

Clinical problems in patients with prosthetic heart valves

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ABSTRACT – Information from the UK Heart Valve Registry, which was established in 1986 and receives data from all centres in the National Health Service, shows that more than 5,000 artificial heart valves are implanted each year in Britain and that almost two-thirds of these are mechanical. This article is intended as a practical outline of the clinical problems and complications which may occur.

Types of valve prosthesis and factors determining selection

A simple classification of prosthetic valves is shown in Table 1. The bare-strut Starr–Edwards valve was the first to be introduced into clinical practice, in 1960, and has the best durability record. The Björk–Shiley valve was introduced in 1969 and has undergone a number of modifications since then [1]. The St Jude medical bileaflet prosthesis has the advantage of haemodynamic excellence and it is less noisy than other mechanical valves [2]. Glutaraldehyde preservation of tissue valves has considerably improved their durability but this remains a significant problem as some reports show a failure rate approaching 20–30% at 8 years [3]. Tissue valves degenerate faster in younger patients and are contraindicated in patients under the age of 35 years. Bioprostheses are selected for elderly patients with a limited life expectancy or for patients with major contraindications to oral anticoagulants. For most other patients a mechanical prosthesis is probably better.

Disabling symptoms due to valvular heart disease remain the clearest indication for valve replacement which results in significant symptomatic benefit in the majority. Additional coronary artery bypass grafting may be required for co-existing coronary artery disease. Data from the UK Heart Valve Registry (1987 figures, with permission) show a mortality rate at 30 days following surgery of 6.5% for isolated mitral valve replacement (123 deaths, 1,883 patients) and 4.2% for isolated aortic valve replacement (99 deaths, 2,343 patients).

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Table 1. Types of prosthetic valve

<i>Mechanical</i>	
Ball and cage	Starr–Edwards prosthesis
Tilting disc	Björk–Shiley prosthesis Medtronic–Hall prosthesis
Bileaflet	St Jude medical valve Duramedics valve (now withdrawn)
<i>Tissue</i>	
Porcine	Wessex bioprosthesis Carpentier–Edwards bioprosthesis Hancock bioprosthesis
Pericardial	Ionescu–Shiley valve (now withdrawn) Hancock pericardial valve (withdrawn)

Clinical evaluation

All patients with prosthetic valves should be seen by their physician at least once a year for a complete clinical evaluation. A full history is mandatory in patients whose condition has recently deteriorated. Their anti-coagulant booklet and current medication must be reviewed for drug-induced problems and interactions such as digoxin toxicity, diuretic resistance from NSAIDs, diuretic-induced electrolyte disturbance and excessive anticoagulation due to drug interaction such as the addition of amiodarone [4]. All pulses need to be checked on each visit because embolism may be silent. The possibility of infective endocarditis must always be in mind. Particular attention should be given to the prosthetic opening and closing sounds and to the auscultatory findings of remaining native valves and comparison made with previous observations. It is not generally realised that significant mitral or aortic prosthetic valve regurgitation may not always produce an audible murmur [5,6]. The annual visit should include an electrocardiogram and chest X-ray.

Echocardiography allows reliable non-invasive assessment of ventricular and prosthetic valve function and should be carried out at least once for baseline documentation in every patient after valve replacement. Regurgitation can be assessed semiquantitatively using a combination of 2D imaging and Doppler colour flow mapping. The peak instantaneous pres-

sure gradient across bioprosthetic aortic valves can be obtained using continuous-wave Doppler. A thrombosed prosthesis, degenerative changes in a bioprosthetic valve or dehiscence [7] may all be identified. Ventricular septal hypokinesia may occur following open heart surgery and usually returns to normal after several months [8]. Transoesophageal echocardiography (TOE), when available, greatly enhances the image quality, detection and quantitation of paraprosthetic regurgitation and the recognition of thrombi and vegetations compared with conventional transthoracic echocardiography (TTE). Cinefluoroscopy can show prosthetic poppet or disc motion or a rocking prosthesis due to extensive dehiscence [9]. Cardiac catheterisation may be required to determine the state of the coronary arteries.

Complications

Thromboembolism

This complication is more common in patients with mechanical prostheses. The presence of atrial fibrillation, an enlarged left atrium and poor left ventricular function further increases the risk [10]. Meticulous anticoagulant control is the best means of prevention [11]. The therapeutic range for prosthetic valve patients is an international normalised ratio (INR) of 3–4.5 [12], although some older patients may show spontaneous bruising when the INR is above 3.

