Most Important Papers in Transcatheter Aortic Valve Replacement and Transcatheter Aortic-Valve Implantation

The Editors

The following are highlights from the series, Circulation: Cardiovascular Interventions Topic Review. This series summarizes the most important manuscripts, as selected by the editors, which have published in the Circulation portfolio. The studies included in this article represent the most noteworthy research in the areas of transcatheter aortic valve replacement and transcatheter aortic-valve implantation. (Circ Cardiovasc Interv. 2012;5:e12-e21.)

Aortic Valve Disease

Natural History of Very Severe Aortic Stenosis

Summary: This is the first study to assess the outcome of a large series of asymptomatic patients with very severe aortic stenosis (AS) managed according to current guidelines. One hundred sixteen consecutive asymptomatic patients with isolated very severe AS, defined by a peak aortic jet velocity ≥5.0 m/s, were prospectively followed up for a median of 61 months. Event-free survival rate (indication for surgery, 90; cardiac death, 6) was poor for patients with a peak aortic jet velocity between 5.0 and 5.5 m/s (n=72), with 76±5% at 1 year, 43±6% at 2 years, 33±6% at 3 years, and 17±5% at 4 years; it was even worse for patients with a peak aortic jet velocity ≥5.5 m/s (n=44), with 44±8% at 1 year, 25±7% at 2 years, 11±5% at 3 years, and 4±4% at 4 years (P<0.0001). In comparison, event-free survival rate for a series of 82 patients with severe AS, defined by a peak aortic jet velocity between 4.0 and 5.0 m/s, was 82±4% at 1 year, 70±5% at 2 years, 49±6% at 3 years, and 39±16% at 4 years. Furthermore, 6 cardiac deaths occurred in previously asymptomatic patients with very severe AS, and symptom onset was more severe for patients with higher peak aortic jet velocities. Peak aortic jet velocity thus yields important prognostic information in the group of patients with severe AS. Because of the high event rate and the possibility of rapid deterioration, considering early elective surgery might be worthwhile in patients with very severe AS, even when they are still asymptomatic.

Conclusions: Despite being asymptomatic, patients with very severe aortic stenosis have a poor prognosis with a high event rate and a risk of rapid functional deterioration. Early elective valve replacement surgery should therefore be considered in these patients.

Editor’s Comment: The optimal timing of aortic valve surgery in patients with asymptomatic severe AS is controversial. In this prospective observational study, the clinical outcomes of patients with very severe AS, defined as a peak aortic jet velocity ≥5.0 m/s, was reported. Within a relatively short span of time, a median of 41 months, more than two thirds of the patients developed an indication and underwent aortic valve surgery, and 5% of patients had cardiac death. These findings support the concept that elective aortic valve surgery for selected asymptomatic patients at high risk for clinical deterioration from severe AS should be studied further in a randomized trial.1

Integrating of 3D Imaging Data in the Assessment of Aortic Stenosis: Impact on Classification of Disease Severity

Summary: In aortic stenosis (AS), the precise assessment of its severity is essential for appropriate therapeutic decision-making. It relies on standard echocardiographic criteria, including transaortic gradients, dimensionless index, and aortic valve area, which is typically calculated by the continuity equation (CE). CE uses left ventricular outflow tract (LVOT) diameter to calculate aortic valve area with the assumption that LVOT is circular; however, LVOT is very often elliptical in shape, potentially creating a discrepancy between the actual and calculated aortic valve area. The discrepancy is more noted in patients with reduced ejection fraction. The use of multidetector computed tomography (MDCT) enables us to 3-dimensionally measure LVOT area, which could be incorporated into the CE. The current study of patients with severe AS demonstrates that integration of 3D LVOT area significantly increases the congruence between various AS severity criteria (including corrected aortic valve area, transaortic gradients, and dimensionless index), leading to improved classification of AS severity, especially in the setting of reduced ejection fraction. Improved congruence in aortic valve area measurements could help in selection of appropriate timing for surgical and percutaneous treatments. In addition, it could also help in further refinements in shape and size of future percutaneous aortic valves.

Conclusions: In patients with suspected severe AS, incorporation of MDCT-LVOT area into the CE improves congruence for AS severity.

Editor’s Comment: The introduction of new treatment options underscores the importance of accurately assessing the severity of AS using noninvasive imaging. Frequently employed 2-dimensional transthoracic echocardiographic CE estimation of aortic valve area is limited in severe AS because of the marked eccentricity of the aortic annulus and LVOT. This single-center observational study reports that, in patients with severe AS, a CE using an MDCT-obtained LVOT area correlated better with MDCT planimetry measured aortic valve area than did a standard transthoracic echocardiographic continuity calculation involving LVOT diameter, which underestimated aortic valve area and overestimated the severity of the AS. This study provides more data supporting the use of 3D imaging to best select appropriate patients with AS to undergo valve replacement.2


Correlates and Causes of Death in Patients With Severe Symptomatic Aortic Stenosis Who Are Not Eligible to Participate in a Clinical Trial of Transcatheter Aortic Valve Implantation

Summary: This study confirms that patients with severe symptomatic aortic stenosis (AS) who are not included in the TAVI trials have exceptionally poor 1-year prognoses. These patients are exposed to high mortality rates, irrespective of the treatment modality, medical or surgical. Importantly, quality of life was often compromised by the morbidity associated with the surgical procedure. Clinical factors such as renal failure, New York Heart Association class, and decreased blood pressure are more predictive of mortality than is the risk score model in medically managed patients. Renal dysfunction was the strongest correlate of outcome in the surgically treated group. It remains to be seen whether this patient population may benefit from TAVI with respect to overall mortality rates and quality of life.

Conclusions: Patients with severe symptomatic AS not included in transcatheter aortic valve implantation (TAVI) trials do poorly and have extremely high mortality rates, especially in nonsurgical groups, and loss of quality of life in surgical groups.

Editor's Comment: Patient selection for transcatheter aortic valve replacement in recently reported clinical trials followed a strict screening protocol. Among those patients randomized to medical therapy, including balloon aortic valvuloplasty when deemed appropriate, the observed mortality rate was significantly higher than for patients randomized to TAVI. Despite this finding, whether or not these results were applicable to patients not eligible for trial study remained unknown. The present study extends our understanding of clinical outcomes for patients not eligible for TAVI trials by identifying risk factors and correlates for mortality in this patient population when they were treated by medical therapy/balloon aortic valvuloplasty or surgical aortic valve replacement. The study also confirms the fact that 1-year mortality rates remain high in patients with high-risk clinical characteristics treated with medical therapy/balloon aortic valvuloplasty.

