Aortic stenosis (AS) is currently the most common cause of AS in adults and the most frequent reason for aortic valve replacement (AVR) in these patients. Its incidence is on the rise since this pathology is a disease of ageing and the population is getting older.1 The natural history of AS has shown that in the absence of surgical management the patient develops progressive invalidating symptoms of syncope and angina. The mortality rate at five and 10 years is 68% and 82%, respectively, from congestive heart failure.2 Indication for surgery arises when the severity of the stenosis becomes significant (valve area <1cm² or 0.6 cm²/m² body surface area) or the patient becomes symptomatic.3

Conventional surgical AVR is the reference treatment and is performed under cardiopulmonary bypass, cardiac arrest and aortic cross-clamping. The native cusps are excised and a prosthesis is sutured into the aortic annulus replacing the native valve (Figure 1).

Isolated AVR carries an average 30 day mortality of 3.8±1.5%.4 AVR is the “gold standard” treatment for symptomatic aortic stenosis and has shown to improve outcome and survival. Following AVR and removal of the obstruction to the left ventricular outflow, the heart function rapidly improves in part because the ventricle has been preconditioned to generate higher pressures. Thus, there are few contraindications to valve replacement for severe aortic stenosis when left ventricular function is not depressed.5

Moreover, the indications for intervention have been revised to perform corrective procedures before establishment of severe myocardial damage and according to some authors even prior to onset of symptoms.6 A multivariate analysis of almost 6,000 patients having AVR, showed that the five most important predictors of mortality were age≥80 years, NYHA class≥III, EF≤30% associated with previous MI, emergent AVR and concomitant coronary artery bypass graft (CABG) surgery.7
Limits related to comorbidity:

Additionally, patients can be refused surgery because of severe comorbidities known to be associated with poor outcome. Since the prevalence of AS increases with age, and as longevity within the general population is increasing, the proportion of patients for whom surgery may be too late due to multiple comorbidities is also expected to increase. These comorbidities may be related to concomitant cardiac diseases which further compromise myocardial function such as poor left ventricular ejection fraction (LVEF), previous cardiac surgery and associated coronary artery disease (CAD). Other comorbidities related to the general condition of the patient such as neurological dysfunction, chronic lung disease, liver cirrhosis and renal insufficiency are also predictors of poor outcome.

These patients are prone to severe postoperative complications as infections and bleeding; and the procedure itself may further compromise vital organ function. The contribution of these factors can increase the odds ratio for operative mortality by a factor of 10.6 for emergency versus elective surgery, 4.9 for renal failure, 3.1 for NYHA class (III-IV versus I-II) and 4.3 for neurological dysfunction. Thus it may too late to perform elective valve replacement on patients with terminal end-organ failure of the liver (Child-Pugh class B or C cirrhosis) or lung.

Despite the increased risk with several comorbidities, survival in elderly patients (≥80 years) with severe AS and low LVEF (≤30%) and/or chronic renal failure was still better in patients who had AVR as compared to those who did not.

Limits related to age:

Cardiologists are reluctant to refer elderly and high-risk patients for AVR. Age was a recurrent factor for refusing surgery for 31.8% of patients with AS of the Euro Heart Survey on Valvular Heart Disease and 62% of patients with AS in another study from the USA. Advanced age is an important predictor of operative risk and survival in cardiac surgery. It has repeatedly and consistently been shown to be a predictor of both poor in-hospital outcome and long-term survival.

In a series of 6,359 patients undergoing aortic valve replacement, Hannan et al. showed an incremental increase in the adjusted hazard ratio for 30-month survival from 1.57 to 2.18 to 3.96 in age ranges 65-74 y, 75-84 y and ≥85 y, respectively. After isolated AVR, the 30-month survival was 90.1% for patients of age <75 and 86.2% for patients ≥75 years of age. A study in octogenarians with severe AS showed that AVR had significant survival benefit with 1-year, 2-year and 5-year survival rates of 87, 78 and 68%, respectively, compared with 52, 40 and 22%, respectively, in those who had no AVR. Elderly patients on the other hand experience increased operative mortality and also are at higher risk for valve-related events.

