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Research paper

Sex disparities in in-hospital outcomes of left ventricular aneurysm complicating acute myocardial infarction: A United States nationwide analysis☆

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ABSTRACT

Background: Previous studies have reported sex-specific differences in the presentation, mechanisms, and outcomes of acute myocardial infarction (AMI). We assessed differences between women and men in the incidence and in-hospital outcomes of left ventricular (LV) aneurysm complicating AMI.

Methods: Hospitalizations for AMI with LV aneurysm were identified retrospectively in the National Inpatient Sample (NIS) from 2001 to 2017. Incidence and trends in in-hospital mortality, complications, length of stay and costs were analyzed in women and men.

Results: A total of 16,334 AMI hospitalizations with concomitant LV aneurysm were identified including 6994 (42.8%) women and 9340 (57.2%) men. Among these hospitalizations, women had a higher incidence of LV aneurysm compared to men (0.16% vs. 0.14%; $p < 0.001$). Unadjusted in-hospital mortality was higher in women than men (12.7% vs. 7.2%; $p < 0.001$). After adjusting for demographic and baseline characteristics and excluding inter-hospital transfers, women with AMI complicated by LV aneurysm had 49% greater odds of in-hospital mortality than men (OR 1.49, 95% confidence interval 1.06–2.10, $p = 0.02$). Women with LV aneurysm were less likely than men to undergo percutaneous coronary intervention (28.5% vs. 35.4%; $p < 0.001$), bypass surgery (15.8% vs. 25.1%; $p < 0.001$), coronary atherectomy (0.8% vs. 1.9%; $p = 0.009$) and LV aneurysm surgery (7.8% vs. 11.1%; $p = 0.001$).

Conclusions: In this large population-based cohort study, women had a slightly higher incidence but dramatically higher in-hospital mortality associated with LV aneurysm complicating AMI compared to men. Further research is necessary to validate strategies to ensure that women receive guideline-directed therapy for AMI and LV aneurysm to address the sex disparity in mortality.

Abbreviations: AMI, acute myocardial infarction; CABG, coronary artery bypass surgery; CAD, coronary artery disease; NSTEMI, non-ST elevation myocardia infarctiom; LV, left ventricular; NIS, national inpatient sample; PCI, percutaneous coronary intervention; STEMI, ST elevation myocardial infarction.

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1. Introduction

Acute myocardial infarction (AMI) is one of the leading causes of cardiovascular morbidity and mortality in the United States (US). Approximately 1 million patients suffer AMI every year, with more than 110,000 deaths annually from this disease in the US [1,2]. Left ventricular (LV) aneurysm is a severe complication known to develop during the post-infarction period, especially after transmural AMI [3].

Since the advent of prompt reperfusion via thrombolysis and primary percutaneous coronary intervention (PCI), the incidence of LV aneurysm has decreased [3]. However, recent studies have demonstrated a resurgence in the prevalence of LV aneurysm following AMI, possibly due to increased detection because of the expanded availability and utilization of cardiac imaging [4]. Current American Heart Association and American College of Cardiology guidelines recommend performing routine noninvasive imaging after AMI to evaluate LV function, thereby increasing the identification of LV aneurysms [5].

Numerous prior studies have reported sex-specific differences in the clinical presentation, pathophysiological mechanisms, outcomes, and health related quality of life following AMI [6–9]. Specifically, women with AMI have atypical symptoms, delayed clinical presentation in the course of AMI, and are undertreated with guideline-directed therapies, leading to poor in-hospital outcomes, reinfarction, excess mortality, and more likely to develop LV aneurysm compared to men [7,10,11]. In addition, sex differences in post-AMI LV aneurysms are important to study as the rate of mechanical complications reflects the downstream catastrophic outcome of sex-based differences in reperfusion therapy utilization. However, data are lacking on the incidence and outcomes of LV aneurysm complicating AMI in women as compared to men. In addition, sex-specific predictors of mortality with LV aneurysm have not been reported. Therefore, we utilized the National Inpatient Sample (NIS) database to assess temporal trends in the incidence and outcomes of LV aneurysm complicating AMI in women compared to men.

2. Methods

2.1. Data

We conducted a retrospective cohort study using the National Inpatient Sample (NIS) database to obtain hospital-related information from January 1, 2001, through December 31, 2017. The NIS is the largest all-payer inpatient care database in the United States and is part of the Healthcare Cost and Utilization Project (HCUP) family of databases sponsored by the Agency for Healthcare Research and Quality (AHRQ) [12]. This study was exempted by the institutional review board of Creighton University because the NIS is publicly available and contains deidentified patient information.