Usefulness of Carvedilol in the Treatment of Chronic Aortic Valve Regurgitation

Summary: The medical treatment of asymptomatic patients with severe aortic valve regurgitation (AR) remains controversial. No pharmacological treatment has been clearly shown to be effective to protect the myocardium against the deleterious effects of chronic volume overload. Despite the recent publication of promising human data, β-blockade in chronic AR remains controversial because of the deleterious effects of bradycardia. More data are needed to support this potentially new treatment strategy. The authors hypothesized that carvedilol might be a safe treatment option in chronic AR, combining its combined β-blocking and α-blocking effects and proven efficacy in patients with established heart failure. They designed a study in a rat model of chronic AR, testing the efficacy of carvedilol at maintaining cardiac function and slowing the development of eccentric left ventricular (LV) hypertrophy over 6 months, starting treatment 2 weeks after surgical AR induction. Carvedilol treatment resulted in less LV dilatation. Ejection fraction was improved, and filling pressures were reduced by carvedilol; β1-adrenoreceptor expression was also improved. These beneficial effects were noted despite the presence of drug-induced bradycardia. The results of this study revealed that carvedilol exerted protective effects against volume-overload cardiomyopathy in this model of AR with preserved ejection fraction. These results, in addition to those shown previously with metoprolol, suggest a protective class effect of β-blockers. Combined with the recent publication of promising human data, these findings support the need to carefully design a prospective study in humans to evaluate the effects of β-blockers in chronic AR.

Conclusions: Carvedilol exerted protective effects against volume-overload cardiomyopathy in this model of AR with preserved ejection fraction. These results suggest a protective class effect of β-blockers.

Editor's Comment: The clinical benefit resulting from the use of β-blockers to treat patients with chronic AR has not been conclusively proven. This preclinical study investigates the cardiovascular effects of carvedilol treatment (combined β- and α-blocking effects) on Wistar rats with severe AR and normal left ventricular ejection fraction (LVEF). Carvedilol was associated with decreased LV hypertrophy and dilatation and improved hemodynamics compared with sham-operated and untreated AR animals. LV remodeling, β1-Receptor expression, and LV capillary density were also improved in the carvedilol treated group. No α-blocking hemodynamic effects were noted in the treated AR group, suggesting that β-blockade played a significant role in these protective findings. These data and the publication of several observational clinical reports supporting the concept that β-blocker therapy offers benefit in human heart failure and AR populations suggest the need for a randomized clinical trial to better address this issue in human patients with AR and a normal LVEF.

The Adverse Impact of Diabetes Mellitus on Left Ventricular Remodeling and Function in Patients With Severe Aortic Stenosis

Summary: Previous studies have shown that diabetes adversely modifies the response of the left ventricle (LV) to various forms of cardiovascular injury, such as a myocardial infarction or systemic hypertension, by provoking worse LV remodeling and function; however, the impact of diabetes on LV remodeling and function has severe MR more high-risk clinical characteristics and worse LV function. Despite these findings, surgical AVR was associated with lower 5-year mortality compared with no surgical intervention. In the era of TAVI, reports are emerging of percutaneous valve replacement for AR. Findings from this study may, therefore, aid in the management of those patients undergoing TAVI with coexisting severe mitral regurgitation.

Summary: The results of this study show that 3 or 4+ mitral regurgitation (MR) is present in a quarter of these patients. It appears to be mechanistically related to a larger left ventricle (LV), with thinner walls and lower ejection fraction (EF). It also predisposes to atrial fibrillation, pulmonary hypertension, and possibly stroke. AVR in these patients confers a mortality benefit, and a concomitant MV repair appears to be additionally beneficial in terms of better survival. Though the issue of MR is extensively studied in severe aortic stenosis (AS), the authors did not come across systematic studies of MR in a severe AR population. It is difficult to apply the findings from aortic stenosis to an AR population because LV in AR has both pressure and volume overload, LV is larger, patients tend to be younger than AS patients by about a decade, and response of the LV to AR is both qualitatively and quantitatively different. The findings of this study give valuable insights into MR mechanisms and outcomes in severe AR.

Conclusions: MR is common in patients with severe AR, with 3 or 4+ MR occurring in a quarter of these patients. It is an independent predictor of reduced survival. Performance of AVR and concomitant mitral valve repair is associated with a better survival. Development of MR should serve as an indication for AVR, even in asymptomatic patients.

Editor's Comment: Patients with severe AR may often have coexisting MR that predisposes them to adverse cardiac events. This observational study highlights the fact that patients with concomitant severe MR have more high-risk clinical characteristics and worse LV function. Despite these findings, surgical AVR was associated with lower 5-year mortality compared with no surgical intervention. In the era of TAVI, reports are emerging of percutaneous valve replacement for AR. Findings from this study may, therefore, aid in the management of those patients undergoing TAVI with coexisting severe mitral regurgitation.

The Adverse Impact of Diabetes Mellitus on Left Ventricular Remodeling and Function in Patients With Severe Aortic Stenosis
not been explored in patients with aortic stenosis (AS). In this article, the authors show that diabetes adversely modifies how the LV responds to the hemodynamic pressure overload of AS. When compared to patients without diabetes, with a similar degree of AS, patients with diabetes had increased LV mass and larger chamber dimensions, independent of body size and other factors known to influence remodeling in patients with AS. After also controlling for differences in LV mass, patients with diabetes also had worse systolic function and a trend toward worse heart failure symptoms. These findings may have important clinical implications because increased LV hypertrophy, worse systolic function, and worse heart failure symptoms are all associated with poor outcomes in patients with AS. In particular, there may be implications for risk stratification, surgical timing, and approach to valve implantation. Further studies are needed to clarify the mechanisms by which diabetes exerts its adverse influence on LV remodeling and function in the setting of pressure overload and to understand how these findings might alter clinical management of patients with diabetes and AS.

Conclusions: Diabetes mellitus (DM) has an additive adverse effect on hypertrophic remodeling (increased LV mass and larger cavity dimensions) and is associated with reduced systolic function in patients with AS beyond known factors of pressure overload.

