Controversies in cardiovascular medicine

Percutaneous transarterial aortic valve implantation: what do we know?

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Transcatheter aortic valve implantation (TAVI) is assuming a major role in the routine management of patients with aortic stenosis. Surgical aortic valve replacement is generally accepted to prolong survival, on the basis of historical comparisons and long experience. However, recently percutaneous transarterial TAVI has assumed the position as the only therapy in any aortic stenosis patient group demonstrated to prolong survival in a randomized trial. Arguably, percutaneous TAVI is now the standard of care in symptomatic patients who are not candidates for conventional surgery. On the basis of almost 10 years of experience TAVI also appears to be a reasonable option for some operable, but high-risk patients. Nevertheless considerable work needs to be done before the indications for TAVI are expanded into lower risk groups. We review what is currently known about percutaneous transarterial implantation of the aortic valve.

Keywords
Aortic valve • Percutaneous • Transcatheter

Introduction
Symptomatic aortic stenosis is associated with a dismal prognosis when managed conservatively. Surgical valve replacement is generally accepted to prolong survival, on the basis of historical comparisons and long experience.1,2 Multiple registries from multiple centres have shown that transcatheter aortic valve implantation (TAVI) can be accomplished in high-risk patients with outcomes that compare favourably with the outcomes of surgical valve replacement, as predicted by operative risk assessment tools.3–8

Recently, percutaneous transarterial TAVI assumed the position as the only therapy in any aortic stenosis patient group demonstrated to prolong survival in a randomized trial.7 An absolute 20% increase in survival at 1 year in patients determined to be too high risk for surgery is dramatic confirmation of this potential. As we approach 10 years of experience with TAVI, over 20 000 cases and over 100 publications, a review of what we now know about percutaneous TAVI seems appropriate. As the bulk of the percutaneous experience to date has been with the Edwards SAPIEN and Medtronic CoreValve devices and with the femoral transarterial approach, this will be the focus of the discussion below.

Current transcatheter valves
There are currently two valves in widespread clinical use, as shown in Figure 1 and described in Table 1. The Edwards transcatheter heart valve (THV) (Edwards Lifesciences, USA) utilizes a balloon-expandable tubular frame (Figure 2). Earlier iterations, including the prototypic Cribier–Edwards and the more widely used SAPIEN THV, required large diameter delivery systems. However, the current SAPIEN XT valve is mounted on a low profile NovaFlex delivery system. In contrast the CoreValve ReValving System (Medtronic Inc., Minneapolis, MN, USA) utilizes a self-expanding multi-staged frame. A unique feature is that this device is anchored not only within the aortic annulus, but also extends superiorly to anchor in the supracoronary aorta. Early versions of both the Edwards and CoreValve devices required large 22–25 F delivery systems. For a period the CoreValve device offered the advantage of a lower profile delivery system. However, both devices are now available with comparable low profile 18–19 F delivery systems; theoretically allowing application in the majority, but by no means all, patients with aortic stenosis.

The CoreValve device is associated with less haemodynamic instability during deployment, more forgiving positioning and is potentially retrievable if positioned incorrectly. The risk of acute
coronary obstruction by a displaced native valve leaflet may be lower. A relatively high rate of acute and delayed heart block may require prolonged electrocardiographic monitoring with temporary indwelling leads and more frequent pacemaker implantation. The late consequences of a CoreValve stent frame extending into the ascending aorta and over the coronary ostia are not known and the SAPIEN valves offer a more focal therapy. The SAPIEN valve is supported by a larger and longer body of publications and early randomized data demonstrating benefit over medical management in non-operative patients. Comparisons with regards to durability are largely speculative, although there is a surgical literature suggesting the superiority of bovine over porcine pericardial tissue valves. In the absence of comparative trials it difficult to definitely determine differences in the potential for clinical benefit. This review will focus, as much as possible, on the similarities between the two clinically available devices.

Future valves

A number of other valves are in early clinical evaluation. In general these incorporate features to reduce delivery catheter diameter, facilitate accurate positioning, reduce paravalvular leaks, or allow for retrieval. Generally these next generation valves are self-expanding rather than balloon-expandable, a feature which facilitates smaller diameter delivery systems and retrieval. Examples include the Lotus (Boston Scientific Inc., USA), Direct Flow (Direct Flow Medical Inc., USA), and HLT (Heart Leaflet Technologies Inc., USA) valves. Some utilize a secondary fixation point in the supra-coronary aorta such as the Accurate (Symetic Inc., CH) and St Jude (St Jude Medical Inc., USA) valves. Some incorporate features which facilitate positioning and anatomical orientation in relation to the native valve and coronaries such as the Engager (Medtronic Inc., USA) and the JenaClip (JenaValve Inc., Germany). Although these valves may incorporate desirable features little information is available on efficacy, procedural outcomes, and durability. It is possible that attempts to improve ease of implantation may lead to unexpected problems or compromise durability.