Nevertheless, age is not, per se, a contraindication to AVR according to published guidelines. Analysis of determinants of operative mortality in regard to age showed that age is not linearly related to the mortality rate after AVR and there is considerable functional improvement after valve replacement.
Limits related to contractile reserve:

Delay in the management of patients with AS may give rise to certain “cardiac” profiles that are intrinsically associated with poor outcome after AVR. When the aortic valve area is less than half of normal, the gradient across the valve becomes important and the increased afterload is associated with concentric myocardial hypertrophy which maintains systolic performance. The EF is decreased because of increased afterload and impaired diastolic function, but contractility is maintained and AVR has an excellent outcome with EF returning to normal values once the afterload excess is removed. However in other patients, hypertrophy fails to normalise wall stress causing the abnormal afterload to reduce ventricular ejection, reducing cardiac output, adding to the heart failure syndrome.

This subset of patients with low gradient AS and low EF is known to be associated with poorer outcomes after AVR. It is seen in 5–10% of all cases of severe AS and defined as patients with a mean gradient <30 mm Hg (or 40 mm Hg), an aortic valve area <1 cm², and an EF <35% (or 40%). In patients with low gradient and low cardiac output, there is severe decrease in EF in excess of what would have occurred through afterload increase alone. The associated myocardial dysfunction contributes to a poor prognosis. Since the transvalvular gradient is small, there is a correspondingly smaller reduction in afterload and thus a smaller improvement in EF following surgery. AVR in this group of patients carries a poor prognosis with an operative mortality reported as high as 21% with a 50% death rate within four years of the procedure. Although AVR is superior to medical management in terms of short-term survival, surgery is not recommended to all low-gradient, low-EF patients. Risk stratification of patients before surgery may decide whether medical or surgical therapy is best.

This stratification is based on:

1) Stenosis severity
2) Inotropic reserve
3) Presence or absence of CAD or other valve disease, and
4) Other comorbidities.

Patients without inotropic reserve and those with a large increase in aortic valve area with increased output are least likely to benefit from AVR and are generally considered a contraindication because of "pseudo-aortic stenosis". Nevertheless, in a recent international multicentre registry of low EF/low gradient AS, AVR was associated with superior survival and was advocated when mean pressure gradient was >20 mm Hg and in the absence of excessive comorbidities or severe CAD with large scarring caused by extensive myocardial infarction. The authors conclude that the lack of contractile reserve in these patients may not systematically be related to irreversible LV dysfunction but probably due to an afterload mismatch that is not corrected by inotropic stimulation with dobutamine infusion.

Technical limits to surgical AVR:

In addition to comorbidities, patients may present with technical difficulties and complexities which make AVR challenging to perform. This is particularly true in patients undergoing redo surgery with patent coronary artery bypass grafts, where the risk of injury to the graft during dissection can be prejudicial to myocardial vascularity. The matter is further complicated by issues related to cardioplegia when the patent grafts are the internal thoracic arteries. Patients those with previous mediastinal radiotherapy and radiation damage to the myocardium are also known to have poor outcomes. Finally, in the presence of heavily calcified and atherosclerotic ascending aorta (porcelain aorta), cross clamping and aortotomy can be impossible.

Role of risk stratification models in predicting outcome

Since operative mortality is a standard parameter of operative success and indirectly a reflection of the operative risk, it is judged a good measure of quality of cardiac surgical care, as long as patient risk factors are taken into consideration, thus several risk scores have been described to calculating predicted operative mortality for patients undergoing cardiac surgery. The most employed surgical scores, namely the EuroSCORE and STS score offer quantitative assessment to establish whether patients are at high risk for surgery. Besides the intrinsic flaw of not having been designed for this population, these scores do not capture all relevant variables. Moreover they collect a large number of preoperative data that are not all incorporated in the calculation of predicted mortality. Thus out of more than 50 variables collected by the STS score, only 24 are actually used in its mortality algorithm for patients having valve surgery. Variables such as hepatic disease, previous chest wall irradiation, nutritional status and frailty that can have profound effects on surgical outcomes are not included in the STS risk algorithm.

Amber et al. described a risk model that can be applied to patients undergoing valve surgery, with or without concomitant CABG surgery based on data from the Great Britain and Ireland National cardiac surgical database. While scores are useful tools to predict operative mortality in a broad sense, clinical judgement and careful preoperative assessment of patients are the key determinants in decision making.

Transcatheter aortic valve implantation (TAVI) techniques

Transcatheter aortic valve implantation (TAVI) techniques have been developed to provide alternative approaches to patients for whom conventional AVR is fraught with a considerable risk (Figure 2). These techniques are performed without cardiopulmonary bypass or aortic cross clamping under general or locoregional anaesthesia, with fluoroscopic and transoesophageal echocardiography (TEE) guidance.