The NIS contains administrative claims data from more than 7 million inpatient hospitalizations annually [12]. These data include primary and secondary discharge diagnoses and procedures as well as sociodemographic and hospital information. NIS is designed to allow researchers and policymakers to make national estimates of health care utilization, charges, quality, and outcomes. The NIS sampling frame includes data from all nonfederal US hospitals (excluding rehabilitation and long-term acute care hospitals) in the 47 participating states plus the District of Columbia, representing more than 97% of the US population. Hospitals were further stratified based on the bed-size and location-teaching status. NIS data have been utilized previously to analyze nationwide trends, disparities, and outcomes following AMI [4,10,11,13,14].

2.2. Study cohort

Patients aged 18 years or older who were admitted with a primary discharge diagnosis of AMI were identified using International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) 410.x and International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) I21.x-I22.x codes. Within these AMI index hospitalizations, we identified secondary diagnoses of LV aneurysm with ICD-9-CM 414.10 and ICD-10-CM I25.31 [4]. Index hospitalizations without data on sex or in-hospital mortality were excluded. We excluded hospitalizations of patients less than 18 years old and diagnoses of unstable angina, Takotsubo cardiomyopathy and/or myocarditis (see Supplementary Table 1 for all ICD-9/10 codes).

2.3. Definition(s)

The term "incidence" indicates new event, and by the sampling design we estimate the rate of all new LV aneurysms for hospitalizations in the United States between 2001 through 2017 in which the patient was an adult and had AMI as the primary discharge diagnosis. So, while calculating the incidence, the number of LV aneurysm events were placed in the numerator and all AMI hospitalizations (excluding patients <18-year-old, unstable angina and/or myocarditis) were placed in the denominator.

2.4. Patient and hospital characteristics

For each hospitalization, we extracted the following characteristics: demographics (age, race, primary payer, income quartile, facility location/teaching status, bed size, and United States region), clinical characteristics associated with increased mortality following AMI [tobacco use, dyslipidemia, prior coronary artery disease (CAD), prior PCI, prior myocardial infarction, prior coronary artery bypass grafting (CABG), atrial fibrillation, anemia, cirrhosis, and body mass index (BMI)], and 29 Elixhauser comorbidities. The major cardiac comorbidities included in the Elixhauser Comorbidity score are: hypertension, diabetes mellitus, congestive heart failure, cardiac arrhythmias, valvular heart disease, renal failure, obesity, anemia, drug and alcohol abuse. The Elixhauser Comorbidity score is a well validated measure of comorbidity used frequently in administrative databases and has been previously utilized in studies assessing in-hospital mortality, inhospital complications and readmissions following AMI [14,15]. We calculated the Elixhauser Comorbidity Index, ranging from −32 to 99, in which negative values imply a protective effect of the comorbidities and higher positive values imply a harmful effect of the comorbidities [16,17].

2.5. Study outcomes

We evaluated year-over-year trends in the rate of AMI hospitalizations that included a secondary diagnosis of LV aneurysm stratified by sex. We also evaluated sex-specific in-hospital mortality, length of stay, hospital costs, and predictors of in-hospital mortality and the rate of in-hospital complications including bleeding, vascular complications, stroke/transient ischemic attack (TIA), cardiogenic shock, cardiac arrest, and recurrent myocardial infarction.

2.6. Statistical analysis

All descriptive statistics were stratified by sex. Continuous variables are presented as median and interquartile range and compared using log-normal regression models to allow nationally-representative NIS weighting. Categorical variables are presented as percentages and compared using the chi-square test with Wilson confidence intervals, as appropriate. Year-over-year trends in the rate of LV aneurysm were evaluated using orthogonal polynomial contrasts. Multivariable logistic regression models were estimated for in-hospital mortality after adjusting for demographic and clinical characteristics. We adjusted for age, race, insurance, income quartile, location/teaching status, bed size, region of the United States, year, CAD, Elixhauser Comorbidity Index, location of STEMI, NSTEMI. These models were estimated including and excluding patients who were transferred to another facility. Further twoway interactions were estimated between sex and each demographic and clinical covariate to determine whether the effect of the covariate on in-hospital mortality differed between women and men. Log-linear regression models were estimated for length of stay and hospital cost given skewed and heteroscedastic residuals. Hospital cost was inflation-adjusted to 2017 US dollars [18]. The functional form of continuous covariates was evaluated using restricted cubic splines with knots specified at the 5th, 27.5th, 50th, 72.5th, and 95th percentiles. All analyses were conducted using SAS v9.4, accounted for the NIS sampling design and used updated trend weights as appropriate.

