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Thoracic Aortic Aneurysm: Reading the Enemy's Playbook

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Imagine if a sports team were able to read the opposing team's playbook; this would be a boon of major proportions. Aortic diseases represent a virulent opponent for cardiac specialists and for our patients. Over the last 10 years, at the Yale Center for Thoracic Aortic Disease, we have made a concerted effort to learn more about the natural history of aortic diseases based on a data set including information on 3000 patients and 9000 years of patient follow-up and 9000 serial imaging studies. This analysis has given us glimpses into the playbook of thoracic aortic diseases; these glimpses have corrolaries in terms of the appropriate role and timing of surgical intervention.

Aortic dissection is one of the most catastrophic acute natural events that can befall the human being. The pain of this disorder is often described by those affected as the most severe pain imaginable. Because acute aortic dissection often masquerades as a heart attack, its true incidence is often underestimated. If a middle-aged or elderly person presents to the emergency room with acute onset of chest pain, clutches his chest, and promptly dies, he is likely to be signed out as a "myocardial infarction". In actual fact, many such presentations represent undiagnosed aortic dissections. It takes autopsy series to document the true incidence of acute aortic dissection. Such series have indicated that aortic dissection is actually the most common lethal condition affecting the human aorta, more common than the better appreciated ruptured abdominal aortic aneurysm. [1]

Furthermore, with the increasing frequency of 3-D imaging of the human body—including the so-called "drive-in" CT scanners—aortic pathology is being diagnosed more thoroughly.

For all these reasons, acute aortic dissection is a condition of great importance not only to the surgical specialist, but also to the generalist and to other specialists such as emergency medicine, radiology, and cardiology.

This chapter will address the natural history of aortic dissection. Its surgical treatment will be covered elsewhere in this text.

ETIOLOGY

Marfan's syndrome, based on any of a large number of mutations on the fibrillin gene, is a well-known cause of aortic dissection. A patient with Marfan's disease, if denied surgical intervention, runs a 50% risk of developing aortic dissection during his lifetime. Marfan's disease accounts for about 5% of all cases of aortic dissection. A small number of other collagen vascular diseases (including Ehler-Danlos syndrome) cause an even smaller percentage of aortic dissections. As is well-known, the condition of cystic medial necrosis provides the anatomic backdrop in which the dissecting

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process can occur. Figure 1 provides a classic example of this pathologic entity. One can easily picture how a tear in the endothelium can permit blood under pressure to enter one of the intramedial lacunae and how such pressurized entry can split the aortic wall and propagate distally. Cystic medial necrosis is a non-specific degenerative condition of the media which can occur from one of the collagen vascular syndromes like Marfan's disease, from the effects of chronic hypertension, or from the aging process itself.

Although the medial degeneration may take decades to develop, the process of dissection itself is literally instantaneous: one moment the aorta is whole, and a split second later, it is dissected. We have visualized this process by direct aortic examination and by echo in our laboratories in an animal model of experimental aortic dissection. [2] By naked eye and by echo, one can see the dissection extend from the proximal descending aorta, where we induce an intimal tear along the entire length of the aorta. By producing an intimal tear and then inducing severe iatrogenic hypertension (BP 300 mmHg, utilizing epinephrine injection), we can reliably produce these aortic phenomena and evaluate various surgical treatments.

We are recognizing that many patients with aortic dissection do not fit any acknowledged syndrome of collagen vascular disease. In fact, Marfan's disease and the similar disorders account for only the "tip of the iceberg" of aortic dissection. Our own studies have indicated a strong genetic component in patients with thoracic aortic aneurysm and dissection among those patients without Marfan's disease. In fact, our construction of nearly 250 family trees of patients with thoracic aortic aneurysm or dissection has indicated that 21% of our probands have at one family member with a known aneurysm somewhere in the arterial tree. [3] Figure 2 shows the positive family trees from among our first hundred family trees. Note that the predominant method of inheritance is autosomal dominant, but that other genetic patterns are also expressed. The true rate of inheritance is likely much higher, as many family members may harbor aneurysms without being aware of their presence. We have undertaken intensive efforts aimed toward identifying the specific genetic aberrations that underlie these family transmissions. The patients with positive family trees showed a higher rate of growth of their aortas and a presentation with clinical disease at an earlier age, strongly supporting an inherent genetic defect of the aortic wall.

