Gender-related differences in outcomes of transcatheter aortic valve replacement in nonagenarians

Darren C Tsang, Marcos Nores, Mark Rothenberg, Larry Lovitz, Cristiano Faber, Sotiris C. Stamou

Tsang DC, Nores M, Rothenberg M, et al. Gender-related differences in outcomes of transcatheter aortic valve replacement in non-agenarians. Clin Cardiol J 2019;3(1):4-8

BACKGROUND: Multiple studies suggest women have lower intermediate-term mortality risk than men following transcatheter aortic valve replacement, yet no published investigations have evaluated this trend in nonagenarians.

OBJECTIVE: We compare early clinical outcomes and actuarial survival of nonagenarians who underwent transcatheter aortic valve replacement, by gender.

METHODS: A concurrent cohort study of 148 consecutive nonagenarians undergoing transcatheter aortic valve replacement from April 2012 to July 2017 was conducted at a tertiary referral center. Relevant baseline demographics between men and women were compared. Major morbidity, operative mortality, and 5-year actuarial survival were compared between groups. Independent predictors of operative and late mortality were examined.

RESULTS: Compared with men, women presented with higher STS risk scores (women: 7.2% [5.9-8.8%] vs. men: 5.8 [3.8-7.5%]; p=0.002). Women experienced more postoperative atrial fibrillation compared with men (women: 20% vs. men: 9%; p=0.049). Overall operative mortality was similar between groups (women: 4% vs. men: 10%; p=0.181). Actuarial survival at 3 and 5-years was lower in women than men, but this difference did not reach statistical significance (69% and 56% for women, and 58% and 40% for men, respectively; p=0.071). Urgent status was associated with increased risk of operative mortality. Predictors of late mortality included urgent status, coronary artery disease, history of atrial fibrillation, and postoperative prolonged ventilatory support, stroke, cardiac arrest, and pacemaker implantation.

CONCLUSION: Significant gender-related differences exist in nonagenarians presenting for transcatheter aortic valve replacement. While women had lower operative and late mortality, actuarial survival did not achieve statistical significance at 3 and 5-years.

Key Words: *Elderly; Sex-related; Women; Survival; Aortic valve; Aortic stenosis*

Acronyms and Abbreviations: *BAV: Balloon Valvuloplasty; CI: Confidence Intervals; IQR: Interquartile Range; POD: Post-operative Day; STS: Society of Thoracic Surgery; TAVR: Transcatheter Aortic Valve Replacement*

INTRODUCTION

Transcatheter aortic valve replacement (TAVR) has emerged as a safe and effective alternative to surgical aortic valve replacement in high and intermediate-risk groups (1-6). Multiple studies suggest that women have a lower intermediate-term mortality risk than men following TAVR, despite higher perioperative rates of vascular and bleeding complications. Yet, to date, there have been no published investigations that evaluate this trend in nonagenarian patients, a rapidly expanding high-risk group for TAVR that is estimated to quadruple in population size by 2050 (7).

Here in, we compare early clinical outcomes, and actuarial survival in nonagenarians who underwent TAVR between men and women. Secondarily, we identify predictors of early and late mortality following TAVR in the nonagenarian population.

PATIENTS AND METHODS

The TAVR registry at JFK Medical Center was queried to identify all nonagenarian patients who underwent TAVR at the institution from April 2012 to July 2017. A total of 148 consecutive nonagenarians were identified and compared based on gender. Baseline demographics, procedural data, and perioperative outcomes were prospectively recorded and entered into a pre-specified database by dedicated data-coordinating personnel.

Patients

Risk factor assessment was performed during preoperative evaluation and included transthoracic Doppler echocardiography, coronary angiography, carotid duplex ultrasonography, pulmonary function testing, frailty assessment (5-meter walk test, grip strength, and Katz Index of Independence in Activities of Daily Living), and computed tomography of the chest, abdomen and pelvis. The Society of Thoracic Surgery (STS) risk score was calculated to estimate patients' risk of morbidity and mortality for surgical aortic valve replacement.

Nonagenarian patients approved for TAVR included those who had intermediate (STS risk score >3%) or high-risk for operative mortality (STS risk score >8%), and those deemed poor surgical candidates (combined risk of morbidity and mortality >50%) for surgical aortic valve replacement with frailty, based on frailty assessment. A structural heart team comprised of interventional cardiologists, cardiac surgeons, and cardiac anesthesiologists participated in the preoperative evaluation, intraoperative management, and postoperative care of each patient.

