Transcutanous aortic valve replacement with Medtronic CoreValve in a public-private partnership hospital complex

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ABSTRACT

Objective: The aim of this study was to assess the initial experience of transcutaneous aortic valve implantation (TAVI) in a high risk aortic stenosis population not suitable for conventional surgical valve replacement.

Background: No data exist for TAVI with Medtronic CoreValve in South Africa and especially not in a public private partnership hospital complex.

Methods: Retrospective data regarding severe aortic stenosis evaluation, risk stratification and management were evaluated over a 24 month period.

Results: A total of 106 patients were evaluated of whom 17 were accepted for surgical valve replacement (SVR) while TAVI was attempted in 25. The CoreValve was successfully implanted in 96% (24/25) of the cases. No procedural or peri-procedural deaths occurred. Three patients required permanent pacemaker insertion in the peri-procedural period and 2 patients had vascular access complications requiring blood transfusion only. Median hospital stay was 3.7days (range: 2 - 7). Aortic valve gradient showed a significant reduction after valve implantation, which was sustained during follow-up (p<0.001). NYHA class symptomatology also improved from a median of 3.3 to 1.0 (p<0.001). During follow-up there were 4 late deaths, not related to the procedure, occurring after 78 to 193 days. Average cost for private and government patients were R268 000.00 and R163 000.00 respectively.

Conclusions: The CoreValve can be implanted with a high success rate. Short term mortality and morbidity are acceptable. Significant symptomatic improvement is gained at follow-up. The financial implications are important.

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INTRODUCTION

In the developed world, aortic stenosis (AS) is the most frequent type of valvular heart lesion found in the elderly. It primarily presents as calcific aortic stenosis in adults of advanced age above 65 years.[1,2] In asymptomatic individuals with severe AS, average event-free survival at 2 years ranges from 20 - 50%. However, in symptomatic patients the prognosis is dismal with survival rates of 15 - 50% at 5 years.[3-5]

Aortic valve replacement is the definitive therapy for severe AS. However, many patients with AS and coexisting conditions are not candidates for surgical aortic valve replacement. In the Euro Heart Survey 33% of 216 patients >75 years presenting with symptomatic severe AS were not referred for surgery.[6] Transcatheter aortic valve implantation (TAVI) is an alternative, less invasive treatment for high risk patients with symptomatic severe AS. In the absence of anatomical contraindications, transfemoral approach is the preferred access route with a procedural success rate of >95%.[7-10] In selected patients, TAVI reduced the rates of both death and hospitalisation. Reported 30 day mortality ranges from 5 - 15%[9-13] with 1 year survival ranging from 60 - 80%.[8,10,14-16] Improvement in symptomatology and valvular hemodynamic were also sustained at 2 years of follow-up.[10,13,16] The long-term durability of TAVI valves still has to be ascertained, but the 3 - 5 year results are promising.[15] Initial results with the Medtronic CoreValve device (Medtronic Inc. Minneapolis, USA) were inferior to those of the rival device. Increasing experience revealed a trend of improved combined safety endpoints.[17] Recent results from the ADVANCE registry have shown procedural success rate of 98%, with 6 month and 1 year survival rates being 88% and 82% respectively.[18]

Recommendations regarding the use of TAVI have been proposed in a recent expert consensus document.[19] These guidelines recommend that TAVI only be attempted in severe symptomatic AS, unsuitable for surgery as assessed by a multi-disciplinary heart team and in hospitals with cardiac surgery facilities on-site.

Universitas Netcare is a Public Private Partnership Hospital complex which forms part of the University of the Free State Medical School of Health Sciences. The aim of this study is to report on the prevalence of aortic stenosis and initial experience with the Medtronic CoreValve.

