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TAVR in Patients with a Low STS Score: A Cohort Study with a Mean Follow Up of 2 Years

Khaled Al-Shaibi [a,*], Waqar Ahmed [a], Walid Abukhudair [a], Yousef Nosir [a], Abdulaziz Al-Shaibi [b], Rayan Kateb [a], Mirvat Alasnag [a]

[a] King Fahd Armed Forces Hospital, Jeddah, Saudi Arabia
[b] King Abdulaziz University, Jeddah, Saudi Arabia

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ABSTRACT

Background: Partner 2 and SURTAVI trials (mean STS score of 5.8 and 4.5) support extending TAVR into the intermediate risk group. We present our results of TAVR in a group with mean STS score of 2.9 and 2 year follow up.
Methods: This is a prospective cohort study of 46 consecutive patients undergoing TAVR between 2011 and 2016. All patients had severe symptomatic AS. Age, functional status, coronary disease, co-morbidity and imaging parameters were assessed. Patients were followed up for 12–60 months.
Results: 46 patients with a mean age of 75 years were enrolled. Mean EF 56%, mean MG 52 mm Hg and mean PG 87 mm Hg. The mean STS score was 2.9. Forty-two underwent transfemoral and 4 transaortic TAVR. Forty-five of 46 valves were implanted successfully. One patient had moderate perivalvular regurgitation (PVR). Post-procedure mean MG was 11 mm Hg. There was one procedure related stroke and one intraprocedural death. Five patients (10.8%) required a permanent pacemaker. 30-day mortality was 2 of 46 (4.3%). Mean follow up was 28 months. Mean MG at 2 years was 12 mm Hg. Late cardiac mortality occurred in 1 patient.
Conclusion: TAVR in this group with a low STS score was successful with excellent valve performance. Although the STS score identifies intermediate and high risk patients, it does not account for the overall frailty and limited mobility of many elderly patients placing them at a higher surgical risk despite their low STS scores. A scoring system that captures all such factors is required. Finally, a large scale randomized trial with long term follow up determining the validity of TAVR in truly low risk individuals is necessary.

1. Background

Severe aortic stenosis has a 50% two year mortality after the onset of symptoms [1]. For many years, elderly patients with significant co-morbidities were denied surgical aortic valve replacement. In fact, in clinical practice, prior to the transcatheter aortic valve replacement (TAVR) era, up to 30% of patients with severe symptomatic aortic stenosis were not offered surgery [2,3]. The era of TAVR for severe symptomatic aortic stenosis was heralded by the first in man experience published by Cribier et al. in 2002 [4,5]. The PARTNER B trial, published in 2010, established transcatheter aortic valve replacement as the preferred method of treatment in patients deemed inoperable [6]. The PARTNER A trial, published a year later, further extended the indications for transcatheter aortic valve replacement to patients deemed high risk for surgical aortic valve replacement (STS score > 10). This trial demonstrated that transcatheter and surgical aortic valve replacement were associated with similar rates of survival at one year although transcatheter procedures were associated with a higher stroke rate as well as a higher major vascular complication rate [7]. In 2014, publication of the US CoreValve pivotal trial demonstrated for the first time that TAVR in patients with a high STS score (mean STS score 7.4) was associated with a higher one year survival compared to those who underwent conventional surgical aortic valve replacement [8]. Refinements in the technology and increasing operator experience have led to progressive reductions in the incidence of stroke, major vascular complications and perivalvular regurgitation (PVR) associated with TAVR. Given the observed reduction in TAVR related procedural complications and reductions in PVR, the PARTNER 2 trial was conducted to test the hypothesis that transcatheter aortic valve replacement was non-inferior to surgical aortic valve replacement in an intermediate risk population. The results of PARTNER 2 Trial published in early 2016 unequivocally demonstrated that in intermediate risk patients (STS = 5.8%) TAVR was similar to surgical aortic valve replacement with respect to the

* Corresponding author at: King Fahd Armed Forces Hospital, PO Box 9862, Jeddah 21159, Saudi Arabia.
E-mail address: kfalshaibi@gmail.com (K. Al-Shaibi).

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primary endpoints of death and disabling stroke. This study suggests that transfemoral TAVR in intermediate risk patients may in fact be superior to surgical aortic valve replacement [9]. The SURTAVI trial demonstrated the non-inferiority of TAVR compared to surgical aortic valve replacement in an intermediate risk group of patients with a mean STS = 4.5% [10]. In our cohort, we identified patients with a low STS score (< 4) who underwent TAVR and followed them up using clinical and echocardiographic parameters for a mean of 28 months.