Study design and conduct

This is a retrospective cohort study of prospectively collected data from consecutive nonagenarians who underwent TAVR via a transfemoral, transapical, transaortic, or trans axillary approach at JFK Medical Center. All patients provided written informed consent. The study was approved by the Western Institutional Review Board and conducted according to Health Insurance Portability and Accountability Act of 1996 regulations.

Definitions

The Society of Thoracic Surgeons' national cardiac surgery database definitions were used for this study. Diabetes was defined as a history of diabetes mellitus, regardless of the duration of disease or need for oral agents or insulin. Prolonged ventilation was defined as pulmonary insufficiency requiring ventilatory support >24 h, postoperatively. Post-operative stroke was defined as any new major (Type I) neurological deficit presenting in-hospital and persisting >72 h. Operative mortality includes both (i) all deaths occurring during the hospitalization in which the operation was performed (even if death occurred after 30 days from the operation); and (ii) those deaths occurring after discharge from the hospital, but within 30 days of the procedure.

DATA ANALYSIS

Univariate analysis

Continuous variables are presented as median (interquartile range), while categorical variables are reported as frequencies and percentages. Differences in continuous variables were tested using the Mann-Whitney U-test. Categorical variables were compared with Pearson's Chi-square or

Departments of Cardiology and Cardiothoracic Surgery, JFK Medical Center, Atlantis, FL, USA

Correspondence: Sotiris C. Stamou, MD, PhD, Departments of Cardiology and Cardiothoracic Surgery, JFK Medical Center, Atlantis, FL, 180 John F Kennedy Drive, Suite 320, Atlantis, FL 33462, USA. Tel: 954-544-0606, e-mail: sotiris.stamou@hcahealthcare.com

Received: January 30, 2019, Accepted: February 15, 2019, Published: February 22, 2019

Fisher's Exact test, as appropriate. All tests were two-tailed, and a $p<0.05$ was considered statistically significant.

Multivariate analysis

Step-wise multivariate logistic regression was used to identify predictors of operative mortality. Cox proportional hazards regression was used to identify predictors of late mortality. A significance level of 0.10 was required to allow variables into the models. Odds ratios (OR), hazard ratios (HR), and 95% confidence intervals [95% CI] were generated.

Survival analysis

Time-related outcome was early (operative) mortality. Non-parametric estimates utilized the Kaplan–Meier estimator. The instantaneous risk across time (the hazard function) was estimated parametrically. Kaplan–Meier univariate unadjusted survival estimates were calculated and compared using a log-rank test for male and female patients. All analyses were conducted using SAS statistical software 14.0 (SAS institute, Cary, NC, USA).

RESULTS

Pre-operative characteristics

Of 810 TAVR patients performed during the study period, 148 patients were nonagenarians. Preoperative patient characteristics are summarized in Table 1.

TABLE 1

Pre-operative patient characteristics

Characteristics	Male N=79	Female N=69	p-value
Age, years	92 [90-93]	92 [90.5-93]	0.366
STS Risk Score	5.8 [3.8-7.5]	7.2 [5.9-8.8]	0.002
Previous cardiac surgery	32 (41)	17 (25)	0.047
Urgent Status	14 (18)	15 (22)	0.539
Ejection Fraction	56 [45-64]	60 [50-65]	0.028
Atrial fibrillation	41 (52)	28 (41)	0.169
Coronary artery disease	7 (9)	6 (9)	0.972
Chronic obstructive pulmonary disease	15 (19)	24 (35)	0.029
Diabetes	12 (15)	11 (16)	0.900
Congestive Heart Failure	45 (57)	47 (68)	0.163
Hypertension	67 (85)	60 (87)	0.709
Prior myocardial infarction	23 (29)	10 (15)	0.037
Previous cerebrovascular accident	9 [11)	2 (3)	0.049

Notes: Values expressed as N (%) or Median [IQR=interquartile range]. STS: Society of Thoracic Surgery.