It is interesting that aortic dissection has been shown to occur in circadian and diurnal patterns, with a preponderance of instances in the winter months and in the early morning hours. The reasons behind these patterns are unknown.

Acute aortic dissection can also occur in pregnancy. Also, bicuspid aortic valve, a very common congenital condition (1-2% of the general population) predisposes to aortic dissection. One in twenty bicuspid patients will develop aortic dissection in his lifetime. Of note, dissection usually occurs before the onset of symptomatic aortic stenosis in these patients. Aortic
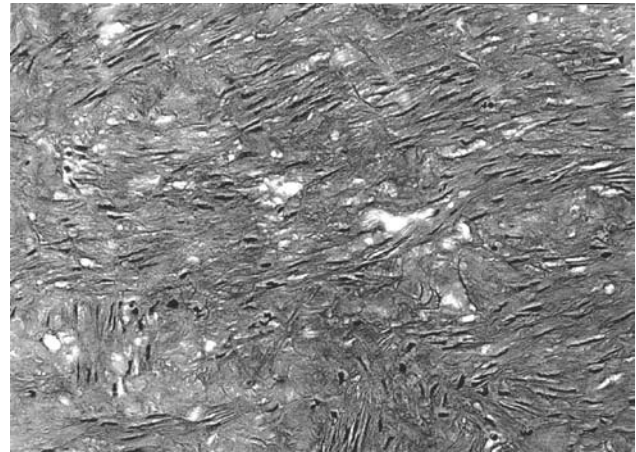

FIGURE 1. Classic cystic medial necrosis. Note the drop-out of medial cell bodies and the cystic spaces within the media.
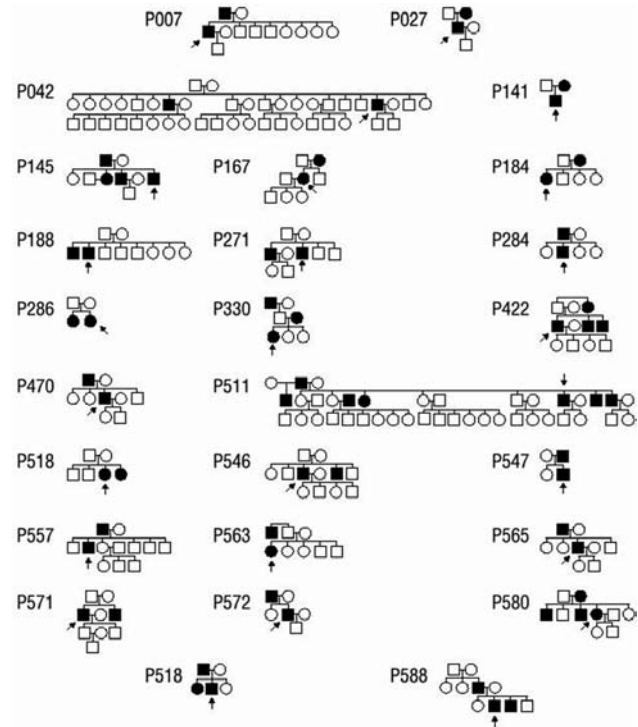

FIGURE 2. Family trees of the first 21 patients in Yale series with positive family histories, drawn from among 100 interviewed families. The predominant pattern of inheritance is autosomal dominant.

coarctation predisposes strongly to aortic dissection. Dissection can occur in pregnancy, threatening both mother and fetus. In the present era, cocaine use is emerging as an increasingly frequent cause of aortic dissection.

