Heart Valve Disease

34

Laura Harvey, Kenneth K. Liao, and Ranjit John

Abstract

This chapter was designed to provide the reader with a brief overview of the current treatment options for heart valve disease. Major topics of discussion are: (1) development of prosthetic valve replacements; (2) current issues with valve replacement; (3) major valvular diseases that affect humans in the Western world; and (4) recent advances in therapeutic options for valvular diseases.

Keywords

Mechanical prosthetic valve • Biologic prosthetic valve • Aortic stenosis • Aortic sclerosis • Aortic regurgitation • Mitral stenosis • Mitral regurgitation • Tricuspid valve disease

34.1 Introduction

The function of the heart is to circulate blood in closed circuit to the lungs where blood is oxygenated, and out to the body where oxygen provides fuel for cellular metabolism. To accomplish this task, blood is pumped by the right heart system from the body to the lungs. Once oxygenated in the lungs, blood is returned to the left heart where it is then pumped out to the body. Although described as a biologic pump, the heart is actually two biological pumps in series, composed of a right and left heart. Each unit of the heart is composed of an atrial and ventricular chamber, whose synchronized contractions result in the forward flow of blood out of the heart. Crucial to the appropriate function of the heart are four valves (the mitral, aortic, tricuspid, and pulmonic valves) that function in concert to maintain forward flow of blood across the heart (Fig. 34.1). Diseases affecting the heart valves result in either obstruction to forward flow (stenosis) or reversal of flow across an incompetent valve (regurgitation). In either case, significant morbidity and mortality will result if no treatment is offered to the patient. This chapter was designed to provide the reader with a brief overview of the current treatment options for heart valve disease. Major topics of discussion are: (1) development of prosthetic valve replacements; (2) current issues with valve replacement; (3) major valvular diseases that affect humans in the Western world; and (4) recent advances in therapeutic options for valvular diseases.

34.2 A New Frontier: Valve Replacement

Before 1950, the ability to safely and effectively operate on the human heart was considered an insurmountable goal. Attempts to operate to correct valvular diseases without stopping the heart resulted in severe, often fatal complications including uncontrollable bleeding and the introduction of air emboli [1]. The ability to maintain forward flow of blood while stopping the heart to allow the surgeon access to the valve would have to wait for the development of cross-circulation, and later for the perfection of the cardiopulmonary bypass procedure by Dr. C. Walton Lillehei, Richard L. Varco, and Dr. F. John Lewis at the University of Minnesota [2] (see also Chap. 25). With this new technology, a new frontier in surgical options for the treatment of heart valve

L. Harvey, MD • K.K. Liao, MD • R. John, MD (✉)
Division of Cardiovascular and Thoracic Surgery, Department of Surgery, University of Minnesota, 420 Delaware Street SE, MMC 207, Minneapolis, MN 55455, USA
e-mail: johnx008@umn.edu

© Springer International Publishing Switzerland 2015

P.A. Iaizzo (ed.), *Handbook of Cardiac Anatomy, Physiology, and Devices*, DOI 10.1007/978-3-319-19464-6_34

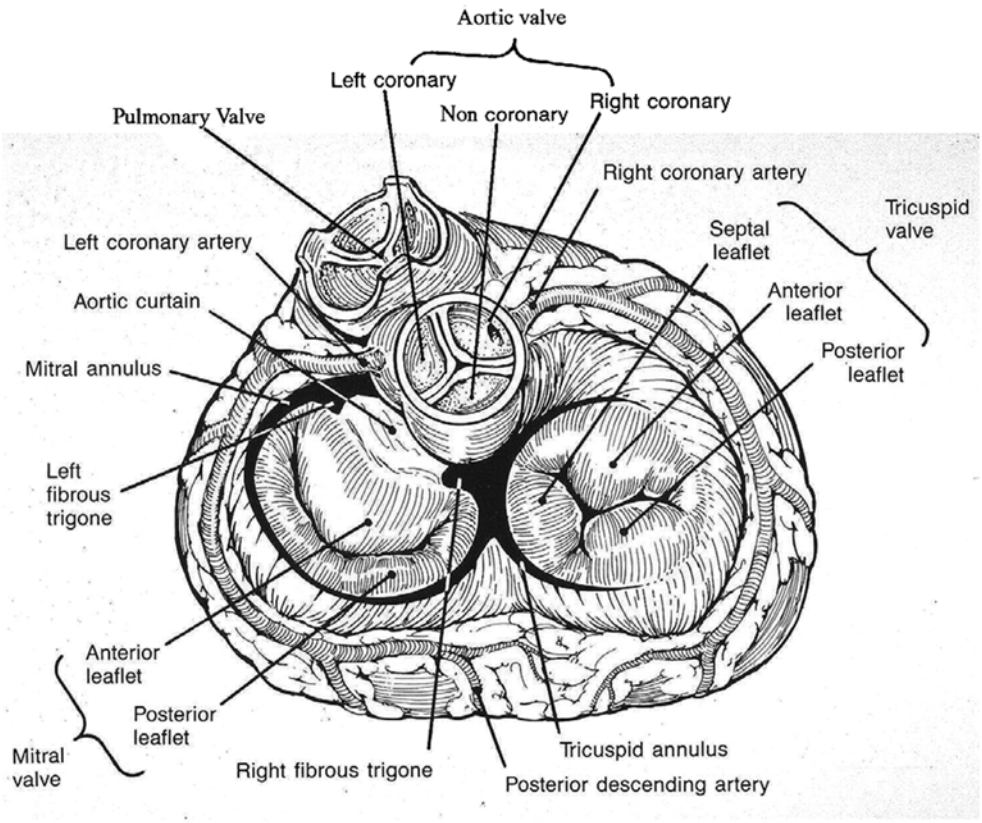

Fig. 34.1 Apical view of the four heart valves—aortic, mitral, pulmonic, and tricuspid

disease began to emerge. During the past several years, major advances have occurred in diagnostic techniques (i.e., imaging) and therapeutic interventions for valvular diseases, as well as improved understanding of the natural history of both treated and untreated valvular disease (for more detail, see Chaps. 35 and 36).

34.2.1 Mechanical Prosthetic Valves

By 1961, Dr. Albert Starr and Lowell Edwards had successfully implanted the world's first mechanical valve into a human to replace a mitral valve that had been deformed by rheumatic fever [3]. Initially, this steel ball and cage design was successful in approximately 50 % of implantations. Major complications were soon recognized, including: (1) clot formation resulting in embolic strokes; (2) significant noise; (3) red blood cell destruction; and/or (4) tissue ingrowth causing subsequent valve obstruction. A complete history of the development of currently used mechanical prostheses is beyond the scope of this text. However, it is important to mention two key aspects of any successful new valve design: (1) improved valve hemodynamics; and (2) reduced thrombogenic (or clot forming) potential. Efforts to optimize valve hemodynamic function date back to the development of the Lillehei/Kaster tilting disk valve which allowed blood to flow centrally through the valve. At that time, this new type of valve emphasized the requirement to design a valve that would reduce turbulent blood flow, reduce cell destruction, and minimize the transvalvular gradients [4]. A transvalvular gradient is defined as the pressure difference across the valve. Despite the advantages of a new steel tilting disk design, careful strict anticoagulation therapy was still required to reduce the risk of clot formation [5]. The next improvements of these valves came with the development of the pyrolytic carbon valve leaflets. The nonthrombogenic weight and strength properties were determined by Drs. Jack Bokros and Vincent Gott. Subsequently, pyrolytic carbon was used in the creation of a bileaflet valve inspired by Dr. Kalke. This valve, originally manufactured by St. Jude Medical (St. Paul, MN, USA), provided exceptional performance, and today this design remains the gold standard for mechanical valves [6]. To date, all patients with mechanical valves require anticoagulation, e.g., with oral warfarin therapy which reduces the risk of thromboembolism to 1–2 %/year (Table 34.1) [7]. It should be noted that numerous studies have demonstrated that the risk of thromboembolism is directly related to the valve implant position, i.e., in the

Table 34.1 Anticoagulation after prosthetic heart valves [8]

		Warfarin INR 2.5	Warfarin INR 3.0	Aspirin 75–100 mg
Mechanical prosthesis				
First 3 months post implantation		+		+
After initial 3 months	Aortic valve	+		
	Aortic valve + Risk factor		+	+
	Mitral valve		+	+
	Mitral valve + Risk factor		+	+
Biological prosthesis				
First 3 months post implantation		+		+
After initial 3 months	Aortic valve			+
	Aortic valve + Risk factor	+		+
	Mitral valve			+
	Mitral valve + Risk factor	+		+

descending order of risk, the tricuspid, mitral, and aortic valves. In addition, this risk of emboli appears to be greatest in the early post-implant period, and then becomes reduced as the valve sewing cuff becomes fully endothelialized.

In general, management of anticoagulation must be individualized to the patient to minimize risk of thromboembolism and, at the same time, prevent bleeding complications. In situations where a patient with a valve prosthesis requires noncardiac surgery, warfarin therapy should be stopped only for procedures where risk of bleeding is substantial. A complete discussion of anticoagulation therapy is beyond the scope of this chapter, however several excellent reviews are available on this subject [7, 8].

34.2.2 Biological Prosthetic Valves

Because of the problems related to anticoagulation, a majority of subsequent valve research focused on developing tissue alternatives that avoid the need for anticoagulation. From a historical perspective, Drs. Lower and Shumway performed the first pulmonary valve autotransplant in an animal model [9]. Later in 1967, Dr. Donald Ross completed the first successful replacement in a human. The *Ross Procedure* is a well-established method still used today to replace a diseased aortic valve with the patient's own pulmonary valve (Fig. 34.2); a donor tissue valve or homograft (Table 34.2) is then used as a prosthetic pulmonary valve. In general, tissue valves are significantly more biocompatible than their mechanical counterparts. These valves are naturally less thrombogenic, and thus the patient does not require aggressive anticoagulation. Specifically, a risk of <0.7 %/year of clinical thromboembolism has been reported in valve replacement patients eliciting sinus rhythm without warfarin therapy [7]. Therefore, this treatment option is advantageous in clinical situations where the use of anticoagulation would significantly increase morbidity and mortality. Yet, to date, a potential major disadvantage of tissue valve implantation is early valvular degeneration as a result of leaflet calcification. Thus, methods for tissue preservation to prevent such calcifications are currently a major focus of research in this field.

34.2.3 Biological Versus Mechanical Valves

The choice of a mechanical or biologic valve for implant will typically depend on various factors: (1) the patient's current disease status; (2) the specific native valve involved; and/or (3) the surgeon's preference and experience. If these factors are not limiting, the choice of valve type should be based on the maximization of benefits over risks for the individual patient. Unfortunately, the ideal prosthetic valve that combines excellent hemodynamic performance and long-term durability without increased thromboembolic risk or the need for lifelong anticoagulation remains elusive. In general, mechanical valves offer greater durability at the cost of requiring lifelong anticoagulation, as well as the risk of thromboembolism. In contrast, bioprosthetic valves have a much lower thromboembolic risk without the need for anticoagulation, but elicit a higher risk for structural degeneration and thus potential need for reoperation. As such, mechanical valves are perhaps most well suited for the younger patient who does not desire future reoperations. Currently, mechanical valve replacement in the USA is quite standardized and commonplace, i.e., yielding satisfactory valve function that is reproducible from patient to patient. Furthermore, the flow gradients with newer bileaflet mechanical valves have dramatically improved from the early ball valve type; currently, a trileaflet valve is in the preclinical stages of development and may eventually not require anticoagulation therapy. Nevertheless in the interim, bioprosthetic or tissue valves offer a safe alternative for patients in

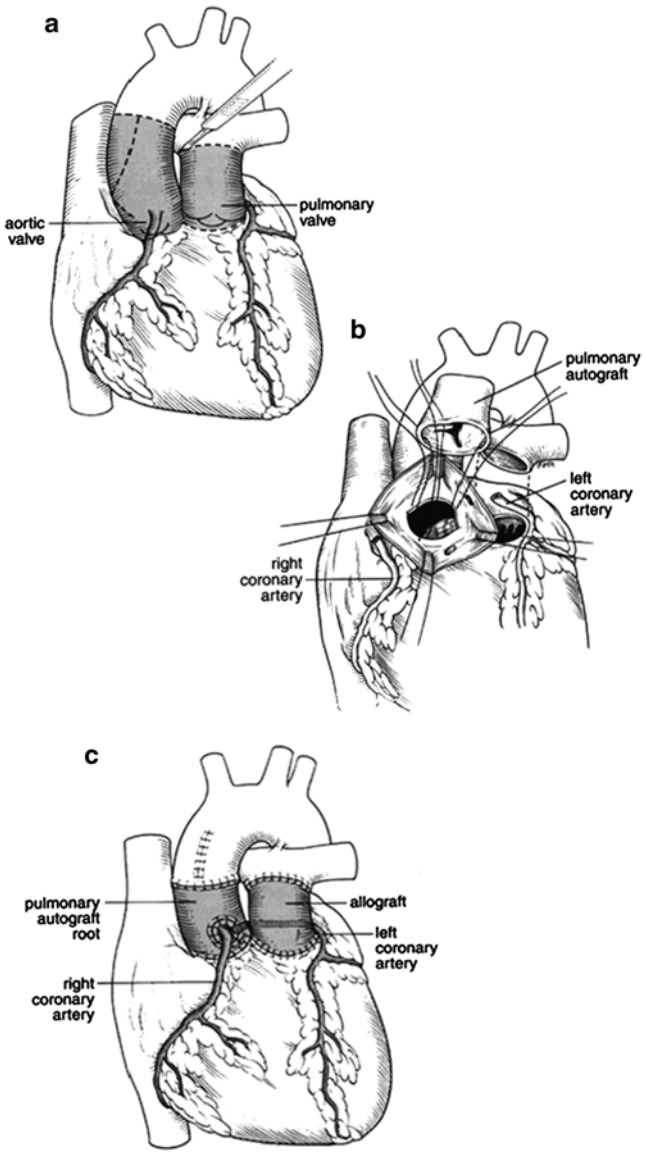

Fig. 34.2 Schematic drawing of the Ross Procedure. (**a**) Resection of the diseased aortic valve. (**b**) Harvesting of native pulmonary valve. (**c**) Implantation of the pulmonic valve in the aortic position and reimplantation of coronary arteries

whom the risk of anticoagulation is prohibitively high (e.g., elderly patients >70 years of age, women of child bearing years desiring pregnancy). Yet, the length of their durability remains a serious concern for tissue valves, and thus a patient whose life expectancy is greater than that of the prosthesis will likely encounter the risk of another surgery for a second valve replacement. Note that a transcatheter-delivered *valve in valve* procedure is a more recent option (Chap. 36).