### Table 1 Comparison of the Edwards SAPIEN XT valve and Medtronic CoreValve prostheses

<table>
<thead>
<tr>
<th></th>
<th>Edwards SAPIEN XT</th>
<th>Medtronic CoreValve</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frame</td>
<td>Cobalt chromium</td>
<td>Nitinol</td>
</tr>
<tr>
<td>Leaflets</td>
<td>Bovine pericardial</td>
<td>Porcine pericardial</td>
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<tr>
<td>Expansion</td>
<td>Balloon-expandable</td>
<td>Self-expanding</td>
</tr>
<tr>
<td>Balloon valvuloplasty required</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Retrievable</td>
<td>No</td>
<td>Prior to release</td>
</tr>
<tr>
<td>Annular/valvar fixation</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Ascending aortastabilization</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Manufacturers diameter</td>
<td>23, 26 mm</td>
<td>26, 29 mm</td>
</tr>
<tr>
<td>Recommended annulus diameter</td>
<td>18–25 mm</td>
<td>20–27 mm</td>
</tr>
<tr>
<td>Length</td>
<td>15–17 mm</td>
<td>53–55 mm</td>
</tr>
<tr>
<td>Delivery system diameter</td>
<td>18F&amp;19F</td>
<td>18F</td>
</tr>
<tr>
<td>Sheath external diameter</td>
<td>7.3 mm</td>
<td>7.3 mm</td>
</tr>
<tr>
<td>Minimum arterial diameter</td>
<td>6 mm</td>
<td>6 mm</td>
</tr>
<tr>
<td>Suitable for</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aortic stenosis</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Aortic insufficiency</td>
<td>If combined with stenosis</td>
<td>Yes</td>
</tr>
<tr>
<td>Pulmonaryposition</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Valve-in-valve</td>
<td>All four valve positions</td>
<td>Aortic only</td>
</tr>
<tr>
<td>Transapical access</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Transaxillary access</td>
<td>Yes, limited experience</td>
<td>Yes</td>
</tr>
<tr>
<td>Longest reported follow-up</td>
<td>5 years</td>
<td>3 years</td>
</tr>
<tr>
<td>Pacemaker</td>
<td>4–8%</td>
<td>15–40%</td>
</tr>
<tr>
<td>CE mark approval</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Randomized trials</td>
<td>PARTNER completed</td>
<td>Results anticipated 2013</td>
</tr>
</tbody>
</table>

*SAPIEN XT 20 and 29 mm valves and CoreValve 23 mm valves anticipated.*
Valve function

The haemodynamic performance of currently available THVs is comparable with surgical heart valves (Figure 3). Mean systolic gradients are typically around 10 mmHg and effective orifice area is generally between 1.2 and 1.9 cm², depending on prosthesis size. Transcatheter heart valves appear associated with better haemodynamics than surgical bioprostheses, in part due to the absence of a bulky sewing ring.

Paravalvular regurgitation, due to incomplete annular sealing, is common with current THVs. With current implant techniques, oversizing and increasingly accurate positioning paravalvular regurgitation is usually trivial or mild and sometimes moderate. Such leaks appear well tolerated, do not worsen with time, and clinical haemolysis has not been reported. Severe regurgitation may occur, but is relatively infrequent. Severe leaks are typically due to technical errors in terms of sizing or positioning. In such instances redilation or implantation of a second, overlapping valve-in-valve implant can be helpful.

The majority of patients with aortic stenosis also have some degree of regurgitation at baseline. However, significant prosthetic transvalvular leaks are uncommon after TAVI. In current large series the general finding is that net aortic regurgitation (both valvular and paravalvular combined) is not increased and is often reduced, after TAVI.

Accelerated wear testing of currently available valves predicts durability in excess of 10 years. There are several reports of echocardiographic follow-up out to 1 and 2 years with both the SAPIEN...
and CoreValve devices.\textsuperscript{5,7,9,15–20} One published report documents late valve function in patients up to 5 years after implantation of the SAPIEN precursor valve.\textsuperscript{24} The longest surviving patient, at 6.5 years in the original Cribier series, still has a normally functioning prosthesis. It is reassuring that structural THV failure has not been reported to date, although admittedly late follow-up remains limited and inadequate.