SYMPTOMS

The symptoms of aortic dissection are well-known. Ascending aortic dissection usually produces substernal pain, and descending dissection produces posterior back pain in the interscapular region. It is interesting that nature perceives the pain of dissection via a "splitting" or "tearing" quality very much a propos to the pathologic process itself.

Other symptoms are reflective of ischemia of the specific vascular branches that may be impaired or occluded by the dissection process. These are depicted in Figure 3. Dissection may produce ischemia of the brain, resulting in stroke; ischemia of the spinal cord, resulting in paraplegia; ischemia of the intestines, resulting in bowel necrosis; ischemia of the kidneys, resulting in renal failure or reno-vascular hypertension; or iliac artery ischemia, resulting in pulseless lower extremities.

Figure 3 also indicates the means by which aortic dissection can lead to mortality. These are four: (1) intrapericardial rupture, producing cardiac tamponade, (2) acute aortic insufficiency, resulting in acute cardiogenic shock, (3) free
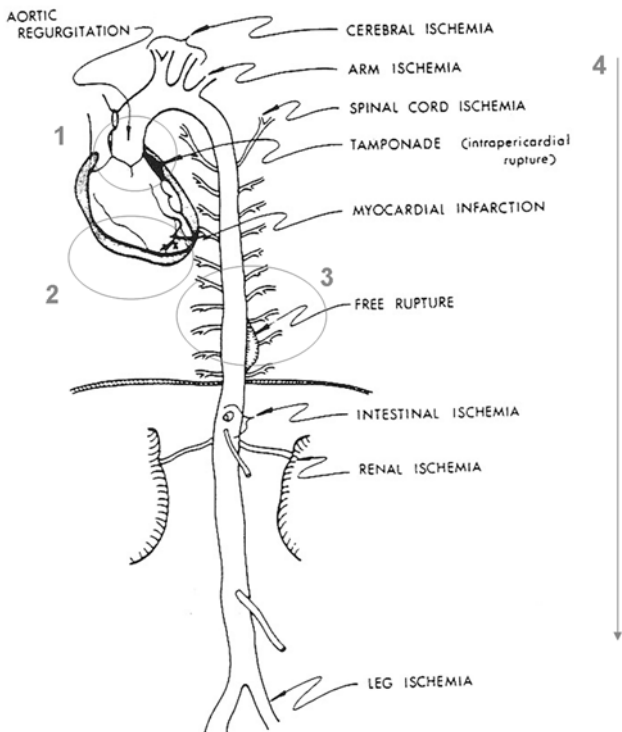

FIGURE 3. Schematic depiction of the manners in which acute aortic dissection can take a patient's life. These include (1) intrapericardial rupture with tamponade, (2) acute aortic insufficiency, resulting in acute cardiogenic shock, (3) free intrapleural rupture, usually on the left side, and (4) vascular compromise, from any of the indicated branch arteries of the aorta.

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SURVIVAL IMPACT

We have followed hundreds of patients longitudinally in our Yale Center for Thoracic Aortic Disease. This serial follow-up has demonstrated that thoracic aortic aneurysm disease is inherently a lethal disease. [4] Five-year survival overall is 63%. In all calculations, regardless of category, patients with aneurysm do more poorly than those with aneurysm without dissection. This can be seen in Figure 4. The five-year survival for patients with dissection is only 42%. This poorer outcome is understandable in view of the fact that, after dissection has occurred, the bloodstream is restrained by only a partial thickness of an intrinsically weak aortic wall. In fact, our data has indicated clearly that the dissected aorta grows more quickly than the non-dissected aorta, 0.37 cm / year, compared to 0.09 cm/year.

This poor prognosis after realized dissection indicates how critically important it is to intervene *before aortic dissection occurs*. Our detailed studies of the natural history of the enlarged aorta have defined criteria which predict when dissection and rupture are likely to occur in an enlarged thoracic aorta. See Figure 5. We have identified "hinge points" for dissection or rupture at 6 cm for the ascending and 7 cm for the descending aorta. [4] We have recommended intervention at sizes smaller than these danger points, namely 5.5 cm for the ascending aorta and 6.5 cm for the descending aorta.