Editor’s Comment: While both AS and DM are known to adversely affect LV remodeling and function, it remains unclear whether these effects are additive. This single-center observational study investigated the impact of diabetes on LV remodeling and function in patients with severe AS. Using 2D echocardiography, the investigators showed increased maladaptive hypertrophic remodeling and reduced LV systolic function in patients with AS and DM compared with patients with AS without DM. This association remained significant after controlling for multiple factors known to influence LV structure and function. Although the mechanisms explaining this relationship are not completely understood, these observations may have potential clinical implications on defining the optimal timing of valve replacement and the use of adjunctive hypoglycemic and antihypertensive medications in patients with DM with AS.6

**TAVI**

**Thirty-Day Results of the SAPIEN Aortic Bioprosthesis European Outcome (SOURCE) Registry: A European Registry of Transcatheter Aortic Valve Implantation Using the Edwards SAPIEN Valve**

**Summary:** The 30-day SAPIEN Aortic Bioprosthesis European Outcome (SOURCE) Registry results represent the most contemporary results that can be expected with the Edwards SAPIEN valve. These data give the interventional community a benchmark from which it can assess future patient cohorts and results. In addition, they allow physicians performing this procedure to accurately refer these high-risk patients with aortic valve for the transcatheter aortic valve implantation (TAVI) procedure. Thirty-day mortality was 8.5% overall, 6.3% for the transfemoral approach, and 10.3% for the transapical approach. The transapical patients were a higher-risk cohort; the logistic EuroSCORE was 29.1% in the transapical group and 25.7% in the transfemoral group. The stroke rate was 2.5%. The requirement for permanent pacemaker was 7%. The major vascular complication rate was 10.6% for the transfemoral approach, but, unlike previous studies, this was not associated with an increased mortality; however, a major vascular complication of the transapical approach did result in increased mortality. Any future change in the technology or procedure will be able to be assessed against these results of a consecutive group of patients undergoing the procedure in centers with surgeons experienced in, or new to, the procedure.

**Conclusions:** Technical proficiency can be learned and adapted readily, as demonstrated by the short-term procedural success rate and low 30-day mortality rates reported in the SOURCE Registry. Specific complication management and refinement of patient selection are needed to further improve outcomes.

**Editor’s Comment:** As the experience with TAVI grows, large-scale registries provide the opportunity to gain important insight into the safety and efficacy of the procedure. In this report of the largest patient experience at the time of publication, clinical and procedural characteristics and short-term outcomes observed in a European registry indicate that patients that underwent TAVI using either the transfemoral or transapical approach continue to have high rates of procedural success with lower rates of adverse events and 30-day mortality than reported in prior clinical trials. The report also reveals that, for patients undergoing TAVI using transfemoral access, but not transapical access, mortality rates were not different when patients were stratified using the logistic EuroSCORE. This observation provides some of the first awareness that this scoring mechanism may not be sufficient to predict mortality in patients undergoing TAVI using the transfemoral approach.7

**Transcatheter Aortic Valve Implantation: Durability of Clinical and Hemodynamic Outcomes Beyond 3 Years in a Large Patient Cohort**

**Summary:** Transcatheter aortic valve implantation (TAVI) is rapidly gaining acceptance as a viable therapy for high-risk patients with severe symptomatic aortic stenosis (AS). Thus far, short-term outcomes have been encouraging, with limited data beyond 1 year. The present study evaluated the medium- to long-term outcomes of an early cohort undergoing TAVI, with all patients evaluated by follow-up at a minimum of 3 years from the procedure. The study demonstrated excellent durability, no evidence of structural valvular failure, and preserved hemodynamics. Small changes in valve area and transvalvular gradients were documented for the first time, which were generally similar to those in previously published surgical series that reported on bioprosthetic valves in the aortic position. Patients showed significant improvement in functional state, which appeared to be preserved over time. Postprocedural aortic regurgitation was generally mild and did not appear to worsen over time. Detailed computed tomographic imaging demonstrated no evidence of valve fracture, deformation, or migration. At a median of 3.7 years, patients surviving more than 30 days after a successful procedure had a survival rate of 57%. The bulk of late mortality in this high-risk cohort was because of significant comorbidities and was generally unrelated to aortic valve disease. Overall, when used in patients who are deemed to be poor surgical candidates, TAVI appears to offer an adequate and lasting resolution of symptomatic AS.

**Conclusions:** TAVI demonstrates good medium- to long-term durability and preserved hemodynamic function, with no evidence of structural failure. The procedure appears to offer an adequate and lasting resolution of aortic stenosis in selected patients.

**Editor’s Comment:** Although there are data to understand the long-term outcomes and mechanisms of failure of bioprosthetic valves after surgical valve replacement, analogous data following TAVI procedures are not yet available, owing to the recent introduction of TAVI. This study provides some of the first longer term follow-up data and shows that, among surviving patients, the valve remains durable up to 3 years. Although there was a statistically significant increase in transaortic gradients and decrease in mean valve area, these findings did not result in device failure. Whether or not these changes proceed on the same trajectory and have long-term sequelae for valve performance remain to be determined with longer follow-up.8
Incidence and Predictors of Early and Late Mortality After Transcatheter Aortic Valve Implantation in 663 Patients With Severe Aortic Stenosis

Summary: Transcatheter aortic valve implantation (TAVI), using the self-expandable CoreValve prosthesis, was performed in 663 patients with severe aortic stenosis (AS) and high surgical risk in 14 Italian centers. Procedural success was 98%, and in procedural mortality was 0.9%. The mortality rates at 30 days and 1 year were 5.4% and 15.0%, respectively. Early mortality was acceptably low compared with the anticipated risk calculated by means of the EuroSCORE and was strongly associated with the occurrence of procedural complications. Late mortality continued to occur from 30 days to 1 year after TAVI, primarily as the effect of postprocedural paravalvular aortic regurgitation (AR) ≥2+ and nonvalve-related comorbidities, such as cerebrovascular disease, chronic kidney disease, and heart failure. Clinical and hemodynamic benefits observed acutely after TAVI were sustained at 1 year.

Conclusions: Benefit of TAVI with the CoreValve ReValving System is maintained over time up to 1 year, with acceptable mortality rates at various time points. Although procedural complications are strongly associated with early mortality at 30 days, comorbidities and postprocedural paravalvular AR ≥2+ mainly impact late outcomes between 30 days and 1 year.

