Recent developments for surgical aortic valve replacement: the concept of sutureless valve technology

Introduction
Aortic stenosis has become the most frequent type of valvular heart disease in Europe and North America, presenting frequently as calcified aortic stenosis in adults of advanced age (2–7% of the population aged >65 years). Valvular aortic stenosis is a chronic progressive disease. Patients may remain asymptomatic for a long time and, when symptoms appear, sudden cardiac death may occur. Early valve replacement should be strongly recommended in all symptomatic patients with severe aortic stenosis who are considered to be candidates for surgery. As long as the mean gradient remains above 40 mmHg, there is virtually no lower ejection fraction limit for surgery.

Treatment of valvular aortic stenosis
For more than 40 years surgical aortic valve replacement (aVR) has been recognised as the definitive therapy for severe aortic stenosis. Recently, operative mortality of isolated aVR for aortic stenosis has varied between 1–3% in low-risk patients younger than 70 years old and between 4–8% in selected older adults. Several factors have been recognised to significantly increase the risk of surgery: older age, associated comorbidities, female gender, higher functional class, emergency operation, left-ventricular dysfunction, pulmonary hypertension, coexisting coronary disease and redo-intervention. Long-term survival following aVR is close to that observed in a control population of similar age. Numerous observational studies have consistently demonstrated that corrective surgery in symptomatic patients is invariably followed by a subjective improvement in quality of life (QoL) and a substantial increase in survival rates. In addition, aVR may also provide survival benefit for selected asymptomatic patients when compared with conservative management. Several considerations must be addressed whenever surgical correction of aortic stenosis is warranted, such as the choice of a mechanical valve versus the use of a bioprosthetic valve, including stented and stentless valves, aortic auto- and homografts. While mechanical valves are more durable in general, bioprosthetic valves do not require lifelong anticoagulation.

Recently, transcatheter aortic valve implantation (TAVI) has been demonstrated to be feasible in patients with high surgical risk using either a retrograde transfemoral or an antegrade transapical access. Reported 30-day mortality ranges between 5 and 15% and is acceptable when compared with the risk predicted by the logistic EuroSCORE (varying between 20 and 35%) and the STS Score, although the EuroScore has been shown to markedly overestimate the effective operative risk. One major concern that remains is the high rate of paravalvular regurgitation, which is observed in up to 85% of patients and requires further follow-up and critical evaluation. In addition, long-term durability of these valves, with a focus on the effects of crimping, remains to be addressed, although 3–5 year results are promising.

Management of asymptomatic severe aortic stenosis remains a matter of controversy. The 2008 update of the ACC/AHA guidelines for the management of patients with valvular heart disease also states that aVR may be considered for asymptomatic patients with severe aortic stenosis and an abnormal response to exercise. The decision to operate on asymptomatic patients requires careful weighing of benefits against risks.

Choice of the prosthetic valve with special emphasis on sutureless valve technology
Despite major advances in available technologies, there are still no perfect valve substitutes; whether mechanical or biological, all prosthetic valves have certain advantages and disadvantages. The most recent bileaflet and tilting-disk mechanical valves are, in theory, long-lasting, but require lifelong anticoagulation. In contrast, all tissue valves do not require long-term anticoagulation unless otherwise indicated, but they are all subject to structural valve deterioration over time. Biological valves can be further subdivided into stented and stentless.
The design of stentless valves was intended to provide a more effective valve area. Although, more favourable haemodynamics have been reported, no improvement in long-term durability has been demonstrated thus far. Sutureless valves are a novel technology that allow quick placement of a bioprosthesis without a sewing cuff. This technology will be discussed hereafter in greater detail.

The choice between a mechanical valve and a bioprosthesis in adult patients is mainly determined by assessing the risk of anticoagulant-related bleeding and thromboembolism with a mechanical valve versus the risk of valve degeneration with a bioprosthesis, and by considering the patient’s goals, values and preferences for life and healthcare. Indeed, a recent trial randomised 310 patients aged 55−70 to a mechanical or biological prosthesis. No differences were found in survival or thromboembolism or bleeding rates, but, as expected, a higher rate of valve failure and reoperation was seen following implantation of bioprostheses.

