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Comparison of in-hospital outcomes between octogenarians and nonagenarians undergoing transcatheter aortic valve replacement: a propensity matched analysis

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Abstract

Background   Aortic valve stenosis (AS) is very common in the elderly patients above 80 years. Transcatheter aortic valve replacement (TAVR) in such patients is being increasingly performed. This study sought to assess in-hospital outcome differences between octogenarians and nonagenarians and predictors of mortality in nonagenarians undergoing TAVR with severe AS. **Method**   The study population was derived from the National Inpatient Sample (NIS) for the years 2012–2014 using ICD-9 CM procedure codes 35.05 and 35.06 for TAVR. Hospitalizations below 80 years of age were excluded. After performing propensity score matching (1: 2), in-hospital outcomes were compared in matched cohorts. Then, multivariate model was developed to analyze predictors of in-hospital mortality in nonagenarians. **Results** There were 11,630 hospitalizations in the octogenarian and 5815 hospitalizations in the nonagenarian group. Primary outcome of in-hospital mortality (6% *vs.* 4.1%, $P \leq 0.001$) was higher in nonagenarians compared to octogenarians. Secondary outcomes including stroke (3.4% *vs.* 2.8%, $P \leq 0.001$), renal failure (18.9% *vs.* 17.3%, $P \leq 0.001$), blood transfusion (35% *vs.* 32.6%, $P \leq 0.001$), vascular complications (4.5% *vs.* 3.5%, $P \leq 0.001$), and pacemaker implantation (27.8% *vs.* 24.8%, $P \leq 0.001$) were higher in nonagenarians. There was no difference in their length of stay. Median cost (70,374$ *vs.* 65,381$, $P \leq 0.001$) was slightly higher with nonagenarian. **Conclusions**   Although in-hospital mortality is slightly higher in nonagenarians, it is acceptable. This difference in mortality is at least partly explained by higher complications in nonagenarians. Efforts should be made to decrease the complications which can further narrow the difference in in-hospital mortality between the groups.

1   Introduction

The prevalence of aortic valve disease increases with age and it is the most common native valve disease.[1] The progression of aortic valve stenosis (AS) is gradual and has a long latency period.[2] However, after the initial appearance of symptoms, the disease progresses rapidly,[3–6] causing high rate of mortality. Mortality rate is near 50% in the first two years after initial symptoms appearance if patient is not treated appropriately.[1,7,8] Generally, elderly patients above 80 years of age with AS are frailer and have more comorbidities compared to younger age group and are considered poor candidates for surgery.[9] Also, functionality and qual-ity of life are markedly decreased in such patients with severe AS.[10] Although, surgical repair was the only option for such patients until few years ago, transcatheter aortic valve repair (TAVR) is now an alternative treatment option for severe AS in high-risk patients who are poor surgical candidates.[2,11] With increase in life expectancy, population of elderly age group is constantly increasing in United States. Between 1980 and 2010, nonagenarian population in the United States more than doubled from 720,000 to 19,000,000.[12] Also, nearly 300,000 patients with AS are TAVR candidate every year.[13] This is one of the major reasons why TAVR quickly gained popularity in such high surgical risk patients after its first introduction in 2002,[14,15] and later became the established therapy.[2,11,16–21] TAVR has also shown promising results in intermediate-risk patients, which is demonstrated by SURTAVI trial.[17,18]

TAVR was first introduced in the United States in January 2005 through the approval of feasibility trial of the Cribier-Edwards percutaneous aortic heart valve by the US

Food and Drug Administration (FDA).[22] After the conclusions of various clinical trials, FDA approved Edwards SAPIEN device for TAVR in patients with inoperable status in November 2011.[23,24] Later, in September 2012, FDA expanded TAVR indication to include patients with high surgical risk.[23,25] In late 2016, TAVR has also been approved for intermediate-risk patients by the FDA.[26] However, the effect of TAVR in nonagenarians is largely unknown, as only a small fraction of patients were enrolled in the pivotal clinical trials.[27–29] As incidence of AS increases with increasing age, more studies are required to establish safety and efficacy in elderly population especially nonagenarians.