It is well-known that patients with Marfan's disease can dissect at quite small sizes, and for this reason, we have decreased the intervention for Marfan's patients to lower levels, namely 5.0 cm for the ascending aorta and 6.0 cm for the descending aorta. We consider patients without Marfan's disease but
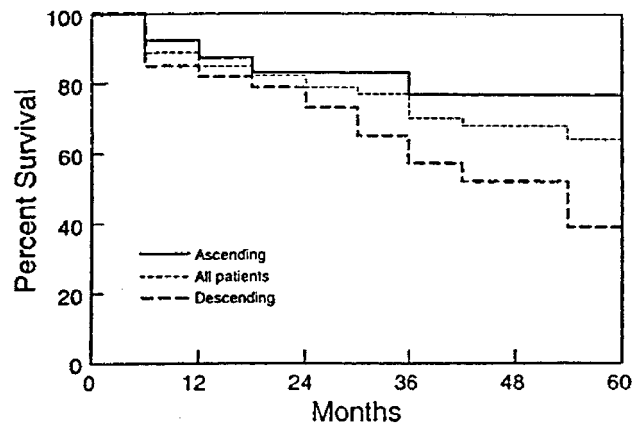

FIGURE 4. Long-term survival of patients with thoracic aortic aneurysms and dissections.
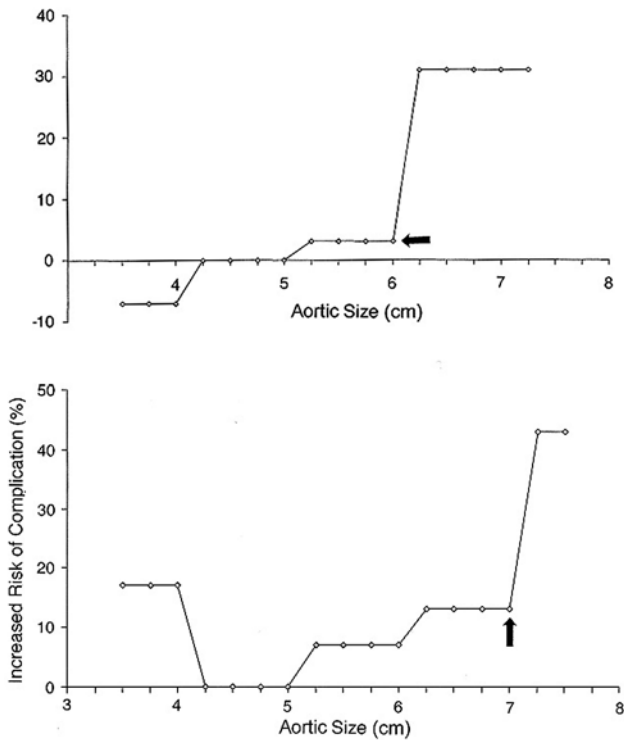
FIGURE 5. Depiction of "hinge points" for lifetime natural history complications at various sizes of the aorta. The y-axis lists the probability of complication; complication refers to rupture or dissection. The x-axis shows aneurysm size. Figure a is for the ascending aorta. Figure b is for the descending aorta.

TABLE 1. Size criteria for resection of asymptomatic thoracic aortic aneurysms.

