

SURGERY FOR MARFAN SYNDROME

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Etiology

Marfan syndrome was first described by the French pediatrician Antoine Marfan in 1896.¹ The disease is the most common inherited connective-tissue disorder and affects approximately 1 in 10,000 adults.^{2,3} It results from mutations in the gene for fibrillin-1 (*FBNI*), located on chromosome 15.⁴ More than 125 different mutations have been identified for the *FBNI* gene, of which 75% are inherited and 25% are sporadic.^{3,5,6} These mutations cause faulty synthesis of fibrillin, the core protein of microfibrils, and result in abnormal formation of the elastic components of the body. In the aorta, this is manifest as disorganized elastic fibers and premature cystic medial degeneration.⁷ The disorder is also associated with ocular, musculoskeletal, central nervous system, and pulmonary abnormalities.

Aneurysm of the ascending aorta in the context of Marfan syndrome was first reported by Baer and Taussig in 1943, at the Johns Hopkins Hospital.⁸ Comprehensive description of Marfan syndrome and its cardiovascular manifestations is generally credited to McKusick's paper in 1955.⁹ Nearly 75% of patients with Marfan syndrome have aortic root dilation, which might or might not be associated with aortic valve regurgitation.¹⁰ Aortic dilation increases wall tension according to the law of Laplace and may accelerate the premature degenerative process and lead to aortic dissection. Most patients with Marfan syndrome die from cardiovascular events, the majority from complications of aortic root dilation, including aortic dissection and aortic rupture.^{10,11} Appropriately timed surgical intervention can prevent these complications and increase survival in patients with Marfan syndrome.^{12,13}

Screening for Aortic Disease in Marfan Syndrome

Traditionally, aneurysmal disease of the aorta is evaluated and followed by either serial computed tomography or ultrasonography, with particular emphasis on size and location of the aneurysm, as well as rate of expansion.

More recently, magnetic resonance imaging (MRI) has assumed a growing role. In general, once the aorta reaches a diameter of 5 cm or expands at a rapid rate between imaging studies (> 1 cm per year), the aorta is considered to be at increased risk for dissection and rupture, and elective prophylactic surgery is undertaken. However, in patients with Marfan syndrome, acute dissection may occur in the absence of marked dilation of the aorta, particularly in patients with a family history of aortic catastrophe.^{14,15,17} Genetic testing may be useful in patients with a family history of Marfan syndrome to help characterize the severity of an individual's disease and stratify risk, but it is not suitable as a screening tool in patients without the typical phenotype.^{3,6,18}

Indications for Surgery

Patients with Marfan syndrome are at risk for life-threatening complications of dilation of the aortic root. Aortic root replacement should be performed when the diameter of the aortic root reaches 5.5 to 6.0 cm.^{10,12,19} Patients with a family history of acute dissection or rupture should undergo surgery earlier, preferably when the aortic root reaches 5 cm in diameter, as there is evidence that aortic dissection can occur without marked dilation of the aortic root in these patients.^{14,19} Other indications for surgery are aortic dissection (acute or chronic), severe aortic regurgitation, progressive dilation of the aorta on serial imaging, and aortic root diameter twice that of the normal aorta.^{14,19-21}

It is now well documented that elective surgery for Marfan disease of the aorta is the preferred method of treatment. Emergent operation for aortic dissection or rupture in these patients carries an unacceptably high mortality and morbidity.

Operative Technique

Surgery for Marfan disease of the aorta is typically aortic root replacement with or without aortic valve replacement. Late complications of dissection in the distal aorta con-

stitute the second most common cause for operation. Surgery is planned with recognition that the disease is not confined to the ascending aorta and that many patients will require additional surgery in the future.

Dilation of the aortic root can result in aortic regurgitation, which may require repair or replacement of the aortic valve. Key to successful surgery of the aortic root in Marfan syndrome is the understanding that the disease is most severe in the aortic sinuses, and therefore, removal of all aortic sinus tissue is vital to a favorable early outcome as well as for prevention of later complications such as dissection and pseudoaneurysm. Replacement of the aortic valve and separate supracoronary ascending aorta with a synthetic graft leaves behind vulnerable aortic sinus tissue and is inadequate treatment for patients with Marfan syndrome.