3. Results

From 2001 to 2017, a total of 16,334 AMI hospitalizations with LV aneurysm were identified. Of these, women represented 6994 (42.8%) and men represented 9340 (57.2%) hospitalizations. The median age was 73 years for women compared to 65 years for men ($p < 0.001$). In addition, the majority of patients aged >75 years were women (56.8%). Since women were older, the composite Elixhauser Comorbidity Index was higher in women than in men ($p = 0.014$). A majority of the patients were racially white (77% of women, 78.5% of men), followed by black (9.6% of women, 7.4% of men), Hispanic (7.2% women & 7% of men), and others (6.2% of women, 7% of men) ($p = 0.194$). Women had significantly higher rates of anemia, hypertension, diabetes mellitus, atrial fibrillation, chronic heart failure, and chronic obstructive pulmonary disease (COPD); women had lower rates of dyslipidemia, atrial flutter, CAD, tobacco use, and illicit drug abuse. Tables 1 and 2 summarize the differences in demographic characteristics, risk factors, and comorbidities between women and men.

Table 1
Demographic characteristics stratified by sex.

	Male ($n = 9340$)	Female ($n = 6994$)	p
Age	65 [56–75]	73 [63–81]	<0.001
18–54	19.9	9.3	<0.001
55–64	27.1	17.2	
65–74	26.1	26.3	
75–84	20.6	32.2	
85+	6.3	15.0	
Race			
White	78.5	77	0.194
Black	7.4	9.6	
Hispanic	7.0	7.2	
Other	7.1	6.2	
Insurance			
Medicare	53.4	70.0	<0.001
Private	30.1	17.9	
Other	16.5	12.1	
Income quartile			
0 to 25th	24.7	24.3	0.905
26th to 50th	25.6	25.7	
51st to 75th	24.9	24.2	
76th to 100th	24.8	25.8	
Location-teaching status			
Rural	5.8	6.9	0.103
Urban nonteaching	33.6	36.1	
Urban teaching	60.6	57.0	
Bed size			
Small	8.9	8.5	0.606
Medium	21.0	22.4	
Large	70.2	69.1	
Region			
Northeast	18.7	20.1	0.437
Midwest	26.2	27.3	
South	36.6	35.6	
West	18.5	16.9	

Note. Data presented as median [IQR] or percent.

Table 2
Baseline characteristics stratified by sex.

	Male ($n = 9340$)	Female ($n = 6994$)	p
Hypertension	58.5	60.2	0.314
Diabetes	30.4	32.1	0.278
Dyslipidemia	51.0	48.0	0.092
Atrial fibrillation	19.1	20.2	0.405
Atrial flutter	3.6	2.0	0.011
CAD	91.7	83.9	<0.001
Chronic heart failure	3.8	4.8	0.149
Chronic renal failure	12.4	12.5	0.962
Anemia	18.8	24.6	<0.001
Cirrhosis	–	–	–
COPD	18.4	23.7	<0.001
Tobacco use	18.3	12.3	<0.001
Alcohol abuse	3.9	–	–
Drug abuse	2.6	1.1	0.002
Peripheral vascular disease	12.3	12.7	0.777
Pulmonary hypertension	–	–	–
Coagulopathy	7.4	7.1	0.734
Obesity	10.2	10.0	0.838
BMI category			
<25	1.1	–	–
25 to <30	0.8	–	–
30 to <35	1.6	1.9	0.394
35 to <40	1.5	1.1	0.398
40+	1.8	1.8	0.930
Elixhauser Comorbidity Index	0 [−1 to 8]	2 [−1 to 9]	0.014

Note. Data presented as median [IQR] or percent. A dash indicates that the observed count of hospitalizations was less than 10 which precludes reporting as defined in the HCUP-NIS Data Use Agreement.
BMI = body mass index.
CAD = coronary artery disease.
COPD = chronic obstructive pulmonary disease.

3.1. *Incidence of LV aneurysm complicating AMI*

The incidence of LV aneurysm among AMI hospitalizations was numerically higher in women than men (0.16% vs. 0.14%, $p < 0.001$; Fig. 1). No temporal trend was observed in the incidence of LV aneurysm complicating AMI in either sex during the study period. The incidence of LV aneurysm had commensurate distribution with STEMI (49.5% vs. 50.1%) and NSTEMI (50.5% vs. 49.9%) in women and men (Table 3).

3.2. *In-hospital outcomes*

In the overall study cohort of patients with AMI complicated by LV aneurysm, unadjusted in-hospital mortality was higher in women than men (9.4% vs. 5.8%; OR1.70, 95% confidence interval [CI] 1.31–2.20; $p < 0.001$; Fig. 2). Similar differences were observed after excluding the patients who were transferred out of the hospital alive to another acute care facility (12.7% vs. 7.2%; $p < 0.001$; Table 4). Unadjusted in-hospital mortality increased with age in both sexes, and women had higher odds of mortality across all age groups compared to men (Fig. 2). After adjusting for demographic and baseline characteristics, the adjusted odds for in-hospital mortality were 39% higher in women than men (OR 1.39, 95% CI 1.00–1.94; $p = 0.049$). Similar results were observed after excluding the transferred-out cohort (OR 1.49, 95% CI 1.06–2.10; $p = 0.022$).

