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Contemporary trans-catheter treatment of severe aortic stenosis

Współczesne przezcewnikowe leczenie zaawansowanej stenozy aortalnej

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INTRODUCTION

Significant improvements in medical care and lifestyle in recent years have resulted in prolongation of life. Among our growing elderly population, aortic stenosis (AS) is becoming an important and increasingly prevalent condition. It is well known to have a poor prognosis once it is symptomatic and moreover is associated with significant morbidity, multiple and prolonged hospital admissions and a significant reduction in the quality of life.

The prevalence of calcific, degenerative AS increases with advancing age and affects ~40% of people aged over 80 years [1]. Once AS becomes symptomatic, life expectancy decreases dramatically (Fig. 1). Until recently, the only definitive treatment for severe AS has been surgical aortic valve replacement (AVR).

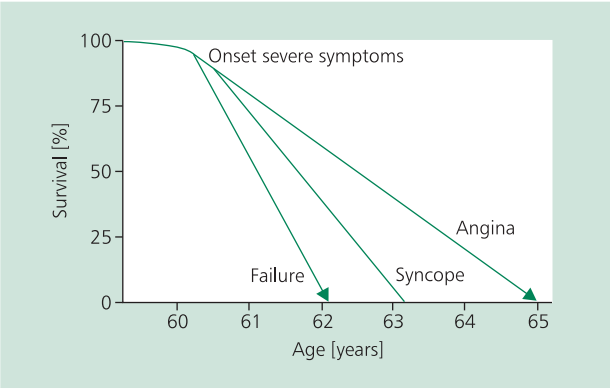

Figure 1. Natural history of symptomatic aortic stenosis without treatment. Survival curves show the interval from the onset of symptoms to the time of death (approximately two years in patient with heart failure, three years for those with syncope, and five years for those with angina)

In the general population, the risk of conventional aortic valve surgery is low (about 3%) and even when valve replacement is associated with concurrent coronary artery by-pass grafting, the operative risk does not exceed 5%. However, the risk of aortic valve surgery is significantly higher in the elderly, who are therefore often denied treatment [2]. It is the combination of an unmet need with a desire to find lower risk and less invasive approaches that has driven the development of percutaneous valve therapy, which is now an extremely fast-growing area of cardiology. Percutaneous and minimally invasive treatment of valvular heart disease presents a very attractive option for this high risk group.

In this article, we discuss the percutaneous alternatives to open valve surgery and review the currently available techniques.

BALLOON AORTIC VALVULOPLASTY

Percutaneous balloon aortic valvuloplasty (BAV) was first described by Cribier et al. [3] a quarter of a century ago in 1986. They reported its successful use in three elderly patients with symptomatic severe AS, who were either unsuitable for AVR or had refused it. After initial enthusiasm, use of the technique tapered off, particularly when it became apparent that there was no mortality benefit [4–6]. Despite this, BAV remained a successful method of increasing aortic valve area and reducing the mean and peak aortic valve gradient. There also appeared to be an increase in cardiac output and decrease in left ventricular (LV) end-diastolic pressure. More importantly, at 30 days, 70% of patients had improvement of symptoms, but this was transient and re-stenosis was frequent (~50% of patients within 3–6 months). Moreover, the procedure itself was considered high risk and cumbersome and therefore declined in popularity in the early 1990s.

In recent years, BAV has experienced something of a renaissance, largely due to the growth and development of trans-

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catheter aortic valve therapy. The BAV technique has been refined by modern balloons, guidewires, vascular closure devices and improved imaging techniques. The introduction of rapid pacing during the procedure has made balloon inflation both more predictable and more effective, and has transformed the ease with which the aortic valve can be dilated. The transcatheter aortic valve implantation (TAVI) experience has taught us that this is a simple and safe thing to do, even in the conscious/sedated patient.

The BAV is finding a well-defined role in the treatment of patients with critical AS. Accepted indications for BAV are now:

— bridge to definitive treatment (either open AVR or TAVI);
— bridge to new technology e.g. those patients whose aortic annulus is too large for the currently available TAVI devices;
— prior to pre-TAVI percutaneous coronary intervention (PCI) which can often be complex and high risk in the setting of severe AS;
— therapeutic trial — particularly in breathless patients with the combination of severe AS, significant coronary artery disease (CAD) and severe airways disease;
— palliative — while this is more controversial, some feel that offering 3–6 months of symptomatic benefit to very elderly patients is ethical and worthwhile.

