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ORIGINAL RESEARCH

Sex differences in trends and outcomes of acute myocardial infarction with mechanical complications in the United States

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ABSTRACT

Background: Mechanical complications (MC) are rare but significant sequelae of acute myocardial infarction (AMI). Current data on sex differences in AMI with MC is limited.
Methods: We queried the National Inpatient Sample database to identify adult patients with the primary diagnosis of AMI and MC. The main outcome of interest was sex difference in-hospital mortality. Secondary outcomes were sex differences in the incidence of acute kidney injury (AKI), major bleeding, use of inotropes, permanent pacemaker implantation (PPMI), performance of percutaneous coronary intervention (PCI), coronary artery bypass grafting (CABG), surgery (VSD repair and MV surgery), pericardiocentesis, use of mechanical circulatory support (MCS), ischemic stroke, and mechanical ventilation.
Results: Among AMI-MC cohort, in-hospital mortality was higher among females compared to males (41.24% vs 28.13%: aOR 1.39. 95% CI 1.079–1.798; $p = 0.01$). Among those who had VSD, females also had higher in-hospital mortality compared to males (56.7% vs 43.1%: aOR 1.74, 95% CI 1.12–2.69; $p = 0.01$). Females were less likely to receive CABG compared to males (12.03% vs 20%: aOR 0.49 95% CI 0.345–0.690; $p < 0.001$).
Conclusion: Despite the decreasing trend in AMI admission, females had higher risk of MC and associated mortality. Significant sex disparities still exist in AMI treatment.

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Sex differences; myocardial infarction; mechanical complications; papillary muscle rupture; ventricular septal defect; in-hospital mortality; admission trend; trends

1. Introduction

Acute myocardial infarction (AMI) accounts for 31% of all deaths globally per year [1]. AMI complications can be broadly divided into electrical, inflammatory, ischemic, embolic and mechanical [2]. Mechanical complications (MCs) are rare, yet very serious complications caused by the transmural necrosis of the myocardium and other affected tissue resulting to rupture and scarring [3]. Patients with AMI and MC have a mortality rate 12 times higher than those without MC [4]. The most common MCs according to the American Heart Association include papillary muscle rupture (PMR), ventricular septal defect (VSD) and free wall rupture (FWR) [5]. However, MCs occur in only about 0.27 to 0.91% of AMI patients [3,6] making it a huge challenge in conducting population-based studies [7,8]. Sex disparities in in-hospital outcomes following AMI is well established [9–12]. However, only a handful of studies have investigated the sex differences in characteristics and outcomes of AMI with MC in the current era of advanced revascularization strategies. Therefore, to address these gaps, we examined sex differences in the trends of hospitalization, patient characteristics, and in-hospital outcomes of AMI with MC in the US using a nationally representative sample in the 2^{nd} decade of 2000.

2. Methods

2.1. Data source

The data source for this analysis is the National Inpatient Sample (NIS). NIS is the subdivision of the Healthcare Cost and Utilization Project (HCUP) sponsored by the Agency for Healthcare Research and Quality. NIS is the largest publicly available database, with information drawn from 49 states participating in HCUP, covering more than 97% of the US population. The data are structured so that every discharge record represents a single hospitalization with a primary diagnosis and several secondary and procedural diagnoses, defined by the *International Classification of Diseases, Ninth Revision* and *Tenth Revision (ICD-9* and *ICD-10*) codes. The internal validity of the database is maintained by annual quality

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assessments. Although representative of ≈ 20% of all US hospitalizations, national estimates of hospitalizations can be obtained using the sampling weights provided. Data are compiled annually from 1988 through 2020, which allows analysis of disease trends over time. However, the database does not provide state and hospital identifiers, therefore protecting patient confidentiality. The NIS has been previously used to describe the trends in the outcomes of AMI in different populations in the US [9,13,14]. This study was deemed exempt from the requirement of an institutional review board approval because the NIS contains de-identified patient information and is publicly available.

2.2. Study sample

We queried the NIS database from 1 January 2012, to 31 December 2020, to identify women and men aged ≥ 18 with the primary diagnosis of AMI (STEMI and NSTEMI) using the *ICD-9* and *ICD-10*, Clinical Modification (*ICD-9-CM* and *ICD-10-CM*) codes (Table S1). These are validated codes with high-specificity and sensitivity and have been used in several other studies [15–17].