2. Methods

2.1. Patients

All patients were referred to our center for surgical aortic valve replacement for severe symptomatic aortic stenosis. The patients were initially reviewed by our cardiac surgery department. All those rejected by the cardiac surgeons for surgical AVR whether due to co-morbidities, prior surgery, porcelain aorta, advanced age or frailty were then referred to the multidisciplinary heart team. Patients for whom TAVR was deemed to be potentially beneficial and not futile were then evaluated for suitability for TAVR. The evaluation included imaging with transesophageal echocardiography, multi-slice CT scan and coronary angiography. The measured parameters included ejection fraction (EF), aortic peak and mean gradients, annulus area, annulus to left main ostium distance, aortic valve morphology, calcium distribution, coronary sinus depth, sinotubular junction diameter, calcification and tortuosity of the aorta and iliofemoral vessels, coronary disease and concomitant valvular disease. Based on the review of our database, all consecutive cases deemed to be appropriate for TAVR with an STS score < 4 were included in this analysis.

2.2. Device and procedure

A total of 46 patients were identified in our database to have a low STS score (< 4). They constitute the cohort for this study. All procedures were performed under general anesthesia with trans-esophageal echocardiographic guidance. Forty-two patients underwent transfemoral TAVR, while 4 patients underwent transaortic TAVR. The selection of the access site was based on the CT scan assessment of the aorta and iliofemoral vessels. Size, calcification and tortuosity were the key determinants. All patient in whom screening coronary angiography had demonstrated a need for percutaneous revascularization (PCI), the PCI was performed 4–6 weeks before the TAVR procedure. Between December 2011 and October 2014 all valves implanted were the EDWARDS SAPIEN XT valves. After November 2014, the valves implanted were EDWARDS SAPIEN 3 valves. The first 13 transfemoral cases were performed via a surgical cutdown. All subsequent transfemoral cases were performed percutaneously and the arteriotomy site closed with two Proglide perclose devices. Aortic Valve prosthesis sizing was primarily based on the aortic annulus diameters as derived from the annulus area obtained by CT scan. In the majority of patients intra-procedural balloon sizing was also used to confirm the appropriateness of the size of the selected valve prosthesis. Procedure related data are summarized in Table 3.

2.3. Statistical analysis

Categorical data are presented as the number of events and frequencies. Kaplan–Meier survival curves summarize time to event outcomes. Continuous data are presented as mean ± SD. All analyses were performed with R version 2.5.13 (R Core Team, 2013).

3. Results

3.1. Patients

The mean STS score of the studied patient population was 2.9. The major reasons for rejection by the cardiac surgery department were patients' age, limited mobility and frailty based on a subjective assessment of two surgeons. Other reasons included prior CABG (5 patients) and porcelain aorta (2 patients). The mean age of this cohort was 75.4 years with 28 males and 18 females. Coronary artery disease was present in 12 patients of which 5 had prior CABG with patent grafts. Five patients underwent planned PCI prior to TAVR and two patients had coronary disease that was non-critical and was treated medically. The mean ejection fraction was 56% with an average peak aortic gradient of 87 mm Hg and an average mean gradient of 52 mm Hg. Only 5 patients had concomitant mitral regurgitation that was not significant. Tables 1 and 2 summarize the baseline characteristics of this cohort of patients.

3.2. Procedure outcomes

Forty-five out of 46 devices were successfully implanted. There were no cases of device embolization or annular disruption. None of the patients required the placement of a second valve. Furthermore, only 3 patients required post-dilatation of the implanted valve at the conclusion of the procedure. PVR that was more than mild was identified by intraprocedural TEE in only 1 patient who had moderate PVR. The mean trans-aortic gradient post-procedure was 11 mm Hg.

Only five patients required the placement of a permanent pacemaker. In two of these patients, the indication for a pacemaker was complete heart block occurring during the procedure (both of these patients had preexisting RBBB). In one patient the indication for a permanent pacemaker implantation was alternating RBBB and LBBB identified in the first 24 h post-procedure. Two other patients had a permanent pacemaker implanted for new LBBB. This was early in our experience and we no longer routinely implant pacemakers for isolated LBBB.

One patient suffered an intraprocedural stroke. Based on neurological/radiological assessment of the infarction pattern seen on a brain CT Scan, this was diagnosed as a watershed infarction by our neurologists likely induced by intra-procedural hypotension. Of note, this was the third TAVR performed in our center for an 84 year old lady with very limited mobility. There was significant hypotension that occurred

Table 1
Baseline characteristics.