METHODS

The TAVI programme in our hospital was initiated in 2011. A dedicated multi-disciplinary TAVI team was assembled consisting of 2 cardiologists, 2 cardiothoracic surgeons, an anesthetist (with TAVI experience), 2 radiologists, 2 echocardiographers, 2 catheterisation laboratory trained senior nurses and 2 radiographers. Between January 2011 and January 2013 transthoracic echocardiographic (TTE) data from patients with significant aortic or mitral valvular lesions (aortic stenosis valve area <1cm², mitral stenosis valve area <1.2cm² and aortic or mitral regurgitation with left ventricular dilatation) were assessed. Patients older than 20 years with aortic stenosis were assessed for TAVI or surgical valve replacement (SVR) on clinical and TTE data. Patients who were considered for TAVI, in addition, all had trans esophageal echocardiography (TEE), contrast aortic and outflow tract computerised tomography (CT) scanning as well as cardiac catheterisation.TTE and TEE were done utilising Philips Sonographic Model I E 33. Measurements were done in long axis, 4 chamber and short axial views. The CT scan (GE 750 HD 64 slice Dual Energy) utilises a multi-planar oblique tool to create a double oblique transverse or axial image of the aortic root. Axial images of the aortic annulus are essential because the aortic annulus and coronary sinus are non cylindrical structures. A dedicated hardware programme (Heart Navigator, Koninklijke Philips Electronics, N.V) was used to allow for different CoreValve sizes to be superimposed on the aortic annulus thus optimising valve selection of appropriate size. Routine blood tests, according to the recommended TAVI protocol, were done. Additive and Logistic Euro and Society of Cardiothoracic Risk (STS) scores were calculated and frailty assessed. A final decision regarding TAVI eligibility and SVR ineligibility was made by the multi-disciplinary team. In this regard age, co-morbid conditions, frailty, Euro and STS scores were taken into account. This was then discussed with the patient and fully informed consent was obtained. An agreement was concluded between the Academic Provincial Health Authority and Medtronic Inc. (Minneapolis, USA) regarding financial funding in patients without private medical benefit funding. In patients with medical funding benefit, authorisations were obtained on an ad hoc basis from the medical funders.

TAVI procedure was performed as described by Grube, et al.[20] and the first 22 patients' procedures were carried out under guidance of a proctor. The standard protocol allows for pre-procedural balloon valvuloplasty (BVP) followed by CoreValve self expanding placement and no deviation from this approach occurred. In all patients the procedure was done under general anesthesia and vascular access was gained through the trans femoral approach. In 24 patients a Prostar (Abbott laboratories, Illinois, USA) closure device was used and in 2 surgical exploration. The first 22 procedures were done under guidance of a proctor with extensive experience in TAVI procedure.

RESULTS

Between January 2011 and January 2013, a total of 1 043 patients with significant valvular lesions were defined by means of TTE (Figure 1). Of these, 106 (10.1%) had significant AS. Age distribution showed that 37.7% and 62.3% respectively were older or younger than 75 years. Eight patients were lost to follow-up. Subsequently a total of 98 patients (54 male and 44 female) with significant AS and a mean age 59.7 years (36 - 89 years) were evaluated for TAVI and SVR. Of these 14 were considered unsuitable for both TAVI and SVR. Seventeen patients (mean age 55 years, ranging from 40 - 73 years) had SVR. The average hospital