2.3. Patient and hospital characteristics

Using the NIS database for each year, all adult patients (age ≥18 years) with a principal diagnosis of AMI, which includes STEMI, NSTEMI, AMI unspecified, and other types of AMI were identified. A separate subgroup analysis each for STEMI and NSTEMI was done. Furthermore, a separate analysis was done for each MC. The patient population was divided into AMI with associated mechanical complications (MC) versus AMI with no MC. For the purposes of this study, MC is defined as having papillary muscle rupture (PMR) and ventricular septal defect (VSD). Free wall rupture (FWR) was not included as FWR from AMI has no specific ICD code. Records with missing data were also excluded. Baseline patient sociodemographic and hospital characteristics including age, race and ethnicity, primary payer, quartile of median household income, hospital region, teaching status, and bed size associated with the primary diagnosis were obtained from the NIS. Coding for race and ethnicity in the NIS combined self-reported race and ethnicity provided by the data source into 1 data element ('RACE'). If both race and ethnicity were available, ethnicity was preferred over race. The NIS database was also used to identify underlying comorbidities, location of myocardial infarction, and inpatient procedures using *ICD-9-CM* and *ICD-10-CM*, and clinical classification software codes.

3. Statistical analysis

Our analyses considered survey design complexity by incorporating sampling weights, primary sampling units, and strata. This allowed us to estimate population proportions, means, and regression coefficients using survey (*svy*) data commands in STATA. Baseline sociodemographic, hospital, and clinical characteristics were categorized according to sex. Categorical variables were compared using the chi-square test and are expressed as numbers and percentages. Continuous variables were compared using the Student's *t*-test and are reported as mean ± SD or median (interquartile range [IQR]) depending on whether they were normally distributed or not. Effect sizes were expressed using odds ratios (ORs) and 95% confidence intervals (CIs). All p values were 2-sided with a conventional significance threshold of $p < 0.05$. The hospitalization rates of AMI, STEMI and NSTEMI in the overall study cohort were reported per 100,000 inpatient hospitalizations. To provide for a robust analysis and minimize confounders, a large number of covariables were included in the analysis. These include age, race, comorbidities (hypothyroidism, diabetes, fluid and electrolyte abnormalities, hypertension, liver disease, heart failure, carotid artery disease, history of smoking, chronic kidney disease, chronic lung disease, peripheral artery disease, anemia, valvular heart disease, obesity), history of percutaneous coronary intervention (PCI), history of coronary artery bypass grafting (CABG), prior acute MI, and hospital size, location and teaching status, and payer status. Most of these covariables were supplied by the NIS database, while comorbidities were derived from the Elixhauser list of comorbidities. Multivariable logistic regression, adjusted for statistically significant baseline variables, was used to estimate the adjusted odds of in-hospital mortality from 2012 to 2020. To determine the statistically significant baseline variables, binomial regression was used to identify sociodemographic, hospital, and clinical variables that were associated with the outcome of interest. All significant variables were then incorporated into the multivariable logistic regression model. Statistical analyses were performed using Stata 17.0 (StataCorp. 2020. Stata Statistical Software: Release 17. College Station, TX: StataCorp LLC.).

4. Study outcomes

The main outcome of interest was sex difference in-hospital mortality among AMI patients with MCs. Secondary outcomes were sex differences in incidence of AKI, major bleeding, use of inotropes, PPMI, performance of PCI, CABG, surgery, pericardiocentesis, use of mechanical circulatory support (MCS), ischemic stroke, and use mechanical ventilation. This study followed the STROBE reporting guideline. (Table S2)

5. Results

There were 5,639,319 AMI admissions from 2012–2020. After excluding missing and incomplete data, a total of 3,635 AMI with MC admissions were included in the final analysis. (Figure 1) For AMI in general, hospitalization among males was 337,675 in 2012 compared to 339,680 in 2020. In contrast, there was a statistically significant decrease in hospitalization for females (217,750 in 2012 to 191,550 in 2020). Over the 9-year study period, the proportion of females who had MCs from AMI was significantly higher compared to males (p = 0.008). (Figure 2) The same finding was seen in the STEMI cohort ($p = 0.014$). However, there was no significant difference between sexes when considering the trend of PMR and VSD individually ($p = 0.435$, $p = 0.909$ respectively). (Figure 3) Among patients who had STEMI-MC, females were older than males (74.1 ± 0.69 vs. 67.3 ± 0.59; $p < 0.001$). Males

