PROSTHETIC HEART VALVES

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I have had a longstanding (> 30 year) interest in patients with several forms of heart disease, including those with valvular disease. As a result, I have had a strong interest (and extensive experience) in dealing with various prosthetic heart valves.

It is estimated that 60,000 to 75,000 valve replacements are performed annually in the United States. General internists often provide ongoing care for these patients, and internal medicine subspecialists in fields other than cardiology often participate in their care as well. My purpose today is to provide an overview of commonly encountered prosthetic valves, hoping to shed light on (a) their basic characteristics, including each type's major advantages and limitations, with special attention to the need for chronic antithrombotic therapy; (b) their normal manifestations on physical examination, with particular attention to their auscultatory characteristics; and (c) the occurrence, recognition, and management of potential complications [1].

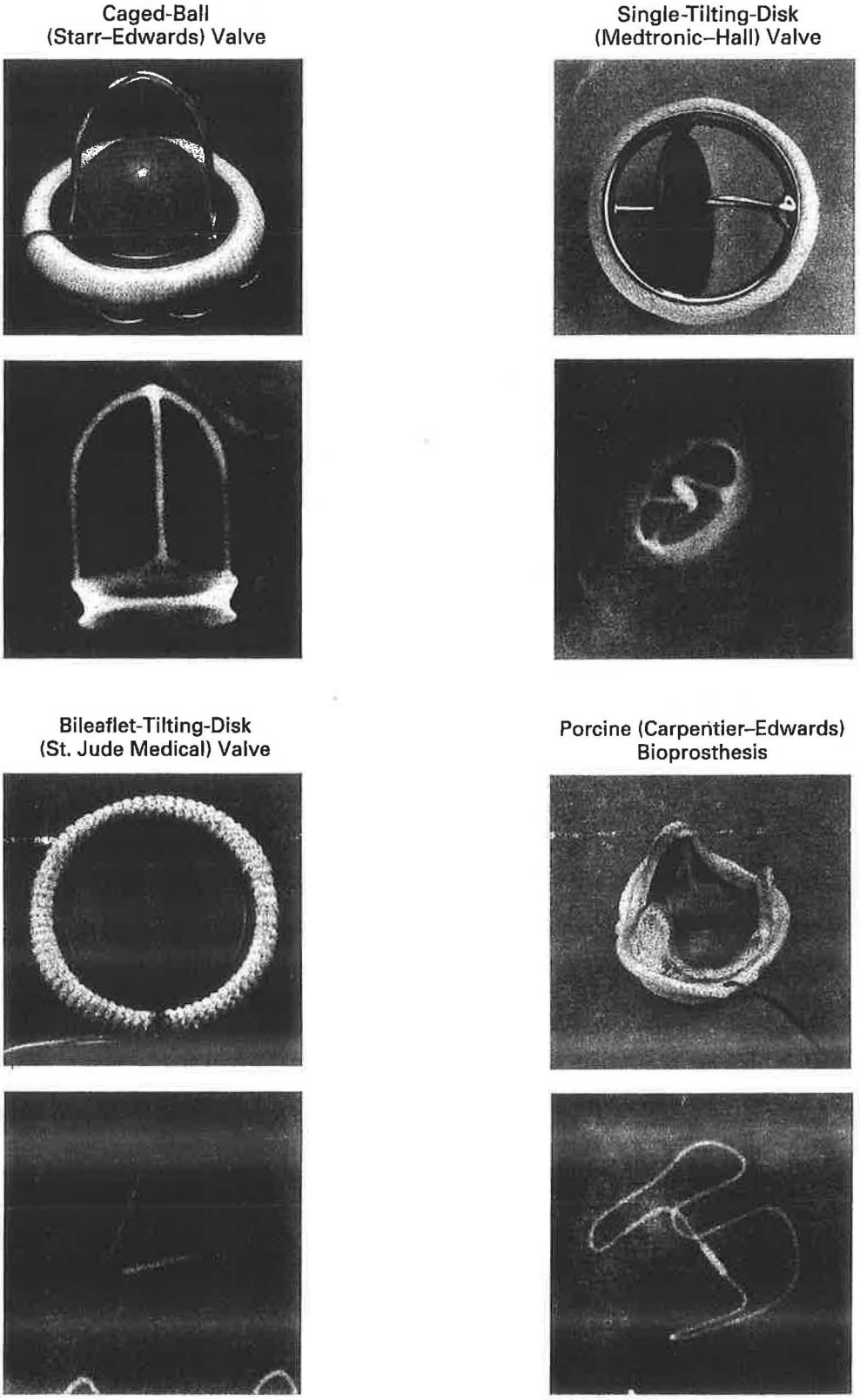
CHARACTERISTICS OF PROSTHETIC VALVES

The first successful replacements of cardiac valves in humans were accomplished in 1960 by Nina Braunwald and colleagues [2], Harken and coworkers [3], and Starr and Edwards [4]. Subsequently, although at least 80 models of prosthetic valves have been developed and implanted, it is reasonable to categorize them as (a) bioprostheses (i.e., tissue prostheses), which may be heterografts (composed of porcine or bovine tissue, which may or may not be mounted on a metal support) or homografts (fresh or preserved human aortic valves); or (b) mechanical valves, which are composed primarily of metal or carbon alloys and which may be ball-in-cage or tilting disc in design and structure. Displayed in Table 1 (below) and shown in Figure 1(next page) are the most commonly implanted prosthetic valves and their respective brand names. Those that are italicized are the most commonly used here at UT Southwestern.