In this study, we compared the in-hospital outcomes between octogenarian and nonagenarian from a large nationwide inpatient database. To better understand what causes high mortality after TAVR in hospitalizations above 90 years of age, we also estimated the predictors of in-hospital mortality in this age group.

2　Methods

We did not require Institutional Review Board (IRB) approval for our study as each individual hospitalization in Healthcare Cost and Utilization Project (HCUP) National Inpatient Sample (NIS) is de-identified.
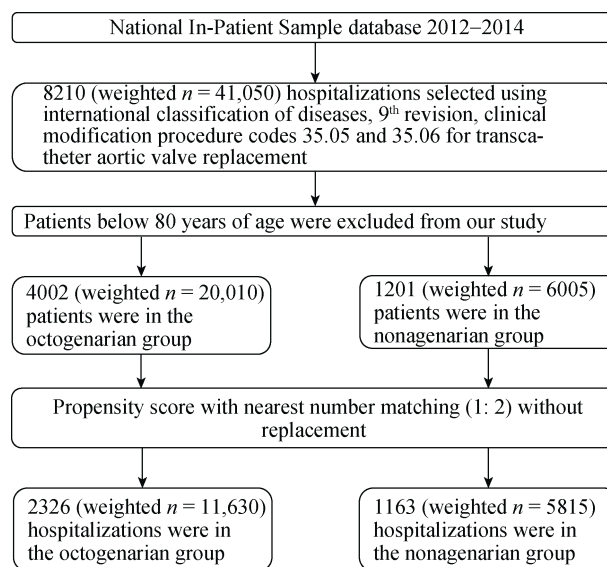
2.1　Data source

Our study population was obtained from National Inpatient Sample (NIS).[30] NIS is the largest, publicly available, all-payers, inpatient care database of the United States. This database is developed for the Healthcare Cost and Utilization Project (HCUP) and is sponsored by Agency for Healthcare Research and Quality (AHRQ). HCUP NIS has 20% stratified sample of discharged records from all HCUP participating hospitals. This database represents more than ninety five percent of the United States population. Each entry in HCUP NIS contains one primary discharge diagnosis, up to thirty secondary diagnosis (up to twenty-five in 2012 and 2013), one primary procedure, up to fifteen secondary procedures, demographic information, insurance status, comorbidities, length of stay, discharge disposition, teaching status of hospital, hospital region, median household income. We performed a retrospective, observational cohort study.

2.2　Study design

We have identified hospitalizations undergoing TAVR between 2012 and 2014. To identify the patient undergoing TAVR, we have used International Classification of Diseases 9th Revision, Clinical Modification (ICD-9-CM) pro-

cedure code 35.05 (Endovascular Replacement of Aortic Valve) and 35.06 (Transapical Replacement of Aortic Valve). Hospitalizations below 80 years of age were excluded. Hospitalizations between 80 and 90 years of age were included in the octogenarian group and above 90 years of age were included in the nonagenarian group (Figure 1). We used Elixhauser comorbidities in our study.[31] ICD 9 CM codes for other comorbidities and in-hospital outcomes are showed in Table 1S. We defined the severity of comorbid conditions using Deyo Modification of Charlson's Comorbidity Index (CCI).[32] This index contains seventeen weighted comorbid conditions. The score ranges from 0–33. Higher score corresponds to a greater burden of comorbid diseases prior to the procedure. Discharge trend weights provided by the HCUP NIS were used to generate national estimate.

The primary end-point of our study was all-cause in-hospital mortality. Secondary in-hospital outcomes included individual end-points of stroke (ischemic and hemorrhagic), acute renal failure, blood loss requiring transfusion, vascular complication, cardiac arrest, permanent pacemaker placement, atrial fibrillation and composite of all complications. Other outcomes included in our study were length of stay and median cost of hospitalization stay. To estimate the cost, HCUP NIS data were merged with cost-to-charge ratio files available from HCUP. We estimated the final cost by multiplying total hospital charge with cost-to-charge ratio.

