

PROSTHETIC HEART VALVES

Risk Stratification for Surgery

Surgical risk can be estimated by online risk calculators from the Society of Thoracic Surgeons (<http://www.sts.org/quality-research-patient-safety/quality/risk-calculator-and-models/risk-calculator>) or the European System for Cardiac Operative Risk Evaluation (EuroSCORE; <http://www.euroscore.org>). Current risk scores (including Euroscore, STS and Ambler score) are useful but may not always provide a reliable estimate of operative mortality regardless of other patient characteristics.¹ The STS score tends to underestimate risk for AVR, whereas the logistic EuroSCORE overestimates risk for isolated valve surgery.² Tables 1-3 presents the surgical risk assessment of patients with VHD.

Heart Valve Centers

Patients with VHD should be ideally treated by a dedicated Heart Team at a Primary or Comprehensive Valve Center (Table 4). Recommendations for follow-up and periodic imaging after intervention are presented in Tables 5 and 6

Prosthetic valve types

Mechanical valves

Prosthetic heart valves (PHV) are either mechanical or bioprotheses (tissue valves).³ Tissue engineering is employed for the creation of tissues analogous to a native human heart valve.⁴

Ball-cage Starr-Edwards.

Tilting disc Medtronic-Hall, Omniscience, the old Lillihei-Kaster, and Bjork-Shiley.

Bileaflet St Jude, CarboMedics, and On-X.

Randomized and observational long-term studies have shown good and comparable outcomes with FDA-approved mechanical valves such as the Starr-Edwards valve, the Medtronic-Hall valve, and the St Jude Medical valve for AVR and MVR.⁵ However, the bileaflet valves are the most commonly implanted due to low bulk and better haemodynamics and lower thrombogenicity in the mitral position. The Starr-Edwards although the most durable valve has a higher risk of haemolysis and thrombogenicity and is not suitable for MVR.

Tissue valves (bioprotheses)

Stented xenografts

Porcine Carpentier-Edwards SAV, Medtronic HancockII, Medtronic Mosaic, Abbott Biocor, Abbot Epic

Pericardial bovine Carpentier-Edwards PERIMOUNT Line, Sorin Mitroflow PRT, Abbott Trifecta, Avalus Medtronic

Stentless xenografts

Porcine Abbott Toronto SPV, Medtronic Freestyle

Pericardial bovine Sorin Solo Smart

Sutureless

Pericardial bovine Edwards INTUITY Elite, Sorin Perceval 5

Homograft (allograft) aortic valves harvested from cadavers

Autograft aortic valves. Fabricated from the patient's own pericardium or pulmonary autografts (Ross principle).

Bioprosthetic valves are usually either **porcine** (assembled aortic valve leaflets or complete aortic valves) or **pericardial bovine**. **Stentless** valves are designed to provide a larger orifice area to achieve a more physiological flow pattern and improve hemodynamics. However, their theoretical hemodynamic advantage, and the expected longevity benefit remains controversial.⁶ An alternative to sutured stented or stentless valves is rapid deployment or **sutureless** valves, which are a hybrid of conventional surgical and transcatheter valves. They have sufficient radial force to allow annular implantation without sutures, and facilitate minimally invasive surgical aortic valve replacement. However, the tissue of the native diseased valve needs to be excised, which requires some suturing. Thus, the benefits and drawbacks of sutureless devices are debated.⁷ Doppler echocardiography may detect haemodynamic valve deterioration (increase in transprosthetic gradient or regurgitation) related to structural valve degeneration in $\approx 30\%$ of patients after surgical aortic valve replacement with a bioprosthetic valve. Haemodynamic valve deterioration was associated with a 2.2-fold higher adjusted mortality. Diabetes mellitus and renal insufficiency were associated with early haemodynamic valve deterioration (2-5 years), whereas female sex, warfarin use, and stented BPs (versus stentless) were associated with late deterioration (>10 years).⁸