Adjusted in-hospital mortality was higher for hospitalizations in which the patient was older, had an ST Elevation Myocardial Infarction (STEMI) diagnosis, and/or required mechanical circulatory support (Table 6). STEMI was associated with higher in-hospital mortality than non-STEMI in both women and men (13.8% vs. 5.1% in women and 8.4 vs. 3.1% in men; Table 4). There were no statistically significant differences in in-hospital mortality noted between women and men when stratified by race, income level, insurance status, region of care and bed size of the hospital (Table 5). Similarly, no statistically significant differences were observed between women and men in the effect of any

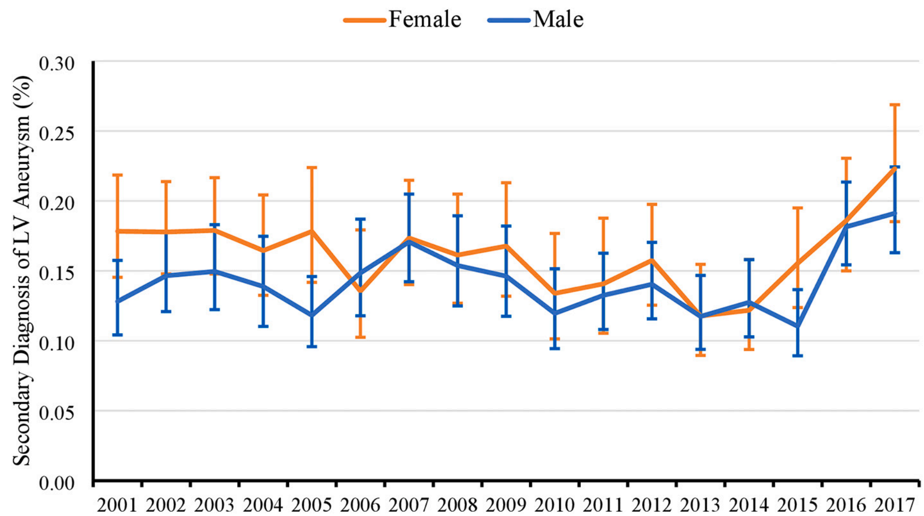

Fig. 1. Year-over-year trend in the rate of hospitalizations for AMI complicated by LV aneurysm. Error bars represent 95% Wilson confidence intervals.

Table 3
In-hospital characteristics stratified by sex.

	Male ($n = 9340$)	Female ($n = 6994$)	p
AMI type			
STEMI	50.1	49.5	0.766
Anterior	60.5	62.4	0.442
Inferior	25.5	22.6	0.157
Other	15.8	17.7	0.323
NSTEMI	49.9	50.5	0.766
Fibrinolysis	1.5	1.3	0.632
Coronary angiography	74.3	71.5	0.082
On day of admission	56.6	53.4	0.159
PCI	35.4	28.5	<0.001
CABG	25.1	15.8	<0.001
Atherectomy	1.9	0.8	0.009
Mechanical Circulatory Support	14.2	9.9	<0.001
LV Aneurysm Surgery	11.1	7.8	0.001

Note. Data presented as percentage (%).
AMI = acute myocardial infarction.
CABG = coronary artery bypass grafting.
LV = left ventricular.
NSTEMI = non-ST-elevation myocardial infarction.
PCI = percutaneous coronary intervention.
STEMI = ST elevation myocardial infarction.

clinical covariates (i.e., no covariate-by-sex interaction effects were statistically significant; Table 6).

During AMI hospitalizations with LV aneurysm, women had more acute systolic heart failure (43.1% vs. 38.8%; $p = 0.01$) and hemodialysis (2.7% vs. 1.6%; $p = 0.014$), while men had more ventricular arrhythmias (13.3% vs. 21.4%; $p < 0.01$). There were not significant differences in the rates of mechanical cardiac complications, mechanical ventilation, cardiogenic shock, LV thrombus, cardiac arrest, and acute stroke. Table 4 summarizes rates of in in-hospital complications in women and men.

Finally, there was no difference in the length of hospital stay between men and women (5.3 days vs. 5.3 days; $p = 0.994$); however, hospital cost was higher in men compared to women ($23,873 vs. $20,068; $p < 0.001$; Table 4).

3.3. In-hospital care

During hospitalization for AMI complicated by LV aneurysm, women were less likely than men to be treated with PCI (28.5% vs. 35.4%; $p < 0.001$), coronary artery bypass grafting (CABG; 15.8% vs. 25.1%; $p < 0.001$), and LV aneurysm surgery (7.8% vs. 11.1%; $p = 0.001$). In addition, compared to men, women underwent complex coronary intervention with atherectomy at lower rates (0.8% vs. 1.9%; $p = 0.009$) and were placed on mechanical circulatory support less frequently (9.9% vs. 14.2%; $p < 0.001$). Table 3 summarizes the differences in in-hospital care between women and men.