The thromboembolic rate per treatment year varies between 0.5% and 5% [10]. Indefinite oral anticoagulation is necessary for all patients with a mechanical prosthesis, and about 50% of patients with tissue valves also need them. The addition of dipyridamole (100 mg qds) may result in fewer embolic episodes than warfarin alone [10] and should be prescribed in those with embolic events despite good anticoagulant control where an underlying complication has been excluded. Patients with tissue valves should be maintained on oral anticoagulants for 3 months following surgery until the sewing ring has endothelialised. Those in atrial fibrillation, with an enlarged left atrium or previous embolic episode, need to be anticoagulated indefinitely [10]. Other patients with tissue valves may benefit from long-term aspirin [13], especially as the valve ages.

In a recent study, 70% of embolic episodes were cerebral, 10% retinal, 10% coronary and 10% peripheral [11]. Transient ischaemic attacks, amaurosis fugax and completed stroke are common modes of presentation. Embolism may be associated with a thrombosed mechanical prosthesis or endocarditis. In every case a search should be made for evidence of prosthetic valve dysfunction or infection. Urgent re-replacement may be necessary.

Haemorrhage

Haemorrhage is the only serious side effect of warfarin therapy in non-pregnant subjects and is closely associ-

ated with excessive anticoagulation [14]. The incidence of serious haemorrhage is approximately 1–2% per treatment year [15]. For life-threatening gastrointestinal tract haemorrhage, oral anticoagulants must be stopped immediately and fresh frozen plasma given. This is preferable to iv vitamin K which can take up to 12 hours to act, results in resistance to coumarins for up to 2 weeks and introduces a serious risk of valve thrombosis. Patients with recurrent peptic ulceration should be indefinitely maintained on H₂ receptor blockers. The source of bleeding in patients with chronic occult gastrointestinal tract blood loss can be difficult to establish despite extensive investigation; it is often caused by angiodysplasia especially associated with aortic valve disease [16]. In patients presenting with a stroke, cerebral haemorrhage is frequently impossible to distinguish from infarction but the prothrombin time on admission provides an important clue. CT scanning establishes the diagnosis and is mandatory on admission because anticoagulation should be continued if there is no CT scan evidence of haemorrhage.

Valve prosthesis – patient mismatch

All prosthetic valves are stenotic since the effective orifice area is less than that of the native healthy valve. The pressure gradient across the prosthesis depends upon its type, model, size and position and on cardiac output. Obstruction to left ventricular outflow or inflow may be severe for prostheses with a small effective orifice area and may be further reduced by endothelialisation and fibrous tissue ingrowth [17]. These considerations become more important in younger physically active people.

Prosthetic valve dysfunction

Prosthetic valve dysfunction may be due to [18]:

- Tissue valve degeneration
- Mechanical valve failure
- Valve dehiscence
- Endocarditis
- Acute thrombosis
- Encapsulation by a pannus of thrombus.

Common clinical presentations of prosthetic valve dysfunction include cardiac failure, acute circulatory failure, a new tachyarrhythmia, endocarditis, an embolic episode and, more rarely, haemolysis. The main differential diagnoses of a malfunctioning prosthesis are from progression of disease in another native valve and ventricular dysfunction.

Degeneration of tissue valves with stenosis and incompetence commonly develops 7–10 years after surgery but may occur much earlier in children, young people and patients with renal failure. The patient may have gradually worsening exertional dyspnoea, fatigue and new murmurs. Echocardiography identifies thickened or calcified prosthetic valve leaflets and enables the functional severity to be assessed.

Acute mechanical failure is rare but has been reported especially with the Björk–Shiley valve [19] after fracture of the minor strut due to metal fatigue with escape of the disc occluder. Since 1982 a monostrut version of this valve seems to have overcome the problem. The patient characteristically presents with sudden severe left ventricular failure, hypotension and absent prosthetic valve sounds on auscultation. Björk–Shiley valves, manufactured after 1975, all contain a radio-opaque disc marker, which is seen to be absent on cinefluoroscopy [9] if the valve is broken. Fracture of the valve housing with escape of a leaflet has been described with Duramedics bileaflet valves; they were withdrawn in August 1988 but not explanted, leaving a number of UK patients with this prosthesis. Fracture of a mechanical valve may be distinguished from thrombosis because the haemodynamic disaster is instantaneous rather than gradual. The patient's condition is not as bad with loss of one leaflet from a bileaflet valve as after escape of a single occluder. The radio-opaque ring is absent (tilting disc) or only one is seen moving normally on echo (bileaflet), but time should not be wasted on these investigations. Emergency surgery will save life, and the deaths that have occurred followed mistaken attempts at thrombolysis. The patient should be taken to the nearest cardiac surgical centre without delay. It cannot be overemphasised that the *only* life-saving action for a patient with a prosthetic valve who has suffered a haemodynamic disaster is immediate notification of the *nearest* cardiac surgery centre and transport to it. Time should not be wasted on securing a diagnosis or on returning the patient to the hospital where the valve replacement was carried out [19].