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│   National In-Patient Sample database 2012–2014  │
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┌─────────────────────────────────────────────────┐
│ 8210 (weighted n = 41,050) hospitalizations      │
│ selected using international classification of    │
│ diseases, 9th revision, clinical modification     │
│ procedure codes 35.05 and 35.06 for transca-     │
│ theter aortic valve replacement                  │
└─────────────────────────────────────────────────┘
                        │
┌─────────────────────────────────────────────────┐
│ Patients below 80 years of age were excluded     │
│ from our study                                   │
└─────────────────────────────────────────────────┘
            │                           │
┌────────────────────┐      ┌────────────────────┐
│ 4002 (weighted      │      │ 1201 (weighted      │
│ n = 20,010)         │      │ n = 6005)           │
│ patients were in the│      │ patients were in the│
│ octogenarian group  │      │ nonagenarian group  │
└────────────────────┘      └────────────────────┘
            │                           │
┌─────────────────────────────────────────────────┐
│ Propensity score with nearest number matching    │
│ (1: 2) without replacement                       │
└─────────────────────────────────────────────────┘
            │                           │
┌────────────────────┐      ┌────────────────────┐
│ 2326 (weighted      │      │ 1163 (weighted      │
│ n = 11,630)         │      │ n = 5815)           │
│ hospitalizations    │      │ hospitalizations    │
│ were in the         │      │ were in the         │
│ octogenarian group  │      │ nonagenarian group  │
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Figure 1.　Flow chart for cohort selection. A total of 5203 hospitalizations from HCUP NIS database between 2012 and 2014 were included in our study. After performing propensity score matching analysis, 1163 hospitalizations in the nonagenarians and 2326 hospitalizations in the octogenarian groups were included and compared.

Table 1. Baseline characteristics of hospitalizations with transcatheter aortic valve replacement (unmatched).

Variable name	Octogenarians (*n* = 20010)	Nonagenarians (*n* = 6005)	*P* value
Unweighted numbers	4002	1201	N/A
Age, yrs	85.1	90.5	< 0.001
*Race			
White	88.5%	87.5%	
Black	2.9%	3.1%	
Hispanic	3.6%	3%	0.18
Asian/Pacific Islander	1%	0.7%	
Native American	0.2%	0.3%	
Other	3.8%	5.2%	
Gender			
Male	50.9%	47.9%	0.08
Female	49.1%	52.1%	
$Admission type			
Elective	76.1%	76.7%	0.73
Non-elective	23.9%	23.3%	
**Charlson's/Deyo comorbidity index			
0	6.1%	8.1%	
1	19%	24.9%	< 0.001
2	21.3%	19.7%	
≥ 3	53.6%	47.3%	
Primary payer			
Medicare	94.7%	94.3%	
Medicaid	0.3%	0.1%	
Private insurance (Including HMOs and PPOs)	3.6%	3.4%	0.30
Self-pay	0.4%	0.1%	
Other	1%	2.1%	
#Median household income for patient's ZIP code			
0–25 percentile	20.4%	17.2%	
26–50 percentile	25.1%	21.1%	< 0.001
51–75 percentile	25%	27.2%	
76–100 percentile	29.5%	34.5%	
Teaching status of hospital			
Rural	0.8%	0.4%	
Urban (non-teaching)	9.6%	11.8%	0.009
Urban (teaching)	89.6%	87.8%	
Hospital region			
Northeast	27%	28%	
Midwest	21.2%	22%	< 0.001
South	33.7%	27.6%	
West	18.1%	22.5%	

*345 missing patients; **Charlson's/Deyo comorbidity index was calculated as per Deyo classification; $3 missing patients; #a quartile classification of the estimated median household income of residents in the patient's ZIP Code. These values are derived from ZIP Code-demographic data obtained from Claritas. The quartiles are identified by values of 1 to 4, indicating the poorest to wealthiest populations. Because these estimates are updated annually; the value ranges vary by year. Http://www.hcupus.ahrq.gov/db/vars/zipinc_qrtl/nisnote.jsp. Frequency is in % or in mean. HMOs: health maintenance organizations; N/A: not applicable; PPOs: preferred provider organizations.

