Aortic stenosis in interventional cardiology

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The ESC guidelines on the management of valvular heart disease (VHD) were published early in 2007 and include recommendations for the evaluation and treatment of aortic stenosis (AS). At that time, transcatheter aortic valve implantation (TAVI) was in its very early stages—at least as far as its clinical use was concerned. Thus, only a brief statement was included: “Preliminary reports show that percutaneous aortic valve replacement is feasible but this procedure is at an early stage and further studies are needed to evaluate its potential role.”

A first position paper on the use of TAVI was published by ESC and EACTS in 2008. Again, conclusions were based on data available at that time as well as the authors’ own experience. The available evidence suggested that this technique was indeed feasible providing haemodynamic and clinical improvement for up to two years in high-risk patients. Safety and long-term durability still needed to be assessed.

Since then, TAVI has experienced an incredible development and thousands of valves have been implanted worldwide. Many (continued on page 4)

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Aortic stenosis today

(continued on page 2) there was a clear majority of women (71%), and a higher incidence of chronic obstructive pulmonary disease. Mortality was 74% during a mean follow-up of 3.6 ±1.4 years. One-year survival was 66% compared with 94% in the surgical group. Among those patients fit for AVR, refusal to undergo surgery (hazard ratio 12.61, p=0.001) was the only predictor of mortality in a multivariate model. This poor prognosis is in line with an earlier Dutch series, which demonstrated the highly negative impact of severe symptoms and left ventricular dysfunction on the survival of non-operated patients (three year survival of 49% with an ~ 5-fold increase in mortality risk, if systolic LV dysfunction was present).

In the Euro Heart Survey data, 32% of patients were surprisingly either denied surgery or simply never referred to surgeons by cardiologists. While the two main reasons not to operate on patients by multivariate analysis were left ventricular dysfunction and older age, this is clearly not in accordance with ESC guidelines, which state that “...old age in itself is not a valid reason to deny AVR... and that, as long as the mean gradient is still >40 mmHg, there is virtually no lower EF limit for surgery.” Further-more, comorbidities (using the Charlson index) were not significantly associated with the decision to operate or not. This fact is all the more surprising when we consider the negative impact of comorbidities on four-year mortality in untreated patients. We have seen, since the introduction of TAVI, that referral for AVR is increasing. As we said above, results from several large TAVI centres point to the fact there has been a strong increase in the number of surgical AVRs in their institutions.

TAKING MESSAGES

A large number of patients with severe symptomatic AS are not treated. Patients with severe AS—patients who do not receive treatment surgery or TAVI—are associated with a higher increase in mortality risk. Surgical AVR continues to be an effective treatment for severe AS. TAVI is an excellent new option for those who are at high risk for surgery. Referring a patient to a centre with a multidisciplinary Heart Team will ensure that all treatment options are fully explored in the best interest of the patient. This Heart Team approach, involving cardiologists, surgeons and anaesthesiologists, is of paramount importance.

Progression of aortic stenosis: an update

Alain Berrebi

A recent editorial by Catherine M. Otto describes the current understanding of the progression of aortic stenosis, concluding that “calcaric aortic valve disease: outflow obstruction is the end stage of a systemic disease process” (Fig. 1). Dr. Otto adds that “this conceptual framework for the natural history of calcific aortic valve disease illustrates the spectrum of disease from the ‘at risk’ patient to the patient with end-stage severe symptomatic aortic stenosis. Once aortic sclerosis is detectable, there is an increased risk of cardiovascular events. At the onset of even mild symptoms, survival deviates even more than expected, with a dramatic decline in survival with severe symptomatic aortic stenosis. Aortic valve replacement (AVR) at the onset of early symptoms prevents these late adverse outcomes. The challenge now is to identify factors that predict transition from an ‘at risk’ patient to a patient with aortic sclerosis and to identify which aortic sclerosis patients will go on to progressive aortic stenosis.” Many severe AS patients who are asymptomatic actually reveal symptoms of their underlying disease when given an exercise/stress test, and exercise testing is recommended.