Valve dehiscence is not uncommon; it occurs soon after surgery if caused by cutting out of sutures or may be associated with early or late prosthetic valve endocarditis. The clinical picture depends on the severity of the paraprosthetic leak. Regurgitant murmurs vary from obvious to absent, as does mechanical haemolysis, but anaemia, wide pulse pressure, hyperkinetic left ventricle or unexplained dyspnoea or heart failure may be the clue. Rocking of the aortic or mitral valve seat on 2D echocardiography may be seen when dehiscence is extensive. Aortic paraprosthetic leaks are usually easily visualised on colour flow mapping. However, mitral paraprosthetic regurgitation can be difficult to see and either missed altogether or underestimated on TTE although well quantitated on TOE.

Thrombosis is linked with inadequate anticoagulation and may be acute or subacute with or without distal embolism. Heart failure, absent or muffled prosthetic sounds and auscultatory features resembling stenosis and regurgitation may be noted. Cinefluoroscopy shows limited or absent disc or poppet motion. Earlier models of the Starr–Edwards and Björk–Shiley valves had a radiolucent occluder; echocardiography is essential in these cases [20,21] and is usually more quickly available and more informative. Immediate surgery is necessary. Intravenous streptokinase or urokinase has a place in the treat-

ment of thrombosis of tricuspid prostheses [22]. It should only be used if cardiac surgical facilities are not immediately available. Significant haemodynamic improvement may follow but immediate definitive surgery is preferable. Thrombolytic therapy is inappropriate for left-sided heart valve thrombosis because of the risk of embolism and because it wastes time, may be ineffective and will be disastrous if the diagnosis was wrong. Thrombosis is not confined to mechanical valves but has also occurred on tissue valves though rarely.

Encapsulation by a pannus of thrombus may present more chronically with worsening dyspnoea or recurrent emboli despite good anticoagulant control and is more common with a mechanical valve in the mitral position.

Prosthetic valve endocarditis

The presenting features are similar to those in native valve endocarditis. Patients with prosthetic valves and suspected or proven endocarditis should be referred at once to a hospital with cardiological and cardiac surgical facilities.

Prosthetic valve endocarditis is divided into early and late infections. Early infections are caused by organisms which gain access at the time of cardiac surgery or through wound infections and generally present within 2 months. Commonly responsible organisms include *Staphylococcus epidermidis*, *Staphylococcus aureus* and *Candida albicans* [23]. The organisms may be sensitive to the prophylactic antibiotics given to cover the peri-operative period [24]. Late infections are caused by the same organisms that are responsible for native valve disease, except that *Candida* and *Staphylococcus epidermidis* are more common for the first year [23] and are really 'early' infections emerging 'late'. Infection tends to cause necrosis of the paravalvular tissue with abscess formation and eventual development of a paraprosthetic leak.

Late prosthetic valve endocarditis is similar to native valve infection but embolic episodes are more common. Transthoracic echocardiography is frequently unsatisfactory with mechanical valves but vegetations may be identified in patients with tissue valves [25]. Transoesophageal echocardiography is particularly indicated. Mortality is still high but early surgery has dramatically improved the prognosis [26]. The indications for this are outlined in Table 2. Close co-operation between the cardiologist, cardiac surgeon and microbiologist is crucial to ensure optimal management. Early prosthetic valve endocarditis usually requires surgery because the responsible organisms are difficult to eradicate by medical means. Medical treatment alone may be successful in cases of prosthetic valve endocarditis caused by antibiotic sensitive micro-organisms, with no prosthetic dysfunction and when embolic events are absent. Early operation combined with antibiotic treatment should be the rule in all other cases.