Editor's Comment: Initial European and US trials of TAVI were performed using the Sapien Edwards valve. The CoreValve ReValving System is fundamentally different in design, being self-expanding and having a different delivery system. It represents an alternative to the Sapien Edwards valve. The early and late mortality results described in over 600 patients with severe AS are encouraging. The association of significant aortic insufficiency with late mortality is concerning, however, given the greater presumed incidence of this complication with the CoreValve compared with the Sapien valve.

Silent and Apparent Cerebral Ischemia After Percutaneous Transfemoral Aortic Valve Implantation: A Diffusion-Weighted Magnetic Resonance Imaging Study

Summary: Ischemic stroke is among the most devastating complications in cardiac surgery and interventional cardiology, associated with a high rate of morbidity and mortality. A 2% to 10% stroke incidence has been reported after transfemoral aortic valve implantation (TAVI), which is an emerging treatment option for elderly high-risk patients with severe aortic stenosis (AS). The rate of clinically silent cerebral embolism during TAVI may be higher but is yet unknown. The authors prospectively examined 32 patients who underwent TAVI with the use of the 2 currently commercially available bioprostheses with serial cerebral diffusion-weighted magnetic resonance imaging (MRI) and compared the results with a historical control group of 21 patients undergoing surgical aortic valve replacement. After the procedure, a total of 115 new foci of restricted diffusion suggestive of embolization were detected by diffusion-weighted MRI in 27 of 32 patients (84%) and were significantly more frequent than after conventional open surgery (10 of 21 patients [48%]; P = 0.011). Interestingly, volumes of cerebral diffusion-weighted imaging lesions were significantly smaller in the elderly patients who underwent TAVI, and there were no periprocedural neurological deficits, despite the high lesion load compared with 1 stroke in the younger, lower-risk surgical control group. After 3 months, 80% of diffusion-weighted imaging lesions had resolved without residual signal change on follow-up MRI. Nevertheless, the high incidence of new foci of restricted diffusion may portend greater clinical importance once younger patients undergo TAVI; thus, future research needs to be directed at strategies to reduce the risk of embolization including development of less traumatic, smaller-bore delivery catheters, as well as protection devices.

Conclusions: Clinically silent new foci of restricted diffusion on cerebral MRI were detected in almost all patients (84%) undergoing TAVI. Although typically multiple, these foci were not associated with apparent neurological events or measurable deterioration of neurocognitive function during 3-month follow-up. Further work needs to be directed to determine the clinical significance of these findings in a larger patient population.

Editor's Comment: In patients with severe AS, stroke is a serious complication that may be more common following TAVI than after aortic valve replacement (AVR). The very high incidence of cerebral restrictive diffusion foci by MRI following TAVI supports this concept that neurological injury, probably embolic, is more common following TAVI than AVR. Although the incidence of apparent or unapparent measurable neurological impairments differed between AVR and TAVI, these findings are of concern for both approaches and provide incentive for efforts to promote cerebral protection and less traumatic techniques.

Comparison Between Transcatheter and Surgical Prosthetic Valve Implantation in Patients With Severe Aortic Stenosis and Reduced Left Ventricular Ejection Fraction

Summary: Patients with severe aortic stenosis (AS) and reduced left ventricular ejection fraction (LVEF) have a poor prognosis with medical treatment but a high operative mortality when treated surgically. These patients pose an important challenge with regard to therapeutic management because they require a valve replacement procedure that ensures optimal valve hemodynamics with complete relief of left ventricular (LV) outflow obstruction although minimizing the operative risk. The results of the present study suggest that transcatheter aortic valve implantation (TAVI) may achieve both of these goals. The most important finding of this study is that, despite a much worse risk profile at baseline, TAVI was associated with faster and better recovery of LVEF compared with surgical aortic valve replacement (AVR). This benefit may be because of, at least in part, better periprocedural myocardial protection and superior prosthetic valve hemodynamics. Hence, TAVI may provide a good alternative to surgical AVR in patients with severe AS and depressed LV systolic function considered at high or prohibitive surgical risk, which includes patients with severe comorbidities, small aortic root, and/or lack of myocardial contractile reserve on dobutamine stress test.

Conclusions: In patients with severe AS and depressed LV systolic function, TAVI is associated with better LVEF recovery compared with surgical AVR. TAVI may provide an interesting alternative to surgical AVR in patients with depressed LV systolic function considered at high surgical risk.

Editor's Comment: TAVI will be compared to surgical AVR across a wide variety of clinical subsets. Patients with severe AS and reduced global LV function are a natural group to explore, given the derangements associated with cardiopulmonary bypass and cardiac arrest. This report is provocative in indicating improvement in LV function was greater following TAVI than AVR. These findings are not conclusive, however, given the imbalance between 2 nonrandomized groups and the use of only echocardiography to evaluate LV performance.

Safety and Efficacy of the Subclavian Approach for Transcatheter Aortic Valve Implantation With the CoreValve ReValving System

Summary: Whether the subclavian artery can be used as the vascular approach for transcatheter aortic valve implantation (TAVI) is a
particularly significant question because a number of patients screened for TAVI have contraindications for femoral access. This report describes the procedural results of TAVI with the CoreValve ReValving System placed through the subclavian artery in 54 consecutive patients. Procedural success was obtained in 100% of the patients who underwent subclavian access, with no inprocedural deaths. The most common in-hospital complications were a new left bundle-branch block (27.8%) and the need for a pacemaker (18.5%). No specific complications related to subclavian access (vessel rupture or vertebral or internal mammary ischemia) were observed. Six-month mortality was 9.4%, whereas the rate of valve-related adverse events was 13.6%. When comparing the outcomes of these patients with those treated by the femoral artery approach, no significant differences were observed. The preliminary data show that the subclavian approach is safe and feasible, with excellent procedural success and low in-hospital complication rates, similar to those of the femoral approach. Interestingly, the subclavian approach did not require a learning curve. Vascular access through the subclavian artery may expand the proportion of patients with AS for treatment by TAVI.

**Conclusions:** TAVI through the subclavian approach appeared feasible and safe, with excellent procedural success and low in-hospital complication rates. This new technique allows patients with contraindications to the femoral approach to be treated with TAVI.

