MONICA S. BETTADAPUR, MD
Department of Cardiovascular Medicine,
The Cleveland Clinic

BRIAN P. GRIFFIN, MD
Department of Cardiovascular Medicine,
The Cleveland Clinic

CRAIG R. ASHER, MD
Department of Cardiovascular Medicine,
The Cleveland Clinic

Caring for patients with prosthetic heart valves

ABSTRACT

Patients with prosthetic heart valves require regular examinations and echocardiograms, antithrombotic therapy, and appropriate antibiotic prophylaxis against endocarditis. Physicians must also be on the alert for several uncommon but potentially devastating complications: valve structural failure, thrombosis, embolism, endocarditis, paravalvular leak, and hemolytic anemia.

KEY POINTS

Doppler echocardiography should be performed regularly to monitor left ventricular function and valve structure and to screen for stenosis or regurgitation.

Auscultation can identify many valvular problems.

Antithrombotic therapy is begun shortly after implantation. Goals are different for different valve types.

Patients with prosthetic valves require antibiotic prophylaxis against endocarditis before dental treatment and other procedures.

If thrombosis is detected, the first goal is to optimize the anticoagulation therapy. Surgery or thrombolysis may be required for larger thromboses.

GENERAL INTERNISTS will be more likely to take a leading role in the care of patients with prosthetic valves as the population ages and the use of replacement valves becomes more common. Since the first prosthetic valve 40 years ago, the number of prosthetic valves implanted has risen steadily to its current figure of 60,000 per year.[1]

Patients with prosthetic valves require antithrombotic therapy and endocarditis prophylaxis. Their routine care should include regular physical examinations and echocardiograms to screen for complications such as valve structural failure, thrombosis, embolism, endocarditis, paravalvular leak, and hemolytic anemia. Some complications can be treated medically, whereas others require a referral for surgery.

In this review, we discuss screening, monitoring, routine medical care, and the diagnosis and treatment of complications in patients with different types of prosthetic heart valves.

TYPES OF PROSTHETIC VALVES

The 80-plus types of prosthetic heart valves can be divided into two categories: mechanical and bioprosthetic (TABLE 1).

Mechanical valves. Three types of mechanical valves are currently in use: bileaflet tilting disk, single tilting disk, and ball-in-cage.

Bioprosthetic valves, also known as tissue valves, can be categorized as heterografts, homografts, or autografts. Heterograft valves (also called xenografts) are either whole porcine aortic valves or hand-fabricated valves made from bovine pericardial tissue. Homograft valves are human aortic valves harvested from cadavers and cryogenically preserved. Autografts are used solely in the Ross

TABLE 1

Common prosthetic heart valves

- **Mechanical valves**
  - Single tilting disk
    - Björk-Shiley (discontinued)
    - Medtronic-Hall (Hall-Kaster)
    - Monostrut
    - OmniScience
    - Omnicarbon
    - Lillehei-Kaster
    - Ultracor (available outside the United States)
  - Bileaflet tilting disk
    - St. Jude Medical
    - Carbomedics
    - Duromedics (discontinued)
    - ATS Medical Open Pivot (listed as an investigational device)
  - Nontilting disk (discontinued)
    - Kay-Suzuki
    - Kay-Shiley
    - Beall
  - Ball-in-cage
    - Starr-Edwards
- **Bioprosthetic valves**
  - Heterograft
    - Porcine, stented
      - Hancock
      - Carpentier-Edwards
      - Biocor
      - Epic valve
      - Intact
      - Mosaic
    - Porcine, unstented
      - St. Jude Toronto SPV
      - Medtronic Freestyle
      - Baxter Prima
      - Cryolife-O'Brien
      - Biocor
    - Bovine pericardial
      - Ionescu-Shiley (discontinued)
      - Hancock (no longer in use)
      - Carpentier-Edwards Perimount (aortic valve)
      - Mitroflow (used outside the United States)
  - Homograft
  - Pulmonary autograft

procedure, in which the native pulmonary valve is replaced with a homograft. The native pulmonary valve is then used to replace the aortic valve.[2]

ROUTINE CARE FOR PATIENTS WITH PROSTHETIC VALVES

The routine care of patients with prosthetic valves should include annual physical examinations and echocardiograms, anticoagulation therapy, and prophylaxis against endocarditis.

Many of the care decisions are made on the basis of the valve type and location; thus, it is important for the physician to know the type, model, size, and year of the prosthetic valve. Every patient should carry a wallet card with this information. If this information is not available, an expert may be able to use chest radiography to identify mechanical valves (FIGURE 1), although x-ray images may not be helpful for identifying stentless tissue valves.

The importance of auscultation

Each valve type and position has a unique set of normal sounds (TABLE 2). Murmurs are common, and many are normal. However, a new or changing murmur may indicate a problem.

Sounds from mechanical valves. With mechanical valves, mechanical clicks should be heard as the valve opens and closes.

With the bileaflet tilting disk valves, the opening click should be softer than the closing click; if the closing click is softer, then the valve may be malfunctioning. With a valve in the aortic position, there is a soft midsystolic ejection murmur that radiates to the carotid arteries. Any diastolic murmur is abnormal and should raise suspicion of aortic insufficiency. If the valve is in the mitral position, the opening click follows the second heart sound in diastole, and there is a low-frequency diastolic rumble. A holosystolic murmur should raise the suspicion of mitral regurgitation.

With the single tilting disk valves, sounds are similar to those from bileaflet tilting disk valves, with one notable difference: a single tilting disk valve in the aortic position may create a short, soft diastolic murmur.

The ball-in-cage valve typically causes a loud opening click, followed by several clicks of different intensities caused by the ball bouncing in the cage. The closing click should be less intense than the opening one; if it is not, valve dysfunction is a possibility. A systolic flow murmur is often heard from ball-in-cage valves in the aortic position. Any diastolic murmur is abnormal and suggests aortic insufficiency.

