Surgical treatment of elderly patients with severe aortic stenosis in the modern era – review

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Kardiochirurgia i Torakochirurgia Polska 2018; 15 (3): 188-195

Abstract

Surgical treatment of severe aortic stenosis offers good early and long-term results, even in elderly patients. Despite the implementation of percutaneous methods for the very high-risk group, surgical valve replacement remains the gold standard. The advanced age of patients should not be the only indicator limiting the possibility of surgery. In this review we present the most important information on the results of aortic stenosis surgical treatment in the groups of older patients. New methods such as percutaneous and minimally invasive methods of surgery are also discussed. Additionally, the presented information is referred to current guidelines for the treatment of severe aortic stenosis.

Key words: elderly patients, aortic valve replacement.

Introduction

Aortic stenosis is the most common primary valvular heart disease. The most common rheumatic pathology in the past, currently due to the appropriate treatment of rheumatic fever it is a rare cause of aortic stenosis. Genetic predisposition, especially the presence of a bicuspid valve, can cause aortic damage even in younger people. Nowadays, however, the development of aortic valve stenosis is strongly related to older age and is associated with the degeneration of this valve, which begins at around 60 years of age and most often causes symptoms in the 7th or 8th decade of life. According to US data (after analysis of 7 studies with a total population of 9723 patients), over 12% of people over 75 years of age present aortic stenosis and 3.4% in severe grade [1]. Data from the Central Statistical Office show that men in Poland lived on average 73.9 years, while women

Streszczenie

Chirurgiczne leczenie ciężkiej stenozy aortalnej przynosi dobre wyniki zarówno krótko-, jak i długoterminowe, nawet u pacjentów w podeszłym wieku. Pomimo wprowadzenia metod przezskórnych przeznaczonych dla pacjentów z grupy wysokiego ryzyka, chirurgiczna wymiana zastawki aortalnej jest złotym standardem. Zaawansowany wiek pacjentów nie powinien być jedynym czynnikiem ograniczającym możliwość wykonania operacji. W artykule zaprezentowano najważniejsze informacje na temat wyników chirurgicznej (klasycznej) wymiany zastawki aortalnej u starszych pacjentów. Omówiono również leczenie przezcewnikowe oraz małoinwazyjną metodę chirurgicznej wymiany zastawki aortalnej. Przedstawione dane odnoszą się do obowiązujących wytycznych dotyczących leczenia ciężkiej stenozy aortalnej.

Słowa kluczowe: pacjenci w podeszłym wieku, wymiana zastawki aortalnej.

lived 81.9 years (7.7 and 6.7 years respectively longer than in 1990). This longer length of life increases the number of patients with degenerative aortic stenosis.

Pathophysiology, diagnosis, medical management

Aortic stenosis, currently occurring mainly in the elderly population, was initially considered as a degenerative process with passive deposits of calcium, resulting primarily from the process of aging of this valve ("wear and tear"). Recent studies indicate the involvement of a chronic inflammatory process, similar to those occurring in atherosclerosis, tissue remodeling with lipoprotein deposition, oxidized lipoproteins and calcium, infiltration of inflammatory cells, and osteoblast activation. It is emphasized that the degeneration of the valve is active, not passive as mentioned earlier.

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This process is based on the interaction between genetically conditioned, biochemical and humoral factors. Risk factors associated with acceleration of the disease and its worse prognosis include age, diabetes, hypertension, smoking, male gender, metabolic syndromes, dyslipidemia, diabetes, hypercholesterolemia, low high-density lipoprotein (HDL) levels, elevated level of apolipoprotein B, endothelial dysfunction, elevated level of cytokines and C-reactive protein (CRP), and decreased adiponectin level. The pathogenesis of aortic stenosis seems to be similar to the pathogenesis of atherosclerosis. Risk factors are defined as cardiometabolic or valvulo-metabolic. A gradual process initiated by remodeling of the tissue leads to significant calcification of the valve, resulting in narrowing of the left ventricle outflow, which leads to overload of the left ventricle and consequently to its systolic and diastolic dysfunction [2-5].