Several surgical approaches are now available for treatment of Marfan patients, allowing the surgeon to tailor the operation to the individual patient. These operations include composite replacement of the ascending aorta and aortic valve (Bentall operation), valve-sparing replacement of the ascending aorta, combined replacement of the ascending aorta and arch (elephant trunk procedure), and single-stage repair of the ascending aorta and arch (arch-first technique).

Composite Replacement of the Ascending Aorta and Aortic Valve (Bentall Operation)

Bentall and De Bono first described the technique for combined replacement of the ascending aorta and aortic valve in 1968.²² After establishment of cardiopulmonary bypass and cardioplegic arrest, the ascending aorta is resected to a point of normal diameter (Figure 32-1). The aortic valve is excised, and the coronary arteries are mobilized with small collars of aortic tissue. The remainder of aortic sinus tissue is trimmed to the level of the aortic annulus. A composite graft consisting of a mechanical aortic valve within a woven synthetic tube graft is then sutured to the aortic annulus. The coronary arteries are anastomosed in anatomic position to small windows in the graft. Finally, the distal end of the graft is anastomosed to the transected ascending aorta in an end-to-end fashion.

The Bentall operation has become the gold standard for patients with concomitant disease of the aortic valve and aortic root and is particularly applicable to patients with Marfan disease. In 1999, Gott and associates reported a 1.5% operative mortality in patients undergoing elective aortic root replacement for Marfan disease of the ascending aorta.²³ Ten-year survival in this series of patients was 75%; the most common causes of late death were dissection or rupture of the residual aorta and congestive failure. Other reports have confirmed the safety and efficacy of this technique, which is suitable for nearly all patients with Marfan syndrome, especially those with aortic regurgitation.^{24,25}

Valve-Sparing Replacement of the Ascending Aorta

Many patients with Marfan sinus aneurysms have competent aortic valves and do not require prosthetic valve replacement. In addition, there are patients, such as children and young adults, for whom anticoagulation mandated by a mechanical valve may be undesirable. These are the same patients for whom bioprostheses have limited durability. Reconstruction of the aortic root and remodeling of the aortic annulus in this setting can restore the native aortic valve to normal function and competence and can eliminate the need for anticoagulation and minimize the risk of endocarditis.

Correction of severe aortic annular dilatation is an important part of valve-sparing root surgery. Depending on the degree of dilation at the sinotubular junction and at the aortic annulus, a prosthetic graft can be tailored to adjust these dimensions back to a normal state. Doty described several methods of graft size selection and modification to remodel the aortic root in valve-sparing operations.²⁶ Figure 32-2 illustrates the method used when both the sinotubular junction and the aortic annulus are dilated.

Techniques for valve-sparing replacement of the aortic root were developed independently by Yacoub in London and David in Toronto.^{27,28} As with the Bentall operation, the ascending aorta and sinus tissue are excised, leaving the mobilized coronary ostia with buttons of aortic tissue. The aortic valve is inspected for normal leaflet mobility and absence of degenerative changes, and the diameter of the aortic annulus is recorded, at which point normal coaptation could be expected to occur.

Several iterations of valve-sparing root replacement have been described. The David I, or implantation technique, slides a tubular Dacron graft around the valve apparatus, anchoring the low end of the graft below the nadir of the three sinuses by interrupted mattress sutures placed from within the left ventricular outflow tract outward (Figure 32-3). The top of each of the three commissures is then fixed to the graft at the appropriate height to promote leaflet coaptation. The annulus, along with a small rim of sinus tissue, is then sutured inside the graft with continuous 4-0 polypropylene suture. Holes are cut in the graft opposite the coronary "buttons," which in our practice are encircled with Teflon felt "lifesaver" pledgets and anastomosed to the graft, also with 4-0 polypropylene. The distal end of the Dacron graft is anastomosed end-to-end to the distal ascending aorta. Placement of a left ventricular vent is useful during the early stages of resuscitation of the heart, to prevent left ventricular dilatation and to assess residual aortic insufficiency.