Table 1: Most Commonly Used Prosthetic Heart Valves

Type	Brand Name
Porcine heterograft: stented	*Hancock* *Carpentier-Edwards*
Porcine heterograft: stentless	Medtronic freestyle Edwards prima St. Jude Toronto SPV
Ball-in-Cage	Starr-Edwards
Single Tilting Disc	*Medtronic-Hall* Omniscience
Bileaflet Tilting Disc	*St. Jude* CarboMedics

Figure 1: Photographs (top panels) and radiographs (bottom panels) of the most commonly used prosthetic valves (From reference # 1)



In assessing the "pluses" and "minuses" of each prosthetic valve, one should consider 3 characteristics: (a) durability or longevity (i.e., how many years are likely to elapse before the patient needs a repeat valve replacement?), (b) thrombogenicity (i.e., will the patient require chronic warfarin therapy and, if so, how intensively?), and (c) hemodynamic "profile" or "effective orifice area" (i.e., once the prosthesis is in place and working normally, how large will the orifice be when the valve is open?). Displayed in Tables 2 and 3 (below) are the characteristics of each type of prosthetic valve in accordance with the 3 aforementioned variables.

Table 2: Characteristics of Various Prosthetic Valves

Valve Type	Durability	Thrombogenicity		Effective Orifice Area	
	mean time to failure	warfarin?	aspirin?	aortic	mitral
BIOPROSTHESES					
Heterograft (porcine)	10-15 yrs	1-3 mos	*	1.0-1.6	1.5-2.7
Homograft	10-15 yrs	no	*	3.0-4.0	NA
MECHANICAL PROSTHESES					
Ball-in-cage	> 40 yrs	yes	*	1.2-1.6	1.4-3.0
Tilting Disc					
Single	> 30 yrs	yes	*	1.5-2.1	1.9-3.2
Bileaflet	> 24 yrs	yes	*	2.4-3.2	2.8-3.4
NORMAL	a lifetime!	no	*	3.0-4.0	4.0-6.0

* Concomitant aspirin is indicated if the patient has (a) atrial fibrillation, (b) previous systemic embolization, (c) a left atrial thrombus, or (d) severe left ventricular systolic dysfunction.

The **stented porcine heterograft prosthesis** has been in widespread use since 1965 [5]. Under sterile conditions, the leaflets from a pig's aortic valve are harvested, preserved in glutaraldehyde, and mounted on semirigid metal struts or "stents." The stented framework facilitates implantation and maintains the 3-dimensional relationship among the leaflets. More recently, **stentless porcine heterograft prostheses** have been

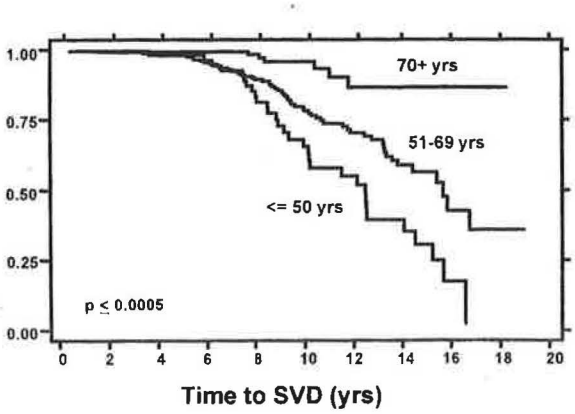
developed. Since the presence of the semirigid metal struts compromises the overall size of the valve orifice, their absence allows the porcine heterograft to have a larger effective orifice area.

Table 3: Characteristics of Various Prosthetic Valves (Simplified)

Valve Type	Durability	Thrombogenicity	Effective Orifice Area
Porcine heterograft	poor	excellent	poor
Ball-in-Cage	excellent	poor	poor
Single tilting disc	excellent	fair	good
Double tilting disc	excellent	fair	very good

The major "minus" of all porcine heterografts (stented or stentless) is their relatively limited durability. Cuspal tears, degeneration, fibrin deposition, disruption of the fibrocollagenous structure, perforation, fibrosis, and calcification often begin to appear within 5 years of implantation. Within 10 years of implantation, roughly 1/3 of them require replacement, and by 15 years a repeat operation is required in about ½. These data are inclusive of all subjects. Importantly, **the rate of structural valve failure is strongly age dependent**: as age increases, the chance of prosthetic valve degeneration and failure decreases. On the one extreme, patients > 70 years of age who undergo aortic valve replacement with a porcine heterograft have a 10% chance of manifesting heterograft structural degeneration within 10 years of the operation. On the other extreme, heterograft prosthetic valve failure occurs in > 40% of subjects who are < 50 years of age within 10 years of the operation (Figure 2, below)[6,7].

