT was found to be more sensitive than aortography (100% vs. 94.4%) but less specific (81.7% vs. 96.3%, respectively) in detecting aortic lesions. False positives are reported in cases of prominent mediastinal vessels adjacent to the aorta (such as a right bronchial artery) or in cases of volume averaging from the left brachiocephalic or left superior intercostal veins. The authors concluded that negative findings on helical CT of the aorta, even in the presence

of mediastinal hematoma, are sufficient to exclude aortic rupture. In a subsequent study, Gavant et al.<sup>40</sup> evaluated a larger number of patients with the addition of two-dimensional and three-dimensional reconstructions including shaded-surface display and maximum intensity projection volume-rendering techniques. The retrospective reconstruction of additional axial images with a 50% overlap proved to be critical for detecting subtle aortic injury. Even if two-dimensional and three-dimensional reconstructions do not produce improvement in terms of diagnosis, they are useful supplements to the axial helical CT examination allowing depiction of important anatomical details such as relationships between the aortic lesion and the major branch vessels.

Since it provides high-quality images with a drastic reduction of acquisition time and motion artefacts, helical CT represents a method of great diagnostic value, potentially the method of first choice in the acute phase, in the evaluation of blunt chest trauma patients with suspected aortic injury, particularly in polytraumatized patients with other associated lesions<sup>41</sup>.

## ECHOCARDIOGRAPHY

Transesophageal echocardiography (TEE) has evolved as the optimal modality in acute nontraumatic aortic pathology. The capability of providing high-resolution images of the aortic wall in a rapid time, even at the patient's bedside, allowed it to become often the first imaging test in suspected acute aortic injuries. The use of TEE in TAR was first reported in the 1990s<sup>42</sup>, initially in small series of patients with blunt chest trauma and successively in wider prospective trials. The diagnosis is based on the identification of the aortic tear as a mobile echogenic flap, perpendicular to the aortic isthmus. The lesion may involve the entire aortic circumference in the case of subadventitial complete aortic disruption or may appear as a limited discontinuity of both intimal and/or media layers. The aortic contour is generally deformed because of the formation of a pseudoaneurysm (Figure 15.4).

There are several advantages in the use of TEE in the evaluation of TAR. Echocardiography can be performed quickly, at the bedside, without interrupting resuscitative and therapeutic measures. It is a noninvasive technique and does not require the administration of contrast media. Moreover, it may provide information on possible associated cardiac contusions or valvular lesion.

Nevertheless, in a polytraumatized patient, some disadvantages of TEE may become particularly problematic. It cannot be performed in patients with facial fractures or cervical spine fractures, representing 5–25% of the trauma victims<sup>7</sup>. The descending aorta is scanned in close proximity to the esophagus, and possible near-field artefacts may occur due to excessive gain and reverberation. Because of the interposition of the trachea, there can be some limitations in visualizing the upper portion of the ascending aorta as well as

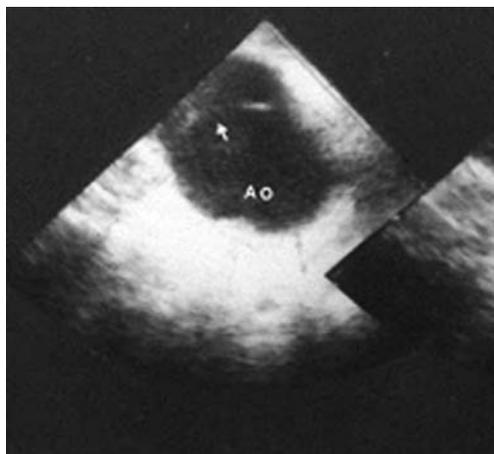


Figure 15.4. Cross-sectional transesophageal echocardiographic view of the aortic isthmus (Ao) in a patient with a partial aortic disruption following car accident. The disrupted aortic wall is mobile (arrow). Localized deformity of the posterior aortic contour is shown corresponding to the formation of acute pseudoaneurysm. Courtesy of Guido Rocchi, MD, Institute of Cardiology, University Hospital, Bologna, Italy.

the arteries of the aortic arch, the next most common locations for TAR after the aortic isthmus. These problems are noted in the literature of several cases of false positive and false negative results<sup>43–47</sup>.

TEE may be considered an effective test in the evaluation of TAR, providing helpful information on the aortic lesion. However, considering the operator dependence of the method and some pitfalls in detecting specific portions of the aortic segments, its use as sole diagnostic test for ruptured thoracic aorta requires a careful approach.

## AORTOGRAPHY

For more than 20 years, aortography has been the unique imaging modality for studying aortic pathology, and it has been considered to be the diagnostic standard to confirming or excluding the presence of traumatic aortic rupture<sup>49</sup>. Biplane cineangiography assures high temporal resolution images and accurate evaluation of the isthmic aorta by a single injection of 50 ml of contrast medium. The entire thoracic aorta as well as the intrathoracic portions of the brachiocephalic vessels should be visualized to exclude location of aortic rupture other than at the isthmus, occurring in 5% of clinical series. The diagnosis is based on the detection of the intimal/medial tear visible as a linear irregular filling defect within the lumen of the aorta (Figure 15.5). When the tear extends deep into the media, the pseudoaneurysm appears on the aortogram as

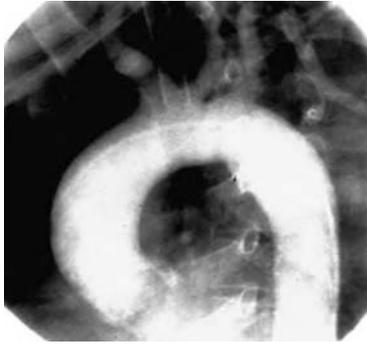


Figure 15.5. Aortography (left anterior oblique view). A longitudinal, subtle tear, extending within the lumen of the aorta, is visible.

a focal bulge in the column of contrast material. The combined findings that are highly specific for aortic rupture are a focal bulge with delayed washout of contrast material, and a linear filling defect at the level of the ligamentum arteriosum.

Focal bulge alone cannot be considered diagnostic of traumatic aortic rupture. A focal convexity, involving the opposite wall asymmetrically, may be present at the thoracic aortic isthmus in some 25% of cases due to ductus diverticulum and tends to be more prominent in older patients. It accounts for 1–2.8% of false positive results of aortography in the diagnosis of TAR<sup>50</sup>. Other abnormalities that can simulate TAR include atherosclerotic plaque, aortitis, and streaming or mixing artefacts. A false negative diagnosis of rupture with angiography may occur up to 12% of cases<sup>51</sup>, due to poor opacification by contrast agents, inadequate projections, or thrombosis of the pouch. By design, small intimal tears or intimal intraparietal lesions cannot be visualized by angiography, as demonstrated in reports comparing angiography with high-resolution tomographic modalities as TEE, MRI, and CT<sup>39,52</sup>. Due to its invasive approach and contrast media administration, aortography generally has a complication rate of 1–2% of cases, which tends to be higher in acute patients. Kram<sup>49</sup> reported 10.5% of complications in 76 victims of blunt chest trauma undergoing aortography, one of whom required blood transfusion for severe groin hemorrhage. Although it is difficult to demonstrate a precise cause and effect relationship, several cases of death during aortography have been reported<sup>22,51,53,54</sup>. Contrast media extravasation into the mediastinum or massive leakage from the aneurysm after injection of contrast media has even been documented by Del Rossi et al.<sup>51</sup> and La Berge et al.<sup>53</sup> Therefore, in the era of high-resolution noninvasive imaging modalities, aortography should not be recommended in polytraumatized patient with suspected TAR.

## MAGNETIC RESONANCE IMAGING

The role of MRI in diagnostic evaluation of aortic diseases has been widely documented, resulting in comparative studies as one of the most accurate diagnostic techniques in the detection of acute and chronic aortic pathology<sup>55</sup>. A long examination time as well as difficult access to the patient has been considered the main limitation in acute aortic pathology. Although the development of fast MRI techniques has enabled the examination to be shortened to a few minutes, MRI has been underutilized in critically ill patients. For this reason, the use of MRI in traumatic aortic rupture for several years has been limited to case reports<sup>56</sup>, regardless of its potential. The value of MRI in detecting traumatic aortic rupture has been reported in a series of 24 consecutive patients in comparison with angiography and CT<sup>52</sup>. The diagnostic accuracy of MRI was 100%, 84% of angiography (two false negative, in two cases of limited partial lesion), and 69% of CT (two false negative and three false positive). Moreover, in almost all cases MRI was able to differentiate the type of lesion, according to Parmley's classification.

Because of the presence of methemoglobin, intimal hemorrhage has high signal intensity and is clearly detected by MRI spin-echo sequences. On the sagittal plane, the longitudinal visualization of the thoracic aorta allows one to distinguish a partial lesion, as a tear limited to the anterior or to the posterior wall (Figure 15.6), from a circumferential lesion, as a tear developing on the entire aortic circumference (Figure 15.7). This discrimination provides prognostic significance because circumferential lesions may have a greater risk of free rupture. The presence of periadventitial hematoma and pleural and mediastinal hemorrhagic effusion, with high signal intensity, may also be considered to be a sign of instability of the lesion. The characteristic of MRI to detect the hematic content of a collection by its high signal intensity is widely useful in a polytraumatized patient. This is applicable to every traumatic lesion such as lung (Figure 15.6A), liver, or splenic hemorrhagic contusions, all characterized by high signal intensity, just like head hematoma. In the same sequence used to evaluate the aortic lesion, without any additional time, the wide field of view of MRI gives a comprehensive evaluation of chest trauma, such as lung contusion and edema, pleural effusion, and rib fractures. All this can compromise the result of emergency surgical repair, considering that respiratory insufficiency is the very common postoperative complication. In the subacute phase, MRI may be considered the ideal modality to monitor the aortic lesion before surgery because of its noninvasiveness, accuracy, and reproducibility of the parameters<sup>57</sup>. The development of fast techniques that reduce examination time to a few minutes and better accessibility to the patient may contribute to a feasible use of this powerful diagnostic tool in traumatic aortic rupture.



Figure 15.6. Sagittal oblique spin-echo MR image demonstrating a partial lesion of the isthmic aorta. An intimal tear involving only the anterior wall is visible with associated pulmonary contusions, periaortic and bilateral pleural effusion. The sagittal plane provides a better visualization of the diverticular aneurysm.



Figure 15.7. Sagittal oblique spin-echo MR image showing a circumferential aortic lesion. The involvement of both the anterior and posterior walls causes the development of a fusiform aneurysm. Note the invagination of the anterior and posterior aortic tears.

## CHRONIC POSTTRAUMATIC ANEURYSM

Conventionally, posttraumatic aneurysm is defined as chronic if it still exists three months or more after trauma. Histological studies<sup>10</sup> provide evidence that fibroblastic proliferation begins soon after injury at the site of the traumatic tear, and after two or three weeks the wall of the pouch becomes lined with endothelial cells. Despite their nature of chronic pathology, the natural history of posttraumatic aneurysm is progressive risk of rupture and the timing is unpredictable. The widest reviews in the literature by Bennet and Cherry on 107 patients<sup>58</sup> and by Finkelmeier on 401 patients<sup>59</sup> clearly demonstrated that rupture may occur even several years after trauma, and sometimes no clinical manifestations precede the lethal event. Sometimes the presence of posttraumatic aneurysm is an occasional finding on a chest X-ray performed for other reasons. An abnormal aortic knob on the right side of the aortic arch, with thin, linear calciphic contour, is the typical aspect on a chest radiogram.