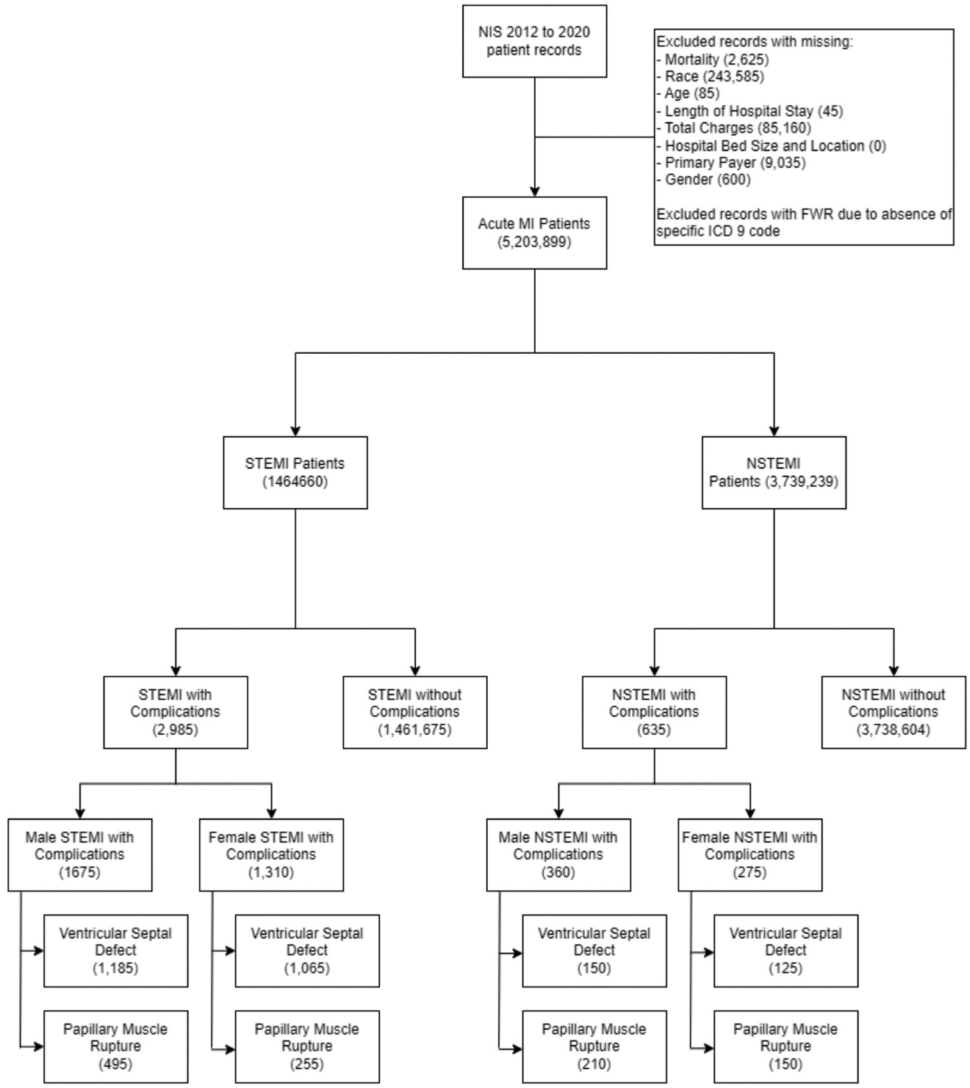

Figure 1. Study flowchart.