4. Discussion

The incidence of LV aneurysm decreased significantly from 35% in the pre-reperfusion era [19] to 11% [3] in the thrombolytic era to as low as 0.5% in the primary PCI era [4]. However, some reports, including our analysis, suggest that this incidence may have increased recently [4], possibly due to technological advancements and increased utilization of echocardiography, cardiovascular magnetic resonance imaging (MRI) and cardiac computed tomography (CT) in the US following AMI [5,20,21]. In the present large population-based study of AMI hospitalizations, we report three major findings regarding the incidence and in-hospital outcomes of LV aneurysm from 2001 through 2017. 1) LV aneurysm complicating AMI occurred at a higher rate in women than men. 2) Women with LV aneurysm underwent less PCI, CABG, and surgical LV aneurysm repair than men. 3) The in-hospital mortality of LV aneurysm complicating AMI was higher in women than men across all age groups.

First, we found a slightly higher incidence of LV aneurysm in women compared to men following AMI. Previous literature has established that women are more likely than men to have delayed AMI presentation and less likely to undergo revascularization procedures [6,7,11]. Nevertheless, data on sex differences in LV aneurysm following AMI are limited. Our study is the largest to date to explore the impact of LV aneurysm on in-hospital outcomes during AMI hospitalization in both sexes. Our findings confirm a prior observation in a retrospective study of 809 AMI patients that female sex was an independent predictor of LV aneurysm following AMI [22]. Aligned with our findings, in a recent STEMI study, women were more than 3 times more likely to develop LV aneurysm compared to men [23]. The increased risk of LV aneurysm formation in women following AMI may be attributable to atypical presentation, delayed diagnosis and reperfusion, less frequent revascularization, no re-flow phenomenon, lower glomerular filtration rate (GFR), and greater burden and severity of heart failure, all of which are predictors of LV aneurysm [3,24–26]. A recent scientific statement from the American Heart Association, as well as the Gender and Sex Determinants of Cardiovascular Disease: From Bench to Beyond Premature Acute Coronary Syndrome (GENESIS PRAXY) study, confirmed sex-specific differences