It is important to note that two historic randomized clinical trials have compared outcomes between early generation tissue and mechanical valves—the Edinburgh Heart Valve trial and the Veteran Affairs Cooperative Study on Valvular Heart Disease [9–11]. Both trials showed increased bleeding associated with mechanical valves and increased reoperations with tissue valves. While the strength of these trials is a prospective randomized design, the disadvantages are that the valves used in these trials are currently obsolete. More recently, a large meta-analysis comparing mechanical versus bioprosthetic aortic valves found no difference in risk-corrected mortality regardless of patient age [12]. Based on this and other studies, the choice of valve should not be based on age alone. Clearly, there is a trend towards increasing use of bioprosthetic valves in younger patients; this is based on the fact that advances in tissue fixation and improved anti-calcification treatments have resulted in superior durability of the newer generation bioprosthetic valves. Specifically, third generation bioprosthetic valves have been shown to have a greater than 90 % freedom from structural generation at 12-year follow-up [13]. Furthermore, improvements in cardiac surgery including better techniques for myocardial preservation, less invasive procedures (i.e., robotic surgery), as well as strategies for cardiac reoperation have significantly reduced the risk for cardiac reoperation. This has further allowed an increasing application of bioprosthetic valves in patients younger than 55–60 years old. In conclusion, in the absence of current randomized trials, physicians must make a choice based on existing data and individualize that choice based on patient-related factors such as age, lifestyle, tolerance for anticoagulation, and/or position of the replacement valve [14].

Table 34.2 Tissue valve graft options: classification of bioprosthetic valves

Bioprosthetic valve	Description
Stented porcine valve (Xenograft)	A three leaflet valve supported by three artificial struts or stents to maintain leaflet structure and geometry.
Stentless porcine valve (Xenograft)	A length of porcine aorta including tissue below (proximal) and above (distal) to the valve, called the "root."
Bovine pericardial valve (Xenograft)	A three leaflet valve created from bovine pericardium attached to a stented frame.
Homograft	A human aortic valve and root.
Autograft	A pulmonary valve and root excised from the patient and reimplanted in the same patient.

Table 34.3 Reportable valve prosthesis complications [9]

Complication	Description
Structural valvular deterioration	Any change in function of an operated valve resulting from an intrinsic abnormality, causing stenosis or regurgitation.
Nonstructural dysfunction	Any stenosis or regurgitation of the operated valve that is not intrinsic to the valve itself, including inappropriate sizing, but excluding thrombosis and infection.
Valve thrombosis	Any thrombus, in the absence of infection, attached to or near an operated valve that occludes part of the blood flow path or interferes with function of the valve.
Embolism	Any embolic event that occurs in the absence of infection after the immediate perioperative period (new temporary or permanent, focal or global neurological deficit, and peripheral embolic event).
Bleeding event (anticoagulant hemorrhage)	Any episode of major internal or external bleeding that causes death, hospitalization, permanent injury, or requires transfusion.
Operated valvular endocarditis	Any infection involving an operated valve, resulting in valve thrombosis, thrombotic embolus, bleeding event, or paravalvular leak.

34.2.4 Prosthetic Heart Valve Endocarditis and Performance Tracking

All patients with prosthetic valves also need appropriate antibiotics for prophylaxis against infective endocarditis. Details of these therapies are beyond the scope of this chapter, but the reader is referred to guidelines published by a joint committee from the American Heart Association (AHA) and American College of Cardiology (ACC) for the applicable protocols. In addition, a registry has been established to track the long-term performance of all clinically approved implanted valve prostheses. Established standards were revised in 1996 and are briefly summarized in Table 34.3. As alluded to in Chap. 27, investigators seeking approval for all new valves must also report any complications that occur in the preclinical animal testing phase to the appropriate regulatory authority.

34.3 Specific Valvular Diseases: Etiologies and Treatments

The remainder of this chapter is devoted to a generalized summary of the most common valvular diseases affecting patients in the Western world. Of the four heart valves, significant clinical disease can primarily affect all but the pulmonary valve. Yet, compromised function of this valve is noted to occur in the adult congenital heart patient who previously underwent reparative surgeries. Indications for diagnostic, therapeutic, and follow-up intervention will be discussed for each disease. Note that a complete evidence-based summary of recommendations for intervention and level of physical activity for individuals with valvular disease is available from several excellent reviews [8, 15, 16].

34.3.1 Aortic Valve Disease

Anatomically, the normal aortic valve is composed of the annulus and the left, right, and noncoronary leaflets (sometimes referred to as *cusps*) (Fig. 34.3). Diseases affecting these structures can be subdivided into aortic stenosis or regurgitation, or some combination thereof. Overall, aortic stenosis is considered a surgical disease with aortic valve replacement considered to be the standard of care. Treatment of aortic regurgitation is also typically surgical, though the exact method chosen will vary widely based on the etiology of the disease.

34.3.1.1 Aortic Stenosis

Aortic stenosis causes varying degrees of left ventricular outflow tract obstruction [17, 18]. The various etiologies of aortic stenosis are subdivided into acquired versus congenital. Regardless of the etiology, the most common two causes of aortic stenosis in adults are calcification of a normal trileaflet or a congenital bicuspid aortic valve. Interestingly, among individuals under the age of 70, bicuspid aortic valve disease is the most common cause of aortic stenosis. These congenitally abnormal valves typically develop progressive fibrosis and calcification of the leaflets over several decades, and can present for surgery at any time during an individual's life, i.e., depending on the degree of deformity and rate of progression of the narrowing. Patients over the age of 70 more typically elicit the so-called *senile aortic stenosis*; these valves start out as normal valves, but develop thickening, calcification, and stenosis with aging. In a patient with any degree of aortic stenosis, careful clinical follow-up is mandatory to follow the progression of stenosis, and typically surgery is indicated at the onset of any symptoms (see below). Congenital malformation (typically presenting in bicuspid aortic valves) results in progressive fibrosis and calcification

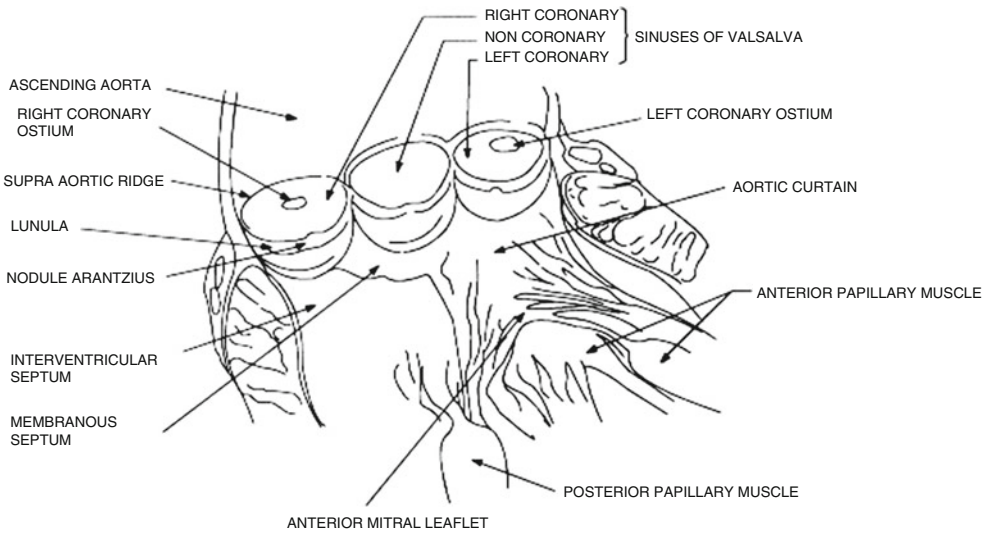

Fig. 34.3 Anatomy of the aortic valve. Adapted from Duran CMG (1994) Conservative valve surgery. In: Zaibag MA, Duran CMG (eds) Valvular heart disease. Marcel Dekker, New York, p 584

Table 34.4 Degree of aortic stenosis [83]

	Valve orifice area (cm^2)	Peak aortic velocity (m/s)
Mild	>1.5	<3.0
Moderate	>1.0 to 1.5	3.0–4.0
Severe	<1.0	>4.0

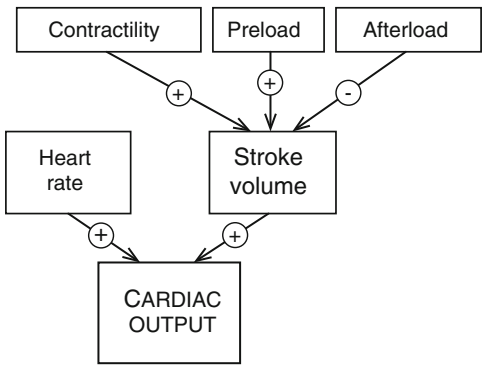

Fig. 34.4 Determinants of cardiac output include contributions from preload and afterload pressures, contractility, and heart rate. Adapted from Lilly LS (ed) (1993) Pathophysiology of heart disease. Lea & Febiger, Philadelphia, p 149

of the leaflets over several decades. The average rates of reduction in valve orifice area have been estimated to be ~0.12 cm^2/year, and valve orifice areas are typically used to grade the relative severity of valve stenosis (Table 34.4) [19]. Nevertheless, progression of aortic stenosis varies significantly and the appearance of symptoms may not correlate well with the given measured valve area. Therefore, careful clinical follow-up is mandatory, as it is difficult to predict an actual individual rate of stenotic progression. In general, aortic stenosis is graded into various categories of severity based on degrees of mean pressure gradient, aortic jet velocity, and/or valve area.

Valve stenosis may also be associated with progressive outflow tract obstruction, which can then cause additional increases in left ventricular pressure. As a result, concentric left ventricular hypertrophy is an early response, which assists initially in maintaining normal left ventricular systolic wall tension and ejection fraction [20]. However, once this response becomes functionally inadequate, afterload tends to increase which, in turn, results in a gradual reduction in overall ejection fraction (Fig. 34.4). In some patients, an initial ventricular hypertrophy itself may also be detrimental, producing subendocardial ischemia even in the absence of coronary artery disease [21, 22]. As such, this results in further systolic and diastolic left ventricular dysfunction and may predispose such patients to a potentially larger degree of myocardial ischemia and higher mortality [7, 8, 17, 18, 23].

Although aortic stenosis may not produce symptoms early in its clinical course, in time symptoms of angina, syncope, heart failure, and/or even sudden death will develop. Although the latter are the classic symptoms of aortic stenosis, more subtle symptoms such as reduced effort tolerance, fatigue, and exertional dyspnea can also occur. Once symptoms are present, average survival without intervention is less than 2–3 years [17, 18, 24–29]. Furthermore, the mortality of patients with aortic stenosis, in the absence of surgical treatment, present with: (1) angina, 50 % within 5 years; (2) syncope, 50 % mortality within 3 years; and (3) heart failure, 50 % mortality within 2 years. Therefore, a high degree of skepticism is necessary to make the diagnosis prior to the onset of symptoms to maximize a given patient's outcome. In general, aortic stenosis can be detected early based on: (1) the presence of a systolic outflow murmur; (2) the occurrence of delayed/diminished carotid upstrokes; (3) a sustained left ventricular impulse; (4) a reduced intensity of the aortic component of the second heart sound; and/or (5)

evidence of left ventricular hypertrophy on exam, chest X-ray, and/or EKG. Typically, results of echocardiography can be further used to confirm the diagnosis of aortic stenosis and also provide for the detailed assessment of: (1) mean transvalvular pressure gradient; (2) derived valve area; (3) relative left ventricle size (degree of hypertrophy) and function; and/or (4) presence of other associated valvular disease. For more details on the clinical use of echocardiography, the reader is referred to Chap. 22. It should also be noted that advances in magnetic resonance imaging may be applied in diagnosing such patients (Chap. 24).

Physicians who follow patients with known aortic stenosis commonly perform an annual history and physical examination, and urge these patients to promptly self-report the development of any new symptoms. Although changes in valve area alone are not totally predictive, annual echocardiography is also useful to assess progression of ventricular hypertrophy and alterations in function. In any case, the development of any new symptoms (e.g., exertional chest discomfort, shortness of breath, or fainting spells) warrants additional clinical assessment, given that aortic stenosis progresses rapidly once such symptoms are present.

In patients being considered for aortic valve replacement secondary to aortic stenosis, cardiac catheterization is generally indicated in individuals >40 years of age to assess for any degree of significant coronary artery disease. Additional indications include the assessment of: (1) hemodynamic severity of the aortic stenosis in situations where there is a discrepancy between clinical and echocardiographic findings; and (2) situations where there is evidence of pulmonary hypertension or other valvular or congenital disease. Complete diagnostic evaluation should include: (1) measurement of transvalvular flows (liters/min); (2) determination of the transvalvular pressure gradients (mmHg); and (3) calculation of the effective valve areas (cm^2) [30].

Stress testing is recommended in patients with equivocal symptoms, and should only be carried out under close monitoring by a physician. Positive findings suggestive of hemodynamically significant aortic stenosis include the development of symptoms, limited exercise tolerance, and a blunted blood pressure response to exercise. In all such cases, surgical replacement of the aortic valve is indicated.

Medical therapy for aortic stenosis is primarily relegated to the prevention of endocarditis and the control of arterial hypertension. As most asymptomatic patients lead a normal life, no interventions are typically considered. Yet, there are some studies that have shown slowing of disease progression with statins. While there are theoretical benefits for the use of ACE inhibitors, studies so far have not shown significant benefits on this disease progression [31, 32]. Nevertheless, once symptoms develop, prompt intervention should be offered to prevent morbidity and mortality. In some patients, interventional radiological therapy using balloon aortic valvotomy can effectively reduce the transvalvular pressure gradients. This procedure uses percutaneously inserted catheters advanced into the aortic valve, then a balloon is inflated to fracture calcific deposits and separate fused commissures [33, 34]. Though successful at providing clinical improvements, the post-procedure valve area rarely exceeds 1.0 cm^2, and aortic regurgitation is often created, thus increasing the burden on the left ventricle. To date, the rate of significant complications (10 %) and symptomatic restenosis (6–12 months) unfortunately makes balloon valvotomy an undesirable substitute for aortic valve replacement in adults with aortic stenosis [7]. Yet, percutaneous aortic balloon dilations may be considered as a bridge to surgical aortic valve replacement or transcatheter aortic valve replacement in patients with severe symptomatic aortic stenosis [8].

