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Feasibility and clinical outcomes in nonagenarians undergoing transcatheter aortic valve replacement with the LOTUS™ valve

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Surgical aortic valve replacement (AVR) is associated with very high peri-operative risk in the nonagenarian population.[1] Patients with severe aortic stenosis treated conservatively have high rates of mortality with poor quality of life and loss of independence.[1] Transcatheter aortic valve replacement (TAVR) has been validated in the high risk elderly population as a viable alternative to surgery with comparable outcomes.[2,3] Results from long term follow up of these patients suggest a clear benefit when compared to medical therapy with regards to mortality and morbidity.[3] However the outcomes and safety of TAVR in the nonagenarian cohort is not well understood. Recent cohort studies have suggested that nonagenarians post TAVR have comparable outcomes to younger patients.[4–6] Traditional surgical risk scores have been poor at predicting risk post TAVR and there is increasing use of other markers of risk such as frailty indices.[7]

The LOTUS™ (Boston Scientific, St Paul, Minnesota) valve is a fully repositionable device which improves precision in delivery with the aim of minimising the risk of paravalvular leak.[8] There is currently limited real world data on the clinical outcomes following LOTUS™ valve implantation. Furthermore, there is currently no literature on the outcomes in the nonagenarian cohort.

The aim of our study was to assess the clinical outcomes of nonagenarian patients who had TAVR with the LOTUS™ valve system and to compare this to a younger cohort. Our hypothesis is that TAVR is a viable and safe treatment option with similar clinical outcomes in nonagenarians.

From April 2012 to October 2015 we prospectively recruited consecutive patients (n = 104) from a single tertiary centre who had TAVR using the LOTUS™ Valve system due to high surgical risk as assessed by the heart team. All patients had baseline investigations including ECG, echocardiography, computed tomography and coronary angiography.

The LOTUS™ valve was used in all patients and sizing was done using multidetector computed tomography measurements based on manufacturer recommendations. All procedures were performed by an experienced TAVR team using a transfemoral approach (using a 18–20 F delivery sheath) in all but one case (transapical) with balloon valvuloplasty prior to implantation. The majority of procedures were done under general anaesthetic (73%) with transoesophageal echocardiography guidance (72%). Patients were admitted to a tertiary coronary care unit with temporary pacing wire backup. Transthoracic echocardiography was routinely performed prior to discharge. Following discharge from hospital patients were reviewed by the heart team or their treating physician.

Ethics approval was obtained from the institution's Human Research Ethics Committee. Patients were divided into two groups. The nonagenarian group were patients with an age at implantation ≥ 88 years to allow for an adequate sample size for statistical analysis whilst patients were allocated to the younger cohort (control group) if age at implantation was < 88 years. As well as baseline demographics, data was collected prospectively for peri-procedural complications and from medical records. Follow-up data was collected either from clinic visits or by telephone calls to patients. Primary endpoint was 30 day mortality and major adverse cardiovascular events. Secondary endpoints included procedure time, length of stay, vascular complications and in-patient rehab rates. Adverse events were defined according to Valve Academic Research Consortium

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(VARC)-2 criteria. All categorical variables were presented as percentages and continuous variables presented as mean ± SD. Statistical significance was performed using the Chi Square test for categorical data or Students *t* test for continuous data. Analyses were considered to be statistically significant if 2 tailed *P* values were < 0.05. Statistical analysis was performed using SPSS v.22.

A total of 104 patients (46% male) were recruited for analysis. Baseline patient characteristics are shown in Table 1. The nonagenarian group had 23 patients with mean age of 90.6 ± 2.6 years. The younger cohort had 81 patients with mean age of 81.1 ± 4.6 years ($P < 0.001$). The younger cohort had a higher proportion with hypertension ($P = 0.013$) whilst surgical risk was higher in the nonagenarian cohort [mean Society of Thoracic Surgeons (STS) score: 5.7 *vs*. 3.6, $P < 0.001$].