According to a study by Pellikka *et al.*, the majority of patients with asymptomatic but haemodynamically significant aortic stenosis will develop characteristic symptoms within 5 years. Sudden cardiac death will occur in 1%. Age, chronic renal failure, and limited physical activity are independent predictors of death. The period without adverse cardiac events (including death) in 1 year was 80%, after 2 years 63% and 25% after 5 years [6]. Chizner *et al.* show that the onset of symptoms is associated with 1-year mortality of 26%, 2-year mortality of 48% and 3-year mortality of 57% [7].

In the assessment of the severity of aortic stenosis the crucial method is echocardiography. Echocardiographic assessment allows confirmation not only of the value of the gradient by the aortic valve, but also of the severity of the disease in the presence of a low-pressure gradient. The aortic valve opening area should be evaluated depending on the size of the flow, pressure gradient and parameters of the left ventricle, such as wall thickness, left ventricular function, calcification, arterial blood pressure, and functional status [3]. The conservative treatment of severe aortic stenosis is ineffective. Also, the treatment of heart failure in the course of this disease has a different character than in the case of circulatory insufficiency of other causes. Therefore, no form of conservative treatment improves the prognosis of patients. The only effective method is intervention on the aortic valve. Three methods of intervention available at the moment are valvuloplasty, surgical valve replacement (SAVR) and transcatheter aortic valve implantation (TAVI). The effectiveness of valvuloplasty is limited, and it is reserved for urgent cases as a bridge for further intervention, as a palliative or as a diagnostic method.

According to the ESC guidelines [3], aortic valve intervention is indicated in symptomatic patients with severe, high-gradient aortic stenosis (IB) and symptomatic patients with severe low-flow, low-gradient stenosis in the presence of low LV ejection fraction and evidence of flow (contractile) reserve excluding pseudosevere aortic stenosis (IC). Intervention should also be considered (IIa) in symptomatic patients with severe low-flow, low-gradient stenosis and normal EF or in patients with reduced EF without flow (contractile) reserve, particularly when CT calcium scoring con-

firms severe aortic stenosis. In the case of the presence of severe comorbidities when the intervention is unlikely to improve quality of life or survival, the intervention should not be performed (IIIC). The choice of treatment method (SAVR or TAVI) in elderly patients should be based on the assessment of risk factors. The surgical method is preferred in patients with low surgical risk (STS risk or EuroSCORE II < 4% or logistic EuroSCORE I < 10%). The surgical method should also be carefully considered in the presence of other risk factors, not included in the above scales, such as frailty (occurring in more than 30% of patients over 80 years of age), porcelain aorta or sequelae of chest radiation. In the presence of these factors or higher than the above-mentioned operative risks resulting from the STS or EuroSCORE calculations, individual patient analysis within the framework of the Heart Team should be performed and the treatment should be determined by SAVR or TAVI depending on other factors (e.g. the possibility of vascular access). For patients who are not candidates for SAVR, a TAVI procedure is recommended, particularly in the case of older patients if endovascular access is available (IB).

Surgical replacement of the aortic valve in asymptomatic patients, eligible for this operation, should be performed in the presence of severe aortic stenosis and left ventricular dysfunction (LVEF < 50%) or if the result of the exercise test documents symptoms associated with stenosis or there is a decrease in the arterial pressure below the baseline (IB). Similarly, in patients with asymptomatic severe aortic stenosis and normal EF without abnormalities in the exercise test, surgery should be considered if one of the parameters is present: very severe stenosis (Vmax > 5.5 m/s), severe calcification and the rate of Vmax \geq 0.3 m/s/year, a significant increase in brain natriuretic peptide (BNP) concentration or severe pulmonary hypertension.

The patient's age and probability of survival more than 1 year after treatment are important factors of Heart Team selection between SAVR and TAVI [8]. Other factors supporting the consideration of TAVI are previous cardiac surgery and reduced mobility or other factors affecting the rehabilitation after cardiac surgery [3].

Important information is that age itself should not be the decisive factor in the choice of treatment strategy (in particular a factor affecting the decision of denial surgical treatment). According to the Euro Heart Survey Study as many as 33% of older patients with symptomatic, severe aortic stenosis are disqualified from surgery. The decisive factors are, apart from a low left ventricle ejection fraction, the patient's advanced age [9]. The decision to deny surgery in older patients results in a significant decrease in survival in the group treated conservatively, even after comparing groups evaluated by propensity matching analysis [10].