Therefore, rather than setting arbitrary age limits, prosthesis choice should be considered on an individual basis and discussed in detail with the patient. Bioprostheses are appropriate in patients whose life expectancy is less than that of the estimated durability of the bioprosthesis (particularly if comorbidities will necessitate other surgical procedures in the future) and in those patients with increased bleeding risk. Although structural valve degeneration is accelerated in chronic renal failure, poor long-term survival with either type of prosthesis and an increased risk of complications with mechanical valves, may favour the choice of a bioprosthesis in these patients.

QoL issues and informed patient preferences must also be taken into account. The inconvenience of oral anticoagulation can be minimised by self-management of anticoagulation. Although bioprothetic recipients can avoid long-term anticoagulation, they face the possibility of deterioration of their clinical condition due to degeneration of the bioprosthesis and the prospect of reoperation if they live long enough. Furthermore, during mid-term follow-up some patients receiving a bioprosthetic valve may develop another condition requiring oral anticoagulation (e.g. atrial fibrillation, stroke and peripheral arterial disease).

Current experience with sutureless valves
The concept of sutureless valves was first tested in the early sixties in order to facilitate implantation and shorten ischaemic and perfusion times. However, the concept was abandoned due to numerous complications, such as paravalvular leaks (PVLs) and valve-related thromboembolic events. Recently, sutureless AVR has become increasing interesting due to the rapid development of transcatheter valve technology. Shortening the time required for AVR may help to reduce morbidity and mortality, especially in patients who require complex multivalve or combined valve and coronary procedures.

To date, there are >40 patents for sutureless valve technologies and three different types of sutureless prostheses have been implanted:

* The 3f Enable® valve from ATS-Medtronic received CE market approval in 2010
* The Perceval S from Sorin received CE market approval in February 2011
* The Odyssee sutureless prosthesis from Edwards has entered pilot clinical investigation

The Enable valve from ATS-Medtronic

Structure and function of device
The 3f Enable Aortic Bioprosthesis Model 6000 (ATS-Medtronic) comprises a 3f® Aortic Bioprosthesis Model 1000 stentless bioprosthesis with a NiTiNOL stent that unfolds at normal temperature. This bioprosthesis has excellent mechanical properties and performance characteristics. It was designed to mimic the physiological function of the native aortic valve as closely as possible. It is known that the aortic valve is initially tubular and adopts in shape to the haemodynamic forces during the cardiac cycle, thus ensuring unidirectional blood flow. The valve is assembled from three equal sections of glutaraldehyde-fixed equine pericardial tissue. Glutaraldehyde is used to preserve the collagen matrix of the pericardium and to reduce its immunogenic and thrombogenic potentials, while preserving strength and flexibility. The anatomical design of the valve is highlighted by the fact that it appears very similar to the native aortic valve both visually and functionally on echocardiography (Figure 1). The stent used in the Model 6000 bioprosthesis is a self-expanding NiTiNOL frame (Figure 2). This material is capable of recoverable deformation (approximately 8−10
times that of steel), regaining its initial shape when stress is removed (a deformation-driven superelastic effect).

The tabs of the ATS 3f valve are reinforced with equal sections of polyester material and are fixed into specially designed eyelets in the superior aspect of the NiTiNOL frame. The self-expanding NiTiNOL frame partly contributes to the fixation of the device in the deployed location, by virtue of outwardly emitted, radial forces inherent in the NiTiNOL material, delivering a constant outward force. This allows for the use of only one guiding stitch for the correct placement of the valve to the annulus. The polyester fabric covering on the inflow aspect of the device, (referred to as the ‘flange’ or skirt; Figure 2), which minimises the potential for perivalvular leaks and migration, and apposes well to the aortic annulus without blocking the coronary ostia, also aids in fixation of the device.

The model 6000 has a polyacetal homopolymer folding sleeve that is attached to the valve and is used in conjunction with an accessory inserter system to aid folding and insertion of the valve.