When a ball-in-cage valve is in the mitral position, turbulence in the left ventricular outflow tract may cause a systolic ejection

murmur. A holosystolic murmur is abnormal and should raise concern about mitral regurgitation. A prolonged diastolic rumble is also abnormal and suggests prosthetic stenosis, a high flow state, or a small prosthesis.

Sounds from bioprosthetic valves. Because bioprosthetic valves are made from tissue, they do not click, and their opening and closing sounds are similar to those of native heart valves.

Stented valves, ie, those with a rigid or semirigid support frame, sound somewhat different from unstented ones. Stented heterograft valves in the aortic position produce a systolic ejection murmur that can radiate to the carotid arteries. Stented bioprosthetic valves in the mitral position may cause an early-to-mid systolic ejection murmur attributable to the turbulent flow in the left ventricular outflow tract; the ejection murmur is followed by the second heart sound and then by an opening sound of the valve. A low-frequency diastolic rumble may also be heard at the apex.

Stentless heterograft valves and homograft valves usually sound similar to native valves, although homograft valves with small effective orifices may create systolic ejection murmurs.

Appropriate use of screening Doppler echocardiography

Doppler echocardiography should be used for serial evaluations of left ventricular function, valve structure, valvular stenosis or regurgitation, and pulmonary artery pressures. Patients should have a baseline echocardiogram within 2 to 3 months after surgery for prosthetic

valve implantation. The guidelines from the American College of Cardiology (ACC) and the American Heart Association (AHA) recommend repeating the echocardiogram annually in patients without symptoms, but some experts suggest less frequent follow-up exams.

The pressure gradient across the valve is measured to screen for valvular stenosis (TABLE 3). The normal gradient for each valve depends upon the ring size, the cardiac output, and the heart rate of the patient. High gradients may be normal in patients with high-output states, such as anemia, hyperthyroidism, pregnancy, sepsis, and tachycardia. However,

in patients with a normal cardiac output, high gradients may indicate valvular stenosis. In patients with decreased cardiac output due to left ventricular dysfunction, a high-normal gradient may signify severe stenosis.

It is also normal for prosthetic mechanical valves to have a slight amount of regurgitation, or backflow, caused by blood leaking between and around the valve assembly. The jets of this normal backflow have low velocities. In contrast, abnormal regurgitant flows have high velocities. In normally functioning bioprosthetic valves, backflow is less common, occurring in fewer than 10% of patients.[3]

Initiation and maintenance of proper anticoagulation

Different types of valves carry different risks of thrombosis, and valves are more thrombogenic in the mitral position than in the aortic. Thus, the level of anticoagulation is adjusted according to the type of valve and the valve position (TABLE 4).

Mechanical valves. Patients with mechanical valves are routinely treated with anticoagulants because without this therapy, they have a lifetime risk of thromboembolism that may be as high as 34%.[4–7] Ideally, anticoagulation therapy with warfarin would be started immediately after surgical implantation, but to prevent surgical bleeding, it is usually started a few days after surgery.

Patients with other risk factors for thromboembolism, such as left atrial thrombus, atrial fibrillation, decreased left ventricular function, multiple prosthetic valves, or any previous thromboembolic event, may be given aspirin in addition to warfarin.

For heterograft bioprosthetic valves, the need for warfarin is controversial. For mitral valves, an international normalized ratio (INR) level of 2.5 to 3.5 is often recommended for the first 3 months after surgery until the

Mechanical valves normally have some low-velocity regurgitation

TABLE 4

The Cleveland Clinic guidelines for anticoagulation therapy in patients with prosthetic valves

PROSTHESIS SITE	TARGET INTERNATIONAL NORMALIZED RATIO (INR)	
	PATIENTS WITH NO OTHER RISK FACTORS	PATIENTS WITH ADDITIONAL RISK FACTORS*
Mitral		
Single tilting disk	3.5	3.5
Other mechanical valves	2.5–3.5	2.5–3.5
Bioprosthetic valves	2.5–3.5 for first 3 months, then aspirin 81 mg daily	2.5–3.5
Aortic		
Bileaflet	2.0–3.0	2.5–3.5
Medtronic-Hall	2.0–3.0	2.5–3.5
Other disk valves	2.5–3.5	2.5–3.5
Starr-Edwards	2.5–3.5	2.5–3.5
Bioprosthetic	Aspirin 325 mg daily for first 3 months	2.5–3.5 for first 3 months, then 2–3

*Additional risk factors for thromboembolism include atrial fibrillation, decreased left ventricular systolic function, left atrial thrombus, multiple prosthetic valves, and any history of thromboembolic events.

Adjust the INR according to valve type and location

valve is fully endothelialized. If the patient has additional risk factors (such as left atrial thrombus, atrial fibrillation, or a prior thromboembolic event), then anticoagulation should be continued beyond the first 3 months. For aortic valves, aspirin 325 mg daily is usually recommended for 6 to 12 weeks until the valve is endothelialized, though some guidelines recommend warfarin instead.

For homograft bioprosthetic valves, no anticoagulation is necessary. However, as with any patient, anticoagulation therapy is required if there is atrial fibrillation, atrial thrombus, or previous thromboembolic events.

Preventing endocarditis

Patients with prosthetic valves of any type have a 2% to 6% lifetime risk of developing endocarditis, which carries a high risk of mortality.[8,9] There are no data to suggest that prophylactic antibiotics reduce the risk. Nevertheless, the ACC/AHA guidelines do recommend prophylactic antibiotics for heart valve patients in certain high-risk situations: dental procedures and tooth cleaning, surgery involving the respiratory mucosa, some respiratory procedures, and some gastrointestinal and genitourinary procedures.[10]

COMMONLY ENCOUNTERED CLINICAL SCENARIOS

Anticoagulation and invasive procedures

Anticoagulation therapy can be continued when the patient undergoes a minor procedure associated with little or no blood loss, such as dental cleaning, dental caries treatment, or minor skin surgery.