Figure 2: Actuarial curves for structural Valve failure in various age groups. From Reference # 7.



The major "plus" of porcine heterografts is freedom from required long-term anticoagulation. During the first 3 months postoperatively, the sewing ring is becoming endothelialized; until this process is complete, the risk of thromboembolism is of sufficient concern that modest anticoagulation is desirable. Subsequently, however,

anticoagulation is not required (unless, of course, it is indicated for another reason [i.e., atrial fibrillation, recent pulmonary embolism, severely depressed left ventricular systolic function, etc]).

Finally, the effective orifice area of stented porcine heterografts is adequate but small in comparison to other prosthetic valves. Relative prosthetic valve stenosis is most often an issue in subjects who undergo aortic valve replacement for aortic stenosis, since these patients sometimes do not have a dilated aortic annulus (as opposed to those with aortic regurgitation, whose annulus is usually dilated). As a result, the insertion of a stented porcine heterograft into a small aortic root may leave the patient with mild or even moderate obstruction. In subjects with a small aortic annulus, a stentless porcine heterograft has a better hemodynamic profile, in that its effective orifice area is substantially larger.

Cryopreserved homograft aortic valves are harvested from cadavers (often along with the kidneys) within 24 hours of the donor's death. They are sterilized with antibiotics and cryopreserved for a long period at –196° C. They are inserted directly, usually in the aortic position, without being mounted on a prosthetic stent. Their overall durability appears to be similar to that of porcine heterografts, with structural deterioration occurring with increasing frequency as time elapses [8]. Their thrombogenicity is low (i.e., no warfarin required), and their hemodynamic profile is excellent (i.e., the effective orifice area, in essence, is that of a normal native valve).

Mechanical prosthetic valves may be classified as (a) ball-in-cage or (b) tilting disc; the latter, in turn, may be single or bileaflet. The **Starr-Edwards ball-in-cage valve** is the oldest prosthetic valve in continuous use, and, therefore, it has the longest record of predictable performance of any. The poppet is made of silicone rubber, the cage of Stellite alloy, and the sewing ring of Teflon/polypropylene cloth. As detailed in Tables 2 and 3 (above), its greatest "plus" is its proven durability: recent manuscripts have noted the 40 year "anniversary" of these valves [9]. Its "minuses" include (a) the need for fairly intensive anticoagulation (Table 4, below), (b) its acceptable, but not optimal, effective orifice area (Table 2), and (c) its bulky cage design (i.e., it is said to be "high profile"). As a result of its bulk, it is not suitable for placement in the mitral position in the patient with a small left ventricular cavity or in the aortic position in the subject with a small aortic root.

Although Starr-Edwards ball-in-cage valves are still used on occasion in this country, their "market share" has steadily declined over the past 10 to 15 years. In developing countries, on the other hand, they are still used frequently, in large part because they cost substantially less than other mechanical valves ($1500 for a ball-in-cage prosthesis, $4500 for a tilting disc prosthesis [10]).

The **single tilting disc prosthetic valve** consists of a pivoting disc mounted in a metal housing with a polyester sewing ring. The **Medtronic-Hall** prosthetic valve has a Teflon sewing ring and a titanium housing, within which is mounted a thin, carbon-coated

Table 4: Recommended anticoagulation for various prosthetic valves in patients without (a) atrial fibrillation, (b) previous systemic embolization, (c) left atrial thrombus, or (d) severe left ventricular systolic dysfunction

Prosthesis	Position	Optimal INR	Aspirin
Ball-in-Cage	aortic	4.0-4.5	no
	mitral	4.5-5.0	no
Single tilting disc	aortic	3.0-3.5	no
	mitral	3.5-4.0	no
Bileaflet tilting disc	aortic	2.0-2.5	no
	mitral	2.5-3.0	no
Porcine	aortic	2.0-2.5	no
(first 3 mos only)	mitral	2.5-3.0	no

pivoting disc. As noted in Tables 2, 3, and 4, its durability is excellent; the first single tilting disc prostheses were placed in the mid-1970s. Warfarin is required, although the intensity of anticoagulation is less than that required for a ball-in-cage prosthesis. Its effective orifice area is good.

The **St. Jude bileaflet valve** presently is the most widely used prosthesis worldwide. The 2 semicircular discs, which are coated with pyrolytic carbon, pivot between the open and closed positions without the need for supporting struts. As a result, it has an excellent hemodynamic profile (i.e., its effective orifice area is large). The first St. Jude was placed in 1982, and thusfar most of those that were implanted at that time are still functioning normally; hence, it appears that durability is excellent. Warfarin is required, but the intensity of anticoagulation is even less than with a single tilting disc (and much less that with a ball-in-cage)(Table 4).

