

Recommendations for the management of patients after heart valve surgery

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Approximately 50 000 valve replacement operations take place in Europe annually and almost as many valve repair procedures. Previous European guidelines on management of patients after valve surgery were last published in 1995 and were limited to recommendations about antithrombotic prophylaxis.¹ American guidelines covering the broader topic of the investigation and treatment of patients with valve disease were published in 1998 but devoted relatively little space to post-surgical management.² This document represents the consensus view of a committee drawn from three European Society of Cardiology (ESC) Working Groups (WG): the WG on Valvular Heart Disease, the WG on Thrombosis, and the WG on Rehabilitation and Exercise Physiology.

In almost all areas of patient management after valve surgery, randomized trials and meta-analyses do not exist. Such randomized trials as do exist are very few in number, are narrowly focused with small numbers, have limited general applicability, and do not lend themselves to meta-analysis because of widely divergent methodologies and different patient characteristics. Recommendations are therefore almost entirely based on non-randomized studies and relevant basic science.

The early post-operative period and rehabilitation

Recommendations

- (i) The benefits of rehabilitation following coronary artery surgery have been well documented, and one study following valve surgery has demonstrated similar benefits from exercise training.³ A multidisciplinary rehabilitation programme should therefore be available for all patients undergoing valve surgery. This is particularly important for patients whose post-operative course has been complicated by heart failure.
- (ii) Whether rehabilitation should be conducted on an inpatient or outpatient basis should be determined by the availability of local facilities and the pattern of the patient's recovery.⁴
- (iii) Baseline echocardiography should be performed on all patients post-operatively and at the completion of rehabilitation to permit comparison with future studies during long-term follow-up.⁵

- (iv) Patients should be educated about anticoagulation, including drug interactions and self-management if appropriate,⁶ about the recognition of important symptoms and about the elements of a healthy lifestyle.
- (v) Selected patients should be offered exercise training, bearing in mind that exercise tolerance after mitral valve replacement (MVR) is much lower than that after aortic valve replacement (AVR), particularly if there is residual pulmonary hypertension.⁷
- (vi) Good candidates for exercise training include patients with AVR and normal left ventricular (LV) function and patients who have undergone successful mitral valve repair with preserved LV function.⁸ Patients likely to be suitable should undergo a submaximal exercise test about 2 weeks after surgery to guide detailed exercise recommendations.

Antithrombotic management

Recommendations

- (i) Antithrombotic management should encompass the effective management of risk factors for thromboembolism (TE) in addition to the prescription of antithrombotic drugs.^{9,10}

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- (ii) Until new direct antithrombin drugs are licensed for patients following valve surgery, vitamin K antagonist drugs will be required for oral anticoagulation.¹¹
- (iii) Oral anticoagulation is recommended for the following situations.
- Lifelong for all patients with mechanical valves irrespective of valve type or date of introduction.¹²
 - Lifelong for patients with bioprostheses or mitral repair who have other indications for anticoagulation, e.g. atrial fibrillation (AF), heart failure, and impaired LV function (ejection fraction <30%).¹²
 - For the first 3 months, in all patients with bioprostheses or mitral valve repair involving the use of a prosthetic annuloplasty ring. Although there is widespread use of aspirin as an alternative to anticoagulation for the first 3 months in patients with no other indications for anticoagulation, there are no randomized studies to support the safety of this strategy.^{13,14}
- (iv) Patients with bioprostheses or mitral valve repair who are not on anticoagulation require close follow-up not only to detect evidence of structural degeneration or recurrence of mitral regurgitation, but also to detect the onset of AF.¹⁵
- (v) The mode of initiation of anticoagulation immediately after valve surgery varies widely with no randomized trials to guide practice. Until data from randomized trials are available, intravenous unfractionated heparin, monitored to an aPTT of 1.5–2.0 until a therapeutic INR is achieved with oral anticoagulation, is probably safer than subcutaneous low molecular weight heparin (LMWH) or subcutaneous unfractionated heparin.¹⁶ If LMWH is used, antifactor Xa monitoring should be employed to ensure optimum anticoagulation,¹⁶ particularly in patients with renal failure or obesity, in whom dosage may be difficult to determine.¹⁷
- (vi) The choice of optimum INR for oral anticoagulation should take into account patient risk factors and the thrombogenicity of the individual prosthesis as determined by reported **valve thrombosis rates** for that prosthesis in relation to specific INR levels.^{18–20} Reported **thrombo-embolic rates** in the literature do not provide sufficient guidance about individual prosthesis thrombogenicity as they are heavily influenced by so many other patient-related factors and the methods of data collection.^{18–20} Unfortunately, currently available randomized trials comparing different INRs offer little general guidance due to limitations imposed by their selection criteria, small numbers of patients with short follow-up, and varied methodologies, making them unsuitable for meta-analysis.^{21–26}
- Certain caveats apply:
- Prostheses cannot be conveniently categorized by basic design (e.g. bileaflet, tilting disc, etc.) or date of introduction for the purpose of determining thrombogenicity.
 - For many prostheses on the market, sufficient data on valve thrombosis rates at different levels of INR do not exist to allow categorization. Until further