In patients with valvular heart disease and persistent LV dysfunction after surgical correction, ICD implantation for primary prevention may be needed, according to recommendations for dilated cardiomyopathy (ESC 2022 GL on VA and SCD, I C).⁹

Mechanical vs Bioprosthetic valves

Three randomized trials have compared mechanical with bioprosthetic valves. In the old VA and Edinburgh randomized trials that were conducted in the 70s, mechanical valves showed better survival (especially in the aortic position) and less reoperation but a higher rate of bleeding.^{10,11} In the third RCT that was conducted with modern valves in the 90s, mechanical

valves had a similar survival rate, thromboembolism, bleeding, and endocarditis with bioprosthetic ones, but a significantly lower risk of valve failure and reoperation for aortic valve replacement.¹² Reports from the STS National and New York State Databases have shown that among AVR and MVR patients, long-term mortality rates were similar for bioprosthetic versus mechanical valve patients. **Bioprostheses** were associated with a higher long-term risk of reoperation and endocarditis, but a lower risk of stroke and hemorrhage.^{13,14} In a registry of patients aged 50–69 years who had undergone AVR in Sweden 1997–2013, those who received mechanical valves had better long-term survival than those with bioprostheses. The risk of stroke was similar; however, patients with bioprostheses had a higher risk of aortic valve reoperation and a lower risk of major bleeding.¹⁵ In a large, population-level comparison of valve prostheses in California, **mechanical** mitral valves were associated with lower mortality than biologic valves among patients up to 70 years of age, whereas the benefit of a mechanical aortic valve disappeared by 55 years of age. In both cases, the implantation of a mechanical prosthesis was associated with a significantly lower risk of reoperation but a higher risk of bleeding and, in some age groups, stroke.¹⁶ Mechanical valves are considerably durable in patients of any age with a low risk of reoperation. They appear to have less structural deterioration beyond 10 years and especially in the young but require anticoagulation for life, and patients are at an increased risk of haemorrhagic and other complications.¹⁷ They are preferred in patients <50 years of age for AVR and 65 years for MVR and in surgery for infective endocarditis, as well as in patients in need of anticoagulation for AF (Tables 7-9, and Figure 1).^{5,18} An exception is women at childbearing age, given the risk of anticoagulation and thromboembolism during pregnancy. Pregnancy in women with a prosthetic valve is high risk, with more favourable outcomes in women with a biological valve, especially in the mitral position.¹⁹ A mechanical valve is recommended in patients on chronic hemodialysis based on the concern of accelerated calcification of bioprosthetic valves in patients with end-stage renal disease, but no significant difference in survival of dialysis patients after cardiac valve replacement with tissue versus mechanical valves has been demonstrated.^{20,21}

Uncertainty and debate continue about which type of AVR is appropriate for patients 50 to 65 years of age. Newer surgical bioprosthetic valves may show greater freedom from structural deterioration, specifically in the older individual, although a high late mortality rate in these studies may preclude recognition of valve dysfunction.²² Several studies have shown a survival advantage with a mechanical prosthesis in this age group. Alternatively, large retrospective observational studies have shown similar long-term survival rates in patients 50 to 69 years of age undergoing mechanical versus bioprosthetic valve replacement.²²

Patients <50 years of age at the time of AVR incur a higher and earlier risk of bioprosthetic valve deterioration. Overall, the predicted 15-year risk of needing reoperation because of structural deterioration is 22% for patients 50 years of age, 30% for patients 40 years of age, and 50% for patients 20 years of age, although it is recognized that all bioprostheses are not alike in terms of durability.²² In a recent STS database, inpatients aged ≤60 years, mechanical AVR was associated with an independent risk-adjusted survival benefit compared with bioprosthetic AVR.²³ Glutaraldehyde-preserved bioprostheses without antimineralization treatment are at high risk of calcification, and recently, a high rate of valve deterioration was reported for Sorin Mitroflow bioprostheses implanted in the aortic position of young patients.^{24 25} Subclinical bioprosthetic valve thrombosis is also not uncommon and may occur several years after surgery or TAVI.^{26,27} Redo surgery for bioprosthetic aortic valve stenosis is associated with an excellent outcomes in experienced centres.²⁸ Continuous evolution of valve technology, especially with bioprostheses, as well as patient preferences should be taken into account for prosthetic valve selection in the current era.²⁹