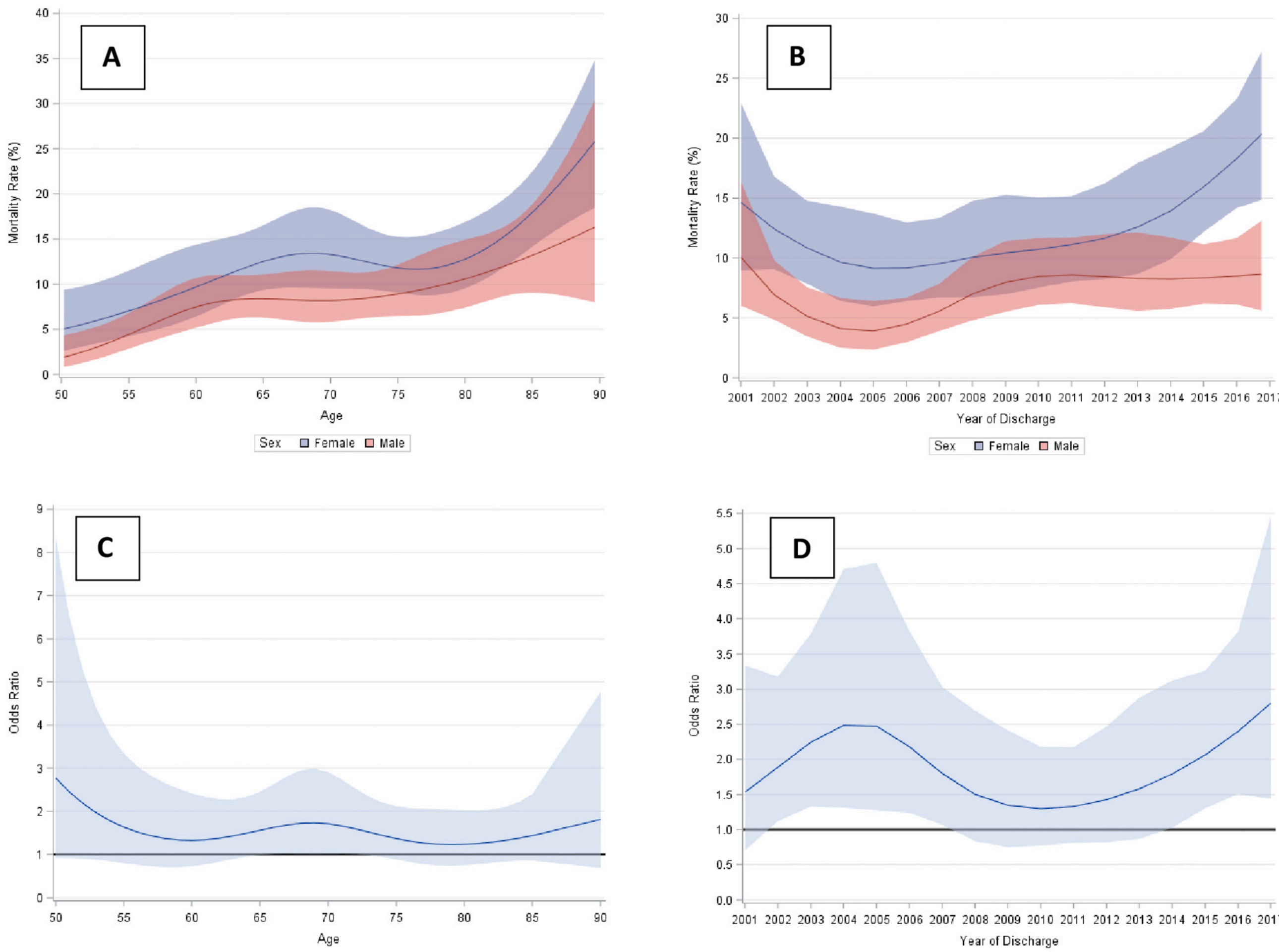

Fig. 2. Unadjusted mortality rate (top) and odds ratio (bottom) for in-hospital mortality between females compared to males across age (left) and year of discharge (right). Odds ratios greater than 1 indicate greater odds of mortality in females (i.e., favors survival in males). Shaded areas represent 95% confidence intervals. For the odds ratios, any confidence interval that includes 1 is not statistically significant.

in clinical presentation, with women presenting more often than men with atypical chest pain or anginal equivalent symptoms [7,27]. These differences in clinical presentation may result in delayed diagnosis, delayed or deferred revascularization and subsequent complications including LV aneurysm [6,7,11]. In addition to these differences in clinical presentation and treatment, unique biologic and pathophysiologic factors could play a role in the greater risk of LV aneurysm in women [28,29]. Furthermore, the results of a 2019 American Heart Association national survey showed that women's awareness of CAD has been declining [30], which could lead to delayed clinical presentation. Accordingly, to improve care for women with acute coronary syndromes, physicians and patients alike must maintain a high index of suspicion in women with atypical symptoms.

Second, our study is the first to report the association between women with LV aneurysm and the lower use of PCI, CABG, coronary atherectomy, and/or LV aneurysm surgery. Multiple previous studies have shown that, in general, women receive cardiac procedures less frequently than men including coronary angiography, PCI, CABG, and other cardiac surgeries [7,10,11,31–33]. In the present retrospective study of an administrative claims database, we were unable to characterize the reasons for underutilization of these potentially life-saving procedures in women. However, a previous study of >6500 acute coronary syndrome patients reported that advanced age, female sex and “physician's risk assessment” were the strongest predictors of underutilization of evidence-based treatments in women compared to men [11,34]. Our study adds to this aspect of the literature, highlighting that women's older age and increased comorbidities (anemia, chronic heart failure, and hemodialysis) could bias physicians' clinical decision-making and diminish utilization of evidence-based AMI treatments in women [34]. Additionally, in alignment with prior research, we found underutilization of mechanical circulatory support (MCS) devices in women compared to men, although the survival benefit associated with these devices remains unproven [11]. This finding can be potentially explained by several reasons: men may have experienced greater hemodynamic instability during and after revascularization procedures, resulting in a greater need for MCS, on the other hand, because, women generally have smaller iliofemoral arteries, and had higher average age at index hospitalization, and so may have had arterial anatomy and/or goals of care discussion resulting in the reduced use of organ support therapies [11]. As such, individual physicians' biases likely play a very significant role in the undertreatment of female patients with LV aneurysm and these biases must be addressed systemically through education and objective professional guidelines.

Third, our study found that women with LV aneurysm complicating AMI had higher unadjusted in-hospital mortality than men (12.7% vs. 7.2%; $p < 0.001$). After adjusting for clinical characteristics and excluding inter-hospital transfers, the magnitude of mortality difference decreased but the relative mortality difference remained large: women had 49% higher odds of adjusted in-hospital mortality than men. In addition, despite numerous advances in medical and procedural therapy since 2001, sex differences in the in-hospital mortality rate have remained stable and high in this AMI-LV aneurysm patient cohort. A multitude of prior studies have definitively established that women suffer higher mortality than men following AMI

Table 4
In-hospital outcomes stratified by sex.