Adjust target INR to intracardiac conditions and prosthesis thrombogenicity		Without risk factors	With risk factors
		SR LA 0 MVgr 0 LV normal SEC 0 AVR	AF LA > 50 mm MVgr + EF < 35% SEC + MVR, TVR, PVR
Prosthesis thrombogenicity (as determined by valve thrombosis rates) ^{19,20,24–27}	Low	2.5	3.0
	Medium	3.0	3.5
	High	3.5	4.0
<p>Low = Medtronic Hall, St Jude Medical (without Silzone), Carbomedics AVR, bioprostheses. Medium = Bileaflet valves with insufficient data, Bjork-Shiley valves. High = Lillehei Kaster, Omniscience, Starr Edwards.</p> <p>SR, sinus rhythm; LA, left atrium; MVgr, mitral valve gradient; EF, ejection fraction; SEC, spontaneous echo contrast; TVR and PVR, tricuspid and pulmonary valve replacement, respectively.</p>			

data become available, they should be placed in the 'medium thrombogenicity' category.

- Newly introduced prostheses require particularly careful evaluation before categorization on the basis of thrombogenicity. History has shown that lower thrombogenicity in comparison with older designs cannot be assumed. These prostheses also should be categorized as of 'medium thrombogenicity' until reliable scientific data become available to re-categorize them.
 - INR recommendations in individual patients may need to be revised downwards if recurrent bleeding occurs from a pathological source not amenable to treatment.
- (vii) The risk of major bleeding begins to rise when the INR exceeds 4.5 and rises steeply and exponentially above an INR of 6.0.²⁸ An INR of ≥ 6.0 therefore requires reversal of anticoagulation. However, in patients with prosthetic valves who are not bleeding, intravenous vitamin K should not be used because of the risk of valve thrombosis if the INR falls rapidly. The patient should be admitted to hospital, the oral anticoagulant stopped, and the INR allowed to fall gradually. If the INR is >10.0, consideration should be given to the use of fresh-frozen plasma.²⁹
- (viii) Bleeding with a therapeutic INR is often related to an underlying pathological cause and it is important to identify and treat it.
- (ix) In patients who are bleeding with a high INR, a risk assessment must be made according to the severity, site, and controllability of bleeding. If the risk to life from continued bleeding, inaccessible to local control, is greater than that of valve thrombosis (e.g. intracranial bleeding), cessation of anticoagulation should be accompanied by prothrombin complex concentrate. Intravenous vitamin K may also be necessary if bleeding continues, as the half-life of

factor VII is only 6 h. However, it should be recognized that both factor concentrates and vitamin K increase the risk of valve thrombosis.²⁹ Intracranial and, in particular, intracerebral haemorrhage always necessitates reversal of anticoagulation.³⁰ The exact timing of the resumption of anticoagulation remains controversial but the committee recommends that it should be resumed after 1 week as the long-term risk of further intracranial bleeding is lower than that of valve thrombosis and TE.

