

## Research Article

# Aortic Stenosis Increases the Risk of Mortality in Hospitalization for Myocardial Infarction

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## Abstract

**Background:** Valvular aortic stenosis (AS) commonly co-exists with coronary artery disease, but there is limited information on the effect of AS on mortality in the setting of acute myocardial infarction (MI). Using National Inpatient Sample data from years 2005-2014, we analyzed the association between presence of AS and in-hospital mortality in MI patients. **Methods:** We assessed frequency and estimated mortality differences in patients who had percutaneous coronary intervention (PCI) versus those patients who did not receive PCI. Generalized estimating equation models were used to control for potential confounders and within-hospital variation. **Results:** We evaluated a total of 1,201,176 patients admitted for MI, including 56,037 patients (4.7%) with concomitant AS. Patients with both MI and AS were more likely to die during hospitalization when compared to patients with MI but without AS (OR 1.15 [95% CI, 1.11-1.19]); this finding was similar for patients admitted for ST-elevation MI or non-ST-elevation MI ( $P=0.35$ ). MI patients with AS less often received PCI (20.2% of AS patients versus 46.1% of non-AS patients;  $p<0.0001$ ). Those patients with AS who received PCI had lower mortality risk compared to AS patients who did not undergo PCI (OR 0.66 [95% CI, 0.59-0.73]). **Conclusion:** Concurrent AS increases odds of in-hospital mortality in patients with acute MI. An important contributing factor for this increased mortality risk may be the significantly lower rate of PCI in AS patients. These results suggest a need to carefully consider the appropriateness of conservative versus aggressive revascularization strategies in patients with valvular AS associated with acute MI.

**Abbreviations:** MI= myocardial infarction; CAD= coronary artery disease; AS= aortic stenosis; PCI= percutaneous coronary intervention; NIS= National Inpatient Sample; ICD-9-CM= International Classification of Diseases-Ninth Edition-Clinical Modification; NSTEMI= Non-ST-elevation MI; STEMI= ST-elevation MI; OR = Odds Ratio; CI= Confidence Interval; CABG= coronary artery bypass graft; SAVR= surgical aortic valve replacement

## Introduction

Despite a significant decrease in death rates associated with cardiovascular diseases in the United States over the last decade, the burden remains high with 1 in every 3 deaths still due to cardiovascular disease [1]. Myocardial infarction (MI) is a major cause of morbidity and mortality and affects a substantial proportion of the population [2-4]. Aortic stenosis (AS) commonly occurs in the elderly and often co-exists in patients with coronary

artery disease (CAD) and it is also a major public health concern with significant associated morbidity and mortality [5]. In patients with AS over the age of 70, over 50% also have CAD and this prevalence rises to 65% in patients over 80 years of age [5]. Further, approximately half of adults with severe symptomatic AS have significant CAD [6]. It is also now well established that degenerative calcific aortic valve disease is not a result of passive wear and tear but represents an active, proliferative, and inflammatory process with risk factors similar to those associated with atherosclerotic vascular disease like age, male gender, hypertension, and smoking [1–5,7,8]. However, there is a paucity of data on the effects of acute MI in patients with AS. In this study, we evaluated the association of AS to mortality and other outcomes along with differences in percutaneous coronary intervention (PCI) rates in MI patients in the United States.

## Methods

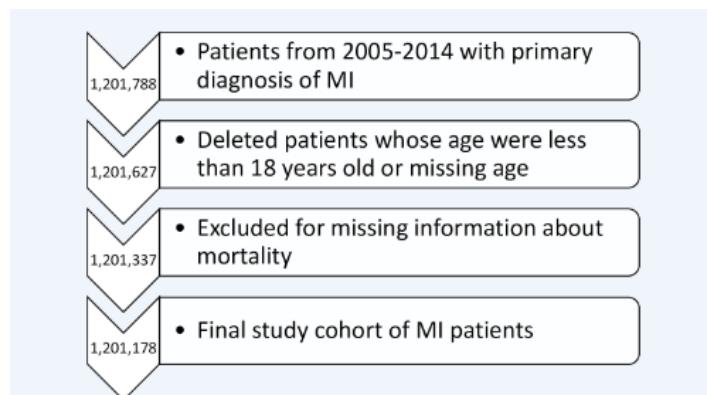
### Data Source

We utilized the National Inpatient Sample (NIS) database, the largest publicly accessible health care database of inpatients in the United States which features a national annual weighted estimate of over 35 million admissions [9]. This database has been widely validated and used in many different studies reporting on inpatient outcomes associated with medical conditions and it favorably compares to other similar administrative databases in the United States. Annually, the NIS provides data on approximately 8 million hospitalizations pooled from around 1,000 hospitals. By design, the NIS can approximate a 20% sample of United States community hospitals, defined as “all non-federal, short-term, general, and other specialty hospitals, excluding hospital units of institutions,” representing more than 95% of the U.S. population [9]. Research utilizing the NIS is institutional review board exempt.