Aortic valve replacement surgery results

In the study of the Society of Thoracic Surgeons (Society of Thoracic Surgeons Adult Cardiac Surgery Database – STS ACSD) evaluating 145 911 patients over 64 years of age operated on for aortic stenosis, perioperative mortality

was 3.9% in patients undergoing isolated AVR (in patients with STS risk < 5%, mortality was 2.5%, in those with STS risk between 5 and 9% it was 10%, and in patients with STS risk > 10% (mean age 81) it was up to 17.2%. However, it should be noted that this analysis included patients who were also operated on in the early 90s (follow-up period 1991–2007) [11]. Dimarakis et al. evaluated SAVR results in high-risk patients who could not undergo the TAVI procedure. The study group included 28 elderly patients (mean age: 78.4 ±9.2), characterized by high predicted operational risk (mean EuroSCORE: 10.0 ±3.6, mean logistic EuroSCORE: 19.9 ±18.8). The perioperative mortality rate in such a high risk group of patients was only 4% and the survival rate in almost 1-year observation was 81%. The authors emphasize that the improvement of mortality and fewer neurological complications after surgical aortic valve replacement had the effect of introducing axillary artery cannulation in patients at risk in order to minimize manipulation of the aorta. Unfortunately, a significant percentage of postoperative complications were observed (renal failure 21%, atrial fibrillation 25%, stimulator implantation 7%, infections 7%, reoperation due to bleeding 7%, tracheostomy 14%). After the operation the patients reported the quality of life as satisfactory. The deterioration in the quality of life was affected by comorbid diseases, but not due to heart disease [12]. Vasques et al. in a meta-analysis reviewed 48 papers with the results of isolated SAVR in patients over 80 years of age. Perioperative mortality was assessed at 6.7%. The authors noted a decrease in perioperative mortality in the last few years, associated with a significant improvement in perioperative care – the mortality of 5.8% was observed in 18 papers published in 2000-2006 whereas it was 7.5% in 30 papers from 1982-1999 [13]. In a study by Smith et al. the outcomes of SAVR and TAVI in high-risk elderly patients with significant aortic stenosis are presented. Perioperative mortality after SAVR was 6.5%, stroke occurred in 2.1%, vascular complications in 3.2%, bleeding in 19.5%, and atrial fibrillation in 16.0% [14]. Langanay et al. observed that the early mortality of the entire cohort of elderly patients after SAVR decreased with time due to medical progress from 6.2% in 1990 to 4.2% in 2010 [15]. Very good postoperative results were published by Dell'Amore et al. Perioperative mortality was only 4.3% in patients with mean age of 82 years. Urgent surgery, left ventricle ejection fraction lower than 35%, prolonged aortic clamp-time, the need of intra-aortic balloon pump, prolonged ventilation, renal failure, postoperative infarction, and reoperation due to bleeding were independent predictors of perioperative mortality. One-, three- and five-year survival was 97.1%, 92.2% and 82.4%, respectively [16]. Similarly satisfactory results of long-term survival in patients over 80 years after SAVR were presented by Costa et al. In this analysis the 1-, 3- and 5-year survival rates were 85%, 81%, and 59%, respectively, and the majority of patients (96%) remained in NYHA functional class I or II at follow-up [17]. In the Leontyev et al. study, the survival of low, intermediate and high risk patients depending on the risk group calculated

