Transcatheter Aortic Valve Replacement: A Potential Option for the Nonsurgical Patient

Address for correspondence:
Thomas A. Hennebry, MB,
BCh, BAO, FSCAI, FACC
PO Box 26901, WP 3010
Oklahoma City, OK 73190
Thomas-Hennebry@ouhsc.edu

Jigar H. Patel, MD; Sunil T. Mathew, MD; Thomas A. Hennebry, MB, BCh, BAO, FSCAI, FACC

Department of Internal Medicine (Patel); Cardiovascular Section (Mathew, Hennebry), University of Oklahoma Health Science Center, Oklahoma City, Oklahoma

ABSTRACT

With improved life expectancy, the incidence of aortic stenosis is rising. However, up to one-third of patients who require lifesaving surgical aortic valve replacement are denied surgery due to a high operative mortality rate. Such patients can only be treated with medical therapy or percutaneous aortic valvuloplasty, neither of which has been shown to improve mortality. With advances in interventional cardiology, transcatheter methods have been developed for aortic valve replacement. Clinical trials are investigating these devices in patients with severe aortic stenosis that have been denied surgery. Preliminary results from these trials suggest that transcatheter aortic valve replacement (TAVR) is not only feasible, but an effective way to improve symptoms. In this review, we describe the current technology and display available outcome data. Though technical challenges and operator learning curve limit optimal use of the current technology, continued experience and advancements in technology may one day make TAVR a viable alternative to traditional surgical aortic valve replacement.

Aortic Valve Disease

As life expectancy improves, aortic valve disease is becoming a significant problem in the elderly. In population-based observational studies, it has been found that 1% to 2% of patients older than 65 have moderate to severe aortic stenosis (assessed by limited mobility of valve leaflet and/or increased velocity across the aortic valve seen on echocardiogram).^{1,2} Figure 1 depicts the incidence of aortic stenosis for patients older than 65.^{1–3} These patients have an increased risk of cardiovascular events and death from cardiovascular events.⁴

Surgical aortic valve replacement is currently the only treatment option for severe aortic stenosis that has been shown to improve survival.^{5–8} Unfortunately, up to one-third of patients with severe aortic stenosis are ineligible for corrective valve surgery,⁹ either because of advanced age or the presence of multiple comorbidities. Current treatment options for those patients not offered surgery include medical treatment or percutaneous balloon aortic valvuloplasty though neither has been shown to reduce mortality. Transcatheter aortic valve replacement (TAVR) methods have been developed recently to address this. Preliminary results are promising. We review the currently available technology for percutaneous valve replacement and reported clinical outcome data.

Transcatheter Aortic Valves

Valves currently in clinical trials with published clinical outcome data are manufactured by Edwards Lifesciences, Inc. (Irvine, CA) (Figure 2A) and CoreValve, Inc. (Irvine, CA) (Figure 2B).

The Edwards Lifesciences SAPIEN THV device is a balloon-expandable valve. It consists of bovine pericardium that is firmly mounted within a tubular, slotted, stainless steel balloon-expandable stent. Two valve sizes have been developed (23 mm and 26 mm).¹⁰ A 26 mm valve is typically used for an aortic annulus diameter of up to 25 mm; a 23 mm valve is typically used for an aortic annulus diameter of up to 21 mm.

The CoreValve, Inc. Revalving device is a self-expanding frame-valve prosthesis. It consists of a porcine pericardial tissue valve that is mounted and sutured in a multilevel self-expanding nitinol frame. This device has a broader upper segment (outflow aspect) which yields proper orientation to the blood flow. The first generation valve used bovine pericardial tissue and was constrained within a 25 French (F) delivery catheter (1F = 0.33 mm).¹¹ The second generation valve was built with porcine pericardial tissue within a 21F catheter to allow access through smaller-diameter vascular beds. The third generation of the device features a catheter with a valve delivery sheath size of 18F and a follow-on shaft of 12F.¹²

Next Generation Devices

Newer devices for TAVR are being developed to help address some problems encountered in first generation valves.

Newer devices that have first-in-man applications¹³ include Paniagua (Endoluminal Technology Research, Miami, FL), Enable (ATS, Minneapolis, MN), AorTx (Hansen Medical, Mountain View, CA), Perceval (Sorin

Figure 1. Incidence of aortic stenosis for population age >65 based on estimated population growth projection data from US Census assuming that 2% of the population age >65 have aortic stenosis.^{1–3}

Figure 2A. Edwards-Sapien Valve.