The possibility of a valve-in-valve approach with **TAVI** in patients with failed surgical bioprostheses may result in implantation of bioprostheses in younger patients.³⁰ To date, the intermediate-term durability of TAVI valves has compared favorably with that of SAVR valves, as reported in randomized trials and registries . For the most part, these data reflect observations made in older patients and may not be applicable to younger populations (eg, <70 years).²²

The **Ross procedure** is usually offered to young patients with bicuspid aortic valves without AR or a dilated aorta, but may be considered for all age groups.³¹ The patient's own PV and adjacent main pulmonary artery are removed and used to replace the AV and if necessary the aortic root with reimplantation of the coronary arteries into the graft. A human pulmonary or aortic homograft is inserted in the pulmonary position. Reoperations after the Ross procedure, when required, may be complex, frequently involve multiple structures, and carry significant morbidity.³² However, in experienced centers, may reduce stroke and cardiac mortality,³³⁻³⁵ and failing autografts can be successfully repaired,³⁶ while the option of TAVR is now available. The value of this approach in adults with rheumatic heart disease or AR, is questionable.

Anticoagulation

Target INR for mechanical prostheses is presented in Tables 10-12 and Figures 2 and 3. As a general rule, for mechanical prostheses in aortic position an INR of 2-3 is indicated for bileaflet and Medtronic-Hall valves and 2.5-3.5 for the others. Lower INR (1.5-2) may be

adequate for new bileaflet valves in the aortic position.³⁷ For MVR an INR of 2.5-3.5 is sought. Bioprostheses (and MV repair) require anticoagulation for 3 months postoperatively according to current guidelines; however, continuation of warfarin for up to 6 months resulted in reduced cardiovascular mortality in a recent large registry.³⁸ REcommendations are provided in Table 13 and Figure 4. The development of portable anticoagulation monitors has enabled self-testing and self-adjustment of anticoagulation therapy.³⁹ In INR > 5 warfarin is withheld, and the INR is determined after 24 h. Oral vitamin K (phytonadione) is necessary only when INR is > 10 in the absence of bleeding.⁴⁰ If bleeding is present, IV vitamin K (5-10 mg) for major bleeding or 2-5 mg oral vitamin K (or 1-2 mg of the IV preparation in a cup of orange juice) for non-major bleeding are given.⁴¹ Pharmacogenetic testing for guiding doses, by means of genotyping for variants CYP2C9 and VKORC1 that are associated with reduced clearance and thus a decrease in warfarin requirement, is not clinically useful.⁴²⁻⁴⁴

Direct oral anticoagulants (DOAC) such as dabigatran should not be used for anticoagulation in the presence of mechanical prosthetic valves. The RE-ALIGN trial was prematurely stopped due to increased incidence of thrombotic events with dabigatran compared to warfarin.⁴⁵ In patients with bioprosthetic valves, rivaroxaban appears to be as effective as warfarin (RIVER trial).⁴⁶

Adding low-dose **aspirin** to oral anticoagulation decreases the risk of systemic embolism or death among patients with prosthetic heart valves, but the risk of major bleeding is increased with antiplatelet therapy.⁴⁷ Thus, the choice in mechanical valves should be individualised. In patients with a history of stroke before prosthetic valve insertion, the addition of aspirin (75-100 mg od) to anticoagulation is recommended.⁴⁸ If the patient has a stroke despite adequate anticoagulation, addition of aspirin 325 mg od or an increased INR target are needed.