Aortic valve replacement is technically possible at any age, and is the treatment of choice for aortic stenosis in most adults [35]. Yet, the degree of stenosis mandating surgery in asymptomatic patients remains an issue of debate. Nevertheless, the degree of improvement following aortic valve replacement is directly related to preoperative left ventricular function; patients with depressed ejection fractions caused by excessive afterloads demonstrate significant improvement in left ventricular function after aortic valve replacement. Conversely, if depressed left ventricular function is caused by myocardial insufficiency, improvement in left ventricular function and resolution of symptoms may not be reversed after valve replacement. In general, survival is improved for patients undergoing aortic valve replacement, with the possible exception of a subset of patients with severe left ventricular dysfunction caused by coronary artery disease [36, 37]. In summary, in contrast to the dismal survival rates for patients with untreated severe aortic stenosis, the long-term survival of patients who have undergone aortic valve replacement approaches the rate in the normal population. Therefore, it is recommended that patients with severe aortic stenosis, with or without symptoms, who are undergoing coronary artery bypass surgery should also undergo aortic valve replacement at the time of the revascularization procedure. Similarly, patients with moderate-to-severe aortic stenosis undergoing surgery for the replacement of other heart valves or an aortic root repair should also undergo an aortic valve replacement as part of their overall surgical procedure. Hence, in the absence of contraindications, aortic valve replacement is indicated in virtually all symptomatic patients with severe aortic stenosis (Table 34.5).

In recent years, transcatheter aortic valve replacements have been increasing in use. According to ACC/AHA guidelines, transcatheter aortic valve replacement is a reasonable alternative to surgical aortic valve replacement in patients who meet an indication for replacement and/or who have a high surgical risk for surgical aortic valve replacement.

Table 34.5 Aortic valve replacement in aortic stenosis [8]

- Symptomatic patients with severe aortic stenosis alone or:
  - Undergoing coronary artery bypass surgery.
  - Undergoing surgery on the aorta or other heart valves.
- Patients with moderate aortic stenosis and:
  - Undergoing coronary artery bypass surgery.
  - Undergoing surgery on the aorta.
  - Undergoing surgery on other heart valves.
- Asymptomatic patients with severe aortic stenosis and left ventricular systolic dysfunction typified by:
  - Abnormal response to exercise (e.g., hypotension).
  - Ventricular tachycardia.
  - Marked or excessive left ventricular hypertrophy (>15 mm).
  - Valve area <0.6 cm2.
  - Prevention of sudden death without the findings listed.

However, transcatheter aortic valve replacement should only be performed in patients with an expected post-procedure survival longer than 12 months [8, 38, 39]. For a more detailed discussion of these valves, see Chap. 36.

Currently, there are two areas of major controversy in the management of aortic stenosis including: (1) the asymptomatic patient with a severe aortic stenosis; and (2) the patient with low ejection fraction with a reduced gradient aortic stenosis [17, 18]. There is low (1–2 %) risk of sudden death or rapid progression to symptoms in the asymptomatic patient with a severe aortic stenosis. Adverse clinical outcomes are more likely in the asymptomatic patient with severe aortic stenosis who demonstrates more rapid progression of hemodynamic parameters, such as: (1) an increase in aortic jet velocity greater than 0.3 m/s/year; or (2) a decreasing aortic valve area greater than 0.1 cm^2/year. Therefore, other than in a small selected group of patients, the risk of surgery may still exceed any potential benefits in this group of patients, i.e., those with a severe aortic stenosis with normal ventricular function who are truly asymptomatic. On the other hand, patients with low ejection fractions and reduced gradient aortic stenosis may present an even more challenging problem. These complexities partly lie in the difficulty to distinguish this entity from those patients with reduced ejection fractions and only mild-to-moderate aortic stenosis; this latter group will not benefit from aortic valve replacement. It should be noted that patients with severe aortic stenosis who present with reduced ejection fractions and reduced gradients will ultimately face increased operative mortality. The use of dobutamine stress echocardiography to measure the pressure gradients and the effective valve areas, both during baseline and at stress, can help determine the true severity of aortic stenosis [40]. It should be noted that, in general, patients with reduced ejection fractions with low transvalvar gradients who elicit no response to stress such as inotropes have poorer outcomes, even with surgery.

34.3.1.2 Aortic Sclerosis

Aortic sclerosis is a common finding in older patients, and is present in approximately 25 % of patients older than 65 years [16, 17]. The classic findings of aortic sclerosis include focal areas of valve thickening with otherwise relatively normal leaflet mobility. It is important to note that, by definition, valvular hemodynamics in these patients are within normal limits. In other words, other than the presence of a systolic murmur, these individuals elicit no clinical signs or associated symptoms. Histologic findings in aortic sclerosis include focal subendocardial plaque-like lesions with accumulations of lipoproteins. The similarity of these findings to atherosclerosis suggests that both are, in some way, an age-related process.

Despite the lack of valve-related symptoms with aortic sclerosis, it is generally associated with an increased risk of cardiovascular mortality. This may be related to the development of coronary artery disease and/or occasionally to a progression to severe aortic stenosis. Thus, while symptoms in the patient identified with aortic sclerosis may be initially benign, these individuals warrant close cardiovascular follow-ups.

34.3.1.3 Aortic Regurgitation

Aortic regurgitation results from a structural defect in the aortic valve that allows for blood flow to reverse direction across the valve during diastole (i.e., re-enter the ventricle). The etiologies of aortic regurgitation are best discussed if one subdivides this disease into acute or chronic regurgitation (Table 34.6). The majority of such lesions result in chronic aortic regurgitation, with insidious dilatation of the left ventricle. In contrast, lesions responsible for acute aortic regurgitation may result in sudden catastrophic elevation of

Table 34.6 Etiologies of aortic regurgitation (subdivided by presentation time)

Acute	Chronic
Infective endocarditis	Idiopathic aortic root dilatation
Aortic dissection	Congenital bicuspid valves
Trauma	Calcific degeneration
	Rheumatic disease
	Infective endocarditis
	Systemic hypertension
	Myxomatous proliferation
	Ascending aortic dissection
	Marfan syndrome
	Syphilitic aortitis
	Rheumatoid arthritis
	Osteogenesis imperfecta
	Giant cell aortitis
	Ehlers-Danlos syndrome
	Reiter's syndrome
	Discrete subaortic stenosis
	Ventricular septal defects with aortic cusp prolapse

left ventricular filling pressures, reduction in cardiac outputs, and/or sudden death.

Chronic Aortic Regurgitation

Valve damage that results in progressively larger retrograde flows across the aortic valve produces the condition of *chronic aortic regurgitation*. The patient's left ventricle responds to the volume load of aortic regurgitation with several compensatory mechanisms such as an increase in end-diastolic volumes and a combination of eccentric and concentric hypertrophy [41]. The increased diastolic volume allows the ventricle to eject a larger total stroke volume, thereby initially maintaining stroke volume within a relative normal range. As a result, the majority of such patients remain asymptomatic for prolonged periods of compensation, during which time they maintain forward stroke volume within the normal ranges. Yet, after a while, the compensatory mechanisms become inadequate, and further increases in afterload result in reduced ejection fractions. Once the left ventricle can no longer compensate, patients typically present with symptoms of: (1) dyspnea and exertional angina, reflecting declining systolic function; (2) elevated filling pressures; and/or (3) diminished coronary flow reserves of the hypertrophied myocardium [42]. Several natural history studies have identified age and left ventricular end-systolic pressures (or volumes) as predictive factors associated with higher risks of mortality in these clinical populations (Table 34.7) [7].

Importantly, although the progression of asymptomatic aortic regurgitation is slow, approximately one-fourth of patients will develop systolic dysfunction, or even die, before the onset of warning symptoms [7]. Therefore, quantitative evaluation of left ventricular function with echocardiography is necessary, as a serial history and physical exam alone are considered as insufficient, in general.

The clinical diagnosis of chronic severe aortic regurgitation by a trained physician can be made on: (1) the presence of a diastolic murmur (the third heart sound) and/or a rumble (Austin–Flint sign) on auscultation; and (2) the detection of a displaced left ventricular impulse and wide pulse pressure [43, 44]. Similar to aortic stenosis, the chest X-ray and ECG will typically reflect left ventricular enlargement/hypertrophy and may also elicit evidence of conduction disorders. Echocardiography is then indicated to: (1) confirm the diagnosis of aortic regurgitation; (2) assess valve morphology; (3) estimate the severity of regurgitation; (4) assess aortic root size; and (5) determine left ventricular dimensions, relative mass, and systolic function. If the patient has severe aortic regurgitation and is sedentary, or has equivocal symptoms, exercise testing is helpful to assess the following: functional capacity, symptomatic responses, and/or the hemodynamic effects of exercise.

In patients who are symptomatic on initial evaluation, cardiac catheterization and angiography is considered indicated for the subsequent evaluation of coronary artery disease for the possible need of revascularization therapy, i.e., if the echocardiogram is of insufficient quality to assess left ventricular function and the severity of aortic regurgitation. The ultimate aim of any serial evaluation of the asymptomatic patient with chronic aortic regurgitation is to detect the onset of symptoms and objectively assess changes in left ventricular size and function that may occur in the absence of physical symptoms (Fig. 34.3). Medical therapy for aortic regurgitation is primarily based on the use of vasodilating agents which are believed to improve forward stroke volumes and reduce regurgitant volumes; note, the use of such agents can often result in regression of both left ventricular dilatation and hypertrophy.

Initial left ventricular systolic dysfunction in chronic aortic regurgitation has been commonly associated with an increased afterload pressure, and is considered to be reversible following aortic valve replacement, i.e., with nearly full recovery of left ventricular size and function [7]. However, if depressed myocardial contractility (rather than volume overload) is responsible for the systolic dysfunction as the ventricle becomes more hypertrophic and dilatation progresses, the chamber becomes more spherical geometry. At this stage, neither return of normal left ventricular function nor improved long-term survival has been documented even after aortic valve replacement [7]. For patients with chronic aortic regurgitation, left ventricular systolic function and end-systolic size have been identified as the most important determinants of postoperative survival and/or normalization of left ventricular function following aortic valve replacement [7].

Medical therapy using vasodilating agents is generally indicated for chronic therapy in patients with severe aortic regurgitation who have symptoms of left ventricular dysfunction and for whom surgery is not recommended, i.e., because of either cardiac or noncardiac factors. The benefits of vasodilating agents are based on their potential ability to improve stroke volume and reduce regurgitant volume [45].

Table 34.7 Natural history of aortic regurgitation

Asymptomatic patients with normal left ventricular systolic function	• Progression to symptoms and/or left ventricular dysfunction	<6 %/year
	• Progression to asymptomatic left ventricular dysfunction	<3.5 %/year
	• Sudden death	<0.2 %/year
Asymptomatic patients with left ventricular systolic dysfunction	• Progression to cardiac symptoms	>25 %/year
Symptomatic patients	• Mortality rate	
	– with angina	>10 %/year
	– with heart failure	>20 %/year

In general, the acute administration of vasodilating agents such as sodium nitroprusside, hydralazine, and nifedipine reduces peripheral vascular resistance and results in immediate augmentation in forward cardiac outputs and decreases in regurgitant volumes. The ACC/AHA recommends three guidelines for the use of vasodilating agents in the patient with severe aortic regurgitation: (1) the long-term treatment of patients with severe aortic regurgitation who have symptoms and/or left ventricular dysfunction who are considered poor candidates for surgery; (2) improvements in the hemodynamic profile of patients with severe heart failure symptoms and severe left ventricular dysfunctions with short-term vasodilator therapy, before proceeding with aortic valve replacement; and (3) prolonged use during the compensated phase of asymptomatic patients who have volume overloads, but have normal systolic functions.

Acute Aortic Regurgitation

When damage to the aortic valve is acute and severe, subsequent and sudden large regurgitant volumes return into the left ventricle, and this will decrease the functional forward stroke volumes dramatically. In contrast to chronic aortic regurgitation, in such acute cases, there has been no time for compensatory ventricular hypertrophy and/or dilatations to develop. As a result, the considered typical exam findings of ventricular enlargement and diastolic murmur associated with chronic aortic regurgitation are absent. Instead, the patient with acute aortic regurgitation presents with pronounced tachycardia, pulmonary edema, and/or potentially life-threatening cardiogenic shock.

Echocardiography, which is considered crucial for the initial workup of the acute aortic regurgitation patient, will likely demonstrate a rapid equilibration of aortic and left ventricular diastolic pressures, and may provide some insights as to the etiologies of aortic regurgitations. Echocardiography also allows for a rapid assessment of the associated valve apparatus, the aorta, and/or the relative degree of pulmonary hypertension (if tricuspid regurgitation is present). Transesophageal echocardiography is indicated when aortic dissection is suspected [46, 47] (Chap. 22). Importantly, acute aortic regurgitation resulting from aortic dissection is a known surgical emergency requiring prompt identification and management. Cardiac catheterization, aortography, and coronary angiography are considered as important components of such an evaluation of aortic dissection with acute aortic regurgitation, and thus should be performed if these procedures do not unduly delay urgent surgery. Additionally, following trauma, computed tomographic imaging can be quite useful in obtaining the appropriate clinical status and underlying diagnoses.

Nevertheless, appropriate treatment of acute aortic regurgitation is dependent on the etiology and severity of the disease. For example, only antibiotic treatment may be required in a hemodynamically stable patient with mild acute aortic regurgitation, i.e., resulting from infective endocarditis. Conversely, severe acute aortic regurgitation is a surgical emergency, particularly if hypotension, pulmonary edema, and/or evidence of low cardiac outputs are present. In such cases, temporary preoperative management may include the use of agents such as nitroprusside (to reduce afterload) and inotropic agents such as dopamine or dobutamine (to augment forward flow and reduce left ventricular end-diastolic pressure). Note that intraaortic balloon counterpulsation is contraindicated in such patients, and beta-blockers should be used cautiously because of their potential to further reduce outputs by blocking the compensatory tachycardia. Typically, mortalities associated with acute aortic regurgitation are usually the result of pulmonary edema, ventricular arrhythmias, electromechanical dissociation, and/or circulatory collapse.

In general, aortic valve replacement is the treatment of choice in aortic regurgitation. In such cases of aortic disease, additional aneurysm repair (Fig. 34.5) or aortic root replacement (Figs. 34.6 and 34.7) needs to be considered. Aortic root replacement with a homograft or autograft should be offered to patients in whom anticoagulation is contraindicated (e.g., elderly with risk, women of child bearing years), as the tissue valve grafts do not require anticoagulation. In addition, patients with disease resulting from endocarditis also benefit, as a homograft appears to have more resistance to subsequent infection. Finally, although the use of mechanical valves is effective, the prosthesis may impose a clinically relevant degree of stenosis in certain patients due to unavoidable size mismatch. Naturally, homografts and autografts are superior as they can be tailored to provide a larger outflow tract. Nevertheless, in certain situations, repair of the aorta may involve the use of an artificial conduit using materials such as Dacron.