The David II, or remodeling procedure, is similar to Yacoub's technique (Figure 32-4). In the David II, a synthetic graft that is the same diameter as the remodeled aortic annulus is selected, and three "tongues" of graft are created for reconstruction of the aortic sinuses. The length of each tongue is approximately two-thirds the

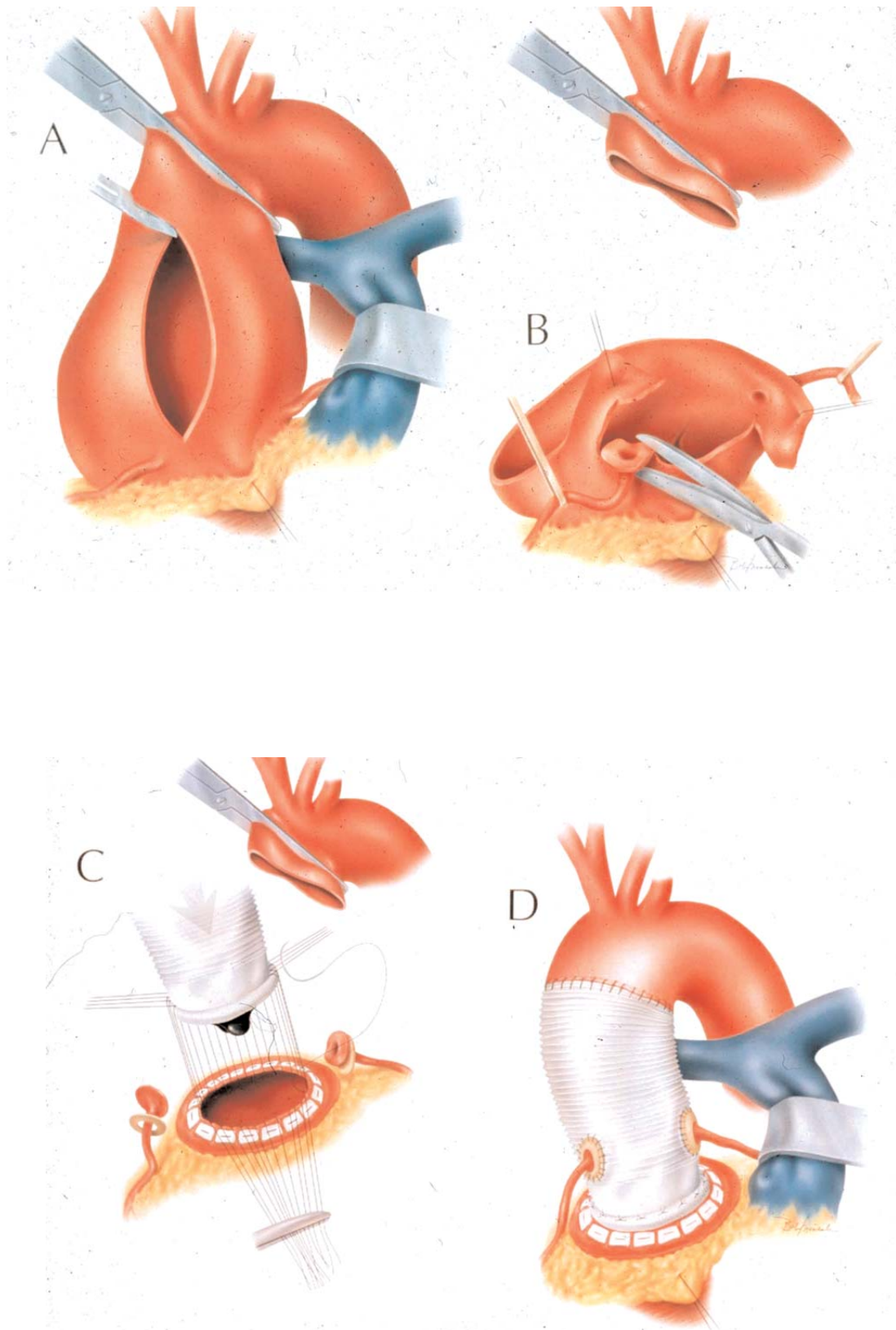


FIGURE 32-1. The Bentall procedure for aortic root replacement. *A*, On cardiopulmonary bypass, the aorta is cross-clamped and the aneurysm opened. *B*, The aneurysm is excised, and the coronary arteries are mobilized with a small collar of sinus tissue. *C*, The prosthesis is secured to the annulus with interrupted pledgeted horizontal mattress sutures and the coronary arteries encircled with Teflon felt "lifesaver" pledgets before anastomosis to side holes in the graft. *D*, The completed prosthesis.