Pain is the most frequent symptom observed in chronic aneurysm, being present in one third of cases. Dyspnea due to compression of the left main stem bronchus is observed in 10% of cases, as well cough and hoarseness due to laryngeal nerve entrapment. Less frequently, dysphagia, hemoptysis, hypertension, and syncope may occur. In the review by Finkelmeier, 42% of patients had signs or symptoms of expansion five years after injury, and one third of the untreated patients died as a result of their aneurysm, mostly asymptomatic. Comparing the mortality between the surgically treated and the untreated group, the survival rates at 5, 10, and 15 years were 20% higher in the operative patients (85% at 10 years after trauma) than in untreated patients (66% at 10 years after the trauma). The superiority of the surgical management is due to the very low operative mortality of elective operation (0–4.6%) in a circumscribed chronic pathology. Given the low operative mortality of chronic aneurysm and the unpredictable evolution of these lesions, elective surgical repair is recommended for both symptomatic and asymptomatic patients.

## SURGERY

### Management of Acute Patients

Despite the ongoing improvement in resuscitation techniques and emergency transport, traumatic aortic rupture secondary to a blunt chest trauma presents a high mortality, and all patients who reach the hospital alive are candidates for surgical repair. What is the best time to intervene in the aortic lesion and whether surgery should be preceded or followed by the treatment of associated traumatic lesions remain a matter of debate since most patients present associated traumatic lesions in other organs, which may influence the patients outcome<sup>60</sup>.

Table 15.1. Mortality and incidence of paraplegia according to different surgical techniques in emergency surgery for traumatic aortic rupture

Surgical technique	Patients	Mortality (%)	Paraplegia (%)
Cross clamping	443/220	15–16	19.2
Passive perfusion	424	12.3	11.1
Passive perfusion (Gott shunt)	52	8	4
Active perfusion	548	12.2	2.5
LHB <sup>a</sup>	100	17	0
PCBP <sup>b</sup>	246	10	2

Source: From references 21 and 61.

<sup>a</sup> Left heart by-pass.

<sup>b</sup> Partial cardiopulmonary by-pass.

Table 15.2. Operative mortality and incidence of paraplegia in patients operated on with delayed surgery for traumatic aortic rupture

Author	Points	Mean time injury-aortic repair	Mortality (%)	Paraplegia (%)
Akins (1981) <sup>62</sup>	19	33 days	10	0
Kiepfer (1994) <sup>63</sup>	10	15 weeks	0	0
Blegvad (1989) <sup>64</sup>	15	6 weeks	6	0
Pacini (2005) <sup>66</sup>	43	7 months	0	0

Immediate surgery has been characterized by a high mortality and morbidity rate (20–40%). In a report of 144 patients undergoing surgery within an average of six hours after arrival in hospital, there was an intraoperative mortality of 10.2% and postoperative mortality of 18.4%, with major postoperative morbidity such as paraplegia reaching 10.5%<sup>5</sup>. In a recent prospective multicenter trial<sup>47</sup> among 274 patients collected over 2.5 years, the overall mortality was 31%, with 14% of operative mortality in stable patients undergoing planned thoracotomy (Table 15.1).

Akins in 1981<sup>62</sup> showed good results on preoperative mortality delaying surgical intervention on the aorta in a small group of severely polytraumatized patients (Table 15.2). His criteria to exclude immediate surgery were severe central nervous system trauma, respiratory insufficiency, extensive burns, contaminated open wounds, and sepsis. According to the data reported by Hartford<sup>65</sup>, the risk of a complete rupture of the aorta is not very high in the posttraumatic period, especially if the lesion is not circumferential, provided the patients, once admitted to hospital, received an immediately aggressive resuscitation and medical treatment with controlled hypotension.

This first phase after the trauma is life threatening, and accident victims should be taken to the hospital as quickly as possible. A prompt diagnosis of aortic wall injury is mandatory, and an aggressive intravenous therapy with vasodilators and beta-blocking drugs must be started to reduce the aortic wall stress and the risk of lethal aortic rupture. According to Pate<sup>23</sup>, the risk of rupture of a periaortic hematoma contained in the mediastinum can be avoided if the systolic blood pressure is constantly maintained below 140 mm Hg. On subsequent days, a process of organization of the hematoma usually develops, and with time it will turn into a strong fibrous tissue, with the formation of a pseudoaneurysm that has the same risk of rupture as a true aneurysm of similar size. Patients must be admitted to an intensive care unit with continuous monitoring of ECG, arterial and central venous pressure, renal function, and peripheral metabolism. An arterial systolic pressure exceeding 90 mm Hg should be an indication to limit fluid replacement and any hemodynamic support in hypotensive patients. Monitoring of respiratory function and eventual intubation and mechanical ventilation are fundamental in polytraumatized patients with respiratory insufficiency due to central nervous system injury, pulmonary contusion, and pleural effusion with measurement of chest tube outputs<sup>66,67</sup>.

Considering this possible evolution, the strategy to delay the surgical repair of posttraumatic aortic aneurysms in selected patients offers some clear advantages. The overall mortality and the incidence of major complications are lower when it is possible to delay surgery than when unstable patients have to undergo an emergency operation. All the necessary procedures of distal aortic perfusion can be safely performed, and mortality is also reduced by prior treatment of potentially lethal associated lesions, often encountered in polytraumatized patients. It is important to remember that 90% of patients with aortic rupture have associated other open and closed traumatic lesions of different areas (orthopedic 81%, abdominal 42%, closed-head injury 40%), which may cause a rapid evolution into shock and coma, thus influencing the patient's outcome. Therefore, the treatment of associated lesions is fundamental in these patients, and it is another incentive to delay surgical intervention in the aorta. CT scan and MRI offer noninvasive assessment of the anatomical characteristics of the aortic lesions and can be used to monitor their evolution. Signs indicative of imminent free rupture (such as an increase in size of the periaortic hematoma), pseudoaneurysm, or recurrent hemothorax (associated with a poorly controlled arterial pressure) can be promptly identified and therefore provide an indication for emergency surgery<sup>40,57</sup>.

### **Surgical Techniques**

The operation is performed with patients under general anesthesia ventilated with a double lumen endotracheal tube, thus permitting the left lung to

be collapsed during the aortic surgery. A right radial catheter and a femoral arterial catheter are inserted to monitor upper and lower blood pressure. A triple-lumen central venous catheter and a pulmonary artery catheter are also inserted. An epidural catheter can also be positioned to ensure the monitoring of intraliquoral pressure, the possible drainage of cerebrospinal fluid, and the infusion of anesthetic drugs.

The patient is positioned as for a left thoracotomy procedure although the left hip is rolled back to expose the left groin sufficiently to allow access to the femoral vessels.

The aortic isthmus is approached via a posterolateral thoracotomy through the fourth or fifth intercostal space. After opening the pleural space and removing any clots that may be present, the aorta must be controlled above and below the adventitial hematoma. The damaged aortic wall is manipulated only after vascular clamping. The proximal clamp can be positioned below or above the left subclavian artery depending on its involvement within the rupture; various techniques can ensure perfusion of the distal aorta and are discussed below.

Once the hematoma is opened, the margins of the rupture can be identified. If the aortic tear is limited enough, a *primary wall repair* with stitches reinforced with Teflon pledges should be considered. If the lesion is wider, the hematoma is removed, and the two transected margins of the aorta are sutured with an end-to-end anastomosis. These procedures are not feasible in the majority of patients because of the tendency of the two aortic intimal margins to retract and to move away from each other, especially if the rupture is circumferential, in which case the interposition of a preclotted dacron graft is advisable. The choice of surgical technique is based on the type of lesion and the time of execution: primary sutures (also with pledges) and end-to-end anastomoses are suitable in patients with linear lesions without extensive dissection and in young patients with an easily mobilized aorta. A *tube prosthesis* is recommended in lacerated or multiple lesions with a wide intimal dissection and in elderly patients with atherosclerotic lesions.

Patients tend to be hypertensive immediately after surgery, probably due to an imbalance of the baroreceptors of the aortic arch. Therefore, during the postoperative course, intensive monitoring of arterial pressure values is mandatory.

Rupture involving the anterior portion of the aortic arch is usually characterized by a partial or complete avulsion of the brachio-cephalic trunk. In these cases, the surgical approach is via a median sternotomy, and the operation is performed with the patient on cardiopulmonary bypass and deep hypothermia with complete circulatory arrest. The extracorporeal circulation can be a right atrium-femoral artery or a femoral vein-femoral artery to be implanted before sternotomy. The operation involves completely detaching the brachio-cephalic trunk, repairing the aortic arch with a dacron patch or replacing it with a dacron



Figure 15.8. Spin-echo axial MRI showing an ascending aorta lesion with intramural hemorrhage.

tube prosthesis and reimplanting the brachio-cephalic trunk on the ascending aorta with the interposition of a prosthesis.

In the case of rupture of the ascending aorta (Figure 15.8), the involved segment needs to be replaced during heart cardioplegic arrest and extracorporeal circulation with right atrium-femoral artery or femoral vein-femoral artery. Small lesions that can be treated with a direct suture and lateral clamping without the need for extracorporeal circulation are very rare.

### Surgical Spinal Cord Protection

The role of the perfusion of the distal aorta in preventing ischemic damage of the spinal cord and renal failure during surgery for traumatic aortic rupture has yet to be clarified.

All surgical techniques that imply the use of aortic clamping at the level of the descending aorta disrupt the balance of blood pressure. Above the cross-clamp, a hypertensive regimen is established with an overload of work for the left ventricle; below, a low blood pressure is established with ischemia that primarily affects the spinal cord and subsequently the kidneys and other abdominal organs. The risk of paraplegia, common in operations on the thoracic descending aorta, is particularly elevated in patients with traumatic aortic rupture, probably due to the lack of a collateral circulation that can potentially develop in cases of chronic disease (such as coarctations, atherosclerotic aneurysms, and chronic dissections). This complication is directly correlated

with the length of time of aortic flow interruption and increases proportionally when the clamp time exceeds 30 min.

For this reason, several efforts have been made to reduce the incidence of cordal ischemia by adopting experimental and clinical methods such as whole-body surface hypothermia, the localized cooling of the spinal cord, the intrathecal administration of drugs such as papaverine, the systemic administration of steroids, and finally the perfusion of the distal aorta<sup>21,68-70</sup>. These last techniques can be divided into two major categories: the active and passive intraoperative perfusion of the descending aorta each of which present some advantages and disadvantages and are the most widely used. The *passive perfusion* consists of the simple interposition of a shunt with heparin-coated tubing, inserted proximally (ascending aorta or left ventricle) and distally. The *active perfusion* consists of the augmentation of distal perfusion by various methods with the insertion of a pump (roller or centrifugal) through the circuit. An extracorporeal circulation can be used with partial bypass between the femoral vein and the artery. This procedure implies a total heparinization of the patients and therefore carries a risk of hemorrhage, mostly in the polytraumatized patients undergoing acute surgery. Left atrium-femoral artery bypass with partial or without heparinization performed with a centrifugal pump offers an adequate blood flow to the distal aorta and the abdominal organs, reduces the blood volume overload and the overall pressure to the cardio circulatory system above the cross-clamp, and prevents possible hemorrhagic complications.

An overview of the English literature by von Opperl in 1994<sup>21</sup> disclosed a 25% incidence of paraplegia when the surgical repair was performed by simple cross-clamping. By significantly increasing the distal perfusion, the incidence of paraplegia was reduced to 5.2%. Moreover, the two types of intraoperative perfusion differed significantly because paraplegia developed in 15.6% of patients submitted to passive perfusion and in 2.5% of patients submitted to active perfusion. Despite these data, the overall operative mortality was 18.2% for cardiopulmonary bypass, 11.9% for perfusion without heparin, 12.5% for shunts, and 16% for simple aortic cross-clamping.