- (x) Poor anticoagulation control with high variability of the INR is the strongest independent predictor of reduced survival after valve replacement.³¹ Self-management of anticoagulation has been shown to reduce INR variability and should therefore be recommended in all patients who, after a period of education and training, have the ability and understanding to control their own anticoagulation.⁶
- (xi) In determining whether an antiplatelet agent should be added to anticoagulation in patients with prosthetic valves, it is important to distinguish between the possible benefits in vascular disease and those specific to prosthetic valves when computing the risk:benefit ratio. Trials showing a benefit from antiplatelet drugs in vascular disease³² and in patients with prosthetic valves and vascular disease³³ should not be taken as evidence that patients with prosthetic valves and no vascular disease will also benefit.
- (xii) With the exception of dipyridamole, the addition of an antiplatelet agent to anticoagulation increases the risk of major bleeding.³³⁻³⁷ Hyper-responders to aspirin (excessive prolongation of the bleeding time) are at particular risk.³⁸ Antiplatelet agents should, therefore, not be prescribed for all patients with prosthetic valves, but should be reserved for specific indications only. In each patient, a balance must be achieved between probable benefit and the increased risk of bleeding, particularly intracerebral haemorrhage, as the latter carries a very high mortality rate. With the possible exception of intracoronary stenting, all indications are thus relative rather than absolute.
- (xiii) Relative indications for the addition of an antiplatelet agent to anticoagulation are as follows.
 - (a) Concomitant arterial disease.³²
 - (b) Following intracoronary stenting.³⁹
 - (c) Recurrent embolism, but only after full investigation, treatment of identified risk factors and optimization of anticoagulation management have failed to abolish the problem.
 - (d) In patients with caged ball valves, in particular, dipyridamole should be considered rather than aspirin in view of its apparent efficacy in prostheses of this unique design, with less risk of bleeding than aspirin.^{34,35}
- (xiv) Relative contraindications to the use of concomitant antiplatelet agents are as follows.
 - (a) Previous history of gastrointestinal bleeding, particularly from ulcer disease or angiodysplasia.⁴⁰
 - (b) Hyper-responders to aspirin, with excessively prolonged bleeding time.³⁸
 - (c) Poorly controlled hypertension, due to the increased risk of intracerebral haemorrhage⁴¹

and the lack of efficacy of aspirin in preventing stroke in hypertension.⁴²⁻⁴⁴

- (d) Elderly patients, particularly women aged >75.⁴³
- (e) Patients on multiple medications, patients who require frequent courses of antibiotics and patients whose anticoagulation control, despite all efforts, is extremely erratic.
- (xv) Although most instances of short-term anticoagulation interruption do not lead to TE or valve thrombosis, the corollary is that most cases of valve thrombosis occur following a period of anticoagulation interruption for bleeding or another operative procedure.^{45,46} Anticoagulation management during subsequent non-cardiac surgery therefore requires very careful management based on risk assessment. High-risk patients include those in the following categories.^{9,10,47}
 - (a) Patients with risk factors for TE, especially patients with multiple risk factors, i.e. AF, past history of TE, heart failure, impaired LV function (ejection fraction $\leq 30\%$), and hypercoagulability.
 - (b) Patients with mechanical prostheses in the mitral position.
 - (c) Patients with particular types of mechanical prostheses known to have a high incidence of valve thrombosis in the presence of a low INR (see table above).
 - (d) Patients undergoing surgery for malignant disease or an infective process, due to the hypercoagulability associated with these conditions.

The risk of anticoagulation interruption increases in proportion to the number of factors in the categories described above.⁴⁷ For very high-risk patients, anticoagulation interruption should be avoided if at all possible. Many minor surgical procedures (including dental extraction) and those where bleeding is easily controlled do not require anticoagulation interruption.⁴⁸ The INR should be gradually lowered to a target of 2.0, surgical haemostasis should be meticulous and, where appropriate, post-operative drainage should be used to prevent haematoma formation.

- (xvi) For major surgical procedures, the risk of bleeding varies according to surgical site.⁴⁹ If interruption of oral anticoagulation is considered essential, patients should be admitted to hospital in advance and transferred to intravenous unfractionated heparin (aPTT 1.5-2.0) while the INR is gradually reduced. The safety of LMWH given subcutaneously at home, as an alternative pre-operative preparation for surgery, has not been established. Effective anticoagulation with intravenous heparin should be resumed as soon as possible after the surgical procedure and maintained until the INR is once again in the therapeutic range.

Follow-up after surgery

Recommendations

- (i) The first post-operative visit to hospital or a cardiac specialist should be within 6 weeks of discharge if there has been no period of inpatient rehabilitation, or within 12 weeks if a rehabilitation programme has been completed.