Careful post-aortic valve replacement follow-ups are necessary during both the early and long-term postoperative courses, to evaluate both prosthetic valve and left ventricular function. An accepted excellent predictor of long-term success of aortic valve replacement is the reduction in left ventricular end-diastolic volume, typically occurring within the first 14 days after the operation. It should be emphasized that, in most patients, as much as 80 % of the overall reduction in end-diastolic volume that will occur will happen within this time period. In addition, the degree of regression in left ventricular dilatation typically correlates well with the magnitude of functional increases in ejection fraction [44]. Nevertheless, long-term follow-ups should include an exam at 6 months post-aortic valve replacement, and then yearly examinations are recommended if the patient's clinical course is uncomplicated. Note that serial postoperative echocardiograms after the initial early postoperative study are usually not indicated. However, repeat echocardiography is warranted at any point when there is evidence of: (1) a new murmur; (2) questions of prosthetic valve integrity; and/or (3) concerns about adequate left ventricular function.

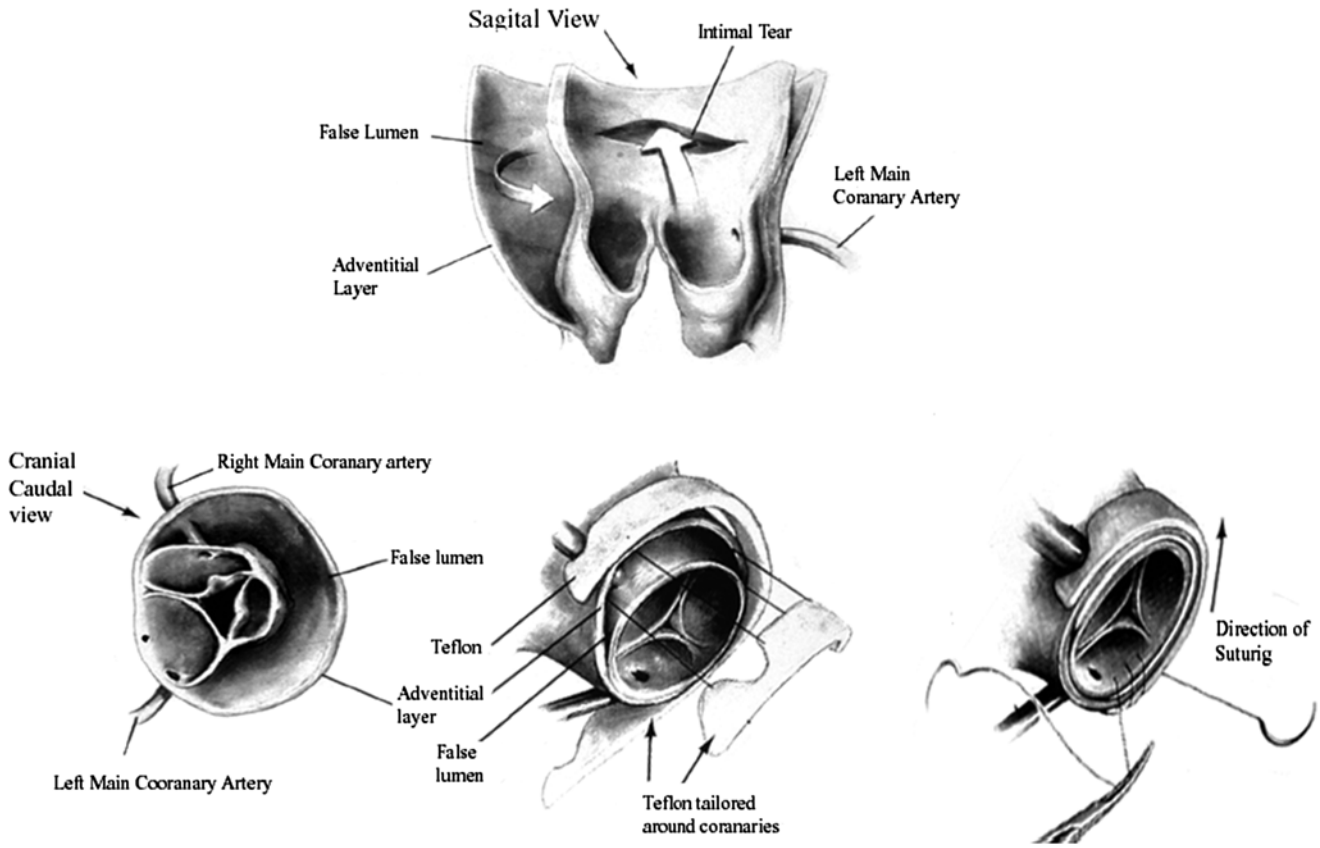

Fig. 34.5 Aortic aneurysm repair using a Teflon felt reinforcement technique preserving the aortic valve and coronary arteries. 81Operative Techniques in Cardiac and Thoracic Surgery: A Comparative Atlas by W.B. Saunders, Co. Reproduced with permission of W.B. Saunders, Co., in the format book via Copyright Clearance Center

Aortic Valve Disease Associated with Disease of the Ascending Aorta

Dilatation of the ascending aorta is a common cause of aortic regurgitation. It is well recognized that patients with bicuspid aortic valves will typically also have disorders of the vascular connective tissue system, which can result in dilatation of the ascending aorta and/or aortic root even in the absence of hemodynamically significant valvular disease. The dilatation of the aorta can be progressive over time, with an increased risk for aortic dissection. Currently, echocardiography is the primary diagnostic modality used for these patients. However, a more detailed anatomic study can be obtained with either computerized tomography or cardiac magnetic resonance imaging (Chap. 24).

Regardless of the etiology of the dilated ascending aorta, the recommended indications for operative intervention include an aortic diameter >5.5 cm or growth of the aorta >0.5 cm/year. In patients with bicuspid aortic valves undergoing aortic valve replacement, repair of the aortic root or replacement of the ascending aorta is commonly indicated if the diameter of the aorta is >4.5 cm [8]. Note that aortic valve-sparing operations are feasible in many patients with dilatation of the aorta who do not elicit significant aortic regurgitation or aortic valve calcification. The techniques for aortic valve-sparing surgery have been pioneered by Yacoub and David [48, 49]. In early stages of this disease, the use of beta-adrenergic blocking agents may slow the progression of aortic dilatations.

34.3.2 Diseases of the Mitral Valve

Diseases of the mitral valve can be subdivided in a similar fashion as those affecting the aortic valve—stenosis and regurgitation. The general anatomy of the mitral valve consists of a pair of leaflets attached to the left ventricle by chordae tendinae. Normal mitral valve area ranges between 4.0 and 5.0 cm^2. However, in the case of mitral stenosis, symptoms do not typically develop until the functional valve area is reduced to <2.5 cm^2 [50]. For more details on valve anatomy, the reader is referred to Chaps. 4, 5, 7 and the Atlas of Human Cardiac Anatomy (www.vhlab.umn.edu/atlas).

34.3.2.1 Mitral Stenosis

Stenosis of the mitral valve orifice typically produces a funnel-shaped mitral apparatus described to resemble a “fish mouth” which then hinders normal diastolic filling of the left ventricle. In the past, roughly 60 % of all patients with mitral

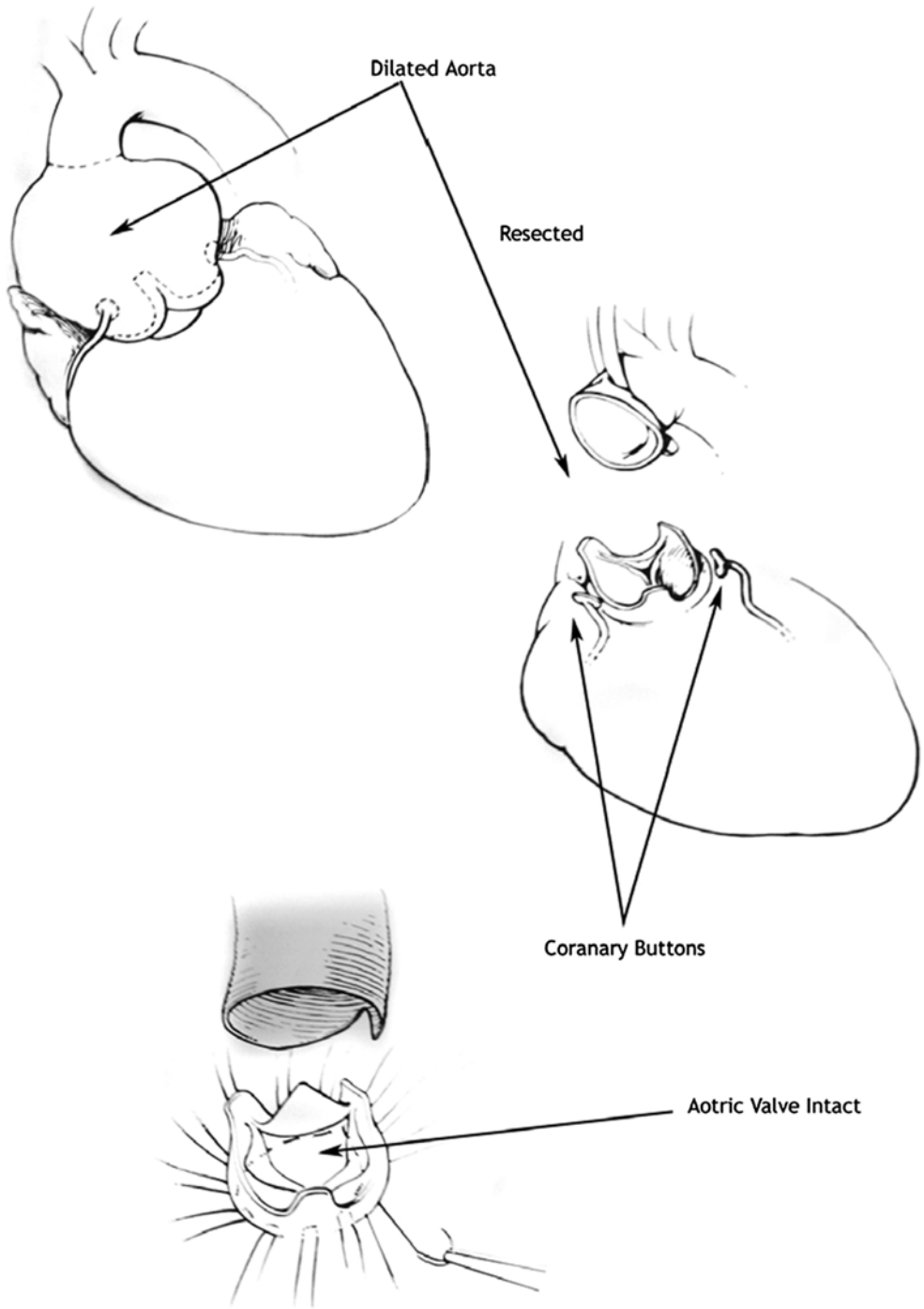

Fig. 34.6 David procedure for aortic root replacement. The dilated aorta is resected, sparing the aortic valve and coronary buttons. The repair is then completed with insertion of a graft with reimplantation of the coronary arteries. Adapted from Smedira NG (2003) Mitral valve replacement with a calcified annulus. In: Cox JL, Sundt TM III (eds) Operative techniques in cardiac and thoracic surgery. Saunders, Philadelphia, pp 2–13

stenosis presented with a history of rheumatic fever [51, 52]. Typical pathological processes observed in such patients include: (1) leaflet thickening and calcification; (2) commissural and chordal fusion; or (3) a combination of these processes [53, 54]. Yet, congenital malformations of the mitral valve, though rare, are usually responsible for mitral stenosis observed in infants and children [54] (see Chap. 10). Currently, women (2:1) account for the overall majority of mitral stenosis cases [51, 52, 55]. Other entities can also simulate the clinical features of rheumatic mitral stenosis, such as left atrial myxoma, infective endocarditis, or mitral annulus calcification in the elderly.

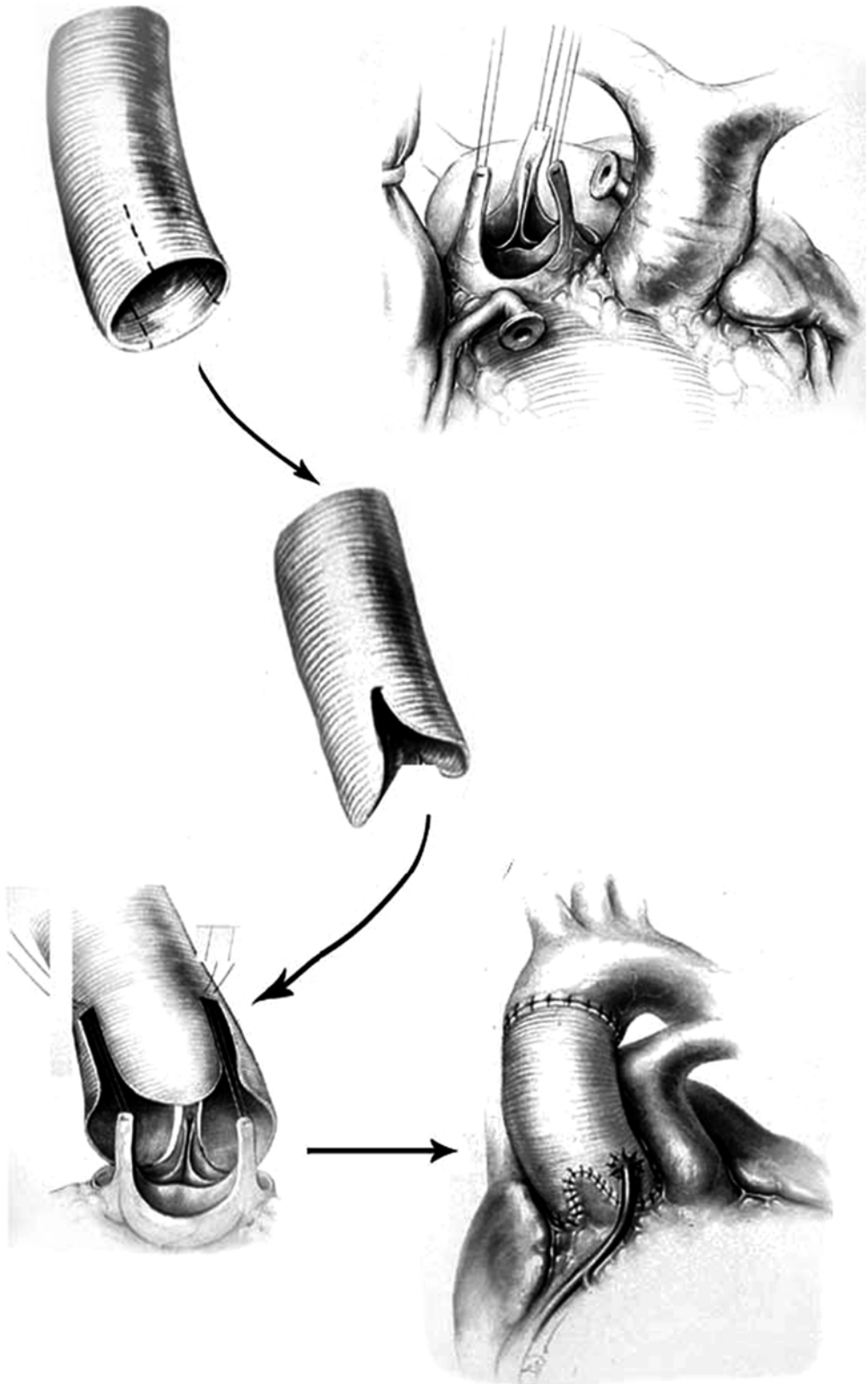

Fig. 34.7 Aortic root replacement using Dacron graft as the technique used for correct sizing, for suturing in place to yield the final graft implantation along with coronary re-implantation. Adapted from Yacoub M. Valve-conserving operation for aortic root aneurysm or dissection. In: Operative techniques in cardiac and thoracic surgery, pp 57–67