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Implantation technique
Surgery is performed under full or mini-sternotomy. Standard cardiopulmonary bypass (CPB) is established by cannulation of the ascending aorta and the right atrium. Myocardial protection is achieved by 100 ml antegrade crystalloid single-shot cardioplegia (Cardioplexol®, Bichsel Laboratory, Interlaken, Switzerland). Transverse aortotomy is performed approximately 2 cm above the commissures. The valve is excised and the annulus decalcified as for conventional AVR.

Sizing of the prosthesis is a crucial step. Neither over- nor under-sizing is recommended, since it is not possible to expand an oversized Enable valve in a smaller annulus and under-sizing may lead to PVLs. Following usual rinsing, the valve is submerged in ice-sludge to allow the folding and insertion of the stented valve into the applicator. A guiding stitch is placed at the level of the lowest point of the native annulus in one of the intracommissural trigones (preferably at the left non-coronary commissure) to avoid rotation or deep insertion of the valve. The stitch is passed through the suture ring of the valve and the prosthesis pushed out of the applicator. Expansion of the NiTiNOL stented valve is performed under constant observation using warm saline solution. The tabs are not sutured to the aortic wall, but attached to the stent; they come in contact with the aortic wall after expansion of the valve. Inspection of the coronary ostia is very easy due to the intra-annular position of the valve. The aortotomy is closed with a running suture and the operation completed in the usual way. Position and function of the valve are assessed by intraoperative transesophageal echocardiography (TEE) immediately after weaning from CPB.
Deployment of the Enable valve with a modified frame is easier since the valve is crimped and a tool provided that ensures simultaneous and circumferential expansion of the frame.

Clinical experience
The midterm results of a prospective, multicentre clinical study evaluating the safety and efficacy of this stented bioprosthesis in patients undergoing isolated AVR with or without concomitant procedures are available at this time. 140 patients (mean age: 76±6 years; 63% of patients in NYHA stage III–IV) received the ATS 3f Enable Bioprosthesis in 10 European centres between March 2007 and December 2009. The mean follow-up was 121.8 patient-years. Valve implantation resulted in significant improvements in patients’ symptoms. The mean systolic gradient was 9.04±3.56 and 8.62±3.16 mmHg with mean effective orifice area of 1.69±0.52 and 1.67±0.44 cm² at 6 months and 1 year, respectively. No significant transvalvular aortic regurgitation was observed. Early complications included three major PVLs (2.1%) resulting in valve explantation and one thromboembolic (0.7%) event. All but one of the early PVLs were evident intraoperatively, but the medical decision was made not to reposition or resolve the issue immediately. Late adverse events included three explantations (2.5%/patient-year): one due to PVL and two due to endocarditis. There was an additional case of late endocarditis (0.8%/patient-year) that resolved through medical management. No structural deterioration, valve-related thrombosis or haemolysis were documented. In conclusion, the sutureless valve implantation technique is feasible and safe with the ATS 3f Enable Bioprosthesis. Valve implantation resulted in excellent haemodynamics and significant clinical improvement. Overall, these data confirm the safety and clinical utility of the Enable Bioprosthesis for AVR.

The Perceval S sutureless valve from Sorin Biomedica Cardio S.r.l
Structure and function of device
Perceval S is a prosthetic valve comprising a bovine pericardium tissue valve attached to a self-expandable NiTiNOL anchoring device, which has the dual role of supporting the valve and providing fixation to the implantation site (Figure 3). The anchoring device design is characterised by two ring segments (outflow and inflow ring), three commissural elements supporting the valve, and three pairs of sinusoidal elements providing fixation in the sinuses of Valsalva. Therefore, the Perceval S prosthesis can be compressed for the implantation and is able to reach its final diameter when released.