### Study Population

We used the International Classification of Diseases-Ninth Edition-Clinical Modification (ICD-9-CM) codes 410.X1 to identify all adult patients (age  $\geq 18$  years old) with a principal diagnosis of MI. We utilize the principal diagnosis because it is considered the primary reason for hospital admission in the NIS database. From 2005-2014, there were 1,201,788 patients with a primary diagnosis of MI. 161 patients were excluded due to age less than 18 years. We further excluded 449 patients because of missing mortality data. The final cohort consisted of 1,201,178 patients with a primary diagnosis of MI. Then, a secondary diagnosis of AS was identified using ICD-9-CM codes 395.0, 395.2, 424.1, 396.2, and 396.0. Patients with a principal diagnosis of non-ST-elevation MI (NSTEMI) were identified using ICD-9-CM codes 410.7X and ST-elevation MI (STEMI) were identified using ICD-9-CM codes 410.11 to 410.61, 410.81 and 410.91. PCI cases in these patients

were identified using the procedure codes 36.01 through 36.07 and 36.09 in the NIS. Coronary artery bypass graft (CABG) cases were identified using the procedure code 36.1X. Surgical aortic valve replacement (SAVR) cases were identified using the procedure codes 35.21 and 35.22 (Figure 1).



**Figure 1:** Study cohort selection

### Patient Characteristics

Baseline patient characteristics included were demographics (age and race/ethnicity) and secondary outcomes were described using ICD-9-CM, clinical classification software (CCS) and NIS documentation (extracted using ICD-9-CM codes). Previous studies have used CCS categories when grouping medical conditions [10]. 29 Elixhauser comorbidities as defined by the Agency for Healthcare Research and Quality were also used in the analysis.

### Outcomes

The primary outcome analyzed was all-cause in-hospital mortality. Secondary in-hospital outcomes included cardiac arrest, shock, acute stroke, gastrointestinal bleed, pneumonia, respiratory failure, acute renal failure, other hemorrhage, balloon counterpulsation, and mechanical ventilation.

### Statistical Analysis

Descriptive analyses, patient demographics, comorbidities, in-hospital procedures/treatments, and in-hospital outcomes were compared between MI patients with AS and MI patients without AS using the Pearson Chi-square test for categorical variables and Student t-test for continuous variables. To determine the association of AS and in-hospital mortality, multivariable logistic models were constructed using generalized estimating equations with an exchangeable working correlation matrix. This was done to account for clustering of outcomes within hospitals. Variables included in the regression model were age, gender, history of PCI, history of CABG, 29 Elixhauser comorbidities, and hospital

characteristics (rural vs urban, teaching vs non-teaching). We used the Wald test for interaction between AS and age and AS and gender with a plan to stratify the odds ratios if the interactions were significant. We used the same model for secondary outcome analyses. Race/ethnicity was missing in 16.01% of the study population and was therefore not included in the model. The Wald test was used to test the significance of MI type effect modification.

We determined the difference in proportion of patients receiving PCI between the MI patients with AS compared to the MI patients without AS. Then, we stratified these patients by age less than 50 years, 50 to 70 years, and greater than 70 years. We subsequently analyzed a subgroup of only MI patients with AS to determine if PCI contributed to a difference in odds of mortality. Then, we stratified these patients by NSTEMI and STEMI. Furthermore, we used a logistic regression model to analyze how AS impacts the odds of receiving PCI, adjusted for age, gender, and comorbidities of diabetes, renal failure, and coagulopathy. These confounders were selected based on previous studies [11,12]. We further analyzed patients with MI and AS who did not receive PCI to determine how many underwent CABG and SAVR and compared their mortality odds to MI patients with AS who did not undergo any coronary revascularization.

All inferences were based on robust standard errors that were corrected for misspecification of the exchangeable correlation

structure. Statistical analysis was performed using SAS 9.4 (SAS Institute, Cary, NC); All p values were 2-sided with a significance threshold of  $p<0.05$ . Categorical variables were expressed as percentage and continuous variables as means. Odds ratios (OR) and 95% confidence interval (CI) were used to report the results of logistic regression.

