Current status of transcatheter aortic valve implantation: a systematic review of non-orthodox deployment strategies

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ABSTRACT

Objectives: The present systematic review objectively assessed the feasibility, safety, clinical effectiveness, & durability of different approaches in deployment of transcatheter aortic valve implantation (TAVI) for patients at high surgical risk with severe aortic stenosis (AS).
Methods: Electronic searches were performed in 2 databases from January 2002 to November 2011 of patients undergoing TAVI via transapical, transaortic, & subclavian approaches. The primary end points included feasibility, safety, efficacy, & durability.
Results: The current literature regarding TAVI is limited to observational studies. Overall procedural success rates ranged from 90% to 100%. The incidence of major adverse events included: 30-day mortality (0%-18%), major adverse cardiovascular and cerebral events ranged from 2-35%. There was statistically significant hemodynamic improvement demonstrated by postoperative echocardiography with no significant deterioration out to 6 months. Survival at 6 months ranged from 59-93%. Only one study with long-term of transapical TAVI follow-up could reliably evaluate long-term survival of 58% at 3 years.
Conclusion: TAVI has proven to be feasible and potentially an effective intervention for non-surgical patients with symptomatic AS and poor femoral access. Although short-term efficacy based on echocardiography has been promising, there is a paucity of data concerning long-term outcomes. The evolution of TAVI will be dependent on the development of a valid tool for estimating the surgical risk.

INTRODUCTION

Aortic stenosis (AS) is the most common form of valvular heart disease in adults in the western world. Severe AS is universally fatal if left untreated, with a 75% mortality rate within 3 years of symptom onset. Although patients are often high-risk candidates for open surgery, aortic valve replacement (AVR) with cardiopulmonary bypass (CPB) has been the longstanding treatment of choice for patients with symptomatic severe AS that not only offers symptomatic relief, but the potential to improve long-term survival. Although longstanding evidence has established that AVR significantly reduces mortality, 30-40% of patients that have a class I indication for AVR are never offered surgical intervention because of extreme preoperative risk. The need for a less invasive device to relieve a fixed mechanical obstruction led to the development of transcatheter aortic valve implantation (TAVI). Clinical effectiveness of a randomized control trial demonstrated an absolute reduction of 20% in all-cause mortality in patients unsuitable for surgery when comparing TAVI against medical therapy. However, the potential for vascular morbidity inherent in the elderly population led to the development of subclavian, transapical, and transaortic access techniques. Each of these techniques provides the advantage of avoiding access difficulty and facilitating device delivery. The use of TAVI has expanded with new access techniques, however its adoption must be tempered with studies regarding feasibility, safety, and clinical effectiveness in the treatment of severe AS.

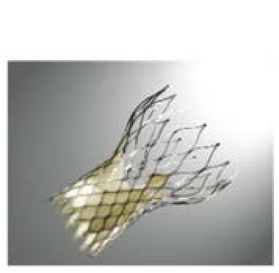
Study	n	Death at 30 d, n (%)	Pacemaker insertion, n (%)	Myocardial infarction, n (%)	Cardiac tamponade, n (%)	Cerebrovascular accident, n (%)	Conversion to surgery, n (%)	IABP Implantation, n (%)	Valve thrombosis, n (%)	Vascular complications, n (%)	Aortic dissection/ perforation, n (%)	Multiple organ failure, n (%)	Procedural duration, min ± SD	ICU stay, median hrs	MACCE, n (%)	Survival at 6 mo, n (%)	Survival at 1 yr, n (%)
Vancouver[1]	71	12 (17)	6 (9)	-	-	1 (1)	1 (1)	-	0	2 (3)	1 (1)	2 (3)	-	-	-	74 ± 5	72 ± 6
Frankfurt[2]	26	4 (15)	-	-	-	0	2 (8)	2 (8)	1 (4)	2 (8)	1 (4)	2 (8)	152 ± 87	18	-	-	-
Paris[3]	18	3 (17)	1 (6)	-	2(11)	-		3 (17)	-	2 (11)	-	-	-	-	-	-	-
Multicenter[4]	59	8 (14)	-	-	-	2 (3)	4 (7)	-	-	-	-	-	148 ± 92	20	-	76 ± 6	-
Multicenter[5]	40	7 (18)	-	6 (15)	-	2 (5)	2 (5)	-	0	-	-	1 (3)	-	-	14 (35)	59 ± 4	-
Munich[6]	137	17 (12)	27 (20)	-	-	7 (5)	1 (1)	-	-	16 (12)	-	-	-	-	-	77	-
Paris[7]	17	2 (12)	-	0	0	0	0	-	-	-	1 (6)	-	-	-	-	-	-
Multicenter[8]	54	0	10 (19)	0	0	1 (2)	0	-	0	0	-	-	106 ± 29	-	1 (2)	93 ± 4	-
Milan[9]	12	1 (8)	3 (25)	-	-	-	0	-	-	2 (17)	1 (8)	-	174 ± 63	-	-	-	-
London[10]	108	9 (8)	-	0	0	6 (6)	-	-	-	3 (3)	-	-	-	-	-	-	-
France[11]	83	13 (16)	7 (8)	0	1 (1)	2 (2)	-	-	-	5 (6)	0	-	-	-	-	-	-
Belgium[12]	96	11 (11)	7 (7)	-	-	5 (5)	-	-	-	-	-	2 (2)	-	-	-	77	71