Calcific aortic stenosis is a progressive disease, and echocardiography can play an important role in defining the different stages of the disease, based upon the peak aortic jet velocity (PAJV) or aortic valve area (AVA).

In an earlier New England Journal of Medicine editorial, Catherine Otto said, “Once symptoms occur, valve replacement is the only effective treatment, and there are no known therapies to prevent disease progression.”

REFERENCES

From the cardiac surgeon’s perspective

TAVI has become a well-established therapeutic option for patients with severe calcified aortic stenosis who are unsuitable for surgery or defined as high risk, according to currently available risk scores (EuroSCORE > 20 and STS > 10). The 30-day mortality has, nevertheless, a significant variation, according to different studies ranging from values as low as 1.8% (the Padua experience) up to 18%. The one- to three-year survival rate after TAVI can also vary significantly among different TAVI series. Current risk scores are certainly inadequate for the precise stratification of patients, and even the adoption of the so-called Leipzig score (EuroSCORE divided by three) is a simple mathematical artefact.

Older patients are at increased risk for postoperative complications. If a complication occurs, it can lead to a cascade of events resulting in disability, loss of independence, diminished quality of life, high health care costs and mortality. Surgical decision-making in this population is challenging because of the heterogeneity of health status in geriatric patients and the inadequacy of tools for predicting operative risk. Commonly used predictors of post-operative complications have substantial limitations; most are based on a single organ system or are subjective, and none estimate a patient’s physiologic reserves. As an example, not all patients with calcific aortic stenosis and CAD have the same risk profile. The SYNTAX score, derived from the SYNTAX trial, has clearly highlighted that not all three-vessel disease patients are exactly the same.

The SYNTAX score has allowed stratification of risk according to the severity of coronary artery disease and the same applies to aortic stenosis and CAD. There is a need for the development of new scores for this specific cohort of patients.

Frailty is increasingly recognised as a unique domain of health status that can be a marker of decreased reserves and resultant vulnerability in older patients. Frailty can be conceptualised as a global phenotype of physiologic reserves and resistance to stressors. It might be that pre-operative assessment of patients for frailty would result in more accurate risk assessment for cardiac surgery and may identify a challenging subset of patients who would benefit from this novel technique for their care. Extensive collection of data and an in-depth analysis of The SOURCE Registry could fulfil this task. However, only randomised trials comparing surgical AVR and TAVI, regardless of patients’ age, can provide a definitive answer.

For all these reasons, and for this continuing uncertainty, it is our opinion that it is of paramount importance to maintain and enhance a solid interaction among cardiac surgeons, cardiologists and anaesthesiologists in the “aortic team,” which seems to be the only way to identify the best therapeutic option for each individual case. I believe, as well, that we need to reject recent statements at valve meetings suggesting that interventional cardiologists should no longer scrub in with the surgical team when performing transapical insertion and that, vice-versa, cardiac surgeons and anaesthesiologists should remain on call when performing transfemoral insertion. Quality control of the final results is achieved only by the team approach, something that has been stated and understood since the beginning of the transcatheter valve experience. To give up such a strategy is not acceptable, either for our patients’ safety or cost control.

Patients should always remain the centrepiece of our actions, with their relative quality of life being of primary consideration.

REFERENCES

Aortic stenosis is life-threatening and progresses rapidly

“Survival after onset of symptoms is 50% at two years and 20% at 5 years.”

“Surgical intervention [for severe AS] should be performed promptly once even...minor symptoms occur.”

**SOURCE Registry update**

**MARTYN THOMAS**
Professor Thomas is the director of cardiothoracic services at Guy's and St Thomas' Hospital in London, UK, and serves as one of the Principal Investigators for The SOURCE Registry.

Over the last decade, the development of the transcatheter aortic valve implantation (TAVI) procedure has been actively underway and we have seen a significant evolution in valve technology, procedural refinement, Heart Team training and clinical evaluation. Today, thousands of procedures have been performed, and the majority of data have been gathered through a multitude of clinical trials and registries.