The majority were male (52%), had hypertension (86%) and congestive heart failure (62%). Median STS risk score for mortality was 6.4% (5.0-8.7%). When compared to men, nonagenarian women had higher STS risk scores (7.2% [5.9-8.8%] *vs.* 5.8% [3.8-7.5%], p=0.002) and higher rates of chronic obstructive pulmonary disease (n=24, 35% *vs.* n=15, 19%; p=0.029). Additionally, they presented with higher left ventricular ejection fractions (60% [50-65%] *vs.* 56% [45-64%]; p=0.028) and lower rates of previous cardiac surgery (n=17, 25% *vs.* n=32, 41%; p=0.047), myocardial infarctions (n=10, 15% *vs.* n=23, 29%; p=0.037), and cerebrovascular accidents (n=2, 3% *vs.* n=9, 11%; p=0.049).

Operative characteristics

Operative patient characteristics are presented in Table 2.

TABLE 2

Operative patient characteristics

Characteristics	Male N=79	Female N=69	p-value
Access Site			
Transfemoral	61 (77)	51 (74)	0.415
Transapical	10 (13)	14 (20)	
Transaxillary	6 (8)	2 (3)	
Transaortic	2 (3)	2 (3)	
Prosthesis			
Edwards Sapien	71 (90)	61 (88)	0.562
Medtronic CoreValve	7 (9)	8 (12)	
Valve in Valve	0 (0)	2 (3)	0.216
Pre-deployment BAV	61 (77)	53 (77)	0.954
Post-deployment BAV	29 (37)	18 (26)	0.166
Conversion to open surgery	0 (0)	2 (3)	0.216
Vascular complications	12 (15)	7 (10)	0.360
Intra-aortic balloon pump	0 (0)	1 (1)	0.466
Operative mortality	8 (10)	3 (4)	0.181

Notes: Values expressed as N (%); BAV: Balloon Valvuloplasty.

Most patients underwent transfemoral access TAVR (n=112, 76%), while 24% necessitated the use of alternative access sites including transapical (n=24, 16%), trans axillary (n=8, 5%), and transaortic (n=4, 3%) approaches. Edwards SAPIEN S3 valve (Edwards Lifesciences, Irvine, California) was implanted in most patients (n=129, 87%). Pre-deployment balloon valvuloplasty (BAV) was utilized in 114 (77%) patients while post-deployment BAV was necessary for about one-third of patients (32%) who had more than mild paravalvular leak as detected by completion aortogram or echocardiography. Vascular complications were encountered in 13% (n=19) of patients, intra-aortic balloon pump placement was required in 1 patient (<1%), and conversion to open surgery was required in 2 patients (1%). Operative characteristics were similar for both groups, and no differences in vascular complication rates were elucidated when comparing women to men (n=7, 10% *vs.* n=12, 15%; p=0.360).

Early hospital outcomes

Post-operative patient characteristics are presented in Table 3.

TABLE 3

Post-operative patient characteristics

Outcomes	Male N=79	Female N=69	p-value
Median follow-up, months	25 [11-41]	29 [20-41]	0.328
Stroke	4 (5)	0 (0)	0.123
Atrial Fibrillation	7 (9)	14 (20)	0.049
Cardiac arrest	2 (3)	1 (1)	1.000
Blood transfusion	29 (37)	26 (38)	0.900
ICU stay, hours	43 [25-73]	47 [25-90]	0.608
Prolonged ventilation	5 (6)	3 (4)	0.595
Hospital length of stay, days	8 [5-10]	8 [5-12]	0.321
Readmission	25 (32)	15 (22)	0.176
Paravalvular leak			
None	40 (51)	28 (41)	0.428
Trace/Mild	35 (44)	38 (55)	
Moderate	4 (5)	3 (4)	
Permanent pacemaker	19 (24)	14 (20)	0.584
Hemodialysis	1 (1)	1 (1)	1.000

Notes: Values expressed as N (%) or Median [IQR=interquartile range].

No significant differences in blood transfusion rates were elucidated between women and men (n=26, 38% *vs.* n=29, 37%; p=0.900). Compared to men, women had higher rates of postoperative atrial fibrillation (n=14, 20% *vs.* n=7, 9%; p=0.049). Of the 4 patients who had a stroke, 3 died within 30-days, while 1 patient with a right-sided infarct was discharged with no residual deficits. All 4 strokes occurred in men. Seventy-two patients (49%) had trace or mild paravalvular leak while moderate paravalvular leak remained in 8 patients (5.4%) following post-deployment BAV. Median ICU and hospitalization times were 46 hours (25-75 hours) and 8 days (5-10 days), respectively. Preoperative and postoperative gradients are shown in Table 4.