However, warfarin should be stopped 3 to 5 days before any major procedure expected to entail substantial blood loss. Patients at the highest risk (those with combinations of risk factors such as a mitral prosthesis, atrial fibrillation, and severe left ventricular dysfunction) should be admitted to the hospital for intravenous heparin at therapeutic levels. The heparin should be stopped 2 to 4 hours before the procedure and then restarted afterwards, followed by oral warfarin.

For a patient at an intermediate level of risk, such as one with a bileaflet disk aortic valve with atrial fibrillation, low-molecular-weight heparin may be considered for use in the outpatient setting. However, the efficacy of low-molecular-weight heparin as a bridge therapy for patients with prosthetic valves has not been studied in a randomized trial.[11,12]

Anticoagulation during pregnancy in patients with mechanical valves

Pregnancy creates a hypercoagulable state, and even with anticoagulation therapy, thromboembolic events may occur in 3% to 14% of pregnant women with mechanical prosthetic valves.[13–16] There is as yet no consensus about anticoagulation therapy for these patients.

Unfortunately, warfarin crosses the placenta and poses a risk to the fetus. It is associated with stillbirths, prematurity, spontaneous abortions, fetal deformity (embryopathy), and neurological abnormalities. The risk of fetal deformity is highest (4% to 10%) when the exposure is during the 6th through 12th weeks of gestation. Furthermore, warfarin may be associated with fetal cerebral hemorrhage during labor and delivery.

Some experts recommend using subcutaneous heparin, which does not cross the placenta, at a dose of 17,500 to 20,000 units twice a day, adjusted to a partial thromboplastin time (PTT) that is 2 to 3 times the control. However, several case series have shown that heparin is associated with an unacceptable risk of thromboembolism.[17–19] Thus, subcutaneous heparin should be considered only for low-risk patients, that is, those with no history of thromboembolism and with newer models of prosthetic valves.

For pregnant women with additional risk factors for thromboembolism (such as a previous thromboembolic event or a ball-in-cage valve in the mitral position), intravenous heparin should be used for the first trimester, with a PTT goal of 2 to 3 times the control. Warfarin can then be used through week 35, when anticoaguation should be converted back to intravenous heparin in anticipation of delivery. Heparin and warfarin can be restarted 4 to 6 hours after delivery in patients who have not had substantial bleeding. Studies are ongoing about the efficacy of low-molecular-weight heparin in these patients.[20]

Intracerebral hemorrhage during anticoagulation

A dilemma occurs when a patient receiving anticoagulation therapy for a mechanical prosthetic valve develops intracerebral bleeding. Several studies have shown that a strategy of withholding anticoagulation for 1 to 2 weeks, followed by reinstitution of anticoagulation, is effective in this situation.[21–23]

Managing excessive anticoagulation

When the INR rises above 5, the risk of hemorrhage rises. In most patients, supratherapeutic INR levels should be managed simply by withholding the warfarin and following serial INR levels or by giving a small dose (1 mg) of oral vitamin K.[24] However, a sudden decrease in INR to subtherapeutic levels increases the risk of thromboembolism. If the patient has significant bleeding in the presence of excessive anticoagulation or needs emergency surgery, fresh frozen plasma should be used to help correct an excessive anticoagulation level. Vitamin K may also be used as adjunctive therapy in these situations, although it may make it more difficult to achieve therapeutic INR levels the next time warfarin is given.

The risk of embryopathy is highest with warfarin exposure in weeks 6–12

No problem with MRI or metal detectors

It is safe for patients with any type of prosthetic valve to undergo magnetic resonance imaging. In addition, patients can pass through metal detectors without triggering the detector.

Strut fractures in the Björk-Shiley valve

The Björk-Shiley convexo-concave valve was withdrawn from the market in 1986 because of a 0.5% to 2% risk per patient-year of strut fracture. This structural problem leads to disk embolization, acute valvular regurgitation, and death.

Patients at highest risk for Björk-Shiley strut fracture are those who were younger than 50 years old at implantation and whose valves have an opening angle of 70˚ and a diameter of more than 29 mm. These patients should undergo valve replacement.[25–27]

Strut fractures may present as sudden syn-

A St. Jude aortic valve with a fixed leaflet

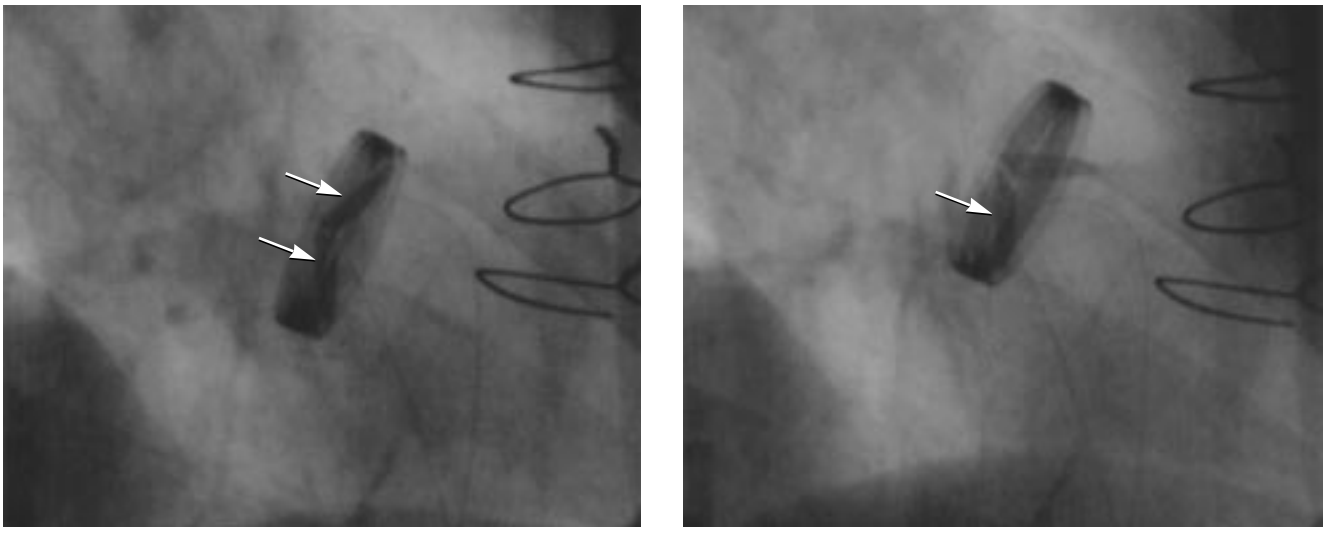

FIGURE 2. The appearance of a St. Jude aortic valve with a fixed leaflet on cinefluoroscopy. **Left**, during diastole the valve leaflets are closed (arrows). **Right**, during systole the top leaflet opens normally, but the bottom leaflet is restricted (arrow).

cope, dyspnea, or cardiogenic shock. Patients with suspected strut fractures require an emergency cardiology consultation because the complication can be fatal within minutes.