The procedure is usually performed retrogradely via the femoral artery. The aortic valve is crossed with an AL-1/2 catheter and straight wire. An extra-stiff guidewire is positioned toward the apex of the LV to allow support for balloon passage across the stenosed valve. The balloons are available in different sizes, lengths and shapes; some of them have a 'dog-bone' shape to ensure a steady position during inflation.

More contemporary series of BAV [7] demonstrate that while long-term survival is still low, procedural complications (in particular vascular) have improved, as has procedural mortality [8, 9]. Large arterial sheaths (9–14 F) are still necessary and procedural complications therefore include bleeding and vascular injury (10–20%). However, the incidence of other complications is low and, rather surprisingly, severe valvular regurgitation is uncommon (~1%).

TRANSCATHETER AORTIC VALVE IMPLANTATION

Until recently, the only definitive treatment for AS was open heart surgical AVR, which remains the gold standard.

However, the novel technique of percutaneous TAVI has become feasible in recent years. Cribier et al. [10] performed the first antegrade percutaneous aortic valve implantation in 2002, with the valve prosthesis advanced from the venous circulation across the inter-atrial septum. This technique proved very technically demanding and difficult to reproduce, prompting the development of two new approaches: retrograde/transfemoral/subclavian approach (Edwards Sapien valve, CoreValve) or the anterograde/transapical (Edwards Sapien valve) approach.

The two devices available for TAVI are currently the Edwards Sapien bioprosthesis (Edwards Lifesciences, Inc., CA, USA) and the CoreValve ReValving system (Medtronic CV, Luxembourg) (Fig. 2). The second generation of the Edwards Sapien (Sapien XT) valve consists of three bovine pericardial leaflets mounted within a balloon expandable, cobalt chromium stent and are currently available in two sizes (23 and 26 mm; 20 and 29 mm are in development). The size of the fourth generation transfemoral delivery system (NovaFlex™), which received its CE mark in March 2010, has been reduced (22 F to 18 F and 24 F to 19 F). The Edwards Sapien THV is deployed transapically using the 'Ascendra 2™' catheter. The most recent iteration of this system enhances procedural control and sheath size has been reduced from 26 F to 22 F (Fig. 3). The second generation of 20 mm and 29 mm valves are currently being tested in clinical trials (PREVAIL). The CoreValve device has three porcine pericardial leaflets within a larger, self-expanding nitinol frame and is available in 26 mm and 29 mm

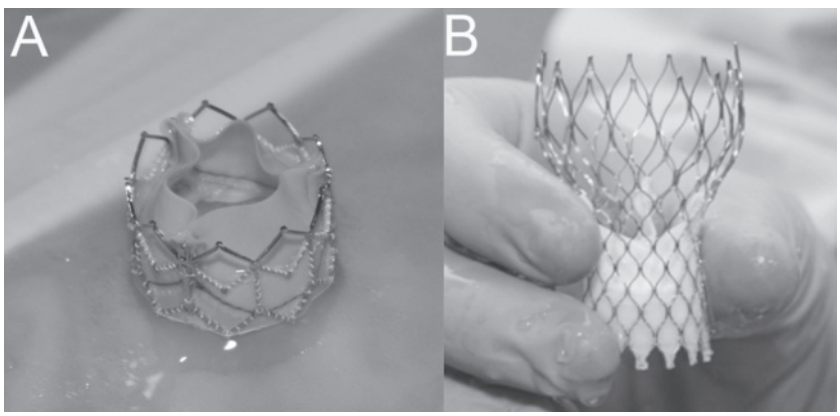

Figure 2. Edwards Sapien XT valve (**A**) and CoreValve prosthesis (**B**) before loading into the delivery system (CoreValve picture from Grube et al. J Am Coll Cardiol, 2007)

