Original Article

Outcomes Following Transcatheter Aortic Valve Replacement for Aortic Stenosis in Patients of Extreme Age: Analysis from a Rural Population

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Abstract

Introduction: Previous single- and multi-center studies done in predominantly metropolitan areas have shown transcatheter aortic valve replacement (TAVR) to be a safe and effective treatment modality for patients of advanced age with severe aortic stenosis. However, it is unknown whether similar patient cohorts from rural areas have similar outcomes or if these initial studies are not representative of the experience in more rural areas. **Setting:** This is a single-center health-care system in a predominantly rural area. **Methods:** A retrospective chart review case–control study of 339 consecutive patients who underwent a TAVR for severe aortic stenosis at Sanford Health in Fargo, ND, was performed to determine if advanced age (>80 years of age) at the time of TAVR affects short- and long-term outcomes. **Results:** Despite higher predicted baseline surgical risk**,** predominantly rural patients of advanced age had no significant difference in overall survival at 1-month (93% vs. 97%, $P = 0.228$), 6-month (88% vs. 90%, $P = 0.695$), 1-year (79% vs. 82%, $P = 0.611$), or 2-year (63% vs. 60%, $P = 0.731$) post-TAVR versus younger patients from the same geographical area. Patients of advanced age also had no significant difference in periprocedural or echocardiographic outcomes out to 1-year post-TAVR. **Conclusion:** This study from a predominantly rural area gives evidence to suggest that there is no association between extreme age (>80 years of age) and decreased overall survival. In addition, high baseline Society of Thoracic Surgeons and European System for Cardiac Operative Risk Evaluation predicted risk was not suggestive of worse outcomes in patients of advanced age. This study gives reassurance of the safety of TAVR in patients of advanced age in rural areas.

Keywords: Age, outcomes, survival, transcatheter aortic valve replacement

Introduction

Previous studies have shown transcatheter aortic valve replacement (TAVR) to be a safe and effective treatment modality for patients of advanced age with severe aortic stenosis.[1-3] However, the studies that have directly compared older cohorts of patients to younger patient groups have been limited to either single large metropolitan area health-care system or multicenter analyses of mostly urban centers. To the best of our knowledge, there have been no studies involving TAVR for severe aortic stenosis in elderly patients from the more rural areas of America.

Studies conducted in other area of cardiology gives reason to believe that the outcomes seen in an urban center and metropolitan-based studies may not be representative of the experience of rural centers. For example, in a study published by Baldwin *et al*., patients presenting to rural hospital for acute myocardial infarction experienced an increase in 30-day mortality compared to urban centers.[4] Likewise, in a study from Canada, urban patients were more likely to have office-based physician visits in the 1st year after a heart failure diagnosis and had lower rates of hospitalization than rural patients.[5]

There also have been documented differences in the management of aortic stenosis between urban and rural America. In a study by Vavalle *et al*., patients in the most rural parts of North Carolina had the highest rates of hospitalizations for aortic stenosis and the lowest rates of valvular surgery.[6] Approximately 19.3% of the US population (60 million people)

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lives in a rural area and the composition of rural America today is disproportionally elderly. These facts underscored the importance of the study of the rural elderly population in today's changing health-care landscape.[7] This study aims to describe the outcomes of TAVR for severe aortic stenosis in patients of extreme age from a predominantly rural area.

Methods

A hospital-based, single-institution case–control study was conducted using data from one upper Midwestern integrated health system. We performed a retrospective chart review of 339 consecutive patients who underwent a TAVR at Sanford Health in Fargo, ND, from August 10, 2012, to November 15, 2016, for severe aortic stenosis, defined as an aortic valve area <1 cm^2. The last date of data acquisition was January 4, 2017. The entire cohort was divided into two groups where the patients aged 80 years or older at the time of TAVR were placed in one "extreme age" cohort, while all other patients were designated as controls. Primary outcomes were overall survival at 1-month, 6-month, 1-year, and 2-year post-TAVR. Secondary outcomes were procedural complications, post-TAVR permanent pacemaker implantation, major adverse cardiovascular and cerebrovascular events defined as death from any cause, myocardial infarction, rehospitalization, or stroke, cardiovascular mortality, myocardial infarction, stroke/transient ischemic attack, heart failure exacerbation, or rehospitalization for any reason in defined time periods. Pre- and postprocedural echocardiographic data were also compared. The clinical outcomes were assessed in accordance with the standardized endpoint definitions for TAVR of the Valve Academic Research Consortium-2.[8] Heart failure exacerbation was defined as a gradual or rapid change in heart failure signs and symptoms resulting in a need for a change in therapy or hospitalization.