A summary of outcomes at 30 days are shown in Table 2. Overall there were similar clinical outcomes in both groups at 30 days. Procedure time was similar in both groups (120.4 min in nonagenarians *vs.* 133.8 min in control group, $P = 0.073$). There was one death in both groups ($P = 0.337$) and no myocardial infarction in either group. There was one disabling stroke in the sample which occurred in a patient in the younger cohort. Length of stay was similar in both groups (mean 9.7 *vs.* 9.5 days, $P = 0.888$), respectively. There was a higher proportion of patients in the nonagenarian group requiring inpatient rehabilitation (43% *vs.* 22%, $P = 0.046$). There was no difference in the rates of new permanent pacemaker insertion post TAVI (30% in nonagenarians *vs*. 22% in younger cohort, $P = 0.416$). Left ventricular ejection fraction was lower in the nonagenarian cohort pre and post implantation (54% *vs.* 59%, $P = 0.077$) and (50.2% *vs.* 60.4%, $P = 0.001$) respectively.

There has been limited evidence of the safety and efficacy of TAVR in nonagenarians. However TAVR is well validated for the treatment of severe aortic stenosis in the elderly and has a mortality benefit when compared to medical therapy alone.[9] Recently, the outcomes of nonagenarian

Table 1. Baseline patient characteristics.

Characteristic	Nonagenarian cohort (age ≥ 88 yrs), *n* = 23	Control (age < 88 yrs) *n* = 81	*P* value
Age, yrs	90.6 ± 2.6	81.1 ± 4.6	< 0.001
Male	12 (52%)	36 (44%)	0.512
Hypertension	13 (57%)	66 (81%)	0.013
Atrial fibrillation	11 (48%)	22 (27%)	0.060
Ischaemic heart disease	5 (22%)	16 (20%)	0.834
Diabetes mellitus	3 (14%)	21 (26%)	0.196
Previous cardiac surgery	3 (13%)	15 (19%)	0.540
Previous PPM/ICD	4 (18%)	5 (6%)	0.091
Previous stroke	2 (9%)	14 (17%)	0.314
Peripheral vascular disease	2 (9%)	8 (10%)	0.865
COPD	6 (27%)	19 (23%)	0.794
NYHA ≥ 3 Prior to TAVI	17 (74%)	56 (69%)	0.658
Mean STS mortality score	5.7 ± 2.2	3.6 ± 1.8	< 0.001
Mean Euroscore mortality	5.5 ± 5.4	4.0 ± 3.3	0.121
Creatinine, μmol/L	109 ± 37	114 ± 103	0.262
Haemoglobin, g/L	118 ± 16	124 ± 16	0.157
Platelets	200 ± 64	204 ± 76	0.217
Mean pulmonary pressure	22.7 ± 6.4	24.1 ± 9.1	0.522
LVEF	53.7% ± 17%	59.1% ± 11%	0.077
Mean gradient, mmHg	44.7 ± 14	49.6 ± 16	0.201
Aortic valve area, cm^2	0.67 ± 0.17	0.73 ± 0.20	0.210
Mitral regurgitation (Grade 3 or 4)	5 (22%)	8 (10%)	0.129

Data are presented as mean ± SD or *n* (%). COPD: chronic obstructive pulmonary disease; ICD: implantable cardioverter defibrillator; LVEF: left ventricular ejection fraction; NYHA: New York Heart Association; PPM: permanent pacemaker; STS: Society of Thoracic Surgeons; TAVI: transcathater aortic valve implantation.

Table 2. Procedural outcomes and follow up data at 30 days.