Following **TAVI**, aspirin alone is probably preferable to dual-agent therapy.^{49,50}

Bridging to Surgery or Interventions

The risk of thromboembolism without anticoagulation in the presence of a mechanical prosthesis is 0.03 to 0.05 per day. For major surgical procedures recommendations are presented in Tables 14-16. However, the optimal periprocedural anticoagulation is not established. In a meta-analysis, heparin bridging in patients receiving vitamin K antagonists for AF, PHV or VTE conferred a >5-fold increased risk for bleeding, whereas the risk of thromboembolic events was not significantly different between bridged and nonbridged patients. The use of therapeutic dose LMWH was associated with an increased risk of bleeding compared with prophylactic or intermediate dose.⁵¹ Minor procedures, such as

dental extraction, do not require interruption of anticoagulation. Patients with bileaflet mechanical aortic valves in sinus rhythm and no previous thromboembolism are low-risk and no bridging is required for interruption of warfarin.⁵² Implantation of pacemakers or defibrillators in patients with moderate to high thromboembolic risk does not necessitate interruption of warfarin (INR: 2- 3.5) since heparin use is associated with more pocket haematomas.⁵³ When bridging is required in high-risk patients, SC LMWH is convenient but in patients with stage IV renal failure anti-Xa monitoring is required, while in stage V IV UFH is recommended.⁵² The management of patients on warfarin who present with an ACS is discussed in the relevant Chapter.

Haemorrhage

In major bleeding four-factor prothrombin complex concentrate is preferred to fresh frozen plasma since >1500 mL of fresh frozen plasma are needed to achieve a meaningful increase in coagulation factor levels (Table 17).⁵⁴ In the case of intracerebral hemorrhage, reversal of anticoagulation with IV vitamin K (1-2 mg to achieve an INR<1.3) is needed. Intensive treatment to lower the blood pressure with a target systolic level of <180 mm Hg is recommended,⁵⁵ but there has been evidence that values <160-140 mm Hg may reduce haematoma enlargement and improve functional outcomes.^{56 57} Therapeutic anticoagulation should be started after 2 weeks of intracranial haemorrhage. In patients at high thromboembolic risk it may be considered after day 6, but the risk of increased haemorrhagic complications.⁵⁸

Thrombosis of Prosthetic Valves

Prosthetic-valve thrombosis in the current era has a reported incidence of 0.03 to 0.13% per patient-year, although it used to be up to 8% with the initial mechanical valves.⁵⁹⁻⁶¹ Bioprosthetic valve thrombosis may also occur.⁶² The major contributing factors are inadequate anticoagulant therapy, and mitral location of the prosthesis. Acquired abnormalities of von Willebrand factor multimers are also associated with aortic and mitral prosthesis dysfunction, with occasional gastrointestinal bleeding and gastrointestinal angiodysplasia. Quantitative von Willebrand factor tests may provide adjunctive value in the difficult assessment of prosthetic valve dysfunction.⁶³ Obstruction of prosthetic valves may be caused by thrombus formation, pannus ingrowth, or both. Transthoracic echocardiography can assess haemodynamic severity and follow resolution of valve dysfunction, and transoesophageal echocardiography is indicated to assess thrombus size and valve motion. Fluoroscopy or CT may also be used for assessing valve motion.

If the prosthesis is obstructed by pannus the valve needs to be replaced. Emergency **surgery** is recommended for a thrombosed left-sided prosthetic valve, and NYHA III-IV symptoms or a large clot (>10 mm) or peripheral embolism (Tables 18 and 19, and Figures 5 and 6). Surgery is associated with a mortality of 15%, but most of reported patients are NYHA class III/IV.⁵⁹ **Fibrinolysis** may be considered if surgery is not an option or is very high risk for the treatment of thrombosis of right-sided prostheses, but carries a risk of bleeding and thromboembolism.^{61,64} Complete success of thrombolysis is achieved in 70% of cases. Fibrinolysis should be considered in thrombosis of **tricuspid or pulmonary valve** replacements, because of the higher success rate and low risk of systemic embolism. Fibrinolytic therapy for a **left-sided** prosthetic valve obstructed by thrombus may be considered for small thrombi <10 mm as determined by transesophageal echocardiography in stable or inoperable patients. Fibrinolysis is less likely to be successful in mitral prostheses, in chronic thrombosis, chronic thrombosis, or in the presence of pannus that may be difficult to distinguish from thrombus. In case of haemodynamic instability, a short protocol is recommended, using either intravenous recombinant tissue plasminogen activator 10mg bolus+90mg in 90 minutes with UFH, or streptokinase 1 500 000 U in 60 minutes without UFH. Longer durations of infusions can be used in stable patients. If fibrinolytic therapy is successful, it should be followed by intravenous UFH until warfarin achieves an INR of 3.5 for aortic and 4 for mitral prosthetic valves. Low-dose aspirin is also given. Fibrinolysis is associated with a mortality of 8%,⁵⁹ and risk of cerebral embolism 12% to 15% depending on the size of the clot (odds ratio of 2.41 per 1-cm² increment).⁶⁵