## Results

### Baseline Characteristics

The final study population included a total of 1,201,178 patients admitted for a primary diagnosis of MI, including a total of 56,033 patients (4.7%) with a secondary diagnosis of AS. MI patients with AS were more likely to be male and were older than patients without AS ( $p<0.0001$ ). The distribution of race in these two groups was also significantly different with AS patients with MI more likely to be Caucasian and less likely to be any other race ( $p<0.0001$ ). When analyzing the distribution of comorbidities, MI patients with AS were also more likely to have hypertension, congestive heart failure, a history of CABG, chronic pulmonary disease, peripheral vascular disease, deficiency anemia, diabetes, pulmonary circulation disease, hypothyroidism, renal failure, and coagulopathy (all  $p<0.0001$ ). MI patients without AS were more likely to have a history of PCI and tobacco smoking, obesity, and hyperlipidemia (all  $p<0.0001$ ) (Table 1).

	Myocardial Infarction without Aortic Stenosis N (%)	Myocardial Infarction with Aortic Stenosis N (%)	P-Value
Number of Cases	1,145,145 (95.3)	56,033 (4.7)	
Male	446,489 (39.0)	26,412 (47.1)	<0.0001
Age, years, mean (SD)	66.7 (14.2)	78.9 (11.1)	<0.0001
Race			
Caucasian	731,680 (76.2)	40,605 (83.7)	
African American	96,358 (10.0)	2,919 (6.0)	
Hispanic	72,857 (7.6)	2,676 (5.5)	<0.0001
Asian	21,660 (2.3)	894 (1.8)	
Native American	5751 (0.6)	217 (0.5)	
Other	31,995 (3.3)	1,203 (2.5)	
Comorbidities			
Hypertension	778,576 (68.0)	40,138 (71.6)	<0.0001
Congestive heart failure	104,107 (9.1)	9,306 (16.6)	<0.0001
History of PCI*	138,602 (12.1)	5,988 (10.7)	<0.0001
History of CABG*	84,070 (7.3)	5,775 (10.3)	<0.0001
Tobacco smoking	272,397 (23.8)	4,901 (8.8)	<0.0001

Chronic pulmonary disease	233,109 (20.3)	14,045 (25.1)	<0.0001
Peripheral vascular disease	121,203 (10.6)	9,777 (17.5)	<0.0001
Deficiency Anemias	160,918 (14.1)	14,015 (25.0)	<0.0001
Obesity	139,628 (12.2)	4,781 (8.5)	<0.0001
Diabetes	391,476 (34.2)	19,861 (35.5)	<0.0001
Pulmonary circulation disease	8,719 (0.8)	1,306 (2.3)	<0.0001
Hypothyroidism	108,591 (9.5)	7,836 (14.0)	<0.0001
Renal failure	188,830 (16.5)	16,788 (30.0)	<0.0001
Liver disease	13,502 (1.2)	661 (1.2)	0.9898
Coagulopathy	48,345 (4.2)	3,826 (6.8)	<0.0001
Hyperlipidemia	650,363 (56.8)	29,032 (51.8)	<0.0001

\*PCI = Percutaneous coronary intervention; CABG = Coronary artery bypass graft

**Table 1:** Baseline Demographics and Comorbidities in Myocardial Infarction Patients with and without Aortic Stenosis

**Association of aortic stenosis complicated by myocardial infarction to mortality and other in-hospital outcomes**

Patients with both MI and AS were more likely to die during hospitalization when compared to patients with MI but without AS (OR 1.18 [95% CI, 1.11-1.19]); this finding was similar for patients admitted for either STEMI or NSTEMI (P=0.35). There was a significant interaction between AS and gender (P=<0.01) and AS and age (P=<0.01). After stratifying by age and sex, AS patients with MI in all age groups were more likely to die in-hospital except for women aged 18-49 (Table 2). MI patients with AS experienced a significantly higher in-hospital odds of developing any type of shock, gastrointestinal bleed, pneumonia, respiratory failure, acute renal failure, and hemorrhage, and need for mechanical ventilation compared to MI patients without AS (all p<0.05). However, there were lower odds of cardiac arrest (p=0.06), acute stroke and balloon counterpulsation (p<0.05) for MI patients with AS compared to MI patients without AS (Table 3).