The Yale Center for Thoracic Aortic Disease Recommended Surgical Intervention Criteria for Thoracic Aortic Aneurysms

1. Rupture

2. Acute Aortic dissection
   a. Ascending requires urgent operation
   b. Descending requires a complication- specific approach

3. Symptomatic states
   a. Pain consistent with rupture and unexplained by other causes
   b. Compression of adjacent organs, especially trachea, esophagus, or left main stem bronchus
   c. Significant aortic insufficiency in conjunction with ascending aortic aneurysm

4. Documented enlargement
   a. growth >1 cm/yr or substantial growth and aneurysm is rapidly approaching absolute size criteria

5. Absolute size (cm)

	Marfan's	Non-Marfan's
Ascending	5.0 cm	5.5 cm
Descending	6.0 cm	6.5 cm
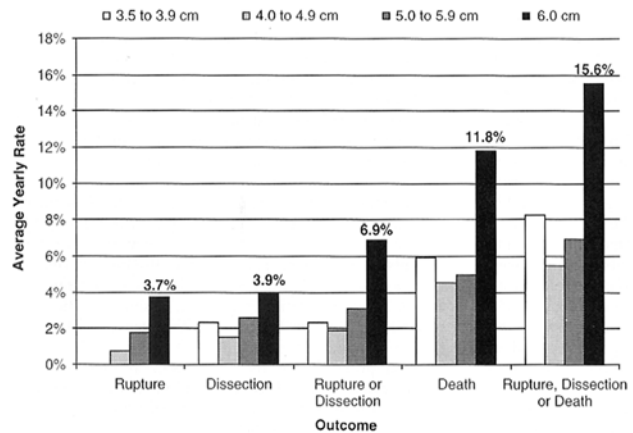
FIGURE 6. Yearly rates of rupture, dissection, or death according to aneurysm size.

with a family pattern of aortic disease just as vulnerable as Marfan's patients. We use these lower criteria for patients with a positive family history.

See Table 1 for criteria for preemptive surgical intervention for aortic enlargement. It is important to emphasize that these criteria are specifically and only for asymptomatic patients. Presence of symptoms requires surgical extirpation of the aorta, regardless of size.

We have recently been able to determine the yearly risk of rupture, dissection, or death for patients with enlarged aortas of various sizes. [5] These are depicted in Figure 6. This analysis was just recently completed, as calculation of yearly rates requires extremely robust statistical data. We now have observed about 150 hard aortic endpoints, permitting such statistical analysis. One can see that an aorta that has reached 6 cm imparts a risk of dissection of 3.9 % per year. The corresponding risks of rupture and death are 3.7 % and 11.8%. The yearly risk of rupture, dissection, or death is 14.1% per year. This data provides further substantiation of the validity of criteria which permit intervention before the dangerous dimension of 6 cm is reached.

Very recently, we have been able to refine our analysis to permit estimation of rupture and dissection risk based on the patient's body size as well as the diameter of the aneurysm. This information is relayed in Table 2. By inputting body surface area and aneurysm size, one can categorize any specific patient into low, moderate, and high risk categories.

TABLE 2. Nomogram for computing risk category based on body size and aneurysm size.

					Aortic Size (cm)					
BSA	**3,5**	**4,0**	**4,5**	**5,0**	**5,5**	**6,0**	**6,5**	**7,0**	**7,5**	**8,0**
1,30	2,69	3,08	3,46	3,85	4,23	4,62	5,00	5,38	5,77	6,15
1,40	2,50	2,86	3,21	3,57	3,93	4,29	4,64	5,00	5,36	5,71
1,50	2,33	2,67	3,00	3,33	3,67	4,00	4,33	4,67	5,00	5,33
1,60	2,19	2,50	2,80	3,13	3,44	3,75	4,06	4,38	4,69	5,00
1,70	2,05	2,35	2,65	2,94	3,24	3,53	3,82	4,12	4,41	4,71
1,80	1,94	2,22	2,50	2,78	3,06	3,33	3,61	3,89	4,17	4,44
1,90	1,84	2,11	2,37	2,63	2,89	3,16	3,42	3,68	3,95	4,22
2,00	1,75	2,00	2,25	2,50	2,75	3,00	3,25	3,50	3,75	4,00
2,10	1,67	1,90	2,14	2,38	2,62	2,86	3,10	3,33	3,57	3,80
2,20	1,59	1,82	2,05	2,27	2,50	2,72	2,95	3,18	3,41	3,64
2,30	1,52	1,74	1,96	2,17	2,39	2,61	2,83	3,04	3,26	3,48
2,40	1,46	1,67	1,88	2,08	2,29	2,50	2,71	2,92	3,13	3,33
2,50	1,40	1,60	1,80	2,00	2,20	2,40	2,60	2,80	3,00	3,20