Group, Arvada, CO), Jena (JenaValve Technology, Wilmington, DE), Lotus Valve (Sadra Medical, Campbell, CA),¹⁴ and Direct Flow percutaneous aortic valve (Direct Flow Medical, Inc., Santa Rosa, CA).¹⁵

Techniques for TAVR

Techniques that are used in currently ongoing clinical trials are the retrograde and transapical approaches. A video animation of the basic methodology may be viewed at: www.clinical-cardiology.com.

Retrograde Approach: The retrograde approach involves using the femoral artery as access. After access is obtained, the valve is guided to the subcoronary position of the stenotic aortic valve.

Transapical Approach: The transapical approach is a more invasive approach that is performed more commonly by surgeons. The pleural space over the left ventricle apex

Figure 2B. Third generation CoreValve.

is first exposed. The prosthesis and balloon catheter are advanced through the left ventricle and positioned to the level of the fluoroscopically visible valvular calcium.¹⁶

Technical Challenges

Delivery Catheters: Relatively large delivery catheters may result in significant problems such as arterial dissection, perforation, or thrombosis if using the retrograde technique. Modifications are currently underway to reduce the diameter (size) of support catheters which may help reduce these risks.

Valve Positioning and Sizing: Valve positioning requires careful attention as improper positioning may obstruct coronary flow at the coronary ostia causing myocardial infarction. Improper positioning may also lead to valve dislodgement with resultant embolization and paravalvular insufficiency.

Selecting the size of valve is also important. Inserting a valve that is smaller than the aortic annulus may result in paravalvular leak or embolization. Likewise, inserting a valve that is too large may result in coronary obstruction.^{17,18}

Transvenous Pacing: To facilitate TAVR, a transient burst pacing of the right ventricle is done to limit blood flow through the aortic outflow tract. An uncommon problem is ventricular arrhythmias which may be responsive to defibrillation.¹⁹ Some devices do not require burst pacing (ie, CoreValve Lotus Valve, and Direct Flow).

Clinical Outcome Data With Transcatheter Aortic Valve Replacement (Table 1)

Cribier-Edwards Valve: Using the retrograde technique, Webb et al attempted implantation of the Cribier valve in 18 patients. The valve was implanted successfully in 14 patients. There were no intraprocedural deaths and 16 out of 18 patients were alive at a follow-up of 73 ± 49 days.¹⁷

Webb et al²⁰ also published their 12-month experience using the Cribier-Edwards valve implanted with the retrograde technique in 50 high risk patients. Procedural success was achieved in 43 patients (86%). Overall 30 day mortality was 12%; mortality of 16% in the first 25 patients falling to 8% in the following 25 patients ($P = 0.10$) suggesting that continued experience may play a role in lowering mortality. For those patients who received successful valve implantations, valve area measured by echocardiogram showed improvement from 0.6 ± 0.2 to 1.7 ± 0.4 cm² ($P < 0.0001$). Also, New York Heart Association (NYHA) functional class improved significantly ($P < 0.0001$) at 1 month follow-up and was maintained at 1 year follow-up.²⁰

Lichtenstein et al reported their initial experience using the Cribier-Edwards valve with the transapical technique in 7 patients. Overall, patients had improvements in aortic valve area (AVA) and left ventricular ejection fraction (LVEF). Paravalvular insufficiency was present though it did not appear to be of a magnitude that was clinically significant.¹⁶ The group recently published their 6 month follow-up. Of the 4 patients who remained alive, AVA, aortic mean gradient, and quality of life as assessed by NYHA class were well maintained at the 6 month follow-up.²¹

CoreValve: The feasibility and safety of this valve was studied in a prospective, multicenter trial. A total of 25 symptomatic patients with AVA < 1 cm² were enrolled in the study. The device was successfully implanted using the retrograde technique in 22 of 25 patients. Procedural success and aortic mean pressure gradients were markedly improved immediately following implantations with preprocedure gradients 44.24 ± 10.79 mm Hg to 12.38 ± 3.03 mm Hg postprocedure and were about the same at 30 day follow-up (11.82 ± 3.42 mm Hg). NYHA class improved by 1 to 2 grades in all patients. Major adverse cardiac events (MACE); (defined as death from any cause, major arrhythmia, myocardial infarction, cardiac tamponade, stroke, urgent or emergent conversion to surgery or balloon valvuloplasty, emergent percutaneous coronary intervention, cardiogenic shock, endocarditis, or aortic dissection) occurred in 8 of the 25 patients while in the hospital.¹¹