by logistic EuroSCORE after 1 year was 90%, 78%, and 69%, after 5 years 70%, 53%, 38%, and after 8 years 38%, 33%, 21%. Factors worsening the survival rate were heart failure, urgency of the procedure, prior stroke or TIA and higher risk [18]. In the afore-mentioned meta-analysis, Vasques et al. observed a very good survival rate after 1, 3, 5 and 10 years – 87.6%, 78.7%, 65.4% and 29.7% [13]. Pierard et al. in the examined group of patients (mean age: 83) with significant aortic stenosis and combined aortic valve disease assessed that the perioperative mortality rate was 5% and mortality predictors were the severity of the disease in terms of pre-operative symptoms. The presence of preoperative chronic obstructive pulmonary disease worsened long-term survival [10]. Interesting observations were presented by Krane et al. The authors analyzed the results of elderly patients undergoing SAVR and SAVR with CABG. Among 303 patients over 79 years of age who underwent isolated aortic valve replacement, the average survival was 6.1 years. In the group of patients who underwent SAVR or SAVR with CABG, the overall survival after 1 year, 5 years and 10 years was 81.6 ±1.2%, 60.4 ±1.9%, and 23.3 ±2.6% and, what is extremely important, showed no significant differences compared to survival of the general population. Creatinine levels higher than 1.3 mg/dl, atrial fibrillation in the preoperative period, and post-operative prolonged ventilation were independent predictors of worse long-term survival [19]. Di Eusanio et al. reported excellent outcomes in octogenarians (mean logistic Euro-SCORE: 13.0%) after SAVR. Hospital mortality was 4.5% and stroke rate 1.3% and at 6 years the survival rate was similar to the expected survival of the age- and sex-matched population [20]. The assessment of patients' quality of life after SAVR was mostly affected by comorbidities, but was not related to heart disease. Comorbidities are common in older people and may impede the assessment whether the patient will benefit from valve replacement surgery. They affect not only the quality of life, but also the length of life, regardless of valvular disease. Nevertheless older patients benefit from aortic valve replacement surgery in the aspect of improving the quality of life [21].

Surgical replacement of the aortic valve recently offers new, minimally invasive approaches, possibly shortening the period of rehabilitation and improving the quality of life in older patients. These methods are associated with limited access (ministernotomy, minithoracotomy) or shortening of the duration of extracorporeal circulation and/or aortic cross-clamp time (sutureless valves) [22]. Gilmanov et al. analyzed two propensity-matched groups of patients aged over 80 years who underwent mini-AVR (thoracotomy) and conventional sternotomy. The minimally invasive group had lower stroke incidence, earlier extubation and shorter hospital stay. The in-hospital mortality and longterm survival at 5 years were similar [23]. Moscarelli et al. in a systematic review of non-randomized studies found mini-AVR to have mortality comparable to full sternotomy, significantly reduced postoperative length of stay, and no significant difference in CPB and aortic cross-clamp times [24]. Santarpino et al. observed patients undergoing sutureless valve implantation with no differences reported between

Table I. Selected results of the treatment of severe aortic stenosis in elderly patients

Comments	Outcomes	es	Patient group size (N),	Author, date, journal and study
	Long-term mortality or survival prediction	In-hospital/30-day mortality (M), in-hospital stay, complications prediction	mean age (MA)	type, operation follow-up (FU)
Advanced age alone cannot be considered as a contraindication to conventional isolated AVR. Mortality rate seems to have markedly decreased during the last years as a result of remarkable advances in perioperative management. The present results are representative only for the very old patients who are fit for surgery	Pooled survival rates at 1, 3, 5, and 10 years after isolated AVR were 88%, 79%, 65%, and 30%, respectively	M = 6.7% (95% CI: 5.8–7.5, 47 studies, 13,092 patients) M = 5.8% (95% CI: 4.8–6.9) in 18 studies with a mid-date from 2000 to 2006 M = 7.5% (95% CI: 6.8–8.2) in 30 studies with a mid-date from 1982 to 1999 Stroke = 2.4% Dialysis = 2.6% Pacemaker = 4.6% Mean length of in-hospital stay was 13.3 days	N = 13 216 79+ years old	Vasques [13], 2012 American Heart Journal Systematic review of the literature and meta-study (publications: 1990–2011) Isolated AVR primary or redo 1982–2006
Long-term survival following surgical AVR in patients over 65 years of age is excellent and up to 8 years is comparable to the matched general population	Survival: 65–69 15.1 years 70–79 10.6 years 80 or over 6.3 years Long-term predictors: chronic kidney disease, severely impaired LVEF or current smoker, age at operation, chronic lung disease, hypertension, diabetes mellitus, extracardiac arteriopathy and preoperative arrhythmia development of a postoperative complication such as CVA, haemofiltration or re-exploration for bleeding	M = 1.5%	N = 356 65+ years old MA = 74.8	Sharabiani [35], 2016 Open heart Retrospective cohort study Isolated AVR 1996–2011
5-year survival is comparable to that of the age-matched Australian population. AVR should still be regarded as the gold standard in the management of aortic stenosis	5-year survival was 72. The 5-year survival of male/female elderly patients undergoing AVR (mean age 83.4 years) male/female, at 65%/75.4% is comparable to the expected survival of age-matched Australian males/females (mean age 83 years) at 64.3%/72.3%. Mortality predictors: age, chronic obstructive pulmonary disease, diabetes mellitus, cerebrovascular disease, renal failure, congestive heart failure, left ventricular ejection fraction < 45% and New York Heart Association classification III or IV	M = 4% Elderly status was not a predictor for 30-day mortality. Elderly status was associated with new renal failure, prolonged ventilation and Gl complications	N = 531 79+ years old MA = 83.4	Saxena [36], 2012, European Journal of Cardio-Thoracic Surgery Retrospective study Isolated AVR 2001–2009
Survivorship among octogenarians is favorable, with more than half the patients surviving more than 6 years after their surgery	Median survivorship for patients undergoing isolated AVR was 6.8 years (80 to 84 years), 6.2 years (85+ years)	M = 6.7% in the 80 to 84 age group M = 11.7% in 84+ age group Older age was associated with increased risk of stroke (2.1%, 80–84 year old group), atrial fibrillation, and longer length of stay	N = 575 79+ years old (419 pts 80–84 years old; 156 pts 84+ years old (24 nonagenarians))	Likosky [37], 2009 Circulation (registry) Isolated AVR 1987–2006