☐ = low risk (~4% per yr) ☐ = moderate risk (~8% per yr) ☐ = severe risk (~20% per yr)

ACUTE AORTIC DISSECTION

We will consider acute aortic dissection by the categories of ascending and descending dissection, as the presentations, sequellae, and treatments vary according to this distinction.

ACUTE ASCENDING DISSECTION

It is well-known that acute aortic dissection of the ascending aorta is a lethal condition. It has been estimated that up to 90% of patients with acute aortic dissection will die from this disease, if not surgically treated, and that patients die at a rate of 20% in the first 24 hours, 60% within 2 weeks, and 90% within 3 months. [6]

Because this natural history is well appreciated, we no longer allow acute ascending aortic dissection to express its natural history. Urgent surgical intervention is performed, to prevent the lethal development of intrapericardial rupture, coronary artery dissection with myocardial infarction, and acute aortic insufficiency with shock.

Occasionally, two or three days have already passed since the onset of symptoms before diagnosis is made or the patient is transferred to a tertiary treatment center. Our review of patients with late recognition or referral has indicated that this subgroup of patient need not be operated in the middle of the night, but can await the next daytime operative slot. [7] This may be helpful to know, as complex aortic surgery usually can be carried much better to a successful outcome during regular working hours, when ideal staff and facilities are available.

Occasionally, a patient presents with acute aortic dissection who cannot be operated because of completed stroke or should not be operated because of overwhelming age, debility, or comorbidity. We have found that vigorous "anti-impulse" therapy can produce some survivors in this setting.

ACUTE DESCENDING DISSECTION

Although an extremely serious disorder, acute descending dissection is less virulent than ascending aortic dissection. Accordingly, urgent surgical intervention is not frequently required. The so-called "anti-impulse" therapy is applied, so as to decrease the mechanical stresses on the aortic wall by means of medical treatment. This therapy usually involves a beta-blocker or calcium channel blocker to decrease strength or cardiac contraction and an afterload reducing agent to lower blood pressure.

We have recommended a "complication-specific" approach to acute descending dissection. [8] For most patients, without rupture or ischemic vascular complications, medical therapy suffices. For patients with acute vascular occlusion, we use the fenestration procedure, which is quick, safe, and effective. Traditional replacement of the proximal descending aorta for acute descending dissection carries a very serious risk, with a mortality of nearly 50% and a rate of paraplegia

or paresis amounting to 32% [9]. Fenestration is much simpler and more effective. Variations of fenestration can now be performed percutaneously at many centers. For realized rupture, only traditional aortic resection and graft replacement is appropriate.

We have recently examined a consecutive series of 100 patients presenting to our center with acute descending aortic dissection. See Figure 7. Nine percent of patients died during the initial hospital admission. As can be seen in the figure, two-thirds of patients did fine with just anti-impulse therapy. The remaining 31% of patients developed specific vascular complications and required early or late surgical intervention. This data indicates again that uncomplicated acute descending dissection is a medical, not a surgical, phenomenon. Whether there is any appropriate role for routine percutaneous stent treatment of all patients with acute descending aortic dissection remains to be determined from clinical trials. Some experts have recommended such therapy, reasoning that reapplying the two layers early in the process may lessen later complications.

