Transcatheter aortic valve implantation for high-risk patients with severe aortic stenosis: A systematic review

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Objectives: The present systematic review objectively assessed the safety and clinical effectiveness of transcatheter aortic valve implantation for patients at high surgical risk with severe aortic stenosis.

Methods: Electronic searches were performed in 6 databases from January 2000 to March 2009. The end points included feasibility, safety, efficacy, and durability. Clinical effectiveness was synthesized through a narrative review with full tabulation of results of all included studies.

Results: The current evidence on transcatheter aortic valve implantation for aortic stenosis is limited to short-term observational studies. The overall procedural success rates ranged from 74% to 100%. The incidence of major adverse events included 30-day mortality (0%–25%), major ventricular tachyarrhythmia (0%–4%), myocardial infarction (0%–15%), cardiac tamponade (2%–10%), stroke (0%–10%), conversion to surgery (0%–8%), moderate to major paravalvular leak (4%–35%), vascular complication (8%–17%), valve-in-valve procedure (2%–12%), and aortic dissection/perforation (0%–4%). The overall 30-day major adverse cardiovascular and cerebral events ranged from 3% to 35%. The mean aortic valve area ranged from 0.5 to 0.8 cm^2 before and 1.3 to 2.0 cm^2 after transcatheter aortic valve implantation. The mean pressure gradient ranged from 34 to 58 mm Hg before and 3 to 12 mm Hg after transcatheter aortic valve implantation. There was no significant deterioration in echocardiography measurements during the assessment period. Death rate at 6 months postprocedure ranged from 18% to 48%. No studies had adequate follow-up to reliably evaluate long-term outcomes.

Conclusions: The procedure has a potential for serious complications. Although short-term efficacy based on echocardiography measurements is good, there is little evidence on long-term outcomes. The use of transcatheter aortic valve implantation should be considered only within the boundaries of clinical trials. (J Thorac Cardiovasc Surg 2010;139:1519-28)

Aortic stenosis (AS) is the most common valvular heart disease in adults.[1] The disorder is becoming more frequent as the age of the population increases, representing a growing public health issue. Severe AS is universally fatal if left untreated, with three-quarters of patients dying within 3 years of symptom onset.[2] No medical treatment improves survival in chronic disease, as the obstruction to outflow tract requires mechanical relief. Mortality rates are significantly reduced in symptomatic patients with AS by aortic valve replacement (AVR).[3] Thus, AVR can be withheld in such patients only when compelling contraindications exist. A recent prospective survey of patients with valvular heart disease throughout Europe suggests that almost one-third of patients over the age of 75 with severe AS do not undergo AVR, due to risks arising from age and comorbidities.[1] These findings have stimulated tremendous interest in reducing patient morbidity and mortality and motivated the development of a less-invasive transcatheter aortic valve (TAV) procedure.[4-31]

The analysis of The Society of Thoracic Surgeons National Cardiac Database evidenced that, among 46,397 patients, mortality for surgical AVR ranges from 4.3% for first isolated AVR to 25% for redo surgery or multiple valve replacement plus coronary artery bypass grafting, with an overall mortality rate of 6.4%.[32] Fish[33] states that surgical results are excellent even in high-risk patients and that adoption of a percutaneous approach must be justified and guarantee high performance. Many issues related to TAV implantation remain to be clarified by clinical data. We performed the present systematic review to objectively assess the safety and clinical effectiveness of TAV implantation in treatment of severe AS.

METHODS

Literature Search Strategy

Electronic searches were performed in 6 databases from January 2000 to March 2009: MEDLINE, EMBASE, PubMed, Cochrane Central Register

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Abbreviations and Acronyms

AS = aortic stenosis
AVR = aortic valve replacement
MACCE = major adverse cardiovascular and cerebral events
NYHA = New York Heart Association
SD = standard deviation
TAV = transcatheter aortic valve

of Controlled Trials, Cochrane Database of Systematic Reviews, and Database of Abstracts of Review of Effectiveness. To achieve the maximum sensitivity of the search strategy and identify all studies, we used appropriate free text and thesaurus terms: ''percutaneous'' OR ''transcutaneous'' OR ''transcatheter'' OR ''transarterial'' OR ''transapical'' AND ''aortic valve'' OR ''aortic valve stenosis.'' The reference lists of all retrieved articles were reviewed for further identification of potentially relevant studies.

Study Population

The study population was defined as patients of high surgical risk with AS or those deemed not suitable for surgical AVR, whereas TAV implantation was considered. The criteria for patient selection for TAV implantation varied among institutions, and the definitions for nonsurgical candidates were not uniform.