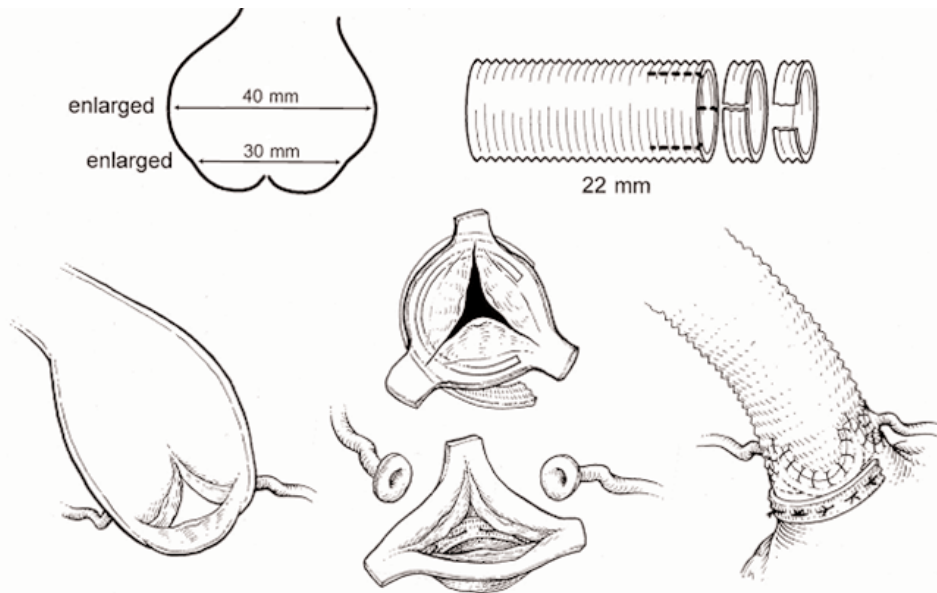


FIGURE 32-2. Method for restoring normal aortic root dimensions in aortic valve-sparing operations. A vascular graft 10% less than the desired diameter of the aortic annulus is chosen. Small strips of the graft are used to reduce the aortic annulus to five-sixths of the circumference of the left ventricular outflow tract. The remainder of the graft is then the appropriate size at the sinotubular junction. Reproduced with permission from Doty DB, Arcidi JM Jr.²⁶