TABLE 4

Preoperative and postoperative aortic valve gradients

Outcomes	Male N=79	Female N=69	p-value
Preoperative, mmHg			
Peak gradient	61 [53-76]	74 [56-91]	0.028
Mean gradient	41 [31-48]	43 [32-55]	0.218
Postoperative, mmHg			
Peak gradient	14 [9-21]	14 [9-19]	0.824
Mean gradient	8 [5-10]	8 [5-12]	0.324

Notes: Variables are expressed as Median [IQR=interquartile range].

While women presented with higher preoperative peak aortic valve gradients (74 mmHg [56-91] *vs.* 61 mmHg [53-76]; p=0.028), postoperative gradients were similar in both groups. No other postoperative differences were elucidated between women and men, including need for blood transfusions (n=26, 38% *vs.* n=29, 37%; p=0.900) and permanent pacemaker implantation (n=14, 20% *vs.* n=19, 24%; p=0.584).

Operative mortality was 7.4%, with 6 in-hospital deaths and 5 deaths occurring within the 30-day postoperative period. Of the 6 in-hospital deaths, one patient died from stroke complications following trans axillary TAVR, while another died on postoperative day (POD) 1 following acute aortic dissection and coagulopathy after transfemoral TAVR. One patient developed an ischemic stroke secondary to blood loss and hemothorax sustained during transapical TAVR and expired on POD 11. Three patients had cardiac arrest and/or developed respiratory failure several days following transfemoral TAVR in the setting of active do-not-resuscitate orders. Five deaths occurred after discharge within the 30-day operative period. One patient had a stroke after transapical TAVR and another developed renal and respiratory failure after transapical TAVR. Both patients were discharged to hospice where they subsequently died. A third patient died of subdural hematoma secondary to a nursing home fall on POD 20. Two patients died of unknown causes following uneventful discharge. While there was no significant gender-related difference in operative mortality, women had less than half the mortality rate of men (n=3, 4% *vs.* n=8, 10%; p=0.181).

Multivariate analysis

Multivariate regression analysis identified urgent TAVR status to be an independent predictor of operative mortality (p=0.006). Independent predictors of late-mortality are summarized in Table 5 and included urgent TAVR (p=0.001), history of atrial fibrillation (p=0.027), history of coronary artery disease (p=0.007), postoperative stroke (p=0.004), postoperative cardiac arrest (p<0.001), prolonged ventilatory support (p=0.007), and postoperative pacemaker implantation (p=0.043). Notably, gender was not identified as an independent predictor of operative or late mortality.

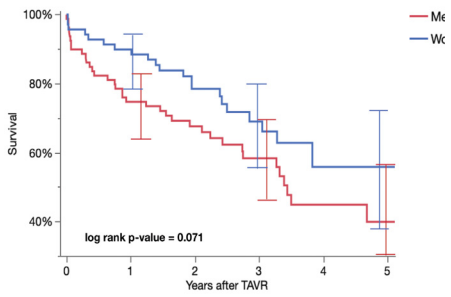
TABLE 5

Cox regression analysis for predictors of late Mortality

Characteristics	Hazard Ratio	95% Confidence Interval	P-value
Urgent Status	2.9	1.6 – 5.2	0.001
Atrial fibrillation	1.9	1.1 – 3.3	0.027
Coronary artery disease	4.6	1.6 – 11.6	0.007
Postoperative stroke	8.6	2.2 – 27.3	0.004
Postoperative cardiac arrest	28.9	6.2 – 97.8	<0.001
Prolonged ventilatory support	4.1	1.5 – 9.6	0.007
Postoperative pacemaker	1.8	1.0 – 3.2	0.043

Survival analysis

Survival outcomes are presented in Figure 1. Actuarial survival at 1, 3, and 5-years for the entire cohort was 81.8%, 63.2%, and 46.6%, respectively.