The next-generation Edwards SAPIEN XT THV has enabled clinicians to weigh a multitude of attributes when selecting the best option for their patients. These include the delivery approach, valve durability and performance, tissue characteristics, frame design, device height and delivery system features.

Of extreme importance and interest to clinicians and patients is the longer-term clinical performance of TAVI devices. Edwards has recently reached the one-year follow-up milestone of more than 1,000 patients in The SOURCE Registry, the company’s post-CE Mark surveillance of the Edwards SAPIEN valve.

The SOURCE Registry is following more than 1,000 consecutively treated patients receiving the valve, and has shown a one-year survival rate of 81.1% in transapical procedures (TF) and 72.1% in transfemoral procedures (TF). The SOURCE Registry is follow¬ing more than 1,000 consecutively treated patients receiving the valve, and has shown a one-year survival rate of 81.1% in transapical procedures (TF) and 72.1% in transfemoral procedures (TF).

**Indications for intervention in AS and the current use of TAVI**

(See full guidelines at www.escardio.org/guidelines-surveys/esc-guidelines/Pages/valvular-heart-disease.aspx)

1. No new, strong data have been published since 2007 that would justify changing the general recommendations of the ESC guidelines regarding the indications for surgery in AS.

2. TAVI will certainly get more attention in the revised ESC guidelines, scheduled for 2011. However, it may still be too early in the development of TAVI to provide strong recommendations.

3. Despite the growing experience with TAVI, availability of small observational studies and sizeable registries, the following facts need to be considered:
   - Currently available mortality data for TAVI can only be compared to risk score calculations with all their well-known major limitations.
   - A randomised trial comparing conventional valve replacement and TAVI is underway, with data for Cohort B (extremely high risk patients randomised between TAVI and medical management) to be released at TCT, Sept 2010. Cohort A (high risk patients randomised between TAVI and surgical AVR) should be available in the first half of 2011.
   - Current experience is mainly restricted to surgical high-risk patients.
   - No long-term results for TAVI are available. In particular, data on valve durability in vivo are missing.

Furthermore, the access to the coronary arteries may be more difficult for future coronary interventions in certain of these patients (particularly when long, self-expanding stents are used). The impact of that is still unknown. Finally, effects on the conduction system (again, in particular when self-expanding stents are used) require further studies as well.

Thus, in 2010, conventional valve replacement must strongly be recommended for patients with low risk for surgery, and TAVI must still be restricted to patients with a significantly elevated risk of surgery.

4. The difficult question remains: When is the surgical risk elevated enough to justify TAVI? A logistic EuroSCORE ≥ 20% and other conditions such as porcelain aorta and previous chest radiation have been proposed. Though the logistic EuroSCORE has been shown to overestimate the actual operative mortality, this appears to remain a helpful screening cutoff for current practice.

However, certain octogenarians and nonagenarians frequently present with EuroSCOREs < 20% and nevertheless appear to be poor candidates for conventional valve surgery, based on our clinical judgement. Geriatric outcome scores may be helpful in this situation. Although octogenarians and nonagenarians can still be good candidates for surgery, a more liberal decision for TAVI in this age group may be justified, but requires careful and balanced discussions with the patient and family. (See www.euroscore.org)

5. In the above defined patient population currently considered suitable for TAVI, spontaneous symptoms will, in general, be the indication for intervention. However, in this patient group, symptomatic status may be difficult to assess. High age and comorbidities can make it challenging to determine whether non-specific symptoms such as fatigue, limitations to physical activity and shortness of breath are primarily related to AS or rather to comorbidities and age. In general, the primary goal of decision-making with regard to intervention may no longer be prognostic considerations, but rather improvement of the quality of life.