HEAD-TO-HEAD COMPARSIONS OF PROSTHETIC VALVES

Two large randomized trials have compared patient outcomes with a single tilting disc valve and a porcine heterograft. Of particular interest are the results of the Department of Veterans Affairs (DVA) trial [11], in which 575 men requiring single valve replacement (aortic or mitral) at one of 13 VA Medical Centers were randomized to receive a Bjork-Shiley tilting disc valve or a Hancock porcine bioprosthesis. Randomization began in 1977 and ended in 1982, after which the patients were followed long-term. The outcomes after 15 years of follow-up are displayed in Table 5 and Figures 3-7 (below).

As noted previously, structural degeneration and subsequent failure of bioprosthetic valves is age-dependent: as age increases, the chance of prosthetic valve degeneration and failure decreases. As displayed in Figure 7, primary valve failure among the subjects who received an aortic bioprosthesis was uncommon in those ≥ 65 years of age, whereas it was more common in those who were < age 65 years.

In summary, this study suggests that patients undergoing aortic valve replacement had a better survival with a mechanical valve than with a bioprosthetic valve, largely because primary structural failure was virtually absent with mechanical valves. Primary structural failure was confined almost completely to the porcine heterografts; furthermore, it occurred much more often in those < 65 years of age. In fact, in the subjects ≥ 65 years of age, primary valve failure was similar in those receiving mechanical and bioprosthetic valves. Bleeding was much more common in those with mechanical valves.

Table 5: Results of the Veterans Affairs Randomized Trial (from Reference # 11).

Variable	Aortic		Mitral	
	mechanical n = 198	bioprosthesis n = 196	mechanical n = 88	bioprosthesis n = 93
1° valve failure	0%	23%*	5%	44%*
Reoperation	10%	29%*	25%	50%
Bleeding	51%	30%*	53%	31%*
Embolism	18%	18%	18%	22%
Endocarditis	7%	15%	11%	17%
Valve thrombosis	2%	1%	1%	1%
Death (all cause)	66%	79% *	81%	79%

* statistically different from mechanical valve

Figure 1: All cause mortality for AVR and MVR [11]

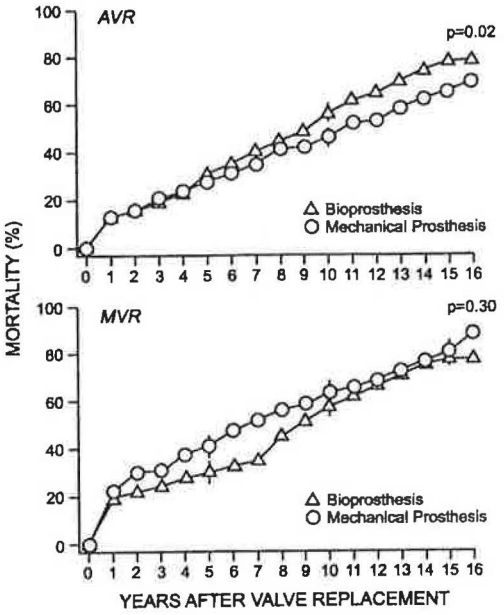


Figure 2: One or more clinically significant bleed(s) [11]

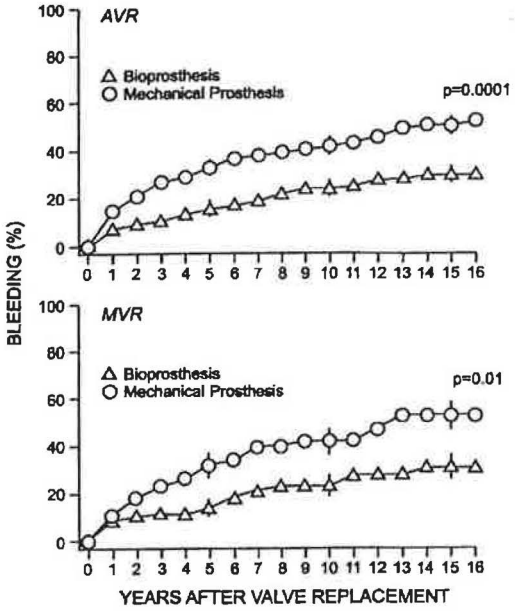


Figure 3: Primary Valve Failure [11]