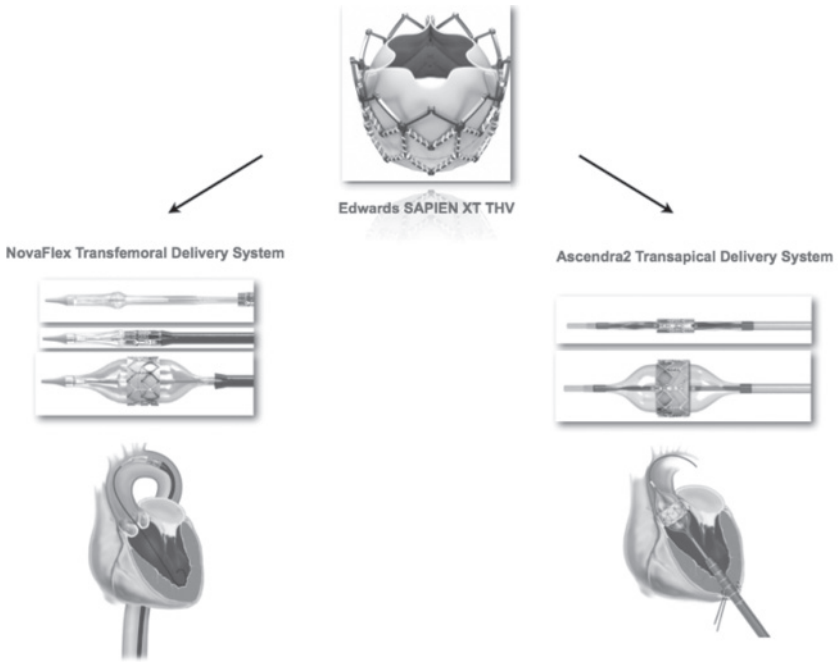

Figure 3. Edwards Sapien valve is deployed using a transfemoral or a transapical approach (picture from Edwards LifeSciences)

Table 1. Comparison of different CE marked transfemoral devices

	Valve size	Stent	Valve	Frame height	Annulus size	Delivery sheath	Minimal vessel diameter
Edwards Sapien XT	23 mm	Cobalt chromium, balloon expandable	Bovine pericardium	14.3 mm	18–22 mm	18 F	> 6 mm
	26 mm	Cobalt chromium, balloon expandable	Bovine pericardium	17.2 mm	21–25 mm	19 F	> 6.5 mm
CoreValve	26 mm	Nitinol self expandable	Porcine pericardium	50 mm	20–23 mm	18 F	> 6 mm
	29 mm	Nitinol self expandable	Porcine pericardium	50 mm	24–27 mm	18 F	> 6 mm

sizes delivered via an 18 F sheath. A summary of currently available transfemoral systems is presented in Table 1.

Retrograde/transfemoral approach

After arterial puncture or surgical exposure of the artery, the vessel is pre-dilated with a series of dilators of increasing size to accommodate the appropriate size of delivery sheath. Depending on the valve size, 18 F or 19 F introducer sheaths are required for implantation of the Edwards Sapien XT valve and 18 F for the CoreValve. As with balloon valvuloplasty, valve implantation with the balloon-mounted Edwards Sapien is achieved using rapid pacing to facilitate accurate deployment of the prosthesis. The Edwards XT valve is crimped proximal to the balloon and is moved onto the balloon in the descending aorta. No rapid pacing is required during deployment of the CoreValve system. Haemostasis is usually achieved by surgical repair or suture-mediated closure devices. With currently available delivery systems, the TAVI procedure becomes a purely percutaneous procedure and in many centres is performed under only local anaesthesia with conscious sedation.

Transapical approach/subclavian/ /transaxillary approach

Only the Edwards Sapien valve is currently available for use via the transapical route. Access to the LV apex is gained through a left anterolateral minithoracotomy, with opening of the pericardium. Under fluoroscopic guidance, the apex is punctured and the valve is crossed anterogradely. After BAV, the 22 F Ascendra 2 delivery system is placed in the ventricle and

the valve is implanted using a similar technique to the transfemoral approach. The transapical sheath is removed and the apex closed with purse-string sutures [11]. In addition, the Edwards valve can be deployed utilising a transaortic approach via a mini sternotomy.

For patients unsuitable for the transfemoral approach, the CoreValve device can be deployed via the subclavian artery. This procedure is usually performed under general anaesthesia but can be performed under regional/local anaesthesia.

INDICATIONS FOR TAVI

The TAVI is currently indicated in patients with severe symptomatic calcific AS who are deemed too high risk for conventional, surgical AVR. This diagnosis should obviously be delineated by standard transthoracic echocardiography and occasionally dobutamine stress echocardiography (in cases of low gradient, low output AS) or/and transoesophageal echocardiography. The TAVI is approved for use in patients with a calculated risk of conventional surgery of > 20% (by EuroSCORE), > 10% (by STS) or those patients turned down for conventional surgery by two cardiothoracic surgeons [12]. However, no scoring system currently exists which is specific to TAVI and the EuroSCORE has significant limitations. Broadly speaking, our own experience and the SOURCE registry suggest that the EuroSCORE is a crude indication of TAVI outcome, but does help to identify patients who may not benefit from TAVI.