Age Group	Adjusted* OR (95% CI)		
	Total	Male	Female
Overall	1.18 (1.13, 1.23)	1.22 (1.16, 1.29)	1.14 (1.08, 1.21)
18-49	1.85 (1.20, 2.85)	2.34 (1.45, 3.79)	0.71 (0.24, 2.14)
50-59	1.36 (1.07, 1.74)	1.41 (1.05, 1.90)	1.27 (0.82, 1.97)
60-69	1.56 (1.37, 1.77)	1.52 (1.29, 1.80)	1.63 (1.32, 2.00)
70-79	1.29 (1.19, 1.40)	1.30 (1.17, 1.45)	1.27 (1.12, 1.45)
>80	1.17 (1.12, 1.23)	1.20 (1.12, 1.29)	1.15 (1.08, 1.23)

\*Generalized estimating equation model controlling for age as a continuous variable, gender, hypertension, congestive heart failure, history of PCI, history of CABG, tobacco of smoking, chronic pulmonary disease, peripheral artery disease, deficiency anemia, obesity, diabetes mellitus, hospital characteristics (rural vs urban, teaching vs non-teaching), valvular disease, pulmonary circulation disease, paralysis, other neurological disorders, hypothyroidism, renal failure, liver disease, peptic ulcer disease, acquired immune deficiency syndrome, lymphoma, metastatic cancer, rheumatoid arthritis, coagulopathy, weight loss, fluid and electrolyte disorders, chronic blood loss anemia, alcohol abuse, drug abuse, psychoses, depression, hyperlipidemia, all shock, pneumonia, hemorrhage, balloon pump, blood transfusion, sepsis, severe sepsis, and within hospital variation.

**Table 2:** Odds ratios\* of in-hospital mortality among patients with and without aortic stenosis by age and gender groups, 2005-2014.

Outcome	Odds Ratio (95% CI)
Cardiac arrest	0.94 (0.89, 0.99)
All shock	1.07 (1.03, 1.12)
Acute stroke	0.89 (0.84, 0.96)
Gastrointestinal bleed	1.21 (1.15, 1.28)
Pneumonia	1.15 (1.11, 1.19)
Respiratory Failure	1.23 (1.19, 1.27)
Renal Failure	1.04 (1.01, 1.07)
Hemorrhage	1.16 (1.12, 1.21)
Balloon Counter pulsation	0.75 (0.71, 0.79)
Mechanical Ventilation	0.98 (0.94, 1.03)

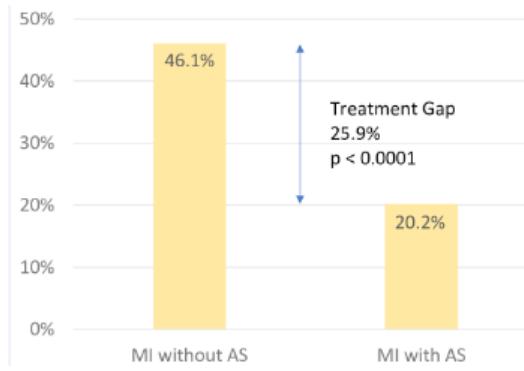
\*Odds ratios were calculated by generalized estimating equation (GEE) model controlling for age as a continuous variable, gender, hypertension, congestive heart failure, history of PCI, history of CABG, tobacco of smoking, chronic pulmonary disease, peripheral artery disease, deficiency anemia, obesity, diabetes mellitus, hospital characteristics (rural vs urban, teaching vs non-teaching), valvular disease, pulmonary circulation disease, paralysis, other neurological disorders, hypothyroidism, renal failure, liver disease, peptic ulcer disease, acquired immune deficiency syndrome, lymphoma, metastatic cancer, rheumatoid arthritis, coagulopathy, weight loss, fluid and electrolyte disorders, chronic blood loss anemia, alcohol abuse, drug abuse, psychoses, depression hyperlipidemia, sepsis, severe sepsis, and within hospital variation.

**Table 3:** Odds ratios of in-hospital complications in MI patients with AS compared to MI patients without AS.

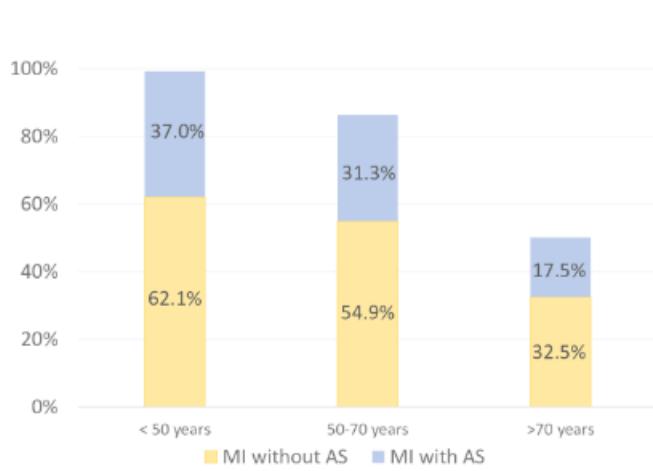
#### Analysis of revascularization in MI patients with AS