- (ii) At the first post-operative visit, it is important to assess the completeness of wound healing and to establish baselines for continued follow-up in terms of:
 - (a) Symptomatic status and physical signs.
 - (b) Heart rhythm and ECG abnormalities.
 - (c) Chest X-ray, to ensure resolution of any post-operative abnormalities.
 - (d) Echocardiography to assess any pericardial effusion, ventricular function, prosthetic function, the competence of valve repair, and disease at other valve sites.
 - (e) Routine haematology and biochemistry and tests for haemolysis.
- (iii) The frequency of future follow-up should be determined by the patient's progress and by local facilities, but ideally all patients who have undergone valve surgery should continue to be followed-up at a cardiac centre in order to detect, at an early stage, deterioration in prosthetic function, recurrence of regurgitation following valve repair, or progression of disease at another valve site, any of which can occur with relatively little or no change in symptoms.²
- (iv) The frequency of echocardiography during follow-up should be determined by the results of previous echocardiography, symptomatic status, the type of surgery and the existence of other pathology.^{5,50} Patients requiring echocardiography at a clinic visit include:
 - (a) Patients in whom a previously identified abnormality requires monitoring for progression or response to treatment, e.g. mitral regurgitation, sewing ring thrombus, previous endocarditis, etc.
 - (b) Patients with new symptoms suggestive of prosthetic dysfunction, progression of another valve lesion, or worsening LV function. If prosthetic dysfunction is suspected, transoesophageal echocardiography and cinefluoroscopy may also be required to supplement transthoracic echocardiography.⁵ Cinefluoroscopy is useful for detecting early limitation of leaflet movement in bileaflet and tilting disc valves.⁵¹
 - (c) Patients with bioprostheses, homografts or autografts, to detect structural deterioration or, in the case of the Ross procedure, to detect aortic root dilatation,⁵² progressive aortic regurgitation, or structural deterioration in the pulmonary homograft.⁵³ The likelihood of these complications increases after the first 5 years.
 - (d) Patients with Marfan's syndrome, to detect progressive dilatation of the aorta or progressive mitral regurgitation.⁵⁴
- early post-operative period.⁵⁵ The risk is also higher in the presence of structural valve deterioration with associated calcification.⁵⁵ Distortion of stentless bioprostheses due to inaccurate implantation technique can also pre-dispose to valve thrombosis.⁵⁶
- (ii) Valve thrombosis should be suspected in any patient with any type of prosthetic valve who presents with a recent increase in shortness of breath or fatigue, because valve thrombosis can develop slowly and insidiously over several days or weeks. Suspicion should be higher if there has been a period of interrupted or sub-therapeutic anticoagulation in the preceding few weeks or if there has been a cause for increased coagulability (e.g. dehydration, infection, etc.).
- (iii) The diagnosis should be confirmed by transthoracic and/or transoesophageal echocardiography⁵⁷ or cinefluoroscopy.⁵¹
- (iv) If valve thrombosis is the suspected or proven diagnosis, the patient should be immediately transferred to a cardiac centre with cardiac surgical facilities after giving 5000 U of heparin intravenously.
- (v) Urgent or emergency valve replacement should be the treatment of choice for obstructive thrombosis of AVR or MVR in critically ill patients without serious co-morbidities to avoid the risks of systemic embolism and recurrent thrombosis with thrombolysis (*vide infra*).
- (vi) Thrombolysis should be considered in:
 - (a) Critically ill patients with AVR or MVR unlikely to survive surgery because of serious co-morbidities and poor performance status prior to developing valve thrombosis.
 - (b) Situations in which surgical treatment is not immediately available and the patient is in extremis and cannot be transferred.
 - (c) Thrombosis of tricuspid or pulmonary valve replacements, because of the high success rate and low incidence of embolism.
- Thrombolysis is less likely to be successful in MVR, in chronic thrombosis, or in the presence of pannus (tissue ingrowth).^{58,59} The risk of systemic embolism from prostheses on the left side of the heart is ~20% and the risk of recurrent valve thrombosis is about the same. The risk of major bleeding is ~5%.^{58,59}
- (vii) In haemodynamically stable patients with mild or no obstruction, in whom acute discontinuation or recent subtherapeutic anticoagulation is considered the most likely cause for valve thrombosis, a short course of intravenous heparin should be used first, closely monitored by echocardiography and/or cinefluoroscopy.⁵¹ A good response with gradual resolution of the thrombus obviates the need for either surgery or thrombolysis.