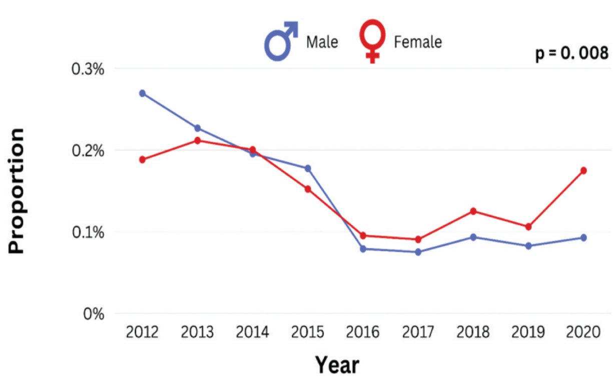

Figure 2. Proportion of females who has mechanical complications from acute myocardial infarction.

had more history of CHF (60.9% vs. 52.3%; $p = 0.04$) while females had more history of stroke (7.6% vs. 3.9%; $p = 0.05$) and obesity (15.6% vs. 10.1%; $p = 0.04$). The majority of patients who had MC had anterior STEMI with females doubling the number of males (46.2% vs. 21.2%; $p < 0.001$). (Table 1)

Among AMI-MC cohort in general, in-hospital mortality was higher among females compared to males (41.24% vs 28.13%: aOR 1.39. 95% CI 1.079–1.798; $p = 0.01$). (Table S3) Among AMI-MC cohorts who had VSD, females had a higher chance of dying in the index hospitalization compared to males aOR 1.74, 95% CI 1.12–2.69; $p = 0.01$). There was no sex difference in in-hospital mortality among AMI cohort with PMR (aOR 0.89, 95% CI 0.43–1.85; $p = 0.75$). (Table 2) Among STEMI-MC cohorts who had VSD, females had a higher in-hospital mortality compared to males (aOR 1.72, 95% CI 1.08–2.74; $p = 0.02$). There was no sex difference in in-hospital mortality among those who had PMR (aOR 1.03, 95% CI 0.41–2.62; $p = 0.94$). (Table 3)

5.1. Subgroup analysis for mortality

Subgroup analysis showed that for AMI with MC in general, age 50 years old and above and female sex were both associated with increased mortality (aOR 3.11; 95% CI 2.977–3.251; $p < 0.001$ and aOR 1.25 95% CI 1.224–1.270; $p < 0.001$, respectively). These findings were also consistent

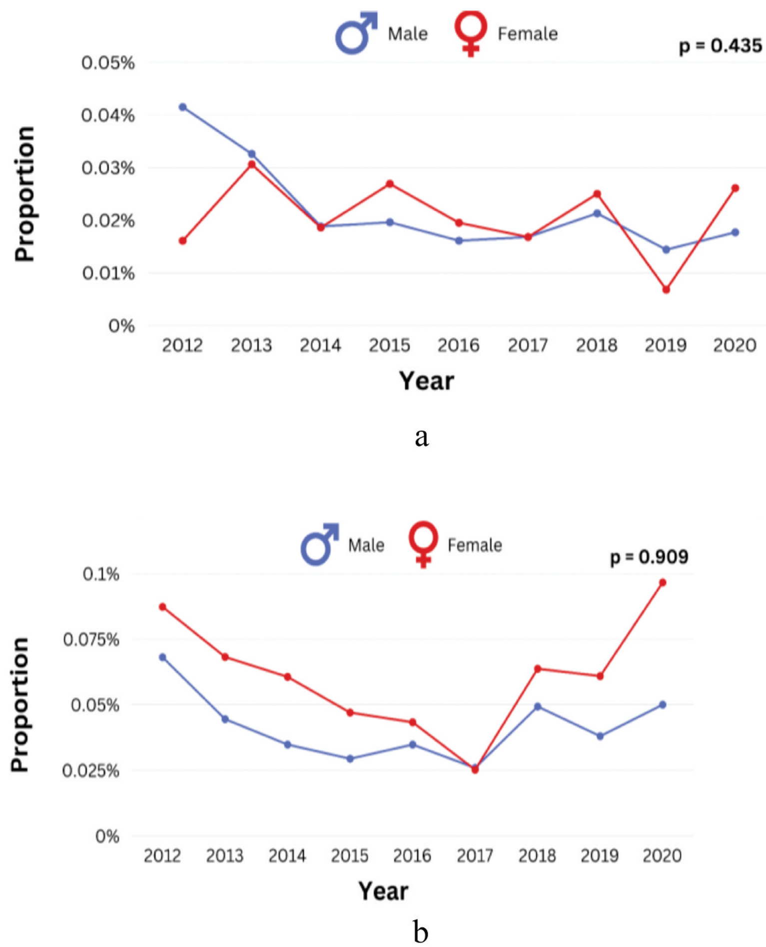

Figure 3. Sex differences in trend on papillary muscle rupture (a) and ventricular septal defect (b) as mechanical complications from acute myocardial infarction.