Two major methods were proposed to identify immediately and very sensitively spinal cord damage: the monitoring of somatosensory evoked potential and of intraliquoral pressure. As shown by Safi, combined cerebral spinal fluid drainage (below 15 cm H<sub>2</sub>O) and distal aortic perfusion cause a reduction in neurological deficits in patients submitted to aortic surgery for thoraco-abdominal aneurysms.

## ENDOVASCULAR TREATMENT

Since 1996, the introduction of endovascular techniques for the thoracic aorta in the clinical practice has opened less invasive options for patients in

which emergency treatment is necessary. After initial limited series and case reports, endovascular treatment is evolving as the method of choice in management of TAR<sup>71-74</sup>. Because of the lower invasivity, avoiding thoracotomy, and the use of heparin, endovascular repair can be applied in the acute patients without the risk of destabilizing pulmonary, head, or abdominal traumatic lesions. At present, standard sizes of thoracic stent grafts are available allowing its use in an emergency. In recent years, initial medical management and delayed surgery of the aortic traumatic injury have represented important advances in the difficult management of polytrauma, substantially reducing operative and overall mortality. However, there are some patients in whom delayed surgery cannot be applied. Even if the majority of traumatic aortic ruptures are stable lesions, in approximately 5% of them the risk of rupture may be high in the acute phase. Signs of impending rupture (such as periaortic hematoma, repeated hemotorax, and uncontrolled blood pressure) are considered signs of instability. Sometimes the aortic tear, acting with a valve mechanism, may cause a pseudocoarctation syndrome, producing a reduction of flow in the descending aorta with lower extremity ischemia. This complication, which represents a surgical emergency, is accounted for in 10% of victims. In these unstable patients, endovascular techniques offer a suitable alternative to open repair. In early clinical series, endovascular treatment demonstrated lower morbidity and mortality in comparison with open surgical repair even in high-risk patients (Figure 15.9). There is no requirement for full heparinization, and blood loss is minimal. The risk of paraplegia seems to be very low even in extensive atherosclerotic aneurysms in which the coverage of the stent graft extends from the left subclavian artery to the celiac axis. At present, no case of paraparesis-paraplegia has been reported in the literature in endovascular treatment of traumatic aortic lesion.

In the chronic posttraumatic aneurysm endovascular treatment represents a favorable alternative treatment of asymptomatic disease that is frequently recognized several years after the trauma. Chronic posttraumatic aneurysms are potential evolving lesions. Death from rupture may occur many years after injury sometimes without any premonitory signs and symptoms. Because it is impossible to predict which aneurysm still remains quiescent, elective repair is always recommended for both symptomatic and asymptomatic lesions. Advances in surgical techniques and spinal cord protection over the years significantly reduced operative mortality and paraplegia in elective surgical repair of the thoracic aorta. In the largest surgical series, operative mortality for chronic posttraumatic aneurysms ranges from 0–10% and paraplegia accounts for 5% of cases. The risk of paraplegia in surgery of chronic posttraumatic aneurysms is very low compared to atherosclerotic aneurysms because of the limited extension of the pseudo-aneurysm that usually does not extend beyond



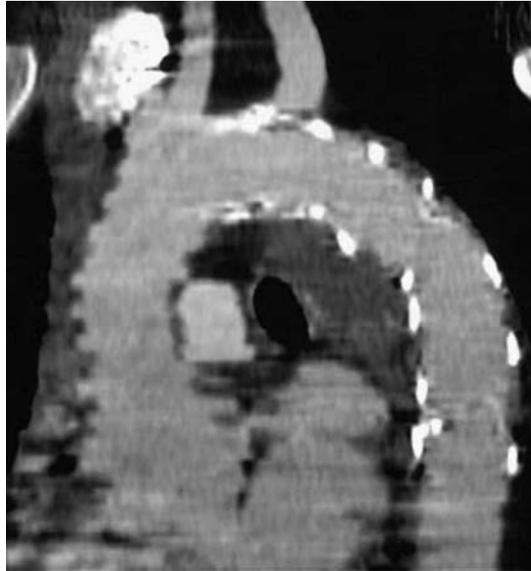
(a)



(b)

Figure 15.9. (a) Intraoperative aortography of a traumatic aortic injury before stent placement. (b) Aortography after stent placement. The stent has been deployed in isthmic aorta, with aneurysm exclusion and patency of left subclavian artery. (c) CT follow-up images (longitudinal reconstruction). Complete thrombosis of aneurysm.

the first pair of intercostals arteries. However, patients with chronic asymptomatic aneurysm are not always prone to accept a major thoracotomy and the risk of dreadful complications. Endovascular treatment may play an important role in chronic posttraumatic aneurysm management.



(c)

Figure 15.9. (Continued).

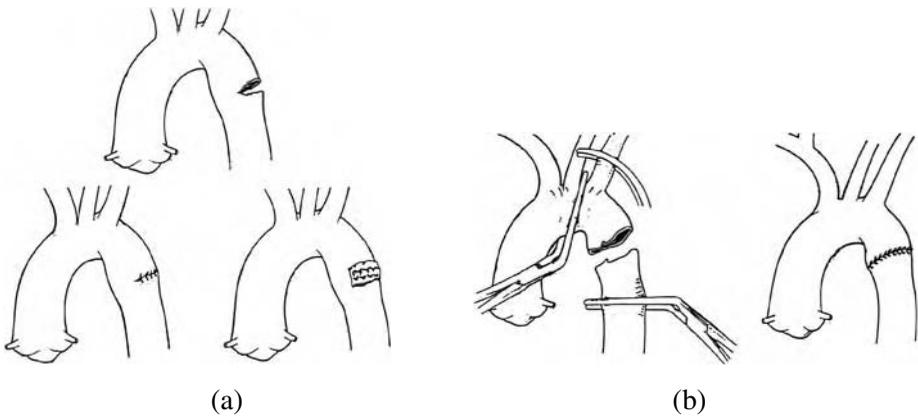


Figure 15.10. (a) Schematic drawing of an incomplete acute traumatic aortic rupture repaired with primary sutures with or without pledgets. (b) End-to-end anastomosis repair of a circumferential linear laceration.

Endovascular treatment needs some peculiar anatomical conditions to be performed, so not all the patients can be treated. At a minimum, a proper peripheral vascular access is requested. The most important anatomical characteristic of a posttraumatic lesion allowing endovascular treatment is the presence of an adequate proximal neck or a distance more than 5 mm from the

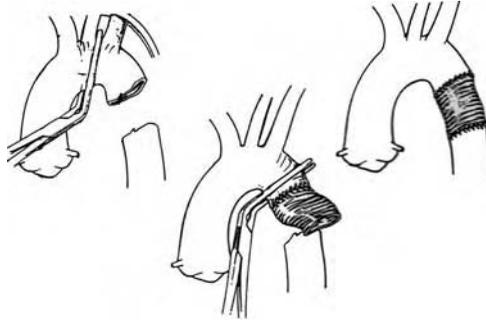


Figure 15.11. Schematic drawing of a complete aortic transection and repair with the interposition of a straight prosthetic graft.

subclavian artery and the absence of mural thrombus or calcifications or hemorrhage on the aortic wall at the neck site. Several studies reported the artificial creation of an aortic neck, covering the left subclavian artery with the stent graft, with or without previous subclavian to carotid transposition or bypass grafting. However, subclavian-to-carotid transposition is an invasive adjunctive procedure that carries the risk of mortality and stroke (4.2%), while the abrupt closure of the left subclavian artery may evolve into chronic or acute subclavian steal syndrome. The risk of vertebral ischemia and cerebellar infarction is reported up to 13% for interventional treatment of intracranial aneurysm treated by vertebral ligation. Therefore, we may expect the same rate of complication for endovascular coverage of the left subclavian artery with a stent graft. Moreover, the long-life expectancy of the uncovered part of the stent graft to the left carotid artery is a potential source of emboli. Preoperative imaging studies are fundamental to define the indication to endovascular treatment and to customize the stent graft. The accuracy of measurements becomes then essential to verify the efficacy of the procedure during long-term follow-up. Both helical CT and MR imaging represent excellent imaging modalities for evaluation of traumatic aortic lesion, displaying the extent of the disease without partial volume errors and providing accurate details of the aortic wall structure. Angiography can provide only luminal information on the aortic vessel and should be reserved to the few cases in which the necessary details have not been achieved by noninvasive methods.

For many years, traumatic aortic injury has been considered a highly lethal lesion and a potential cause of death in blunt chest trauma. Despite evidence in the literature of lower morbidity and mortality, initial medical management of uncomplicated aortic injury and subsequent delayed surgery have not been easily accepted in the clinical practice. The development of endovascular techniques represents a viable alternative with a very low risk and a limited impact on further multisystem destabilization.

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**SECTION VI:**  
**FUTURE FRONTIERS**

# 16

## FUTURE DIRECTIONS OF AORTIC DISSECTION

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Aortic dissection is characterized by separation of the layers within the aortic wall and the subsequent inflow of blood into the intima-media space with further propagation of the dissection. The clinical onset of aortic dissection may mimic a wide array of conditions, such as myocardial ischemia, heart failure, neurologic event, visceral ischemia, or peripheral vascular insufficiency. Clinical signs of aortic dissection include among others chest pain with a ripping nature and immediate onset, widening of the mediastinum and the aortic knob, pulse and blood pressure differentials, limb ischemia, presence of a diastolic aortic murmur due to aortic regurgitation<sup>1-3</sup>, or physical findings may be totally absent<sup>1,4</sup>.

Table 16.1. Diagnostic value of different imaging modalities in the evaluation of suspect aortic dissection with various organ involvement. Modified from: Task Force Report, Eur. Heart J. (2001) 22, 1642–1681

Clinical variables	TTE/TEE	CT	MRI	Angio	IVUS
Sensitivity	++	++	+++	++	+++
Specificity	+++	++	+++	++	+++
Classification	+++	++	++	+	++
Entry tear localization	+++	—	++	+	+
Aortic insufficiency	+++	—	++	++	—
Pericardial effusion	+++	++	++	—	—
Mediastinal hematoma	++	+++	+++	—	+
Side branch involvement	+	++	++	+++	+++
Coronary involvement	++	—	+	+++	++
Follow-up studies	++	++	+++	—	—
Patient comfort	+	++	+	—	—

+++ Excellent; ++ Good; + Sufficient; — Insufficient

Once aortic dissection is suspected, time is critical to improve survival. In-hospital mortality is approximately 27%, with most deaths occurring soon after the onset of symptoms<sup>4</sup> and can be as high as 1 percent per hour among untreated patients<sup>5</sup>. Therefore, one of the remaining challenges for aortic dissection is a rapid and accurate diagnosis in the first hours from symptoms onset, which is essential to reduce complications and to select appropriate medical and surgical treatment.

Nowadays, given the rapidly evolving state of imaging diagnosis involving transesophageal echocardiography, magnetic resonance imaging, and computed tomography scan (preferably helical), aortic dissection can be accurately diagnosed and defined non-invasively with high sensitivity<sup>5–8</sup> (Table 16.1). The choice of imaging modality may reflect hospital availability rather than preference<sup>4</sup>. In this setting, computed tomography is more frequently used for initial assessment although transesophageal echocardiography is accurate and easily applicable at the bedside, and magnetic resonance imaging is accompanied by high sensitivity and specificity<sup>4</sup>. Moreover, time delay, physicians' familiarity with different imaging methods, restricted ability to monitor patients during imaging, and high cost for sophisticated imaging examination are other logical explanations for differential diagnostic approach in suspected aortic dissection.