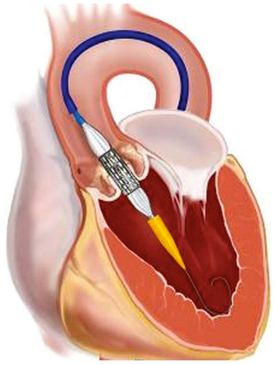
SD, standard deviation; *IABP*, Intra Aortic Balloon Pump; *us*, units; *MACCE*, Major adverse cardiovascular and cerebral events

Figure 1: Procedural, 30-d clinical outcomes & long-term survival following transcatheter aortic valve implantation

METHODS

Electronic searches were performed in 2 databases from January 2002 to November 2011: PubMed and Cochrane Database of Systematic Reviews. The study population was classified as patients who would be considered for TAVI in the United States, therefore of high surgical risk with AS or those deemed not suitable for surgical AVR. The Edwards SAPIEN bioprosthesis is a balloon-expandable stent and the Medtronic CoreValve is a self-expanding percutaneous porcine aortic valve stent. A 5-cm skin incision for exposure was used for axillary/subclavian access. Antegrade transapical aortic valve implantation was performed via a left anterolateral mini-thoracotomy while retrograde aortic implantation was performed through a partial upper mini-sternotomy. The primary end points included feasibility, safety, efficacy, and durability of the device based on echocardiographic findings and clinical status. A meta-analysis was not appropriate because no comparisons among different devices or techniques of insertion have been reported, sample sizes are relatively small, and potential differences in different generations of prostheses may also exist. Prospective and retrospective experimental or observational studies were included, however case reports, case series, abstracts, editorials, and expert opinions were excluded. This systematic review only targeted studies & patient subsets that included high-risk patients with severe AS that only received TAVI via a subclavian/axillary artery, transapical, or transaortic approach.





RESULTS

The overall procedural success rates ranged from 90% to 100%. All studies determined procedural success based on 3 distinct end points: adequate technical placement, normal bioprosthesis performance, & operative outcome. The range of these adverse events was the following: 30-day mortality (0%-18%); myocardial infarction (0%-15%); cerebrovascular accident (0%-6%); aortic dissection/perforation/rupture (1%-8%). The overall 30-day MACCE (major adverse cardiovascular & cerebral events) ranged from 2-35%, while survival at 6 months was between 59-93%. Survival at 1 year (70-72%), 2 years (66%), & 3 years (58%). All studies demonstrated significant improvement in hemodynamic performance ($p < .05$). Mean aortic valve area increased from 0.5-0.7 cm^2 to 1.4-1.7 cm^2, mean pressure gradient decreased from 40-56 cm^2 to 6-12 cm^2, left ventricular ejection fraction ranged from 47-56% before and 54-61% after TAVI. At 1-month follow-up, the study patients had on average improved their NYHA functional class at least by 1 grade, limited only by their previous medical conditions. These outcomes were followed out to 3 months, 6 months, 12 months, & 24 months establishing a stable improvement in functional class. There was no significant functional valvular deterioration upon echocardiography during the assessment period. Quality-of-life scores improved with statistical significance ($p=0.002$). A quality-of-life evaluation collected a self-assessed general health state on a scale of 0-100%. Preoperatively the patients rated themselves at 55±17%, this improved to 68±16% at 30 days postoperative ($p<0.001$).