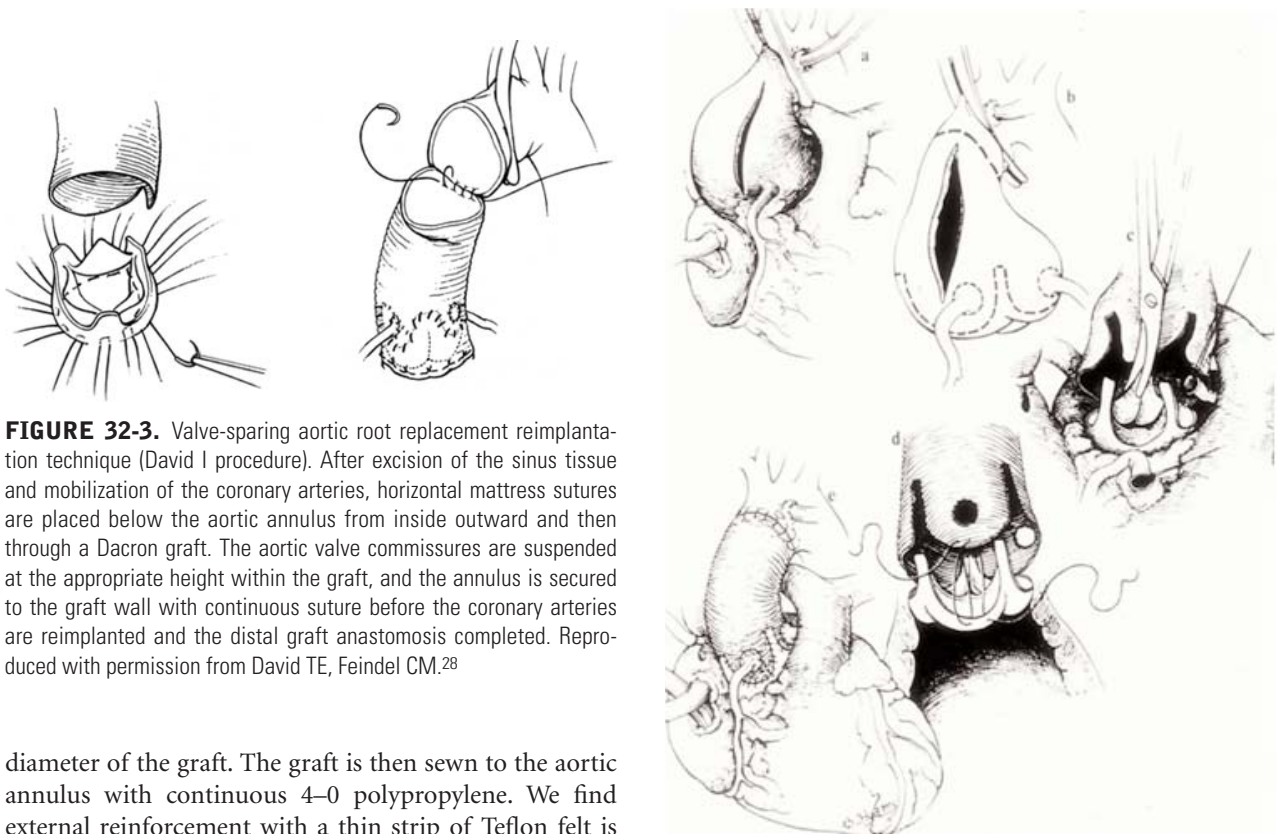


FIGURE 32-3. Valve-sparing aortic root replacement reimplantation technique (David I procedure). After excision of the sinus tissue and mobilization of the coronary arteries, horizontal mattress sutures are placed below the aortic annulus from inside outward and then through a Dacron graft. The aortic valve commissures are suspended at the appropriate height within the graft, and the annulus is secured to the graft wall with continuous suture before the coronary arteries are reimplanted and the distal graft anastomosis completed. Reproduced with permission from David TE, Feindel CM.²⁸

diameter of the graft. The graft is then sewn to the aortic annulus with continuous 4-0 polypropylene. We find external reinforcement with a thin strip of Teflon felt is helpful for hemostasis. The coronary ostia are reimplanted on the graft just as in the David I, and the distal end of the graft is anastomosed to the transected ascending aorta in an end-to-end fashion.

FIGURE 32-4. Valve-sparing aortic root replacement remodeling technique (David II or Yacoub procedure). The graft is trimmed to fit the excised sinuses, and the coronary arteries are reimplanted onto the graft. Reproduced with permission from Yacoub MH et al.²⁷

Recent studies on late outcomes after valve-sparing operations are encouraging. David and associates reported low operative mortality, 90% freedom from moderate or severe aortic regurgitation, and 97% freedom from reoperation at 5 years.²⁹ Birks and associates described a 4.9% operative mortality with the Yacoub valve-sparing operation specifically applied to patients with Marfan disease.³⁰ In that report, 10-year survival ranged from 64% for patients undergoing surgery for acute dissection to 94% for chronic aneurysm. Freedom from reoperation was 83% at 10 years, and 79% of patients had no or only mild aortic regurgitation. There is some concern that the native aortic leaflets may be subject to stress and repetitive injury from contacting the surface of the prosthesis. New graft prostheses have been developed with preformed aortic sinuses that may help reduce stress on the native aortic leaflets by creating a more normal root architecture.³¹