Until now, routine laboratory testing has played only a minor role in the assessment of acute aortic dissection, and tests are performed only for the exclusion of other diseases. To improve intensive care admission practices, a number of prediction models and new diagnostic screening tools have been developed. The prediction models include assessment of various clinical variables

while the new diagnostic tools evaluate the use of screening of biochemical markers in the peripheral blood that will aid the initial diagnostic screening<sup>9</sup>. The concept of early recognition with the use of biochemical markers has gained much popularity recently, attracting the interest of many researchers. Biochemical diagnosis provides a chemical marker reflective of the pathogenic activity and state, which when used in conjunction with other independent diagnostic modalities (such as imaging), may provide a more comprehensive understanding of the pathogenic state. Biochemical diagnosis is also inexpensive, readily available, nonspecialized, and noninvasive, making it an ideal modality for use in the rapid diagnosis in the ER and CCU. Thus, those types of tests have the potential to become very attractive for diagnosis if they are rapid and accurate. This chapter reviews different markers recently proposed for the diagnosis of aortic dissection and explores their usefulness in preclinical and clinical settings.

## **SMOOTH-MUSCLE MYOSIN HEAVY-CHAIN PROTEIN**

Smooth-muscle myosin heavy chain is a smooth-muscle-specific form of the myosin protein. Myosin along with actin is the major constituent of muscle cells' contractile apparatus and is one of the most abundant proteins in muscles. Smooth-muscle myosin is a specific isoform of the smooth-muscle lineage, and thus, it can be biochemically differentiated from cardiac or skeletal muscle myosin isoforms<sup>10,11</sup>. Smooth-muscle myosin heavy chain is present in the aortic medial smooth-muscle cells and, at time of the vascular insult, is released into the circulation allowing for its detection.

Although the technical details of the assay will not be discussed here, the immunoassay of smooth-muscle myosin heavy chain has been improved since its introduction and has reached clinically applicable stages. The kinetics of the protein release into the circulation show that similar to the kinetics of myoglobin in acute myocardial ischemia, smooth-muscle myosin heavy-chain form is rapidly cleared after an initial peak. Indeed, in contrast to cardiac myosin, which is tightly bound to the fibers and is therefore only slowly released, smooth-muscle myosin is loosely dispersed after the injury allowing for immediate release into the circulation. Levels of smooth-muscle myosin heavy-chain protein can be used to diagnose aortic dissection soon after symptom onset with the use of a rapid 30-minute assay<sup>10,11</sup>. The diagnostic implications of the assay show that aortic dissection can be reliably detected within the first six hours of the disease, with the most accurate range of detection in De Bakey type I and II dissection within the first three hours of symptom onset<sup>12</sup> (Figure 16.1). This is likely because the thoracic aorta is not only anatomically different from the abdominal aorta but is also characterized by a different aortic response to atherosclerotic disease.

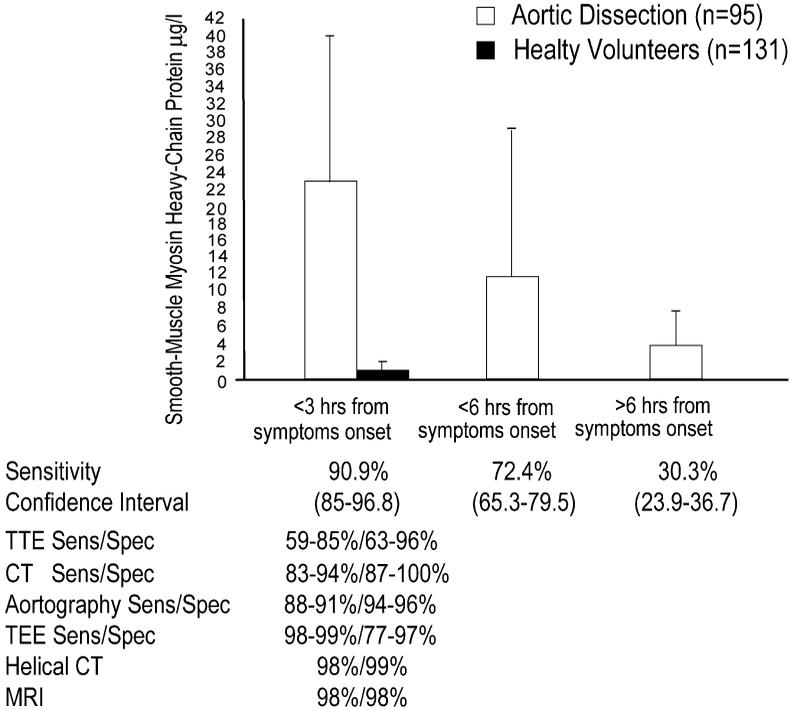


Figure 16.1. Blood levels and sensitivity of smooth-muscle myosin heavy-chain protein measurement in acute aortic dissection at different time intervals from symptom onset. For comparison, the sensitivity and specificity of several imaging technique are reported. Modified from reference 13.

In this setting, it is possible to demonstrate intact smooth muscle content in atherosclerotic segments of the thoracic aorta, whereas segments of the abdominal aorta show often gross fatty change with loss of smooth-muscle content. For this reason, it is likely that some patients with a dissection involving a distal aortic tract do not have elevated smooth-muscle myosin heavy-chain levels. The diagnostic performance of the assay alone is comparable if not superior to transthoracic echocardiography, conventional CT, and aortography but less effective than transesophageal echocardiography, helical CT, or MRI<sup>13,14</sup> (Figure 16.2). The main advantages of this assay are obvious: it is rapid, it can be done at a fraction of the cost of computed tomography or magnetic resonance imaging, and it can be repeated in a manner similar to that of other conventional immunoassays. One must take into account that this test would be most useful in the initial patient triage at the emergency department, especially with its negative predictive role, helping physicians to determine whether an aortic dissection is a possibility. Since biochemical diagnosis is an independent diagnostic modality compared to noninvasive imaging proce-

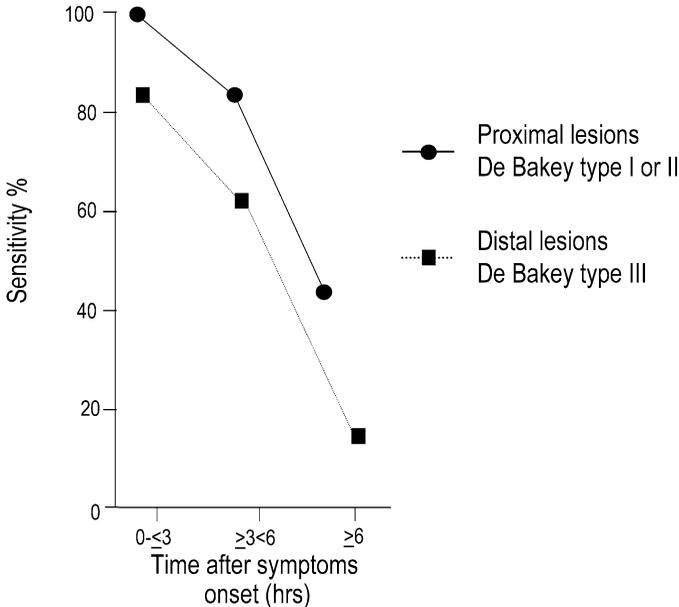


Figure 16.2. Temporal sensitivity curves based on the site of the entry tear for smooth muscle myosin heavy-chain protein measurement with a cutoff level of 2.5  $\mu\text{g/l}$ . Modified from reference 13.

dures, the combined use of one technique with the biochemical test should markedly increase the sensitivity and specificity in detecting aortic dissection. A multicenter international clinical study aimed at validating the clinical use of the assay is ongoing and additional analysis to define a vascular-specific smooth-muscle assay, which will also improve the usefulness of the assay, is under evaluation.

## CREATINE KINASE BB-ISOZYME

The BB-isozyme of creatine kinase has been also investigated as a potential marker for aortic dissection since it is abundantly present both in smooth-muscle fibers and in the neurological system. Analogous to the use of the MB-isozyme of creatine kinase for the detection of cardiac ischemia, a small study has shown that creatine kinase BB-isozyme is elevated in acute aortic dissection<sup>15</sup>. In addition, the study demonstrated that the temporal profiles of the peak level is delayed compared to smooth-muscle myosin heavy chain. Combined use of the two tests may therefore be extremely useful for temporal profiling of aortic dissection.

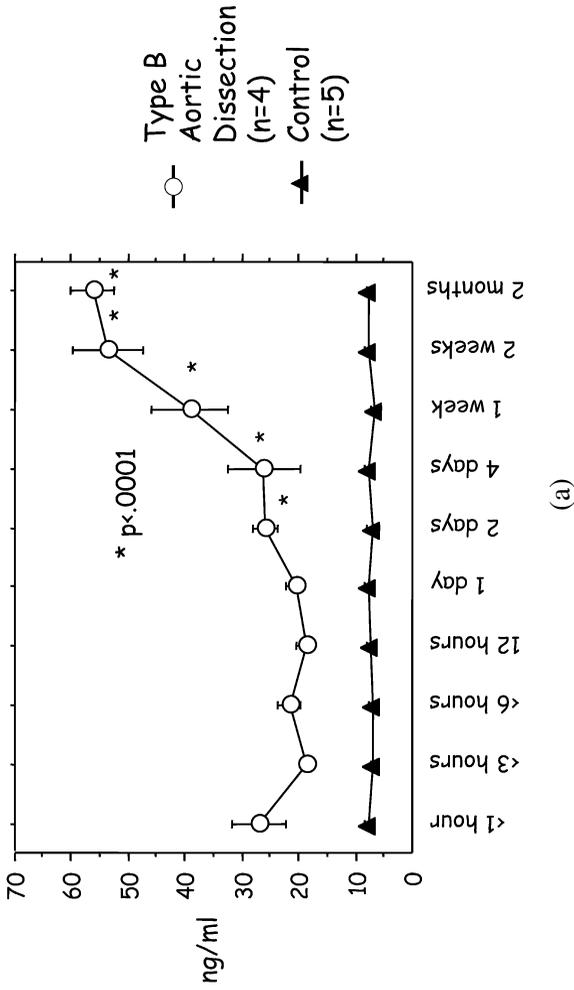
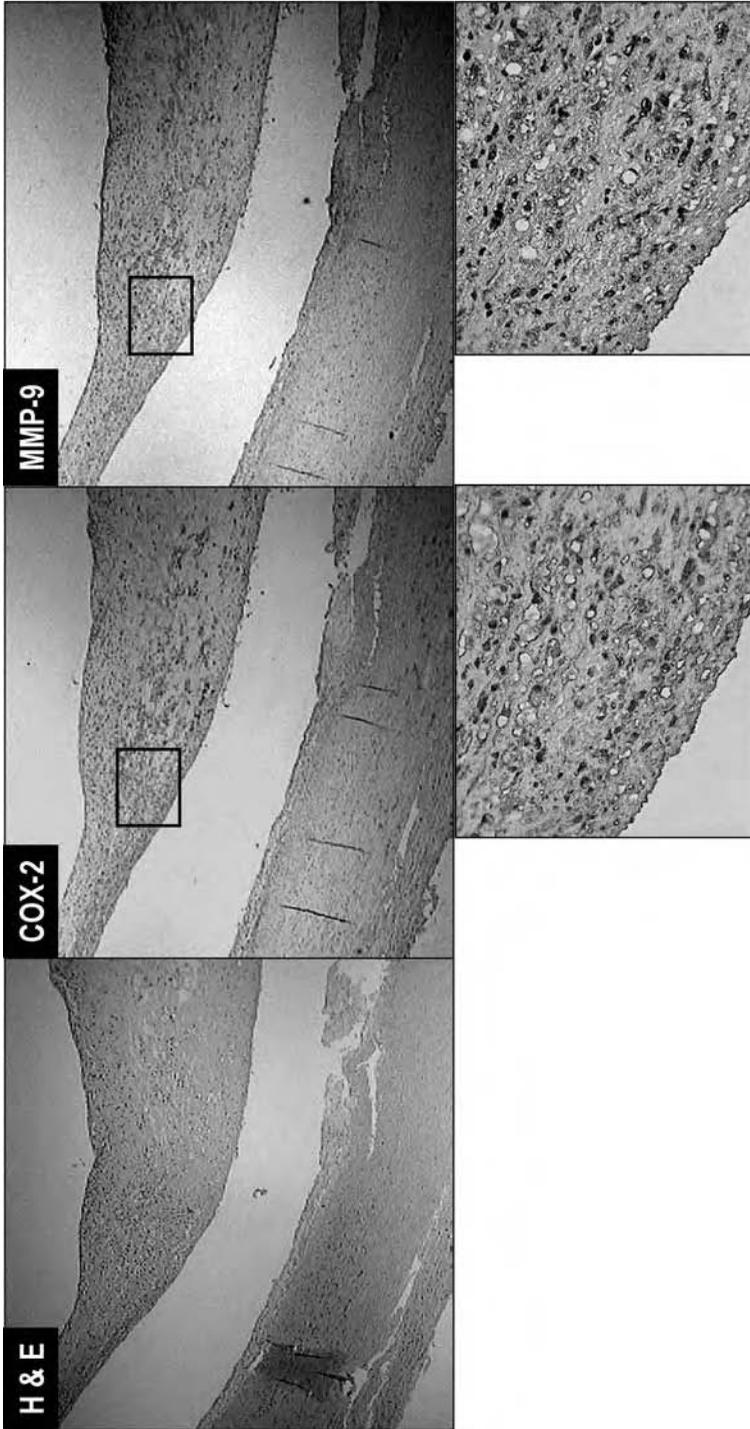