MI patients with AS received less PCI ( $p<0.0001$ ) (Figure 2), and those who received PCI had lower odds of mortality compared to those who did not (OR 0.66; 95% CI: 0.59-0.73). When stratifying by MI type, 34.2% of NSTEMI patients without AS received PCI and 15.9% of NSTEMI patients with AS received PCI ( $p<0.0001$ ). STEMI patients without AS received PCI in 71.9% of cases and STEMI patients with AS received PCI in 45.9% of cases ( $p<0.0001$ ). When stratifying the PCI rate differences by age in MI patients with and without AS, we found that in MI patients less than 50 years of age, 62.1% of patients without AS received PCI compared to 37.0% of patients with AS ( $p<0.0001$ ). In patients between age 50-70 years of age, 54.9% of patients without AS received PCI compared to 31.3% of patients with AS ( $p<0.0001$ ). In patients older than 70 years of age, 32.5% of patients without AS received PCI compared to 17.5% of patients with AS ( $p<0.0001$ ). As a proportion, the percentage of MI patients with AS receiving PCI compared to the percentage of MI patients without AS receiving PCI decreases from 62.1% to 54.9% to 32.5% as age increases (Figure 3). Acute MI patients with AS were 52% less likely to receive PCI compared to MI patients without AS after adjusting for age, gender, and comorbidities of diabetes, renal failure and coagulopathy (OR 0.48; 95% CI 0.47-0.49). In the group of patients with acute MI and AS who did not receive PCI, 5,030 (11.3%) patients underwent CABG. Of these patients who underwent CABG, 2,933 (58.3%) also underwent SAVR. These

acute MI patients with AS who underwent CABG instead of PCI had lower odds of mortality compared to the acute MI patients with AS who had no coronary revascularization (OR 0.78; 95% CI: 0.69-0.89). 4.8% of MI patients without AS and 4.8% of MI patients with AS were presented with cardiogenic shock. However, 53.9% of MI patients without AS in cardiogenic shock received PCI compared with only 28.9% of MI patients with AS in cardiogenic shock ( $P<0.0001$ ).



**Figure 2:** Percentage of acute myocardial infarction (MI) patients receiving percutaneous coronary intervention (PCI) stratified by presence of aortic stenosis (AS). The treatment gap (shown by the arrow) is defined as the difference in percentages between the two patient groups, which was statistically significant. MI patients with AS receive PCI less than half as often as MI patients without AS.



**Figure 3:** Percentage of acute myocardial infarction (MI) patients receiving percutaneous coronary intervention (PCI) stratified by presence of aortic stenosis (AS) and stratified by age. As a proportion, the percentage of MI patients with AS receiving PCI compared to the percentage of MI patients without AS receiving PCI decreases from 62.1% to 54.9% to 32.5% as age increases.

## Discussion

Acute MI and AS are commonly comorbid conditions though the effects of AS on MI mortality and other in-hospital outcomes are not well described, especially in large populations. Reports regarding the potential differences in treatment of this subset of MI patients are lacking. Identification of PCI treatment gaps in MI patients with concomitant AS can facilitate improved selection of an early invasive versus non-invasive, medical management strategy in order to improve patient in-hospital mortality and other outcomes.

The major new findings of our large, multi-institutional, population-level observational study of adults in the United States, are (1) patients hospitalized for acute MI who have concomitant AS have markedly higher odds of in-hospital mortality compared to MI patients without AS (2). The observed increased mortality of MI patients with AS was associated with much lower rates of PCI (3). These disparities in mortality and PCI rates were similar in patients admitted for NSTEMI and STEMI.

Patients with AS often have myocardial fibrosis as part of a hypertrophic response to AS and those who have an infarct pattern detected on cardiac magnetic resonance imaging with late gadolinium enhancement have an increased mortality [13]. Patients with aortic sclerosis also have an increased incidence of cardiovascular events associated with CAD and inflammation. There is conflicting data regarding aortic sclerosis itself – while not found to be an independent predictor of cardiac death in a study

by Otto et al, Chandra and colleagues found it was associated with a nearly 50% increase in risk of death from cardiovascular causes and risk of MI [14,15].