PATIENT SELECTION

The key to successful implementation of this new technique is case selection and this is achieved via teamwork and a multidisciplinary approach. The team should consist of two interventional cardiologists, two cardiothoracic surgeons, an imaging/echo specialist and a cardiac anaesthetist. Involvement of other specialists (vascular surgeons, vascular radiologists, physicians specialising in care of the elderly) is also necessary. Cases should be discussed and decisions made at a formal multidisciplinary meeting.

The TAVI work-up investigations are shown in Table 2 and include a coronary (and ileofemoral) angiogram, right heart catheterisation, computed tomography (CT) of aorta and iliac arteries (often with 3D reconstruction), lung function tests and duplex ultrasound of the carotid arteries. Co-existing CAD is not a contraindication for TAVI and PCI can be performed pre-valve implantation in a patient with severe proximal coronary stenosis. The consensus is that concurrent coronary disease should only be treated if the amount of myocardium that is potentially ischaemic is large and likely to cause significant problems during the TAVI procedure.

One of the most important components of the work-up is the assessment of valve morphology and the sizing of the aortic annulus. Correct valve sizing is critical to minimise the potential for paravalvular regurgitation and to avoid prosthesis migration. 3D TOE and CT are ideal in this regard, as the aortic annulus is an oval structure and 3D techniques allow measurements in multiple planes. The assessment of valve morphology is vital as it helps to predict the severity and localisation of periprosthetic regurgitation or the risk of coronary artery obstruction. The decision about valve size depends not only on annulus size, but also on the severity of valve calcification, the size of the LV outflow tract (LVOT), and the size of the aortic root/sinuses.

Table 2. Pre-operative investigations necessary during patient selection for transcatheter aortic valve implantation

Cardiac catheterisation:
Coronary angiography
Aortography
Ilio-femoral angiogram
Echo studies:
Transthoracic study (with annulus measurement)
Transoesophageal study (if annulus borderline or if any doubt regarding anatomy)
Computed tomography scan of aorta:
3D reconstruction if available
Precise localisation of vessel wall calcium — particularly with non-contrast-enhanced scans
Annulus measurement
Carotid Dopplers
Lung function tests

As the commonest and most serious complications of the transfemoral route are vascular, special attention should be paid to the evaluation of size, tortuosity and calcification of peripheral vessels to assess suitability for the transfemoral approach. Angiography of the femoral and iliac arteries is the gold standard to measure vessel diameter, but CT is also helpful in estimating calcification and tortuosity, particularly with additional 3D reconstruction. The contraindications for transfemoral access include small calibre vessels (< 6 mm, depending on the device used), severe tortuosity/calcification of the iliac arteries, and severe intraluminal aortic atheroma. In general terms, tortuosity is much more difficult to negotiate with any device in conjunction with calcification.

Clinical outcome

Early experience of TAVI was analysed in the Registry of Endovascular Critical Aortic Stenosis Treatment (RECAST) trial from Cribier's group [13]. Anatomical and procedural success using the transfemoral technique exceeded 90% with a low 30-day mortality (less than 10%). John Webb's group [14] initially reported a valve implantation success rate of 86% with a 30-day mortality of about 12%. These initial results

Table 3. Thirty-day mortality and clinical outcome

	Edwards Sapien valve			CoreValve	
	SOURCE	TAVI UK Registry	Kings Health Partners	European Registry	TAVI UK Registry
	n = 1,038 [19]	n = 402 [21]	n = 151 [20]	n = 1,243 [22]	n = 460 [21]
30-day mortality	6.2%	8.9%	9.9%	6.7%	5.5%
TF	6.3%	NA	6%	NA	NA
TA/subclavian approach	10.3%	NA	13.1%	9.4%	NA
Stroke	2.5%	NA	6%	1.7%	NA
Pacemaker	7%	7%	5.3%	12%	26%
Major vascular complications	7%	2.5%	8.6%	1.9%	4%

TF — transfemoral; TA — transapical

were influenced by a marked learning curve; procedural success increased to 96% when experience had been gained.

The first CoreValve prosthesis was implanted in a human in 2004. Again, the CoreValve was implanted in high-risk elderly patients with a procedural success rate of 92% and an initial 30-day mortality of 15% [15].