Table I. Cont.

The results obtained with isolated AVR were favorable with no operative deaths. It may be desirable to perform surgery before symptomatic deterioration (during the asymptomatic period). In elderly patients undergoing cardiac surgery, postoperative complications have amplor influence on mortality. Concomitant surgery amplor influence on mortality. Concomitant surgery including CABG also had an influence on early mortality. While the present study suggested that the indications for surgery should not be determined by age alone, severe CKD was found to be a strong contraindication with a 6-month mortality rate of 57.1%. Thus, TAVI severe CKD was found to be a strong contraindication with a 6-month mortality rate of 57.1%. Thus, TAVI school probably be considered for dialysis patients cardlent, although patients with a high society of Thoracic Surgeons perioperative risk of mortality and those with certain comorbidities carry a particularly poor long-term prognosis Among unselected intermediate- and high-risk patients, of factorion in median survival mortality and were more likely to be care lobogital mortality and were more likely to be care loss death and stroke, but TAVR patients and were more likely to be care loss of a particulary of in-hosoital mortality and were more likely to be care loss of a particulary of race ally early of an acute more likely to be			
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arly nts,	## A = 0% ## A = 0%	N = 49 79+ years old	Sezai [38], 2015 Ann Thorac Cardiovasc Surg retrospective study Subgroup Isolated AVR FU = 96.0% follow-up rate, 4.3 ±2.8 years (maximum: 14.3 years)
	ival in patients And > 80 years y, and > 80 years isolated AVR was rs, respectively. ease and renal associated with ion in median s left ventricular d prior cardiac associated with median median median median	N = 43 809 65+ years old Median age 75 (71– 80)	Brennan [11], 2012 Circulation Retrospective study, registry Subgroup Isolated AVR 1991–2007 FU = 6.2 median (3.4–10.8) maximum follow-up of 18 years
r) dy :-	ollowing hospital M = 5% % of patients Stroke = 2.7% out of an acute Pacemaker = 6.3%, at least 11 of 12 ths. matched cohort ears, 48% female; M 5.6%), TAVR its experienced 1-year rates of vs. 17.9%; hazard 95% confidence -1.04) and stroke %; HR 1.18,	N = 4,732 (SAVR) Median age = 82 years (77–85)	Brennan [39], 2017 J Am Coll Cardiol Retrospective registry study Subgroup isolated AVR 2011–2013, 2014–2015