Management of valve thrombosis

Recommendations

- (i) There should be awareness of the possibility of valve thrombosis in any patient with a prosthetic valve, whether mechanical or bioprosthetic. Obstructive valve thrombosis can also occur in stentless bioprostheses and has even been witnessed in an aortic homograft. In patients with bioprostheses, the risk of valve thrombosis is highest in unanticoagulated patients in the presence of low cardiac output in the

Management of thromboembolism

Recommendations

- (i) It should be recognized that TE after valve surgery is multifactorial both in its aetiology and in its origin.⁹ Although many TE events will have originated from thrombus or a vegetation on a prosthesis or as a result of the abnormal flow conditions created by a prosthesis, many others will have arisen from other

sources as a result of other pathogenetic mechanisms⁶⁰ and be part of the background incidence of stroke and TIA in the general population.⁶¹ This underlines the importance of thorough investigation of each episode of TE, rather than simply increasing the target INR or adding an antiplatelet agent.

- (ii) Investigation of TE should include:
 - (a) Review of the quality of anticoagulation control.
 - (b) Thorough auscultation to detect new murmurs or muffling of prosthetic heart sounds.
 - (c) Checking for evidence of endocarditis, especially if there has been a recent infective focus, recent dental treatment, or recent surgery.
 - (d) A search for new risk factors, e.g. AF, hypertension, and diabetes.
 - (e) Blood tests for prothrombotic factors.⁹
 - (f) Transthoracic and transoesophageal echocardiography to search for aortic atheroma and intracardiac or prosthetic thrombus and to assess prothrombotic flow conditions. Cinefluoroscopy may also be useful in detecting restricted leaflet movement if a small thrombus at the hinge of a bileaflet valve is suspected.⁵¹
 - (g) Carotid Doppler examination to identify carotid atheroma as a possible source in TE events causing stroke or TIA.
 - (h) In the case of cerebrovascular TE events, cerebral imaging using either CT or MRI should be performed to exclude intracerebral haemorrhage, to document the size of the recent infarction, and to detect other previously 'silent' areas of infarction.
- (iii) Treatment strategy of recent cerebrovascular events remains controversial, balancing the risk of recurrent embolism, if anticoagulation is withheld or reversed, against the risk of haemorrhagic transformation if it is continued or increased. The risk of recurrent embolism depends on the source and the mechanism involved (e.g. high risk if there is left atrial or prosthetic thrombus still present), but overall, in the first 2 weeks, the risk of early recurrent embolism is lower than the risk of haemorrhagic transformation in a large infarct. If the infarct is >35% of the cerebral hemisphere or if there is uncontrolled hypertension, oral anticoagulation should be withheld for at least 5 days, until hypertension is controlled, and until a repeat CT scan shows no haemorrhagic transformation. In the meantime, intravenous heparin (aPTT 1.5–2.0) can be used.
- (iv) Prevention of further TE events involves:
 - (a) Treatment or reversal of remediable risk factors such as AF, hypertension, hypercholesterolaemia, diabetes, smoking, chronic infection, and prothrombotic blood test abnormalities.
 - (b) Optimization of anticoagulation control, if possible with patient self-management, on the basis that better control is more effective than simply increasing the target INR.
 - (c) Because of the increased risk of bleeding, antiplatelet drugs should not be prescribed 'automatically' in all cases, but rather targeted to specific situations in which there is likely to be a benefit, e.g. in arterial disease. If aspirin is used, it

should be prescribed in a low-dose formulation (≤ 100 mg daily) and combined with low-intensity anticoagulation (INR ≤ 2.5 – 3.5 depending on the site of the prosthesis and its thrombogenicity).