	30 days*	1 year	3 year	5 year
TAVR	93%	82%	63%	47%
Women	95.7% (69)	89.9% (66)	69.0% (62)	55.8% (2
Men	89.9% (79)	74.7% (71)	58.3% (59)	39.9% (2
Number at risk	N = 148	N = 137	N = 121	N = 53

Figure 1) *Actuarial 5-year survival curves for male and female nonagenarian patients.*

Median follow-up time was 28 months (16-41 months). While women overall had a higher 5-year survival, this difference did not achieve statistical significance (log rank p-value=0.071, Figure 1).

DISCUSSION

Since its US Food and Drug Administration approval for inoperable patients in 2011, TAVR has revolutionized the management of aortic stenosis in elderly patients, especially those considered to be at prohibitive or high-risk for conventional, surgical aortic valve replacement such as nonagenarians. Prior studies suggest that female gender is associated with better intermediate-term outcomes after TAVR, despite increased periprocedural complications (8-10). Our study demonstrates that this trend is largely consistent in the nonagenarian TAVR population, with acceptable early and late clinical outcomes.

Principal findings

Pre-operative risk profile

Prior investigations into gender-based differences in TAVR have elucidated that women often have fewer comorbidities, but a different risk profile compared to men which include older age, increased frailty, and higher STS score, among others (8,9,11). As expected, the nonagenarian women in our series had higher STS risk scores and peak aortic valve gradients. Additionally, they had higher left ventricular ejection fractions and lower rates of previous cardiac surgery, myocardial infractions, and strokes, in-line with other studies (8,9). However, in contrast to the literature, nonagenarian women presented for TAVR with higher rates of chronic obstructive pulmonary disease than men (9,12). This discrepancy may be attributable to changes in disease prevalence in the very elderly or regional differences in disease burden.

Operative mortality

Our TAVR experience is consistent with previously published reports that documented acceptable morbidity and mortality in this high-risk group (7,13-16). Operative mortality did not significantly differ between women and men (4 *vs.* 10%; p=0.181) in our series, a finding consistent with several reports in the literature (11). Post-hoc analysis of the PARTNER-1 randomized trial found no sex-related difference in all-cause mortality at 30 days (6.5 *vs.* 5.9%; p=0.52) (8). Similarly, analysis of the STS/ACC TVT registry did not elucidate a gender-based difference in in-hospital mortality (5.6 *vs.* 4.28%; p=0.294) (9).

Postoperative morbidity

While postoperative stroke was the most devastating complication in our series, the issue of gender-related differences in stroke following TAVR remains a contentious topic. Two recent meta-analyses concluded that women have an increased 30-day risk of stroke compared to men (OR 1.23, 95% CI 1.06-1.43) (11,12), yet several large studies found similar 30-day stroke risks between women and men (8,9). Although gender-related differences in perioperative stroke were clinically insignificant in our series, interestingly, all 4 instances of postoperative stroke occurred in men. Moreover, contrast to several studies that found higher rates of vascular complication and blood transfusion rates in women, no gender-related differences in vascular complication and blood transfusion rates were observed in our nonagenarian series (8,9,11).

Additionally, women in our study experienced higher rates of post-operative atrial fibrillation following TAVR when compared to men, a finding that was not elucidated in the ACC/STS TVT registry (9). This relative lack of gender-related differences may be attributable to changes in risk profile in the nonagenarian population. Analysis of the National Inpatient Sample found that nonagenarians had higher rates of in-hospital mortality, stroke, and vascular complications following TAVR when compared to a propensity-score matched cohort of octogenarians (17).

Actuarial survival

Several investigations found that female gender is associated with better 1-year survival after TAVR (3,8-11). While nonagenarian women in our series had better actuarial survival estimates, this difference did not achieve statistical significance (log rank p-value=0.071). This can possibly be attributed to the overall reduced life expectancy of the nonagenarian population. Estimated actuarial survival for our entire nonagenarian cohort at 1, 3, and 5-years was 82%, 63%, and 47%, respectively. In subgroup analysis of the PARTNER-1 trial, 1-year and 3-year survival rates were estimated at 70% and 46% for nonagenarians who underwent TAVR (18). This finding suggests that

women's intermediate-term survival advantage following TAVR may not persist in the nonagenarian population and the very elderly.