ACC/AHA guidelines call for a yearly echocardiogram

POTENTIAL COMPLICATIONS OF PROSTHETIC VALVES

Complications are rare, but when they do occur, they can cause valve dysfunction. Complications include structural deterioration, paravalvular regurgitation, patient-prosthetic mismatch, thrombosis, embolism, endocarditis, and hemolytic anemia.

When prosthetic valve dysfunction is suspected, a careful history and physical examination is vital. Transthoracic echocardiography should then be performed to evaluate the valve structure, assess the transvalvular gradients for possible stenosis, identify regurgitation, and visualize any thrombi or vegetations.

If transthoracic echocardiography is inadequate, then transesophageal echocardiography will provide better visualization. Transesophageal echocardiography is often considered the imaging method of choice in evaluating prosthetic valve dysfunction. Unfortunately, it may still be insufficient for aortic valves. In these instances, cinefluoroscopy may aid in visualizing the function of the valve and seeing if the valve leaflets are mobile (FIGURE 2).

Rarely, cardiac catheterization may be warranted to further assess hemodynamics. If these studies are unrevealing and a patient has exertional symptoms, then stress echocardiography should be performed to evaluate the valve hemodynamics at higher cardiac outputs (FIGURE 3).

Structural deterioration

Valve dysfunction can be caused by structural problems including valve wear, leaflet tear, fracture, calcification, and suture line disruption. These problems usually present as valvular stenosis or regurgitation.

Structural problems are much less common in most mechanical valves than in bioprosthetic valves.[28] About 30% of heterograft valves and 10% to 20% of homograft valves require replacement within 10 to 15 years because of structural failure.[29–31] After 10 years, the rate of deterioration rapidly accelerates.

A primary mechanism of failure is deposition of calcium, which can restrict leaflet motion and produce leaflet tears. These problems are manifested by valvular stenosis and regurgitation. Calcium deposition is particularly common in stented heterograft