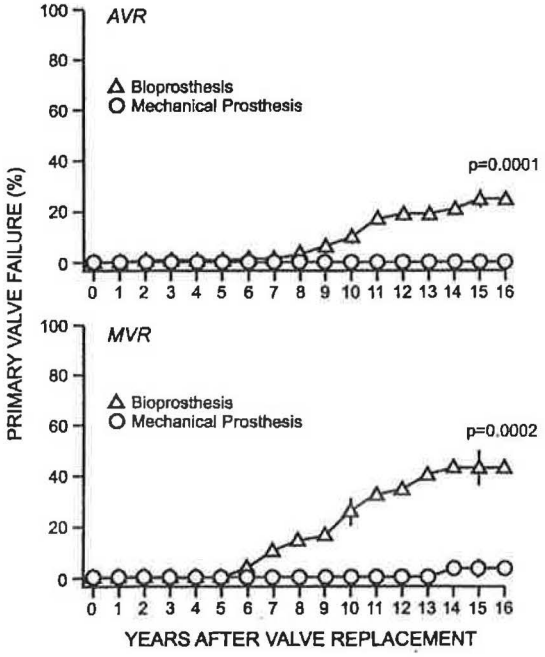
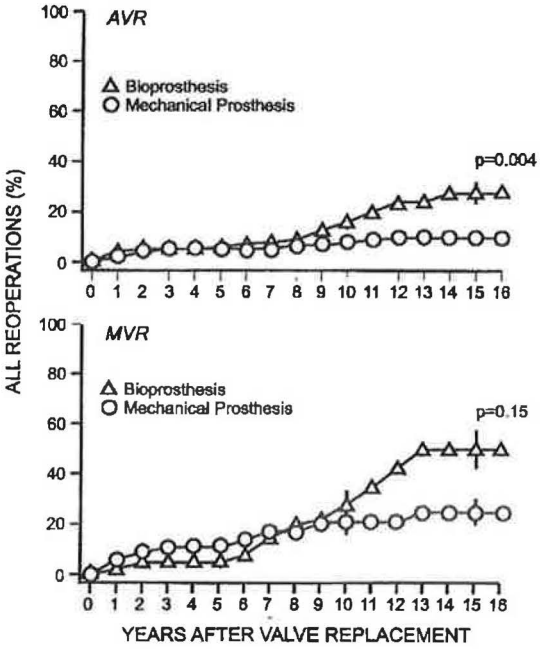


Figure 4: All reoperations [11]



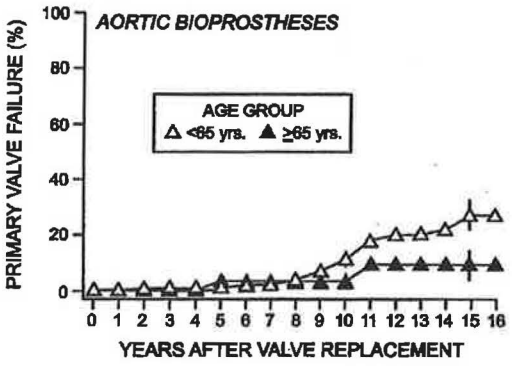


Figure 7 :Primary valve failure among aortic valve replacement patients as a function of age [11].

ASSESSMENT OF PROSTHETIC VALVE FUNCTION

Central to an assessment of prosthetic valve function is an understanding of the normal auscultatory finding for each type in each location (Figure 8 , next page)[1,12]. Valve dysfunction may be suggested by a change in the intensity or quality of a previously audible sound, the appearance of a new murmur, or a change in the characteristics of a preexisting murmur. Mechanical valves produce crisp and high-pitched opening and closing sounds, whereas bioprosthetic valves produce sounds that are similar in quality to those of a native valve. With a ball-in-cage valve, the opening sound is louder than the closing sound; the opposite is true with a tilting disc valve.

In patients in whom prosthetic valve dysfunction is suspected, several imaging methods may be used to assess the function of the valve. **Cinefluoroscopy** is a simple, rapid, inexpensive, and frequently neglected technique for evaluating prosthetic valve function. Although it cannot be used to visualize the leaflets of bioprosthetic valves, it is very useful for assessing the structural integrity of mechanical valves. Diminished motion of the disc or poppet suggests obstruction of the valve from thrombus or ingrowth of tissue, whereas excessive tilt (so-called "rocking") of the base ring is consistent with partial dehiscence of the valve [13].

Two-dimensional transthoracic **echocardiography** (TTE) can be used to assess sewing ring stability and leaflet motion of bioprosthetic valves, but mechanical valves often are difficult to visualize because of intense echo reverberations from the metal (so-called "acoustic shadowing"). Since transesophageal echocardiography (TEE) provides an unobstructed view of the atria and the mitral valve and a higher resolution image than that obtained with TTE [14,15], TEE should be performed in a subject in whom dysfunction of a prosthetic mitral valve is suspected. TEE is limited in its ability to detect aortic prosthetic valve obstruction or regurgitation, especially when a mitral prosthesis is present [16]. The recipient of a prosthetic valve should undergo transthoracic echocardiography before hospital discharge to provide baseline data with