2.3 Statistical analysis

SAS 9.4 (SAS Institute Inc., Cary NC) was used for statistical analyses. Differences between categorical and continuous baseline variables were tested using Chi-square test and Student's *t*-test, respectively. Wherever Chi-square test was considered an inappropriate test due to very low frequency, we substituted it with Fischer's Exact Test. Level of significance was set at *P* value of less than 0.05. We used propensity score matched model to establish matched cohorts for baseline and procedural characteristics imbalances between two groups. The propensity score has been developed using a logistic regression model according to a non-parsimonious approach, and all baseline (gender, comorbidities) as well as procedural (any mechanical circulatory support, trans-femoral access) characteristics were included in the analysis. In the end, hospitalizations with similar propensity score in both groups were matched using two-to-one scheme without replacement using the matching algorithm.[33] To calculate in-hospital outcomes in matched cohorts, we used McNemar's test and Wilcoxon-rank-sum test. To analyze predictors of in-hospital mortality in nonagenarians, we developed multivariate logistic regression model. In this model, we included age, gender, admission type, primary payer, median household income, teaching status of the hospital, all Elixhauser comorbidities, approach for TAVR and all mechanical circulatory devices.

3 Results

3.1 Baseline characteristics

In the unadjusted cohorts, a total of 26,015 hospitalizations with severe AS underwent TAVR above 80 years of age. On an average, TAVR procedures increased from year 2012 through 2014, with highest procedure performance in 2014 (Figure 1S). Table 1 shows baseline characteristics (unadjusted) in the two groups. Nonagenarian hospitalizations were more likely to be females (52.1%) while octogenarian hospitalizations were more likely to be males (50.9%). The hospitalizations were predominantly white (88%) in both groups. In both the groups, TAVR procedures were more often performed electively (76.4%). Most common primary payment method was Medicare (94.5%). Most hospitalizations had a significant baseline burden of comorbidities with CCI score ≥ 3 (53.6% in octogenarians and 47.3% in nonagenarians). There was a significant geographical variability in utilization of TAVR procedure, with highest being in the Southern US. Most procedures were performed at urban teaching hospital (88.7%). Interestingly, higher comorbidities like uncomplicated and complicated

diabetes mellitus, obesity, peripheral vascular disease, chronic pulmonary disease, ischemic cardiomyopathy and composite of hemo and peritoneal dialysis were noted in octogenarian group before matching. Only coagulopathies were significantly higher in nonagenarians before matching (Table 2S).

3.2 In-hospital outcomes after propensity score matching

After performing propensity score matched analysis, 11,630 hospitalizations were in the octogenarian group and 5815 hospitalizations were in the nonagenarians group. Nonagenarian hospitalizations had higher in-hospital mortality (6% *vs*. 4.1%, $P \leq 0.001$). Secondary in-hospital outcomes of stroke (3.4% *vs*. 2.8%, $P \leq 0.01$), renal failure (18.9% *vs*. 17.3%, $P \leq 0.01$), blood transfusion (35% *vs*. 32.6%, $P \leq 0.01$), vascular complications (4.5% *vs*. 3.5%, $P \leq 0.01$), and pacemaker implantation (27.8% *vs*. 24.8%, $P \leq 0.01$) were higher in nonagenarians as well. Cardiac arrest and rates of atrial fibrillation were comparable in both groups. Higher composite of all complications was noted with nonagenarians (79.6% *vs*. 78.4%, $P \leq 0.001$). No difference in the length of hospital stay was noted between the groups (7.9 *vs*. 7.7 days, $P = 0.45$). Median cost of hospitalization was higher with admission of nonagenarians (70,374\$ *vs*. 65,381\$, $P = 0.014$) (Table 2).

Multivariate predictor model for in-hospital mortality was generated to assess predictors in nonagenarian hospitalizations undergoing TAVR with severe AS. Increasing age and female gender were associated with greater risk of in-hospital mortality. Interestingly, hospitalizations with median household income between 75 and 100 percentiles were associated with higher in-hospital mortality. Comorbidities like fluid and electrolyte disorders, peripheral vascular disease, coagulopathies, chronic pulmonary disease, mitral stenosis, mitral insufficiency, chronic kidney disease and hospitalizations on dialysis were associated with a greater risk of in-hospital mortality. Also, hospitalizations which required mechanical circulatory support such as intra-aortic balloon pump, percutaneous left ventricular assist device (Impella™, Tandem Heart™, etc.) and extracorporeal membrane oxygenation were associated with greater risk of in-hospital mortality. Transapical approach was not a predictor of higher in-hospital mortality in nonagenarians. In contrast, hospitalizations with uncomplicated diabetes mellitus, hypertension and ischemic cardiomyopathy were predictive of a lower incidence of in-hospital mortality (Table 3).