Algorithm for evaluating patients with suspected prosthetic valve dysfunction

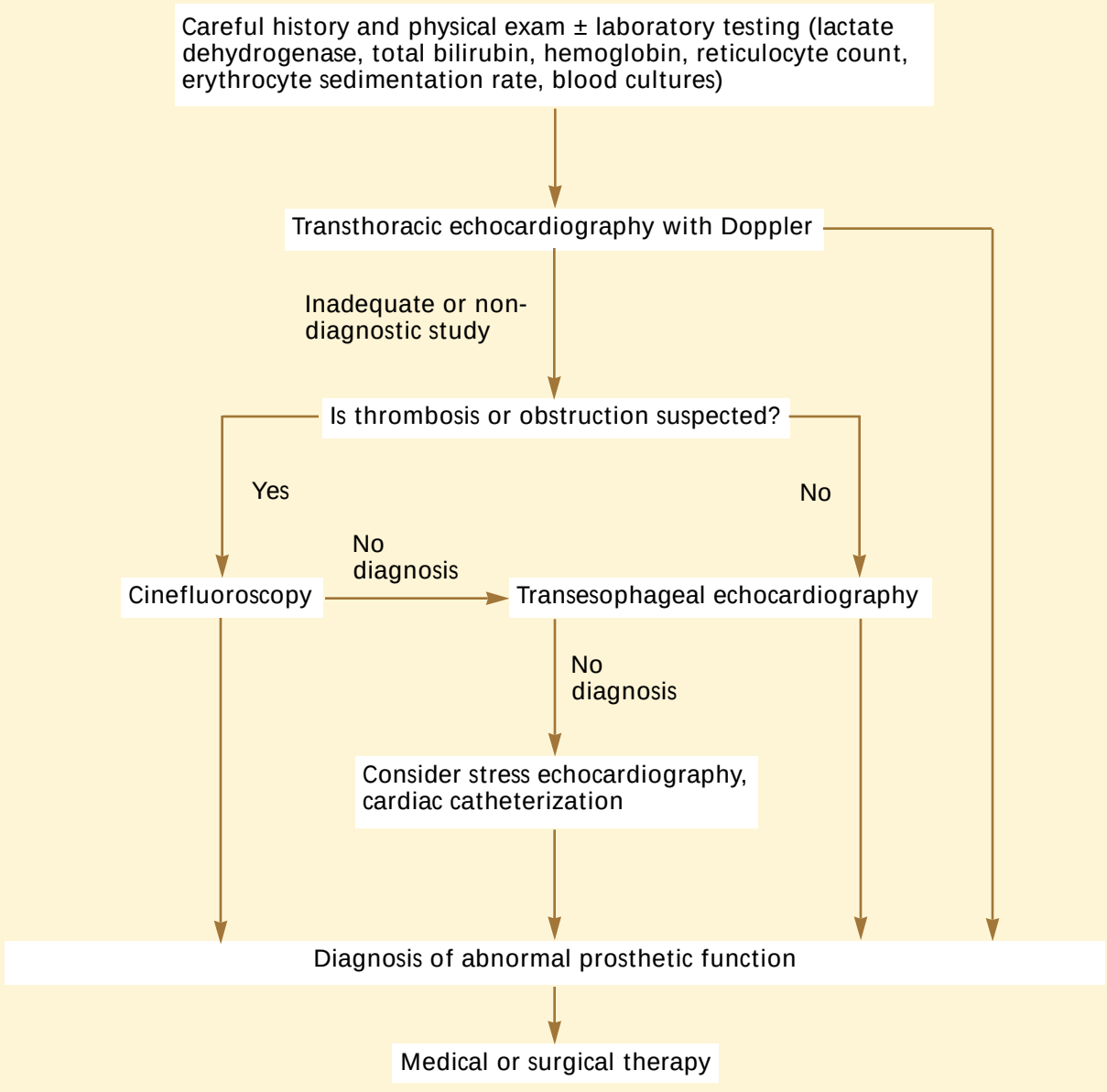

FIGURE 3

valves 6 to 8 years after implantation. Calcific degeneration occurs more quickly in patients under 20 years old and in patients with abnormal calcium metabolism (caused by chronic renal failure, hyperparathyroidism, Paget disease of bone, and other causes of hypercalcemia).[32]

Pregnancy also increases calcium turnover and thus accelerates the process of premature valve failure.[33] In addition, the failure rate is higher in patients who have mitral valve prostheses.[31,34–36] For these reasons, bioprosthetic valves are usually used in patients over 65 years old. In patients over 70, only 10% have had to have reoperation for valve replacement at 12 to 15 years.[36,37]

Paravalvular leak

Paravalvular regurgitation is uncommon and is usually due to endocarditis. However, it can occur soon after implantation if the valve is positioned poorly. Progressively increasing leakage (identified during the physical exam and Doppler echocardiography) is an indication for reoperation. Occasionally, suture or patch repair is feasible; if not, the valve must be replaced.

Patient-prosthetic mismatch

Valve dysfunction can also result from inappropriate sizing of the valve. The mismatch is usually due to the valve area being relatively small for the patient's size (effective orifice area ≤ 0.85 cm^2/m^2) and is usually seen in patients who underwent aortic valve replacement for aortic stenosis.[38]

Patients with mismatched valves generally do not improve clinically after valve implantation and may even worsen.[39] Echocardiography shows a structurally normal prosthesis, but one with a higher-than-expected gradient.[38] Intrinsic valve dysfunction must be excluded before mismatch is diagnosed. Stress echocardiography may be useful in identifying a large increase in transvalvular gradient with exercise, which, if the valve is structurally normal, suggests that the valve may be too small for the patient.

The problem may be corrected by replacing the valve with a larger one or one of a different type, and enlarging the annulus.

Thrombosis is usually sudden with disk valves, but gradual with ball-in-cage valves

Valvular thrombosis

Thrombosis is a risk with all prosthetic valves. Thromboses can develop gradually or abruptly. With disk valves, thrombosis usually occurs suddenly and can be fatal; with ball-in-cage valves, thrombosis often develops over several weeks and manifests as heart failure, decreased perfusion, or embolization.

Mechanical valves are more likely to trigger thrombosis than are tissue valves. The risk is highest for ball-in-cage valves, followed by single tilting disk prostheses and then bileaflet tilting disk prostheses. However, when anticoagulation therapy is adequate, all mechanical and bioprosthetic valves have similar thrombotic complication rates, approximately 0.1% to 5.7% per patient-year.[28,40–44]

The risk of thrombosis also depends on the valve location. The risk of thrombosis is higher for right-sided prostheses than for left-sided ones, and may be as high as 5% per patient-year.[45] Of the left-sided valves, those in the mitral position are more prone to thrombosis than those in the aortic position.

Treating valvular thrombosis. When thrombosis is detected, the first goal should be to optimize the anticoagulation therapy. Patients not already taking anticoagulants should be started, and patients whose level of anticoagulation is subtherapeutic should receive higher doses. If the thrombus is less than 5 mm in diameter (as measured by echocardiography) and is not obstructing the valve, then anticoagulation therapy is sufficient.

Surgery or thrombolysis is required for larger thrombi. Valve replacement surgery for valve thrombosis is associated with a mortality rate of approximately 9%, but the rate can be as high as 67% in an emergency situation.[46–49] Factors associated with higher mortality rates include higher preoperative New York Heart Association functional class, worse left ventricular systolic function, more urgent surgery, and worse coronary artery disease status.[47,48]

In patients with high surgical risk or with any contraindication to surgery, thrombolytic therapy should be considered. Thrombolysis has a success rate of 70% to 80%, a stroke risk of 3% to 10%, and a mortality rate of 6% to 10% when used for left-sided valves.[14,44,50,51] In general, the mortality rate is lower when thrombolysis is used to treat right-sided thromboses, and thus thrombolysis is often used for such cases. It is also more effective for thromboses affecting the aortic valve than for thromboses affecting the mitral valve. Thrombolysis also works better if the symptoms have been present for less than 2 weeks.

After valve thrombosis is detected, the target INR should be 3.0 to 4.0 for aortic valves and 3.5 to 4.5 for mitral valves. If the thrombosis occurred while anticoagulation levels were therapeutic, then the addition of aspirin may also be considered.

Embolism

One of the most feared complications of thrombosis is a cerebral or peripheral embolic event.

Embolic events occur more often in patients with mechanical valves than in those with bioprosthetic valves, though the rates become similar with adequate anticoagulation therapy. In patients with mechanical valves without any antithrombotic therapy, the risk for embolization is approximately 4% per patient-year; with antiplatelet therapy, the risk decreases to 2.2% per patient-year; and with warfarin, the risk further decreases to 1% per patient-year.[7] In patients with bioprosthetic valves, the risk of embolism is approximately 0.7% per year.[14]

Factors that increase the risk of systemic embolization include age over 70 years, atrial fibrillation, mitral valve position, and, perhaps, decreased systolic function. The risk of embolization is highest in the first few months after valve insertion before the valve is fully endothelialized.