Using the second (50 patients) and third generations (36 patients) of the CoreValve, Grube et al reported their single center experience and clinical outcome at 30 days in 86 patients enrolled in their study from August 2005 through February 2007. Acute procedural success was achieved in 76 out of the 86 patients. Overall procedural success rate was 74% and all MACE were evident in the first 48 hours. Five procedural deaths occurred. Mortality at 30 days was 12% in the intent-to-treat population. NYHA class improved from 2.85 ± 0.73 to 1.85 ± 0.60 after valve implantations ($P < 0.001$).¹²

Preliminary data from an expanded registry of 536 inoperable patients using the CoreValve 18F device implanted

via the retrograde technique shows procedural success was achieved in 97% of patients with a procedure related mortality of 4%. All-cause mortality at 30 days was 8%. Overall, the percentage of patients categorized in NYHA class III-IV improved from 86% to 8% at 30 days. Quality of life continued to be good in those patients with a mid-term and long-term follow-up ($n = 282$).

Sapien Valve: The Sapien Valve (Edwards SAPIEN THV, Edwards Lifesciences Inc., Irvine, CA) is currently being studied in the Placement of Aortic Transcatheter Valve (PARTNER) Trial. Both retrograde and transapical techniques will be tested in this trial. Preliminary results of the first 100 patients show procedural success using retrograde technique was low at 76% in the first quartile of patients but increased to 96% in the subsequent 3 quartiles. NYHA class decreased from a mean of more than 3 to about 1.5 at 12 months in 31 patients with 1 year follow-up. The investigators also observed a lower than predicted 30 day mortality of 15%.²² Using only the transapical technique in this trial, feasibility data of 40 patients show successful deployment of the valve in all patients and seating of the valve successful in all but 4 patients. NYHA class improved from 3.33 at baseline to 2.25 ($P < 0.0001$) at 30 day follow-up. Thirty day mortality was 17.5% with 6 more deaths occurring at a mean follow-up of 143 days.²³

Using the transapical technique and the Sapien valve, Walther et al has reported their initial multicenter results of 59 consecutive patients which is the largest feasibility study published thus far. Procedural success using the transapical technique was achieved in 53 patients. Thirty day mortality was 13.6% and none of these were thought to be valve related as there was good valve function at autopsy.²⁴

Conclusion

Early results of percutaneous valve replacement do show some promising results and with continued experience, this procedure may show better safety and efficacy. With more data, we may be able to develop a scheme that helps us best determine the route of treatment. The European Association of Cardio-Thoracic Surgery (EACTS) and the European Society of Cardiology (ESC) have formulated a joint statement regarding when to consider TAVR.²⁵ We propose a schematic based on this as well as current guidelines in Figure 3.²⁵⁻²⁹

As interventional cardiologists and cardiothoracic surgeons become more familiar with this technique and learn how to avoid or minimize risk, percutaneous valve replacement may show survival benefits similar to surgical aortic valve replacement when studied in larger clinical trials. TAVR may in the future prove to be a less invasive alternative for patients with aortic valve disease that have minimal surgical operative mortality risk.

*Since no definitive surgical risk assessment guidelines exist on patient selection for TAVR, risk assessment (high risk vs low risk) should be a combination of these objective risk scores as well as expert opinions of physicians.

Figure 3. Proposed algorithm to determine traditional vs TAVR. Abbreviations: ACC, America College of Cardiology; AHA, American Heart Association; AVA, aortic valve area; AVR, aortic valve replacement; euroSCORE, European system for cardiac operative risk evaluation; STS, Society of Thoracic Surgeons; TAVR, transcatheter aortic valve replacement; TEE, transesophageal echocardiogram.