Figure 16.3. (a) Plasmatric levels detected by ELISA of metalloproteinase-9 from symptom onset to two months' follow-up in type B aortic dissection. No MMP-9 are measurable in the control population presenting in the emergency room with chest pain.



(b)

Figure 16.3. (Continued) (b) Micrograph showing the aortic wall (hematoxylin eosin, left upper panel, magnification  $\times 4$ ) with immunohistochemical staining for Cox2 (central upper panel, magnification  $\times 4$ ) and MMP-9 (right upper panel, magnification  $\times 4$ ) from a patient affected by type A aortic dissection and operated in the subacute phase (7–10 days after symptom onset). Note the marked inflammatory infiltrate demonstrated by strong positivity to Cox2 (small black insert, magnification  $\times 20$ ) and the presence of MMP-9 within inflammatory cells (small black insert, magnification  $\times 20$ ) in the same region of the aortic wall.

## MATRIX METALLOPROTEINASES DETECTION

The matrix metalloproteinases (MMP) constitute a family of endopeptidases that typically have in their molecule the presence of zinc in their active state, a dependency on calcium for their activity, and their ability to react with specific tissue inhibitors of metalloproteinases to form enzymatically inactive complexes<sup>16</sup>. These proteins are synthesized by variety of connective tissue, parenchymal, and inflammatory cells and have been found to play important roles in the pathogenesis of vascular disorders, especially in aortic and aneurismal lesions<sup>17</sup>. Various MMPs have been studied in the context of aortic disease, and their importance in the pathogenesis of various vascular disorders (such as atherosclerotic lesions, aneurysms, and Marfan syndrome) has gradually been recognized<sup>18</sup>. It is well known that patients with abdominal aortic aneurysms (AAAs) exhibit arterial dilation and altered matrix composition throughout the vasculature<sup>17,19</sup>. Degradation occurs as a consequence of complex interactions between genetic factors, inflammatory cytokines, MMPs, and others<sup>20–22</sup>. Phenotypically, there is dissolution and fragmentation of collagen and elastin, which leads to expansion of the vessel wall that can no longer withhold the repetitive expansible force of systolic contraction<sup>20</sup>. The ability of some of the MMPs (MMP-2, -3, -9, and -12) to hydrolyze elastin is of great importance in terms of their effects on the vascular system and especially for the aortic wall<sup>16</sup>. We have recently shown that plasma MMP-9 and MMP-3 levels are significantly elevated in patients with AAA compared with healthy control subjects and that after endovascular graft exclusion, these proteins decreased to a level similar to that of patients undergoing open surgical repair<sup>23</sup>. Additionally, we showed that a lack of decrease in MMP levels, after endovascular graft exclusion may help identify patients who will have endoleakage and consequent aneurysm expansion caused by continuous sac pressurization during follow-up.

During the last few years, several studies have demonstrated increase in the activities of various MMPs not only in the atherosclerotic aortic aneurysms but also in aortic dissection<sup>24</sup>. Schneiderman and associates demonstrated increased expression of fibrinolytic genes and MMPs 9 in different phases of aortic dissection, suggesting that these enzymes may be coupled with reparation of the vascular wall after the initial insult<sup>25</sup>. Our group has recently demonstrated that it is possible to detect elevated MMPs plasma levels in the acute phase of both type A and type B aortic dissection.

In this study, we evaluated plasma levels of MMPs by ELISA technique in 13 patients affected by acute aortic dissection (9 type A and 4 type B). In patients with type B aortic dissection treated medically, plasma curves at different time intervals (1, 3, 6, 12, 24, 48, 96 hours, 1 week, 2 weeks and 2 months

from symptom onset) were generated and aortic tissue samples obtained during surgery were evaluated by immunohistochemistry and western blot for MMP-9 and TIMP-1 expression<sup>26</sup>. MMP-9 plasma levels were increased in patients affected by type A and type B aortic dissection presenting within 1 hour from onset of symptoms compared to controls ( $29.3 \pm 16.1$  ng/ml and  $16.7 \pm 2.1$  ng/ml vs.  $7.74 \pm 1.6$ ,  $p < 0.03$ , respectively). In addition, in type B aortic dissection, mean MMP-9 plasma levels increased significantly from hospital admission to two months follow-up ( $16.7 \pm 2.1$  ng/ml vs.  $58.0 \pm 8.2$  ng/ml,  $p < 0.0001$ ). Low-moderate expression of MMP-9 was evident at immunohistochemistry in the acute phase while a marked expression was detected in the subacute phase.

Thus, it is possible to hypothesize that the increase in plasma levels of MMP9 in the subacute phase of medically treated type B aortic dissection is an expression of aortic wall remodeling. This increase of proteolytic activity could accompany the dissected aorta's attempts to heal itself but in fact such a phenomena might further weaken the aortic wall, predisposing it to dilation and/or rupture. Thus, our study also suggests a potential role for biomarker measurement done serially to follow subacute or chronic dissections. For example, immediate operation for an acute type B dissection is appropriate only under particular circumstances<sup>27</sup>. The indications for surgery among those patients who survive the acute phase of acute type B AD are not as clear. Because serious complications such as aneurysm formation or extension are not uncommon and unexpected late rupture cannot be predicted reliably by clinical examination, multiple CT examinations are mandatory during follow-up. Given the high cost of repeated imaging, there is great interest in identifying particular subgroups of patients who are at particular risk of aortic expansion and eventual rupture. Because MMPs plasma levels represent excess enzyme released into the circulation during periods of active matrix catabolism, elevated MMPs may reflect a more active state of degeneration of the aortic wall in the natural history of aortic dissection. In this context, MMPs plasma levels determination by ELISA may represent a simple, low-cost, and readily available technique to monitor patients who have been operated or not for aortic dissection in the long-term follow-up. The reappearance or sudden increase in these enzymes in the peripheral circulation may identify high-risk patients who are prone to develop aneurysm formation and rupture. Future larger prospective study with longer follow-up will obviously be required to confirm these possibilities.

## D-DIMER DETECTION

D-dimer is a typical degradation product of cross-linked fibrin and its plasma levels are detectable at levels  $>0.5$   $\mu\text{g/ml}$  fibrinogen equivalent units

in nearly all patients with venous thromboembolism<sup>28</sup>. Despite being non-specific, since elevated plasma levels can be found in intravascular activation of the coagulation system and secondary fibrinolysis (i.e., various forms of malignancies, infections, renal disease, recent trauma and surgery, disseminated intravascular coagulation, postfibrinolysis), it can be used effectively mainly due to its high negative predictive value to exclude deep venous thromboembolism and pulmonary embolism<sup>28-30</sup>.

Recently, elevated plasma levels of D-dimer were found in a small series of patients who experienced aortic dissection<sup>31</sup> and in patients treated with endovascular graft for aortic dissection repair<sup>32</sup>. The authors suggested that this finding could be explained by the extrinsic pathway of the coagulation cascade at the site of the aortic vessel wall injury by tissue factor. They also observed that the extent of the dissection correlates with the absolute degree of D-dimer elevation. Since aortic dissection is associated with disorders of the coagulation system not only in acute stages but also in the later stages which are associated with DIC, not only D-dimer but also other coagulopathic markers should be occasionally examined to rule out this condition<sup>33</sup>. More recently, Eggebrecht and associates have showed that D-dimers are highly elevated in acute aortic dissection<sup>34</sup>. In this study, all acute AD patients showed highly elevated D-dimer values that were similar to the levels of patients affected by pulmonary embolism ( $2,238 \pm 1,765 \mu\text{g/l}$  vs.  $1,531 \pm 837 \mu\text{g/l}$ ,  $p = 0.15$ ) but significantly higher than in chronic AD, AMI, or patients presenting with chest pain ( $p < 0.001$ ).

## SERUM MARKERS OF ELASTIN AND COLLAGEN METABOLISM

Elastin is a major component of the human abdominal aorta<sup>35</sup>. It has been shown that the structure and the amount of elastin is changed in aortic diseases, and increased levels of elastase and other elastolytic proteases in the aortic wall have been demonstrated in several aortic diseases<sup>35-37</sup>. In particular, the study of serum elastin peptides (SEP), plasma elastin alpha1 antitrypsin complex, and procollagen III-N-terminal propeptide (all measured by enzyme linked immunoassay and indicative of increased elastolysis) has suggested that increased elastolysis is associated with increased aortic wall distensibility, whereas increased collagen turnover is associated with reduced distensibility<sup>38</sup>. In addition, SEP have been prospectively described as a strong predictor of expansion in small aortic aneurysm sized 3-5 cm<sup>39</sup>. Elastin has also been explored as a possible marker for aortic dissection.

It is reasonable that this protein has been investigated given its vascular selectively. However, the relative abundance in the circulation that can be quan-

tified by blood testing may be questionable. Limited initial experience has shown that elastin is marginally elevated in aortic dissection, but the dynamic range of the assay is a matter of concern as it crosses considerably with normals, and thus its diagnostic use still warrants further investigation. Technical improvements to the assay to increase dynamic range may show that the assay is useful.