6. The question of whether a patient can be considered for...
TAVI rather than for conventional surgery is not the only difficult one at hand. At the other end of the spectrum, we need to decide when patients are no longer eligible for TAVI because they are too sick and their life expectancy too short. Although a life expectancy of at least 1 year with regard to comorbidities is required, this may be difficult to predict in an individual patient. Here again, geriatric outcome scores may be helpful. Nevertheless, our ability to predict at this end of the patient spectrum whether TAVI will significantly improve quality of life for a reasonable time needs to improve, and further investigation is required with respect to this.

7. TAVI should still be restricted to centres with cardiac surgery available on-site. A team approach involving cardiology, cardiac surgery and vascular surgery is crucial. Despite the rapidly increasing number of interventions, TAVI must still be considered a procedure under investigation. Thus, careful documentation and continuous data analysis must be requested.

Screening requirements for TAVI

In addition to the above discussed clinical selection criteria, appropriate screening in experienced hands is required to determine the “anatomic” eligibility for TAVI in an individual patient. This is crucial to avoid unnecessary complications. In addition to confirmation of AS severity, detailed basic information is required regarding:

- Valve morphology (tricuspid or bicuspid, extent of calcification)
- Annulus diameter
- Left ventricular outflow tract (LVOT) morphology
- Morphology of the aortic root (sinuses and their relation to extensive valve calcification)
- Distance between coronary arteries and annulus (relation to sinus morphology and extensive valve calcification)
- Size, pathology (complex plaques, aneurysms) and course (kinking) of the entire aorta
- Size, pathology (calcification) and course (tortuosity) of iliac and femoral arteries

While some criteria, such as valve diameter and minimum vessel diameter, have been relatively well-defined, others are still awaiting better standardisation.

It is crucial that an experienced TAVI Heart Team reviews all imaging material prior to deciding on the appropriateness of the procedure for a patient, not relying on written reports, particularly when they are not provided by somebody experienced with the procedure.

Currently, echocardiography provides assessment of stenosis severity and valve morphology, LVOT morphology and annulus diameter. Although CT and MRI can also provide annulus measurements, values obtained with the different methods vary significantly. It has to be emphasised that at present most experience is available for transoesophageal echo, which is still the standard for deciding valve size for TAVI.

Even with experience, uncertainty about choosing the appropriate valve size may remain. In this case, angiography during balloon dilatation may be helpful.

At the time of heart catheterisation, mandatory for the evaluation of coronary arteries, aortic root angiography (10° LAO / 10° cranial) is advisable. Angiography of the iliac arteries may also provide primary information and direct further evaluation.

However, CT angiography is the ideal method for evaluation and should be performed in most cases. It provides comprehensive evaluation of the entire aorta, iliac and femoral arteries, aortic root morphology and coronary arteries (see above). Duplex sonography may also be helpful, particularly for the evaluation of the entry site.

REFERENCES


Important considerations in transcatheter aortic valve technology

A state-of-the-art heart valve bioprosthesis is designed to provide immediate and sustained long-term haemodynamic performance and structural integrity. The valve also needs to be easy to position and implant, while respecting anatomical structures within the heart. For these reasons, Edwards’ primary considerations for valve design are durability, haemodynamics and ease of use. Factors involving durability include choice of leaflet material, shape, tissue processing and frame design.

With more than 50 years of experience in creating and developing heart valves, Edwards Lifesciences recognises the importance of a continuing partnership between engineers and the experienced physicians implanting the company’s valves.

LEAFLET TISSUE PROPERTIES The Edwards SAPIEN XT transcatheter heart valve uses bioengineered bovine pericardial tissue, which has demonstrated sustained long-term performance in more than 20 years of clinical follow-up data on Carpentier Edwards PERIMOUNT surgical valves. The bovine pericardial tissue’s multiple layers of collagen improve its resistance and strength.

THERMAFIX™ TISSUE TREATMENT PROCESS The proprietary Edwards ThermaFix anti-calcification treatment applied to the bovine pericardial tissue helps eliminate up to 98% of calcium binding sites on the tissue (see figure below).