**Access**

Transvenous access was utilized to establish the feasibility of TAVI, but successful implantation was difficult to reproduce and this route is no longer utilized. Percutaneous implantation is currently performed utilizing retrograde access from the femoral artery.\textsuperscript{25,26} Originally requiring open cutdown, arterial access this is now typically accomplished with percutaneous puncture and percutaneous suture closure (Figure 4). Alternatives include open surgical access to the retroperitoneal iliac artery, subclavian artery, ascending aorta, or left ventricular apex. All have been used very successfully to avoid problematic peripheral arterial or aortic disease. Greater proximity to the valve with these open central access techniques may, in some cases, facilitate improved catheter control during implantation. The transaxillary/subclavian route has found particular favour in conjunction with the CoreValve device, while the apical route is widely utilized with SAPIEN device. Disadvantages include the need for open surgical access and, in the case of the transapical procedure, concerns about thoracotomy and left ventricular injury.

Although this review is focused on percutaneous TAVI, most of the following discussion is relevant to TAVI regardless of the route of access. Regardless of access route an optimal facility should be able to provide excellent fluoroscopic imaging, surgical sterility, and ready access to anaesthetic, echocardiographic, vascular, and cardiac surgical support (Figure 5). Moreover a multidisciplinary heart team combining interventionalists, surgeons, anaesthesia, and nursing is necessary for appropriate patient evaluation, selection, management, and optimal outcomes.

**Patient outcomes**

Procedural success rates (defined loosely here as implantation of a functional valve with the patient surviving the procedure) have increased steadily from 82\% in the initial transvenous experience,\textsuperscript{15} to over 95\% in more recent series.\textsuperscript{17,19} It appears that, when patients are appropriately selected, TAVI is a procedure that can be reproducibly and reliably performed. In a recent review 82 reports, representing 2356 patients receiving the Edwards Lifesciences and Medtronic THVs, were identified.\textsuperscript{19} Survival at 30 days was 89\%, similar for both valves. Similarly, survival continues to improve, with recent reports documenting 30-day survival rates of 93–95\%.\textsuperscript{3,5,9,22,27} To date the literature has largely consisted of registries, without the oversight expected from a prospective trial.

To put this into perspective it is useful to look at outcomes in the recent PARTNER B trial (Figure 6). Patients were declined surgery due to prohibitive risk based on a rigorously monitored consensus amongst multiple senior surgeons from multiple centres. Despite early generation, large profile systems and minimal operator experience with TAVI before the trial, the low 30-day mortality of 6.4\% amongst patients undergoing TAVI compares very favourably with the Society of Thoracic Surgeons (STS) surgical risk estimate of 11.6\%. Moreover, the STS National Cardiac Database reports that, among 46,397 patients undergoing surgical aortic valve replacement surgery in the USA, overall mortality was also 6.4\%.\textsuperscript{28} In this trial there was a dramatic 20\% absolute improvement in survival at 1 year follow-up with percutaneous TAVI, with the survival curves continuing to diverge. Non-operative patients not receiving TAVI had a dismal survival of <50\% at 1 year, with the survival curves

![Figure 4](image-url) Percutaneous access (left) and closure (right). The technique of ‘preclosure’ involves percutaneous placement of sutures in the arterial wall prior to insertion of a large access sheath to facilitate haemostatic closure of the arteriotomy without a surgical cutdown.
continuing to diverge. Randomized comparisons of surgery and the SAPIEN valve in high risk, but operable, patients may be available in early 2011. Evaluations in lower risk operable patients with the CoreValve and SAPIEN XT devices can be anticipated to start enrolment shortly.

Survival rates at 1 year ranging from 69 to 85% have been reported after TAVI. This somewhat disappointing late survival is invariably the consequence of an array of comorbidities and very rarely due to the aortic valve. Among the factors commonly tracked, logistic EuroSCORE, STS score, age, liver disease, severe mitral regurgitation, anaemia, prior stroke, pulmonary disease, and renal failure are predictors of late mortality following TAVI.

Improvement in functional class has been reported in most published series. Typically New York Heart Association class improves from class III to IV at baseline to I–II after TAVI. Functional benefit appears to be durable. Still, the disappointing late survival in some very high-risk groups begs the question as to whether some elderly patients with comorbidities who may be able to tolerate this therapy may not derive significant benefit from it. This points to the need for multidisciplinary assessment of the complex, often frail and elderly patient currently being considered for this procedure.