Interventions

The balloon-expandable TAV consists of 3 pericardial leaflets, initially equine (Cribier-Edwards; Edwards Life Sciences Inc, Irving, Calif) and currently bovine (Edwards-Sapien; Edwards Life Sciences), mounted within a tubular, slotted, stainless steel balloon-expandable stent. Initial devices were 14 mm in length and 23 mm in expanded diameter, with a larger device available subsequently (length 16 mm, expanded diameter 26 mm). Current devices require either a 22F or 24F (transfemoral) or 26F (transapical) sheath for delivery. Three different insertion techniques have been used for Edwards TAV: the original antegrade approach where the TAV is delivered via the venous route; the retrograde approach by which it is delivered via an arterial route; and the transapical route requiring a minithoracotomy for delivery of the device via the apex of the left ventricle. The self-expandable percutaneous aortic valve (CoreValve; CoreValve, Irving, Calif) consists of 3 pericardial tissue leaflets, initially bovine and currently porcine, mounted and sutured in a self-expandable nitinol stent. The available valve diameters are 22 and 26 mm. Early devices required 25F sheaths. Second-generation devices incorporated porcine pericardial tissue that allowed decrease in profile to 21F sheaths. The current device was further redesigned in the fixing of the valve tissue onto the stent, decreasing the profile to 18F sheaths.

Outcome Measures

The findings from initial scoping searches were used in deciding which outcomes to include in the present review. The primary end points included feasibility and safety (procedural success rate, 30-day mortality, major tachyarrhythmia, bradyarrythmia requiring permanent pacemaker insertion, myocardial infarction, cardiac tamponade, cerebrovascular accident, conversion to surgery, conversion to valvuloplasty, vascular complication, moderate to severe paravalvular leak, valve-in-valve procedure, emergency percutaneous coronary intervention, endocarditis, aortic dissection/perforation, blood transfusion>2 U, procedure duration, and length of hospital stay). The secondary outcomes included efficacy and durability based on echocardiographic findings and clinical outcomes at 1, 6, and 12 months (mean aortic valve area before and after TAV implantation, peak and mean pressure gradient before and after TAV implantation, left ventricular ejection fraction before and after TAV implantation, New York Heart Association [NYHA] functional class improvement versus baseline, numbers of patients at risk at 6-month and 12-month reviews, and number of patients deceased at 6-month follow-up).

Study Design and Selection Criteria

A meta-analysis was not appropriate because no comparisons among different devices or techniques of insertion have been reported, and the potential differences in prostheses might exist. Experimental or observational studies were included in the present review. Case reports, abstracts, editorials, and expert opinions were excluded. Studies eligible for this systematic review included high-risk patients with AS who received TAV implantation. When centers had published duplicate trials with accumulating numbers of patients or increased lengths of follow-up, only the most complete reports were included for qualitative appraisal and data extraction.

Data Extraction and Critical Appraisal

The 2 investigators (T.D.Y. and R.P.) independently appraised each included article, using a critical review checklist as recommended by the National Health Service Center for Reviews and Dissemination case series quality assessment criteria (University of York).[34] This consisted of representativeness of study sample, explicitness of inclusion criteria, similarity of disease progression at the time of treatment, adequacy of follow-up, objectivity of outcome measures, and appropriateness of subseries analysis. The criteria for assessing the quality of morbidity and mortality data included the following 4 points: whether there was an adequate explanation of how adverse effects were identified; whether a standardized or validated measurement instrument was used; how the adverse effect(s) was attributed to the intervention; and whether the terms were clearly explained.

All data were extracted from the relevant articles' texts, tables, and figures. Clinical effectiveness was synthesized through a narrative review with full tabulation of results of all included studies. Discrepancies between the 2 reviewers were resolved by discussion and consensus with a third investigator (J.M.-N.). The final results were reviewed by all 3 senior investigators (M.N., M.P.V., and P.G.B.).

RESULTS

Quantity of Studies

The titles and abstracts of 571 peer-reviewed publications were identified through searching the 6 electronic databases. Initial evaluation of these abstracts identified 57 potentially relevant publications. Manual search of the reference lists identified 4 additional publications of interest. When the inclusion and exclusion criteria were applied to these 61 publications, 28 articles[4-31] remained for assessment (Table 1). Serial publications reporting accumulating numbers of patients or increased length of follow-up were identified. The publication with most complete data set from each center was retained. In total, 17 studies were included for appraisal and data extraction (Table 2).[6,9,11-13,16,18-23,25,27,29-31] All studies evaluated the feasibility and safety of TAV implantation. All except 1 study[23] assessed the efficacy and durability of TAV using hemodynamic measurements by use of echocardiography.