**Editor's Comment:** One of the major complications of TAVI is local vascular complications. This is in part because of the large sheath needed and the high incidence of vascular disease in these elderly patients. Although a transapical approach has been successfully used, it is associated with an increased risk of complications and mortality. As shown in this study, a subclavian approach is a reasonable alternative when a femoral approach is not feasible. Like any vascular access, there is a learning curve, but, overall, the in-hospital complications were not different and the outcomes were similar to a femoral approach.12

### Transarterial Medtronic CoreValve System Implantation for Degenerated Surgically Implanted Aortic Prostheses

**Summary:** Redo surgery is the standard treatment for failing bioprostheses, but it may lead to high mortality and morbidity in the presence of comorbidities. Transcatheter aortic valve implantation (TAVI) might be an attractive option in this high-risk setting, but experience is still limited. The authors report a series of transarterial valve-in-valve implantation, using the Medtronic CoreValve ReValving System for degenerated aortic surgically implanted stented or stentless bioprostheses in high-risk patients. These results suggest the feasibility of such an approach, with a high procedural success rate, immediate hemodynamic improvement, and acceptable clinical outcomes. If mid- and long-term outcomes remain favorable, this will have important clinical implications for treatment strategies of aortic stenosis (AS) in high-risk patients.

**Conclusions:** These results suggest that transarterial Medtronic CoreValve System implantation in patients with degenerated surgically implanted aortic bioprosthesis is feasible and may lead to hemodynamic and clinical improvement in patients who are poor candidates for repeated surgery, pending confirmation in larger series with longer follow-up.

**Editor's Comment:** The off-label use of TAVI for the treatment of degenerated aortic and mitral bioprosthesis has gained significant interest, although the experience remains limited. The initial experience was with the use of the Edwards valve, and only a few case reports suggested that the CoreValve ReValving System could be used. This study reports on 10 cases of the use of the CoreValve ReValving System and shows that this valve is also effective. The study is limited by both small numbers of cases and the lack of long term follow-up. Also, selection of CoreValve versus the Edwards valve is unclear, and more studies are clearly needed.13

### Atrioventricular Conduction Disturbance Characterization in Transcatheter Aortic Valve Implantation With the CoreValve Prosthesis

**Summary:** Atrioventricular (AV) block is one of the most frequent complications of CoreValve transcatheter aortic valve implantation (TAVI). Although several studies have analyzed the effect of TAVI on ECG parameters, none have analyzed the electrophysiological study conduction parameters. The present study demonstrates that both the AV node and His bundle also may be affected by the procedure. Disturbances may arise from both balloon valvuloplasty and TAVI and may be transient and go unnoticed if continuous recording is not performed. Short-term follow-up also provides insight into the evolution of these disturbances to better define the optimal timing and indications for pacemaker implantation.

**Conclusions:** CoreValve implantation worsens AV conduction in most patients, either transiently or permanently. This worsening is the result of direct damage either on the His bundle or on the AV node.

**Editor's Comment:** The CoreValve has been shown to cause significant conduction abnormalities after placement that result in the need for permanent pacemakers in 15% to 30% of patients. This study more carefully evaluated the impact of valve placement on intracardiac electrograms in 18 patients. It demonstrated significant prolongation of AH and HV intervals in 14/18 patients; however, only 5 experienced AV block or left bundle branch block. This study emphasizes the high incidence of conduction abnormalities with this self-expanding valve. The risk factors for conduction abnormalities cannot be determined by this small study but other trials have shown right bundle branch block to be a predictor of the need for pacemaker placement.14

### Incidence and Management of CoreValve Dislocation During Transcatheter Aortic Valve Implantation

**Summary:** Transcatheter aortic valve replacement (TAVR) is a highly specialized technique, offering patients at high risk a new therapeutic option. With more than 20,000 implantations worldwide, it gained reliability as a feasible alternative to open heart surgery. Complications associated with this invasive procedure are different from those after conventional aortic valve replacement (AVR) and require individual specific management. Between June 2007 and September 2009, 212 patients with severe aortic stenosis (AS) had implanted the self-expandable CoreValve prosthesis (Medtronic Inc) through a transfemoral or subclavian access at the German Heart Centre Munich. CoreValve dislocation during transcatheter aortic valve implantation (TAVI) occurred in 10% of the cases. Patients with dislocation of the valve showed a remarkably higher incidence of severe complications, such as coronary ischemia, stroke, and renal failure. Mortality significantly increased when dislocation occurred. In the present study, the authors report their experience with intraprocedural valve dislocation with special focus on possible causes and different management strategies of dislocation, as well as possibilities of how this complication might be avoided.

**Conclusions:** CoreValve dislocation during TAVI occurred in 10% of the cases and significantly increases perioperative risk for severe complications or death. It requires individual specific management and can be managed either interventionaly or, rarely, results in open surgery.

**Editor's Comment:** The self-expanding CoreValve has the advantage of being retrieved into the delivery sheath and repositioned if not in the optimal location. This feature distinguishes it from the Edwards
Midterm Stability and Hemodynamic Performance of a Transfemorally Implantable Nonmetallic, Retrievable, and Repositionable Aortic Valve in Patients With Severe Aortic Stenosis: Up to 2-Year Follow-Up of the Direct-Flow Medical Valve: A Pilot Study

Summary: Misplacement during transcatheter aortic valve implantation (TAVI) can be associated with significant complications and severe aortic regurgitation (AR). Percutaneous valves, which are repositionable and retrievable, may overcome these problems. To the authors’ knowledge, this is the first report on the midterm performance of a catheter-based, repositionable, retrievable, nonmetallic aortic valve prosthesis for percutaneous implantation, evaluated by echocardiography and computed tomography.

Conclusions: In this preliminary series, the 2-year follow-up data of patients, in whom the nonmetallic, repositionable, and retrievable direct-flow medical (DFM) valve was successfully implanted, showed stability of the position, shape, and hemodynamic performance, with no AR in most patients.

Editor’s Comment: Misplacement of TAVI is a serious complication and can lead to embolization, obstruction, and severe AR. The 2 available valves have a small but significant incidence of misplacement, often because of inadequate sizing of the valve. This study evaluated a new nonmetallic, repositionable, and retrievable valve in 25 patients. The valve has 2 inflatable rings that conform to the aortic annulus, making it less likely for misplacement. The study demonstrated a stable position of the valve over 2 years and an outcome similar to the 2 other valves. Clearly, a larger properly sized trial is needed to determine the safety and efficacy of this valve.

Short-Term Performance of the Transcatheter Melody Valve in High-Pressure Hemodynamic Environments in the Pulmonary and Systemic Circulations

Summary: The Melody valve is approved for percutaneous pulmonary valve replacement in dysfunctional right ventricular outflow tracts. The functioning of this valve in a low-pressure environment is well-established. This initial small series describes the unique use of the Melody valve in the high-pressure environment of the aortic and mitral valves. Short-term follow-up of the Melody valve in a high-pressure environment demonstrates good valve function over 1 year.