Shinohara and associates developed soluble elastin fragment (sELAF) enzyme-linked immunosorbent assay to measure human aortic elastin in different clinical settings. The study enrolled 25 AAD patients, 50 patients with acute myocardial infarction, and 474 healthy individuals. The sELAF levels from healthy subjects gradually increased with aging. When the cutoff point for positivity was set at the mean+3 SD, 16 AD patients (64.0%) were found to be positive, whereas only 1 AMI patient was found to be positive (2.0%). AD patients with either an open or a partially open pseudolumen were found to be 88.9% positive for sELAF, whereas those with its early closure were negative. The difference in the sELAF levels between AD patients with and without a thrombotic closure of false lumen was significant ( $60.3 \pm 15.6$  versus  $135.4 \pm 53.2$  ng/ml;  $p < 0.005$ , respectively) suggesting that the presence of sELAF in serum may be a useful marker for helping in the diagnosis and screening of AAD and may also help to distinguish AD from AMI. Another inflammatory marker, c-reactive protein, has also been investigated. Although elevations are to be expected in such catastrophic pathologies, it has been reported that thrombotic state may affect profiles of CRP elevations, which may prove to be of additional use in the diagnosis. Other nonspecific elevated markers would be leukocyte count and LDH, but the implications of their use in diagnosis remains to be addressed.

## GENETICS OF AORTIC DISSECTION

The understanding of the underlying genetic disorders to aortic dissection remain to be addressed. Numerous genetic disorders with aortic phenotypes have been reported, which may add insight to our understanding of specific facets of genetic mutations linked with aortic dissection<sup>40</sup>. One notable disease is the connective tissue disorder, Marfan's syndrome, which is associated with manifestation of aortic dissection and which is linked with mutations in the fibrillin genes<sup>41</sup>. It is most likely that instability of the aortic structure is the main pathology associated with aortic dissection in Marfan's syndrome. Supravalvular aortic stenosis is associated with the elastin gene and Ehlers–Danlos syndrome (type I) with the procollagen gene for other diseases in which disorders of genes associated with structural integrity of the aortic wall may show a possible link<sup>42</sup>. Familial aortic aneurysms have been reported to be linked to the procollagen and fibrillin-1 genes<sup>43</sup>. Other remote

possibilities include the PKD-1 gene, which is associated with polycystic kidney disease (which may manifest aortic disease), the endoglin gene (which is associated with hereditary hemorrhagic teleangiectasia), and HLA B-27/Dw-12/B52 (which have been implicated in aortic inflammation).

Numerous families with aortic dissection have been reported. The study of such families may be the key to finding the susceptible genes involved. One study narrowed the linkage to a locus at 5q13-14, but none of the known genes—which included Versican (encoding a proteoglycan found in the ECM), thrombospondin (encoding an extracellular Ca-binding protein), and CRTL (encoding a cartilage link protein)—were accountable for the disease<sup>44</sup>. Another locus has been mapped to 3p24-25, which overlaps a previously mapped second locus for Marfan's syndrome named the MFS locus<sup>41</sup>. Further investigation will be necessary to determine whether there is a link. The chromosome 11q23.2-q24 has also been shown to be a locus for familial aortic aneurysm disease<sup>45</sup>. Perhaps there is an unknown gene associated with aortic dissection, but further investigations will be necessary to dissect the genes directly involved in aortic dissection.

Such studies suggesting association of genes associated with aortic stability will provide important insight into at least one of the facets of the disease as will do studies linking monogenic abnormalities. However, given the multifactorial nature of aortic dissection (including acquired changes of the wall due to atherosclerosis and hypertension in addition to multigenic associations), how the complicated regulation by environmental cues on top of genetic abnormalities increases specific risk for the disease will be the ultimate question that needs to be answered.

## CONCLUSIONS

The rapidly aging patient population in Western societies and the resultant increase in aortic disease makes advances in biochemical diagnosis of the aortic wall dissecting process increasingly needed. Indeed, assessment of aortic dissection risk with the use of biochemical markers is likely to help triage patients and recognize the urgency for definite diagnosis with an optimal imaging modality, facilitate the prompt and timely initiation of medical therapy, and finally define the need for potential emergency intervention. In patients presenting in the emergency room who are highly suspicious for dissection as recognized by the "right" biochemical marker, a rapid action scheme would include the timely initiation of intravenous therapy with beta-adrenergic blockers, the urgent diagnostic confirmation, and immediate arrangements for transportation to a tertiary care center for adequate imaging and surgical intervention. Although several cytokines and acute-phase reactants potentially

might be predictive of clinical disease, the laboratory tests to assess aortic disease are limited to those that are employable in the clinical settings and have commercially available assays with adequate precision that can be standardized in large clinical studies. On the basis of these considerations at this time, it is most reasonable to limit current assays to smooth-muscle myosin heavy-chain protein and to serum metalloproteinases until more data from the ongoing studies are reported. The utilization of biomarkers could lead to further improvements in diagnostic pathways in acute and chronic aortic diseases, to help in establishing uniform follow-up programs and in formatting regional referral networks and allocation systems.

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# 17

## VASCULAR SURGICAL OPTIONS

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In the last decade, the surgical therapy for acute type A aortic dissections (AAAD) has been modified by new techniques that have improved the outcome. Continuous efforts have led to safer, more rapid, and more durable operations using new technology and new knowledge concerning the pathophysiology of the disease and the surgical long-term results. Some of these procedures (like the use of glue or other adjuncts to reinforce the aortic stumps) are already established techniques. Others “in progress” (like different modes of cerebral protection, sites of arterial cannulation, aortic valve management, and the extended aortic arch replacement) are still debated. Finally, procedures like the combined treatment of ascending aortic replacement associated with a stent graft positioned in the aortic arch and other endovascular techniques (hybrid procedures) seem to be the vascular surgical options for the future. These procedures appear as adjuncts to conventional surgical interventions but need to be evaluated for indications, feasibility, and long-term results.

## TRENDS IN CEREBRAL PROTECTION

The “open aortic anastomosis” technique represents the most frequently adopted surgical procedure for the distal anastomosis in acute type A aortic dissections<sup>1-6</sup>. The rationale for this approach has been to identify and remove intimal tears in the arch, perform a more hemostatic anastomosis by avoiding the crowding and distortion induced by the aortic clamp, avoid clamp injuries, and permit a more extensive resection of the dissected aorta at the level of the innominate artery. Concomitantly, the use of deep hypothermic circulatory arrest (DHCA), in association with antegrade or retrograde cerebral perfusion, has become routine<sup>1-6</sup>. This original method of cerebral protection, developed by Griep in 1975, permits an approach to the aortic arch by creating a bloodless field. However, it does not provide adequate protection of the brain for prolonged procedures exceeding 30 minutes<sup>7</sup>. In the last decade, the introduction of new techniques for cerebral protection during aortic arch surgery have significantly contributed to improvement in hospital survival and neurologic outcome<sup>8-11</sup>. Different experiences reported that mortality has diminished from 12% to 9% and the stroke rate from 7% to 4% using DHCA with no cerebral perfusion and moderate hypothermic circulatory arrest with selective antegrade cerebral blood flow, respectively. However, these patient series include all patients with arch pathology, not only acute dissections<sup>11-14</sup>. In these reports, cardiopulmonary bypass (CPB) time has been found to be a predictor for increased risk of early death<sup>9-14</sup> regardless of the cerebral protection, while the duration of antegrade selective cerebral perfusion has not had adverse impact on hospital mortality. In these patients, the complexity of

the aortic repair traditionally has played a major role in determining the outcome. However, during time-consuming aortic repairs, such as surgical interventions for acute dissections, antegrade selective cerebral perfusion (ASCP) has been effective in extending the safe period of circulatory arrest up to 60 minutes. This technique of cerebral protection gives better and more physiologic metabolic supply of oxygenated cerebral blood through adequate flow levels and utilization of moderate hypothermia instead of deep hypothermia. These methods are continuously developing, particularly through employment of moderate hypothermic temperatures, to reduce CPB times and its whole-body-trauma.

## ACTUAL AND FUTURE MANAGEMENT IN ARTERIAL PERFUSION

The selection of the arterial cannulation site for institution of cardiopulmonary bypass is a critical point during surgery for acute aortic dissection. Historically, in these patients the femoral artery has been adopted as primary site for arterial access<sup>15</sup>. However, a number of relevant complications have been associated with this procedure, including propagation of a retrograde dissection, retrograde embolization of lumen debris, and malperfusion causing end-organ ischemia<sup>16-18</sup>. In particular, cerebral injury can occur during retrograde blood-flow perfusion due to occlusion of the origin of the supra-aortic arterial trunks by the aortic false lumen or by a subtotal occlusion in the descending aorta by a thrombosed false lumen (Figure 17.1). The right axillary artery, on the other hand, has been found to be involved in the dissection only rarely and also is seldomly affected by extensive atherosclerotic lesions, so commonly found in the femoral artery<sup>18-21</sup>. The utilization of this artery has been developed as a safe access. Axillary artery cannulation secures continuous antegrade blood flow in the true lumen, avoiding the phenomenon of the compressed true channel. Also, this access eliminates the extra surgical step of having to cannulate the aortic graft after distal aortic reconstruction to have an antegrade aortic perfusion after completion of the distal anastomosis. In cases of small or deeply placed axillary arteries, a side graft of 8–12 mm can be used to avoid damage to the artery or inadequate flow, particularly in large, overweight male patients<sup>20,22,23</sup>. Most important, arterial inflow through the axillary artery facilitates the use of selective cerebral perfusion during open aortic surgery, which can be directly administered through the right common carotid artery, occluding the innominate artery (Figure 17.2). For the usefulness in reducing perfusion-related morbidity and adverse outcome in AAAD patients, the right axillary artery cannulation is becoming increasingly widespread, representing the preferred site of arterial perfusion in many centers<sup>21-23</sup>.

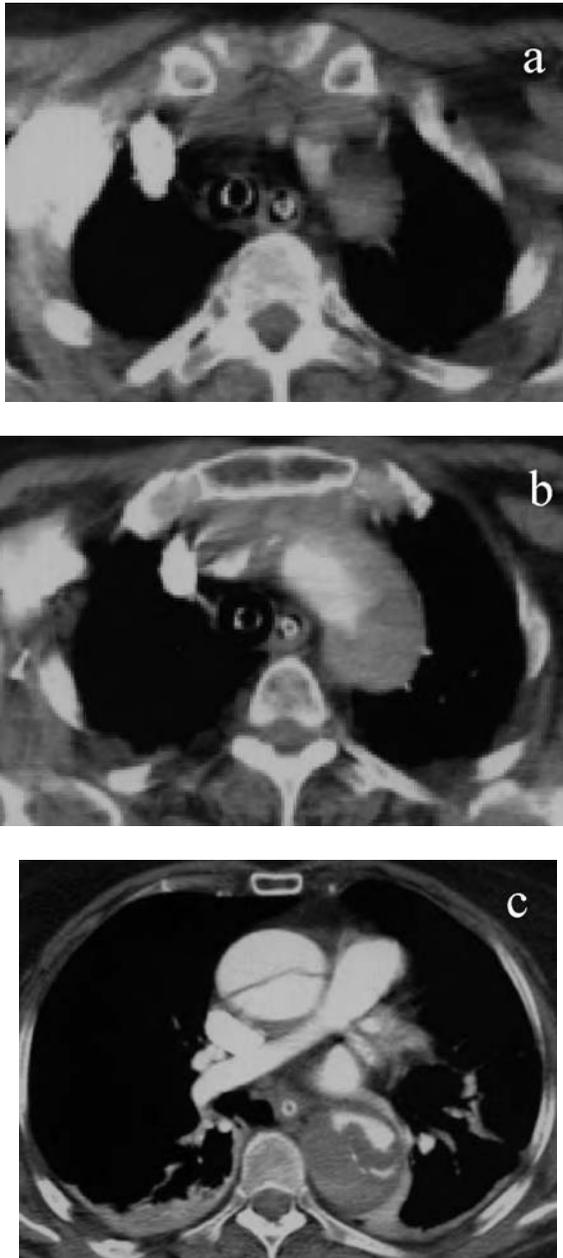


Figure 17.1. 68-year-old patient affected by acute type A aortic dissection presenting with both carotid and femoral pulses absent. CT scan showing absence of blood perfusion in the supra-aortic trunks (panels a, b), and descending aorta largely interested by thrombosed false lumen (panel c).