among those who had STEMI with MC (aOR 2.50; 95% CI 1.076–5.797; $p < 0.033$ and aOR 1.63 95% CI 1.171–2.260; $p < 0.001$ for female sex and age respectively). However, this was not the case for patients who had NSTEMI and MC. (Figure 4)

5.2. Secondary outcomes

Among AMI-MC cohort in general, females were less likely to receive CABG compared to males (12.03% vs 20%, aOR: 0.49 95% CI 0.345–0.690; $p < 0.001$). (Table S3) Among those who had VSD, females were less likely to get surgery compared to males aOR 0.55, 95% CI 0.34–0.88; $p = 0.01$). Among those with PMR, females had more major bleeding (aOR 3.50, 95% CI 1.00–12.22; $p = 0.05$) and ischemic stroke (aOR 5.70, 95% CI 1.00–32.48; $p = 0.05$) compared to males. (Table 2) Among STEMI-MC cohorts who had VSD, females were less likely to get surgery compared to males (aOR 0.60, 95% CI 0.37–1.00; $p = 0.05$). Among STEMI-MC cohort with PMR, females had a lesser chance of getting CABG (aOR 0.33, 95% CI 0.11–0.94; $p = 0.04$). (Table 3) There was no sex difference in the performance of PCI for AMI with MC admissions (aOR 0.89 95% CI 0.708–1.120; $p = 0.320$). There was no sex difference in the utilization of mechanical circulatory support, use of vasopressor, insertion of permanent pacemaker, and pericardiocentesis, and use of mechanical ventilation for respiratory complications. Lastly, the prevalence of ischemic stroke was similar in both sexes. See Figure 5 Central Illustration.

6. Discussion

The most important findings of our study can be summarized as follows: 1) There is decreasing trend in hospitalization for AMI among females 2) The proportion of females who had MC was significantly higher compared to males; 3) Females who had MC had higher odds of dying during the index hospitalization compared to males; 4) Age >/ = 50 years old and female sex were associated with increased mortality during index hospitalization; 5) Men were more likely to undergo CABG compared to females; 6) Females who had VSD had a higher odds of dying in the index admission compared to males 7) For both MC, females were less likely to get surgery compared to males.

In the US, a 20-year trend study of AMI in older patients from 1995–2014 revealed an initial increase in admissions from 1995–2000, followed by a steady decline in the following years [18]. This is perhaps partly because of the changes in methods of diagnosis over time leading to increased detection, followed by a decrease brought about by increased public awareness on risk factors and measures in preventing AMI [18]. Our study is in keeping with the current data

Table 1. Comparison of baseline characteristics among STEMI and NSTEMI patients with mechanical complications stratified according to sex.