Conclusions: Short-term performance of the Melody valve in high-pressure environments is encouraging, with good valve function in all patients.

Editor’s Comment: The Melody valve uses a jugular venous valve and was the first percutaneous valve introduced. It has been largely used for the treatment of dysfunctional pulmonic valves. This report suggests that it may be effective in the short term when placed into a high pressure system as well. This preliminary experience, with 30 implants in a variety of situations, demonstrates excellent short-term outcomes over one year, without any significant valvular regurgitation. Since this valve is smaller than the approved valves used in adults, use in the pediatric population is ideal, and this study suggests that it may be appropriate for a wider group of patients.

Comparison of Aortic Root Dimensions and Geometries Before and After Transcatheter Aortic Valve Implantation by 2- and 3-Dimensional Transesophageal Echocardiography and Multislice Computed Tomography

Summary: Current 2D echocardiographic techniques assume circular aortic root geometry when calculating cross-sectional areas. Previous studies have demonstrated that the aortic annulus and left ventricular outflow tract (LVOT) have an ellipsoid geometry but fail to quantify the extent of underestimation caused by this geometric assumption. This may have important clinical implications for selection of appropriate transcatheter aortic valve sizes, which is currently based on 2D echocardiographic measurements. Furthermore, changes in the aortic root dimensions and geometries after transcatheter aortic valve implantations are unknown. Using multislice computed tomography (MSCT) as the “clinical gold standard,” the present study quantified the degree of aortic root cross-sectional area underestimation caused by the assumption of circular aortic annular and LVOT geometry. Furthermore, the authors demonstrated that 3D transesophageal echocardiography (TEE) had the best agreement with multislice computed tomography. Finally, after transcatheter aortic valve implantations (TAVI), the LVOT and aortic valve annulus became more circular-shaped. The use of 3D imaging may have implications in the calculation of aortic valve area by continuity equation and the selection of appropriate transcatheter aortic valve sizes.

Conclusions: Before TAVI, 2D and 3D TEE aortic annular/LVOT circular geometric assumption underestimated the respective MSCT planimetrized areas. After TAVI, 3D TEE and MSCT planimetrized annular areas decreased as it assumes the internal dimensions of the prosthetic valve. However, planimetrized LVOT areas increased due to a more circular geometry.

Editor’s Comment: Determining the preferable noninvasive imaging modality to best assess aortic annular and left ventricular outflow tract (LVOT) size in patients with aortic stenosis (AS) presenting for transcatheter aortic valve replacement (TAVI) has important diagnostic and procedural implications. The underestimation of aortic annular and LVOT size using 2D transesophageal echocardiographic (TEE) circular area calculations has been demonstrated and attributed to the elliptical shape of these areas in patients with AS. However, the accuracy of calculated circular and planimetrized area assessments obtained by 3D TEE is unknown. Using a multislice computed tomography (MSCT) derived planimetrized measurement as a gold standard, the investigators determined that while all TEE derived measurements underestimated areas pre-TAVI, direct planimetry of the aortic annular/LVOT areas by 3D TEE volumetric imaging provided the best agreement with MSCT findings compared with 2D and 3D TEE calculated circular measurements. Post-TAVI, the aortic annular size decreased as the new annulus assumed the internal dimensions of the prosthetic valve, although the LVOT area increased as a result of the more circular geometry. 3D TEE was able to assess these changes accurately, suggesting this imaging modality as a valuable tool to facilitate both pre- and post-TAVI care.

Aortic Valve Surgery

Percutaneous Repair of Paravalvular Prosthetic Regurgitation: Acute and 30-Day Outcomes in 115 Patients

Summary: Paravalvular prosthetic regurgitation is a recognized complication in patients who otherwise have had successful heart
valve surgery. Although many patients have minimal or no morbidity, paravalvular regurgitation can lead to profound symptoms of heart failure, hemolytic anemia, or both. The treatment of paravalvular prosthetic regurgitation traditionally has been open surgical repair, which may lead to increased risk because of the need for reoperation, patient morbidity, and technical challenges that could have initially contributed to the regurgitation. As a less-invasive alternative, percutaneous approaches to treatment of paravalvular prosthetic regurgitation have emerged. The present study examined the early outcomes of percutaneous repair of symptomatic paravalvular prosthetic regurgitation in a cohort of 115 patients (age, 67 years; men, 53%) who were at high risk of open heart surgery (estimated surgical mortality, 6.9%). Successful percutaneous closure, defined as ≤1+ residual regurgitation, was achieved in 77% of patients, with a 30-day complication rate of 8.7%. The majority of complications were related to bleeding. No procedural deaths occurred, but 2 (1.7%) patients died within 30 days. Procedural time decreased with increasing case experience. The present investigation demonstrates a high rate of favorable clinical outcome, but there is a significant learning curve because of the complexity of the procedure. These data support percutaneous repair as part of a comprehensive therapeutic strategy for this challenging subset of patients and may be an initial therapeutic option, particularly in patients at significant risk for open heart surgery.

Conclusions: Percutaneous repair of paravalvular prosthetic regurgitation can be performed with a reasonable rate of procedural success and may be an initial therapeutic option, particularly in patients at significant risk for open surgery. Increased case experience is associated with shorter procedural time.

Editor’s Comment: Paraprosthetic valvular regurgitation is a well-recognized but undesirable complication of surgical valve replacement. When severe, this disorder has required surgical correction. This report describes the percutaneous, catheter-based approach for the treatment of paraprosthetic regurgitation, involving the aortic and mitral valves. A 77% success rate was achieved in more than 100 consecutive patients. Notable, however, is the complexity of these procedures and the need for multiple cardiology subspecialists. Also, there is great variability between patients in the nature of their structural and functional abnormalities and, thus, the need for unique, individualized solutions. We are fortunate to have nonsurgical treatment for patients with paraprosthetic valve regurgitation and recognize the importance of regional, specialized centers for application of this therapy.19

Valve Configuration Determines Long-Term Results After Repair of the Bicuspid Aortic Valve

Summary: Valve replacement has been a reliable therapy for bicuspid aortic valve dysfunction for decades. To minimize valve-related complications, repair techniques have been developed in the last 2 decades. Repair of the bicuspid valve has been less challenging geometrically because only 1 coaptation line has to be corrected. Different publicati-
Conclusions: Perioperative treatment with GIK was associated with a significant reduction in the incidence of low cardiac output state and the need for inotropic support. This benefit was associated with increased signaling protein phosphorylation and O-GlcNAcylation. Multicenter studies and late follow-up will determine whether routine use of GIK improves patient prognosis.