Management of haemolysis

Recommendations

- (i) As 'subclinical' haemolysis is common with normally functioning prostheses of all types (more common with mechanical valves),⁶² haemolysis only becomes a serious issue if it is severe enough to cause anaemia.⁶³ Nevertheless, blood tests to detect haemolysis (LDH, haptoglobin, reticulocyte count) should be part of routine follow-up in order that trends can be monitored. Absence of anaemia does not exclude significant haemolysis compensated by enhanced erythropoiesis.⁶²
- (ii) If anaemia occurs in association with haemolysis, it is important to establish that it is entirely caused by haemolysis and not due to the co-existence of conditions (deficiency of iron, vitamin B₁₂, or folates), which limit the bone marrow capacity to compensate for red cell loss.
- (iii) Identification of true haemolytic anaemia necessitates thorough investigation of the prosthetic valve, as severe haemolysis is almost always associated with abnormal function, usually either paravalvular leak (PVL) or, in the case of bioprostheses, structural deterioration. Transoesophageal echocardiography is often required in addition to transthoracic echocardiography as the latter may not detect significant PVL, particularly in the mitral position.⁶⁴ Haemolytic anaemia due to prosthetic dysfunction is an indication for re-operation in patients who are otherwise fit for surgery.
- (iv) In patients with haemolytic anaemia in whom re-operation would be associated with high risk, medical treatment can often keep the anaemia under control. It comprises:
 - (a) Iron supplementation and correction of any other deficiency, adjusted according to the response to treatment.
 - (b) Beta-blockers to reduce transvalvular flow velocities and associated shear stress.
 - (c) Erythropoietin therapy for particularly severe haemolytic anaemia, when other measures have been unsuccessful.⁶⁵

Endocarditis prophylaxis

Recommendations

- (i) The risk of prosthetic valve endocarditis (PVE) is highest in the first 3–6 months after prosthetic valve implantation, but thereafter remains relatively constant.⁶⁶ Therefore, there is a lifelong requirement for antibiotic prophylaxis for dental, endoscopic, and surgical procedures.⁶⁷ Patients with annuloplasty rings are also at risk, although the risk is lower than that of prosthetic valves.
- (ii) Vigilance for the symptoms and signs of PVE throughout follow-up is essential, particularly in those

patients with risk factors for PVE which include previous endocarditis, diabetes, renal failure, advanced NYHA class, double valve replacement, and poor anticoagulation control.^{31,68-70} Vigilance should be enhanced in high-risk patients with more frequent follow-up in the early months after any surgical procedure.

- (iii) Prevention of early PVE (PVE occurring in the first few months after implantation) requires measures to be taken at the time of valve surgery and during the early post-operative period, comprising:
 - (a) Pre-operative intranasal treatment for patients who are nasal carriers of *Staphylococcus aureus*.
 - (b) Meticulous skin preparation and avoidance of wound haematoma and haemopericardium.
 - (c) Antibiotic prophylaxis of short duration (48 h or until chest drains are removed), directed mainly against staphylococci, the most common pathogens in early PVE. Vancomycin or teicoplanin should be used where the risk of MRSA is high (patients who have been in hospital for a prolonged period prior to surgery).
 - (d) Scrupulous care and early removal of intravenous lines and urinary catheters.
- (iv) Prevention of late PVE involves commonsense measures in addition to antibiotic prophylaxis.
 - (a) Patient education about oral hygiene, regular dental care, and antibiotic prophylaxis.
 - (b) Patient education about the early symptoms and signs of PVE. In particular, it should be stressed that any fever that lasts more than 2 or 3 days should be a matter for medical consultation and that self-administration of antibiotics should be avoided before blood cultures have been taken.
 - (c) Wherever possible, invasive procedures such as intravenous lines and urinary catheterization should be avoided unless absolutely essential.
 - (d) Surgical procedures, even minor procedures, require scrupulous asepsis and avoidance of wound haematoma formation.
- (v) Appropriate antibiotic prophylaxis is the mainstay of late PVE prevention and needs to be adjusted to the type of procedure which the patient is about to undergo.^{71,72}
 - (a) For dental, oral, respiratory, and oesophageal procedures, prophylaxis is required mainly against streptococci. Amoxicillin is the preferred antibiotic in a single dose of 2 or 3G 1 h prior to the procedure. Patients allergic to penicillin should receive clindamycin, azithromycin, or clarithromycin.
 - (b) For gastrointestinal and genitourinary procedures, prophylaxis should be directed mainly against *Enterococcus faecalis*, using ampicillin 2G intravenously plus gentamycin 30 min before starting the procedure with a second dose 6 h after the procedure. Patients allergic to penicillin should receive vancomycin plus gentamycin.
 - (c) For procedures on infected tissues, antibiotics appropriate to the particular organism(s) causing the infection should be continued.