It is important not to delay treatment for the results

Table 2. Indications for valve re-replacement in prosthetic valve endocarditis

Early prosthetic valve endocarditis
Cardiac failure (except when caused by myocardial dysfunction)
Prosthetic valve dysfunction
New paravalvular leak
Obstruction by vegetation or thrombus
Aggressive or resistant organism
<i>Staphylococcus epidermidis</i>
<i>Staphylococcus aureus</i>
Fungi
Abscess formation
Persistent sepsis
Relapse of prosthetic valve endocarditis
Embolism

of blood cultures because bacterial multiplication and tissue destruction are most rapid early in the course of infection [27]. Initial therapy should be with benzylpenicillin, flucloxacillin and gentamicin [28]. In cases due to streptococci, benzylpenicillin [2 mega units (1.2 g) 4-hourly iv] and gentamicin should be used [28]. *Staphylococcus aureus* infection should be treated with flucloxacillin (2 g 4-hourly iv) plus fusidic acid (500 mg 8-hourly orally) or gentamicin and treatment continued for at least 4 weeks [28]. Netilmicin can be considered as an alternative to gentamicin in the elderly and those with impaired renal function since there is some evidence to suggest that it is less toxic [29]. The final choice of antibiotic is determined by the micro-organism isolated and its sensitivities. Anticoagulation should be continued and carefully monitored in those already on it before the development of the infection [30].

Mechanical haemolysis

Prosthetic valve dysfunction significantly increases the incidence of this problem with all types of prosthesis. Endocarditis, prosthetic valve dysfunction, cardiac haemolysis and chronic occult gastrointestinal blood loss need to be considered in any patient with a prosthetic valve presenting with anaemia.

Typically the blood film shows distorted and fragmented cells with microspherocytes and polychromasia. Serum haptoglobin levels are decreased, lactate dehydrogenase (LDH) levels raised and haemosiderinuria is present. Iron and folic acid should be prescribed, but re-operation is advisable where haemolysis is severe and associated with significant prosthetic valve dysfunction.

Myocardial problems

These are common in patients with prosthetic heart valves and have an important bearing on the long-term prognosis. Possible causes include:

- Myocardial damage due to the primary pathology responsible for the valvular disease, eg rheumatic myocardial damage
- Myocardial damage secondary to long-standing native valve disease
- Co-existing coronary artery disease or previous coronary emboli
- Incomplete myocardial preservation during cardiac surgery
- The development of pulmonary vascular disease
- Relative stenosis of an aortic prosthesis: eg smaller sizes of Starr-Edwards aortic valve replacement have an 'effective' orifice area of 1.5 cm² which compares with a cross-sectional area of the native aortic valve of 3.5–4 cm².
- The rigid ring of a mitral valve replacement further compromises left ventricular function, as does removal of papillary muscles; these may be critical factors when function was poor pre-operatively.

Cardiac arrhythmias

Cardiac arrhythmias are common in this patient group. Important remediable causes include diuretic-induced hypokalaemia and digoxin toxicity. A new arrhythmia with or without haemodynamic compromise may be a presenting feature of prosthetic valve dysfunction. As in other patients, proven symptomatic bradyarrhythmia due to conduction tissue disease is a definite indication for permanent pacing. Second-degree and complete atrioventricular block (which may follow aortic valve or mitral plus tricuspid valve replacement) and symptomatic sinus node dysfunction require permanent pacing [31]. Ongoing therapy with agents that depress conduction tissue function may confuse the assessment. Discontinuing the drug or reducing the dose may solve the problem, but these drugs may be required to control additional symptomatic tachyarrhythmias, making permanent pacing necessary to control the bradyarrhythmia.

Sudden death accounts for 15–20% of the late deaths after aortic valve replacement and is probably most commonly due to a malignant ventricular arrhythmia [32]. Although anti-arrhythmic therapy is commonly prescribed there is no firm evidence that this decreases the incidence of late sudden death in patients with ventricular tachycardia on ambulatory ECG monitoring.

Clinical presentations and problems

Cardiac failure

Possible causes or precipitating factors include:

- Prosthetic valve dysfunction
- Prosthetic valve endocarditis
- Valve prosthesis-patient mismatch
- An additional uncorrected valvular lesion
- Any of the previously mentioned causes of myocardial dysfunction, particularly coronary artery disease

- A complicating cardiac arrhythmia, eg uncontrolled atrial fibrillation
- Significant anaemia

Global left and/or right ventricular failure may develop insidiously or present acutely even years after uncomplicated successful valve replacement. The reason may occasionally be obscure. In patients with chronic myocardial failure where a correctable underlying cause has been excluded, long-term therapy with diuretics and angiotensin converting enzyme inhibitors is appropriate [33].