4 Discussion

Our study compared octogenarians with nonagenarians in

Table 2. Baseline characteristics outcomes after performing propensity score matched analysis (1: 2).

Variables	Octogenarians ($n = 11630$)	Nonagenarians ($n = 5815$)	P value
Unweighted numbers	2326	1163	N/A
Age, yrs	85.1	90.5	< 0.001
Male	49.3%	47.1%	0.24
Female	50.7%	52.9%	
Comorbidities			
Diabetes mellitus (uncomplicated)	16.7%	16.3%	0.78
Diabetes mellitus (with chronic complications)	2%	2.1%	0.93
Hypertension	79.4%	78.6%	0.58
Liver disease	1%	0.5%	0.11
Fluid and electrolytes Disorder	26.1%	25.5%	0.07
Neurological disorder	7.1%	6.1%	0.24
Obesity	2.8%	2.7%	0.94
Peripheral vascular disease	26.4%	26.6%	0.93
Smoking	1.5%	0.9%	0.20
Alcohol	0.6%	0.3%	0.39
Prior MI	11.6%	11.5%	0.97
Family history of CAD	1.5%	0.9%	0.20
Coagulopathy	24.3%	25.4%	0.48
Chronic pulmonary disease	22%	21.3%	0.68
Congestive heart failure	12.2%	10.8%	0.29
AIDS	0	0	N/A
Ischemic cardiomyopathy	4.1%	4.6%	0.44
Mitral stenosis	1.1%	1.3%	0.58
Mitral insufficiency	18.1%	18.6%	0.74
Chronic kidney disease	36.9%	36.5%	0.81
Composite of hemo and peritoneal dialysis	1.7%	2.1%	0.36
Procedural details			
IABP	1.7%	1.5%	0.67
pLVAD	0.3%	0.2%	0.82
ECMO	0.3%	0.2	0.62
Trans-femoral approach	84.5%	83.9	0.65
In-hospital outcome			
In-hospital mortality	4.1%	6%	< 0.001
Stroke (ischemic and hemorrhagic)	2.8%	3.4%	< 0.001
Acute renal failure	17.3%	18.9%	< 0.001
Blood loss requiring transfusion	32.6%	35%	< 0.001
Vascular complication	3.5%	4.5%	< 0.001
Cardiac arrest	5%	5%	1.00
Iatrogenic cardiac complication	0%	0%	N/A
Permanent pacemaker	24.8%	27.8%	< 0.001
Atrial fibrillation	47.3%	48%	0.21
Composite of all complications	78.4%	79.6%	< 0.001
Median length of stay (IQR), days	6 (1–11)	6 (1–11)	0.45
Cost (median)	\$65,381	\$70,374	0.014

AIDS: acquired immuno deficiency syndrome; CAD: coronary artery disease; ECMO: extracorporeal membrane oxygenation; IABP: intra-aortic balloon pump; IQR: interquartile range; MI: myocardial infarction; N/A: not applicable; pLVAD: percutaneous left ventricular assist device.

Table 3. Multi-variate predictors of in-hospital mortality for nonagenarian hospitalizations with transcatheter aortic valve replacement (*n* = 6005).