Quality of Studies

No randomized controlled trials or matched comparative studies were identified. All 17 included articles were experimental studies without control groups.[6,9,11-13,16,18-23,25,27,29-31]

TABLE 1. Summary of outcomes presented in relevant publications on transcatheter aortic valve implantation for high-risk patients with aortic stenosis

Treatment center	Reference	Year	n	Success rate	Post-TAV mortality	Post-TAV morbidity	Myocardial infarction	Emergency cardiac surgery	Cerebrovascular accident	Blood transfusion	Length of hospital stay	Echocardiography findings	NYHA functional class	Learning curve	Survival
Antegrade Edwards valve															
Rouen, France	4	2004	6	●	●	●						●			
	5	2004	8	●								●			
	6	2006	36	●	●	●		●	●			●	●		●
	7	2007	36	●	●	●						●			●
Retrograde Edwards valve															
Vancouver, Canada	8	2006	18	●	●	●		●	●	●	●	●	●		●
	9	2007	50	●	●	●		●	●	●	●	●	●	●	●
	10	2008	40	●	●	●	●		●	●		●			
Paris, France	11	2008	12	●	●	●		●	●	●	●	●	●		●
Athens, Greece	12	2008	12	●	●	●					●	●	●		
Quebec, Canada	13	2008	24	●	●	●		●	●		●	●	●		●
Transapical Edwards valve															
Vancouver, Canada	14	2006	7	●	●	●				●	●	●			
	15	2007	7	●	●	●				●	●	●	●		●
	16	2009	26	●	●	●	●		●	●	●	●	●		●
Leipzig, Germany	17	2007	30	●	●	●	●	●	●		●	●			
	18	2008	50	●	●	●		●	●			●		●	●
Frankfurt, Germany	19	2008	26	●	●	●	●	●	●			●			
Multicenter	20	2007	59		●	●		●	●			●			●
Bicenter	21	2008	40	●	●	●	●	●	●			●	●		●
CoreValve retrograde valve															
Siegburg, Germany	22	2006	25	●	●	●		●	●			●	●		●
Brighton, UK	23	2008	12		●	●					●				
Montreal, Canada	24	2007	10	●	●	●	●	●	●	●	●	●	●		
	25	2007	13	●	●	●		●	●	●	●	●	●		●
	26	2008	13	●	●	●						●		●	
Rotterdam, Netherlands	27	2008	33	●	●							●			
	28	2008	39									●			●
Catania, Italy	29	2009	30	●	●	●	●	●	●			●	●		●
Multicenter	30	2007	86	●	●	●		●	●			●	●		
Multicenter	31	2008	646	●	●	●	●	●	●			●			

TAV, Transcatheter aortic valve.

TABLE 2. Summary of the 17 trials included in the present systematic review

Study	Referred (n)	Attempted (n)	Study period	Age (mean ± SD)	Logistic EuroSCORE (mean ± SD)	Procedure	Procedural success, n (%)
Antegrade Edwards valve							
Rouen, France[6]	36	33	2003–2005	80 ± 7	12 ± 2	LA/sedation, antegrade (26); retrograde (7); rapid ventricular pacing; no CPB	27 (82)
Retrograde Edwards valve							
Vancouver, Canada[9]	—	50	2005–2006	82 ± 7	28	GA; retrograde; rapid ventricular pacing; no CPB	43 (86)
Paris, France[11]	39	12	2006–2007	85 ± 6	31 ± 14	GA; retrograde, rapid ventricular pacing	10 (83)
Athens, Greece[12]	—	12	2007–2008	81 ± 5	34 ± 15	GA; retrograde (8); transapical (4); rapid ventricular pacing; by cardiologists and cardiac surgeons	12 (100)
Quebec, Canada[13]	29	22	2007–2008	84 ± 7	26 ± 16	GA; retrograde (11); apical (11); rapid ventricular pacing; by cardiologists and cardiac surgeons	20 (91)
Transapical Edwards valve							
Vancouver, Canada[16]	—	26	2005–2007	80 ± 9	37 ± 20	GA; minithoracotomy;	26 (100)
Leipzig, Germany[18]	83	50	2006–2007	82 ± 5	28 ± 12	transapical; rapid	47 (94)
Frankfurt, Germany[19]	—	26	2006–2008	84 ± 7	37 ± 6	ventricular	26 (100)
Multicenter[20]	—	59	2006	81 ± 6	27 ± 14	pacing; by cardiac	55 (93)
Bicenter[21]	163	40	2006–2008	83 ± 8	36 ± 15	surgeons	35 (88)
Retrograde CoreValve valve							
Siegburg, Germany[22]	25	25	2005	80 ± 5	11*	GA; retrograde; 24 and 21F sheaths; fem-fem CPB	21 (84)
Brighton, UK[23]	—	12	2007–2008	80*	22*	GA (3); LA/sedation (9); retrograde; 18F sheaths; rapid ventricular pacing	12 (100)
Montreal, Canada[25]	29	11	2005–2006	82 ± 7	36*	GA; retrograde; CPB	11 (100)
Rotterdam, Netherlands[27]	—	33	2005–2007	81 ± 7	20 ± 12	Retrograde; rapid ventricular pacing; 21 and 18F sheaths; ± CPB	33 (100)
Catania, Italy[29]	69	30	2007–2008	82 ± 5	25 ± 8	LA/sedation or GA, retrograde; 18F; rapid ventricular pacing	28 (93)
Multicenter[30]	—	86	2005–2007	82 ± 6	22 ± 13	GA or LA/sedation; retrograde; 21F and 18F sheaths; ± fem-fem CPB	64 (74)
Multicenter[31]	—	646	2007–2008	81 ± 7	23 ± 14	LA/sedation or GA, retrograde; 18F; rapid ventricular pacing	628 (97)

CPB, Cardiopulmonary bypass; *GA,* general anesthetic; *LA,* local anesthetic; *fem,* femeral. *Median.