	$N = 46$
Age (years)	75.43 ± 6.66
Gender - female	18 (39.13%)
Creatinine	81.3 ± 24.07
Diabetes	22 (47.83%)
Hypertension	36 (78.26%)
Hyperlipidemia	28 (60.87%)
Liver disease	0 (0.0%)
Renal insufficiency	3 (6.52%)
Pulmonary disease	6 (13.04%)
Coronary artery disease	12 (26.09%)
Peripheral vascular disease	1 (2.17%)
Mitral regurgitation (Grade 1–2)	5
LV systolic dysfunction	13 (28.26%)
Cerebrovascular disease	2 (4.35%)
Coagulopathy	0 (0.0%)
Porcelain aorta	2 (4.35%)
Prior PCI	5 (10.87%)
Prior CABG	5 (10.87%)
STS score (%)	Mortality 2.85 ± 1.35 M&M 16.42 ± 4.26

Table 2
Baseline imaging.

		N = 46
EF (%)		55.98 ± 8.59
Annular diameter (mm)		
TTE	N = 33	21.45 ± 1.67
TEE		22.11 ± 1.97
MSCT		22.48 ± 1.67
MR		0.89 ± 0.74
AVA		0.69 ± 0.18
Mean gradient (mm Hg)		51.54 ± 12.63
Peak gradient (mm Hg)		87.31 ± 19.58

during the procedure while positioning the valve with rapid ventricular pacing.

Two patients had left main occlusion after valve implantation. One was successfully treated with stent implantation. This patient has now completed a 3 year follow up and is doing very well. The second case was our only procedural death. In this patient, the possibility of left main occlusion was anticipated based on the CT scan measurements. The left main artery was engaged with a guiding catheter. A drug eluting stent was positioned in the coronary artery before the valve was deployed. The left main occlusion was promptly recognized after the valve was implanted at which point the stent was deployed successfully with an excellent immediate angiographic result. There was immediate resolution of the hypotension, acute LV dysfunction and acute mitral regurgitation that had been documented by intra-procedural TEE. The patient developed acute stent thrombosis 20 min following reversal of heparin with protamine sulphate prior to sheath removal. Unfortunately, in spite of our attempts to revascularize the LM, she could not be saved. It is noteworthy that this patient did not receive loading doses of clopidogrel and aspirin.

Peripheral vascular complications occurred in (7/46, 15%) patients and mainly during our early experience when surgical cutdowns were used routinely (3/13, 23%). Vascular complications decreased significantly after the adoption of a percutaneous approach (4/29, 13%). All peripheral complications were treated successfully using percutaneous approaches and did not require surgical intervention. Peripheral rescue was in the form of a covered stent, local thrombin injection for a pseudoaneurysm (day 4), placement of a common femoral stent and balloon dilatation of a narrowed arteriotomy site. The immediate post-procedure outcomes are summarized in Table 4.

All patients were treated post-TAVR with dual antiplatelet therapy (aspirin and clopidogrel). If the patient had atrial fibrillation, he or she was treated with warfarin alone and a target INR of 2–3 was recommended.

4. Clinical & echocardiographic follow up

The 46 patients were followed for a mean duration of 28 months. None were lost to follow up. Our follow up consisted of both clinical and echocardiographic evaluations at 3, 6, 12, 18 and 24 months and annually thereafter.

In addition to the one procedural death described above, one further 30-day mortality occurred. This patient suddenly collapsed on day 6 post-TAVR after going to the bathroom. She was immediately resuscitated and bedside echocardiography demonstrated a normally functioning transcatheter heart valve in the aortic position with an acutely dilated right ventricle and severe pulmonary hypertension not previously present. Of note, the patient had received local thrombin injection to treat a pseudoaneurysm of the common femoral artery 48 h before her collapse. A diagnosis of acute massive pulmonary embolism was made. Despite our best efforts, including administration of thrombolytic therapy, the patient could not be saved.

Table 3
Procedure related data.

		N = 46
Access	TA	4 (8.7%)
	TF	42 (91.3%)
Size of valve	23	33 (71.74%)
	26	13 (28.26%)
Type of valve	SAPIEN XT	25 (54.35%)
	SAPIEN-3	21 (45.65%)
Technical success	Yes	45 (97.83%)
	No	1 (2.17%)

Table 4
Immediate procedure outcome.