LEAFLET DESIGN The Edwards SAPIEN XT valve, Edwards’ latest transcatheter heart valve, incorporates a proprietary surgical leaflet shape, more closely resembling the design of the Edwards PERIMOUNT Magna surgical valve leaflets. This design optimises the distribution of stresses along the body of the leaflets, with continued haemodynamic performance for an extended period of time.

Critical design factors in the Edwards SAPIEN XT transcatheter heart valve frame

Two cornerstones for optimising valve performance and durability are the frame design and radial strength.

Why is the valve frame height important?

The valve is designed to treat severe aortic stenosis while minimising secondary patient compromises. A low frame height is key, as it is important that the valve frame does not interfere with the anatomical parts surrounding the native annulus. Designed with an optimal frame height, the Edwards SAPIEN XT valve—between 14 and 17 mm—may be safely anchored in the aortic annulus. This minimises the risk of coronary obstruction (less than 1%, according to The SOURCE Registry), and leaves free access for future coronary interventions (e.g., angioplasty or stenting). The risks of mitral apparatus interference and/or conduction system disturbance are also reduced with our optimal height design.

Why is the radial force of a valve frame important?

Radial force is a key component to providing durable and positive clinical results. The Edwards SAPIEN XT valve was designed with high radial strength for proper hemodynamics and valve durability. Frame strength results in a large effective orifice area (EOA), even in heavily calcified annuli.

Where does frame radial strength come from?

Frame radial strength comes from a combination of frame geometry and frame material. The Edwards SAPIEN XT frame was designed using extensive computer analysis to determine the optimal geometric shape and material. It is made from cobalt chromium and features this new geometry to allow for low profile crimping, while maintaining high radial strength.

REFERENCES
2) Data on file at Edwards Lifesciences
Transcatheter Aortic Valve Implantation (TAVI) is an alternative approach to surgical aortic valve replacement (surgical AVR). A less-invasive procedure, it avoids cardiopulmonary bypass and cardiac arrest, takes less time and requires less anaesthesia compared to open-heart surgery and is an alternative option for patients at high risk for traditional open heart surgery.

TAVI is performed via transfemoral or transapical access without cardiopulmonary bypass. Both approaches involve inserting and deploying a crimped valve across the native aortic valve after it has been initially widened by balloon valvuloplasty (BAV). The transcatheter heart valve, after being carefully crimped (compressed), is mounted onto the NovaFlex transfemoral or Ascendra2 transapical balloon-expandable delivery catheter system. The Edwards SAPIEN XT THV is designed to be implanted through either of these transfemoral (TF) or transapical (TA) approaches.

Your patient may be suitable for either approach, and the Heart Team will decide with you the best option, taking into consideration whether it would be better for your patient to be treated by TAVI, or surgical AVR.

Edwards is proud to announce CE Mark approval for the Edwards SAPIEN pulmonic transcatheter heart valve. The valve is designed to be an alternative to surgical valve replacement for patients suffering from congenital heart disease of the pulmonic valve. Patients with this congenital disease often face the burden of multiple open-heart surgeries, either to replace their “native” diseased valves or, as they age, their bioprosthetic replacement valves. As every re-operation can increase a patient’s risk of infection, illness and death, a minimally invasive procedure is essential for the long-term survival and quality of life for these patients.

Managing patient expectations is key

“When evaluating patients with severe aortic stenosis, it is extremely important to review the multitude of options available—including surgery—and to refer them to a hospital where a multidisciplinary Heart Team will review all the information. Managing patients and family expectations is key, as many patients will be better suited to surgical valve replacement—still the gold standard for patients with lower risk profiles. It is difficult for all concerned when a patient arrives with his/her heart set on TAVI and is not a suitable candidate.”

Pilar TorNoS mas, md, FESC
Hospital General Universitari Vall d’Hebron, Barcelona, Spain
Head of ESC Task Force of the European Society of Cardiology for the management of valvular heart disease

What is TAVI?