Management of prosthetic valve endocarditis

Recommendations

- (i) PVE is an extremely serious condition with a high mortality rate. A high index of suspicion needs to be maintained, particularly in those patients at higher risk of PVE (discussed earlier). If PVE is suspected, the patient should be referred immediately to a cardiac centre with facilities for cardiac surgery, as early and effective treatment reduces mortality.
- (ii) If PVE is suspected, several blood cultures must be taken before any antibiotics are administered. The diagnosis rests predominantly on the combination of positive blood cultures and echocardiographic evidence of prosthetic infection, including vegetations, paraprothestic abscesses, or a new paraprothestic leak.⁷³ Transoesophageal echocardiography is essential because of its greater sensitivity in detecting these abnormalities.⁶⁴ However, negative blood cultures or inconclusive echocardiographic findings do not exclude the diagnosis of PVE. Early in the course of PVE, echocardiographic changes may be absent or extremely subtle. Serial transoesophageal echocardiography performed by an experienced operator is therefore very important. Serial blood cultures should also be performed.
- (iii) Treatment of PVE requires a specialist multidisciplinary approach involving cardiologists, cardiac surgeons, microbiologists, and, if necessary, intensivists.
- (iv) A minority of cases of PVE can be cured with intravenous antibiotics alone if the diagnosis is made early enough and there are no indications for surgery (discussed below). Medical cure is more likely in late PVE (occurring more than 6 months following surgery) and in non-staphylococcal infections.⁷⁴ Intravenous antibiotics should be continued for 4-6 weeks, and for a minimum of 2-3 weeks after normalization of body temperature.
- (v) Surgical treatment should be considered in the following circumstances:⁷⁵
 - (a) Failure of medical treatment to control the infection, as indicated by persistent fever, persistently elevated or rising inflammatory markers, and progression of echocardiographic abnormalities.
 - (b) Haemodynamically significant PVL, particularly if there is evidence of deteriorating ventricular function.
 - (c) Large vegetations, particularly if they have given rise to embolism.
 - (d) Development of intracardiac fistulae.
- (vi) The timing of surgical treatment remains controversial. Decision-making should be individualized, taking into account co-morbidities, the infecting organism, the risks of surgery, the degree of cardiac decompensation, and the extent to which infection can be controlled. If infection can be brought under control without detriment to cardiac function, firmer tissues allow more secure fixation of a replacement prosthesis and may permit repair of damage at another valve site, thus avoiding the need for a second prosthesis. However, in many cases, progressive cardiac decompensation necessitates urgent surgery before the

infection is controlled. Staphylococcal infections are particularly destructive and nearly always require urgent surgery before control of infection can be achieved.

- (vii) Surgical principles in re-operation for PVE involve:⁷⁵
- Removal of the infected prosthesis and extensive debridement of the annulus and abscesses to remove all infected and non-viable tissue.
 - Laboratory examination of debrided tissue to identify organisms (particularly important, if blood cultures have been negative).
 - If extensive destruction requires patch reconstruction, autologous or heterologous pericardium should be used because of its greater resistance to bacterial colonization than synthetic materials.
 - As there is no significant difference in susceptibility to recurrent PVE between mechanical and bioprosthetic valves, the choice of replacement prosthesis should be determined by other factors (age, necessity for anticoagulation in AF, etc.).
 - In aortic PVE with extensive destruction of the aortic root, homograft root replacement is the treatment of choice. Alternatively, a valved Dacron conduit can be used if a homograft is not available.
 - In aortic PVE with associated mitral valve endocarditis, it is often possible to excise infective leaflet tissue and repair the mitral valve with glutaraldehyde-treated pericardium.
 - Following surgical treatment, intravenous antibiotics should be continued for 6 weeks. In the case of fungal endocarditis, lifelong oral antifungal therapy should be considered.

Management during pregnancy

Anticoagulation management

Recommendations

- Anticoagulation management in pregnancy requires close collaboration between cardiologist and obstetrician and a thorough discussion of the risks and benefits of various anticoagulation strategies with the patient.
- As LMWH is not approved for use in prosthetic valve patients in pregnancy due to the high risk of valve thrombosis, and as subcutaneous unfractionated heparin throughout pregnancy carries a similarly high risk, strategies which should be discussed with the patient are:
 - Heparin during the first trimester (to avoid warfarin embryopathy), followed by oral anticoagulation up to the 36th week with subsequent replacement by heparin until delivery.
 - Oral anticoagulation throughout pregnancy, until the 36th week, followed by heparin until delivery.