For peripheral embolism, anticoagulation therapy should be started or intensified. However, in cases of cerebral embolism, intracerebral hemorrhage and extensive cerebral infarction must be excluded before anticoagulation therapy is started. Even when hemorrhage is ruled out, anticoagulants should not be started until 3 days after the event to ensure that there is no hemorrhagic conversion from the infarct.[21]

Endocarditis

Endocarditis carries a high mortality rate in prosthetic valve patients and must be quickly diagnosed and treated. However, its diagnosis can be difficult. Endocarditis should be suspected in any patient with a prosthetic valve who develops a new or changing murmur or who has a fever, but the diagnosis should be confirmed by the Duke criteria.[52]

Early endocarditis. Early prosthetic valve endocarditis, ie, infection developing within 2 months of implantation, has a worse prognosis than an infection that occurs later. Early prosthetic valve endocarditis carries a mortality rate between 20% and 80%.[9] It is usually caused by skin contamination and is often associated with ring abscesses, conduction disturbances, and paravalvular leaks. The most common causative organisms are coagulase-negative *Staphylococcus*, *Staphylococcus aureus*, gram-negative bacteria, diphtheroids, and fungi.

A patient with early prosthetic valve endocarditis may not have the typical symptoms of endocarditis. Fever, diaphoresis, and back pain are the most common symptoms,[53] and the physical exam may reveal a murmur and signs of heart failure. Peripheral findings, such as splinter hemorrhages, Osler nodes, or Janeway lesions, are found in only 10% of these patients.[53,54]

About 74% of patients are anemic,[53] although recent surgery is a contributing factor. The erythrocyte sedimentation rate is not usually elevated.

Late endocarditis. The signs, symptoms, and prognosis of late prosthetic valve endocarditis (ie, developing more than 2 months after implantation) are similar to those of native valve endocarditis. Mortality may be as high as 46%.

Late prosthetic valve endocarditis is usually caused by infections or procedures involving the mouth, urinary system, gastrointestinal tract, or skin. Causative organisms include streptococci, coagulase-negative *Staphylococcus*, and the HACEK organisms (*Haemophilus parainfluenzae*, *H aphrophilus*, *Actinobacillus*, *Cardiobacterium*, *Eikenella*, and *Kingella*).

Almost 30% of patients with late prosthetic valve endocarditis may have cerebrovascular embolization in addition to the regular signs of endocarditis.[54] Hemolytic anemia and heart block are also more common than in native endocarditis.

Treating prosthetic valve endocarditis. For any patient with suspected endocarditis, at least three sets of blood cultures should be obtained serially over a period of hours. These cultures should be saved for at least 3 weeks in an attempt to grow any fastidious organisms. In addition, special culture media may be required to grow some organisms such as Rickettsiae, Legionellae, and Mycobacteria.

Empiric antibiotic therapy should be started only after blood cultures have been obtained. Once an organism is identified, antibiotic therapy should be tailored to that organism and should be continued for at least 6 weeks.

Echocardiography should be performed to look for vegetations and abscesses and to eval-

For suspected endocarditis, get at least 3 sets of blood cultures

uate valve function. Transthoracic echocardiography can visualize large vegetations well, but transesophageal echocardiography is better for detecting small vegetations and tissue invasion. Its sensitivity is about 95% and its specificity is 90%,[55–59] making it the imaging method of choice.

Surgery with valve replacement and debridement is necessary if the blood cultures remain positive after several days of appropriate antibiotics or if the infection recurs after 6 weeks of appropriate antibiotic therapy. Surgery is also indicated if the patient has signs of refractory heart failure, valve obstruction, significant valve dysfunction, recurrent embolization, myocardial abscess, fungal infection, mycotic aneurysm, or any new electrocardiographically detected conduction abnormalities. Delaying surgery carries the risk of further embolization, complete valve dehiscence, and death.

Most cases of endocarditis associated with mechanical prosthetic valves require surgery. For infections of bioprosthetic valves, the need for surgery is more variable.

Hemolytic anemia

Severe hemolytic anemia is uncommon but may occur when red blood cells are sheared by turbulent blood flow within the prosthetic valve apparatus. Hemolytic anemia often suggests infection or endocarditis that has led to dehiscence of the valve and subsequent paravalvular regurgitation. Hemolytic anemia is more common in patients with ball-in-cage valves and in patients with multiple prosthetic valves.

When hemolytic anemia is suspected, the clinician should examine and follow the levels of lactate dehydrogenase, haptoglobin, and bilirubin, and the reticulocyte count.

Patients with hemolytic anemia should be given iron and folate supplementation, possibly with blood transfusions as well. Beta-blockers decrease the heart rate and heart contractility, which may also decrease the amount of hemolysis. Valve replacement should be considered when severe hemolytic anemia does not respond to medical therapy.

CONCLUSION

As the prevalence of patients with prosthetic valves rises, the primary care physician is becoming increasingly responsible for caring for these patients. In general, management is straightforward and consists primarily of routine history and physical examinations, annual echocardiograms, maintaining adequate anticoagulation therapy, and ensuring appropriate antibiotic prophylaxis for endocarditis. However, there are several potential devastating complications that can occur in these patients. Recognizing these complications early is imperative to prevent serious morbidity and mortality. It is hoped that attention to these issues will lead to optimal care for patients with prosthetic valves.