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New hope for pulmonic patients

A TAVI anniversary—a dialogue between early-timers!

Do you remember May 18th five years ago?

It was the first implant of the Cribier-Edwards Transcatheter valve in Germany, which took place at my former hospital in Essen. My co-workers in Munich remembered today with a cake with five candles on it. I had a telephone call with the first patient a couple of minutes ago. He feels very well and is in good shape, full of power and without any heart problems. Thanks to all of you and particularly to Alain Cribier for the confidence doing this procedure.

Best regards, Stefan

An actual email exchange between Professors Alain Cribier, Stefan Sack (the primary interventionalist for the first German patient treated at the University Hospital in Essen. Prof. Sack is now at the Schwabing Hospital in Munich. For more information, see TAVItalk 3.)

From: Stefan Sack
Subject: TAVI Anniversary
Date: May 18, 2010

So good to hear the great news! And it was obtained with the first-generation valve! There are no limits to our expectations with the new generation devices.

Sadly, our world champion, Mrs S., who was beyond 6.5 years follow-up, passed away two days ago due to non-cardiac disease (terminal renal failure) with a valve which had been checked echographically, live, during a training session in Rouen, a month earlier. Valvular function was perfect, with no change in gradient (9 mmHg) and EOA (1.68 cm²), no AR. Congratulations...and Stefan, thanks for having been an early believer! I really needed people like you at that time! With best regards, Alain

Congratulations to Professor Alain G. Cribier, the ESC 2010 Andreas Gruentalig Award winner, honouring his more than 20-year commitment to finding catheter-based valve solutions for patients with severe AS!
Patient focus

A GRAND GIFT FOR AN 89TH BIRTHDAY!

An 88-year-old retired seamstress was referred to our service for severe aortic stenosis (mean systolic pressure gradient = 81 mmHg, aortic valve area = 0.6 cm²), with prior acute heart failure 3 months earlier. Although she was recompensated, she continued to be short of breath on exertion (NYHA III), which clearly hindered her ability to live independently. It was on this basis that she wished further evaluation and treatment.

Madame R. was on puffers for mild to moderate chronic pulmonary disease. Her past medical history showed she had experienced an incident of deep vein thrombosis some years before. Further assessment revealed concomitant coronary artery disease, with a well-collateralised chronic total occlusion of the distal circumflex, pulmonary hypertension (systolic pulmonary artery pressure = 71 mmHg) and moderate mitral regurgitation. Systolic left ventricular function was preserved (LVEF 59%) and her carotids were unremarkable. Based on a 30-day mortality of 35.7% for conventional aortic valve replacement (estimated by logistic EuroSCORE), our interdisciplinary Heart Team decided she would be best served with TAVI. Given an annulus size of 21 mm and femoral arteries with a minimal luminal diameter of 8.1 mm, a transfemoral access was chosen and a 23 mm Edwards SAPIEN Transcatheter Heart Valve (THV) was successfully implanted the day of her 89th birthday. The procedure, as well as the rest of the hospital stay, were both uncomplicated. Pre-discharge echo revealed an excellent result with a mean transaortic systolic pressure gradient of 9 mmHg, trivial paravalvular leak, reduced mitral regurgitation (2+) and normalised pulmonary pressures. She was discharged to go home on day 10 without any readmissions. Six months after the procedure, she is in functional class I, choosing to climb 4 flights of stairs rather than take the elevator to her apartment.

Six months after her successful transfemoral implantation with an Edwards SAPIEN THV on her 89th birthday, Madame R. (above) insists that, “This valve must be the most wonderful birthday gift I ever received”!

The transcatheter Heart Team at Andreas Grünzig Labs, University Hospital of Zurich. Back row from the left: Lukas Altwegg, MD (interventional cardiologist), Roberto Corti, MD (interventional cardiologist), Juerg Gruenenfelder, MD (cardiac surgeon). Front row from the left: Ines Buehler (study nurse) and Dominique Bettx (cardiac anaesthesiologist).