Mitral stenosis is normally a slowly progressive process with a typical mean age of presentation of symptoms in the fifth to sixth decade of life [56, 57], i.e., with narrowing of the valve to <2.5 cm^2 before the development of symptoms. As the severity of stenosis increases, cardiac output becomes reduced even at rest and will fail to be increased with exercise. The relative degree of pulmonary vascular resistance also influences the development of symptoms. The diagnosis of mitral stenosis may be made solely on the presence of abnormal physical exam findings, or may be suggested by symptoms of fatigue, dyspnea, frank pulmonary edema, atrial fibrillation, and/or embolus [52]. In the asymptomatic patient survival is 80 % at 10 years, with 60 % of these patients eliciting no progression of symptoms [7]. However, once symptoms related to pulmonary hypertension develop, to date, there remains a dismal 10-year survival rate of 0–15 % [7]. Common causes of death in these untreated patients with mitral stenosis are due to: (1) progressive heart failure (60–70 %); (2) systemic embolism (20–30 %); (3) pulmonary embolism (10 %); or (4) infection (1–5 %) [54, 55].

It should be noted that shortness of breath (dyspnea) precipitated by exercise, emotional stress, infection, pregnancy, or atrial fibrillation are typically the first symptoms which present in patients with underlying mild mitral stenosis [58]. Yet, as the obstructions across the mitral valve increase, there will typically be progressive symptoms of dyspnea, as the left atrial and pulmonary venous pressures increase [59]. Increased pulmonary artery pressures and distension of the pulmonary capillaries can lead to pulmonary edema, which occurs as pulmonary venous pressure exceeds that of plasma oncotic pressure. Subsequently, the pulmonary arterioles will elicit vasoconstriction, intimal hyperplasia, and medial hypertrophy, which then further exacerbate pulmonary arterial hypertension.

Commonly, the diagnosis of mitral stenosis can be made based on a given patient's history, physical examination, chest X-ray, and ECG. Nevertheless, at the initial examination, a patient may be asymptomatic although abnormal physical findings, including a diastolic murmur, may be present [56, 57]. In such patients, diagnostic imaging is recommended and currently the tool of choice is 2D and Doppler transthoracic echocardiography. Transesophageal echocardiography or cardiac catheterization is not required unless questions concerning diagnoses remain [7]. Yet, heart catheterization may be indicated to: (1) assess the potential for either coronary artery or aortic valve disease; (2) assess pulmonary artery pressures; (3) perform balloon valvotomy; and/or (4) evaluate the situations when the clinical status of a symptomatic patient is not consistent with the echocardiography findings.

Typically, echocardiography is capable of providing an appropriate assessment of: (1) the morphological appearance of the mitral valve apparatus; (2) ventricular chamber size/function; (3) the mean transmitral gradient [60, 61]; (4) the relative functional mitral valve area; and (5) the relative pulmonary artery pressures [62]. In addition, if deemed necessary, noninvasive dobutamine or exercise stress testing can be completed with either the patient supine (using a bicycle) or upright (on a treadmill) to assess changes in heart rate and blood pressure in response to their overall exercise tolerance. Patients who are symptomatic with a significant elevation of pulmonary artery pressure (>60 mmHg), mean transmitral gradient (>15 mmHg), or pulmonary artery wedge pressure (>25 mmHg) on exertion have, by definition, hemodynamically significant mitral stenosis that may require further intervention [7].

In mitral stenosis, medical treatment is typically indicated for the prevention of emboli (10–20 %), which is primarily associated with the onset of atrial fibrillation [51, 52, 63–65]. Atrial fibrillation ultimately develops in 30–40 % of patients with symptomatic mitral stenosis and, importantly, ~65 % of all embolic events occur within the first year after the onset of atrial fibrillation [51, 52]. The etiology behind atrial fibrillation is thought to be a disruption of the normal conduction pathways caused by structural changes in the myocardium resulting from a pressure/volume overloaded atrium; in fewer cases, it may also result from rheumatic fibrosis of the atrium [57]. The development of atrial fibrillation associated with mitral stenosis occurs more commonly in older patients and has been associated with a decreased 10-year survival rate (25 % versus 46 %) [52, 55]. In addition to the thromboembolic potential, acute onset of atrial fibrillation can herald sudden deterioration in patients with mitral stenosis. This is considered as secondary to an acute reduction in left ventricular ejection fractions and elevated pulmonary artery pressures, which will result from loss of the atrial contribution to left ventricular filling. The urgent treatment for an acute episode of atrial fibrillation with a rapid rate typically consists of: (1) anticoagulation with heparin; (2) heart rate control (digoxin, calcium channel blockers, beta-blockers, or amiodarone); and/or (3) electrical cardioversion. It should be noted that in patients with atrial fibrillation for more than 24–48 h without anticoagulation, cardioversion is then associated with an increased risk of embolism. Today, in chronic or recurrent atrial fibrillation that is resistant to prevention or cardioversion, heart rate control (digoxin, calcium channel blockers, beta-blockers, or amiodarone), and long-term anticoagulation are considered as the mainstay of therapy [65, 66]. Yet, use of anticoagulation for patients with mitral stenosis who have not had atrial fibrillation or embolic events is not indicated due to the risk of bleeding complications. For more details on this topic, the reader is referred to Chaps. 30 and 31.

The principle for treating symptomatic mitral stenosis rests on alleviation of the fixed left ventricular inflow obstruction, thereby reducing the transvalvular gradient. Methods of disrupting the fused valve apparatus (open or

closed mitral commissurotomy, or percutaneous mitral balloon valvotomy) or mitral valve replacement have both demonstrated significant post-procedural improvement in both symptoms and survival rates. The timing of intervention is commonly related to the identified severity of disease, while the method of intervention is chosen based on: (1) morphology of the mitral valve apparatus; (2) presence of other comorbid diseases; and/or (3) expertise at each specific clinical center. Significant calcification, fibrosis, and subvalvular fusion of the valve apparatus can make either commissurotomy or percutaneous balloon valvotomy less likely to be successful. It should also be noted that the presence of mitral regurgitation is a contraindication for valvotomy/commisurotomy, and it is considered best to treat such patients with a mitral valve replacement.

Closed commissurotomy is a surgical technique that uses finger fracture of the calcified valve (Fig. 34.8). This procedure has the advantage of not requiring cardiopulmonary bypass, however the operator is not afforded direct visual examination of the valve apparatus. In contrast, open commissurotomy, which commonly employs cardiopulmonary bypass, has gained favor in the United States because it allows inspection of the mitral valve apparatus under direct vision. During such a procedure, division of the commissures, splitting of fused chordae tendinae/ papillary muscles, debridement of calcium deposits [7], and/or mitral valve replacement can be completed to attain optimal functional results. The 5-year reoperation rate following open commissurotomy has been reported to be between 4 % and 7 %, and the 5-year complication-free survival rate ranges from 80 to 90 %.

More recently, both these operative techniques have given way to percutaneous balloon valvotomy. This is now the initial procedure of choice for the symptomatic patient with moderate-to-severe mitral stenosis, or those patients with favorable valve morphologies and non-significant mitral regurgitation and/or left atrial thrombus (Fig. 34.9). Immediate reduction in the transvalvular gradient (by at least 50–60 %) has been associated with gradual regression of pulmonary hypertension over several months [8]. If selected appropriately, 80–95 % of patients undergoing this procedure will achieve a functional mitral valve area >1.5 cm^2 and a resultant decrease in left atrial pressures without complications. Yet, potential acute complications include: subsequent mitral regurgitation (10 %), an induced atrial septal defect (5 %), left ventricle perforation (0.5–4.0 %), emboli formation (0.5–3 %), myocardial infarction (0.3–0.5 %), and/or increased mortality (<1 %) [67]. Currently, echocardiographic assessments of mitral valve morphology are the most important predictor of outcomes for percutaneous balloon valvotomy. Patients with valvular calcification, thickened fibrotic leaflets with decreased mobility, and/or subvalvular fusion have higher incidence of acute complications following balloon valvotomy and higher rates of recurrent stenosis on follow-up. Presence of left atrial thrombus, detected by transesophageal echocardiography, is a relative contraindication and, at a minimum, warrants 3 months of oral warfarin anticoagulation in an attempt to resolve the thrombus prior to any planned procedure. A post-procedure echocardiogram, typically within 72 h after the procedure, is useful to assess postoperative hemodynamics, as well as to exclude significant complications such as mitral regurgitation, left ventricular dysfunction, and/or an atrial septal defect. However, recurrent symptoms have been reported to occur in as many as 60 % of patients 9 years post-procedure [62, 68, 69]; it should be noted that recurrent stenoses account for such symptoms in <20 % of such patients [68]. In patients with an adequate initial result, progressive mitral regurgitation and development of other valvular or coronary problems are more frequently responsible for the subsequent presentation of symptoms [68]. Thus, in the patient presenting with symptoms late after commissurotomy, a comprehensive evaluation is required to look for other causes.

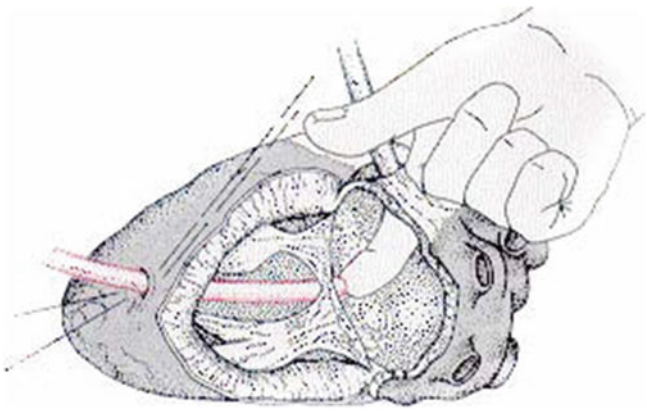

Fig. 34.8 Treatment of mitral stenosis using the finger fracture closed mitral commissurotomy technique. Adapted from Zipes DP (ed) (1992) Braunwald's heart disease: a textbook of cardiovascular medicine. W.B. Saunders Co., Philadelphia, p 1016

Mitral valve replacement is an accepted surgical procedure for patients with severe mitral stenosis who are not candidates for surgical commissurotomy or percutaneous mitral valvotomy (Table 34.8, Figs. 34.10 and 34.11). In addition, patients with recurrent severe symptoms, severe deformities of their mitral apparatus, severe mitral regurgitation, or a large atrial septal defect should be offered mitral valve replacement. The risks associated with mitral valve replacement are also highly dependent on patient age, left ventricular functional status, low cardiac outputs, presence of comorbid medical problems, and/or concomitant coronary artery disease. More specifically, morbidity and mortality associated with mitral valve replacements are directly correlated with age, with risks in a young healthy person of <5 %, increasing to as high as 10–20 % in the older patient with concomitant medical problems or pulmonary hypertension.

