Transcatheter Aortic Valve Implantation (TAVI) – The Time Has Come

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Introduction

Although much attention has been focused on the prevention and treatment of ischaemic heart disease in the last few decades, valvular heart disease has also resulted in significant cardiovascular mortality and morbidity. In the ageing population, aortic stenosis (AS) is the most common valvular heart disease, with a prevalence of 4.6% in adults ≥ 75 years of age. When the patients become symptomatic with congestive heart failure, syncope or chest pain, the average survival is only 2-3 years with a high risk of sudden death. Surgical aortic valve replacement (SAVR) is the recommended treatment for symptomatic AS patients with a major improvement in long-term outcomes. However, many symptomatic AS patients do not undergo SAVR because of underlying co-morbidities, patients’ refusal or deemed inoperable by the surgeons because of advanced age or presence of co-existing diseases. 27-41% of patients with severe symptomatic AS do not receive SAVR. Transcatheter Aortic Valve Implantation (TAVI) has recently provided another treatment option for the high-risk or inoperable symptomatic AS patients.

The Device

TAVI was first described by Andersen in 1992 by implanting an expandable aortic valve by a catheter technique in a closed chest pig model. Several different types of aortic prosthesis have been developed since then and have been implanted in humans with success by using different transcatheter approaches. To date, the two most widespread use with the most clinical data are from two valves approved for clinical use in Europe under CE (European Conformity) Mark, namely the CoreValve (Medtronic, Minneapolis, MN) and Edwards Sapien valve (Edwards Lifesciences, Irvine, CA). Several other second generation TAVI devices have also been developed and are undergoing human feasibility studies with success.

The CoreValve

Medtronic CoreValve has developed the ReValving System which consists of a trileaflet porcine pericardial bioprosthetic valve mounted and sutured in a multi-level self-expanding Nitinol frame. The bioprosthesis is housed in a position for percutaneous delivery via a catheter-based technique, and implanted within the diseased aortic valve. The stent is carefully designed with three contiguous leaves of structure and function. The upper third of the frame has a low radial force and sits within the ascending aorta to orient the prosthesis in the aortic root. The middle third of the frame has high hoop strength and the valve leaflets are attached to this portion of the stent. It is also designed to avoid impinging the coronaries. The lower third of the frame exerts a high radial force and sits within the left ventricular outflow tract. A skirt of pericardium borders the lower portion of the valve to create a seal and prevents paravalvular aortic regurgitation. The 18-F CoreValve allows the use of a percutaneous approach under local anaesthesia (with or without conscious sedation) or under general anaesthesia (with or without haemodynamic support or cardiac assistance). Rapid ventricular burst pacing or transient bradycardia may be initiated or induced during the pre-implantation balloon aortic valvuloplasty (BAV) but the implantation of the CoreValve per se can usually be done under the patients’ intrinsic rhythm and heart rate. Two sizes are available: for aortic annular size of 20-23mm, a 26mm valve should be used and for 24-27mm, a 29mm valve should be deployed. The CoreValve can be implanted through the transfemoral, transaxillary, subclavian and direct aortic approaches. Recently, the delivery catheter of the CoreValve device has added the AccuTrak Stability Layer to enhance stability and accuracy during deployment.

The Edwards Sapien Valve

The Edwards Sapien XT valve consists of a trileaflet bovine pericardial valve mounted in a balloon-expandable stainless steel frame. The proximal portion of the stent is covered by a fabric skirt on its outer perimeter to minimise paravalvular leak. The 23mm Sapien valve can be introduced via a 22F sheath, whereas the 26mm valve needs a 22F to 24F sheath, depending on the type of catheter on which the stent is mounted. The new Sapien XT valve has a significantly lower profile and is compatible with an 18F sheath. The Edwards Sapien valve has been successfully implanted via the retrograde and antegrade methods by using the transfemoral and transapical approaches. Rapid ventricular pacing is needed during Edwards Sapien valve deployment.

Indications

Currently, the TAVI procedure is indicated for patients with symptomatic severe aortic stenosis who have an elevated surgical risk and cannot be considered for open heart surgery.