	Male (*n* = 9340)	Female (*n* = 6994)	p
In-hospital mortality, %			
Total cohort	5.8	9.4	<0.001
Exclude transfer out	7.2	12.7	<0.001
Age category			
<55	–	–	–
55–74	6.2	8.8	0.049
75+	7.8	11.0	0.058
STEMI	8.4	13.8	<0.001
NSTEMI	3.1	5.1	0.040
In-hospital complications, %			
Cardiac			
Arrhythmias (VT/VF)	21.4	13.3	<0.001
Acute systolic HF	38.8	43.1	0.012
Cardiogenic shock	10.5	10.2	0.727
LV thrombus	1.3	1.0	0.505
Mechanical complications	1.6	1.9	0.496
Cardiac arrest	4.1	3.2	0.157
Respiratory			
Acute respiratory failure	14.6	13.2	0.215
Mechanical ventilation	9.0	9.3	0.820
Pulmonary embolism	0.6	–	–
Kidney			
Acute renal failure	14.6	13.2	0.215
Hemodialysis	1.6	2.7	0.014
Gastrointestinal			
GI bleed	2.1	3.3	0.043
Hepatic failure	2.4	1.6	0.145
Bleeding requiring transfusion	9.9	10.5	0.540
Vascular			
Acute in-hospital stroke	2.4	3.1	0.220
Intracranial hemorrhage	–	–	–
Length of stay, days	5.3	5.3	0.994
Hospital cost, 2017$	23,873	20,068	<0.001

Note. A dash indicates that the observed count of hospitalizations was less than 10 which precludes reporting as defined in the HCUP-NIS Data Use Agreement.
GI = gastrointestinal.
HF = heart failure.
LV = left ventricular.
NSTEMI = non-ST-elevation myocardial infarction.
STEMI = ST elevation myocardial infarction.
VT = ventricular tachycardia.
VF = ventricular fibrillation.

Table 5
In-hospital mortality within demographic characteristics stratified by biological sex.

	Mortality rate (%)		OR (95% CI)	p
	Male (*n* = 9340)	Female (*n* = 6994)		
Age	Fig. 2		Fig. 2	0.682
Race				
White	8.1	13.6	1.78 (1.29–2.46)	0.610
Black	5.6	10.6	1.98 (0.65–6.05)	
Hispanic	5.3	11.6	2.34 (0.63–8.66)	
Other	3.5	14.4	4.62 (1.15–18.5)	
Insurance				
Medicare	9.8	15.3	1.66 (1.22–2.25)	0.656
Private	4.8	6.4	1.34 (0.67–2.70)	
Other	4.2	8.9	2.25 (0.97–5.27)	
Income quartile				
0 to 25th	8.7	11.1	1.32 (0.77–2.26)	0.369
26th to 50th	4.7	12.0	2.75 (1.48–5.11)	
51st to 75th	7.5	14.0	2.00 (1.18–3.39)	
76th to 100th	7.6	13.1	1.84 (1.12–3.01)	
Location-Teaching status				
Rural	6.5	20.6	3.73 (1.21–11.39)	0.455
Urban nonteaching	6.5	11.3	1.83 (1.15–2.89)	
Urban teaching	7.6	12.7	1.77 (1.26–2.48)	
Bed size				
Small	7.1	14.4	2.19 (0.96–4.99)	0.778
Medium	7.9	12.0	1.59 (0.91–2.80)	
Large	7.0	12.7	1.93 (1.41–2.65)	
Region				
Northeast	5.4	15.7	3.26 (1.67–6.37)	0.088
Midwest	8.0	14.1	1.89 (1.16–3.05)	
South	6.9	12.2	1.89 (1.22–2.91)	
West	8.3	8.3	1.00 (0.54–1.86)	
Year of discharge	Fig. 2		Fig. 2	0.476

Note. Odds ratios greater than 1 indicate greater odds of in-hospital mortality in females (i.e., favor males). The p-value compares the odds ratio within each demographic characteristic (i.e., an interaction effect). If not statistically significant, then all within-characteristic odds ratios are statistically similar.

[6,7,10,11,13,31,35,36], and that female sex was an independent predictor of in-hospital mortality after AMI [35,36]. While the lower PCI frequency following AMI partially explains the higher LV aneurysm incidence and mortality in women, additional factors that may contribute to this difference are women's greater likelihood to have delayed presentation, delayed revascularization, incomplete revascularization, and less comprehensive medical therapy [7,8,13,22]. Furthermore, CABG and cardiac surgeries are rarely performed at the time of active infarction, and they possibly had little impact on the sex differences in the rates of LV aneurysm formation and mortality. However, it is likely that the prospective differences in the prescription of cardioprotective medications between men and women with prognostic benefit after infarction, especially in patients with left ventricular dysfunction, would have had an impact on the mortality in women with LV aneurysm [28]. Nonetheless, women with AMI-LV aneurysm represent a higher risk patient cohort with excess mortality, and further research studies are essential to focus on optimizing patient access to cardioprotective pharmacological therapies as part of guideline-directed AMI care [28,37].