All reports originated from specialized tertiary referral centers. Five series had ≥50 patients (range, 50–646),[9,18,20,30,31] and the remaining 12 series had <50 patients (range, 11–40).[6,11-13,16,19,21-23,25,27,29] The definitions of high-risk patients with AS not suitable for surgical AVR varied among the institutions. For example, age >70,[11,21] >75,[18-20,31] >80[25,30]; NYHA functional class III/IV[6,11,12]; AVA <1 cm^2,[22,29-31] <0.8 cm^2,[12,19] <0.7 cm^2,[6,11] <0.6 cm^2,[21,25]; logistic EuroSCORE >20%,[11,12,19,25,30] additive EuroSCORE ≥9,[18,20] Society of Thoracic Surgeons score >15%,[21] and Parsonnet's ≥30.[6]

In 16 studies,[6,9,11-13,16,18-23,25,27,29,30] the number of patients evaluated was relatively small and the patients were highly selected. The study sample in these 16 series was unlikely to be fully representative of the study population and was not large enough to provide definitive estimates of incidence of all adverse events. It is acknowledged that the lack of evidence of a rare adverse effect is not proof that such an adverse effect is not associated with the procedure. One multicenter study assessed the procedural and 30-day outcomes of 18F CoreValve in 646 patients.[31] Thirteen studies reported explicit priori inclusion criteria,[6,11,12,18-22,25,27,29-31] and 4 studies did not.[9,13,16,23] All studies reported procedure-related or 30-day morbidity and mortality.[6,9,11-13,16,18-23,25,27,29-31] Ten studies reported follow-up data at 6 months.[6,9,11,13,16,18,20,22,25,29] Eight studies reported follow-up data at 12 months.[6,9,16,18,20,22,25,29] Two studies had follow-up data on 2 and 3 patients beyond 2 years, respectively.[2,16] No studies provided adequate long-term follow-up data. All but 1 study[23] evaluated hemodynamic measurements by echocardiography. Blinding was not reported. Three studies performed subgroup analysis assessing procedural learning curve.[9,18,30] Morbidity, mortality, hemodynamic measurements, and survival rates were objective outcome measures.

All studies clearly defined the techniques of TAV intervention, and there was reasonable consistency in the description of the techniques used for each approach. Clinical adverse events were adjudicated by an independent clinical committee in 3 studies,[22,29,30] not in 3 other studies,[9,16,31] and not reported in the remaining 11 studies.[6,11,12,16,18-21,23,25,27] The duration of follow-up was reported in 14 studies[6,9,11-13,16,18-22,25,29,30] and not in 3 studies.[23,27,31] Six studies reported data according to periprocedural major adverse cardiovascular and cerebral events (MACCE).[6,21,22,29-31] In 11 studies, no standardized measurement instrument was used for reporting adverse events.[9,11-13,16,18-20,23,25,27] The definitions of adverse events were clearly explained in 8 studies[6,9,16,21,22,29-31] and not in 9 studies.[11-13,18-20,23,25,27]

Assessment of Feasibility

The overall procedural success rates ranged from 74% to 100% (Table 2).[6,9,11-13,16,18-23,25,27,29-31] Cribier and associates[6] reported that 22 of the 26 antegrade implantations (85%) of Edwards TAV were performed successfully with 4 technical failures. Two of these patients did not hemodynamically tolerate the guide wire across the mitral valve. In the other 2 patients, valve migration occurred immediately after implantation.

With the retrograde implantation of the Edwards prosthesis, Webb and colleagues[9] achieved successful implantation in 43 patients (86%). Reasons for failure included inability to pass through the iliac artery (n = 1) and cross the aortic valve (n = 3), a defective prototype delivery catheter (n = 1), and malpositioning (n = 2). Descoutures and coworkers[11] reported procedural success in 10 of 12 patients (83%). Reasons for failure included inability to pass though the iliac artery (n = 1) and intraprocedural death from hemopericardium, because of perforation of the left ventricle by the wire (n = 1). Rodes-Cabau and colleagues[13] reported that procedural success was obtained in all but 2 patients (91%). One transfemoral procedure was aborted due to severely calcified femoral arteries, and the other patient died during the procedure, presumably from ischemic heart disease.