Informed consent was not required for inclusion in our retrospective study due to the nature of the study and the absence of any direct interventions. This study protocol received dual Institutional Review Board (IRB) approval from the University of North Dakota IRB and from the Sanford Health IRB. The Fisher's exact test was performed to determine the statistical significance of categorical data, and *t*-test or Wilcoxon two-sample test was used to determine the statistical significance continuous variables. All *P* values were two-sided, and $P < 0.05$ was considered statistically significant.

Results

A total of 195 of the 339 patients met study criteria for inclusion in advanced age cohort. Baseline characteristics for both groups are given in Table 1. Statistically significant

Table 1: Baseline characteristics

	Extreme age (*n*=195)	Control (*n*=144)	*P*
Age	85.3 (3.77)	71.1 (7.04)	<0.001
Male sex	107 (55)	81 (56)	0.826
BMI	29.4 (6.15)	32.0 (5.95)	<0.001
Caucasian race	193 (99)	143 (99)	1.000
EuroSCORE (%)	10.41 (6.82)	6.16 (4.61)	<0.001
STS risk score (%)	7.95 (4.14)	5.82 (3.57)	<0.001
Preprocedural HTN	170 (87)	128 (89)	0.737
Preprocedural CAD	148 (76)	100 (69)	0.215
Baseline ejection fraction <40%	23 (12)	27 (19)	0.088
Preprocedural NYHA Class III or IV symptoms	90 (46)	59 (41)	0.376
Preprocedural DM	52 (27)	68 (47)	<0.001
Prior stroke/TIA	21 (11)	17 (12)	0.862
Preprocedural atrial fibrillation	65 (33)	38 (26)	0.190
Preprocedural serum creatinine (mg/dL)	1.25 (0.81)	1.26 (0.90)	0.877
Preprocedural eGFR <60 mL/min	102 (52)	61 (42)	0.079
Preprocedural AAA	25 (13)	12 (8)	0.220
Preprocedural carotid artery stenosis >50% or prior CEA	55 (28)	37 (26)	0.623
Preprocedural dyslipidemia	172 (88)	129 (90)	0.731
Prior CABG	43 (22)	52 (27)	0.005
Prior PCI	82 (42)	42 (29)	0.017
Prior permanent pacemaker	27 (14)	12 (8)	0.125
Prior aortic valvuloplasty	36 (18)	23 (16)	0.566
HMG-CoA reductase inhibitor	135 (69)	105 (73)	0.471
Beta-blocker	141 (72)	109 (76)	0.533
Any anticoagulant	49 (25)	34 (24)	0.799

Values are mean (standard deviation) or *n* (%). STS: Society of Thoracic Surgeons, HTN: Hypertension, CAD: Coronary artery disease, NYHA: New York Heart Association, DM: Diabetes mellitus, TIA: Transient ischemic attack, eGFR: Estimated glomerular filtration rate, CEA: Carotid endarterectomy, CABG: Coronary artery bypass surgery, PCI: Percutaneous coronary intervention, HMG-CoA: 3-hydroxy-3-methylglutaryl-coenzyme, AAA: Abdominal aortic aneurysm, EuroSCORE: European System for Cardiac Operative Risk Evaluation, BMI: Body mass index

differences were noted in age, body mass index, Society of Thoracic Surgeons (STS) risk score, European System for Cardiac Operative Risk Evaluation (EuroSCORE), preprocedural diabetes mellitus, and prior coronary artery revascularization procedures. There were a high amount of significant comorbidities in both groups including an 88% prevalence of hypertension in the entire cohort. Mean age of the entire cohort was 79.2 years of age. Procedural characteristics for both groups are given in Table 2. There were no statistical differences in the specific type of valve used; however, there was small but statistically significant increase in the utilization of the transaortic approach in the younger cohort. Pre- and postprocedural echocardiographic data are given in Table 3. A difference in baseline ejection was found which was not sustained at 1-year post-TAVR. Finally, the primary and secondary outcome data for this study are given in Table 4. Overall survival for the entire study cohort was 80.2% at 1 year and 61.4% at 2 years.