Variable name	Odds ratio (95% CI)	*P*
*Age	1.08 (1.05–1.10)	< 0.01
Female *vs.* Male	1.58 (1.38–1.81)	< 0.01
Admission type		
Non-elective *vs.* elective	1.02 (0.89–1.18)	0.75
Primary payer		
Medicare	Referent	
Medicaid	1.31 (0.48–3.55)	0.59
Private insurance (Including HMOs and PPOs)	1.23 (0.86–1.76)	0.26
Self-pay/other	0.48 (0.19–1.23)	0.13
Median household income for patient's ZIP code		
0–25 Percentile	Referent	
26–50 Percentile	1.02 (0.83–1.25)	0.86
51–75 Percentile	0.98 (0.80–1.19)	0.81
76–100 Percentile	1.33 (1.10–1.59)	< 0.01
Teaching status of hospital		
Rural	Referent	
Urban (Non-teaching)	0.67 (0.34–1.32)	0.25
Urban (Teaching)	0.54 (0.28–1.05)	0.07
**Comorbidities		
Diabetes mellitus (uncomplicated)	0.67 (0.56–0.80)	< 0.01
Diabetes mellitus (with chronic complications)	1.07 (0.79–1.44)	0.67
Hypertension	0.45 (0.39–0.52)	< 0.01
Liver disease	1.45 (0.86–2.44)	0.17
Fluid and electrolytes disorder	1.98 (1.73–2.27)	< 0.01
Neurological disorder	0.88 (0.67–1.14)	0.33
Obesity	0.87 (0.66–1.15)	0.32
Peripheral vascular disease	1.25 (1.09–1.44)	< 0.01
Smoking	0.77 (0.44–1.36)	0.37
Alcohol	1.14 (0.46–2.84)	0.78
Prior MI	0.94 (0.75–1.16)	0.55
Coagulopathy	1.28 (1.11–1.48)	< 0.01
Chronic pulmonary disease	1.41 (1.22–1.62)	< 0.01
Congestive heart failure	0.95 (0.79–1.16)	0.63
Ischemic cardiomyopathy	0.55 (0.40–0.77)	< 0.01
Mitral stenosis	2.80 (1.91–4.11)	< 0.01
Mitral insufficiency	1.34 (1.15–1.56)	< 0.01
Chronic kidney disease	1.19 (1.04–1.37)	0.01
Composite of hemo and peritoneal dialysis	4.85 (3.88–6.04)	< 0.01
Procedural details		
**IABP	11.78 (9.25–15.00)	< 0.01
pLVAD or ECMO	21.34 (14.0–32.55)	< 0.01
#Trans-apical approach	0.97 (0.83–1.14)	0.76

*Age is a continuous variable; **Reference group was not available; #Transfemoral approach was taken as a reference. ECMO: extracorporeal membrane oxygenation; HMOs: health maintenance organizations; IABP: intra-aortic balloon pump; MI: myocardial infarction; pLVAD: percutaneous left ventricular assist device; PPOs: preferred provider organizations.

high surgical risk hospitalizations between 2012 and 2014 from the national inpatient sample database who underwent TAVR. We found higher all-cause in-hospital mortality in nonagenarians compared to octogenarians. Also, secondary in-hospital outcomes including stroke (ischemic or hemorrhagic), acute renal failure, blood loss requiring transfusion, vascular complication, and permanent pacemaker placement were higher in nonagenarians. Additionally, we demonstrated positive predictors of in-hospital mortality in nonagenarian hospitalizations which included higher age, female gender, high income, fluid and electrolyte disorder, peripheral vascular disease, coagulopathy, chronic pulmonary disease, mitral stenosis, mitral insufficiency, chronic kidney disease and hospitalizations on dialysis.

PARTNER-1 trial demonstrated that TAVR can safely be performed in nonagenarians with acceptable short and mid-terms outcomes and it improves quality of life.[29] Our study demonstrated clinically acceptable outcomes in nonagenarians who underwent TAVR. The study by Tamburino, *et al*.[34] demonstrated that the patients who presented with comorbidities like diabetes mellitus, pre-procedural mitral regurgitation, prior acute pulmonary edema, and systolic pulmonary artery pressure > 60 mmHg are more likely to have increased early mortality after the TAVR procedure. Arsalan, *et al*.[35] analyzed TVT registry and compared nonagenarians with those below 90 years of age. They demonstrated higher stroke, major access site complications, bleeding, and in-hospital mortality with nonagenarians. Our study supported these results and showed higher in-hospital mortality, composite of stroke, vascular complications and blood transfusion with nonagenarians. As elderly patients in nonagenarian group generally have higher comorbidities and frailty, higher in-hospital complications are likely with any percutaneous intervention. Mack, *et al*.[9] also mentioned about the higher frailty in nonagenarians by using frailty test. This higher composite of complications including acute kidney injury may in turn explain short-term in-hospital mortality in our study.[36] Stroke is an important secondary outcome after aortic valve replacement. Few studies have mentioned the association of post-procedural neurological events with the older age.[37] Higher stroke rates in nonagenarians were also showed by few studies in the past.[35] Our study supported the prior findings of higher stroke rates in nonagenarians and this may additionally explain higher mortality rates in this age group. Another study found that nonagenarians requires more permanent pacemaker implantation post TAVR.[38] This is much higher compared with what is showed in PARTNER-1 trial (7.6%). Prevalence of various conduction disorders increase with age which may explain higher permanent pacemaker in non-

agenarians.[39] However, implantation of permanent pacemaker varies widely.[40]