Table 1. Clinical Outcome Data for TAVR

Valve	Study/Date	Number of Patients	Approach	Procedural Success Rate	30-d Outcome	Clinical Improvement
Cribier-Edwards	Webb et al. (2006)	n = 18	Retrograde	77%	11% mortality rate	
	Webb et al. (2007)	n = 50	Retrograde	86%	12% mortality rate	Significant NYHA class improvement at 30 d maintained through 1 y
	Leichtstein et al. (2006)	n = 7	Transapical	100%	14% mortality rate	NYHA class well maintained at 6 mo follow-up
CoreValve (first generation)	Grube et al. (2006)	n = 25	Retrograde	88%	32% MACE rate	NYHA class improved by 1 to 2 grades in all patients
CoreValve (second and third generation)	Grube et al. (2007)	n = 86	Retrograde	88%	12% mortality rate	NYHA class improvement from 2.85 ± 0.73 before and 1.85 ± 0.60 after procedure ($P < .001$)
	Presentation at EuroPCR 2008 by M. Buchbinder	n = 536	Retrograde	97%	8% mortality rate	Percentage of patients categorized in NYHA class III-IV improved from 86% to 8% at 30 d
Sapien Valve	PARTNER Trial (unpublished) Pasupati et al. (2007)	n = 100	Retrograde and Transapical	First 25 patients: 76% Following 75 patients: 96%	15% mortality rate	NYHA class decreased from a mean of >3 to ~ 1.5 at 12 mo in the 31 patients with 1 y follow-up
	Svensson et al. (2008)	40	Transapical	90%	17.5% mortality rate	NYHA class improved from 3.33 to 2.25 ($P < .0001$) at 30 d follow-up
	Walther et al. (2008)	59	Transapical	90%	13.6%	

Abbreviations: NYHA, New York Heart Association; PARTNER, placement of aortic transcatheter valve; PCR, Paris Course on Revascularization; TAVR, transcatheter aortic valve replacement.

Hopefully, the approach of thoughtful teams of surgeons and cardiologists will avoid some of the usual reticence to new technologies and turf wars that have unfounded the appraisal of other new devices.

Acknowledgments

The authors would like to acknowledge Edwards Lifesciences (Irvine, CA) and CoreValve, Inc., (Irvine, CA) for providing them with images and unpublished data for their products.