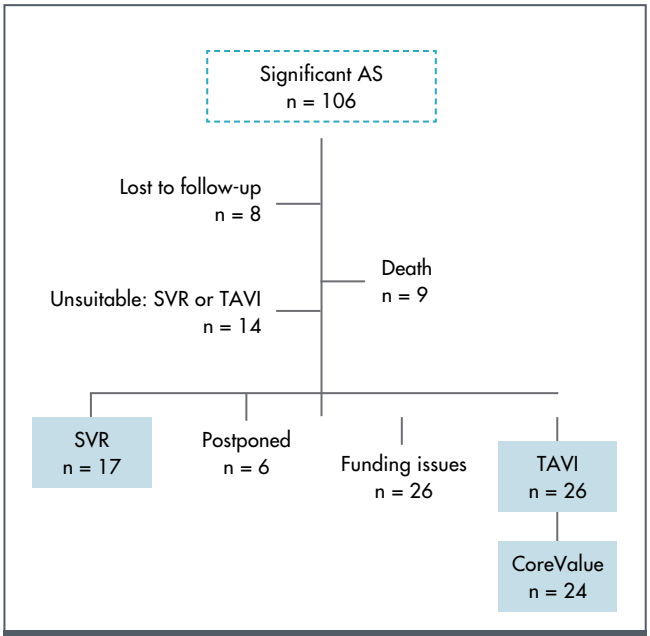

FIGURE 1: Aortic valve stenosis evaluation and outcome

AS = aortic stenosis; SVR = surgical valve replacement; TAVI = transcatheter aortic valve implantation.

stay was 11 days and 2 died during the peri-operative period. Nine patients (average age 76 years) died while awaiting TAVI procedure. Of these, 5 died during hospitalisation (average hospitalisation period 11 days) and 4 at home. Inadequate financial funding (9 government and 17 private) in 26 patients (19 male and 7 female, mean age 76 years) was the reason for delay in the TAVI. In 6 patients TAVI procedure was postponed as the degree of AS was considered to be non critical.

Twenty six patients (14 males and 12 females, median age 82.3 years; range 63 - 88 years) were evaluated for possible TAVI. Of these, 16 were private and 10 public sector patients. All patients were symptomatic with median NYHA class symptoms of 3.3. Median Logistic Euro and STS scores predicted 52.0% and 19.4% mortality rates respectively. The co-morbid conditions reflect on these calculations. Two patients experienced palpitations, 5 patients had had previous syncopal or presyncopal attacks, while 7 other patients complained of angina like symptoms. Co-morbid conditions were present in the form of COPD and pulmonary hypertension in 10 patients, concomitant significant coronary artery disease in 10, previous aortic tissue valve replacement in 3 and impaired renal function (creatinine >140mmol/l) in 4 patients. Renal function was acceptable (average creatinine = 102.7, range 59 - 195mmol/l). Pre-procedural pro BNP values were markedly elevated with a median value of 1154pg/ml. Pre-procedural echocardiographic, cardiac catheterisation and computerised tomographic data are shown in Table 1.

Balloon valvuloplasty with a Nucleus Balloon (NuMED, Hopkinton, NY, USA) size ranging from 18 - 25mm was done before CoreValve placement in 22 patients. In 3 patients with previous tissue SVR, balloon valvuloplasty was not attempted. Both BVP and valve placement was done during short bursts of rapid ventricular pacing at a rate of 120 - 160 beats per minute. In 1 patient aortic valve measurement after BVP was indicative of insignificant residual AS (transvalvular gradient <10mmHg) and no further attempt at valve replacement was undertaken. In our experience the residual transvalvular gradient following BVP is >30mmHg thus explaining the position taken not to continue with CoreValve placement.

TABLE 1: Echocardiographic, catheterisation and CT measurements of the aorta

	Echo	Cath	CT
Gradient (mmHg)	41 (23 - 86)	55 (24 - 123)	
Ava (cm^2)	0.6 (0.3 - 0.9)	0.6 (0.3 - 0.8)	
Annulus (mm)	23 (19 - 30)	23 (18 - 30)	24 (20 - 31)
Cor sinus (mm)		31 (21 - 39)	33 (28 - 40)
ST junction (mm)	25 (15 - 32)	26 (17 - 35)	28 (22 -35)

CoreValve placement with intention to treat was done in 25 patients and implanted in 24 (96% success) using 26mm, 29mm and 31mm valves in 10, 9 and 5 patients respectively. Average contrast volume used, procedural and screening time was 139ml, 92 minutes and 46 minutes respectively. In 1 patient CoreValve placement was unsuccessful as a result of valve displacement into the left ventricular cavity. The valve was retrieved, but due to technical issues the valve was eventually placed in the descending aorta. No further attempt at secondary valve placement was undertaken. Post-procedural echocardiographic and hemodynamic data can be viewed in Figures 2 and 3.