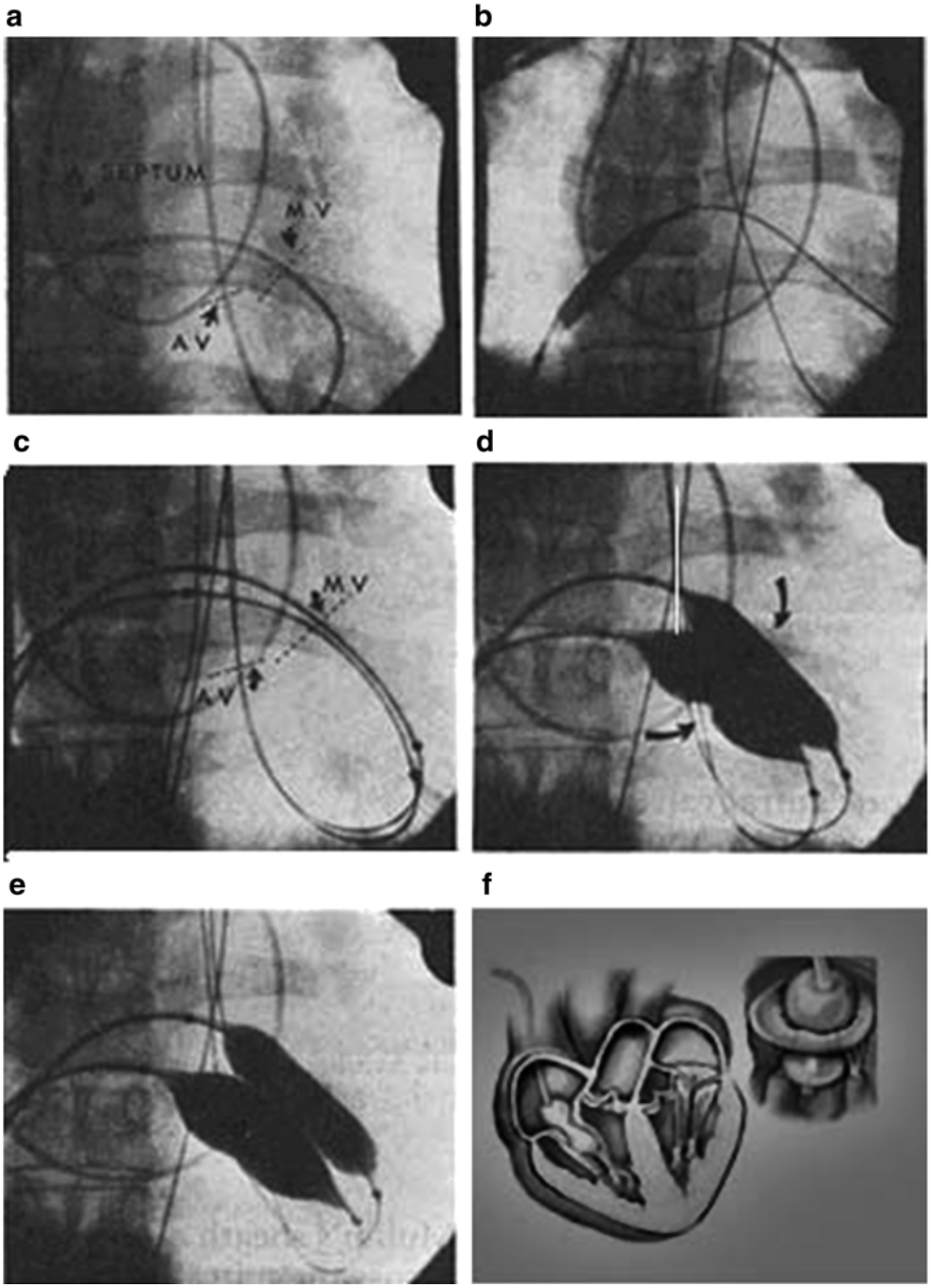

Fig. 34.9 Treatment of mitral stenosis using balloon valvotomy. Sequence of percutaneous mitral valvotomy: (**a**) floating balloon catheter in position across the atrial septum through the mitral and aortic valves. The tip is in the ascending aorta; (**b**) an 8 mm dilating balloon catheter enlarging the atrial septal puncture site; (**c**) two 20 mm dilating balloon catheters advanced into position across the stenotic mitral valve over two separate 0.038 in transfer guide wires; (**d**) partially inflated dilating balloon catheters across the mitral valve; note the "waist" produced by the stenotic valve (*arrows*); (**e**) fully inflated dilating balloon catheters in position across the mitral valve; (**f**) illustration of balloon commissurotomy technique. Adapted from www.rjmatthews.com and Zipes DP (ed) (2003) Braunwald's heart disease: a textbook of cardiovascular medicine. Saunders, Philadelphia

Table 34.8 Mitral valve replacement for mitral stenosis [8]

- Moderate to severe mitral stenosis (mitral valve area <1.5 cm^2):
  - With NYHA functional Class III–IV symptoms.
  - Who are not considered candidates for percutaneous balloon valvotomy or mitral valve repair.
- Patients with severe mitral stenosis (mitral valve area <1 cm^2):
  - With severe pulmonary hypertension (pulmonary artery systolic pressure >60-80 mmHg).
  - With NYHA functional Class I–II symptoms who are not considered candidates for percutaneous balloon valvotomy or mitral valve repair.

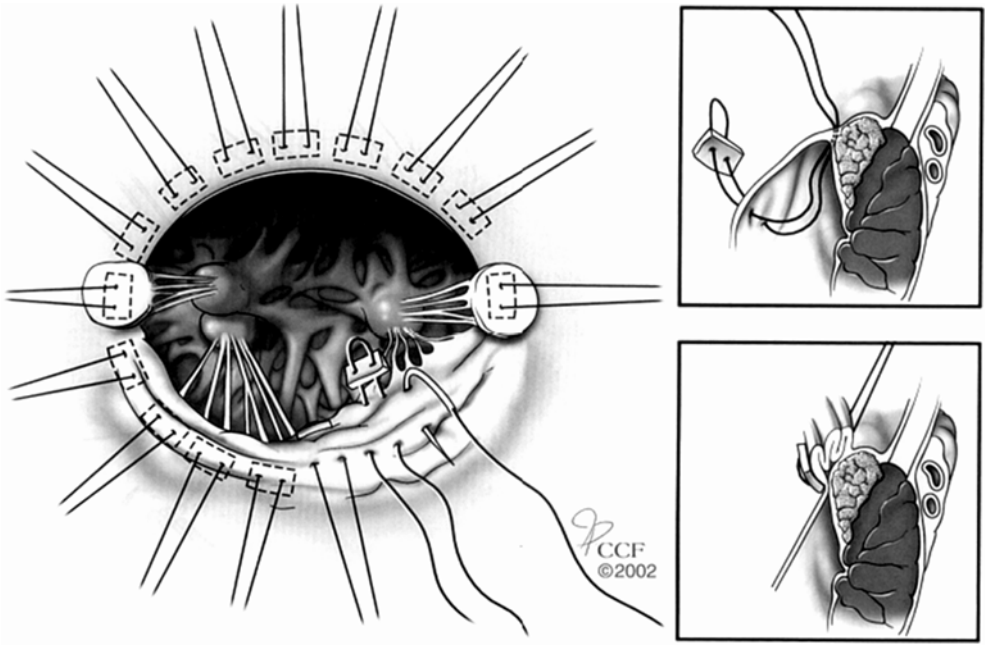

Fig. 34.10 Placement of circumferential sutures and plication of the anterior leaflet of the mitral valve. Adapted from Smedira NG (2003) Mitral valve replacement with a calcified annulus. In: Cox JL (ed) Operative techniques in thoracic and cardiovascular surgery. Saunders, Philadelphia, pp 2–13

Mitral valve replacement can be further complicated by the: (1) potential for embolic events; (2) need for (and risk of) long-term anticoagulation therapy; and/or (3) potential for valve thrombosis, dehiscence, infection, or malfunction.

34.3.2.2 Mitral Regurgitation

The common etiologies for mitral regurgitation include: (1) mitral valve prolapse secondary to myxomatou degeneration; (2) rheumatic heart disease; (3) coronary artery disease; (4) infective endocarditis; or (5) collagen vascular disease. As with aortic regurgitation, mitral regurgitation can be categorized as both acute and chronic presentations. In some cases, mitral regurgitation due to ruptured chordae tendinae or infective endocarditis may present as both acute and severe. Alternatively, mitral regurgitation may worsen gradually over a prolonged period of time. Yet, these very different presentations of mitral regurgitation are both treated with surgical intervention as dictated by the character of the symptoms presented.

Acute Severe Mitral Regurgitation

In acute severe mitral regurgitation, a sudden volume overload is imposed on the left atrium and the left ventricle is without time for typical compensatory hypertrophy. Thus, sudden drops in forward stroke volume and cardiac output occur (cardiogenic shock) in such a patient, with simultaneous pulmonary congestion. In severe mitral regurgitation, the hemodynamic overload often cannot be tolerated, and mitral valve repair or replacement must be performed urgently.

The acute nature of this form of mitral regurgitation results in patients who almost always present with symptoms upon physical exams; they are typically positive for a holosystolic murmur and a third heart sound (see Chap. 18). Transthoracic echocardiography is commonly used to confirm the diagnosis and also to assess the general degree of disruptions within the mitral valve apparatus. Furthermore, the use of transesophageal echocardiography is warranted if mitral valve morphology and regurgitation are still not clearly elucidated following transthoracic echocardiography. Note that it is the high level

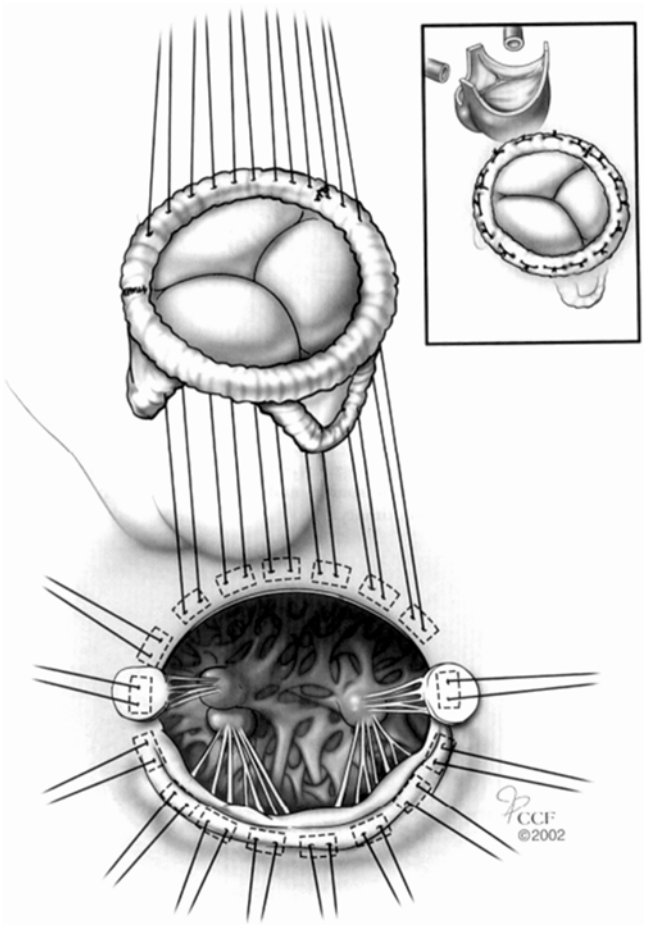

Fig. 34.11 Mitral valve positioning into the mitral oriface. Adapted from Smedira NG (2003) Mitral valve replacement with a calcified annulus. In: Cox JL (ed) Operative techniques in thoracic and cardiovascular surgery. Saunders, Philadelphia, pp 2–13

of details provided by transesophageal echocardiography that is also helpful in demonstrating the anatomic causes of mitral regurgitation and, subsequently, directing successful surgical repairs (see Chap. 22). Coronary arteriography is necessary before surgery in all such patients >40 years of age, unless hemodynamic stability is of concern. If necessary, myocardial revascularization should be performed during mitral valve surgery in those patients with concomitant coronary artery disease [70, 71].

If the patient is not a candidate for surgery or if preoperative stabilization is required, medical therapy can help to diminish the relative amount of mitral regurgitation, thus increasing forward output and reducing pulmonary congestion, yet this therapy should be initiated promptly. However, in cases of acute severe mitral regurgitation, medical therapy has a limited role and is primarily used to stabilize patients prior to surgery. In normotensive patients, nitroprusside has been used to increase forward outputs, not only by preferentially increasing aortic flows, but also by partially restoring mitral valve competence as the left ventricular size diminishes [72, 73]. In hypotensive patients with severe reductions in forward output, aortic balloon counterpulsation can be employed to increase forward output and mean arterial pressure while, at the same time, diminishing mitral valve regurgitant volume and left ventricular filling pressure. If infective endocarditis is the cause of acute mitral regurgitation, identification and treatment of the infectious organism is important to optimize successful clinical outcomes.

Chronic Asymptomatic Mitral Regurgitation

As with chronic aortic regurgitation, time for hypertrophy and chamber dilatation is typically present in the patient presenting with chronic severe mitral regurgitation [33, 74]. These dilatations, or increases in left ventricular end-diastolic volume, are a compensatory mechanism which permits an increased total stroke volume and allows for restoration of forward cardiac outputs [75]. At the same time, increases in left ventricular and left atrial sizes accommodate the regurgitant volume with lower filling pressure; consequentially, symptoms of pulmonary congestion abate. Such patients with mild-to-moderate mitral regurgitation may remain without symptoms for several years with very little hemodynamic compromise. This compensated phase of mitral regurgitation is variable and in many cases can last several years. However, the prolonged burden of volume overloads may eventually result in left ventricular dysfunction. At this time, contractile dysfunction impairs myocardial ejection and end-systolic volume increases; there may also be further left ventricular dilatations and increased left ventricular filling pressures. Therefore, correction of mitral regurgitation is generally recommended shortly following the diagnosis of severe mitral regurgitation, irrespective of the presence or absence of symptoms.

The initial diagnosis of chronic mitral regurgitation is commonly accomplished by physical examination which may demonstrate findings of left ventricular apical impulse displacement, indicating that the mitral regurgitation is severe and chronic and has likely caused cardiac enlargement. Typically, ECG and chest X-ray can be useful to evaluate rhythm changes and heart size, respectively. Nevertheless, an initial echocardiogram, including Doppler interrogation of the mitral valve, is considered indispensable for the subsequent management of the patient with mitral regurgitation. Such an echocardiogram typically provides a baseline estimation of left ventricular and left atrial volumes, an estimation of the left ventricular ejection fraction, and an approximation of the severity of regurgitation. Note that any presence of pulmonary hypertension is worrisome because it likely indicates advanced disease with a worsened prognosis [76]. Serial clinical follow-ups are used to assess changes in symptomatic status, left ventricular function, and/or exercise tolerance. Annual echocardiography is also recommended once patients elicit a moderate mitral regurgitation.

Left ventricular end-systolic dimensions (or volumes) can typically aid in the planned timing for mitral valve surgery. For example, an end-systolic dimension, which may be less load-dependent than ejection fraction, should be <45 mm preoperatively to ensure normal postoperative left ventricular function [75, 77]. If patients become symptomatic, they should undergo mitral valve surgery even if left ventricular function is considered appropriately normal. Similar to acute mitral regurgitation, cardiac catheterization is considered indicated if: (1) there is discrepancy between clinical and noninvasive findings; (2) there is a need for preoperative coronary assessment for potential revascularization at the time of mitral valve replacement; and/or (3) an absence of chamber enlargement raises the question of the accuracy of the diagnosis, which should then be assessed with ventriculography at cardiac catheterization.

To date, there is no generally accepted therapy for asymptomatic patients with chronic mitral regurgitation. In such patients who develop symptoms, but have preserved left ventricular function, surgery is considered as the most appropriate therapy. Atrial fibrillation is commonly associated with mitral regurgitation, and preoperative atrial fibrillation can be an independent predictor of reduced long-term survival after mitral valve surgery for chronic mitral regurgitation [78]. Atrial fibrillation should be treated with heart rate control (digitalis, calcium channel blockers, beta-blockers, or amiodarone) and anticoagulation to avoid embolism [79, 80]. Common predictors for the persistence of atrial fibrillation after successful valve surgery include the presence of atrial fibrillation for >1 year and/or a left atrial size >50 mm [81]. Although patients who develop atrial fibrillation also usually manifest other symptomatic or functional changes that would warrant mitral valve repair or replacement, today many clinicians would also consider the onset of episodic or chronic atrial fibrillation to be an indication, in and of itself, for valvular surgery [82, 83].