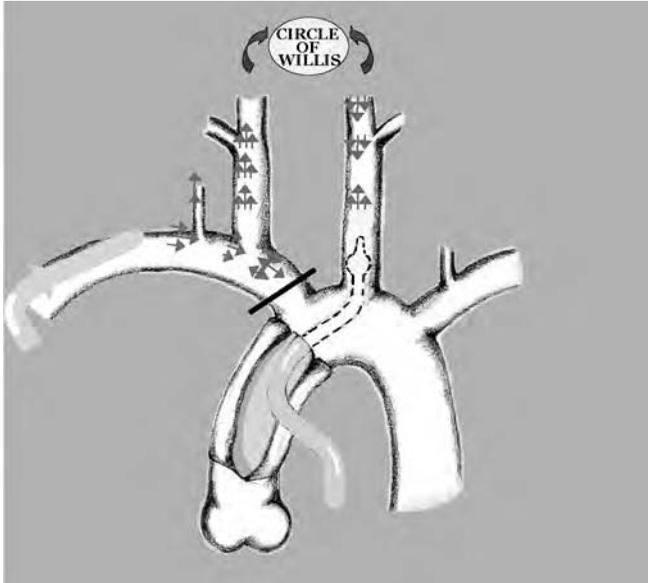


Figure 17.2. Antegrade selective cerebral perfusion through the right axillary artery, after occlusion of innominate artery. A separate arterial cannula can be positioned in the left common artery after aortotomy.

## SURGERY OF THE AORTIC ROOT

In the past, a conservative root repair has been preferred in the setting of acute aortic dissections due to a presumed increased risk related to more extensive procedures<sup>24,25</sup>. Subsequent concerns have been raised regarding a tendency for future aneurysmal expansion of the native aortic root or a recurrency of aortic valve regurgitation. Freedom from reoperation at 10 years has been reported to be around 80% in patients with composite valve-graft replacement and 70% in patients treated with aortic valve resuspension<sup>26</sup>. In this group of patients, it was noted that if the sinuses of Valsalva were not involved, and the aortic regurgitation was secondary to dilatation at the sinotubular ridge, the most frequent cause of proximal reoperation was represented by root dilatation rather than the recurrence of aortic insufficiency<sup>26,27</sup>.

Two morphological aspects play a fundamental role in deciding the most appropriate technique for repairing the aortic root in acute type A dissection—namely, the status of the functional aortic annulus and the condition of the aortic leaflets. The functional aortic annulus is composed of the aortic annulus, the Valsalva sinuses, the commissures and the sinotubular aortic junction. If the ascending aortic and aortic root diameters are normal without downstream displacement of the coronary ostia, and with no commissural detachment of

the aortic valve leaflets or other acute or chronic pathological changes of the leaflets, a supracommissural tubular graft is usually anastomosed to the sinotubular ridge. Whenever one or more of the commissures are detached, with secondary aortic regurgitation, the valve needs to be resuspended prior to graft insertion. In a previously ectatic proximal aorta (i.e., in patients with Marfan's syndrome), implantation of a composite graft is preferred<sup>28,29</sup>.

In patients with a normal aortic valve, Yacoub<sup>30</sup> and David<sup>31</sup> have proposed to replace the aortic root with preservation of the native valve, even in the emergency situation of an acute type A dissection. Sparing the native valve avoids the uncertainties and risks associated with prosthetic valves. Patients receiving a mechanical prosthesis and therefore indefinite anticoagulation are threatened by a potential catastrophe related to a persistent false lumen rupture or a new dissection that can occur distally, highlighting the desirability of preserving the native valve whenever possible<sup>32,33</sup>. Kallenbach and coworkers<sup>34</sup> assessed the outcome of three different proximal surgical approaches for the treatment of acute aortic dissection type A: a supracommissural graft replacement (SCR), root replacement with composite valve-graft (CVG), and an aorta valve-sparing (AVS) reimplantation technique, reporting an operative mortality not significantly different between the groups. Major advantages of valve-sparing operations are the complete removal of diseased tissue, low incidence of reoperation, and lack of anticoagulation. However, these procedures are complicated and time consuming and require great surgical competence. Therefore, at present they appear indicated in centers with accumulated expertise in elective cases<sup>34,35</sup>.

## AORTIC ARCH MANAGEMENT

In acute type A aortic dissection, the primary surgical target is the excision of the intimal tear with replacement of the ascending aorta and, if necessary, the aortic valve apparatus. The remaining false lumen and potential remodeling of the dissected arch and descending aorta currently play a secondary role. While there is concordance about the necessity of resecting the site of primary intimal tear in the ascending aorta, controversy still exists as to what extent the arch should be involved in the reconstruction.

Crawford and colleagues were the first to propose an analytical solution to this dilemma, suggesting that a more extensive aortic replacement may be associated with a lower probability of reoperation. They recommended replacing the arch only when it is aneurysmatic—when there is an excessive enlargement or impending rupture of the false channel or when the dissection originated from an arch tear<sup>37</sup>. It has been reported that a primary intimal tear in the arch is associated with poorer long-term survival in comparison with entry tears

localized in other aortic segments<sup>38</sup>. The increased mortality and rate of reoperation in this group is probably related to a persistently patent distal aortic false lumen secondary to the unresolved arch entry tear.

Lansmann reported that patients with a patent false lumen had a trend toward a lower five-year survival rate (95% with closed vs. 76% with a patent false lumen) and event-free survival (84% with closed vs. 63% with a patent false lumen)<sup>39</sup>. A correlation between an untouched arch primary intimal tear, patent distal false lumen, and late reoperation and mortality rate was also demonstrated by Yeh and colleagues<sup>40</sup>. Arch procedures (total arch or hemiarch operation) decreased the patency rate of a false lumen in the descending aorta, and a patent false lumen was the only significant risk factor in determining a three-year increment in aortic diameter. Moreover, a reduction in the rate of persistent false lumen and a concomitant decrease of aortic reoperations has been reported using open distal anastomosis and resection of arch tears<sup>41-43</sup>.

On the other hand, other authors<sup>44</sup> have shown that primary intimal tear resection had no significant bearing on the likelihood either of late death or of subsequent reoperation, even in case of total arch replacement<sup>45</sup>. Kazui and coworkers evidenced that a complete arch substitution did not translate into a lower 10-year reoperation rate (77%) compared to isolated ascending aortic (79%) or hemiarch replacements (82%). None of the patients requiring reoperation in their series had a redo median sternotomy approach. A right hemiarch or total arch replacement does not cancel the need for late reoperation on the distal thoracoabdominal aorta, but it can eliminate the risk of aneurysmal dilatation of the distal ascending aorta that remains following classic reconstruction of the ascending aorta<sup>27,45-49</sup>. Recent advances in cerebral protection during circulatory arrest have lead some authors to do a routine aortic arch replacement, irrespective of the location of the intimal tear. The rationale for this is to achieve a better control of the residual dissection. The results of this approach was an in-hospital mortality of 10%, an incidence of residual thoracic patent false lumen of 26-46%, and a seven-year freedom from reoperation of 93%<sup>48,49</sup>.

At present, there is somewhat of a consensus<sup>27,37,38,40,41,45,50-54</sup> that any dissected arch should be explored during a period of hypothermic circulatory arrest and that if an entry tear is detected in the aortic arch, the distal aortic anastomosis is usually made in such a manner as to replace the arch beyond the intimal tear. If extensive tears are found that continue beyond the junction of the transverse and descending aortic segments or with an acute dissection of a previously aneurysmal arch, a total arch procedure may be required with reconnection of some or all supraaortic vessels to the graft during hypothermic circulatory arrest and antegrade cerebral perfusion<sup>45,47-49</sup>. The distal false lumen closure has been defined as an end-point in the surgical treatment of acute dissections, but despite continuous efforts, this goal is still difficult to

obtain, probably due to the existence of multiple distal tears in patients with a completely dissected aorta.

## IS THE ELEPHANT TRUNK USEFUL?

A surgical challenge occurs when an acute type A dissection is associated with dilatation of the thoracic or thoraco-abdominal aortic segments. The treatment of such extensive aortic diseases had a primary effort from the introduction of the elephant trunk procedure by Borst and colleagues in 1983<sup>51</sup>. This technique was initially developed for aneurysms and allowed a staged replacement of the thoracic aorta, with a following lower risk of mortality and morbidity<sup>55</sup>. In patients with acute dissections, to facilitate the treatment of a future possible aneurysmal expansion of the thoracic aorta false channel, the elephant trunk extension of the arch graft is an option. However, it is not routinely indicated due to the fragility of the tissues of the left subclavian area that may not be a strong hold to the sutures and the uncertain distal perfusion when inserting the trunk into the true aortic lumen in a dissected aorta<sup>55,56</sup>.

In patients affected by acute type A dissection treated with an elephant trunk procedure, a high incidence of paraplegia/paraparesis (21%) was reported by Miyairi<sup>57</sup>, underlining the concept that in patients with nondilated aortas, long elephant trunks may occlude intercostals arteries leading to paraplegia. However, in some cases there is evidence that this surgical strategy seems to prevent further aortic dilatation<sup>58</sup>. The principle to create a proximal blind pocket that subsequently thromboses spontaneously has also been adopted by Buffolo<sup>59</sup> when treating acute type B patients.

For both type A and B dissections, no data are available concerning the incidence of a second-stage operation in patients whom had a first-stage elephant trunk<sup>56,60,61</sup>. In many of the dissected patients with no significant aortic enlargement of the distal thoracic aorta, the risk of early death for aortic rupture appear to be lower compared to patients with extensive aneurysms waiting for second-stage surgical treatment<sup>60-62</sup>. In highly selected patients, recent experiences have also reported a second-stage elephant trunk stent-graft procedure<sup>15,58,62</sup>. This approach could be performed after a short period from surgical intervention, when an early second-stage operation would not be tolerated.