MI patients with AS are more likely to be older and male, which is consistent with studies showing increasing prevalence of valvular heart disease with age and that male gender is a risk factor for development of AS [8,16]. The increased odds of mortality observed in MI patients with AS may be partly due to the increased proportion of cardiogenic shock at presentation as well as a larger proportion of elderly patients, who have a poorer prognosis in the setting of severe symptomatic AS and a higher comorbidity burden [17]. The increased proportion of comorbidities in AS patients is also consistent with a prior study revealing that in AS patients, 52.7% had renal disease, 25.4% had chronic obstructive pulmonary disease, 11.6% had peripheral artery disease, and 30% had diabetes, all of which were significantly more common in AS patients in our population. That same study's cohort of AS patients had a mean age of 78.6 years, similar to our finding of a mean age of 78.9 years [18]. Despite the increase in comorbidity burden in the elderly, a previous study analyzing the NIS showed that there is an overall downward trend in the in-hospital mortality rate for acute coronary syndrome patients aged 70 years and older from years 1998-2013 [19]. This suggests that the increased odds of mortality seen in acute MI patients with AS may be due to pathophysiology associated with this valvular heart disease.

For secondary outcomes, MI patients with AS had higher odds of a myriad of in-hospital complications which may also contribute to the increased odds of mortality. The increased proportion of AS patients with comorbid chronic pulmonary disease may explain our outcomes findings of why this group is more likely to have respiratory failure and require mechanical ventilation. Also, we found that AS patients have a higher likelihood of having coagulopathy and iron deficiency anemia. AS patients can have Heyde syndrome, characterized by acquired coagulopathy, anemia, and intestinal angiodyplasia. The coagulopathy is due to AS-induced von Willebrand syndrome type 2A caused by degradation of large von Willebrand factor multimers by shear stress across the aortic valve [20]. One study showed that 31.7% of patients with arteriovenous malformations had AS [21]. This may explain our finding of increased likelihood of in-hospital gastrointestinal bleed and other hemorrhage.

We also found that MI patients with AS received PCI significantly less often compared to MI patients without AS. In the subgroup of MI patients with AS, those who received PCI had a significantly lower odds of mortality compared to those who did not receive PCI. The pattern of MI patients with AS receiving less PCI holds true even after stratifying by age. This would suggest that the treatment difference in MI patients with AS receiving PCI may

be a contributing factor to the risk of mortality. Given that MI patients with AS who underwent CABG also had lower odds of mortality compared to MI patients with AS who did not undergo any revascularization, it appears that coronary revascularization benefits this patient population.

The treatment difference in PCI exhibits an increasing trend with age given the smaller ratio of MI patients with AS receiving PCI compared to MI patients without AS. The oldest patient group had the lowest rate of PCI, regardless of presence of AS. One explanation for the decreased PCI rate in patients 70 years and older may be prior studies showing that elderly patients (age 75 years and older) with acute coronary syndrome (ACS) or stable angina undergoing PCI had significantly more comorbidities, more severe coronary pathology and higher procedural complication rates [22,23]. One of those studies also showed the highest incidence of in-hospital mortality occurred in ACS patients age 75 years and older compared to those younger than 75 years [23]. Further, octogenarians with MI undergoing PCI had over three times higher odds of mortality [24]. Elderly patients often have more calcified plaque and greater dilatation and tortuosity of coronary arteries and have a blunted acetylcholine response with reduced endothelium-dependent vasodilation [24,25]. These factors may contribute to a reluctance in choosing an invasive treatment strategy in this demographic, especially since AS patients tend to be older.

However, there are potential reasons why PCI was not performed in MI patients with AS. Given the older age and higher comorbidity burden of this group, a more conservative approach may have been warranted due to their higher risk. Older AS patients, especially those in cardiogenic shock, may have been offered palliative treatment options instead of aggressive measures. It is also possible that the treating physicians may have attributed MI in the AS patients to a type 2 MI caused by demand ischemia rather than an acute coronary plaque rupture leading to a type 1 MI. Additionally, when analyzing the factors associated with a lower likelihood of receiving PCI, we adjusted for presence of diabetes since diabetics often have more involved CAD that has exhibited a mortality benefit from coronary artery bypass graft, resulting in a decreased likelihood of receiving PCI. Renal failure also presents a risk to patients undergoing PCI due to uremia-induced platelet dysfunction increasing the risk of bleeding [26]. Thus, patients with end stage renal disease or those undergoing dialysis who receive PCI are at increased risk of developing heart failure and death [27]. MI patients with AS had a higher incidence of anemia, coagulopathy, and renal failure which may in part explain the markedly lower rate of PCI in this group.