The anchoring device is coated with Carbofilm™, a thin turbostratic carbon film that improves material haemo- and bio-compatibility. The tissue valve is manufactured in the same way as other Sorin (Saluggia, Italy) bovine pericardial valves. A button hole is provided on the inflow ring, corresponding to each valve sinus, through which temporary guide threads are passed to aid prosthesis positioning. The bovine pericardial tissue used

![fig. 2](image-url)

A. 3f stentless valve model 1000
B. NiTiNOL frame
C. 3f Enable aortic bioprosthesis model 6000
Implantation technique
The procedure is performed through median sternotomy or through upper right mini-sternotomy. The aorta is cannulated as high as possible to allow a transverse aortotomy approximately 3–3.5 cm above the expected level of the aortic anulus. Excision of the leaflets is performed in a standard fashion, as is the removal of irregular protruding anular calcifications, and there is no need to decalcify the annulus itself. Three guiding sutures are placed below the aortic annulus at the nadir of each sinus.

The device is prepared on a side table by collapsing it (not crimping), and is mounted on a dedicated delivery device. Guiding sutures are passed within the loops present on the external aspect of the inflow ring and the device can be now parachuted into the root. The guiding sutures assure correct alignment and prevent too low positioning into the left ventricular outflow tract. Correct intra-anular positioning is checked before final release and is facilitated due to optimal visualisation and low profile of the delivery device. The inflow and the outflow are released sequentially and the guiding sutures are removed. Final sealing is ensured by dedicated balloon-dilation at 4 atmospheres for 30” under direct vision. Finally the aortotomy is closed as normal.

Clinical experience
At the present time, the Perceval S prosthesis has been investigated in three clinical studies:

- The "PERCEVAL" TRIAL – Perceval S valve pilot trial – V10601
- The "PERCEVAL" Pivotal Trial – V10801
- The "CAVALIER" – Perceval S valve clinical trial for extended CE mark – TPS001

The pilot trial aimed to demonstrate the 30-day safety of the Perceval S valve in 30 high-risk patients (e.g. subjects older than 75 years of age, with NYHA class III and IV, Logistic EuroSCORE >5%, without aortic dilatation) requiring AVR due to stenosis or steno-insufficiency. The valve was implanted following sternotomy, extracorporeal circulation (ECC), aortic cross-clamping, cardioplegic arrest, and removal of the native valve. The prevalence of pure aortic stenosis was 76.7%, and that of mixed lesion 23.3%. The mean logistic EuroSCORE was 13.2%, and the NYHA class was III and IV in 93.3% and 6.7% of patients, respectively. The mean aortic cross-clamp and ECC times were 34±15 min and 59±21 min, respectively. There was one in-hospital death (3.3%), and three deaths occurred within 12 months of follow-up.
The PERCEVAL pivotal trial aimed to confirm the safety and performance results of the first trial in a larger patient population, and enrolled 150 of the same high-risk patients in nine European centres between January 2009 and January 2010. The most recent study, CAVALIER, will enroll between 300 and 500 patients in order to evaluate the safety and effectiveness of the PERCEVAL S sutureless aortic valve. In this high-risk subset of patients, shortening the aortic cross-clamp and ECC times may help reduce mortality and morbidity.32-33

According to the current experience with the PERCEVAL S sutureless bioprosthesis, it is user-friendly and is a low profile device. Implantation can be performed easily after a short learning curve, even in small and/or calcified aortic roots. The procedure has the advantages that sutures are not required and the deployment starts from a completely collapsed prosthesis. Overall, the PERCEVAL S system allows for at least a 50% reduction in aortic cross-clamp time, the shortest clamping time being around 15–18 minutes. This may have a positive impact on post-operative outcomes, especially if pre-operative conditions are border-line (severe chronic obstructive pulmonary disease/renal dysfunction), or in older patients, as well as in situations where concomitant procedures are needed (e.g. CAGB, atrial fibrillation ablation and patent foramen ovale closure).

Conclusion

Degenerative calcified aortic stenosis is the most common valvular disease, the incidence of which is continuing to rise in the western countries. Surgical valve replacement represents the gold standard of treatment. However, since the proportion of older and high-risk patients is rising, alternatives that minimise the need for surgical valve replacement should be sought. There is already a growing interest in less invasive valve replacement as well as for quicker release of sutureless valves and transcatheter technologies. Future studies must determine which therapeutic option is preferred in each category of patients.