	N = 46
Post-procedural mean gradient (mm Hg)	10.93 ± 4.68
Post-dilation	3 (6.52%)
PVR	
0	39 (84.78%)
1	6 (13.04%)
2	1 (2.17%)
Complete heart block	5 (10.87%)
Bundle branch block	6 (13.04%)
Permanent pacemaker	5 (10.87%)
Vascular complications	7 (15.22%)
Stroke	1 (2.17%)
Coronary obstruction	2 (4.35%)
Device embolization	0 (0.0%)
Annular rupture	0 (0.0%)
Bleeding requiring transfusion	3 (6.52%)
Pericardial effusion or tamponade	6 (13.04%)
Death	1 (2.17%)

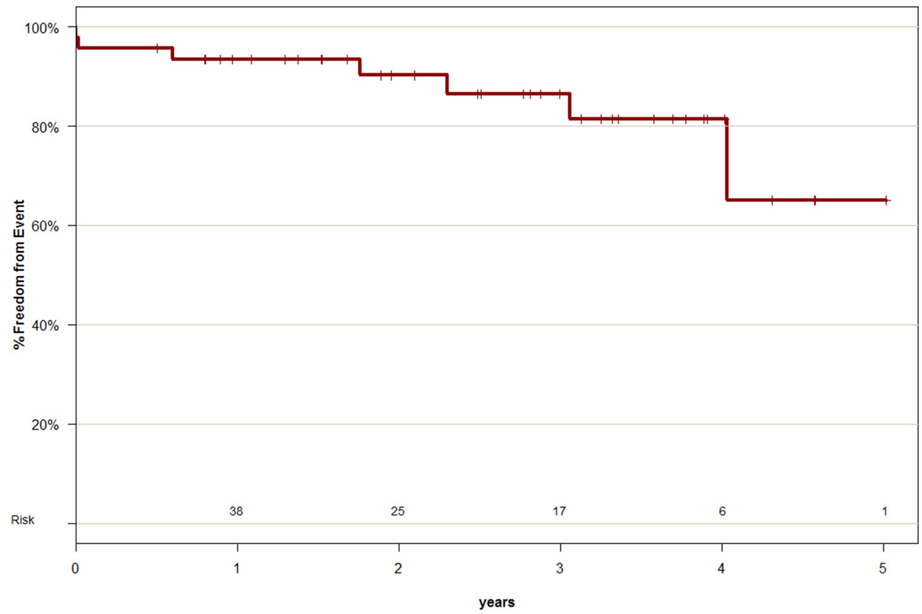
Five more deaths occurred during the 60 month follow up period (4 non-cardiac and 1 sudden death). The one sudden death occurred at home with no prior illness or warning 48 months post-TAVR. Two deaths were due to community acquired pneumonia occurring 21 and 28 months respectively post-TAVR with a documented normally functioning TAVR valve. One death was due to hepatocellular carcinoma and occurred 37 months post-TAVR. The fifth mortality was due to a massive intracerebral bleed that occurred 8 months post-TAVR.

In summary, for those patients who were discharged alive from the hospital after a successful TAVR procedure, the mean 2 year survival was 93% (Graph 1). Only one late death occurred possibly attributable to an unknown cardiac cause. All other deaths were of a non-cardiac cause as the echocardiograms revealed a normally functioning aortic valve prosthesis. Only two strokes occurred in this cohort. One was an intraprocedural stroke early in our TAVI experience. The second was an intracerebral hemorrhage that occurred nine months post-procedure. That patient was on dual antiplatelet therapy (Graph 2).

During the post-procedure echocardiographic evaluation, the mean aortic valve gradient remained stable with a pre-hospital discharge gradient of 11 mm Hg and at 2 year follow up a mean aortic gradient of 12 mm Hg was recorded. Furthermore, for all those in whom trace to mild paravalvular regurgitation was identified, the paravalvular regurgitation did not worsen over time. In the one patient with moderate

Table 5
Echocardiographic follow-up.

	N = 44
Last Echo (days from procedure)	
Mean ± SD	742.95 ± 437.13
Min; max	72;1714
Last ECHO mean gradient (mm Hg)	
Mean ± SD	12.84 ± 4.51
Last ECHO PVR	
None	23/45 (51.11%)
Trace	12/45 (26.67%)
Trivial	3/45 (6.67%)
Mild	6/45 (13.33%)
Mod	1/45 (2.22%)



Graph 1. 5-year survival.

paravalvular regurgitation immediately post-TAVR, the degree of regurgitation regressed over a 2 years follow up period until his death from hepatocellular carcinoma 37 months post-TAVR (Table 5).