Predictors of early and late mortality

Urgent TAVR emerged as an independent predictor of both early and late mortality, echoing previous reports (19). Urgent TAVR was associated with higher 1-year mortality in the STS/ACC TVT registry (29% *vs.* 17%) (19). Postoperative stroke and cardiac arrest are also well-established risk factors known to portend poorer outcomes. Moreover, older adults have higher mortality risks attributable to coronary artery disease. Prolonged ventilatory support and respiratory insufficiency was encountered more frequently in patients with chronic obstructive pulmonary disease and congestive heart failure and thus an expected predictor of late mortality. History of atrial fibrillation was an unexpected predictor of late-mortality. Analysis of the BRAVO-3 trial found similar mortality rates in patients with and without atrial fibrillation at 30-days (6.0% *vs.* 4.5%; p=0.324), suggesting the risks of atrial fibrillation may present later (20). Lastly, postoperative permanent pacemaker implantation was a predictor for late-mortality. The impact of pacemaker implantation on morbidity and mortality is a controversial topic in TAVR, where the development of left ventricular dysfunction and failure of improvement in ejection fraction has been previously demonstrated (21). In the nonagenarian population, our analysis found that postoperative pacemaker implantation nearly doubled the hazard for late-mortality. Interestingly, female gender was not identified as an independent predictor of either early or late mortality.

CLINICAL IMPLICATIONS

To our knowledge, this is the first study evaluating gender-specific outcome differences of TAVR in nonagenarians. We used a real-world, unselected cohort of patients with prospectively acquired data by dedicated data management personnel to evaluate early hospital outcomes and actuarial survival in nonagenarian patients who underwent TAVR. Among the strengths of this study are the prospective entry of all data elements into a surgical registry with strict definitions and careful selection of patients for TAVR. Our study showed that female nonagenarian TAVR patients have a different risk profile than men, akin to prior studies investigating gender-related differences in TAVR. Our study did not find a significant gender-related difference in actuarial survival, suggesting that women's intermediate-term survival advantage following TAVR may not persist in the nonagenarian population. However, the incidence of operative mortality in women was less than half of men, despite women presenting with higher STS risk scores and peak aortic valve gradients. Further studies are required to confirm the findings of our study.

LIMITATIONS

Inherent limitations of a retrospective single institution investigation inevitably affected our study. The small sample size precluded use of more appropriate and robust statistical techniques, such as propensity score matching to adjust for the differences in preoperative characteristics between groups. Additionally, one-quarter of our study cohort included TAVR patients that necessitated the use of alternative access sites. The transapical, trans-axillary, and transaortic approaches included in this experience have unique operative risks that differ from the preferred, transfemoral approach.

CONCLUSION

Female nonagenarian TAVR patients have a different risk profile compared with male patients. While there were lower rates of early and late mortality in women, estimated actuarial survival did not achieve statistical significance at 3 and 5-years.

DISCLAIMER

This research was supported (in whole or in part) by HCA Healthcare and/or an HCA Healthcare affiliated entity. The views expressed in this publication represent those of the author(s) and do not necessarily represent the official views of HCA Healthcare or any of its affiliated entities.

FUTURE PERSPECTIVES

Competency in Medical Knowledge 1

Female nonagenarian TAVR patients have a different risk profile compared with male patients, yet no significant difference in operative or late mortality was elucidated from a large single-center cohort, suggesting women's intermediate-term survival advantage following TAVR may not persist in the very elderly.

Competency in Medical Knowledge 2

Predictors of late mortality in nonagenarians following transcatheter aortic valve replacement include urgent status, coronary artery disease, history of atrial fibrillation, and postoperative prolonged ventilatory support, stroke, cardiac arrest, and pacemaker implantation.

Translational Outlook

The incidence of operative mortality in women was less than half of men, despite women presenting with higher STS risk scores and peak aortic valve gradients. r studies are required to confirm our findings.