Editor’s Comment: Left ventricular (LV) remodeling that occurs as a result of hemodynamically significant aortic stenosis (AS) is subject to ischemia-reperfusion injury when the LV is unloaded, as occurs at the time of AVR. Strategies used to improve LV energetics, such as GIK, have been shown to limit LV pump failure when given during ischemia and aortic coronary bypass surgery. This study applies the same principle of GIK for myocardial protection in patients undergoing surgical AVR. In this patient population, GIK decreased LV pump failure in the postoperative period. Moreover, this finding was associated with cellular evidence that GIK enhanced cardiomyocyte energetics and metabolism. As some degree of myocardial injury has been observed with transcatheter valve replacement, based on these findings, GIK may be an attractive adjunctive therapy for patients with left ventricular hypertrophy undergoing transcatheter aortic valve replacement as well.22

Survival Comparison of the Ross Procedure and Mechanical Valve Replacement With Optimal Self-Management Anticoagulation Therapy: Propensity-Matched Cohort Study

Summary: Survival in young adult patients after mechanical aortic valve replacement (AVR) is reported to be significantly reduced compared with the general age- and gender-matched population, whereas survival after the Ross procedure is excellent and comparable with that in the general population. There is ongoing debate about whether the excellent survival rates observed in patients undergoing the Ross procedure are a consequence of a hemodynamically superior valve and low valve-related complication rates or of patient selection. This is the first study to compare survival in young adult patients after mechanical AVR and the Ross procedure, using propensity score matching. In comparable patients, there was no late-survival advantage in the first postoperative decade for the Ross procedure over mechanical aortic valve implantation with optimal anticoagulation self-management. In contrast to older reports, the relative survival in these selected young adult patients closely resembles that of the general population, possibly a result of better timing of surgery, improved patient selection, and highly specialized self-management anticoagulation treatment in more recent years. In the absence of late mortality differences between comparable patients who received either a mechanical prosthesis or the Ross procedure, the weight of the prosthetic valve selection decision-making process shifts toward quality of life and patient preference. Clinicians are therefore encouraged to systematically elicit patient preferences when discussing prosthesis valve selection in this young adult population.

Conclusions: In comparable patients, there is no late-survival difference in the first postoperative decade between the Ross procedure and mechanical aortic valve implantation with optimal anticoagulation self-management. Survival in these selected young adult patients closely resembles that of the general population, possibly a result of better timing of surgery, improved patient selection, and highly specialized anticoagulation self-management treatment in more recent years. In the absence of late mortality differences between comparable patients who received either a mechanical prosthesis or the Ross procedure, the weight of the prosthetic valve selection decision-making process shifts toward quality of life and patient preference. Clinicians are therefore encouraged to systematically elicit patient preferences when discussing prosthesis valve selection in this young adult population.

Editor’s Comment: Young adults who require AVR face challenges related to the choice of valve prosthesis. Although the Ross procedure offers a period free from anticoagulation, the risk of reoperation is inevitable for most patients. With mechanical valves, durability is superior, but bleeding and thrombotic events are concerns. Whether long-term survival is superior in patients receiving the Ross procedure compared with those receiving a mechanical valve is unknown. In this nonrandomized investigation, patients receiving the Ross procedure were compared to a selected group of patients receiving mechanical valves who were able to self-manage their anticoagulation. Although survival was similar at a mean of 5 to 6 years, this time period is short compared with potential life duration, and, therefore, selection of valve prosthesis in young patients should remain individualized until longer follow-up is available.23

Prosthesis-Patient Mismatch Predicts Structural Valve Degeneration in Bioprosthetic Heart Valves

Summary: Prosthesis-patient mismatch can be predicted at the time of operation. On the basis of this information, the surgical technique and/or the selection of the prosthesis can be modified to prevent prosthesis-patient mismatch or reduce its severity. By avoiding prosthesis-patient mismatch, the incidence of structural valve deterioration (SVD) should be reduced by ≥50%, which, in turn, can influence the choice for a bioprosthetic valve instead of a mechanical one. Furthermore, because intrinsically stentless bioprostheses are less prone to prosthesis-patient mismatch, this type of bioprosthesis should then be preferred over stented valves.

Conclusions: These data suggest that stenosis-type SVD is related to an early, prosthesis-patient mismatch and is, thus, a preventable phenomenon. Incompetent-type SVD is a time-dependent, nonspecific wear damage to bioprosthetic valves, which is not related to prosthesis-patient mismatch.

Editor’s Comment: SVD of bioprosthetic valves in the aortic position can be divided into 2 broad categories, stenotic or regurgitant. Prosthesis-patient mismatch, which is common, occurs when the effective orifice area of the valve is small in relation to body size and results in elevated transvalvular hemodynamics. Whether prosthesis-patient mismatch contributes to SVD has been debated and the type of degeneration unclear. This investigation provides evidence that prosthesis-patient mismatch, independent of valve design, is, in fact, an important contributor to bioprosthetic valve stenosis. Efforts to optimize valve size, therefore, may delay the development of bioprosthetic valve failure.24

Long-Term Clinical and Hemodynamic Performance of the Hancock II Versus the Perimount Aortic Bioprostheses

Summary: The Medtronic Hancock II and the Carpentier-Edwards Perimount are among the world’s most commonly used aortic bioprostheses; however, a direct comparison of their clinical performance is lacking. To minimize biases inherent to between-center comparisons, the authors examined these prostheses within a large, contemporary, single-center cohort. Between 1990 and 2007, 1659 patients (mean age, 73.1±9.3 years) underwent aortic valve replacement (AVR) with either the Hancock II (N=1021) or the Perimount (N=638). Patients were prospectively followed up with serial clinic visits and echocardiograms for up to 16 years (mean, 5.0±3.3 years). There was no significant difference in aortic root size preoperatively (P=0.7). Aortic root enlargement was more commonly performed with the Perimount (P<0.001), and the manufacturer valve size of the implanted prosthesis was larger with the Hancock II (P<0.001). Postoperatively, peak and mean transprosthesis gradients were higher for the Hancock II (32.7±0.7 and 16.0±0.3 mm Hg, respectively) than for the Perimount (24.9±0.7 and 13.4±0.4 mm Hg, respectively; P<0.001); however, no difference in left ventricular (LV) mass regression was observed at late follow-up (P=0.9). Unadjusted 10-year survival was 59.4%±2.4% for the Hancock II and 70.2%±3.8% for the Perimount (P=0.07). Multivariable predictors of survival did not include prosthesis type (P=0.2).