Females are always subject to higher in-hospital mortality when undergoing percutaneous approach. This is showed by multiple previous studies,[41,42] however the reason is not clear yet. Our study showed that chronic pulmonary disease was one of the predictor for in-hospital mortality. One study by Suri, *et al*.[43] showed that moderate to severe chronic pulmonary disease increases risk of mortality.[43] As shown by Tamburino, *et al*.,[34] chronic kidney disease, through multiple mechanisms, leads to mortality in TAVR patients. In our study, chronic kidney disease was associated with higher mortality in nonagenarians. Also, patients on any type of dialysis (hemo or peritoneal dialysis) are associated with worse outcomes. The similar finding of increased early mortality in patients with dialysis dependent renal failure is demonstrated in the review article by Tjang, *et al*.[44] Intraoperative procedures like intra-aortic balloon pump, percutaneous left ventricular assist device and extracorporeal membrane oxygenation are associated with the increased in-hospital mortality as they are usually utilized in high-risk patients with unstable hemodynamics. Patients with multiple comorbidity and poor cardiac function requires mechanical circulatory supports which makes them more prone to adverse events. A study from Peura, *et al*.[45] reported that in-hospital mortality in high risk patients requiring MCS is 10 times higher as compared to that seen in patients with low risk. Another study from Singh, *et al*.[46] states that MCS, when utilized during TAVR in extremely high risk patients, leads to higher in-hospital and long term mortality.

PARTNER trial[29] and SURTAVI trial[17,18] demonstrated that TAVR is non-inferior to SAVR in high and intermediate risk patients, respectively. Similarly, a separate clinical trial is required to see if those results with high and intermediate surgical risk exist in octogenarians and nonagenarians age group. We explained results from observational study from the NIS database which needs to be confirmed with prospective clinical trials. In PARTNER-IIB trial, Edward Sapien XT transcatheter aortic valve were used. Newer generation valves may show further improvement in outcomes.[47] Studies with long term follow up are needed to see if such result persists at 30 days and at 1 year.

4.1 Limitations

Our study has several limitations inherent to the large administrative database such as potential coding errors and misinterpretations of diagnosis or procedures. Further, such database could have under reporting of comorbid conditions and missing data may also introduce bias. Secondly, medications data and other important procedural data (valve type,

defect size, concomitant procedure performed) were not given which may have improved our analysis. Thirdly, long term complications have not been described because of the nature of the database. Also, we were not able to calculate risk scores such as STS score because of the nature of our database. We did not have information on Kansas City Cardiomyopathy Questionnaire (KCCQ-12) which may accurately predict the quality of life post-TAVR.[48] We did not have follow up information because of the inpatient nature of the database. Finally, we have hospitalizations between 2012 and 2014; database after 2014 has not been publically available yet. Also, this database is different from TVT Registry patients. However, HCUP NIS database has been widely used in the research in the past as it represents nationally representative "real-world" sample without any selection bias which we may see with any clinical trial.

4.2 Conclusions

Our study is the largest to compare the in-hospital outcomes between octogenarians and nonagenarians. Although in-hospital outcomes are slightly worse in nonagenarians, TAVR is a feasible option in patients above 90 years of age with appropriate patient selection. Patients who are older (especially above 90 years of age), females, those with chronic pulmonary disease, on dialysis or in those with need for mechanical circulatory device should be followed more closely. TAVR is an evolving technology, and naturally there is a learning curve, and we can expect lower in-hospital mortality and morbidity with more experienced interventional cardiologist in coming years.