REFERENCES

1. Smith CR, Leon MB, Mack MJ, et al. Transcatheter versus surgical aortic-valve replacement in high-risk patients. N Engl J Med. 2011;364:2187-2198.
2. Leon MB, Smith CR, Mack M, et al. Transcatheter aortic-valve implantation for aortic stenosis in patients who cannot undergo surgery. N Engl J Med. 2010;363:1597-1607.
3. Baron SJ, Arnold SV, Wang K, et al. Health status benefits of transcatheter *vs.* surgical aortic valve replacement in patients with severe aortic stenosis at intermediate surgical risk: Results from the PARTNER 2 Randomized Clinical Trial. JAMA Cardiol. 2017;2:837-845.
4. Leon MB, Smith CR, Mack MJ, et al. Transcatheter or surgical aortic-valve replacement in intermediate-risk patients. N Engl J Med. 2016;374:1609-1620.
5. Adams DH, Popma JJ, Reardon MJ, et al. Transcatheter aortic-valve replacement with a self-expanding prosthesis. N Engl J Med. 2014;371:967-968.
6. Havakuk O, Finkelstein A, Steinvil A, et al. Comparison of outcomes in patients </=85 versus >85 years of age undergoing transcatheter aortic-valve implantation. Am J Cardiol. 2014;113:138-141.
7. Kayatta MO, Thourani VH, Jensen HA, et al. Outcomes for transcatheter aortic valve replacement in nonagenarians. Ann Thorac Surg. 2015;100:1261-1267.
8. Kodali S, Williams MR, Doshi D, et al. Sex-specific differences at presentation and outcomes among patients undergoing transcatheter aortic valve replacement: A cohort study. Ann Intern Med. 2016;164:377-384.
9. Chandrasekhar J, Dangas G, Yu J, et al. Sex-based differences in outcomes with transcatheter aortic valve therapy: TVT Registry From 2011 to 2014. J Am Coll Cardiol. 2016;68:2733-2744.
10. Williams M, Kodali SK, Hahn RT, et al. Sex-related differences in outcomes after transcatheter or surgical aortic valve replacement in patients with severe aortic stenosis: Insights from the PARTNER Trial (Placement of Aortic Transcatheter Valve). J Am Coll Cardiol. 2014;63:1522-1528.
11. Saad M, Nairooz R, Pothineni NVK, et al. Long-term outcomes with transcatheter aortic valve replacement in women compared with men: Evidence from a meta-analysis. JACC Cardiovasc Interv. 2018;11:24-35.
12. O'Connor SA, Morice MC, Gilard M, et al. Revisiting sex equality with transcatheter aortic valve replacement outcomes: A collaborative, patient-level meta-analysis of 11,310 patients. J Am Coll Cardiol 2015; 66: 221-228.
13. McNeely C, Zajarias A, Robbs R, et al. Transcatheter aortic valve replacement outcomes in nonagenarians stratified by transfemoral and transapical approach. Ann Thorac Surg. 2017;103:1808-1814.
14. Yamamoto M, Mouillet G, Meguro K, et al. Clinical results of transcatheter aortic valve implantation in octogenarians and nonagenarians: insights from the FRANCE-2 registry. Ann Thorac Surg. 2014;97:29-36.
15. Escarcega RO, Baker NC, Lipinski MJ, et al. Clinical profiles and correlates of mortality in nonagenarians with severe aortic stenosis

undergoing transcatheter aortic valve replacement. Am Heart J. 2016;173:118-125.

16. Noble S, Frangos E, Samaras N, et al. Transcatheter aortic valve implantation in nonagenarians: effective and safe. Eur J Intern Med. 2013;24:750-755.
17. Doshi R, Patel V, Shah P, et al. Comparison of in-hospital outcomes between octogenarians and nonagenarians undergoing transcatheter aortic valve replacement: a
18. propensity matched analysis. J Geriatr Cardiol. 2018;15:123-130.
19. Thourani VH, Jensen HA, Babaliaros V, et al. Outcomes in nonagenarians undergoing transcatheter aortic valve replacement in the PARTNER-I Trial. Ann Thorac Surg. 2015;100:785-792.
20. Kolte D, Khera S, Vemulapalli S, et al. Outcomes following urgent/emergent transcatheter aortic valve replacement: Insights from the STS/ACC TVT Registry. JACC Cardiovasc Interv. 2018;11:1175-1185.
21. Hengstenberg C, Chandrasekhar J, Sartori S, et al. Impact of pre-existing or new-onset atrial fibrillation on 30-day clinical outcomes following transcatheter aortic valve replacement: Results from the BRAVO 3 randomized trial. Catheter Cardiovasc Interv. 2017;90:1027-1037.
22. Kapadia SR, Wazni O, Krishnaswamy A, e al. Pacemaker implantation after TAVR. JACC Cardiovasc Imaging. 2017;10:1148-1150.