Conclusions: For the same manufacturer valve size, the Perimount is larger, which may warrant enlarging the aortic root more often, and it is associated with better hemodynamics than the Hancock II. These differences do not impact survival or LV mass regression, and the
long-term clinical performances of the Hancock II and Perimount bioprostheses are equivalent.

Editor's Comment: The characteristics of surgical aortic bioprostheses, such as size and transprosthesis gradients may influence long-term performance of the valve and cardiovascular outcomes. Although several companies manufacture aortic bioprostheses, randomized comparisons of individual valves are lacking. The present observational study, performed at a single center with high surgical volume and long-term echocardiographic and clinical follow-up, compared 2 commonly used aortic bioprostheses: the Hancock II and the Perimount. Despite differences in the need for aortic root enlargement and post-surgical hemodynamics, mortality was similar and valve type was not independently associated with survival. In addition, while limited by lack of data on medical therapy, LV mass regression was similar with the 2 valves. These findings, along with similar rates of valve-related complications, suggest that valve choice can be left to the discretion of the surgeon.25

Early Surgery Versus Conventional Treatment in Asymptomatic Very Severe Aortic Stenosis

Summary: Management of asymptomatic patients with very severe aortic stenosis (AS) remains controversial, and the combined risks of aortic valve surgery and late complications of aortic valve prosthesis need to be balanced against the possibility of preventing sudden death and lowering cardiac mortality. The authors prospectively evaluated 197 consecutive asymptomatic patients with very severe AS to compare clinical outcomes of early surgery with those of the conventional treatment strategy. Very severe aortic stenosis was defined as a critical stenosis in the aortic valve area \( \leq 0.75 \) cm\(^2\), accompanied by a peak aortic jet velocity \( \geq 4.5 \) m/s or a mean transaortic pressure gradient \( \geq 50 \) mm Hg on Doppler echocardiography. Early surgery was performed on 102 patients, and a conventional treatment strategy was used for 95 patients. There were no operative deaths and no cardiac deaths in the early surgery group, compared with 18 cardiac deaths in the conventional treatment group, and the risk of all-cause mortality was significantly lower in the early surgery group than in the conventional treatment group (hazard ratio, 0.135; 95% confidence interval, 0.030 to 0.597; \( P = 0.008 \)). Compared with the conventional treatment strategy, early surgery is associated with improved long-term survival by effectually decreasing cardiac mortality and sudden cardiac death. This result suggests that early surgery can be a therapeutic option to further improve clinical outcomes in asymptomatic patients with very severe AS and low operative risk. A prospective randomized trial is required to confirm the efficacy of early surgery.

Conclusions: Compared with the conventional treatment strategy, early surgery in patients with very severe AS is associated with improved long-term survival by decreasing cardiac mortality. Early surgery is, therefore, a therapeutic option to further improve clinical outcomes in asymptomatic patients with very severe AS and low operative risk.

Editor's Comment: The recommendation and criteria for aortic valve surgery in asymptomatic patients with severe AS is unclear, as the risk of cardiac mortality from AS must be weighed against surgical morbidity and mortality. This prospective registry of patients with very severe AS demonstrates several important findings. Compared to a conventional approach of deferring surgery until onset of symptoms, early surgery for very severe AS resulted in a substantially lower risk of all cause and cardiac mortality. In addition, surgical mortality was lower than expected; the annual rate of sudden death in the conventional group was higher than expected at 1.7%, and a baseline aortic jet velocity of \( > 5 \) m/s was independently associated with cardiac mortality. Although the study is limited by its nonrandomized nature, the findings suggest that echocardiographic parameters may be useful in determining which asymptomatic patients benefit from early surgery for severe AS.26

Quality-of-Life Implications of Immediate Surgery and Watchful Waiting in Asymptomatic Aortic Stenosis: A Decision-Analytic Model

Summary: Traditionally, aortic valve replacement (AVR) for severe but asymptomatic aortic stenosis (AS) is delayed until the development of symptoms. Earlier surgery may reduce the small risk of sudden death before AVR and avoid heart failure after AVR, but a trial to compare these options has not been performed and seems unlikely. Novel therapeutic strategies, such as percutaneous aortic valve insertions, may cause practitioners to rethink current recommendations. In this study, a Markov model, using literature-derived parameters for a representative 65-year-old patient, shows that the utility with watchful waiting is superior to that of immediate mechanical or tissue AVR (quality-adjusted life-years, 7.4 versus 5.3 versus 5.3), at a lower cost. Sensitivity analyses show that immediate surgery is unlikely to be justified, on basis of preventing heart failure, unless the pre-AVR annual mortality reaches 13%. This decision analysis suggests the current guidelines of frequent clinical follow-up in asymptomatic AS.

Conclusions: Immediate surgery in asymptomatic severe AS does not improve outcomes unless risk of sudden death pre-AVR and heart failure after AVR are higher than currently reported.

Editor's Comment: Current guidelines support a policy of watchful waiting, with frequent monitoring for the emergence of symptoms when managing asymptomatic patients with severe AS. Clinicians are often uncomfortable employing this strategy, fearing the occurrence of sudden cardiac death or the development of subclinical LV dysfunction. Using literature-derived parameters, the investigators constructed a Markov simulation model, testing a strategy of watchful waiting versus immediate surgical mechanical or tissue AVR. A watchful waiting strategy was shown to be superior to an immediate surgical AVR strategy, resulting in greater quality-adjusted life-years at lower cost. Although these findings are concordant with current guideline recommendations, they are based on a model generated from a broad population with severe AS, which may not necessarily represent the optimal strategy for an individual patient. These types of analyses are of importance in light of the introduction of less-invasive transcatheter aortic valve replacement (TAVR) capabilities, for which there may be less hesitation in recommending an asymptomatic patient with AS to undergo valve replacement. Dedicated comparisons with TAVR are warranted.27

References


Most Important Papers in Transcatheter Aortic Valve Replacement and Transcatheter Aortic-Valve Implantation
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