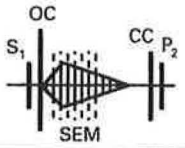
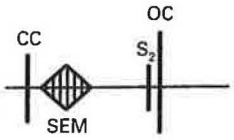
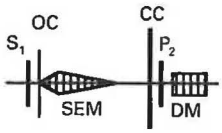
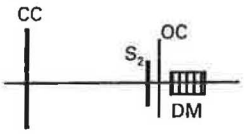
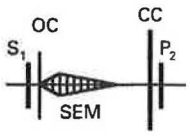
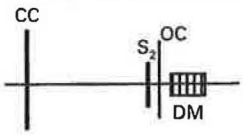
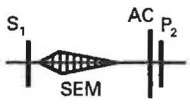
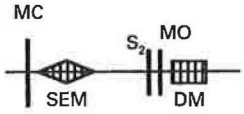
Type of Valve	Aortic Prosthesis		Mitral Prosthesis	
	Normal Findings	Abnormal Findings	Normal Findings	Abnormal Findings
Caged-Ball (Starr–Edwards)		Aortic diastolic murmur Decreased intensity of opening or closing click		Low-frequency apical diastolic murmur High-frequency holosystolic murmur
Single-Tilting-Disk (Bjork–Shiley or Medtronic–Hall)		Decreased intensity of closing click		High-frequency holosystolic murmur Decreased intensity of closing click
Bileaflet-Tilting-Disk (St. Jude Medical)		Aortic diastolic murmur Decreased intensity of closing click		High-frequency holosystolic murmur Decreased intensity of closing click
Heterograft Bioprosthesis (Hancock or Carpentier–Edwards)		Aortic diastolic murmur		High-frequency holosystolic murmur

Fig 8 Auscultatory Characteristics of Various Prosthetic Valves in the Aortic and Mitral Positions, with Schematic Diagrams of Normal Findings and Descriptions of Abnormal Findings.

The caged-ball aortic prosthesis produces a loud opening click (OC) after the first heart sound (S_1) and a less prominent closing click (CC); an early-to-mid-peaking systolic ejection murmur (SEM) is audible, along with multiple systolic clicks (broken lines) of the bouncing poppet within the cage. P_2 denotes the pulmonic component of the second heart sound. The caged-ball mitral prosthesis produces a loud opening click after the second heart sound (S_2). An early-to-mid-systolic ejection murmur, usually loudest at the left sternal border, is caused by turbulent flow in the left ventricular outflow tract. The aortic single-tilting-disk valve has a louder closing click than opening click. An early-to-mid-peaking systolic ejection murmur is usually best heard at the base and often radiates to the carotid arteries. A soft diastolic murmur (DM) may be noted in an occasional patient. The mitral single-tilting-disk valve has a louder closing click than opening click. A low-frequency diastolic rumbling murmur, which represents turbulent flow across the open valve, is usually audible. The aortic bileaflet-tilting-disk prosthetic valve produces a loud closing click. An early-to-mid-peaking systolic ejection murmur is best heard at the base and often radiates to the carotid arteries. A diastolic murmur is not audible. The mitral bileaflet-tilting-disk valve has auscultatory characteristics similar to those of the mitral single-tilting-disk valve. The aortic heterograft bioprosthesis has a closing sound (AC) similar to that of a normal valve. An early-to-mid-peaking systolic ejection murmur is audible and often radiates to the carotid arteries. The mitral heterograft bioprosthesis has a closing sound (MC) that may be indistinguishable from a normal first heart sound; an opening sound (MO) is usually audible after the second heart sound, as is an early-to-mid-systolic ejection murmur, representing turbulent flow in the left ventricular outflow tract. A low-frequency diastolic rumbling murmur may also be audible at the apex.

From reference # 1

which future echocardiograms (performed if prosthetic valve dysfunction is suspected) can be compared.

Magnetic resonance imaging (MRI) can be performed safely in patients with prosthetic heart valves, except those with a Pre 6000 Starr-Edwards ball-in-cage prosthesis (available from 1960 to 1964)[17]. However, MRI is not useful in assessing prosthetic valve structure. With **cardiac catheterization**, one can measure the transvalvular pressure gradient, from which the effective orifice area can be calculated. In addition, one can visualize and quantify valvular and paravalvular regurgitation. A catheter can be passed safely through the orifice of a bioprosthetic valve. Since it may become entrapped in a tilting disc valve or cause substantial prosthetic valvular regurgitation of a ball-in-cage valve, **I recommend that catheters not be advanced across any mechanical prosthesis.**

POTENTIAL COMPLICATIONS & THEIR MANAGEMENT

A. Valve Thrombosis Prosthetic valve thrombosis has a reported incidence of 0.1 to 5.7% per patient year. The major contributing factors are (a) inadequate anticoagulant therapy [18] and (b) mitral location of the prosthesis [19]. Valve thrombosis may manifest itself clinically as pulmonary congestion, poor peripheral perfusion, or systemic embolization. The typical patient has acute hemodynamic deterioration requiring immediate medical attention, but on occasion they may have a more insidious onset and course. Physical examination, cinefluoroscopy, echocardiography, and catheterization may demonstrate or suggest valve obstruction due to thrombus.