With the transapical approach, 2 single-institutional studies reported 100% success rate.[16,19] Walther and associates[18] reported that 47 of 50 patients (94%) had successful implantation, with 3 patients requiring early conversion to open AVR. One multicenter study from Leipzig, Vienna, Frankfurt, and Dallas[20] reported successful transapical valve positioning in 55 patients (93%) with the remaining 4 patients requiring conversion to sternotomy, as the valves were incorrectly positioned. In a bicenter study from Dallas and Cleveland,[21] 35 of the 40 TAVs (88%) were successfully seated. Two valves embolized and required open AVR, and 1 case of severe regurgitation later required AVR. Two additional patients required cardiopulmonary support: 1 valve later embolized and 1 migrated.

With the CoreValve prosthesis, 3 studies reported 100% success rate.[23,25,27] Grube and colleagues[22] reported acute procedural success achieved in 21 of 25 patients (84%). In 2 patients, significant paravalvular leakage occurred, requiring open AVR. In 1 patient, the device could not cross the heavily calcified native valve and the patient died suddenly 12 hours after the balloon valvuloplasty. One additional patient died on the second postprocedural day after successful device implantation as a result of delayed pericardial tamponade secondary to wire perforation of the left ventricle. Tamburino and coworkers[29] achieved procedural success in 28 of 30 patients (93%), with 1 malpositioning of the prosthesis requiring a valve-in-valve procedure, and another patient sustained a nonfatal pericardial tamponade. In the multicenter study from Siegburg, Leipzig, and Montreal, acute device success was achieved in 76 of 86 patients (88%), but the procedural success was 74%.[30] In 6 patients, misplacement of

TABLE 3. Procedural and 30-d clinical outcomes following transcatheter aortic valve implantation

Study	n	Death at 30 d, n (%)	Major tachyarrhythmia, n (%)	Pacemaker insertion, n (%)	Myocardial infarction, n (%)	Cardiac tamponade, n (%)	Cerebrovascular accident, n (%)	Conversion to surgery, n (%)
Antegrade Edwards valve								
Rouen[6]	33	6 (18)	1 (3)	1 (3)	0	2 (6)	1 (3)	0
Retrograde Edwards valve								
Vancouver[9]	50	6 (12)	2 (4)	2 (4)	1 (2)	1 (2)	2 (4)	0
Paris[11]	12	3 (25)	—	1 (8)	0	1 (8)	0	0
Athens[12]	12	0	—	—	—	—	—	—
Quebec[13]	22	2 (9)	1 (5)*	0	0	1 (5)	0	1 (5)
Transapical Edwards valve								
Vancouver[16]	26	6 (23)	0	3 (12)	1 (4)	—	1 (4)	0
Leipzig[18]	50	4 (8)	—	—	—	—	—	3 (6)
Frankfurt[19]	26	4 (15)	5 (19)*	—	—	—	0	2 (8)
Multicenter[20]	59	8 (14)	18 (31)*	—	—	—	2 (3)	4 (7)
Bicenter[21]	40	7 (18)	—	—	6 (15)	—	2 (5)	2 (5)
Retrograde CoreValve valve								
Siegburg[22]	25	5 (20)	0	—	0	1 (4)	1 (4)	2 (8)
Brighton[23]	12	1 (8)	-	3 (25)	—	—	—	—
Montreal[25]	11	2 (18)	-	4 (36)	—	—	1 (9)	0
Rotterdam[27]	33	2 (6)	-	—	—	1 (3)	—	—
Catania[29]	30	2 (7)	0	—	0	1 (3)	0	0
Multicenter[30]	86	10 (12)	-	—	1 (1)	9 (10)	9 (10)	6 (7)
Multicenter[31]	646	52 (8)	-	60 (9)	4 (1)	9 (1)	12 (2)	3 (1)

SD, Standard deviation. *Supraventricular arrhythmia. †Mean.

ACD

the valve led to emergency conversion to open AVR. In 2 patients, the device did not cross heavily calcified native valves despite balloon predilatation. In 2 patients, suboptimal placement of the prosthesis resulted in aortic regurgitation, requiring implantation of a second CoreValve prosthesis. Finally, the largest collaborative study on 646 patients who had 18F CoreValve implantation demonstrated a procedural success in 97% of the patients, and the details of failure were not provided.[31]

Assessment of Safety

Table 3 demonstrates 30-day major cardiovascular and cerebral adverse events following TAV across all studies.[6,9,11-13,16,18-23,25,27,29-31] The range of these adverse events was as following: 30-day mortality (0%–25%); major ventricular tachyarrhythmia (0%–4%); supraventricular tachyarrhythmia (5%–31%); bradyarrhythmia requiring permanent pace maker insertion (0%–36%); myocardial infarction (0%–15%); cardiac tamponade (2%–10%); cerebrovascular accident (0%–10%); conversion to surgery (0%–8%); conversion to valvuloplasty (0%–4%); vascular complication (8%–17%); moderate to major paravalvular leak (4%–35%); valve-in-valve procedure (2%–12%); emergency percutaneous coronary intervention (0%–8%); endocarditis (0%); aortic dissection/rupture (0%–4%); and blood transfusion >2 U (3%–24%). The mean procedure duration varied from 2.5 to 2.9 hours. The mean length of hospital stay ranged from 7 to 17 days. The overall 30-day MACCE ranged from 3% to 35%.[6,21,22,29-31]