Specifically, our study found that women with LV aneurysm complicating AMI had higher in-hospital mortality than men across all age-groups and across all years during the study period. These findings concur with a prior microsimulation analysis from the nationwide French database of>74,000 patients showing excess mortality after AMI in women across all age groups compared to men [38]. In fact, the excess mortality burden in women persisted even in those, undergoing revascularization at rates similar to men [26,38]. A number of potential factors other than traditional clinical characteristics can explain this persistent excess mortality in women following AMI including psychosocial factors, lower socioeconomic status, delayed emergency room presentation, higher AMI clinical severity, and consistent underuse of guideline-directed medical therapy both at the time of index hospitalization and for secondary prevention of AMI at the time of discharge [7,37]. In an analysis of 6558 acute coronary syndrome patients by Bugiardinini et al. from a Canadian registry, female sex was a strongest

Table 6
In-hospital mortality within clinical characteristics stratified by biological sex.

	Mortality rate (%)		OR (95% CI)	p
	Male (n = 9340)	Female (n = 6994)		
Diabetes				
No	7.0	12.9	1.97 (1.45–2.67)	0.592
Yes	7.5	12.1	1.69 (1.05–2.72)	
Type of AMI				
NSTEMI	3.9	6.8	1.78 (1.09–2.91)	0.693
STEMI	10.3	18.8	2.00 (1.46–2.74)	
PCI				
No	8.2	12.1	1.54 (1.13–2.10)	0.039
Yes	5.5	13.8	2.75 (1.74–4.36)	
CABG				
No	6.9	12.1	1.84 (1.36–2.47)	0.449
Yes	7.9	16.5	2.32 (1.36–3.94)	
Mechanical circulatory support				
No	5.2	9.6	1.94 (1.43–2.63)	0.162
Yes	21.2	44.8	3.02 (1.75–5.22)	

Note. Odds ratios greater than 1 indicate greater odds of in-hospital mortality in females (i.e., favor males). The p-value compares the odds ratio within each clinical characteristic (i.e., an interaction effect). If not statistically significant, then all within-characteristic odds ratios are statistically similar.

predictor of significantly lower prescription of lipid lowering therapies, beta-blockers, ACE-inhibitors, and slightly lower prescription of anti-platelet agents at the time of discharge [34]. Therefore, to reduce the mortality of women with LV aneurysm, not only must women's AMI care be improved systemically, but also care pathways must be implemented to identify aneurysms promptly after AMI, utilize quality indicator (QI) tools to implement and improve the utility of evidence-based mechanical and pharmacological therapies to mitigate the associated mortality and improve the quality of AMI care [39].

4.1. Limitations and strengths

Several design and data limitations should be considered in the interpretation of our findings. First, we conducted a retrospective study using the NIS database, which is primarily designed for administrative purposes. Hence, coding inaccuracy could impact our findings, and in particular, comorbidities may not be captured accurately. Second, imaging data, procedural characteristics like culprit vessel, and post-procedural medical care were unavailable and could differ between the sexes, resulting in unmeasured bias. Importantly, the exact location and extent of the LV aneurysm on echocardiogram, cardiac MRI, or cardiac CT were unavailable. Third, we were unable to assess many crucial AMI parameters such as delay in clinical presentation, door-to-balloon time, duration from AMI presentation to LV aneurysm identification and medications at the time of discharge. Fourth, we were unable to identify concomitant diagnoses like Takotsubo cardiomyopathy as the data use agreement (DUA) for the NIS prohibits reporting tabulated data with values $\leq$10, which could increase the risk for identification of specific patients personally.

Despite these limitations, the NIS database employs stringent data accuracy checks and quality control and has been used successfully for many prior cardiovascular outcomes studies. Due to the large size of the NIS database, our study had the power to capture mortality differences not evident in smaller retrospective studies. Finally, the data are ethnically and geographically diverse, including a wide variety of centers and operators, therefore likely accurately representing real-world practice and outcomes.

5. Conclusions

In this large, population-based analysis of 16,334 hospitalizations for AMI complicated by LV aneurysm between 2001 and 2017, women had a modestly higher incidence of this severe condition than men, but women had dramatically higher in-hospital mortality than men across all age groups. Women with AMI and LV aneurysm were less likely to receive PCI, CABG, and surgical LV aneurysm repair than men. Further research is necessary to validate strategies to ensure that women receive guideline-directed therapy for AMI and for LV aneurysm to address the sex disparity in mortality in these patients.

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Study design, literature review, data curation, formal analysis: VSP, AT, BNP, RWW, AA, VMA, AMG
Data management, drafting manuscript: VSP, AT, RWW, BNP, AA, VMA, AMG
Access to data: VSP, AT, RWW, BNP, AA, VMA, AMG
Manuscript revision, intellectual revisions, mentorship: SV, SEA, NRS, VMA, AMG
Final approval: VSP, AT, RWW, BNP, AA, SV, SEA, NRS, VMA, AMG.

Declaration of competing interest

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