Once a diagnosis of valve thrombosis is established, intravenous heparin should be initiated promptly. If the thrombus is < 5 mm in diameter on echocardiography and is not obstructing the valve, the patient can be treated with anticoagulation alone [20]. The presence of a thrombus > 5 mm in diameter is usually associated with a complicated course, so more aggressive therapy (i.e., urgent valve replacement or fibrinolysis) is warranted. The mortality associated with urgent valve replacement for valve obstruction is approximately 15% [21,22], but it may be substantially higher in those with hemodynamic instability [23,24]. Valve replacement is preferred to thrombectomy, since it has a lower incidence of recurrent thrombosis [22]. In patients with prosthetic valve thrombosis, thrombolytic therapy has a success rate of 70% and a mortality rate of 10% [25,26]. It is more effective for aortic than for mitral valve thrombosis, and it is more effective in subjects whose symptoms have been present for < 2 weeks [26]. Since thrombolytic therapy carries a risk of systemic embolization that is reported to be as high as almost 20%, it should be reserved for critically ill patients whose operative risk is high. The hemodynamically stable patient with a relatively low operative risk should undergo valve replacement.

B. Embolization In patients with mechanical valves, the incidence of major embolization (resulting in death or a persistent neurologic deficit) is roughly 4% per patient-year in the absence of antithrombotic therapy, 2% per patient-year with antiplatelet therapy, and 1% per patient-year with warfarin therapy. The risk of embolization is increased in subjects with (a) mitral valve prostheses, (b) ball-in-cage valves, and (c) multiple prosthetic valves. Other variables that increase the risk of systemic embolization in patients with prosthetic valves include (d) atrial fibrillation, (e) age > 70 years, and (f) depressed left ventricular systolic function [27].

C. Hemolysis Although subclinical intravascular hemolysis (as evidenced by an elevated serum LDH, a decreased serum haptoglobin, and reticulocytosis) is noted in most patients with a normally functioning mechanical prosthetic valve, severe hemolytic anemia is uncommon and suggests paravalvular leakage due to partial dehiscence of the valve's sewing ring [28]. Subjects with a ball-in-cage valve or with multiple prosthetic valves have an increased incidence and severity of hemolysis [29]. Since the decreased blood viscosity and increased cardiac output associated with anemia may increase the

magnitude of hemolysis, patients with hemolytic anemia should receive iron and folate supplements or blood transfusion, and those with paravalvular leakage and severe or intractable hemolysis should have their valves replaced or repaired. In those in whom an operation is high-risk or contraindicated, beta-adrenergic blockade may reduce the magnitude of hemolysis [30].

D. Paravalvular Leakage, with Resultant Regurgitation is an infrequent complication of valve replacement. Although it occasionally results from improper implantation of a prosthetic valve, it is most often caused by prosthetic valve endocarditis [31]. Thus, in patients with paravalvular regurgitation, blood should be obtained for culture. The subject with mild or even moderate paravalvular leakage with no or minimal symptoms and only mild hemolytic anemia can be observed carefully with serial echocardiographic examinations. Patients with severe paravalvular leakage usually have symptoms of pulmonary congestion or severe anemia and should undergo surgical repair or replacement.

E. Endocarditis Prosthetic valve infection occurs at some time in 3 to 6% of patients [32]. Importantly, the risk of endocarditis is similar for mechanical and bioprosthetic valves [33]. So-called "early" endocarditis (occurring within 60 days after valve replacement) usually results from perioperative bacteremia arising from skin or wound infections or contaminated intravascular devices. The most common organisms are *Staphylococcus epidermidis*, *Staphylococcus aureus*, gram negative bacteria, diphtheroids, and fungi. In contrast, "late" prosthetic valve endocarditis (occurring > 60 days postoperatively) is usually caused by the organisms responsible for native-valve endocarditis, most often streptococci.

In patients with prosthetic valve endocarditis, fever is the most common symptom. Unexplained fever in a subject with a prosthetic valve should be presumed to be due to endocarditis until proved otherwise. In addition, patients with prosthetic valve endocarditis may have a new or changing murmur, evidence of systemic embolization, or the appearance of congestive heart failure [34]. Many patients manifest poor peripheral perfusion, rapid hemodynamic deterioration, or new conduction abnormalities.

Transthoracic echocardiography allows one to assess prosthetic valvular hemodynamics and chamber dimensions, but – as noted previously – intense reverberations from the metallic structures limit its ability to detect endocarditis, particularly on the mitral valve. Transesophageal echo is superior for detecting paravalvular abscess or leakage, valve dehiscence, and small (i.e., 1 to 2 mm in diameter) vegetations [15]. Although a negative transesophageal study makes endocarditis unlikely, a second examination should be considered if clinical suspicion is high [35].

The mortality is 30 to 80% in patients with early prosthetic valve endocarditis and 20 to 40% in those with late endocarditis. It is particularly high in subjects with concomitant congestive heart failure, persistent fever, new conduction abnormalities, staphylococcal infection, neurologic complications, and azotemia [36].

About 50% of the patients with streptococcal prosthetic valve endocarditis are cured with parenteral antibiotics. Surgery is indicated if blood cultures remain positive after 3 to 5 days of appropriate antibiotic therapy or if infection recurs after the cessation of antibiotics [37]. Infection with an organism other than streptococcus usually requires valve replacement for cure. In subjects with heart failure, valve obstruction, recurrent systemic embolization, myocardial abscess, fungal infection, new ECG conduction abnormalities, or persistent bacteremia despite antibiotic therapy, valve replacement should be performed promptly even if the course of antibiotic therapy is incomplete.