Prevention of endocarditis

Good oral hygiene with regular dental attendances is essential in patients with prosthetic valves. Patients having a dental procedure under general anaesthesia should be referred to hospital [34]. The recommendations for antibiotic prophylaxis are shown in Table 3. All patients should carry a card (available free from the British Heart Foundation) warning of the danger of endocarditis and listing the recommendations for prophylaxis.

Prosthetic heart valves and surgery

Temporary cessation of oral anticoagulant therapy is necessary prior to surgery for all but the most minor procedures. Discontinuation of oral anticoagulants 2–4 days before surgery and resumption 1–3 days afterwards is not accompanied by an increased risk of thromboembolism [36]. Subcutaneous heparin (5,000 units) tds or low molecular weight heparin bd should be substituted.

Prosthetic heart valves and pregnancy

Ideally, women with valvular heart disease should complete their families before valve replacement but, if

this is not possible, a mechanical valve should be used because of the problems with durability of tissue valves.

Pregnancy in patients with mechanical prosthetic valves poses special management problems because of increased fetal risks [37–39]. The maternal hazards are not increased by pregnancy. Coumarin anticoagulants cross the placenta and are teratogenic if the fetus is exposed to them in the first trimester. A warfarin embryopathy with mental retardation, blindness and skeletal abnormalities may occur but the risk of this appears to be less than 5% when warfarin is used throughout pregnancy [39]. There is also an increased incidence of fetal loss, premature delivery and CNS abnormality, due in part at least to fetal and placental haemorrhage induced by warfarin. In one series there were 22 fetal or neonatal deaths in 71 pregnancies [37]. However, single-centre series invariably come from the Third World where facilities for accurate anticoagulant control may be less than ideal and the true fetal risk is probably very much less than this [40].

Heparin therapy is associated with increased fetal loss comparable to that seen with warfarin (presumably because of retroplacental haemorrhage), must be given parenterally and can cause maternal osteoporosis, alopecia and thrombocytopaenia. However, heparin does not cross the placenta and therefore is not teratogenic. An alternative to using warfarin throughout pregnancy is to change to subcutaneous heparin once pregnancy is confirmed and to continue this to 16 weeks, keeping the activated partial thromboplastin time (APTT) at about twice the control. Unfortunately this may not prevent valve thrombosis and larger doses endanger both mother and fetus. Warfarin is then substituted to keep the INR close to 2.5 and then changed for iv heparin again at 38 weeks. Phenindione may be used instead of warfarin with transfer to intravenous heparin for the last 2 weeks of pregnancy [39], but evidence that this is safer than coumarin drugs is still awaited.

Table 3. Antibiotic prophylaxis of infective endocarditis in patients with prosthetic heart valves

	No penicillin allergy	Penicillin allergy
Dental procedures under local anaesthesia in general dental practice	Amoxycillin 3 g orally ^a 1 hour pre-operatively	Clindamycin 600 mg orally 1 hour pre-operatively [35] ^b
Dental procedures under local anaesthesia in patients who have received penicillin in the previous month	Clindamycin 600 mg orally 1 hour pre-operatively [35] ^b	
Dental procedures under general anaesthesia	Amoxycillin 1 g im in 2.5 ml of 1% lignocaine and gentamicin 120 mg im before induction, then 0.5 g amoxycillin orally 6 hours later	Vancomycin 1 g iv over 60 min, then gentamicin 120 mg iv before induction
Genitourinary, obstetric and gynaecological, gastrointestinal and upper respiratory tract surgery or instrumentation	As above. The subsequent 0.5 g of amoxycillin may be given orally or im	As above

im, intramuscular; **iv**, intravenous.

^a May be given with 1 g of probenecid to retard excretion, or may be followed by a second 3 g dose of amoxycillin 6 hours later.

^b An alternative is erythromycin stearate 1.5 g orally 1 hour pre-operatively, then 0.5 g 6 hours later.

Patients with prosthetic valves who have transient ischaemic attacks are debarred from holding an ordinary driving licence and should report these attacks to the licensing centre [41]. Those who have had no such attacks may hold an ordinary driving licence. Those on long-term oral anticoagulants cannot hold a heavy goods or public service vehicle licence, and a number of criteria must be satisfied before a patient with a tissue prosthesis not taking oral anticoagulants can hold such a licence [41].

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