Combined Replacement of the Ascending Aorta, Arch, and Descending Aorta (Elephant Trunk Procedure)

In some patients, dilation of the aorta extends into the aortic arch and descending aorta. Because patients with Marfan syndrome have a higher risk of rupture and dissection, resection of all aneurysmal aorta should be attempted. Borst first described the two-stage approach for extensive aneurysmal disease of the aorta, known as the elephant trunk procedure.³² This technique traditionally requires a period of hypothermic circulatory arrest to complete the distal anastomosis and attachment of the arch vessels, although use of right axillary arterial cannulation and snaring of the neck vessels can substantially shorten arrest time. In the first stage, the ascending aorta and arch are resected just beyond the origin of the left subclavian artery, leaving the arch vessels on an island of aortic tissue. A prosthetic graft is sewn to the internal orifice of the descending aorta, leaving a short 4 to 6 cm cuff that is intussuscepted into the lumen of the descending aorta (Figure 32-5). The arch vessels are then reimplemented along the superior surface of the graft. Cardiopulmonary bypass is resumed after inserting the arterial cannula into the graft. A second graft is then used to replace the ascending aorta, and the two grafts are anastomosed end-to-end to complete the first stage of the repair.

The second stage is performed after adequate patient recovery. A thoracoabdominal incision is made, and the descending aorta is dissected to expose the remainder of the aneurysmal disease, as well as to expose the distal end of the graft from the first stage. Partial or full cardiopulmonary bypass with or without circulatory arrest is employed according to surgeon preference, and the distal end of the graft is clamped. The descending aortic aneurysm is then opened and the “elephant trunk” identified, which is the short cuff of graft that was intussuscepted into the descending aorta during the first stage.

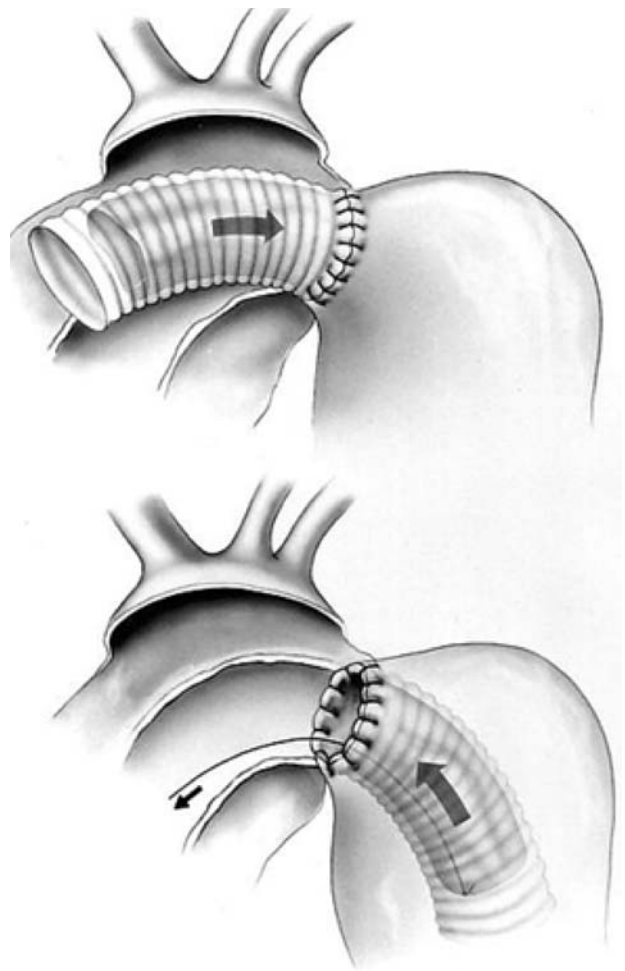


FIGURE 32-5. The elephant trunk technique. The original method as described by Borst is depicted in the top panel, in which the distal “trunk” portion is pushed into the descending aorta after completion of the anastomosis. Crawford’s modification is depicted in the bottom panel, in which the proximal portion of the graft is inverted into the descending aorta and then retrieved after completion of the anastomosis. Reproduced with permission from Heinemann HK et al.³⁵

A prosthetic graft is anastomosed to the “elephant trunk” proximally, intercostal islands are implanted into the body of the graft, and the distal end of the graft is anastomosed to the aorta beyond the aneurysm.