Uncertainty exists regarding continued warfarin therapy in patients with prosthetic valve endocarditis: some studies have shown a reduced incidence of cerebral embolization when warfarin is continued, whereas others have suggested an increased risk of intracranial hemorrhage. I generally recommend continued warfarin treatment in patients with prosthetic valve endocarditis. If a cerebrovascular complication occurs, warfarin should be discontinued. Subsequently, if there is no evidence of intracerebral hemorrhage or hemorrhagic infarction, it can be resumed 3-4 days later [38,39].

ANTITHROMBOTIC THERAPY IN PATIENTS WITH PROSTHETIC VALVES

As noted previously and displayed in Table 4, patients with mechanical prosthetic valves require long-term anticoagulant therapy; the precise amount varies with the type of mechanical prosthesis. Repeated in Table 6 (below) are the suggested optimal INRs for the various types of prosthetic valves. In addition to warfarin, should these patients receive antiplatelet therapy (i.e., low-dose aspirin)? If he/she does not have (a) atrial fibrillation, (b) previous systemic embolization, (c) a left atrial thrombus, or (d) severely depressed left ventricular systolic function, he/she is considered to be "low risk," and concomitant antiplatelet therapy is not indicated. If he/she has 1 or more of these 4 "risk factors," low-dose aspirin should be given concomitantly with warfarin.

Table 6: Recommended anticoagulation for various prosthetic valves

Prosthesis	Position	Optimal INR
Ball-in-Cage	aortic	4.0-4.5
	mitral	4.5-5.0
Single tilting disc	aortic	3.0-3.5
	mitral	3.5-4.0
Bileaflet tilting disc	aortic	2.0-2.5
	mitral	2.5-3.0

The addition of low-dose aspirin to warfarin in patients with prosthetic valves offers additional protection against thromboembolism at the risk of more frequent bleeding

complications. For this reason, concomitant warfarin-aspirin is recommended only for those whose risk of a thromboembolic event is high, as defined by the presence of 1 or more of these 4 risk factors.

A. Management of Anticoagulation in Patients with Prosthetic Valves who are Undergoing a Noncardiac Surgical Procedure For minor procedures with which blood loss is expected to be minimal and easily managed (i.e., a dental procedure), anticoagulant therapy can be continued. For major procedures with which substantial blood loss is expected, warfarin should be discontinued several days preoperatively. For those with a single or bileaflet tilting disc prosthesis in the aortic position without any of the 4 aforementioned "risk factors," (a) warfarin is discontinued several days preoperatively, allowing the INR to fall to < 1.5; (b) the operation is performed; and (c) warfarin is reinstituted promptly postoperatively. In total, then, although the patient is inadequately anticoagulated for 7 to 10 days, the risk of valve thrombosis and subsequent systemic embolization is extremely low.

For all others (i.e., patients with 1 or more of the 4 "risk factors," a ball-in-cage valve in the aortic position, or any prosthetic valve in the mitral position), (a) warfarin is discontinued several days preoperatively; (b) when the INR falls to < 3.0, intravenous unfractionated heparin, adequate in amount to prolong the activated PTT to 2.0-2.5 times the upper limit of normal, is initiated, then discontinued 3 to 6 hours preoperatively; (c) the operation is performed; (d) intravenous heparin is reinstituted as soon as possible postoperatively, at the same time that (e) warfarin is reinstituted; and (f) heparin is continued until the INR is sufficiently prolonged. In total, then, the patient is inadequately anticoagulated for the least possible amount of time (usually < 24 hours).

B. Management of Anticoagulation During Pregnancy Since the incidence of thromboembolic complications is increased in pregnant women with prosthetic valves [40,41], adequate anticoagulation is particularly important in this group. Warfarin use in the first trimester of pregnancy is associated with a high incidence of embryopathy and fetal death [42,43]. Therefore, warfarin should be discontinued when pregnancy is detected, and twice daily subcutaneous unfractionated heparin (in a dose sufficient to prolong the aPTT to > 2.0 times the upper limit of normal, usually approximately 20,000 units BID) should be initiated.

Once subcutaneous unfractionated heparin is begun, one of 2 management strategies can be pursued. First, one may continue the patient on BID subcutaneous heparin throughout the entire pregnancy, discontinuing it within hours of delivery. Immediately after delivery, it is reinstituted, as is warfarin. Second, one may switch back to warfarin during trimesters 2 and 3, then switch back to subcutaneous unfractionated heparin within a few days of induction. Immediately after delivery, heparin is reinstituted, as is warfarin. Unfortunately, low molecular weight heparin is contraindicated in pregnant women with prosthetic valves; a disturbingly high incidence of prosthetic valve thrombosis has been reported in these patients when they have been treated with LMW heparin.

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