To date, three categories of surgical procedures are now in vogue for correction of mitral regurgitation: (1) mitral valve repair; (2) mitral valve replacement with preservation of part or all of the mitral apparatus; and (3) mitral valve replacement with prior removal of the mitral apparatus. Each procedure has its advantages and disadvantages, as well as separate indications. Still today, with the appropriate valve morphology and sufficient surgical expertise, mitral valve repair is the operation of choice. Yet, valve repair may require longer extracorporeal circulation time and may also occasionally fail, then again requiring mitral valve replacement. Valve calcification, rheumatic involvement, and anterior leaflet involvement all decrease the likelihood of an adequate repair, whereas uncalcified posterior leaflet disease is almost always repairable. The primary advantage of repair is the avoidance of anticoagulation and/or a rare prosthetic valve failure. In addition, postoperative left ventricular function and survival are improved with preservation of the mitral apparatus, as the mitral apparatus is considered essential for maintenance of normal left ventricular chamber shape, volume, and function [7]. Similar advantages are gleaned with the use of mitral valve replacement with preservation of the mitral chordal apparatus, except that it adds both the risk of deterioration inherent in tissue valves and the need for anticoagulation with mechanical valves. It is generally considered today that mitral valve replacement, in which the mitral valve apparatus is excised, should be performed only in circumstances when the native valve and apparatus are so distorted by the preoperative pathology (rheumatic disease, for example) that the mitral apparatus cannot be spared.

In an asymptomatic patient with normal left ventricular function, repair of a severely regurgitant valve may be offered as a means to: (1) preserve left ventricular size and function; and/or (2) prevent the sequelae of chronic mitral regurgitation (Fig. 34.12). Similarly, this approach has proven successful in the hemodynamically stable patient with newly acquired severe mitral regurgitation as the result of a ruptured chordae or recent onset of atrial fibrillation. The timing of surgery in asymptomatic patients is indicated by the appearance of echocardiographic indicators of left ventricular dysfunction (i.e., left ventricular ejection fraction <60 % or left ventricular end-systolic dimension >45 mm). Mitral valve repair or replacement at this stage will likely prevent further deterioration in left ventricular function and thus improve overall survival [78]. Patients with symptoms of congestive heart failure, despite normal left ventricular function, as determined by echocardiography (ejection fraction >60 %, end-systolic dimension <45 mm), will likely require surgery. In both situations, mitral repair is preferred when possible. Mitral valve surgery is recommended for severe symptomatic mitral regurgitation with evidence of left ventricular systolic dysfunction; it is likely to both improve symptoms and prevent further deterioration of left ventricular function [84].

Ischemic mitral regurgitation is, by common definition, caused by left ventricular myocardial infarction, resulting in an associated papillary muscle dysfunction. The prognosis for such a patient with ischemic mitral regurgitation is substantially worse when compared with other etiologies [71, 85]. Following an acute infarction with the development of severe mitral regurgitation, hypotension and pulmonary edema often also occur. Hemodynamic stabilization, usually with insertion of an intraaortic balloon pump, is completed preoperatively followed by coronary revascularization; note that this only rarely improves mitral valve function. Unlike the case with nonischemic mitral regurgitation, it is more difficult to demonstrate a benefit of repair over replacement with ischemic mitral regurgitation. In general, operative mortality increases and survival is reduced in patients >75 years of age with coronary artery disease, especially if mitral valve

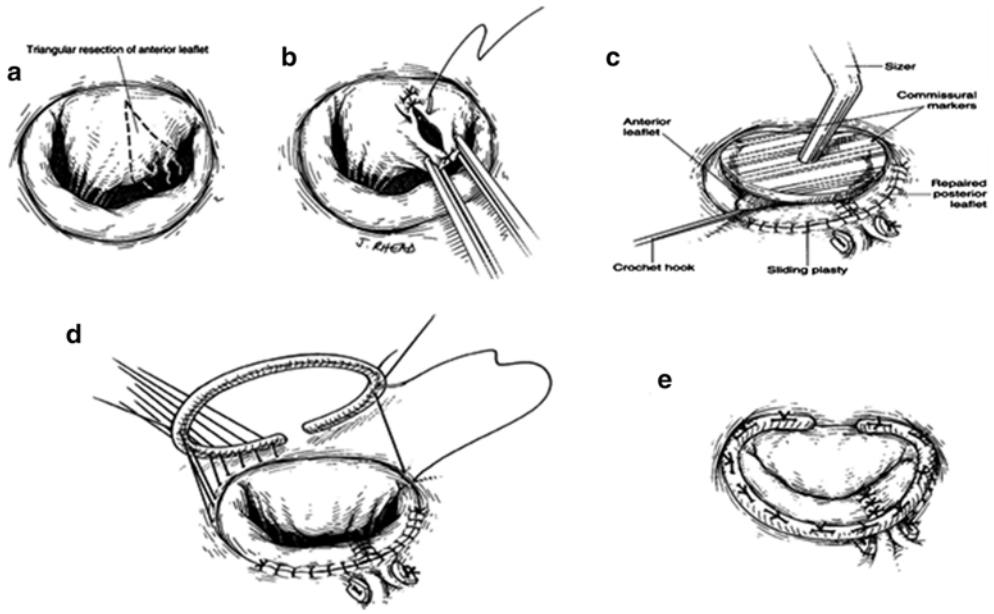

Fig. 34.12 Operative repair of the mitral valve using a technique developed by Carpentier. (**a**) Triangular resection of anterior leaflet; (**b**) Anterior leaflet repair; (**c**) Sizing of annulus; (**d**) Annuplasty ring suture technique; and (**e**) Completed repair. Adapted from Kirklin JW (2003) Cardiac surgery, 3rd edn. Churchill Livingstone, New York, pp 673–675

replacement must be performed [86]. In these patients, the goal of therapy is typically to improve the quality of life rather than prolong it, and medical therapy may be utilized to a greater extent to control cardiac symptoms.

34.3.3 Tricuspid Valve Disease

Tricuspid valve disease can be subclassified as regurgitation, stenosis, or a combination of both; it is most commonly the result of rheumatic fever, with rare cases attributed to infective endocarditis, congenital anomalies, carcinoid, Fabry's disease, Whipple's disease, or methysergide therapy [7]. Rheumatic tricuspid disease commonly presents as a combination of tricuspid stenosis and regurgitation. Furthermore, tricuspid disease commonly presents with concomitant mitral or aortic valve defects since acute rheumatic fever is also a common etiology for these disorders. It should be noted that right atrial myxomas or any type of large vegetations that produce an outflow tract obstruction will mimic tricuspid stenosis; however, regurgitation may also result, as it often causes associated damage to the leaflet apparatus. Pure tricuspid regurgitation may result from rheumatic fever, infective endocarditis, carcinoid syndrome, rheumatoid arthritis, radiation therapy, anorectic drugs, trauma, Marfan's syndrome, tricuspid valve prolapse, papillary muscle dysfunction, and/or congenital disorders [7]. In addition, pressure/volume overload conditions that do not cause direct damage to the leaflets themselves, such as those associated mitral stenosis and mitral regurgitation, typically cause ventricular enlargement, resultant tricuspid annular dilatation, and thus a sole tricuspid regurgitation [7].

The clinical features of tricuspid stenosis include auscultation of a tricuspid opening snap and a characteristic murmur. Auscultation may reveal a holosystolic murmur in the lower left parasternal region that may increase on inspiration (Carvallo's sign; see also Chap. 18). In rare instances, severe tricuspid regurgitation may produce systolic propulsion of the eyeballs, pulsatile varicose veins, or a venous systolic thrill and detectable murmur in the neck. Echocardiography is commonly used to: (1) assess tricuspid valve structure and function; (2) measure annular sizes; (3) evaluate right pressures; and (4) rule out other abnormalities influencing tricuspid valve function. Systolic pulmonary artery pressure estimations, combined with information about annular circumferences, further improve the accuracy of clinical assessments [7].

The etiology of tricuspid valve disease and the overall condition of the patient ultimately dictate the therapeutic approach. Tricuspid balloon valvotomy can be used to treat tricuspid stenosis, however one must be aware of the potential for subsequently inducing severe tricuspid regurgitation. It has been documented that a poor long-term outcome is associated with right ventricular dysfunction and/or systemic venous congestion associated with severe tricuspid regurgitation [7]. In the situation where pulmonary hypertension is the underlying cause of tricuspid annular dilatation, medical management alone may result in substantial improvement of the tricuspid regurgitation, and thus minimize the need for surgical intervention. Surgical options for treating tricuspid regurgitation include valve repair or valve replacement (Fig. 34.13).

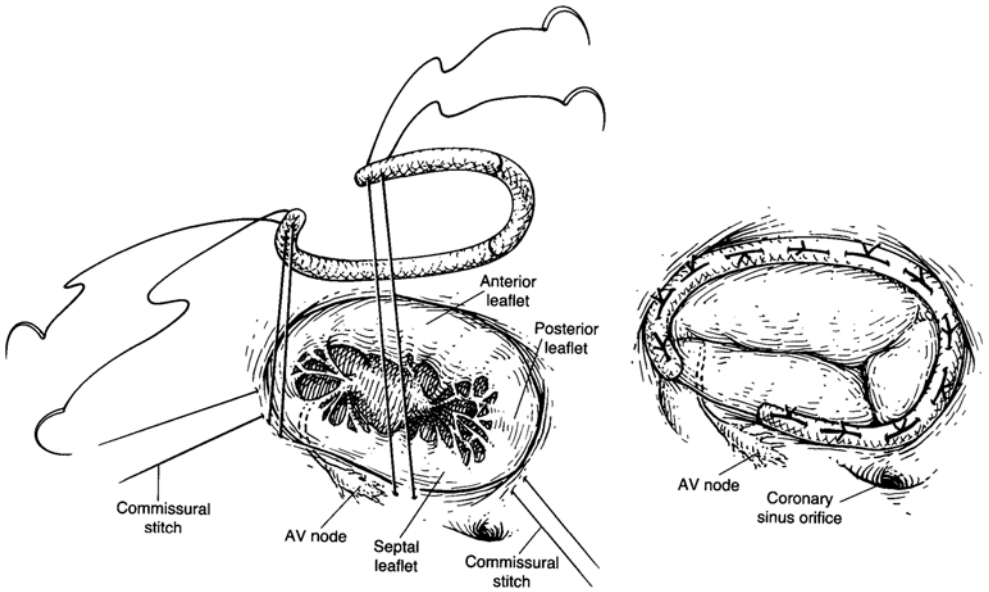

Fig. 34.13 Tricuspid annuloplasty procedure

Today in the United States, the vast majority of diseased tricuspid valves are repaired. The basic techniques for tricuspid valve repair include bicuspidization, annular placation, and various types of annuloplasty, commonly using artificial rings. Tricuspid regurgitation annuloplasty is effective and can be optimized using intraoperative transesophageal echocardiography. Valve replacement with a low profile mechanical valve or bioprosthesis is often necessary when the valve leaflets themselves are diseased, abnormal, or totally destroyed [87]. In both procedures, care must be taken to avoid causing damage to the heart's conduction system. In such cases, use of biological prostheses is preferred to avoid the high rate of thromboembolic complications known to occur with mechanical prostheses placed in the tricuspid position. Combined tricuspid and mitral valve procedures are often completed in the same interventions, as in the setting of rheumatic disease; however, to date, no long-term data regarding the value of such an approach exist. There is an increasing awareness of the importance of correcting tricuspid valve disease in the setting of associated cardiac diseases, most commonly mitral valve disease. In patients with associated conduction defects, insertion of a pacing system at the time of valve replacement is also suggested.

34.4 Summary

The use of cross-circulation followed by the development of the bubble oxygenator for cardiopulmonary bypass was the turning point in the history of cardiac surgery. However, cardiac valvular surgery may be considered to still be in its infancy, with most of the major developments occurring only in the last 50 years. Tremendous advances in the field of cardiac surgery are certain to result from the numerous ongoing efforts of researchers and clinicians alike. This chapter was designed to give the reader an introduction to the complex nature of valve diseases. Several excellent textbooks have been written that provide greater detail for each valve procedure discussed. Such reference texts are valuable for both the clinician and the engineer interested in understanding the underlying etiologies and the current treatment techniques for these diseases. In other words, this basis of understanding, along with the use of further animal and clinical research, will allow for the development of the next generation of treatment options for heart valve disease. The reader is also referred to Chaps. 35 and 37. These topics will have a dramatic impact in this field into the future.