Median post-procedural stay in the intensive care unit (ICU) was 96 hours. No decline in renal function occurred in the peri-procedural period with average creatinine being 99.7mmol/l at discharge. In the 4 patients with pre-procedural elevated creatinine no further deterioration occurred after the procedure. All patients were discharged directly from the ICU. Post procedural complications occurred in 5 patients before discharge. Three patients developed complete atrioventricular dissociation and permanent pacemaker insertion was needed. In 2 patients blood transfusion was required. In one of these, the fall in hemoglobin was related to femoral bleeding from the contra lateral puncture site for additional arterial and venous access required for temporary pacemaker placement. In another, bleeding from the access site closed by means of the Prostar device (Abott laboratories, Illinois, USA) occurred and was treated using conservative measures only.

In an attempt to calculate the private cost component of TAVI, total individual hospital fees were obtained from the private hospital finance division. An average value was the calculated. Average government patient cost was obtained from Universitas Academic public sector hospital finance division according to the individual account of each patient should such an individual have been classified as a private paying patient. According to the finance division such figures reflect the actuarial cost in the public sector.

Average total (CoreValve, delivery system, disposables, hospitalisation and permanent pacemaker if needed) procedural cost for medical aid funded patients was R268 414.00. The corresponding amount for government funded patients was R163 203.00. No professional fees could be charged for government patients. The difference in procedural costs can largely, but not only be ascribed

to the special financial arrangement concluded regarding CoreValve cost between Medtronic and the Universitas Academic public sector component of the private public partnership complex in Bloemfontein. TAVI, in both groups of patients, were done in the same shared cardiac catheterisation theatre according to the local private public partnership agreement. Post-procedural care however took place in different government and private onsite intensive care units.

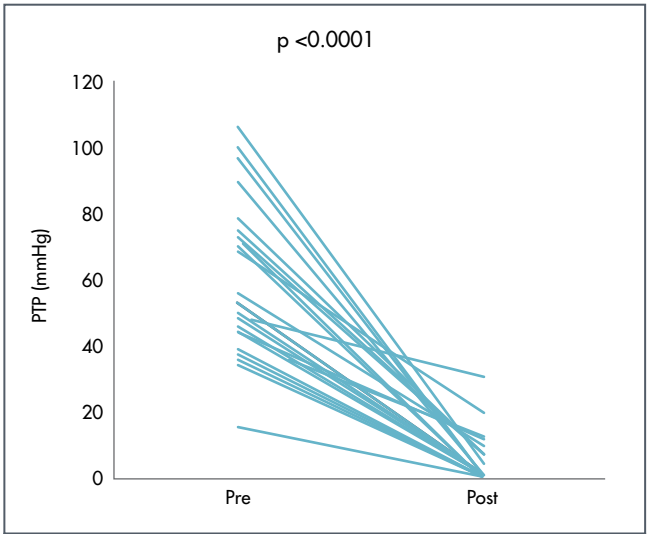

FIGURE 2: Hemodynamic data before and after TAVI
Peak to peak (PTP) pressure gradients immediately before and after valve implantation (mmHg).