Table 2: Procedural characteristics

	Extreme Age (*n*=195)	Control (*n*=144)	*P*
Approach			
Transfemoral	159 (82)	116 (81)	0.889
Transapical	33 (17)	17 (12)	0.217
Transaortic	1 (1)	6 (4)	0.045
Trans-subclavian	2 (1)	4 (3)	0.410
Transcaval	0 (0)	1 (1)	0.425
Mean LOS after TAVR (days)	4.7 (8.1)	4.8 (5.8)	0.874
Valve type			
First-generation Sapien	57 (29)	35 (24)	0.326
Sapien XT	27 (14)	23 (16)	0.643
Sapien S3	68 (35)	46 (32)	0.642
First-generation CoreValve	35 (18)	37 (26)	0.107
CoreValve evolut	8 (4)	3 (2)	0.366

Values are mean (standard deviation) or *n* (%). TAVR: Transcatheter aortic valve replacement, LOS: Length of stay

Table 3: Echocardiographic characteristics

	Extreme age	Control	*P*
Preprocedural			
Aortic valve area (VTI) (cm^2)	0.83 (0.26)	0.88 (0.29)	0.084
Peak aortic velocity (cm/s)	419.0 (60.1)	414.7 (65.1)	0.528
Peak aortic gradient (mmHg)	72.0 (19.4)	70.5 (21.3)	0.501
Mean aortic gradient (mmHg)	45.2 (12.0)	44.8 (13.4)	0.794
Ejection fraction (%)	59.3 (11.5)	55.4 (13.7)	0.005
Stroke volume (mL)	85.7 (21.9)	86.2 (19.0)	0.845
Moderate aortic regurgitation (%)	17	22	0.326
Moderate mitral regurgitation (%)	24	21	0.599
Severe mitral regurgitation (%)	4	3	1.000
1-year post-TAVR			
Aortic valve area (VTI) (cm^2)	1.99 (0.58)	2.01 (0.63)	0.794
Peak aortic velocity (cm/s)	218.7 (49.3)	223.3 (50.6)	0.585
Peak aortic gradient (mmHg)	20.4 (10.7)	21.0 (9.4)	0.754
Mean aortic gradient (mmHg)	11.8 (6.2)	11.7 (5.4)	0.966
Ejection fraction (%)	57.7 (12.1)	58.6 (14.1)	0.683
Stroke volume (mL)	94.8 (29.5)	91.8 (27.0)	0.550
Moderate aortic regurgitation (%)	15	10	0.330
Moderate mitral regurgitation (%)	16	6	0.076
Severe mitral regurgitation (%)	7	3	0.467

Values are mean (standard deviation) or percentage. VTI: Velocity time integral, TAVR: Transcatheter aortic valve replacement

Discussion

This study adds to the previously published data and gives evidence to suggest that patients of extreme age (>80 years of age) at the time of TAVR do not have asignificantly increased mortality out to 2-year post-TAVR. To the best of our knowledge, this study is the first of its kind and demonstrates this important clinical finding in a patient cohort from a predominantly rural area. The findings of this study help to establish the clinical acceptability of TAVR in the most elderly population, especially those in rural America who may be underrepresented in previous studies.

Much like the study published by Orvin *et al*., this study did find some important differences in baseline characteristics between the older and younger patient cohorts.[2] The "extreme age" cohort had a significantly higher predicted surgical risk, noted in the cohort's STS score and EuroSCORE risk. This finding underlines the limited utility of these scores in TAVR, particularity in older cohorts. The previous work by Beohar *et al*. found that STS risk scores overestimated 30-day and inhospital mortality, which is consistent with the finding of this study.[9] These surgical risk scores should likely not be used for patient selection in the patient over the age of 80.

Correspondingly, like the study done by Orvin *et al*., this study also found that older patients chosen for TAVR have some differences in baseline characteristics as well. In our study, this is notably in the significantly lower rates of diabetes mellitus, prior coronary artery bypass graft surgery, reduced ejection fraction at baseline, and lower average body mass index. This finding was largely consistent with the previous study although our larger study had less statistically significant differences overall.[2] This suggests that the predictors of a poor outcomes that have been derived from larger cohorts may not be useful in older cohorts.[10]

The physical location of this single-center study and its finding which are consistent with data from urban multicenter clinical studies imply many other important corollaries as well. First, this study helps to establish that the limited access to advanced cardiac care does not imply worse outcomes after TAVR. This finding is particularly important given the overall physician shortage in rural states such as North Dakota and the forecast