Acknowledgment: *We gratefully acknowledge Dr. Umesh N. Khot for his review and thoughtful comments on this manuscript.*

REFERENCES

1. **Vongpatanasin W, Hillis LD, Lange RA.** Prosthetic heart valves. N Engl J Med 1996; 335:407–416.
2. **Schmidtke C, Bechtel JF, Noetzold A, Sievers HH.** Up to seven years of experience with the Ross procedure in patients >60 years of age. J Am Coll Cardiol 2000; 36:1173–1177.
3. **Zabalgoitia M.** Echocardiographic assessment of heart valves. Curr Prob Cardiol 2000; 25:157–220.
4. **Moggio RA, Hammond GL, Stansel HC Jr, Glenn WW.** Incidence of emboli with cloth-covered Starr-Edwards valve without anticoagulation and with varying forms of anticoagulation. Analysis of 183 patients followed for 3 1/2 years. J Thorac Cardiovasc Surg 1978; 75:296–299.
5. **Akbarian M, Austen G, Yurchak PM, Scannell JG.** Thromboembolic complications of prosthetic cardiac valves. Circulation 1968; 37:826–831.
6. **Duvoisin GE, Brandenburg RO, McGoon DC.** Factors affecting thromboembolism associated with prosthetic heart valves. Circulation 1967; 35:I-70–I-76.
7. **Cannegieter SC, Rosendaal FR, Briet E.** Thromboembolic and bleeding complications in patients with mechanical heart valve prostheses. Circulation 1994; 89:635–641.
8. **Calderwood SB, Swinski LA, Waternaux CM, Karchmer AW, Buckley MJ.** Risk factors for the development of prosthetic valve endocarditis. Circulation 1985; 72:31–37.
9. **Wilson WR, Danielson GK, Giuliani ER, Geraci JE.** Prosthetic valve endocarditis. Mayo Clin Proc 1982; 57:155–161.
10. **Dajani AS, Taubert KA, Wilson W, et al.** Prevention of bacterial endocarditis. Recommendations by the American Heart Association. JAMA 1997; 277:1794–1801.
11. **Montalescot G, Polle V, Collet JP, et al.** Low molecular weight heparin after mechanical heart valve replacement. Circulation 2000; 101:1083–1086.
12. **Lev-Ran O, Kramer A, Gurevitch J, Shapira I, Mohr R.** Low-molecular-weight heparin for prosthetic heart valves: treatment failure. Ann Thorac Surg 2000; 69:264–265.
13. **Chan WS, Anand S, Ginsberg JS.** Anticoagulation of pregnant women with mechanical heart valves: a systematic review of the literature. Arch Intern Med 2000; 160:191–196.
14. **Bonow RO, Carabello B, de Leon AC Jr, et al.** Guidelines 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 (Committee on Management of Patients with Valvular Heart Disease). Circulation 1998; 98:1949–1984.
15. **Larrea JL, Nunez L, Reque JA, Gil Aguado M, Matarros R, Minguez JA.** Pregnancy and mechanical valve prostheses: a high-risk situation for the mother and the fetus. Ann Thorac Surg 1983; 36:459–463.
16. **Salazar E, Zajarias A, Gutierrez N, Iturbe I.** The problem of cardiac valve prostheses, anticoagulants, and pregnancy. Circulation 1984; 70:I-169–I-177.
17. **Meschengieser SS, Fondevila CG, Santarelli MT, Lazzari MA.** Anticoagulation in pregnant women with mechanical heart valve prostheses. Heart 1999; 82:23–26.
18. **Watson WJ, Freeman J, O'Brien C, Benson M.** Embolic stroke in a pregnant patient with a mechanical heart valve on optimal heparin therapy. Am J Perinatol 1996; 13:371–372.
19. **Wang RY, Lee PK, Chow JS, Chen WW.** Efficacy of low-dose, subcutaneously administered heparin in treatment of pregnant women with artificial heart valves. Med J Aust 1983; 2:126–128.
20. **Arnaout MS, Kazma H, Khalil A, et al.** Is there a safe anticoagulation protocol for pregnant women with prosthetic valves? Clin Exp Obstet Gynecol 1998; 25:101–104.
21. **Sherman DG.** Cardiac embolism: the neurologist's perspective. Am J Cardiol 1990; 65:32C–37C.
22. **Wijdicks EF, Schievink WI, Brown RD, Mullany CJ.** The dilemma of discontinuation of anticoagulation therapy for patients with intracranial hemorrhage and mechanical heart valves. Neurosurgery 1998; 42:769–773.
23. **Butler AC, Tait RC.** Management of oral anticoagulant-induced intracranial haemorrhage. Blood Rev 1998; 12:35–44.
24. **Crowther MA, Julian J, McCarty D, et al.** Treatment of warfarin-associated coagulopathy with oral vitamin K: a randomised controlled trial. Lancet 2000; 356:1551–1553.
25. **van der Meulen JH, Steyerberg EW, van der Graaf Y, et al.** Age thresholds for prophylactic replacement of Björk-Shiley convexo-concave heart valves. A clinical and economic evaluation. Circulation 1993; 88:156–164.
26. **Hiratzka LF, Kouchoukos NT, Grunkemeier GL, Miller DC, Scully HE, Wechsler AS.** Outlet strut fracture of the Björk-Shiley 60 degrees convexo-concave valve: current information and recommendations for patient care. J Am Coll Cardiol 1988; 11:1130–1137.
27. **Birkmeyer JD, Marrin CA, O'Connor GT.** Should patients with Björk-Shiley valves undergo prophylactic replacement? Lancet 1992; 340:520–523.
28. **Hammermeister K, Sethi GK, Henderson WG, Grover FL, Oprian C, Rahimtoola SH.** 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 2000; 36:1152–1158.
29. **Yacoub M, Rasmi NR, Sundt TM, et al.** Fourteen-year experience with homovital homografts for aortic valve replacement. J Thorac Cardiovasc Surg 1995; 110:186–193.
30. **O'Brien MF, Stafford EG, Gardner MA, et al.** Allograft aortic valve replacement: long-term follow-up. Ann Thorac Surg 1995; 60:S65–S70.
31. **Gallo I, Ruiz B, Nistal F, Duran CM.** Degeneration in porcine bioprosthetic cardiac valves: incidence of primary tissue failures among 938 bioprostheses at risk. Am J Cardiol 1984; 53:1061–1065.