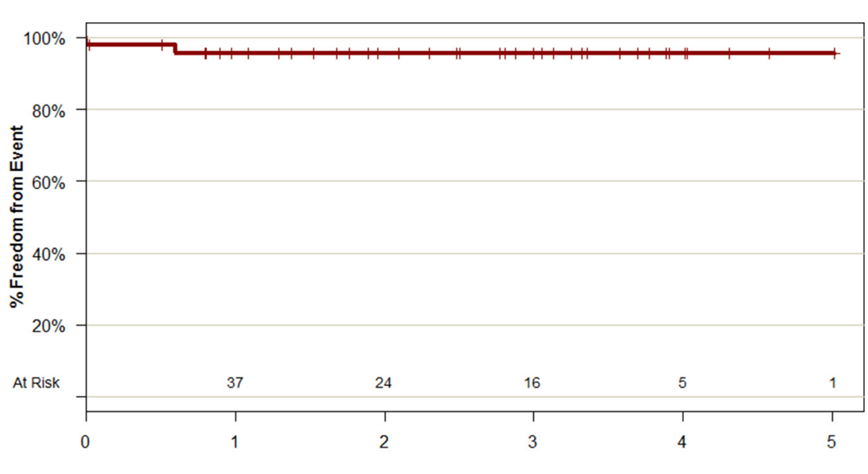
5. Discussion

Many factors are taken into consideration when determining the appropriate treatment options for patients with severe symptomatic aortic stenosis, namely conventional surgical valve replacement or TAVR. The surgical risk scoring system alone does not capture other important variables such as advanced age, patient mobility and frailty which add to the risk of any surgery. In such patients, we believe TAVR offers an excellent alternative treatment.

This is certainly in keeping with the trends observed with TAVR as both the procedure and device technology have been refined. In addition, with increasing operator experience, procedure related complications have significantly decreased especially the vascular complications, stroke and paravalvular regurgitation. In fact, the rate of death from any cause at one year reported in the CoreValve pivotal trial was 14.2% for TAVR in a group of patients with a STS score of 7.4. It is notable, that in our group of patients with a lower STS-score of 2.9, the one year all-cause mortality was substantially lower at 6.5%.

Furthermore, the two year rate of death from any cause or disabling stroke at 2 years was reported to be 19.5% for TAVR in PARTNER 2 (mean STS-score 5.8) and 12.6% for TAVR in SURTAVI (mean STS-score 4.5). Once again, in our cohort of patients with a low STS score the rate of death or disabling stroke at 2 years was lower (10.8%) (Graph 2). Additionally, during the two years of follow up there was no deterioration in valve function as assessed by echocardiography. This is in keeping with published transcatheter heart valve trials. Permanent pacemaker implantation is another concern frequently raised when discussing TAVR in a low risk population. In our series with the Sapien 3 valve, the permanent pacemaker implantation rate was only 10.8%. In this lower risk elderly population issues related to pacemaker implantation and valve durability are less of a concern given these patients' shorter predicted life expectancy.

The two in-hospital mortalities that occurred we believe could have been prevented (acute stent thrombosis and pulmonary embolism). Since the patient died of acute stent thrombosis described above, we have modified our protocol to include loading with aspirin and clopidogrel in all patients prior to any TAVR procedure. The late



Graph 2. Stroke.

mortalities were for the most part non-cardiac and unrelated to the aortic valve prosthesis.

6. Limitations

This cohort is an observational study of select patients that does not have the same implications of a randomized controlled trial comparing TAVR to surgery in individuals with a low STS score. It is also a small size with a mean follow up of only 28 months. A large scale randomized trial with longer follow up is necessary to demonstrate the utility of TAVR in low risk patients. Clearly, the results of our observational cohort study cannot be extended to a low risk group of younger patients or patients with bicuspid valve pathology.

7. Conclusions

In our group of elderly patients with a low STS score (mean 2.9), TAVR was successful and safe. Excellent immediate results were obtained and valve performance remained durable out to a mean follow up of 28 months. Although the STS score can identify intermediate and high risk patients, it doesn't account for the overall frailty and limited mobility of many elderly patients. Frailty in particular places elderly individuals at a higher surgical risk despite their low STS scores. A scoring system that captures all such factors is required. Finally, a large scale randomized controlled trial with long term follow up determining the validity of TAVR in truly low risk individuals is necessary.

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