

Transcatheter Aortic Valve Replacement: The Future Is Here!

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Aortic valve replacement (AVR) is the only effective treatment for symptomatic aortic stenosis (AS). In the ideal candidate, the operative mortality associated with AVR is 4%.¹ With increasing age, patients with AS acquire other comorbidities that increase their surgical risk to prohibitive levels, limiting their surgical options. It is estimated that at least 30% of the patients with severe AS are not referred for AVR due to their other underlying illnesses.² The search for a less invasive, less morbid, and equally effective strategy for the treatment of AS started soon after surgical AVR was described. Improvement in valvular prosthetic design increased the valve durability while decreasing the risk of malfunction and thrombosis. Surgical advances have also decreased the perioperative morbidity and mortality to its current rate. However, surgical AVR is still accompanied by the inherent risks of cardiopulmonary bypass and significant rehabilitation after a median sternotomy. These limitations triggered the search for a percutaneous option for the treatment of AS. Balloon aortic valvuloplasty (BAV) emerged as an effective way of postponing AVR in patients with congenital AS. However its application in patients with calcific/degenerative AS yielded a high rate of early restenosis, complications, and no increase in survival.³

Suboptimal results with BAV prompted a re-evaluation of the percutaneous options and led to the development of transcatheter AVR (TAVR). This concept consists of replacing the native aortic valve with a stent mounted prosthesis which is placed percutaneously through the femoral artery, vein, or directly through the left ventricle. After significant animal experimentation, the first human TAVR was performed by us in Rouen, France in 2002.⁴ TAVR opened the possibility for treating patients who had been left untreated as it was believed that their operative mortality outweighed the benefits of traditional AVR.

Initial reports using a balloon expandable bioprosthesis (Percutaneous Valve Technology [PVT] New-Jersey,

USA) advanced to the native aortic valve through the femoral vein (antegrade transeptal technique) on compassionate basis in extremely sick patients, consistently demonstrated an increase in the aortic valve area (0.6 cm² to 1.6 cm²), a fall in mean transvalvular gradient (37 mm Hg to 9 mm Hg), and an increase in left ventricular ejection fraction (LVEF) (45% to 53%) confirming the feasibility of the procedure. The 30-day mortality rate was 23%.^{5,6} Patient survival was limited due to the severity of their co-morbidities. However long term survival of greater than 4.5 years has been observed without bioprosthesis dysfunction. After acquisition of PVT by Edwards Lifesciences (Irvine, CA, USA) in 2004, significant technical and prosthetic modification followed, solving the majority of the previously encountered limitations: appropriate sizing of the left ventricular outflow tract and the availability of a second valve size decreased perivalvular leaks. Landmark identification for optimal positioning decreased the rate of valve migration. The development of a catheter with a deflectable tip (Retroflex™ catheter) which aids in the atraumatic passage across the aortic arch and in centering the guidewire through the aortic orifice facilitated valve delivery and revitalized the retrograde approach. After applying these modifications, procedural success increased to 96% after the first 25 cases, while the operative mortality decreased to 8%.^{7,8}

Multicenter registries from the United States (REVIVAL II), European Union (REVIVE II), and Canada (Canadian Special Access) included patients with severe AS with a valve area <0.8 cm² and a high predicted operative mortality (logistic EuroSCORE >20%) were started to evaluate procedural safety and efficacy. New valve modifications were added to improve long-term prosthetic function, and included the use of a bovine pericardial prosthesis and the addition of an anticalcification treatment, culminating in the prosthesis that is currently used. With over 200 patients enrolled (Cribier, personal communication, 2007), overall implant success persisted at 88% and the 1-year survival in successfully implanted patients was 74%. The improvement in effective orifice area (EOA), LVEF, and mean aortic gradient echoed the previously reported results. In addition, 48% had aortic insufficiency grade 1/4, and 41% had grade 2/4. Symptomatic improvement of ≥1 New York Heart Association (NYHA) functional class was seen in 77% of the patients at 6 months.

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Unsuccessful valve deployment was seen in 12%, and was due primarily to failed arterial access, inability to cross the aortic valve, and acute valve embolization from misplacement reflecting the learning curve. Thirty-day mortality was 12%, strokes were seen in 4.6%, and vascular complications were documented in 14.8% of the cases, reflecting a frank improvement with the added experience.