When subclinical valve thrombosis is suspected in bioprosthetic valve recipients who present with dyspnoea and/or rising transprosthetic gradients, echocardiographic and possibly computed tomographic imaging is recommended to evaluate bioprosthetic leaflet morphology and motion. In the absence of clinically overt BPV obstruction, oral anticoagulation therapy is recommended, with follow-up echocardiography scheduled 1 to 2 months following treatment initiation.⁶⁶

Following **TAVI**, The reported incidence of **valve thrombosis** ranges from 0.6% to 7%.^{67 68} Hypo-attenuating leaflet thickening (HALT) may be detected in up to 13% of patients, and may progress to hypo-attenuation affecting motion (HAM), and subclinical or clinical leaflet thrombosis.^{69,70} A detailed discussion is provided in the Chapter on AS.

Prosthetic valve stenosis and regurgitation

Mechanical valve stenosis is rare and typically due to valve thrombosis or pannus formation (Tables 21-23, and Figure 7). Paravalvular regurgitation affects 5%-17% of all surgically implanted prosthetic heart valves, and mainly the mitral valve.⁷¹ Patients may be

asymptomatic or present with hemolysis or heart failure. Reoperation is associated with increased morbidity and is not always successful because of underlying tissue friability, inflammation, or calcification. Percutaneous closure should be considered for closure of clinically symptomatic paravalvular leaks and in experienced centers it is successful in up to 90% of the cases with <10% complications rate (obstruction of the titling valve leaflet, embolization of the device, coronary artery obstruction, or stroke).⁷² Prosthetic heart valve **endocarditis** is discussed in the Chapter on Endocarditis.

Haemolysis

Subclinical intravascular hemolysis is noted in most patients with a normally functioning mechanical prosthetic valve, severe hemolytic anemia is uncommon and suggests paravalvular leakage due to partial dehiscence of the valve or infection (Table 18). Diagnosis of valve-induced hemolysis is established by increased serum lactate dehydrogenase concentrations, decreased serum haptoglobin concentrations, and reticulocytosis.⁷³

MRI

Magnetic resonance imaging can be performed safely in patients with prosthetic heart valves, except those with a Pre 6000 Starr–Edwards caged-ball prosthesis.⁷⁴

Pregnancy

Women with a mechanical heart valve have in average a 5-24% risk of valve thrombosis and only a 58% chance of experiencing an uncomplicated pregnancy with a live birth.^{75,76}

In pregnant women with mechanical valves, the anticoagulation management is not established. Usually LMWH (or UFH) for the first trimester followed by warfarin with an INR target of 2.5-3.5 is recommended, although the option of warfarin between weeks 6 and 12, or even the first trimester provided that the necessary dose is <5mg/day is now available.⁷⁷⁻⁷⁹ Warfarin throughout pregnancy is associated with a 2.7% thrombotic events, 0.9% maternal mortality, 65% live births, and 2% embryopathy or foetopathy, whereas with first trimester heparin followed by warfarin corresponding numbers are 2%, 5.8%, 80%, and 2.2%. LMWH throughout pregnancy is associated with no embryopathy but high maternal mortality of 2.7% and thrombotic events of 8.7%.⁸⁰ Recommendations are provided in Table 24-26, and Figures 8 and 9.

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