#### **Strengths/Limitations of study**

The strength of our study is the large sample size that is pooled from hospitals across the entire nation. The most substantial limitations

of our study are related to the commonly encountered restrictions in the NIS. The database does not contain clinical variables like vital signs, laboratory or imaging results, electrocardiogram (ECG) data, echocardiography data or other similar patient-level data that are typically used to confirm diagnoses. In addition, patient symptoms and other subjective data are excluded. The reliance of the database on ICD codes means we are limited in our ability to parse the data for AS in the population, which would certainly be useful for future analyses. Another limitation is possible miscoding of MI as STEMI in AS patients due to often pre-existing left ventricular hypertrophy notable on ECG [28,29]. Despite these limitations, the NIS is a validated database that attempts to reduce errors by using multiple quality control measures and has been extensively used in multiple studies.

Clinically, aortic stenosis can be classified as mild, moderate and severe, but our study used aortic stenosis as a general term since ICD codes lack specificity of severity so the distribution of patients and stratification of outcomes by AS severity is unknown [6]. Some studies have shown that patients with different degrees of aortic stenosis have different prognoses, so relevant future studies can be conducted on patients with different degrees of aortic stenosis. This study was a cross-sectional study of inpatients with no follow-up data available, and the study objectives were all point studies during hospitalization. If a cohort study conducted on a cross-sectional basis for these patients demonstrates similar results, that may provide further evidence for pursuing more aggressive use of PCI in MI patients with AS.

#### **Conclusion**

Patients hospitalized for MI with concomitant AS have higher odds of in-hospital mortality and other complications and are less likely to receive PCI, even after adjustment for increased age and comorbidity burden. However, our findings demonstrate that PCI and CABG are associated with reduced mortality in AS patients with acute MI. Closing this apparent treatment gap may translate into improved outcomes in this population.

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#### **Perspectives**

##### **Competency in Medical Knowledge**

Valvular aortic stenosis commonly co-exists with coronary artery disease.

##### **Translational Outlook**

Further study into the association between aortic stenosis and mortality in acute myocardial infarction can be done by stratifying

by severity of aortic stenosis and degree of coronary lesion.