This is a formidable operation; mortality and morbidity are expectedly higher than isolated root replacement. However, Safi and associates reported low operative mortality rates of 5.1% and 6.2% for first and second stages of the operation, respectively.³³ Most deaths occurred from aortic rupture, either during the interval between stages or in patients who did not return for the second stage. Schepens and associates described a hospital mortality of 8% and permanent neurologic damage in 4%.³⁴ Heinemann and associates reported an operative mortality of 12.5%; only one-third of patients completed the second stage of the operation.³⁵

Single-Stage Repair of the Ascending Aorta, Arch, and Descending Aorta (Arch-First Technique)

In a subset of patients with extensive marked dilation of the ascending aorta, arch, and descending aorta, the aneurysmal disease of the descending aorta prevents application of a staged repair such as the elephant trunk technique. In these patients, single-stage repair using hypothermic circulatory arrest can be employed to replace the entire aorta in one setting. This approach is best suited for patients in whom the aorta distal to the subclavian artery is greater than 4.5 to 5.0 cm in diameter and the aneurysm does not extend to the abdominal aorta. It is also useful in patients requiring reoperation for recurrent aneurysm or chronic dissection.

In Kouchoukos' arch-first technique, the arch vessels are reimplanted first to allow for early restoration of cerebral perfusion via a small side graft, illustrated in Figure 32-6.³⁶ The distal aortic anastomosis is completed during a period of hypothermic low flow, and the proximal aortic anastomosis is completed during rewarming. Although this is a technically challenging operation, Kouchoukos and colleagues reported a 6.2% operative mortality rate without a single stroke or spinal cord injury.³⁷ In that series, all patients were alive and well at a mean follow-up of 13 months.

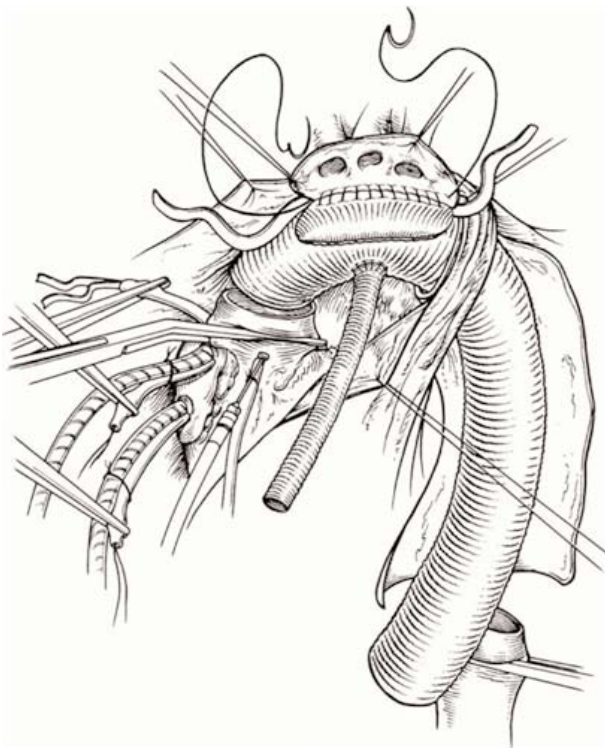


FIGURE 32-6. Single-stage replacement of the ascending aorta, arch, and descending aorta, using the arch-first technique. Hypothermic circulatory arrest is used to implant the arch vessels first. The distal aortic anastomosis is completed during a hypothermic low-flow state, and the proximal aortic anastomosis is completed during rewarming. Reproduced with permission from Rokkas CK, Kouchoukos NT.³⁶

Conclusion

In summary, Marfan disease of the aorta is a pathologic entity with lethal implications because of the risk of rupture and dissection. Surgical intervention at the appropriate time can prevent these complications, save lives, and provide excellent quality of life. Complications from surgery are infrequent if performed in the elective setting, and most patients can anticipate good long-term results from any of the operations currently available for managing this disease.

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