Acknowledgement

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**Table 1S.   International classification of diseases, ninth revision, clinical modification codes.**

Variable name	ICD 9 CM Code Used
Smoking	v15.82, 305.1
Family history of coronary artery disease	v17.3
Prior myocardial infarction	412
Ischemic cardiomyopathy	414.8
Mitral stenosis	396.0
Mitral insufficiency	396.2, 396.8, 394.2, 424.0
Chronic kidney disease	585.x
Dialysis (procedural code)	Haemodialysis: 39.95 Peritoneal dialysis: 54.98
IABP (procedural code)	37.61
pLVAD (procedural code)	37.68
ECMO (procedural code)	39.65
Trans-femoral approach for TAVR (procedural code)	35.05
Transapical approach for TAVR (procedural code)	35.06
Composite of stroke (ischemic and hemorrhagic combined)	430, 431, 432, 997.02, 433.01, 433.11, 433.21, 433.31, 433.81, 433.91, 434.01, 434.11, 434.91, or 436
Acute renal failure	584
Cardiac arrest	427.5
Blood transfusion	998.11, 998.12, 285.1, 99.0
Iatrogenic cardiac complication	997.1
Vascular injury requiring surgery (procedure code)	39.31, 39.41, 39.49, 39.52, 39.53, 39.56, 39.57, 39.58, 39.59, 39.79
Perioperative stroke	997.02
Perioperative infection	998.5, 998.59, 998.62
Postoperative shock	998.0
Permanent pacemaker implantation (procedural code)	37.70 to 37.79, 37.80 to 37.89, 00.50, 00.52, 00.53
Atrial fibrillation	427.31

IABP: intra-aortic balloon pump; ICD 9 CM: international classification of diseases, ninth revision, clinical modification codes; ECMO: extra-corporeal membrane oxygenation; pLVAD: percutaneous left ventricle assist device; TAVR: transcatheter aortic valve replacement.

Table 2S.   Comorbidities in hospitalizations with transcatheter aortic valve replacement (unmatched).

Variable name	Octogenarians ($n = 4002$)	Nonagenarians ($n = 1201$)	P value
Weighted numbers	20010	6005	N/A
Diabetes mellitus (uncomplicated)	26.2%	15.8%	< 0.001
Diabetes mellitus (with chronic complications)	4.7%	2%	< 0.001
Hypertension	80.6%	78.9%	0.24
Liver disease	1%	0.6%	0.15
Fluid and electrolytes disorder	26.5%	25.6%	0.53
Other neurological disorder	6.8%	6.1%	0.36
Obesity	9.5%	2.7%	<0.001
Peripheral vascular disease	30.2%	25.7%	0.002
Smoking	1.7%	1%	0.08
Alcohol	0.5%	0.4%	0.71
Prior MI	12.2%	11.5%	0.53
Family history of CAD	1.7%	1%	0.08
Coagulopathy	23.9%	27.7%	0.009
Chronic pulmonary disease	31%	20.6%	<0.001
Congestive heart failure	12.5%	11%	0.21
AIDS	0%	0%	N/A
Ischemic cardiomyopathy	7%	4.5%	0.001
Mitral stenosis	1.1%	1.3%	0.58
Mitral insufficiency	18.2%	18.7%	0.68
Chronic kidney disease	37.9%	38.5%	0.66
Composite of hemo and peritoneal dialysis	3.4%	2.1%	0.014

HMOs: health maintenance organizations; PPOs: Preferred Provider Organizations, MI: Myocardial Infarction, CAD: Coronary Artery Disease, N/A: Not Applicable
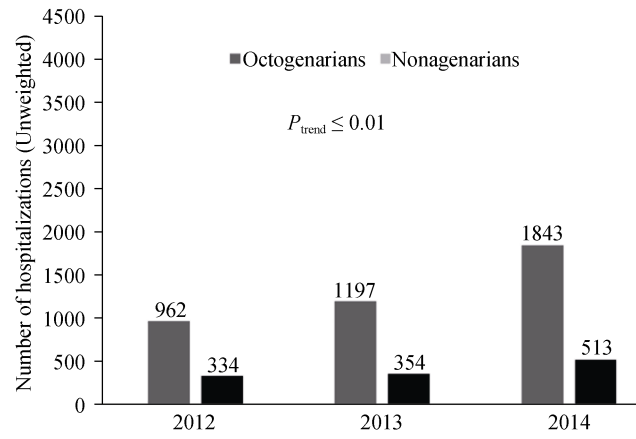
Figure 1S.   Trends in hospitalization: stratified by octogenarians and nonagenarians.