Baseline Characteristics	STEMI with mechanical complications			NSTEMI with mechanical complications		
	Male (n = 1,675)	Female (n = 1,310)	p-value	Male (n = 360)	Female (n = 275)	p-value
Age (mean ± SD)	67.3 ± 0.59	74.1 ± 0.69	$p < 0.001$	67.2 ± 1.36	73.9 ± 1.42	$p < 0.001$
Location of STEMI						
Anterior STEMI	355 (21.2%)	605 (46.2%)	0.00			
Inferior STEMI	1,120 (66.9%)	530 (40.5%)				
STEMI of other site	80 (4.8%)	95 (7.3%)				
STEMI, unspecified site	120 (7.2%)	80 (6.1%)				
Race						
White	1,365 (81.5%)	1,180 (90.1%)	0.09	290 (80.6%)	210 (76.4%)	0.19
Black	60 (3.6%)	35 (2.7%)		15 (4.2%)	25 (9.1%)	
Hispanic	115 (6.9%)	50 (3.8%)		15 (4.2%)	20 (7.3%)	
Asian Pacific Islander	25 (1.5%)	5 (0.4%)		15 (4.2%)	0 (0.0%)	
Native American	25 (1.5%)	10 (10.8%)		0 (0.0%)	10 (3.6%)	
Other races	85 (5.1%)	30 (2.3%)		25 (6.9%)	10 (3.6%)	
Hypertension	640 (38.2%)	585 (44.7%)	0.11	140 (38.9%)	130 (47.3%)	0.35
Diabetes	445 (26.6%)	425 (32.4%)	0.12	75 (20.8%)	85 (30.9%)	0.20
Congestive heart failure	1,020 (60.9%)	685 (52.3%)	0.04	235 (65.3%)	175 (63.6%)	0.85
Hypothyroidism	80 (4.8%)	275 (21.0%)	0.00	15 (4.2%)	60 (21.8%)	0.00
Smokers	290 (17.3%)	170 (13.0%)	0.14	105 (29.2%)	50 (18.2%)	0.15
Chronic kidney disease	350 (20.9%)	230 (1706%)	0.31	75 (20.8%)	65 (23.6%)	0.70
COPD	115 (6.9%)	120 (9.2%)	0.30	65 (18.1%)	35 (12.7%)	0.42
Peripheral Vascular disease	190 (11.3%)	160 (12.2%)	0.74	45 (12.5%)	35 (12.7%)	0.97
Carotid artery disease	30 (1.8%)	20 (1.5%)	0.80	5 (1.4%)	0 (0.0%)	0.38
Obesity	170 (10.1%)	205 (15.6%)	0.04	65 (18.1%)	40 (14.5%)	0.59
Anemia	695 (41.5%)	470 (35.9%)	0.17	145 (40.3%)	120 (43.6%)	0.71
Valvular disease	585 (34.9%)	410 (31.3%)	0.35	195 (54.2%)	145 (52.7%)	0.87
Fluid and electrolyte disorders	1,030 (61.5%)	790 (60.3%)	0.77	160 (44.4%)	130 (47.3%)	0.75
History of PCI	120 (7.2%)	65 (5.0%)	0.26	20 (5.6%)	10 (3.6%)	0.61
History of CABG	100 (6.0%)	75 (5.7%)	0.90	15 (4.2%)	20 (7.3%)	0.45
Prior MI	65 (3.9%)	80 (6.1%)	0.21	15 (4.2%)	35 (12.7%)	0.08
Prior Stroke	65 (3.9%)	100 (7.6%)	0.05	20 (5.6%)	10 (3.6%)	0.62
History of dialysis	10 (0.6%)	0 (0.0%)	0.21	5 (1.4%)	0 (0.0%)	0.38
Liver disease	530 (31.6%)	530 (40.5%)	0.04	35 (9.7%)	20 (7.3%)	0.63
Hospital bed size						
Bed size small	65 (3.9%)	110 (8.4%)	0.07	60 (16.7%)	15 (5.5%)	0.13
Bed size medium	430 (25.7%)	325 (24.8%)		65 (18.1%)	65 (23.6%)	
Bed size large	1,180 (70.4%)	875 (66.8%)		235 (65.3%)	195 (70.9%)	
Hospital location						
Rural hospital	75 (4.5%)	65 (5.0%)	0.63	10 (2.8%)	0 (0.0%)	0.01
Urban non-teaching	340 (20.3%)	225 (17.2%)		40 (11.1%)	90 (32.7%)	
Urban teaching	1,260 (75.2%)	1,020 (77.9%)		310 (86.1%)	185 (67.3%)	
Primary payment coverage						
Payer Medicare	845 (50.4%)	990 (75.6%)	<0.001	175 (48.6%)	220 (80.0%)	<0.001
Payer Medicaid	110 (6.6%)	90 (6.9%)		35 (9.7%)	10 (3.6%)	
Payer Private Insurance	505 (30.1%)	190 (14.5%)		120 (33.3%)	45 (16.4%)	
Payer self-pay	125 (7.5%)	35 (2.7%)		15 (4.2%)	0 (0.0%)	
Payer no charge	0 (0.0%)	0 (0.0%)		0 (0.0%)	0 (0.0%)	
Payer other	90 (5.4%)	5 (0.4%)		15 (4.2%)	0 (0.0%)	