VARIANT FORMS OF AORTIC DISSECTION: INTRAMURAL HEMATOMA AND PENETRATING UCLER OF THE AORTA

In the current era of 3-D aortic imaging by transesophageal echocardiography, CT scan, and MRI imaging, it has become clear that variants of aortic dissection exist, which have been called *intramural hematoma* of the aorta and *penetrating ulcer* of the aorta. In interpreting these imaging studies, we use the principle "no flap, no dissection"; that is, if there is no flap going obliquely across the aortic lumen, it is not a typical dissection. See Figure 8. In contradistinction to aortic dissection, with an intimal flap, intramural hematoma and penetrating ulcer have no flap. Intramural hematoma is a concentric collection of blood in the wall of the aorta. Penetrating ulcer is an extension of blood beyond the media of the aortic wall. This looks just like a duodenal ulcer, but it is located in the aorta. See Figure 9.

We have found these variant lesions to be even more virulent that typical aortic dissection. The rate of rupture at initial presentation is even higher than for typical dissection. [10] See Figure 10. Also, intramural hematoma and penetrating ulcer have a 50% or more likelihood of worsening or progressing to typical dissection, in mid-term follow-up. Also, patients treated medically for these variant dissection processes continue to die of rupture on medical treatment. For these reasons, we recommend nearly routing surgical therapy during the initial hospital admission for patients with intramural hematoma or penetrating ulcer of the aorta. Some centers have found
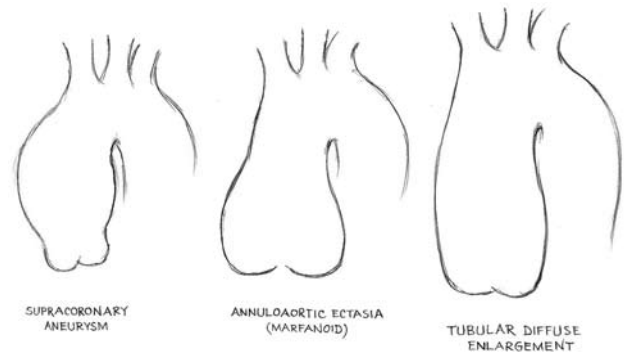

FIGURE 8. Schematic representation of three types of acute aortic dissection pathologies.
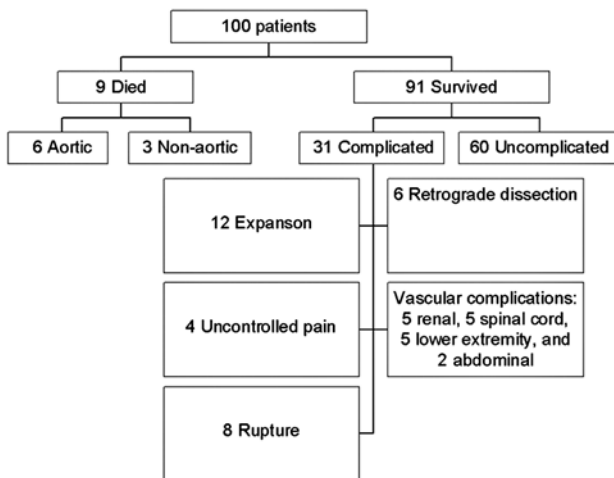

FIGURE 7. Flow diagram of natural behavior of 100 consecutive cases of acute descending aortic dissection.
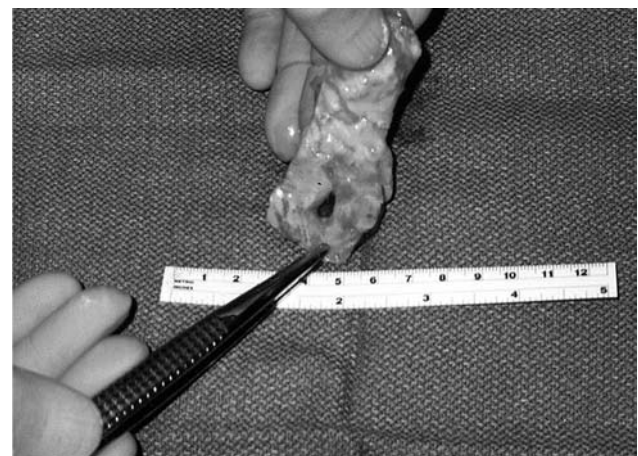

FIGURE 9. An example of a penetrating ulcer of the thoracic aorta. Note the resemblance to duodenal ulcer.

lower virulence than we have seen for these lesions; this may be related to the fact that all of our patients presented with acutely symptomatic hematoma or ulcer—none were incidental findings on scans done for other reasons.