## References

1. Bobrowska B, Zasada W, Dziewierz A, Kruszelnicka O, Surdacki A, et al. (2017) Comparison of demographics, cardiovascular risk factors profile and prevalence of coexistent atherosclerotic vascular disease in patients with severe aortic stenosis stratified according to dichotomized stenosis severity. *Postepy Kardiol Interwencyjnej*. 13:331-334.
2. Kannel WB, Dawber TR, Kagan A, Revotskie N, Stokes J (1961) Factors of risk in the development of coronary heart disease—six year follow-up experience. The Framingham Study. *Ann Intern Med*. 55:33-50.
3. Ortlepp JR, Schmitz F, Bozoglu T, Hanrath P, Hoffmann R (2003) Cardiovascular risk factors in patients with aortic stenosis predict prevalence of coronary artery disease but not of aortic stenosis: An angiographic pair matched case-control study. *Heart*. 89:1019-22.
4. Malakar AK, Choudhury D, Halder B, Paul P, Uddin A, et al. (2019) A review on coronary artery disease, its risk factors, and therapeutics. *J Cell Physiol*. 34:16812-16823.
5. Paradis JM, Fried J, Nazif T, Kirtane A, Harjai K, et al. (2014) Aortic stenosis and coronary artery disease: What do we know? What don't we know? A comprehensive review of the literature with proposed treatment algorithms. *Eur Heart J*. 35:2069-82.
6. Lindman BR, Bonow RO, Otto CM (2013) Current management of calcific aortic stenosis. *Circ Res*. 113:223-37.
7. Stewart BF, Siscovick D, Lind BK, Gardin JM, Gottdiener JS, et al. (1997) Clinical factors associated with calcific aortic valve disease. *Cardiovascular Health Study*. *J Am Coll Cardiol*. 29:630-4.
8. Rajamannan NM (2008) Update on the pathophysiology of aortic stenosis. *Eur Hear J*. 29: E4-E10.
9. Agency for Healthcare Research and Quality (2010) The H-CUP Nationwide Inpatient Sample (NIS).
10. Alshekhlee A, Horn C, Jung R, Alawi AA, Cruz-Flores S (2011) In-hospital mortality in acute ischemic stroke treated with hemicraniectomy in US hospitals. *J Stroke Cerebrovasc Dis*. 20:196-201.
11. Cola C, Brugaletta S, Yuste VM, Campos B, Angiolillo DJ, et al. (2009) Diabetes mellitus: A prothrombotic state. Implications for outcomes after coronary revascularization. *Vasc Health Risk Manag*. 5:101-19.
12. Prabhakar SK, Abbott JD (2012) Factors influencing the outcomes of percutaneous coronary intervention in the stent era. *Interv Cardiol*. 4.
13. Dweck MR, Joshi S, Murigu T, Alpendurada F, Jabbour A, et al. (2011) Midwall fibrosis is an independent predictor of mortality in patients with aortic stenosis. *J Am Coll Cardiol*. 58:1271-9.
14. Otto CM, Lind BK, Kitzman DW, Gersh BJ, Siscovick DS (1999) Association of Aortic-Valve Sclerosis with Cardiovascular Mortality and Morbidity in the Elderly. *N Engl J Med*. 341:142-7.
15. Chandra HR, Goldstein JA, Choudhary N, O'Neill CS, George PB, et al. (2004) Adverse outcome in aortic sclerosis is associated with coronary artery disease and inflammation. *J Am Coll Cardiol*. 43:169-75.
16. Nkomo VT, Gardin JM, Skelton TN, Gottdiener JS, Scott CG, et al. (2006) Burden of valvular heart diseases: a population-based study. *Lancet*. 368:1005-11.
17. Martínez-Sellés M, Díez-Villanueva P, Sánchez-Sendin D, Hevia AC, Doblas JJG, et al. (2015) Comorbidity and intervention in octogenarians with severe symptomatic aortic stenosis. *Int J Cardiol*. 189:61-6.
18. Faggiano P, Frattini S, Zilioli V, Rossi A, Nistri S, et al. (2012) Prevalence of comorbidities and associated cardiac diseases in patients with valve aortic stenosis. Potential implications for the decision-making process. *Int J Cardiol*. 159:94-9.
19. Elbadawi A, Elgendi IY, Ha LD, Mahmoud K, Lenka J, et al. (2019) National Trends and Outcomes of Percutaneous Coronary Intervention in Patients  $\geq$ 70 Years of Age With Acute Coronary Syndrome (from the National Inpatient Sample Database). *Am J Cardiol*. 123:25-32.
20. Massyn MW, Khan SA (2009) Heyde syndrome: A common diagnosis in older patients with severe aortic stenosis. *Age Ageing*. 38:267-70.
21. Batur P, Stewart WJ, Isaacson JH (2003) Increased prevalence of aortic stenosis in patients with arteriovenous malformations of the gastrointestinal tract in Heyde syndrome. *Arch Intern Med*. 163:1821-4.
22. Wang TY, Gutierrez A, Peterson ED (2011) Percutaneous coronary intervention in the elderly. *Nat Rev Cardiol*. 8:79-90.
23. Bauer T, Möllmann H, Weidinger F, Zeymer U, Seabra-Gomes R, et al. (2011) Predictors of hospital mortality in the elderly undergoing percutaneous coronary intervention for acute coronary syndromes and stable angina. *Int J Cardiol*. 151:164-9.
24. Batchelor WB, Anstrom KJ, Muhlbauer LH, Grosswald R, Weintraub WS, et al. (2000) Contemporary outcome trends in the elderly undergoing percutaneous coronary interventions: Results in 7,472 octogenarians. *J Am Coll Cardiol*. 36:723-30.
25. Taddei S, Virdis A, Mattei P, Ghiadoni L, Gennari A, et al. (1995) Aging and endothelial function in normotensive subjects and patients with essential hypertension. *Circulation*. 91:1981-7.
26. Sohal AS, Gangji AS, Crowther MA, Treleaven D (2006) Uremic bleeding: Pathophysiology and clinical risk factors. *Thromb Res*. 118:417-22.
27. Narala KR, Hassan S, LaLonde TA, McCullough PA (2013) Management of Coronary Atherosclerosis and Acute Coronary Syndromes in Patients With Chronic Kidney Disease. *Curr Probl Cardiol*. 38:165-206.
28. Birnbaum Y, Alam M (2014) LVH and the diagnosis of STEMI - How should we apply the current guidelines? *J Electrocardiol*. 47:655-60.
29. Shah ASV, Chin CWL, Vassiliou V, Cowell SJ, Doris M, et al. (2014) Left ventricular hypertrophy with strain and aortic stenosis. *Circulation*. 130:1607-1616.