Abbreviations: AMI: Acute Myocardial Infarction; CABG: Coronary Artery Bypass Graft; COPD: Chronic Obstructive Pulmonary Disease; MI: Myocardial Infarction; MC: Mechanical Complications (includes Ventricular Septal Defect and Papillary Muscle Rupture); PCI: Percutaneous Coronary Intervention.

showing a decreasing trend in both NSTEMI and STEMI admissions among females [15–17]. Following the advent of early reperfusion and revascularization strategies, the incidence of MC from AMI has decreased dramatically [5]. However, despite newer strategies, mortality in patients with MC has not declined [5]. Current evidence on the trend in incidence of MC is outdated, as most recently published studies report data from the 1970s to 2015. In general, studies conducted in Europe and Asia all reported a decreasing incidence of MC [7,19,20]. In the US, one population-based study showed no significant change in the trend of MC incidence from 2003–2015 [3]. Following this result, our study reported a similar pattern from 2012–2020, indicating that this trend has not changed in recent years. Our analysis revealed that a higher proportion of patients who had MC from AMI were females. Furthermore, we established females had a higher in-hospital mortality compared to males. In the study by Sanchez-Jimenez et al., majority of female patients admitted for AMI had MC (43.5% versus 37.4%, $p < 0.001$) [4]. Furthermore, they established that female sex was a predictor for MC following AMI. Data from the Get With The Guidelines – Coronary Artery Disease (GWTG-CAD) Registry with 78,254 patients from 2001 to 2006 revealed that female sex was associated with a higher in hospital mortality particularly in the STEMI group (10.2% versus 5.5%; $p < 0.001$) [21]. In addition, females were less likely to receive early aspirin and β-blocker treatment, timely reperfusion therapy, as well as lower use of cardiac catheterization and revascularization procedure post-MI [22]. Moreover, the International Survey of Acute Coronary Syndromes in Transitional Countries (ISACS-TC) Registry also reported female sex to be associated with a significantly higher 30-day mortality rate compared to males (11.6% vs.

Table 2. Adjusted comparative outcomes among patients with STEMI who had mechanical complications stratified according to sex.

	Males (*n* = 1,185)	Females (*n* = 1,065)	aOR	95% CI	P value
STEMI patients who developed VSD					
In-hospital mortality	550 (46.4%)	630 (59.2%)	1.72	1.08–2.74	0.02
Acute kidney injury	765 (64.6%)	580 (54.5%)	0.90	0.51–1.59	0.72
Major bleeding	60 (5.1%)	60 (5.6%)	0.55	0.17–1.80	0.32
Use of vasopressors	145 (12.2%)	160 (15.0%)	1.53	0.84–2.77	0.17
PPM Implantation	15 (1.3%)	15 (1.4%)	0.69	0.06–8.41	0.77
PCI	575 (48.5%)	555 (52.1%)	0.84	0.54–1.30	0.43
CABG	285 (24.1%)	145 (13.6%)	0.71	0.40–1.24	0.23
Surgery	510 (43.0%)	285 (26.8%)	0.60	0.37–1.00	0.05
Pericardiocentesis	30 (2.5%)	20 (1.9%)	1.18	0.34–4.14	0.79
Mechanical circulatory support	880 (74.3%)	620 (58.2%)	0.65	0.40–1.24	0.09
Ischemic stroke	65 (5.5%)	35 (3.3%)	0.47	0.13–1.67	0.24
Mechanical ventilation	470 (39.7%)	405 (38.0%)	1.12	0.71–1.79	0.62
	Males (*n* = 495)	Females (*n* = 255)	aOR	95% CI	P value
STEMI patients who developed PMR					
In-hospital mortality	215 (43.4%)	120 (47.1%)	1.03	0.41–2.62	0.94
Acute kidney injury	325 (65.7%)	155 (60.8%)	0.44	0.16–1.24	0.12
Major bleeding	25 (5.1%)	15 (5.9%)	1.35	0.24–7.57	0.73
Use of vasopressors	65 (13.1%)	45 (17.6%)	1.14	0.30–4.31	0.85
PPM Implantation	0 (0.0%)	0 (0.0%)	N/A*	N/A*	N/A*
PCI	255 (51.5%)	155 (60.8%)	1.41	0.62–3.17	0.41
CABG	155 (31.3%)	45 (17.6%)	0.33	0.11–0.94	0.04
Surgery	280 (56.6%)	140 (54.9%)	0.62	0.24–1.61	0.33
Pericardiocentesis	5 (1.0%)	5 (2.0%)	N/A*	N/A*	N/A*
Mechanical circulatory support	380 (76.8%)	200 (78.4%)	0.94	0.35–2.56	0.91
Ischemic stroke	30 (6.1%)	25 (9.8%)	8.59	0.69–107.53	0.10
Mechanical ventilation	300 (60.6%)	165 (64.7%)	0.92	0.40–2.11	0.84