References

- Stewart BF, Siscovick D, Lind BK, et al. Clinical factors associated with calcific aortic valve disease. Cardiovascular Health Study. *J Am Coll Cardiol*. 1997;29(3):630–634.
- Nkomo VT, Gardin JM, Skelton TN, Gottdiener JS, Scott CG, Enriquez-Sarano M. Burden of valvular heart diseases: a population-based study. *Lancet*. 2006;368(9540):1005–1011.
- US Census Bureau. *US Interim Projections by Age, Sex, Race, and Hispanic Origin*. In 2004.
- Otto CM, Lind BK, Kitzman DW, Gersh BJ, Siscovick DS. Association of aortic-valve sclerosis with cardiovascular mortality and morbidity in the elderly. *N Engl J Med*. 1999;341(3):142–147.
- Tarantini G, Buja P, Scognamiglio R, et al. Aortic valve replacement in severe aortic stenosis with left ventricular dysfunction: determinants of cardiac mortality and ventricular function recovery. *Eur J Cardiothorac Surg*. 2003;24(6):879–885.
- Murphy ES, Lawson RM, Starr A, Rahimtoola SH. Severe aortic stenosis in patients 60 years of age or older: left ventricular function and 10-year survival after valve replacement. *Circulation*. 1981;64(2 pt 2):II184–II188.
- Connolly HM, Oh JK, Orszulak TA, et al. Aortic valve replacement for aortic stenosis with severe left ventricular dysfunction. Prognostic indicators. *Circulation*. 1997;95(10):2395–2400.
- Kvidal P, Bergstrom R, Horte LG, Stahle E. Observed and relative survival after aortic valve replacement. *J Am Coll Cardiol*. 2000;35(3):747–756.
- Iung B, Cachier A, Baron G, et al. Decision-making in elderly patients with severe aortic stenosis: why are so many denied surgery? *Eur Heart J*. 2005;26(24):2714–2720.
- Cribier A, Eltchaninoff H, Tron C, et al. Early experience with percutaneous transcatheter implantation of heart valve prosthesis for the treatment of end-stage inoperable patients with calcific aortic stenosis. *J Am Coll Cardiol*. 2004;43(4):698–703.
- Grube E, Laborde JC, Gerckens U, et al. Percutaneous implantation of the CoreValve self-expanding valve prosthesis in high-risk patients with aortic valve disease: the Siegburg first-in-man study. *Circulation*. 2006;114(15):1616–1624.
- Grube E, Schuler G, Buellesfeld L, et al. Percutaneous aortic valve replacement for severe aortic stenosis in high-risk patients using the second- and current third-generation self-expanding CoreValve prosthesis: device success and 30-day clinical outcome. *J Am Coll Cardiol*. 2007;50(1):69–76.
- Chiam P, Ruiz C. Percutaneous transcatheter aortic valve implantations: assessing results, judging outcomes, and planning trials. *JACC: Cardiovasc Interv*. 2008;1(4):341–350.
- Buellesfeld L, Gerckens U, Grube E. Percutaneous implantation of the first repositionable aortic valve prosthesis in a patient with severe aortic stenosis. *Catheter Cardiovasc Interv*. 2008;71(5):579–584.
- Low RI BS, Yeo KK, Ebner A. Direct flow medical percutaneous aortic valve: proof of concept. *Eurointervention*. 2008;4:256–261.
- Lichtenstein SV, Cheung A, Ye J, et al. Transapical transcatheter aortic valve implantation in humans: initial clinical experience. *Circulation*. 2006;114(6):591–596.
- Webb JG, Chandavimol M, Thompson CR, et al. Percutaneous aortic valve implantation retrograde from the femoral artery. *Circulation*. 2006;113(6):842–850.
- Cribier A, Eltchaninoff H, Tron C, et al. Treatment of calcific aortic stenosis with the percutaneous heart valve: mid-term follow-up from the initial feasibility studies: the French experience. *J Am Coll Cardiol*. 2006;47(6):1214–1223.
- Webb JG, Pasupati S, Achtem L, Thompson CR. Rapid pacing to facilitate transcatheter prosthetic heart valve implantation. *Catheter Cardiovasc Interv*. 2006;68(2):199–204.
- Webb JG, Pasupati S, Humphries K, et al. Percutaneous transarterial aortic valve replacement in selected high-risk patients with aortic stenosis. *Circulation*. 2007;116(7):755–763.
- Ye J, Cheung A, Lichtenstein SV, et al. Six-month outcome of transapical transcatheter aortic valve implantation in the initial seven patients. *Eur J Cardiothorac Surg*. 2007;31(1):16–21.
- Pasupati S, Humphries K, AlAli A, et al. Abstract 1700: Balloon Expandable Aortic Valve [BEAV] Implantation. The first 100 Canadian patients. *Circulation*. Oct 2007; 116: IL357.
- Svensson LG, Dewey T, Kapadia S, et al. United States feasibility study of transcatheter insertion of a stented aortic valve by the left ventricular apex. *Ann Thorac Surg*. 2008;86(1):46–55.
- Walther T, Simon P, Dewey T, et al. Transapical minimally invasive aortic valve implantation: multicenter experience. *Circulation*. 2007;116(suppl 1):I240–I245.
- Vahanian A, Alfieri O, Al-Attar N, et al. Transcatheter valve implantation for patients with aortic stenosis: a position statement from the European Association of Cardio-Thoracic Surgery (EACTS) and the European Society of Cardiology (ESC), in collaboration with the European Association of Percutaneous Cardiovascular Interventions (EAPCI). *Eur Heart J*. 2008;29(11):1463–1470.
- Nashef SA, Roques F, Michel P, Gauducheau E, Lemeshow S, Salamon R. European system for cardiac operative risk evaluation (EuroSCORE). *Eur J Cardiothorac Surg*. 1999;16(1):9–13.
- Shroyer AL, Coombs LP, Peterson ED, et al. The Society of Thoracic Surgeons: 30-day operative mortality and morbidity risk models. *Ann Thorac Surg*. 2003;75(6):1856–1865.
- Ambler G, Omar RZ, Royston P, Kinsman R, Keogh BE, Taylor KM. Generic, simple risk stratification model for heart valve surgery. *Circulation*. 2005;112(2):224–231.
- Bonow RO, Carabello BA, Chatterjee K, et al. ACC/AHA 2006 guidelines for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (writing Committee to Revise the 1998 guidelines for the management of patients with valvular heart disease) developed in collaboration with the Society of Cardiovascular Anesthesiologists endorsed by the Society for Cardiovascular Angiography and Interventions and the Society of Thoracic Surgeons. *J Am Coll Cardiol*. 2006;48(3):e1–e148.