Patients might be considered a TAVI candidate if they...
fulfil the following criteria:

1. Documented severe aortic valve stenosis
2. Access vessel diameter >6 mm as defined pre-procedure via echocardiographic measure
3. Aortic valve annulus diameter >20 mm and < 27 mm as defined pre-procedure by echocardiographic measure
4. Ascending aorta diameter < 43 mm at the sinotubular junction
5. Native aortic valve disease, defined as valve stenosis with an aortic valve area <1cm² (<0.6cm²/m²) as defined pre-procedure by echocardiographic measure
6. Age > 80 years

Or

Surgical risk calculated with logistic EuroSCORE > 20%,

Or

Age > 65 years with one or two (but not more than 2) of the following criteria:

- Cirrhosis of the liver (Child class A or B)
- Pulmonary insufficiency : VMS < 1 liter
- Previous cardiac surgery (CABG, valvular surgery)
- Porcelain aorta
- Pulmonary hypertension > 60 mmHg and high probability of cardiac surgery for other than valve replacement
- Recurrent pulmonary emboli
- Right ventricular insufficiency
- Thoracic burning sequelae contraindicating open chest surgery
- History of mediastinum radiotherapy
- Severe connective tissue disease resulting in a contraindication to surgery
- Cachexia (clinical impression)

Patients will be excluded if they have the following conditions:

1. Known hypersensitivity or contraindication to aspirin, heparin, ticlopidine, clopidogrel, nitinol, porcine products, or contrast media which cannot be adequately pre-medicated
2. Any sepsis, including active endocarditis
3. Recent myocardial infarction (< 30 days)
4. Any left ventricular or atrial thrombus as determined pre-procedure by echocardiography
5. Uncontrolled atrial fibrillation
6. Mitral or tricuspid valvular insufficiency (> grade II)
7. Previous aortic valve replacement (mechanical valve or stented bioprosthetic valve)
8. Evolutionary or recent CVA (cerebrovascular accident), (< 3 months)
9. Femoral, iliac or aortic vascular conditions (e.g. stenosis, tortuosity), that make insertion and endovascular access to the aortic valve impossible
10. Symptomatic carotid or vertebral arteries narrowing (> 70%) disease
11. Abdominal or thoracic aortic aneurysm
12. Bleeding diathesis or coagulopathy, or patients who refuse blood transfusion
13. Evolutive disease with life expectancy less than one year
14. Creatinine clearance < 20 ml/min
15. Active gastritis or known peptic ulcer disease
16. Pregnancy

Complications

Both the CoveValve and the Edwards Sapien Valve are associated with several procedural-related complications, some of which can be prevented by proper patient selection and attention to procedure details.

Access site related complications

The relatively large diameter of the early delivery catheters, using 22- to 25-F sheath and in the absence of adequate pre-operative screening of the peripheral vasculature have caused relatively high incidence of vascular complications and it was as high as 30% in the early experiences. However, dissection and perforation of the ilio-femoral arteries leading to retroperitoneal haemorrhage might still occur with the smaller 18-F sheath in the presence of excessive traumatic sheath insertion. Dissection of the ascending and descending aorta has also been reported. An extreme case of such complications can occur during sheath withdrawal and when it is met with excessive resistance, causing complete arterial avulsion and sudden haemorrhage. Successful management requires a high level of suspicion during the procedure, especially when sudden unexplained hypotension is observed. Immediate resuscitation with volume expansion and prompt angiographic assessment should be performed without delay. Occlusive balloons and covered stents have been used with success, although surgical repair might sometimes be necessary. Even after an uncomplicated vascular closure at the end of the procedure, ilio-femoral angiography should always be performed from the contralateral femoral access site to look for potential vascular complications. With proper pre-procedural CT angiography and meticulous patient selection, vascular complications have been reduced to as low as 5-6%.