The foetal and maternal complications of anticoagulation strategies are summarized in the following tables.⁷⁶⁻⁷⁹

Because of the high rate of maternal complications with heparin therapy, particularly when given throughout pregnancy, the committee strongly recommends strategy (b), i.e. oral anticoagulation throughout pregnancy until the 36th week. If the warfarin dose does not exceed 5 mg daily, the risk of embryopathy is extremely small.⁸⁰

Foetal complications in % (n) with different anticoagulation regimes

Regime	Spontaneous abortions	Embryopathy	Spontaneous foetal death
UF heparin total	23.8 (5/21)	0.0 (0/17)	42.9 (9/21)
UF heparin first trim	24.8 (57/230)	3.4 (6/174)	26.5 (61/230)
OAC total	24.7 (196/792)	6.4 (35/549)	33.6 (266/792)

UF, unfractionated; total, during whole pregnancy; OAC, oral anticoagulation; Trim, trimester.

Maternal complications in % (n) with different anticoagulation regimes

Regime	Thrombo-embolic complications	Death
UF heparin total	33.3 (7/21)	15.0 (3/20)
UF heparin first trim	9.2 (57/230)	4.2 (7/167)
OAC total	3.9 (31/788)	1.8 (10/561)

Management of delivery

Recommendations

- There should be close collaboration between cardiologist, obstetrician, and obstetric anaesthetist.
- The patient should be transferred to heparin therapy at the 36th week, with close monitoring, preferably using antifactor Xa activity and aiming for activity >0.55 U/mL. If antifactor Xa activity assays are not available, the aPTT ratio should be maintained at or above 2.0 to allow for the increased heparin resistance in the third trimester. Heparin should be discontinued at the start of labour and restarted 4–6 h after delivery. Oral anticoagulation should be resumed after 24 h.
- If labour occurs pre-term while the patient is still on oral anticoagulants, a caesarean section should be performed after reducing the INR to 2.0. A vaginal delivery should be avoided under oral anticoagulation because of the danger of foetal intracranial bleeding.
- Vaginal delivery can be recommended:⁸¹
 - If the patient is not on oral anticoagulation at the onset of labour.
 - If there is no significant prosthetic dysfunction.
 - If there is no other significant cardiovascular disease, e.g. disease at another valve site, impairment of LV function, aortic dilatation, etc.
 - If a specialist obstetric anaesthetist is available to provide epidural anaesthesia.

Management of the malfunctioning valve

Recommendations

- All patients with prosthetic valves or valve repair should undergo cardiological examination and echocardiography as soon as pregnancy is confirmed,

if there has been no such recent assessment. It is important to document prosthetic function or the competence of valve repair, ventricular function, and disease at any other valve site in order to determine the frequency of further examinations during pregnancy. Cardiac medication should also be reviewed.

- (ii) In the case of regurgitation due to anything more than a minor PVL, or minor recurrent regurgitation following valve repair, the regurgitation should be monitored with echocardiography at intervals during the pregnancy, to determine its effect on LV function, in view of the additional volume load on the LV during pregnancy. Diuretics and vasodilators may be required. Hydralazine should be used rather than ACE-inhibitors which should be avoided in pregnancy because of their adverse effects on the foetus.⁸² If regurgitation increases, LV function deteriorates and the patient becomes increasingly symptomatic, the mother's interests should be put ahead of those of the foetus and surgical treatment recommended. If the foetus is sufficiently mature, it is sometimes possible to combine caesarean section with valve replacement under the same anaesthetic.
- (iii) Valve thrombosis is the most serious cardiac complication of pregnancy and is associated with a high mortality rate. Extra vigilance for this complication is necessary during pregnancy, particularly in patients at higher risk, such as patients with mechanical mitral prostheses of higher thrombogenicity (see table in Anticoagulation Management section), and patients with a record of poor compliance with anticoagulation. If valve thrombosis occurs, the mother's interests again should be paramount and urgent operation recommended.

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