In order to address the patients with peripheral vascular disease and those with tortuous calcified iliac arteries, the transapical approach was created. The procedure consists of a direct puncture and sheath insertion into the left ventricular chamber. A guide wire is used to cross the aortic valve and the rest of the procedure follows the same steps involved in valve preparation and deployment as described for the retrograde approach. Traversing the aortic valve is simple as it is done through the smooth ventricular side. Initial published series revealed a high success rate and a low mortality rate.⁹ A recent report by Walther,¹⁰ showed an 89% rate of successful implants with a rate of conversion to conventional AVR in 6.8%. These high-risk patients had a median ICU stay of 20 hours. Perivalvular aortic insufficiency was mild in the majority of patients that experienced it. The 30-day mortality was 13.6%, while the predicted operative mortality was 27%. Use of extracorporeal circulatory support was frequent during the initial procedures, and thereafter abandoned. The largest series (n=125) of high-risk patients treated with the transapical AVR are included in the TRAVERCE registry. Patients with severe symptomatic AS, multiple comorbidities and a logistic EuroSCORE of 26.7% (16.2%) had successful valve placement in 92% of the cases (Walther, personal communication, 2007). The procedural stroke rate is 9.2% reflecting that even with the avoidance of aortic cross-clamping there is still a risk of cerebrovascular accident. Valve malpositioning was the most common reason for an unsuccessful procedure followed by perivalvular aortic insufficiency. The latest Source registry (unpublished data) in Europe show an increase in procedural success >95%, whatever the route used for TAVR. Finally, a huge pivotal randomized study is ongoing in the US (PARTNER trial) aimed at comparing the results of TAVR with surgery in a cohort of high surgical risk patients and with medical treatment in those with formal contra-indication to surgery (400 patients from 15 centers have already been included in the trial).

The Corevalve ReValving™ system (Corevalve Inc, Irvine, CA) is a percutaneously placed self expanding porcine pericardial bioprosthesis designed for the treatment of aortic stenosis. This prosthesis was the second system to be used in humans with severe AS and with the Sapien valve, contribute to the largest patient experience. It is a self centering, partially repositionable, prosthesis which may allow more freedom during deployment. Through its three previous iterations, the device has decreased in size from a 25 Fr to 18 Fr system.

The most recent and comprehensive published series (n=86) with the utilization of 21 Fr and 18 Fr devices showed an acute device success rate of 88% and a 48 hour procedural success of 74%.¹¹ The aortic valve area increased from 0.6 cm² to 1.67 cm².¹² Post procedural aortic insufficiency improved or remained unchanged in 66%. Severe aortic insufficiency was not seen after successful device deployment.¹³ With the use of the 18 Fr delivery system, procedural duration diminished, circulatory support was no longer utilized, and the procedure became truly percutaneous without the need of a surgical cut down. The 30-day mortality rate was significantly lower than the estimated mortality rate (12% vs 27%). Procedural MACCE was seen in 22%, stroke in 10%, and tamponade in 7%. The prosthesis delivered by 21 Fr and 18 Fr catheters performed comparably. Twenty four percent of the patients required a permanent pacemaker after the procedure.

With such promising results, the Edwards Sapien valve and the Corevalve ReValving™ system obtained the CE mark in October 2007. This marked a new beginning in the transcatheter valve therapeutics as the procedure has expanded to select centers throughout Europe. It is estimated that >50 TAVR procedures are performed in Europe weekly. With new physicians being trained the number of eligible centers will grow exponentially and the diffusion of this technology will expand, providing patients the opportunity to be treated with an effective and innovative procedure. However, appropriate training and collaboration between everyone involved in the valve replacement team is imperative to maintain the high standard of success and low complication rate.

Future catheter and device modifications will decrease the sheath size, improve durability, facilitate valve positioning, and reduce perivalvular leaks. A number of other percutaneous valvular technologies are being developed which try to simplify the technique, avoid the previously known limitations, and improve the results. It is an exciting time in the field of interventional cardiology. One can only imagine what the future will add...

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