Improper positioning of the valve

Accurate positioning of the valve in the proper location is of paramount importance in TAVI. Both devices cannot be retrieved or repositioned once they are deployed. If the Edwards Sapien valve is placed too high in the aorta, it might embolise into the aorta causing significant paravalvular regurgitation or even coronary artery obstruction. Occlusion of the coronary ostia is a potential catastrophic complication and the incidence is reported to be about 1%26. Left coronary occlusion is most commonly seen when the coronary ostium lies low in the sinus (< 7mm from the bottom of the leaflet), the native leaflet is long and has bulky calcification of the tips, and the prosthetic valve is slightly oversized. Successful percutaneous coronary intervention has been successfully performed through the CoreValve which might be life-saving27. If it is placed too deep into the left ventricle, it may embolise into the ventricle or the overhang of the native leaflet may prevent proper functioning of the prosthetic valve leaflets, leading to significant central aortic regurgitation. Heart block is more commonly observed with the self-expandable CoreValve system as a result of the pressure applied on the conducting tissues located subendocardially in the LV outflow tract and interventricular septum. Permanent pacemaker implantation rate was 7% and 18% respectively for Edwards Sapien valve and CoreValve26,27. Mitral valve injury causing acute mitral regurgitation as a result of a prosthesis extending too low into the left ventricle has also been reported although it is rare28.
Systemic complications
Systemic complications include infection, bleeding, stroke and cardiac tamponade. The most frequent aetiology of procedural-related strokes is likely to be atheroembolism from the ascending aorta or the aortic arch. Other potential causes include calcific embolism from the aortic valve, thromboembolism from catheters, air embolism from LV cannulation, prolonged hypotension, and dissection of arch vessels. The incidence of strokes ranges widely from 0% to 10%\(^{14,19,24,25,27}\), depending on the access route and the level of manipulation of the catheter in the aortic arch. Cardiac tamponade might be a fatal complication as a result of the super-stiff guidewire in a hypertrophic left ventricle with small ventricular cavity. Immediate pericardiocentesis or even surgical repair has proven to be life-saving.

Clinical Data
Percutaneous aortic valve replacement was first performed via the transseptal route by Dr. Allan Cribier in Rouen, France in April 2002. The initial experience from the compassionate use of the balloon-expandable 23mm valve from the antegrade approach was reported in the I-REVIVE (Initial Registry of Endovascular Implantation of Valves in Europe) and RECAST (Registry of Endovascular Critical Aortic Stenosis Treatment). The procedural success rate was 75%, with a 30-day mortality rate of 23%. Moderate to severe aortic regurgitation was reported in 63% of patients, partly as a result of the valve size.

In Vancouver, John Webb has implanted the Cribier-Edwards valve retrogradely via the transfemoral route, successfully in 14 of 18 patients\(^{20}\). The early mortality rate was 11% at a mean follow-up of 75 days. The same group reported both short- and long-term outcomes in an extended cohort of 50 patients\(^{21}\). Procedural success increased from 76% in the first 25 patients to 96% in the second and 30-day mortality decreased from 16% to 8%.

The first human recipient of the CoreValve was reported in 2005 by Grube et al\(^{22}\). In a single centre series reported by Grube et al, the safety and efficacy of the second (21-F)- and third (18-F)-generation CoreValve aortic valve prostheses were evaluated\(^{23}\). The 18-F device allowed the use of a percutaneous approach under local anaesthesia without haemodynamic support. In this series, a total of 86 patients with a mean valve area of 0.66±0.19 cm\(^2\) (21-F) and 0.54±0.15 cm\(^2\) (18-F), a mean age of 81.3±5.2 years (21-F) and 83.4±6.7 years (18-F), and a mean logistic EuroSCORE of 23.4±13.5% (21-F) and 19.1±11.1% (18-F) were enrolled. Acute device success was 88%. Successful device implantation resulted in a marked reduction of aortic transvalvular gradients (mean pre 43.7 mm Hg vs. post 9.0 mm Hg, \(p<0.001\)) with aortic regurgitation grade remaining unchanged. Procedural mortality was 6%. Overall 30-day with a combined mortality rate was 12%. The combined rate of deaths, strokes, and myocardial infarctions was 22%.

Based on these initial data, the CoreValve and Edwards Sapien valve were approved in Europe under the CE mark in 2007 and in several other non-US countries thereafter.