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Comments	0	Outcomes	Patient group size (N),	Author, date, journal and
	Long-term mortality or survival prediction	In-hospital/30-day mortality (M), in-hospital stay, complications prediction	mean age (MA), mean EuroSCORE (ME)	study type, operation follow-p (FU)
In patients 85 years and older, SAVR seems to offer good short- and mid-term clinical outcomes compared to TAVI. Advanced age alone would not be an indication for TAVI in old patients	1-, 3- and 5-year overall survival rates were 90%, 79%, 71%	M = 5%	N = 40 85+ years old	Sponga [40], 2017 Interactive CardioVascular and Thoracic Surgery Retrospective study Subgroup AVR with concomitant surgery. The median follow-up period was 47 months (range: 0.1–108) in SAVR group
After adjusting for confounders, TAVR, SAVR, and mAVR had comparable operative mortality and mid-term survival	Survival at 12, 24, 36, and 48 months was 86%, 82%, 78% and 73% respectively	M = 5.1% Stroke = 6.4%	N = 722 (378 miniAVR) MA = 84.2 years old	Hirji [32], 2017, Annals of Cardiothoracic Surgery Retrospective study 2002–2015 FU = Median follow-up was 35 (14–65) months
Minimally invasive AVR through right anterior minithoracotomy can be safely performed in patients aged ≥ 80 years with acceptable morbidity and mortality rates. It is an effective alternative to full sternotomy AVR and might be associated with lower postoperative stroke incidence, earlier extubation and shorter hospital stay	Survival rates at 5 years 80%	M = 6% Stroke: RAMT = 0%, FS = 4%	N = 200 (100 RAMT, 100 FS) Age = 80+ MA = FS 81.9 (80.9–83.6) RAMT 82.9 (81.4–84.5)	Gilmanov [23], 2015 Interactive CardioVascular and Thoracic Surgery Retrospective study 2004–2013, Isolated AVR (RAMT-right anterior mini thoracotomy FS-full sternotomy) (minor associated procedures) FU = The median follow-up period was 33.7 months (21.8–69.5); follow-up data were 100% complete

the mini-AVR groups (age \geq 80 years and \leq 80 years) [25]. In the study by Lamelas et~al. a mini-AVR (mini-thoracotomy) group was compared with a full sternotomy group. The composite of mortality and morbidity was significantly lower in the minimally invasive group due to a lower incidence of renal failure, reduced intubation time, less wound infection and fewer deaths [26]. Selected results of the treatment of severe aortic stenosis in elderly patients are presented in Table I.

Recently, TAVI has emerged as an alternative treatment option to SAVR for patients with severe aortic stenosis with improved short-term quality of life in the surgical high-risk patients. The PARTNER B trial (with a medical therapy only control group) and CoreValve U.S. Extreme Risk Pivotal Trial showed similar results in improvements in both diseasespecific and generic health status through 1-year follow-up [27, 28]. Siontis et al. in their meta-analysis of trials comparing TAVI and SAVR concluded that TAVI is associated with a significant survival benefit throughout 2 years of follow-up and this superiority is observed irrespective of the TAVI device, particularly pronounced among patients undergoing transfemoral TAVI and in females [29]. On the other hand, the data from the STS/ACC Transcatheter Valve Therapies Registry on 12,182 patients (mean age: 84 years) indicated that only 60% of TAVI patients were discharged home and the 30-day mortality was 7% [30]. In the SURTAVI trial, the event rate for all-cause mortality at 30 days was 2.2% for TAVR and 1.7% for SAVR, with comparable incidence rates at 1 year (6.7% vs. 6.8%) and 2 years (11.4% vs. 11.6%) [31]. The study by Hirji et al. showed that TAVR (regardless of approach), SAVR, and mini-AVR had comparable operative mortality and mid-term survival [32]. The very good results of SAVR were confirmed in the analysis of PARTNER 2a trial by Thourani et al. The authors concluded that SAVR in intermediate-risk patients had a hospital mortality of 4.1% and excellent results at 2 years [33]. Khan et al. in meta-analysis suggest that TAVI can provide a similar mortality outcome compared with SAVR in low to intermediate surgical risk patients with critical aortic stenosis. However, both procedures are associated with their own array of adverse events. In the analysis stratified by study design, no significant differences were noted in the RCTs for stroke, whereas TAVI was better than SAVR in matched studies in the short term only [34]. The lack of long-term data after TAVI is still the largest weakness of this procedure in non-high-risk patients. However, there is no doubt that transcatheter aortic valve replacement is an alternative treatment for elderly, high-risk or inoperable patients with aortic stenosis. Future technical developments and randomized trials will probably establish indications for elderly, lower-risk patients for SAVR or TAVI.

Disclosure

The authors report no conflict of interest.

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