## HYBRID SURGICAL-ENDOVASCULAR OPTIONS

The treatment of acute type A aortic dissections with extended aortic arch replacements in patients with proximal intimal tears is a controversial issue. In

these patients, with no obligated current indication for a surgical arch management, recent series have reported positive results, even if this technique appears complex with a significant mortality rate<sup>45,63</sup>. To reduce the surgical impact of this procedure, mainly in high risk cases, Roux and colleagues have proposed to insert an uncovered stent graft in the aortic arch to coapt the aortic layers<sup>64</sup>. This Djumbodis dissection system (Saint-Come-Chirurgie, Marseille, France) consists of a large-meshed web (Figure 17.3) that can be positioned over the origin of the supra-aortic trunks without obstruction (Figure 17.4). It is in-

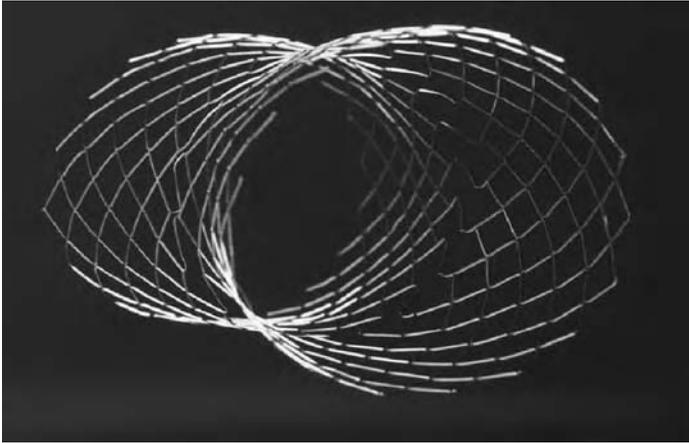


Figure 17.3. The Djumbodis dissection system is an uncovered stent graft that can be positioned in the aortic arch to facilitate coaptation of the aortic layers.

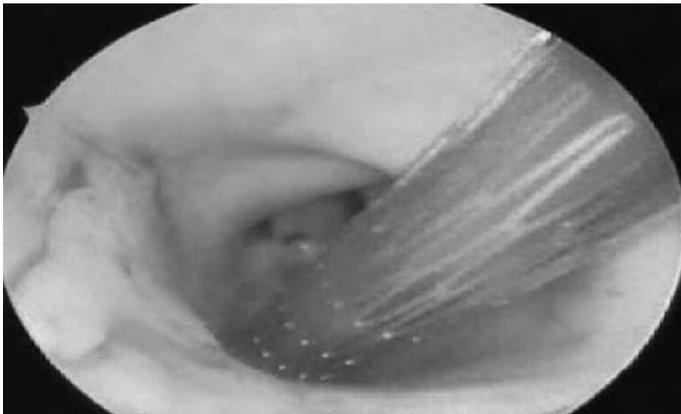


Figure 17.4. Intra-aortic view showing the Djumbodis dissection system superimposed over the origin of the supra-aortic trunks.

serted in the aortic arch during moderate hypothermic circulatory arrest and secured to the aortic wall with transfixing stitches.

This system has been further developed by using a traditional transfemoral artery stent grafting of the thoracic aorta<sup>65</sup>. In an effort to improve the closure of the distal false lumen, other combined endovascular-surgical approaches have been proposed (such as a transaortic stent-graft implantation into the descending aorta during ascending and aortic arch replacements)<sup>52,53</sup>. Both these series have reported an 80% clotting of preoperatively patent false lumen at six months follow-up. This combined surgical and endovascular procedure seems to be a feasible, reproducible, and effective alternative to an extended surgical aortic treatment. However, even though this double technique appears to be a highly valuable option for the future, it obviously needs further evaluation with defined indications and follow-up.

## FUTURE IMAGINATIONS

A feasible complete endovascular treatment of an acute type A aortic dissection has not been developed. Stent-graft procedures have been conducted for aortic arch aneurysms, including intentional covering of one or more of the supraaortic trunks, occasionally associated with surgical implant of intrathoracic bypasses in cases of debranching of the aortic arch (Figure 17.5).



Figure 17.5. Complete debranching of the aortic arch covered by a stent graft for arch aneurysm and intrathoracic bypass between ascending aorta, innominate artery, and left common carotid artery.

In spite the fact that aortic aneurysms and dissections have different characteristics, a total endovascular approach for type A dissections could be hypothesized as well, with the accomplishment of new endografts. In the future, treatment of this catastrophic disease can also foresee indications for limited surgery in patients admitted in hospital in extreme conditions. The IRAD experience shows that an unstable hemodynamic preoperative condition is associated with a particularly poor outcome<sup>4</sup>, making surgical intervention an heroic attempt.

Currently, new methods of preventions of the disease are developing. Causes of dissections, as ascending aortic aneurysms or Marfan's patients are treated with more aggressive surgical approaches, when the aortic diameter is less than 6 cm and less than 5.5 cm, respectively<sup>66</sup>. Specific hypotensive drugs, like beta-blockers, are more frequently administrate in the young population affected by hypertension. Genetics knowledge today allows us to assess high-risk patients; soon, it could became therapy. In the future, we could expect a lower expectancy of acute dissections and probably a limited traditional surgical approach, clarifying the basis for a more specific and effective role of surgery.

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# 18

## PREVENTION OF AORTIC DISSECTION

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The best way to prevent aortic dissection is optimal control of blood pressure, even for people with inherited forms of aortic wall weakness. Beta blockers are the antihypertensive agents of choice in individuals at risk for aortic dissection. Beta blockers lower blood pressure and decrease  $dp/dt$ . They have been shown to retard aortic expansion associated with Marfan's syndrome<sup>1</sup> and with chronic abdominal aortic aneurysms<sup>2</sup>. In a cohort of patients with the Marfan syndrome, Shores et al. demonstrated that the mean slope of the regression line for the aortic-root dimensions, which reflect the rate of dilatation, was significantly lower in the beta-blocker group than in the control group (0.023 vs. 0.084 per year,  $p < 0.001$ )<sup>1</sup>. Current guidelines recommend titration of these agents to achieve a heart rate of  $\leq 60$  beats per minute and a blood pressure  $< 135/80$  mm Hg in usual patients and  $< 130/80$  mm Hg in those with Marfan's syndrome<sup>3-5</sup>.

Optimal lipid lowering with statins is also indicated in individuals at risk for aortic dissection. Mechanistically, statins can directly modulate the biology of the aortic wall and suppress MMP-9 production by inhibiting the activation of neutrophils and macrophages. It is likely that such therapy could be useful for the prevention or treatment of aortic aneurysms<sup>6</sup>.

**mts-1**

gatgaacaatgatgatgaagaaaaagaagaaaaggaaaagatggcaacaagaaggagaaacagaaccggaaa  
 aggaagaagaagaacacaaaaaaaaaaaaaaaaaac [CA]<sub>n</sub> aatgaaaccctgcctctggaatacattgtctt  
 ataataaagatattaccatactcagttcaaacatgaaactgacagcagacaatgtgtctttagggcaga

**mts-2**

cttcagataagtagtggatctctgcagagctccaattaatcatggcacacgagtagctctcattaaaggaaaaagaaagaa  
 ggaaaaaaaaata [CA]<sub>n</sub> tcttagagctctagagggcagaaataatctggggagctttgcaagacgtatatgcctggg  
 ggggatcctctagagctgacctgcaggcatgcaag

**mts-3**

aaaacaagaaagataagtaaaagtagcgatgaaaacaaaatctcagagtagatagtggttagggagagatgaaata  
 aaataaaataaaataacataacataacataaaaaataag [TAAA]<sub>n</sub> aagaacttaccacacaaaaatagc  
 ctatcgggagtggaatggtagccagggtgcaggcacactgatactccctatgagg

**mts-4**

ggaaagtggtttagtattctcaattgctattcgttgatgtccctattgccatcaccaccaccaactgcacg [CA]<sub>n</sub> c  
 gcacgcactttccatctgtcttaccctgcacagggatccgcccgccttagctcccaaagtctaggattacaggtgtgagca  
 accg

Figure 18.1. DNA sequences flanking the microsatellite polymorphisms in the FBN1 gene. The lines above and below the sequences indicate the location of the sense and antisense PCR primers, respectively. The polymorphic markers allowed identification of the particular copy of the fibrillin gene that cosegregated with Marfan's syndrome in 13 of the 14 families tested. Adapted from reference 7.

## PRESYMPTOMATIC DIAGNOSIS

Fibrillin (FBN) is a major glycoprotein component of the extracellular microfibril widely distributed in elastic tissues. Pereira et al. demonstrated that intragenic markers can be used to follow the segregation pattern of FBN1 alleles in most families with Marfan's syndrome<sup>7</sup>. Although the 5/11/2/7 haplotype was observed in homozygosity in approximately 14% of unrelated persons in the general population, haplotype-segregation analysis identified 13 of the 14 families tested in their study (Figures 18.1 and 18.2)<sup>7</sup>. Since earlier beta-blocker therapy is likely to be more effective in patients with Marfan's syndrome, presymptomatic diagnosis may have a significant effect on med-

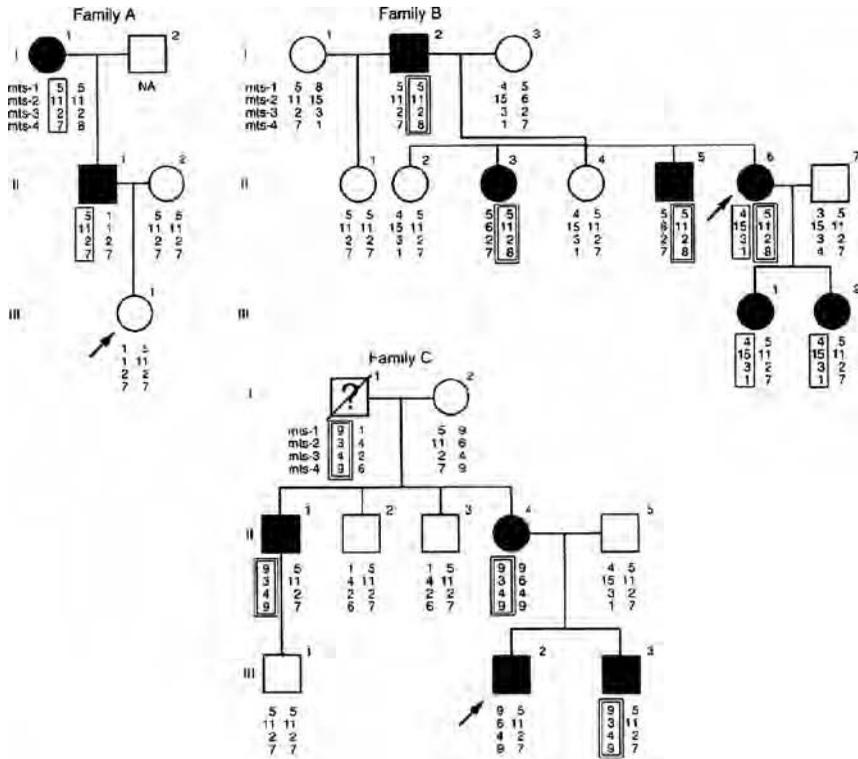


Figure 18.2. Haplotype-segregation analysis in three families. Squares denote male family members, circles female family members, black symbols persons affected by Marfan's syndrome or the MASS phenotype, gray symbols persons with a milder connective-tissue phenotype, white symbols unaffected persons, the slash a deceased person, arrows probands, and NA not analyzed. In Family A, with classic Marfan's syndrome, presymptomatic diagnosis in an infant was requested. The haplotype that segregated with the disease is shown in a box. Analysis of Families B and C revealed Marfan's syndrome in Family B, the MASS phenotype in Family C, and a milder connective-tissue phenotype in both families. The haplotype segregating with Marfan's syndrome in Family B is shown in a single box, and those segregating with the milder phenotypes in Families B and C are shown in double boxes. The question mark indicates that the phenotypic assessment of Subject I-1 in Family C was incomplete because of his early death. Adapted from reference 7.

ical management and prognosis. Contrariwise, early exclusion of the diagnosis would avoid the need for the routine use of expensive diagnostic testing in the follow-up of clinically equivocal individuals. The knowledge of these polymorphisms will contribute to increased understanding of the mechanism of aortic dissection and may lead to the development of new, innovative, and more effective drugs in the near future.

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