32. **Milano A, Bortolotti U, Talenti E, et al.** Calcific degeneration as the main cause of porcine bioprosthetic valve failure. Am J Cardiol 1984; 53:1066–1070.
33. **Sbarouni E, Oakley CM.** Outcome of pregnancy in women with valve prostheses. Br Heart J 1994; 71:196–201.
34. **Bloomfield P, Wheatley DJ, Prescott RJ, Miller HC.** Twelve-year comparison of a Björk-Shiley mechanical heart valve with porcine bioprostheses. N Engl J Med 1991; 324:573–579.
35. **Grunkemeier GL, Jamieson WR, Miller DC, Starr A.** Actuarial versus actual risk of porcine structural valve deterioration. J Thorac Cardiovasc Surg 1994; 108:709–718.
36. **Jones EL, Weintraub WS, Craver JM, et al.** Ten-year experience with the porcine bioprosthetic valve: interrelationship of valve survival and patient survival in 1,050 valve replacements. Ann Thorac Surg 1990; 49:370–383.
37. **Cohn LH, Collins JJ Jr, DiSesa VJ, et al.** Fifteen-year experience with 1678 Hancock porcine bioprosthetic heart valve replacements. Ann Surg 1989; 210:435–442.
38. **Pibarot P, Dumesnil JG.** Hemodynamic and clinical impact of prosthesis-patient mismatch in the aortic valve position and its prevention. J Am Coll Cardiol 2000; 36:1131–1141.
39. **Rao V, Jamieson WR, Ivanov J, Armstrong S, David TE.** Prosthesis-patient mismatch affects survival after aortic valve replacement. Circulation 2000; 102:III-5–III-9.
40. **Edmunds LH Jr.** Thromboembolic complications of current cardiac valvular prostheses. Ann Thorac Surg 1982; 34:96–106.
41. **Metzdorff MT, Grunkemeier GL, Pinson CW, Starr A.** Thrombosis of mechanical cardiac valves: a qualitative comparison of the silastic ball valve and the tilting disc valve. J Am Coll Cardiol 1984; 4:50–53.
42. **Fuster V, Pumphrey CW, McGoon MD, Chesebro JH, Pluth JR, McGoon DC.** Systemic thromboembolism in mitral and aortic Starr-Edwards prostheses: a 10–19 year follow-up. Circulation 1982; 66:I-157–I-161.
43. **Baudet EM, Oca CC, Roques XF, et al.** A 5 1/2 year experience with the St. Jude Medical cardiac valve prosthesis. Early and late results of 737 valve replacements in 671 patients. J Thorac Cardiovasc Surg 1985; 90:137–144.
44. **Roudaut MF, Ledain L, Roudaut R, Besse P, Boisseau MR.** Thrombolytic treatment of acute thrombotic obstruction with disk valve prostheses: experience with 26 cases. Semin Thromb Hemost 1987; 13:201–205.
45. **Lin SS, Tiong IY, Asher CR, Murphy MT, Thomas JD, Griffin BP.** Prediction of thrombus-related mechanical prosthetic valve dysfunction using transesophageal echocardiography. Am J Cardiol 2000; 86:1097–1101.
46. **Gueret P, Vignon P, Fournier P, et al.** Transesophageal echocardiography for the diagnosis and management of nonobstructive thrombosis of mechanical mitral valve prosthesis. Circulation 1995; 91:103–110.
47. **Husebye DG, Pluth JR, Piehler JM, et al.** Reoperation on prosthetic heart valves. An analysis of risk factors in 552 patients. J Thorac Cardiovasc Surg 1983; 86:543–552.
48. **Christakis GT, Weisel RD, David TE, Salerno TA, Ivanov J.** Predictors of operative survival after valve replacement. Circulation 1988; 78:I-25–I-34.
49. **Hurrell DG, Schaff HV, Tajik A.** Thrombolytic therapy for obstruction of mechanical prosthetic valves. Mayo Clin Proc 1996; 71:605–613.
50. **Witchitz S, Veyrat C, Moisson P, Scheinman N, Rozenstajn L.** Fibrinolytic treatment of thrombus on prosthetic heart valves. Br Heart J 1980; 44:545–554.
51. **Ledain LD, Ohayon JP, Colle JP, Lorient-Roudaut FM, Roudaut RP, Besse PM.** Acute thrombotic obstruction with disc valve prostheses: diagnostic considerations and fibrinolytic treatment. J Am Coll Cardiol 1986; 7:743–751.
52. **Durack DT, Lukes AS, Bright DK.** New criteria for diagnosis of infective endocarditis: utilization of specific echocardiographic findings. Duke Endocarditis Service. Am J Med 1994; 96:200–209.
53. **Garcia MJ.** Prosthetic valve disease. In: Topol EJ, editor. Textbook of Cardiovascular Medicine. Philadelphia: Lippincott Williams & Wilkins, 1998:579–606.
54. **Chastre J, Trouillet JL.** Early infective endocarditis on prosthetic valves. Eur Heart J 1995; 16(suppl B):32–38.
55. **Erbel R, Rohmann S, Drexler M, et al.** Improved diagnostic value of echocardiography in patients with infective endocarditis by transoesophageal approach. A prospective study. Eur Heart J 1988; 9:43–53.
56. **Daniel WG, Mugge A, Martin RP, et al.** Improvement in the diagnosis of abscesses associated with endocarditis by transesophageal echocardiography. N Engl J Med 1991; 324:795–800.
57. **Daniel WG, Mugge A, Grote J, et al.** Comparison of transthoracic and transesophageal echocardiography for detection of abnormalities of prosthetic and bioprosthetic valves in the mitral and aortic positions. Am J Cardiol 1993; 71:210–215.
58. **Pedersen WR, Walker M, Olson JD, et al.** Value of transesophageal echocardiography as an adjunct to transthoracic echocardiography in evaluation of native and prosthetic valve endocarditis. Chest 1991; 100:351–356.
59. **Lowry RW, Zoghbi WA, Baker WB, Wray RA, Quinones MA.** Clinical impact of transesophageal echocardiography in the diagnosis and management of infective endocarditis. Am J Cardiol 1994; 73:1089–1091.

ADDRESS: *Craig R. Asher, MD, Department of Cardiology, F15, The Cleveland Clinic Foundation, 9500 Euclid Avenue, Cleveland, OH 44195; e-mail asherc@ccf.org.*