Figure 2: Heavily calcified and atherosclerotic ascending (porcelain) aorta (arrows). Conventional AVR would be a considerable technical challenge and fraught with hazards. A transcatheter valve has been successfully inserted into the aortic annulus (asterisk).
They have been performed via two distinct approaches, namely the transfemoral (TF) and transapical (TA) approaches with established feasibility and have been described in detail. Each approach has its advantages and the selection strategy of patients for one technique or the other depends on centre and physician preference. The decision for performing TAVI is considered in patients with severe symptomatic AS having:

- Contraindications to, or high risk for AVR (quantified by a EuroSCORE ≥20% or STS score ≥10%)
- Life expectancy >1 year
- Favourable anatomy for valve implantation

Patients undergo complete clinical examination, transthoracic echocardiography (TTE), TEE, coronary angiography, aortic and femorolac angiography and multislice computed tomography prior to surgery. This screening process is necessary to establish feasibility of TAVI and conformity of the aortic root geometry and anatomy. The contraindications for TAVI are listed in Table 1. Despite opening new horizons for patients refused or contraindicated conventional surgery, several questions remain unanswered concerning the durability of the prosthesis, the influence of paravalvular leaks on survival, and LV function, and the incidence of endocarditis after TAVI.

### Table 1: Contraindications and limits for TAVI

<table>
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<tr>
<th>I. Related to the aortic valve</th>
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<td>1. Congenital aortic stenosis, unicuspid or bicuspid aortic valve</td>
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<td>2. Non-valvular aortic stenosis</td>
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<td>3. Aortic annulus &lt;18mm or &gt;27mm</td>
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<th>II. Associated cardiac disease</th>
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<tbody>
<tr>
<td>1. Presence of intracardiac mass, thrombus or vegetation</td>
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<tr>
<td>2. Untreated clinically significant coronary artery disease requiring revascularisation</td>
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<tr>
<td>3. Hypertrophic cardiomyopathy (HOCM)</td>
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<td>4. Active bacterial endocarditis or other active infections</td>
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<th>III. Related to the approach</th>
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<tr>
<td>A. TF approach</td>
</tr>
<tr>
<td>1. Femoral and iliac vessels with significant atheroma or diameter &lt;6-7mm</td>
</tr>
<tr>
<td>2. Severe tortuosity / calcifications of the femoral - iliac vessels</td>
</tr>
<tr>
<td>3. Patients with bilateral iliofemoral bypasses</td>
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<tr>
<td>4. Severe angulation or aneurysm of the abdominal aorta with thrombosis</td>
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<th>B. TA approach</th>
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<tbody>
<tr>
<td>1. Previous surgery of the LV</td>
</tr>
<tr>
<td>2. Calcified pericardium</td>
</tr>
<tr>
<td>3. Non-reachable LV apex</td>
</tr>
<tr>
<td>4. Severe respiratory insufficiency</td>
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They have been performed via two distinct approaches, namely the transfemoral (TF) and transapical (TA) approaches with established feasibility and have been described in detail. Each approach has its advantages and the selection strategy of patients for one technique or the other depends on centre and physician preference.

### Aortic regurgitation

In aortic regurgitation (AR), the main strain comes from volume overload on the LV increasing left ventricular work and leading to ventricular remodelling. Initially this allows the heart to cope with the increased load but will eventually lead to the development of heart failure. AVR improves LV function and forward cardiac output and is should be performed before LVEF falls below 50% or when end-systolic dimension increases above 55 mm. It may be too late in patients with extremely dilated LV with depressed LVEF to gain significant benefit from surgical AVR. Development of pulmonary hypertension in patients with severe AR also increases the surgical risk. However, AVR in patients with severe AR and LVEF<40% was still associated with a mortality benefit compared to those left on medical management. Likewise, AVR in patients with pulmonary hypertension was associated with an acceptable operative risk (23% in-hospital mortality) and the 5-year survival was significantly better (62%) when compared to the conservatively treated group (22%).

### CONCLUSIONS

The prevalence of valvular heart disease is rising with the ageing population. The aortic valves are most commonly affected, generally by degenerative disease. Valve surgery is currently the reference treatment of stenotic and regurgitant lesions. However, if left untreated severe valvular disease may lead to severe myocardial damage with poor ventricular function and loss of inotropic reserve and may be associated with significant morbidity and mortality. Surgical intervention may also be fraught with high risk in the presence of several severe comorbidities or technical problems making the procedure hazardous. Advances in monitoring systems and perioperative pharmacological manipulation together with surgical experience and novel transcatheter approaches push the limits of surgery and can further improve outcomes for selected patients with aortic valvular heart disease.
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