Assessment of Efficacy

The efficacy of TAV implantation was assessed based on echocardiographic findings (Table 4).[6,9,11-13,16,18-23,25,27,29-31] One study[23] did not report echocardiographic measurements. The remaining 16 studies[6,9,11-13,16,18-22,25,27,29-31] all demonstrated significant improvement in hemodynamic performance ($P < .05$) when comparing preprocedural with postprocedural (in-hospital) echocardiography measurements. Left ventricular ejection fraction ranged from 41% to 56% before and 46% to 63% after TAV implantation.

Assessment of Durability

Fifty percent to 100% of patients had improved NYHA functional class at least by 1 grade at 1-month follow-up.[6,9,12,13,16,21,22,30] As stated before, no studies had adequate follow-up to reliably evaluate long-term outcomes. Follow-up echocardiographic findings were available in 9 studies at 1 month,[6,9,13,16,21,22,25,27,30] 5 studies at 6 months,[6,9,13,16,21] and 3 studies at 12 months.[6,9,16] According to this information, there was no significant deterioration in echocardiographic measurements during the assessment period. Death rate at 6 months postprocedure ranged from 18% to 48%.[6,9,11,16,18,20,21,25] One study by Cribier and colleagues[6] reported that at 6 months, 16 of 27 patients (60%)

TABLE 3. Continued

Conversion to valvuloplasty, n (%)	Vascular complications, n (%)	Paravalvular leak >2+, n (%)	Valve-in-valve procedure, n (%)	Aortic dissection/ perforation, n (%)	Transfusion >2 U, n (%)	Procedural duration, hours ± SD	Length of stay, days ± SD
—	—	5 (15)	—	—	—	—	—
—	6 (12)	3 (6)	—	1 (2)	9 (18)	—	5†
—	2 (17)	4 (33)	—	—	2 (17)	2.9 ± 1.2	17 ± 8
—	1 (8)	1 (8)	1 (8)	—	—	—	8 ± 2
—	0	4 (18)	1 (5)	—	1 (5)	—	7 ± 3
0	—	1 (4)	1 (4)	—	3 (12)	—	9 ± 5
—	—	—	—	1 (2)	—	—	—
—	2 (8)	6 (23)	—	1 (4)	—	2.5 ± 1.5	—
—	—	3 (5)	—	—	—	2.5 ± 1.5	—
—	—	14 (35)	—	—	1 (3)	—	—
1 (4)	—	2 (8)	—	0	6 (24)	—	—
—	1 (8)	—	—	—	—	1.8–2.3†	3–5†
—	—	—	—	—	2 (18)	.5†	13.5†
—	—	—	4 (12)	—	—	—	—
0	5 (17)	2 (7)	1 (3)	0	—	1.0 ± 0.3	—
2 (2)	—	—	2 (2)	0	—	2.9 ± 1.1	—
—	12 (2)	—	17 (3)	4 (1)	—	2†	—

with successful implantation were dead. Further follow-up of their patients was reported in a subsequent paper.[7] One patient died at 10 months (reason unknown) and another at 30 months (renal failure). Ten patients were followed for at least 1 year, 4 of them for 2 years, and 2 of them for 3 years.

Svensson and associates[21] reported on a Food and Drug Administration–approved feasibility study incorporating 40 patients treated with a transapical inserted the Edwards equine or bovine valve. This is the only published study reporting on quality-of-life data. Quality-of-life scores improved from preoperatively (SF-12 Physical 28.7, standard deviation 6.1; Mental 48.1, standard deviation 11.5) to postoperatively at 6 months (SF-12 Physical 35.2, standard deviation 7.4; Mental 50.4, standard deviation 11.7). The physical improvement was significant ($P = .002$).