Study	n	Mean aortic valve area before TAVI (cm2) ± SD	Mean aortic valve area after TAVI (cm2) ± SD	Peak pressure gradient before TAVI (cm2) ± SD	Peak pressure gradient after TAVI (cm2) ± SD	Mean pressure gradient before TAVI (cm2) ± SD	Mean pressure gradient after TAVI (cm2) ± SD	LV ejection fraction before TAVI (%) ± SD	LV ejection fraction after TAVI (%) ± SD	NYHA functional class at baseline	NYHA functional class after TAVI	Death at 6 mo, n (%)
Vancouver[1]	71	0.6 ± 0.2	1.4 ± 0.3	-	-	44 ± 16	10 ± 4	56 ± 13	61 ± 7	3.3 ± 0.8	1.7 ± 0.8	-
Frankfurt[2]	26	0.6 ± 0.1	-	-	-	-	6 ± 2	-	-	3.5 ± 0.4	-	-
Paris[3]	18	-	-	-	-	-	-	-	-	3.3 ± 0.7	-	-
Multicenter[4]	59	0.5 ± 0.2	-	-	18 ± 11	-	9 ± 6	47 ± 16	-	3.4 ± 0.5	-	13 (22)
Multicenter[5]	40	0.6 ± 0.1	1.6 ± 0.4	65 ± 15	15 ± 5	40 ± 10	8 ± 3	52 ± 15	55 ± 19	3.3 ± 0.5	2.3 ± 0.8	13 (33)
Munich[6]	137	-	1.6 ± 0.4	-	-	-	12 ± 4	-	-	3.1 ± 0.3	1.7 ± 0.6	-
Paris[7]	17	0.6 ± 0.3	1.4 ± 0.4	-	-	47 ± 13	8 ± 4	52 ± 14	-	-	-	-
Multicenter[8]	54	-	-	85	17	51	10	-	-	-	-	3 (9)
Milan[9]	12	0.7 ± 0.2	-	97 ± 19	-	56 ± 11	10 ± 4	54 ± 14	54 ± 9	-	1.2 ± 0.4	1 (8)
London[10]	108	-	-	-	-	-	-	49 ± 13	-	-	-	30 (27)
France[11]	83	0.7 ± 0.2	1.7 ± 0.5	-	-	46 ± 16	11 ± 5	51 ± 14	55 ± 13	-	-	-
Belgium[12]	96	0.6 ± 0.2	-	-	-	49 ± 16	8	55 ± 14	58	-	-	-

TAVI, Transcatheter aortic valve implantation; *NYHA*, New York Heart Association; *SD*, standard deviation; *LV*, left ventricular

Figure 2: Echocardiography measurements & clinical data following transcatheter aortic valve implantation

DISCUSSION

The ongoing U.S. PARTNER trial (Placement of AoRTic TraNscathetER Valve) compares TAVI versus surgical AVR in patients at high or extreme surgical risk. Large centers enrolled in this massive nationwide study have already released extremely promising data.
Feasibility: Procedure success rate ranged from 90% to 100%. However the majority of studies included in this systematic review demonstrated procedural success rates of 100%, demonstrating a definite feasibility of the procedure.
Safety: Ye and colleagues demonstrated survival at 1, 2, and 3 years of 72%, 66%, and 58% with the most definitive and long-term dataset following patients that had transapical TAVI, which is the longest standing non-traditional access. In a report by Kojodjojo and associates, 62 patients who were declined by surgeons for conventional AVR had approximate survivals of 50%, 25%, and 10% at 1, 2, and 3 years. This demonstrated significant survival benefit after TAVI.
Durability: Echocardiographic measurements up to 12-24 months of follow-up did not demonstrate significant functional deterioration. Assessment of the long-term durability will require a minimum of 5-10 years of follow-up. Given the limited life expectancy of this select population currently considered for TAVI, this may not be practical.
Efficacy: NYHA functional class was clinically lower by an entire unit from one month to up to 36 months postoperatively. After successful insertion, patients demonstrated remarkable improved quality of life, decreased gradients, improved orifice area, and return to a better functional performance. There was also statistically significant improvement in a self-assessment of general health state from 55% to 68% on a scale of 0-100%.

CONCLUSION

There is a lack of comparative studies and data on long-term efficacy and durability in non-femoral delivery of TAVI in the current literature. The relatively unproven nature and inherent risks of this new therapy mandate a formal team approach to patient selection with randomized controlled trials and rigorous follow-up to show whether different techniques for access are superior to conventional approaches. Before further convincing evidence becomes available, there is a definite need for further investigation in implantation technique, device positioning, as well as these devices themselves. However many of the basic questions of durability, safety, and efficacy compared to open surgical AVR will be demonstrated in time by the high-risk surgical arm of the current FDA-approved PARTNER trial. Meanwhile, decision on eligibility and approach must be individualized and assessed by a multidisciplinary team of cardiologists, cardiac surgeons, and cardiac anesthesiologists. One of the main challenges in the future will be the determination of clear indications with accurate risk stratification for surgical and interventional treatment of aortic stenosis. 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 approaches for TAVI and its clinical implications.