Placement of AoRTic traNscathetER valves (PARTNER) is the first randomised controlled trial to compare standard surgical AVR to TAVI using the Edwards Sapien valve. At one year, the rate of death from any cause was 30.7% with TAVI, compared to 50.7% with standard therapy ($p < 0.001$). In addition, among survivors at one year, the rate of cardiac symptoms (New York Heart Association [NYHA] class III or IV) was lower among patients who had undergone TAVI than among those who had received standard therapy [16].

The largest series of transapical procedures has been performed by Walther et al. [17], who reported a similar success rate to the transfemoral procedure (exceeding 90%) with a very small risk of needing urgent femoro-femoral cardiopulmonary bypass. The mortality rate is slightly higher using the transapical approach, probably because trans-apical TAVI patients have a significantly higher risk due to peripheral vascular disease and renal failure, which are markers for a high atheroma burden and a poor outcome.

Access site complications were the commonest serious complications, but smaller delivery systems are likely to reduce this. The risk of stroke is relatively low and varies from 2–6%. Atrioventricular block occurs relatively rarely after Edwards Sapien valve implantation, but is more frequent with self-expanding devices (e.g. CoreValve) with a need for pacemaker implantation in up to 20% of cases [18].

Severe aortic regurgitation after valve implantation is very rare, although mild to moderate para-valvular regurgitation with no haemodynamic consequence is frequently observed (93.8% in the SOURCE registry). Thirty-day mortality was 6.3% in transfemoral patients and 10.3% in transapical patients [19]. In our own series published recently, procedural success was achieved in 98%. Postoperative complications included stroke (6%), complete atrioventricular block (5.3%), renal failure requiring haemofiltration (9.3%), and vascular injury (8.6%). Overall 30-day mortality was 9.9% (n = 15), 6% for transfemoral approach and 13.1% for transapical approach (Table 3) [20].

Table 4. Peri-procedural complications of TAVI apparent during the procedure (immediate) or during days 0–7 post-op (delayed)

Immediate:
- Iliac/aortic dissection
- Iliac/aortic/cardiac rupture
- Device migration/embolisation
- Coronary ostial occlusion
- Coronary embolisation (air/debris)
- Mitral regurgitation
- Cerebrovascular accident
- Aortic regurgitation (paravalvular or intravalvular)
- Atrioventricular block

Delayed:
- Delayed haemorrhage (e.g. retroperitoneal)
- Renal failure
- Respiratory failure
- Sepsis
- Peripheral vascular insufficiency
- Aortic regurgitation (paravalvular)

COMPLICATIONS AND THEIR MANAGEMENT

A variety of complications can occur during the TAVI procedure (Table 4) which can have important haemodynamic consequences. We have found real-time 3D TOE invaluable for the rapid identification of these problems, which can often be quickly rectified. Such phenomena include:

— coronary air embolus — manifests as a wall motion abnormality;

— acute increase in mitral regurgitation – can be caused by passage of the guidewire through the mitral subvalvular apparatus, usually clearly seen with 3D TOE;

— severe aortic regurgitation — either after BAV or valve deployment. Echo will quickly identify whether this is intra- or para-prosthetic;
— cardiac/aortic rupture with haemopericardium.

Vascular complications should be identified and treated promptly. It is mandatory to perform an iliac-femorogram at the end of the procedure. Flow-limiting dissections of the iliac arteries should be stented and ruptures of the iliacs or aorta treated with covered stents if possible. Vascular radiologists/ /surgeons should be closely involved with any TAVI programme for this reason.

Based on preclinical tests, the anticipated durability of the Edwards Sapien and the CoreValve should be similar to currently available bioprosthetic valves. So far, there has been no structural deterioration observed on routine follow-up documented beyond seven years with the Cribier-Edwards valve, and beyond five years with the CoreValve device. However, long-term follow-up data is needed from larger groups of patients.

SUMMARY

Percutaneous treatment of valvular heart disease is now a reality. The successful implementation of these interventions depends on appropriate case selection, itself achieved via excellent imaging techniques and a multidisciplinary approach. Rapidly advancing technology is making the procedures safer, but awareness of potential complications and their rapid identification is vital. This new field of transcatheter treatment will involve even closer working between cardiologists and cardiothoracic surgeons and is likely to increase, rather than decrease, cardiothoracic workload.

Conflict of interest: *none declared*

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