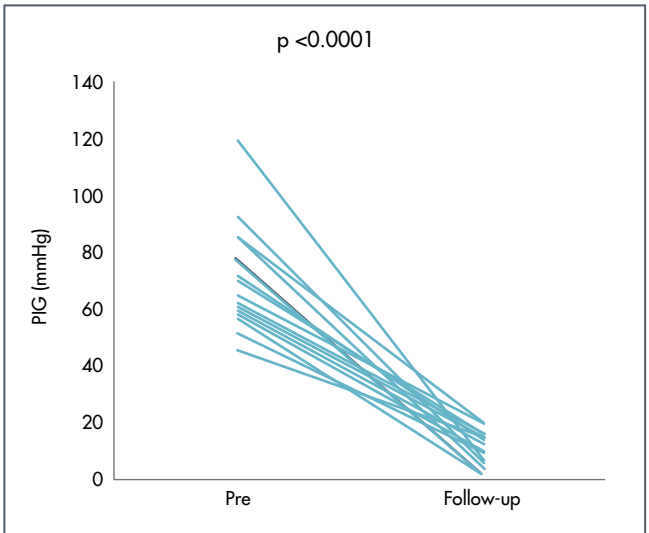

FIGURE 3: Echocardiographic (TTE) aortic valve gradient pre and post TAVI
Routine (awake) peak instantaneous gradient (PIG) on transthoracic echocardiography before (pre) TAVI implantation and at first follow-up visit (post) 30 days following procedure.

Patients were followed up for a period ranging from 3 - 15 months. There were 4 deaths. Of these, 3 had previous tissue SVR prior to TAVI. One male patient demised due to severe chronic obstructive airways disease with severe respiratory failure (day 80 after TAVI). One urinary incontinent male patient developed E.coli septicaemia without echocardiographic evidence of infective endocarditis and died 94 days after implantation. A female patient with a history of major depression died after 5 months because of failure to thrive but with apparent improvement in cardiac symptomatology noted during initial follow-up at 30 days. Death occurred in a male patient related to septicaemia as a result of gangrenous involvement of the left lower leg (non procedural site) 7 months post-procedure. The patient was treated in another hospital and according to the treating surgeon was in a stable cardiac condition. According to this communication, and also the fact that death occurred seven months post-procedure, we have no reason to suspect that this was related to the TAVI procedure. None of these deaths occurred in patients who required permanent pacemaker insertion. Late complete heart block (n = 1) occurred 16 days after the procedure and required permanent pacemaker. All surviving patients at months 6 to 15 experienced substantial symptomatic improvement. Echocardiographic ejection fraction was unchanged but New York Heart Association class improved significantly from a median of 3.3 to 1.0 (p<0.001)(Figure 4). Pro BNP values decreased to a median value of 495pg/ml (p=0.3).

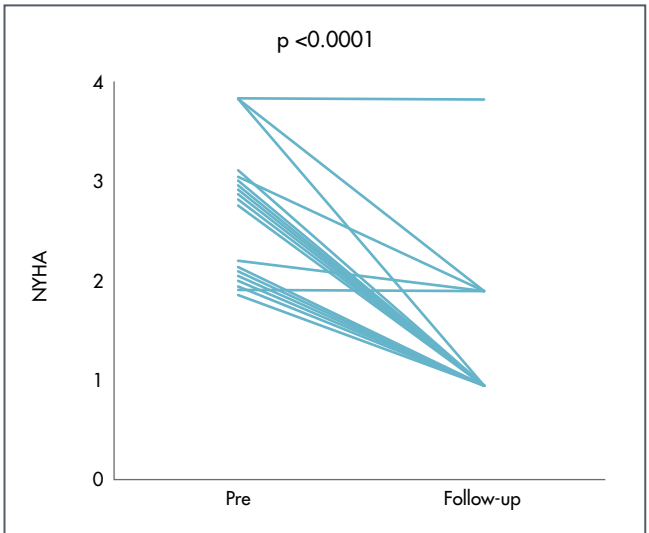

FIGURE 4: NYHA
New York heart association grading of exercise capability before TAVI and at first follow-up visit.

DISCUSSION

In our institution severe aortic stenosis represents 10.1% of all significant valvular lesions. Demographically, our study population included both first and third world individuals and subsequently showed a predominant age distribution less than 75 years which differs noticeably from experience in developed countries where patients are much older.[1,2] In a geriatric population symptomatology may be difficult to interpret, but it is significant that only a minority of patients presented with classical symptoms of angina, syncope or palpitations. Our data have confirmed the adverse outcome of aortic stenosis if treated medically.[3] Many such patients die in hospital with obvious subsequent financial implications.