CHRONIC ASCENDING DISSECTION

Occasionally, a patient will present for evaluation with a chronic ascending aortic dissection. This presentation implies that the patient was one of the small minority (<10%) who survive this event without the benefit of surgical therapy. In some cases, there was an acute event, possibly weeks, months, or even years ago, and the diagnosis was missed. In other cases, no acute symptomatic event can be recalled whatsoever.

In any case, this disorder does not require urgent therapy. Associated aortic insufficiency may mandate surgical intervention. Severe aortic enlargement may warrant intervention. We apply the same size criteria as for chronic non-dissected aneurysm, namely attainment of a diameter of 5.5 cm. Most patients need intervention for one of these reasons. Also, pain requires surgery. For the few patients who have a chronic dissection but do not have aortic insufficiency, dangerous aortic enlargement, or pain, optimal treatment is controversial. The natural history may not be very poor. Nonetheless, most authorities operate on these patients, albeit electively.

CHRONIC DESCENDING AORTIC DISSECTION

In our experience, longitudinal extension and new branch vessel occlusion are quite rare in chronic descending aortic dissection. The real issue with these cases is rupture. Rupture can and does occur, usually preceded by dilatation of the involved segment of aorta. In most patients, this dilatation occurs gradually, at one to three millimeters per year. In some patients, especially those with Marfan's disease, dilatation may occur very rapidly.

For chronic descending aortic dissection, we operate pre-emptively to prevent rupture when the aorta has reached the same criterion that we apply for chronic non-dissected aneurysm, namely 6.5 cm. As always, if the patient has pain, surgery is always indicated, to prevent catastrophic rupture. A recent review by Dr. Griepp's group has found that, in patients with chronic descending aortic dissection, older age, chronic obstructive pulmonary disease, and elevated mean blood pressure were strongly predictive of rupture. [11] They make a strong point for earlier intervention for chronic descending aortic dissection, especially when those identified risk factors are operative.

LOCALIZED DISSECTIONS

On occasion, dissection may be limited in longitudinal extent to the abdominal aorta or be confined to the carotid artery or the coronary arteries. The natural history of these localized dissections is being elucidated.

Only about 1% of dissections are limited to the abdominal aorta. Natural history appears similar to that of descending aortic dissection, and complication-specific management, similar to that of descending aortic dissection, appears most appropriate. [12]

Isolated coronary artery dissection is seen once or twice yearly in a busy catheterization laboratory, often manifesting on the basis of myocardial ischemia in a patient without traditional risk factors for arteriosclerosis. Myocardial infarction may result from coronary artery dissection, so, in the current era, stent therapy is applied at the time of angiographic diagnosis.

CONCLUSION

Regarding the natural history of aortic dissection, one can say that this beast is quite a fierce one. Once it occurs, the impact on both short and long-term survival is severe. Although advances in imaging techniques and surgical sciences have succeeded to some extent in taming this disorder, it continues to exert quite a fierce impact on the human race. Once the aorta has been rent into two dissected layers, despite the most talented surgical efforts, the outlook for that aorta—and consequently, for the patient—will be irrevocably impaired.

The best hope for taming this disorder in the future resides in *predicting and preventing* aortic dissection *before it actually occurs*. From the point of view of aortic size, natural history investigations have clarified quite well appropriate criterion levels for pre-emptive intervention. If the genetic studies underway bear fruit, it may be possible to predict the diathesis for dissection from a simple blood test. Perhaps understanding the genetic underpinnings of dissection disease may, in the future, permit conventional therapies aimed at strengthening the abnormal structural proteins coded by those genes. Even specific genetic remedies can be envisioned for the future.

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