Table 4: Primary and secondary outcomes

	Extreme age	Control	*P*
Percentage survival >1 month	93 (182/195)	97 (139/144)	0.228
Percentage survival >6 month	88 (139/158)	90 (102/113)	0.695
Percentage survival >1 year	79 (100/127)	82 (78/95)	0.611
Percentage survival >2 year	63 (55/88)	60 (34/57)	0.731
Periprocedural major vascular	8 (15)	10 (14)	0.558
Periprocedural minor vascular	10 (19)	7 (10)	0.434
Periprocedural blood transfusion	11 (21)	8 (12)	0.579
Post-TAVR PPM implantation	9 (18)	10 (14)	0.551
Periprocedural increase in serum creatinine >1.5× baseline	5 (10)	6 (9)	0.812
In hospital			
CV mortality	6 (12)	4 (6)	0.472
MI	1 (1)	1 (1)	1.000
Stroke/TIA	2 (4)	3 (4)	0.727
HF exacerbation	22 (42)	19 (28)	0.685
Discharge to 30 days			
MACCE	18 (32)	18 (24)	1.000
CV mortality	1 (1)	0 (0)	1.000
Myocardial infraction	2 (4)	0 (0)	0.138
Stroke/TIA	1 (2)	1 (1)	1.000
HF exacerbation	18 (32)	13 (18)	0.351
Rehospitalization for any reason	17 (31)	18 (24)	1.000
30 days to 6 months			
MACCE	28 (40)	27 (29)	1.000
CV mortality	1 (2)	3 (3)	0.653
Myocardial infraction	2 (3)	1 (1)	0.639
Stroke/TIA	3 (4)	2 (2)	1.000
HF exacerbation	17 (24)	13 (14)	0.482
Rehospitalization for any reason	27 (38)	22 (24)	0.554
6 months to 1 year			
MACCE	28 (28)	33 (26)	0.513
CV mortality	2 (2)	3 (2)	1.000
Myocardial infraction	2 (2)	3 (2)	1.000
Stroke/TIA	2 (2)	1 (1)	1.000
HF exacerbation	21 (21)	18 (14)	0.709
Rehospitalization for any reason	24 (24)	33 (26)	0.182

Values are percentage (*n*). MACCE events, defined as death from any cause, MI, rehospitalization, and stroke. PPM: Permanent pacemaker, TAVR: Transcatheter aortic valve replacement, CV: Cardiovascular, MI: Myocardial infarction, TIA: Transient ischemic attack, HF: Heart failure, MACCE: Major adverse cardiovascular and cerebrovascular events

for future shortages in cardiologists both nationwide and in rural areas.[11-13] Second, this study implies that geriatric patients can be safety monitored following TAVR in areas affected the most by these shortages. Third, this study infers the safety of TAVR performed at a moderate-sized center as compared to large tertiary care centers.

Finally, our data indicate that unlike other common cardiac conditions, the treatment of aortic stenosis in high surgical risk patients does not suffer any urban to rural differences in overall outcomes. We believe that it is increasingly important that the potential impact of geography and practice setting be continually evaluated to establish the widespread efficacy and safety of cardiovascular care, especially as it relates to cardiac device implantation. The current mechanism for cardiovascular research does not adequately address the specific challenges of rural health care nor do they sufficiently represent the roughly one-fifth of Americans who live in these areas. Pragmatic clinical studies like the one we present here could serve as a model for the efficient study of rural patients undergoing similar procedures in the future.

This study does have some limitations including its retrospective design, single-center experience, and inequalities in the length of post-TAVR follow-up. Like all retrospective analyses, the potential for confounding factors which were not identified and addressed in the study's baseline patient characteristics does exist. This study was designed to capture as many pertinent baseline characteristics as possible to effectively isolate the independent variable as much as possible. Patients in both groups were reasonably well-matched overall; however, we did find a significant difference in TAVR approach, in that

patients in the younger cohort had a higher rate of transapical approach utilization. The impact of this on our result is unclear, in that previous studies that have compared the outcomes of transapical to transfemoral TAVR have yielded conflicting results.[14,15]

Conclusion

In this study from a predominantly rural area, no association between extreme age (>80 years of age) and decrease overall survival was found. In addition, high baseline STS and EuroSCORE predicted risk was not suggestive of worse outcomes in patients of advanced age. This study gives reassurance of the safety of TAVR in patients of advanced age and in rural areas with ongoing physician and cardiology access difficulties.

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Conflicts of interest

There are no conflicts of interest.

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