An expanded 18F Registry after CE Mark approval has now included elderly and inoperable patients with severe aortic stenosis according to the IFU. A total of 1243 patients have been included in this Registry (TCT Presentation 2008). The procedure success rate was 98.2% with an increase in the aortic valve area from 0.64±0.19 cm\(^2\) to 1.50±0.51 cm\(^2\) at 30-days follow-up. The mean gradient was reduced from 49.6±16.8 mmHg to 9.0±6.8 mmHg at 30 days follow-up. Procedural complications included early (<24 hours mortality) 1.7%, major bleeding (2.3%), cardiac tamponade (2.3%) access site complications (1.9%), and aortic dissection (0.4%). At time of discharge, aortic regurgitation was 0 (25.9%), 1+ (58.5%), 2+ (14.8%), or 3+ (0.8%). Thirty day all cause mortality rate was 6.7%, including cardiac death in 3.9%, pacemaker requirement in 12.2%, and a neurologic event in 1.7% (stroke in 1.4%; transient ischaemic event in 0.3%). There were no cases of strut fracture or valve migration found in this series.

The UK TAVI Registry from 1st Jan 2007 to 31st Dec 2009 in 26 centres had very encouraging results. There were 860 patients enrolled, with 460 patients implanted with CoreValve and 400 patients with Edwards Sapien. 30-days mortality was 6.9% and mid-term 1 year mortality rate was 19.7%\(^{31}\).

In the CoreValve Australia-New Zealand Study, six months results from TAVI patients implanted with the Medtronic CoreValve system of 375 patients in 10 Australia-New Zealand centres have recently been presented at the 2009 Transcatheter Cardiovascular Therapeutics Scientific Session. It showed a 30-day all-cause mortality of 5.6% and 1 year all-cause mortality 10.5%. Among all the patients, 46.5% showed at least one NYHA class improvement\(^{32}\).

The Italian CoreValve Registry recruited 772 patients also showed an one-year all-cause mortality of 21.2% and an one-year cardiac death rate of 11.4%. More than 50% of patients sustained improvement of at least one functional class at 1 year\(^{21}\).

The results of a groundbreaking PARTNERS Trial were recently published\(^{34}\). A total of 358 patients with Aortic Stenosis who were not suitable candidates for surgery were randomised 1:1 to TAVI versus standard therapy including BAV. The study successfully met both primary and co-primary endpoints with significant reduction in 1-year mortality of 30.7% for TAVI versus 50.7% for standard therapy \((p<0.001)\). It also demonstrated there was a significant reduction in composite endpoint of death from any cause or repeat hospitalisation of 42.5% for TAVI versus 71.6% for standard therapy \((p<0.001)\). Among survivors at 1 year, the rate of cardiac symptoms was lower among patients who had undergone TAVI than among those who had received standard therapy (25.2% versus 58.0%, \(p<0.001)\). However, TAVI, as compared with standard therapy, was associated with a higher incidence of major strokes (5.0% versus 1.1%, \(p=0.06\)) and major vascular complications (16.2% versus 1.1%, \(p<0.001)\).

Medications post-TAVI
There is still no randomised trial on the duration of
anti-platelet agents used after TAVI but the general consensus is to prescribe Aspirin for life and Plavix for 3 months after successful TAVI procedure. If the patient is on anticoagulation for atrial fibrillation or other indications, Warfarin plus Plavix should be given for 1 month post-TAVI, followed by Warfarin plus Aspirin for 1 year and then continue Warfarin only.

Conclusions and Future of TAVI

TAVI has developed at an escalating pace and its wide application in Europe, Canada and Australasia has provided a viable alternative treatment for elderly symptomatic patients with severe aortic stenosis who are deemed high-risk for surgery. Its further development rests on the long-term data on valve function and patient survival, as well as the generalisability to other patient subsets with bicuspid and rheumatic AS, and patients with previous bioprosthesis. With continual refinement of the device which can be repositioned, with a lower still profile of the delivery system and the availability of multiple valve sizes, further expansion of the procedure to the lower risk patients may be possible when it is safer and more reliable. A number of next generation devices are on the horizon and several human studies are in the pipeline. Despite continual technical advancement of TAVI devices and procedures, the combined mortality and morbidity is still high in the range of 5-10%, especially when we are facing a group of high surgical risk patients. The multi-disciplinary team approach to involve the cardiologists, cardiac surgeons, cardiac anaesthesiologists, cardiac radiologists and nurse specialists working in dedicated hybrid interventional suites will form the cornerstone for the overall success of this fascinating new era of transcatheter treatment of valvular heart disease.

References

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