At present selection criteria for TAVI favour an already high risk population for both morbidity and mortality. The expected survival rates for healthy geriatric patients aged 65, 75, 85 and 95 are 15, 10, 5 and 3 years respectively.[21] Corresponding statistics for patients with severe aortic stenosis are unavailable. In a high risk geriatric population it is thus impossible to draw conclusions regarding impact on mortality and morbidity if treated by means of TAVI. Long term benefits after 10 years will, however, unlikely differ from conventional surgical valve replacement. For the foreseeable future SVR will be the treatment of choice in low risk patients and TAVI will be offered to moderate or high risk and relatively elderly patients.[22]

In our experience, TAVI is a technically demanding interventional cardiologic procedure with a challenging learning curve and initial proctor guidance is a non-negotiable necessity. A multi-disciplinary approach towards patient selection was very meaningful. From a practical perspective, computerised tomography of the aortic valve was the most valuable method for determining CoreValve size prior to implantation. This was related to axial reconstruction of the aortic annulus and coronary sinuses and utilisation of the dedicated hardware programme. The programme allows for different valve sizes to be superimposed on aortic annular reconstructions in axial, sagittal and coronal planes. This represents a huge advantage over TEE, TTE and contrast angiography. Our success rate with the Medtronic CoreValve system compares favourably with previous data.[7-9,12,18] Rapid ventricular pacing is helpful during both BVP and valve deployment. Particular care was taken to limit screening time but despite this it was still more than 30 minutes which is not unexpected in view of the challenging nature of the procedure and our initial inexperience. Although contrast volume used was high, renal function was unaffected. Total procedural time was acceptable.

Post-procedural intensive care stay was remarkably short. This certainly had an influence on procedural cost. Although aortic stenosis is a primary medical benefit (PMB) condition, private medical funders at present reimburse only for medical therapy and SVR as management modalities. Their position is based on the view that present day scientific data regarding the merit of TAVI, as opposed to SVR, are inadequate and that it is not a financially viable option. Also, the fact that in our country TAVI is not available in the public sector precludes them from refunding TAVI even though AS is a PMB. Our data certainly refute the notion that TAVI is unavailable in the public sector. The council of medical schemes has in individual disputed cases advised that TAVI be reimbursed to the amount of R330 000.00. Their position in such financial disputes was that this amount is an estimated reflection of the costs for SVR in the private sector. Figures obtained from a major hospital group (personal communication not to be revealed) showed an average cost for all complicated SVR procedures (78%) amounting to R266 691.00 for 2012. TAVI cost in private medical aid funded patients in our experience was comparable to this amount. The cost difference between private and public funded patients reflects on the financial agreement reached between Medtronic Company and the academic public sector authorities in our center.

The incidence of peri-procedural complications in the form of atrioventricular conduction disturbance was not different from previously reported data.[9,10,12,18] At 3 - 15 months follow-up, mortality rates were also comparable to other studies.[12,13,15,16] Our experience regarding short term mortality for valve-in-valve TAVI differs from other data.[23, 24] In 47 patients reported by Webb, et al. the success rate was 98% with 30 day mortality of 17%. In 3 out of 8 fatalities non cardiac septicaemia was reported. In our limited experience none of the deaths were cardiac related but in 2 patients underlying non cardiac septicaemia was noted. Also, post-procedural death occurred much later in our patients. The significance of post-procedural septicaemia in this patient group probably warrants further investigation. In all the remaining patients, symptomatic improvement was noted. The declines in pro BNP values were substantial, although not significant but the small patient cohort may have had an influence on this result.

CONCLUSIONS

TAVI is technically, logistically and financially a very demanding procedure. Our initial experience with Medtronic CoreValve TAVI was acceptable with a good immediate success and low complication rate. The favourable procedural financial implications are important. Present day guidelines regarding patient selection to include only patients in the highest 10th percentile of risk preclude meaningful long term outcome assessment.[25]

Conflict of interest: none declared.

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