### Patient evaluation

Evaluation of the potential TAVI candidate is a complex process involving multidisciplinary review. The basics are similar to what is standard in the setting of surgical valve replacement. The standard TAVI work up includes transthoracic echocardiography to confirm aortic stenosis, assess other valvular lesions, left ventricular function and, notably, the diameter of the aortic annulus. Coronary angiography is performed to assess the need for revascularization. Invasive ascending and descending aortography and/or computed tomographic angiography is needed for assessment of the dimensions and characteristics of the aortic root as well as the diameter, tortuosity, and calcification of the iliac and femoral arteries. The nuances of evaluation are largely dictated by the specific risks of TAVI, as discussed below.

### The brain

Stroke rates of 0–10% have been reported in association with TAVI. To put this in perspective, the large post-marketing source self-reported registry reported a stroke rate of 2.4%, while the more rigorously monitored PARTNER B trial found a major stroke (permanent disability) rate of 5.0% (both with the older large profile SAPIEN delivery system). Despite this increased risk of stroke there was a dramatic 18.3% reduction in the combined risk of death or major stroke at 1 year (Figure 6).

Procedural stroke is often due to embolization of the friable material found in the diseased aortic valve, as demonstrated by transcranial Doppler. New cerebral lesions, as assessed by diffusion-weighted magnetic resonance imaging, have been reported in 58–91% of patients undergoing TAVI. Although these findings do not appear to correlate with clinical neurologic deficits. Experimental approaches to mitigation include catheters...
percutaneous coronary intervention can be performed as a staged or single stage procedure.

The conduction system

Injury to the atrioventricular conduction system as it courses through the interventricular septum below the aortic valve may be associated with new left bundle or complete heart block. Surgical AVR is associated with a need for permanent pacing in 3–18%. Reportedly TAVI is associated with new pacemaker implantation in 3–36% of patients. Comparisons are difficult, as current TAVI patients represent a particularly high-risk group and local practise varies widely in terms of the threshold for pacemaker implantation. Nevertheless the 9–36% rate of new pacemaker implantation with the CoreValve device is clearly higher than the 3–12% rate reported with the Edwards Lifesciences device, presumably as this device often extends further into the left ventricular outflow tract. Additional risk factors for new heart block may include advanced age, pre-existing right bundle branch block or atrioventricular delay and oversizing.

The heart

Left ventricular function typically improves to a small degree shortly after TAVI and may continue to improve with time. Preliminary analyses suggest a reduction in left ventricular volumes and hypertrophy. Mitral regurgitation is common in patients with aortic stenosis, increasing both surgical and TAVI procedural risk. As with isolated surgical aortic valve replacement, mitral regurgitation may improve and/or be better tolerated following TAVI. This is more likely when regurgitation is functional, unassociated with structural abnormalities such as annular calcification, tethering, or left atrial enlargement. A therapeutic strategy of replacing the aortic valve alone may be desirable in many patients in whom the risk of double valve surgery might be prohibitive.

Valve-in-valve

Reoperation for degenerated surgical bioprostheses carries significant risk. Early reported experience with valve-in-valve implantation in aortic degenerated surgical bioprostheses with both the SAPIEN and CoreValve devices has been favourable typically the surgical valve facilitates positioning, paravalvular sealing and shields the atrioventricular conduction system and left main ostium. However, some surgical valves are difficult to image, compromise coronary ostia, or are too small for a valve-in-valve implant. For instance, one widely used 21 mm surgical tissue valve has an internal diameter of 17 mm meaning that even the smallest currently available THV will be underexpanded resulting in moderate stenosis. Fortunately, early experience with damaged, incorrectly positioned or undersized THVs confirms that a second transcatheter valve can be implanted within the first with a good functional result. To some degree TAVI, like percutaneous coronary intervention, may be a repeatable therapeutic strategy.
Summary

Surgical valve replacement remains standard therapy for symptomatic severe aortic stenosis due to a long and established track record. Arguably TAVI is becoming the standard of care for symptomatic patients who are not operative candidates. As outcomes improve and durability is documented TAVI is also becoming an option for selected patients who are eligible for surgery, but at high risk of morbidity. Where this line is drawn is a moving target and remains controversial. Careful and responsible patient selection, high-quality facilities, formal training, multidisciplinary collaboration, and concentration of expertise are fundamental to optimal outcomes.

Conflict of interest: A.C. and J.W. are consultants to Edwards Lifesciences.

References