References

1. Miller GW (ed) (2000) King of hearts. Times Books, New York
2. Bolman RM 3rd, Black SM (2003) Open cardiac repair under direct vision: F. John Lewis and the University of Minnesota. J Card Surg 18:328–332, discussion 333
3. Lewis RP, Herr RH, Starr A, Griswold HE (1966) Aortic valve replacement with the Starr-Edwards ball-valve prosthesis. Indications and results. Am Heart J 71:549–563
4. Lillehei CW, Kaster RL, Coleman M, Bloch JH (1974) Heart-valve replacement with Lillehei-Kaster pivoting disk prosthesis. N Y State J Med 74:1426–1438
5. Lillehei CW, Kaster RL, Bloch JH (1972) New central flow pivoting disk aortic and mitral prosthesis. Clinical experience. N Y State J Med 72:1738
6. Emery RW, Palmquist WE, Mettler E, Nicoloff DM (1978) A new cardiac valve prosthesis: in vitro results. Trans Am Soc Artif Intern Organs 24:550–556

7. Bonow RO, Carabello BA, Kanu C et al (2006) ACC/AHA guidelines for the management of patients with valvular heart disease. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Circulation 114: e84–e234
8. Nishimura RA, Otto CM, Bonow RO et al (2014) 2014 AHA/ACC guideline for the management of patients with valvular heart disease: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 63:2438–2488
9. El Oakley R, Kleine P, Bach DS (2008) Choice of prosthetic heart valve in today's practice. Circulation 117:253–256
10. Oxenham H, Bloomfield P, Wheatley DJ et al (2003) Twenty year comparison of a Bjork-Shiley mechanical heart valve with porcine bioprosthesis. Heart 89:715–721
11. Hammermeister K, Sethi GK, Henderson WG, Grover FL, Oprian C, Rahimtoola SH (2000) Outcomes 15 years after valve replacement with a mechanical versus a bioprosthetic valve: final report of the Veterans Affairs randomized trial. J Am Coll Cardiol 36: 1152–1158
12. Lund O, Bland M (2006) Risk-corrected impact of mechanical versus bioprosthetic valves on long-term mortality after aortic valve replacement. J Thorac Cardiovasc Surg 131:1267–1273
13. Bach DS, Metras J, Doty JR, Yun KL, Dumesnil JG, Kon ND (2008) Freedom from structural valve deterioration among patients 60 years of age and younger undergoing Freestyle aortic valve replacement. J Heart Valve Dis 16:649–655
14. Pibarot P, Dumesnil JG (2009) Prosthetic heart valves: selection of the optimal prosthesis and long-term management. Circulation 119:1034–1048
15. Edmunds LH Jr, Clark RE, Cohn LH, Grunkemeier GL, Miller DC, Weisel RD (1996) Guidelines for reporting morbidity and mortality after cardiac valvular operations. Thorac Cardiovasc Surg 112: 708–711
16. Cheitlin MD, Douglas PS, Parmley WW (1994) 26th Bethesda conference: recommendations for determining eligibility for competition in athletes with cardiovascular abnormalities. Task Force 2: Acquired valvular heart disease. J Am Coll Cardiol 24:874–880
17. Carabello BA (2002) Aortic stenosis. N Engl J Med 346:677–682
18. Freeman RV, Otto CM (2005) Spectrum of calcific aortic valve disease: pathogenesis, disease progression, and treatment strategies. Circulation 111:3316–3326
19. Otto CM, Pearlman AS, Kraft CD, Miyake-Hull CY, Burwash IG, Gardner CJ (1992) Physiologic changes with maximal exercise in asymptomatic valvular aortic stenosis assessed by Doppler echocardiography. J Am Coll Cardiol 20:1160–1167
20. Krayenbuehl HP, Hess OM, Ritter M, Monrad ES, Hoppeler H (1988) Left ventricular systolic function in aortic stenosis. Eur Heart J 9:E19–E23
21. Marcus ML, Doty DB, Hiratzka LF, Wright CB, Eastham CL (1982) Decreased coronary reserve: a mechanism for angina pectoris in patients with aortic stenosis and normal coronary arteries. N Engl J Med 307:1362–1366
22. Bache RJ, Vrobel TR, Ring WS, Emery RW, Andersen RW (1981) Regional myocardial blood flow during exercise in dogs with chronic left ventricular hypertrophy. Circ Res 48:76–87
23. Koyanagi S, Eastham C, Marcus ML (1982) Effects of chronic hypertension and left ventricular hypertrophy on the incidence of sudden cardiac death after coronary artery occlusion in conscious dogs. Circulation 65:1192–1197
24. Ross J Jr, Braunwald E (1968) Aortic stenosis. Circulation 38:61–67
25. Schwarz F, Baumann P, Manthey J et al (1982) The effect of aortic valve replacement on survival. Circulation 66:1105–1110
26. Sprigings DC, Forfar JC (1995) How should we manage symptomatic aortic stenosis in the patient who is 80 or older? Br Heart J 74:481–484
27. Horstkotte D, Loogen F (1988) The natural history of aortic valve stenosis. Eur Heart J 9:E57–E64
28. Iivanainen AM, Lindroos M, Tilvis R, Heikkila J, Kupari M (1996) Natural history of aortic valve stenosis of varying severity in the elderly. Am J Cardiol 78:97–101
29. Kelly TA, Rothbart RM, Cooper CM, Kaiser DL, Smucker ML, Gibson RS (1988) Comparison of outcome of asymptomatic to symptomatic patients older than 20 years of age with valvular aortic stenosis. Am J Cardiol 61:123–130
30. Cheitlin MD, Alpert JS, Armstrong WF et al (1997) ACC/AHA guidelines for the clinical application of echocardiography. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on Clinical Application of Echocardiography). Circulation 95:1686–1744
31. Rosenhek R, Rader F, Loho N et al (2004) Statins but not angiotensin-converting enzyme inhibitors delay progression of aortic stenosis. Circulation 10:1291–1295
32. Rajamannan NM, Otto CM (2004) Targeted therapy to prevent progression of calcific aortic stenosis. Circulation 110:1180–1182
33. McKay RG, Safian RD, Lock JE et al (1986) Balloon dilatation of calcific aortic stenosis in elderly patients: postmortem, intraoperative, and percutaneous valvuloplasty studies. Circulation 74:119–125
34. Safian RD, Mandell VS, Thurer RE et al (1998) Postmortem and intraoperative balloon valvuloplasty of calcific aortic stenosis in elderly patients: mechanisms of successful dilation. J Am Coll Cardiol 9:655–660
35. Tsai TP, Denton TA, Chaux A et al (1994) Results of coronary artery bypass grafting and/or aortic or mitral valve operation in patients > or = 90 years of age. Am J Cardiol 74:960–962
36. Smith N, McAnulty JH, Rahimtoola SH (1978) Severe aortic stenosis with impaired left ventricular function and clinical heart failure: results of valve replacement. Circulation 58:255–264
37. Connolly HM, Oh JK, Orszulak TA et al (1997) Aortic valve replacement for aortic stenosis with severe left ventricular dysfunction. Prognostic indicators. Circulation 95:2395–2400
38. Makkar RR, Fontana GP, Jilaihawi H et al (2012) Transcatheter aortic-valve replacement for inoperable severe aortic stenosis. N Engl J Med 366:1696–1704
39. Smith CR, Leon MB, Mack MJ et al (2011) Transcatheter versus surgical aortic-valve replacement in high-risk patients. N Engl J Med 364:2187–2198
40. Monin JL, Monchi M, Gest V, Duval-Moulin AM, Dubois-Rande JL, Gueret P (2001) Aortic stenosis with severe left ventricular dysfunction and low transvalvular pressure gradients: risk stratification by low-dose dobutamine echocardiography. J Am Coll Cardiol 37:2101–2107
41. Grossman W, Jones D, McLaurin LP (1975) Wall stress and patterns of hypertrophy in the human left ventricle. J Clin Invest 56:56–64
42. Nitenberg A, Foult JM, Antony I, Blanchet F, Rahali M (1988) Coronary flow and resistance reserve in patients with chronic aortic regurgitation, angina pectoris and normal coronary arteries. J Am Coll Cardiol 11:478–486
43. Fortuin NJ, Craige E (1972) On the mechanism of the Austin Flint murmur. Circulation 45:558–570
44. Parker E, Craige E, Hood WP Jr (1971) The Austin Flint murmur and the A wave of the apexcardiogram in aortic regurgitation. Circulation 43:349–359
45. Miller RR, Vismara LA, DeMaria AN, Salel AF, Mason DT (1976) Afterload reduction therapy with nitroprusside in severe aortic regurgitation: improved cardiac performance and reduced regurgitant volume. Am J Cardiol 38:564–567

46. Smith MD, Cassidy JM, Souther S et al (1995) Transesophageal echocardiography in the diagnosis of traumatic rupture of the aorta. N Engl J Med 332:356–362
47. Cigarroa JE, Isselbacher EM, DeSanctis RW, Eagle KA (1993) Diagnostic imaging in the evaluation of suspected aortic dissection. Old standards and new directions. N Engl J Med 328:35–43
48. Yacoub MH et al (1983) Results of valve sparing operations for aortic regurgitation. Circulation 68:311–321
49. David TE (2001) Aortic valve-sparing operations for aortic root aneurysm. Semin Thorac Cardiovasc Surg 13:291–296
50. Gorlin R, Gorlin S (1951) Hydraulic formula for calculation of the area of stenotic mitral valve, other cardiac values and central circulatory shunts. Am Heart J 41:1–29
51. Rowe JC, Bland EF, Sprague HB, White PD (1960) The course of mitral stenosis without surgery: ten- and twenty-year perspectives. Ann Intern Med 52:741–749
52. Wood P (1954) An appreciation of mitral stenosis. I. Clinical features. Br Med J 4870:1051–1063
53. Edwards JE, Rusted IE, Scheifley CH (1956) Studies of the mitral valve. II. Certain anatomic features of the mitral valve and associated structures in mitral stenosis. Circulation 14:398–406
54. Roberts WC, Perloff JK (1972) Mitral valvular disease. A clinicopathologic survey of the conditions causing the mitral valve to function abnormally. Ann Intern Med 77:939–975
55. Olesen KH (1962) The natural history of 271 patients with mitral stenosis under medical treatment. Br Heart J 24:349–357
56. Carroll JD, Feldman T (1993) Percutaneous mitral balloon valvotomy and the new demographics of mitral stenosis. JAMA 270:1731–1736
57. Selzer A, Cohn KE (1972) Natural history of mitral stenosis: a review. Circulation 45:878–890
58. Hugenholtz PG, Ryan TJ, Stein SW, Abelmann WH (1962) The spectrum of pure mitral stenosis. Hemodynamic studies in relation to clinical disability. Am J Cardiol 10:773–784
59. Braunwald E, Moscovitz HL, Amram SS et al (1955) The hemodynamics of the left side of the heart as studied by simultaneous left atrial, left ventricular, and aortic pressures; particular reference to mitral stenosis. Circulation 12:69–81
60. Holen J, Aaslid R, Landmark K, Simonsen S (1976) Determination of pressure gradient in mitral stenosis with a non-invasive ultrasound Doppler technique. Acta Med Scand 199:455–460
61. Hatle L, Brubakk A, Tromsdal A, Angelsen B (1978) Noninvasive assessment of pressure drop in mitral stenosis by Doppler ultrasound. Br Heart J 40:131–140
62. Currie PJ, Seward JB, Chan KL et al (1985) Continuous wave Doppler determination of right ventricular pressure: a simultaneous Doppler-catheterization study in 127 patients. J Am Coll Cardiol 6:750–756
63. Coulshed N, Epstein EJ, McKendrick CS, Galloway RW, Walker E (1970) Systemic embolism in mitral valve disease. Br Heart J 32:26–34
64. Daley R, Mattingly TW, Holt CL, Bland EF, White PD (1951) Systemic arterial embolism in rheumatic heart disease. Am Heart J 42:566
65. Abernathy WS, Willis PW 3rd (1973) Thromboembolic complications of rheumatic heart disease. Cardiovasc Clin 5:131–175
66. Adams GF, Merrett JD, Hutchinson WM, Pollock AM (1974) Cerebral embolism and mitral stenosis: survival with and without anticoagulants. J Neurol Neurosurg Psychiatry 37:378–383
67. Orrange SE, Kawanishi DT, Lopez BM, Curry SM, Rahimtoola SH (1997) Actuarial outcome after catheter balloon commissurotomy in patients with mitral stenosis. Circulation 95:382–389
68. Higgs LM, Glancy DL, O'Brien KP, Epstein SE, Morrow AG (1970) Mitral restenosis: an uncommon cause of recurrent symptoms following mitral commissurotomy. Am J Cardiol 26:34–37
69. Dahl JC, Winchell P, Borden CW (1967) Mitral stenosis. A long term postoperative follow-up. Arch Intern Med 119:92–97
70. Cohn LH, Couper GS, Kinchla NM, Collins JJ Jr (1990) Decreased operative risk of surgical treatment of mitral regurgitation with or without coronary artery disease. J Am Coll Cardiol 16:1575–1578
71. Connolly MW, Gelbfish JS, Jacobowitz IJ et al (1986) Surgical results for mitral regurgitation from coronary artery disease. J Thorac Cardiovasc Surg 91:379–388
72. Chatterjee K, Parmley WW, Swan HJ, Berman G, Forrester J, Marcus HS (1973) Beneficial effects of vasodilator agents in severe mitral regurgitation due to dysfunction of subvalvar apparatus. Circulation 48:684–690
73. Yoran C, Yellin EL, Becker RM, Gabbay S, Frater RW, Sonnenblick EH (1979) Mechanism of reduction of mitral regurgitation with vasodilator therapy. Am J Cardiol 43:773–777
74. Carabello BA (1988) Mitral regurgitation: basic pathophysiologic principles. Part 1. Mod Concepts Cardiovasc Dis 57:53–58
75. Zile MR, Gaasch WH, Carroll JD, Levine HJ (1984) Chronic mitral regurgitation: predictive value of preoperative echocardiographic indexes of left ventricular function and wall stress. J Am Coll Cardiol 3:235–242
76. Crawford MH, Souchek J, Oprian CA et al (1990) Determinants of survival and left ventricular performance after mitral valve replacement. Department of Veterans Affairs Cooperative Study on Valvular Heart Disease. Circulation 81:1173–1181
77. Wisenbaugh T, Skudicky D, Sareli P (1994) Prediction of outcome after valve replacement for rheumatic mitral regurgitation in the era of chordal preservation. Circulation 89:191–197
78. Enriquez-Sarano M, Tajik AJ, Schaff HV, Orszulak TA, Bailey KR, Frye RL (1994) Echocardiographic prediction of survival after surgical correction of organic mitral regurgitation. Circulation 90:830–837
79. Blackshear JL, Pearce LA, Asinger RW et al (1993) Mitral regurgitation associated with reduced thromboembolic events in high-risk patients with nonrheumatic atrial fibrillation. Am J Cardiol 72: 840–843
80. Beppu S, Nimura Y, Sakakibara H, Nagata S, Park YD, Izumi S (1985) Smoke-like echo in the left atrial cavity in mitral valve disease: its features and significance. J Am Coll Cardiol 6:744–749
81. Betriu A, Chaitman BR (1982) Preoperative determinants of return to sinus rhythm after valve replacement. In: Cohn LH, Gallucci V (eds) Cardiac bioprosthesis. Yorke Medical Books, New York, pp 184–191
82. Chua YL, Schaff HV, Orszulak TA, Morris JJ (1994) Outcome of mitral valve repair in patients with preoperative atrial fibrillation. Should the maze procedure be combined with mitral valvuloplasty? J Thorac Cardiovasc Surg 107:408–415
83. Horskotte D, Schulte HD, Bircks W, Strauer BE (1993) The effect of chordal preservation on late outcome after mitral valve replacement: a randomized study. J Heart Valve Dis 2:150–158
84. Bonow RO, Nikas D, Elefteriades JA (1995) Valve replacement for regurgitant lesions of the aortic or mitral valve in advanced left ventricular dysfunction. Cardiol Clin 13(73-83):85
85. Akins CW, Hilgenberg AD, Buckley MJ et al (1994) Mitral valve reconstruction versus replacement for degenerative or ischemic mitral regurgitation. Ann Thorac Surg 58:668–675, discussion 675–676
86. Enriquez-Sarano M, Schaff HV, Orszulak TA, Tajik AJ, Bailey KR, Frye RL (1995) Valve repair improves the outcome of surgery for mitral regurgitation. A multivariate analysis. Circulation 91:1022–1028
87. Silverman N (1998) Tricuspid valve. In: Kaiser K (ed) Mastery of cardiac surgery. Lippincott-Raven, Philadelphia, pp 354–360