Outcome	Nonagenarian cohort (age ≥ 88 yrs) *n* = 23	Control group (age < 88 yrs) *n* = 81	*P* value
Procedural/In hospital outcomes			
Procedure time, min	120.4 ± 26.2	133.8 ± 44.1	0.073
Screening time, min	38.3 ± 12.3	38.0 ± 14.2	0.932
Emergency surgery	1 (5%)	2 (2%)	0.635
Major vascular complications	3 (13%)	10 (12%)	0.929
AKIN stage II/III acute kidney injury (%)	0	6 (7%)	0.179
Major bleeding	4 (17%)	12 (15%)	0.762
Clinical outcomes at 30 days			
Death	1 (4%)	1 (1%)	0.337
Myocardial infarction	0	0	-
Disabling stroke	0	1 (1.2%)	0.595
Mean length of hospital stay, days	9.7 (7.4%)	9.5 (8.6%)	0.888
Rehab admission	10 (43%)	18 (22%)	0.046
New PPM Insertion post TAVI	7 (30%)	18 (22%)	0.416
Echocardiography post implantation			
LVEF	50.2% ± 15.7%	60.4% ± 10.3%	0.001
Aortic velocity, m/s	2.1 ± 0.4	2.5 ± 0.4	0.590
Mean aortic gradient, mmHg	10.0 ± 3.7	13.4 ± 4.5	0.277
Mild or greater aortic regurgitation	4 (17%)	15 (19%)	0.952
Mild or greater mitral regurgitation	13 (59%)	34 (42%)	0.216
Estimated pulmonary systolic pressure > 40 mmHg	8/16 (50%)	23/56 (41%)	0.525

Data are presented as mean ± SD or *n* (%). AKIN: acute kidney injury network; LVEF: left ventricular ejection fraction; PPM: permanent pacemaker; TAVI: transcathater aortic valve implantation.

patients from the PARTNER-1 trial were reported showing that TAVR in this high risk group offered significant improvements in quality of life, valve haemodynamics with an acceptable safety profile. Age alone was not found to be associated with increased mortality.[3] However in clinical practice there is a tendency for treatment decisions to be influenced by age. A multidisciplinary approach incorporating frailty indices, nutrition, assessment of cognition and mobility used in context with age and co-morbidities may be a better system of assessing risk compared with traditional surgical risk scores.

The repositionable LOTUS^{TM} valve offers the advantage of improved precision at the time of implant with the aim of minimising the risk of paravalvular leak.[8] Our study is the first to report on the clinical outcomes in nonagenarian patients using the LOTUS^{TM} valve. Overall complication rates in the nonagenarian cohort appeared to be similar to younger patients. Mortality at 30 days was similar in both groups and overall lower that what has been reported in other cohort studies using the Core-Valve and Edwards valve.[3,5] This could be due to the device's unique repositionable mechanism. We observed similar rates of stroke, myocardial infarction and vascular complications. Valve haemodynamics significantly improved post TAVR and was comparable to other patients. There was no significant increase in length of stay in the nonagenarian cohort which is surprising given the potential risk for post-operative medical complications in the elderly. We did observe a significant increase in inpatient rehabilitation admissions which is not unexpected given that many of our elderly patients are frail and previously living alone. This further confirms the importance of frailty indices as a screening tool in elderly patients.

Rates of new pacemaker insertion were similar in both groups. High grade atrio-ventricular and left bundle branch block have been widely reported post TAVR and pacemaker insertion is a known complication.[10] The mechanical stress associated with resheathing and repositioning of the LOTUS valve may also contribute to higher rates of pacemaker insertion observed due to higher rates of atrio-ventricular nodal and bundle branch block associated with oedema, inflammation and possibly transient ischaemia.

There are several limitations in our study. This single centre non randomized study has the potential for selection bias in the nonagenarian group. The sample size for the nonagenarian group was small and long term follow up data was not available for the majority of our patients, so 30 day outcome measures were used for analysis. Similar outcomes measures were not available in patients treated with medical therapy or with surgical AVR.

In conclusion, TAVR using the new repositionable LOTUS^{TM} valve is a feasible and safe treatment option for the treatment of severe aortic stenosis in the nonagenarian population. We suggest the use of a multidisciplinary approach with incorporation of frailty indices rather than age alone as a guide to treatment.

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