DISCUSSION

With the population aging, AS is becoming a more prevalent public health issue. Medical therapy is unlikely to modify the course of the disease, especially once symptoms or left ventricular dysfunction become manifest. Percutaneous balloon aortic valvuloplasty has only a limited role in the treatment of AS, as the results are not durable. Surgical AVR remains the mainstay of definitive treatment.[3] Although surgical therapy is effective, it entails the risks and morbidity associated with cardiopulmonary bypass and median sternotomy. When a frail and elderly patient with significant comorbidities presents with severe AS, he or she may be precluded from surgical AVR due to potentially high operative risks. TAV implantation with its less invasive nature is believed to offer a safer treatment solution for these patients.[35]

In the current literature, no randomized controlled trials have compared TAV implantation with conservative medical treatment, balloon valvuloplasty, or standard AVR. The clinical experience with TAV is substantiated mainly by short-term results. There is an ongoing randomized trial (Placement of AoRTic TraNscathetER Valve trial in the U.S. [PARTNER US]; ClinicalTrials.gov identifier NCT00530894) using this valve comparing TAV implantation versus surgical AVR in patients at high surgical risk and TAV implantation versus medical treatment or balloon aortic valvuloplasty in patients at extreme surgical risk. The present systematic review based on the available observational series demonstrated the following key points. First, in view of the feasibility and safety results of TAV implantation, the procedure success rate ranged from 74% to 100% but there is a potential for serious complications. The 30-day mortality (0%–25%), 30-day MACCE (range 3%–35%), and 6-month mortality (18%–48%) were high, especially in the initial reports.[6,21,22,30] Without randomized trials, it is not clear whether the high interventional mortality risk associated with TAV insertion is lower than the risk associated with conventional surgery. The procedural and short-term outcomes appeared to be improving in more recent studies

TABLE 4. Echocardiography measurements and clinical data following transcatheter aortic valve implantation

Study	n	Mean aortic valve area before TAV (cm^2) ± SD	Mean aortic valve area after TAV (cm^2) ± SD	Peak pressure gradient before TAV (mm Hg) ± SD	Peak pressure gradient after TAV (mm Hg) ± SD	Mean pressure gradient before TAV (mm Hg) ± SD
Antegrade Edwards valve						
Rouen[6]	33	0.6 ± 0.1	1.7 ± 0.1	—	—	37 ± 13
Retrograde Edwards valve						
Vancouver[9]	50	0.6 ± 0.2	1.7 ± 0.4	—	—	46 ± 17
Paris[11]	12	0.5 ± 0.1	1.7 ± 0.5	—	—	50 ± 19
Athens[12]	12	0.6 ± 0.1	1.8 ± 0.1	91 ± 33	22 ± 7	57 ± 23
Quebec[13]	22	0.6 ± 0.2	1.5 ± 0.3	56 ± 15	17 ± 5	34 ± 10
Transapical Edwards valve						
Vancouver[16]	26	0.5 ± 0.1	1.7 ± 0.5	—	—	45 ± 14
Leipzig[18]	50	—	—	—	15 ± 7	—
Frankfurt[19]	26	0.6 ± 0.1	—	—	—	—
Multicenter[20]	59	0.5 ± 0.2	—	—	18 ± 11	—
Bicenter[21]	40	0.6 ± 0.1	1.6 ± 0.4	65 ± 15	15 ± 5	40 ± 10
Retrograde CoreValve valve						
Siegburg[22]	25	0.7 ± 0.1	—	70 ± 14	21 ± 5	44 ± 11
Brighton[23]	12	—	—	—	—	—
Montreal[25]	11	0.6 ± 0.2	1.3 ± 0.4	—	—	51 ± 19
Rotterdam[27]	33	0.8 ± 0.2	2.0 ± 0.9	77 ± 28	20 ± 12	46 ± 16
Catania[29]	30	0.6 ± 0.2	1.5 ± 0.4	86 ± 22	—	58 ± 18
Multicenter[30]	86	0.6 ± 0.2	—	71 ± 23	—	44 ± 15
Multicenter[31]	646	0.6 ± 0.2	—	78 ± 26	—	49 ± 14

TAV, Transcatheter aortic valve; *NYHA*, New York Heart Association; *SD*, standard deviation.

with accumulating number of patients. In the earlier reports, Cribier and colleagues[6] reported a procedural success rate of 82% in 33 patients received Cribier-Edwards prosthesis.[6] Grube and collaborators[22] obtained a procedural success rate of 84% using the first- and second-generation CoreValve devices. Webb and colleagues[9] demonstrated procedural success increased from 76% in the first 25 patients to 96% in the subsequent 25 patients and an associated decrease in 30-day mortality from 16% to 8%, respectively. In a recent multicenter study on 646 patients receiving the third-generation CoreValve, the overall procedural success rate was 97%, and the 30-day all-cause mortality was 8%.[31] Main aspects of the learning curve for TAV intervention are device technology, procedural skills, and decision making involving case selection, intraprocedural strategic plans, and alterations as well as decision making in management of complications. At this stage, the number of patients required to regard a specialized center well trained is not certain. This procedure requires a high level of training, expertise, and infrastructure to optimize safety for both staff and patients. Therefore, concentration of the services at centers with experience is likely to increase quality of care for these patients.

Second, the short-term efficacy based on echocardiography measurements and NYHA functional class for patients who had successful TAV, irrespective of the procedural approach used, seems to be encouraging. Based on the limited data available, echocardiography measurements at 1-, 6-, and 12-month follow-up did not demonstrate significant functional deterioration. However, long-term follow-up data are not available and the durability of the prostheses is uncertain. Assessment of the long-term durability will require at least 5 years of follow-up. Given the limited life expectancy of patients currently considered for TAV, this may not be practical. It is also noted that although there are significant improvements in valve hemodynamic performance and echocardiography findings, impact on patients' quality of life is less clear.

Currently, TAV is restricted to elderly patients who are considered at very high risk for conventional surgery. In a joint position statement published in 2005, the Society of Thoracic Surgeons, the American Association for Thoracic Surgery, and the Society for Cardiovascular Angiography and Interventions cautioned against the widespread use of these technologies without proper evaluation.[36] In the absence of published guidelines, the selection of cases must be multidisciplinary. All studies evaluated aimed to recruit patients at ''high surgical risk'' or ''nonsurgical'' candidates with AS. The eligibility of patients for TAV is poorly defined or not reported in 4 studies,[9,13,16,23] and in the other studies, the operability is mostly based on assessment by clinicians, supplemented with information obtained from an operative risk score, mostly the EuroSCORE, which provides an estimation of the operative mortality risk.

However, the validity of this risk tool for estimating the surgical risk incurred by high-risk patients has been

TABLE 4. Continued

Mean pressure gradient after TAV (mm Hg) ± SD	LV ejection fraction before TAV (%) ± SD	LV ejection fraction after TAV (%) ± SD	NYHA functional class improved vs baseline, n (%)	Patients at risk at 6-mo follow-up, n (%)	Patients at risk at 12-mo follow-up, n (%)	Death at 6 mo, n (%)
9 ± 2	45 ± 18	53 ± 14	21 (64)	11 (33)	5 (15)	16 (48)
11 ± 5	53 ± 15	57 ± 13	25 (50)	35 (70)	17 (34)	9 (18)
11 ± 3	47 ± 16	—	7 (58)	9 (75)	—	3 (25)
10 ± 3	—	—	12 (100)	—	—	—
9 ± 3	51 ± 16	54 ± 11	17 (77)	10 (45)	—	—
9 ± 5	56 ± 13	63 ± 9	Most	17 (65)	17 (65)	9 (35)
7 ± 4	53 ± 14	—	—	37 (74)	36 (72)	13 (26)
6 ± 2	—	—	—	—	—	—
9 ± 6	47 ± 16	—	—	15 (25)	5 (8)	13 (22)
8 ± 3	52 ± 15	55 ± 19	—	—	—	13 (33)
12 ± 3	54 ± 16	—	18 (72)	7 (28)	2 (8)	—
—	—	—	—	—	—	—
9 ± 4	49 ± 17	56 ± 11	11 (100)	1 (9)	1 (9)	5 (45)
12 ± 7	41 ± 12	46 ± 15	—	—	—	—
9 ± 4	53 ± 8	—	—	13 (43)	5 (17)	—
9	54 ± 16	—	—	—	—	—
3 ± 2	52 ± 14	—	—	—	—	—

criticized. Recent observational data indicate that the EuroSCORE severely overestimates operative risk in high-risk patients having isolated surgical AVR.[37,38] In surgical series from the Mayo Clinic, an estimated 30-day mortality of 23.6% was significantly higher than an observed mortality of only 5.8%.[37] By comparison, Cribier and associates[6] enrolled patients with a mean predicted operative risk of 12 ± 2 for TAV implantation and experienced a 30-day mortality of 18%.[6] Grube and colleagues[30] conducted a multi-institutional study using the CoreValve percutaneous aortic valve on 86 patients with a EuroSCORE of 22 ± 13 and achieved 30-day mortality of 12%. This implies that patients with AS who are considered at high risk for conventional AVR may actually present lower mortality rates if treated surgically than if treated by means of TAV insertion. Clinicians must be cautious in estimating operative risk from models that were not intended for this specific use. The definition of ''high surgical risk'' is difficult, as evidenced by the conversion of such patients to open AVR after failure of TAV implantation. In the multicenter study by Grube and colleagues,[30] 6 patients required emergency conversion to open procedure to retrieve the devices and successfully implanted aortic prostheses with only 1 operative death.

We attempted to evaluate the durability of TAV, but there is a lack of comparative studies and the data on long-term efficacy and durability of TAV in the current literature. The relatively unproven nature and inherent risks of this new therapy mandate a formal team approach to patient selection and outcome analysis. The inclusion and exclusion criteria of the PARTNER trial provide some indication of the limits of this new technology. Before further convincing evidence becomes available, the use of TAV implantation should be considered only within the boundaries of clinical trials with special arrangements for clinical governance, consent, and audit or research. Decision on eligibility must be individualized and assessed by a multidisciplinary team of cardiologists, cardiac surgeons, and cardiac anesthesiologists. It is likely that progressive development of technology, familiarity with techniques, and better understanding of appropriate criteria for patient selection will continue to refine the indications for TAV procedures.

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