Abbreviations: CABG=coronary artery bypass grafting; CI=confidence interval; PCI=percutaneous coronary intervention; PMR=papillary muscle rupture; PPM=permanent pacemaker; STEMI=ST segment elevation myocardial infarction; VSD=ventricular septal defect.

Table 3. Adjusted comparative outcomes among patients with AMI who had mechanical complications stratified according to sex.

	Males (*n* = 1,335)	Females (*n* = 1,190)	aOR	95% CI	P value
AMI patients who developed VSD					
In-hospital mortality	575 (43.1%)	675 (56.7%)	1.74	1.12–2.69	0.01
Acute kidney injury	855 (64.0%)	625 (52.5%)	0.69	0.41–1.18	0.18
Major bleeding	60 (4.5%)	25 (2.1%)	0.58	0.18–1.85	0.36
Use of vasopressors	145 (10.9%)	165 (13.9%)	1.58	0.87–2.89	0.13
PPM Implantation	15 (1.1%)	15 (1.3%)	0.79	0.09–7.12	0.84
PCI	620 (46.4%)	570 (47.9%)	0.82	0.55–1.24	0.35
CABG	310 (23.2%)	160 (13.4%)	0.65	0.38–1.12	0.12
Surgery	545 (40.8%)	300 (25.2%)	0.55	0.34–0.88	0.01
Pericardiocentesis	30 (2.2%)	20 (1.7%)	1.20	0.33–4.28	0.78
Mechanical circulatory support	935 (70.0%)	655 (55.0%)	0.66	0.42–1.04	0.07
Ischemic stroke	70 (5.2%)	40 (3.4%)	0.57	0.15–2.17	0.41
Mechanical ventilation	505 (37.8%)	415 (34.9%)	0.98	0.63–1.53	0.94
	Males (*n* = 705)	Females (*n* = 405)	aOR	95% CI	P value
AMI patients who developed PMR					
In-hospital mortality	265 (37.6%)	160 (39.5%)	0.89	0.43–1.85	0.75
Acute kidney injury	455 (64.5%)	230 (56.8%)	0.40	0.18–0.91	0.03
Major bleeding	25 (3.5%)	25 (6.2%)	3.50	1.00–12.22	0.05
Use of vasopressors	95 (13.5%)	55 (13.6%)	1.08	0.36–3.21	0.89
PPM Implantation	5 (0.7%)	0 (0.0%)	N/A*	N/A*	N/A*
PCI	320 (45.4%)	215 (53.1%)	1.24	0.66–2.33	0.51
CABG	260 (36.9%)	105 (25.9%)	0.51	0.23–1.12	0.09
Surgery	410 (58.2%)	235 (58.0%)	1.00	0.48–2.10	0.99
Pericardiocentesis	5 (0.7%)	10 (2.5%)	N/A*	N/A*	N/A*
Mechanical circulatory support	510 (72.3%)	285 (70.4%)	0.84	0.39–1.82	0.66
Ischemic stroke	35 (5.0%)	25 (6.2%)	5.70	1.00–32.48	0.05
Mechanical ventilation	390 (55.3%)	230 (56.8%)	0.88	0.45–1.72	0.72

Abbreviations: AMI=Acute myocardial infarction; CABG=coronary artery bypass grafting; CI=confidence interval; PCI=percutaneous coronary intervention; PMR=papillary muscle rupture; PPM=permanent pacemaker; STEMI=ST segment elevation myocardial infarction; VSD=ventricular septal defect.

6.0%, $p < 0.001$) [23]. In this study, sex disparity was prominent in females under 60 years of age, with older age associated with less significant gap in mortality. We established that females who had MC from STEMI also had a higher mortality during the index admission compared to their male counterparts, with similar results reported in earlier studies [5,24,25].

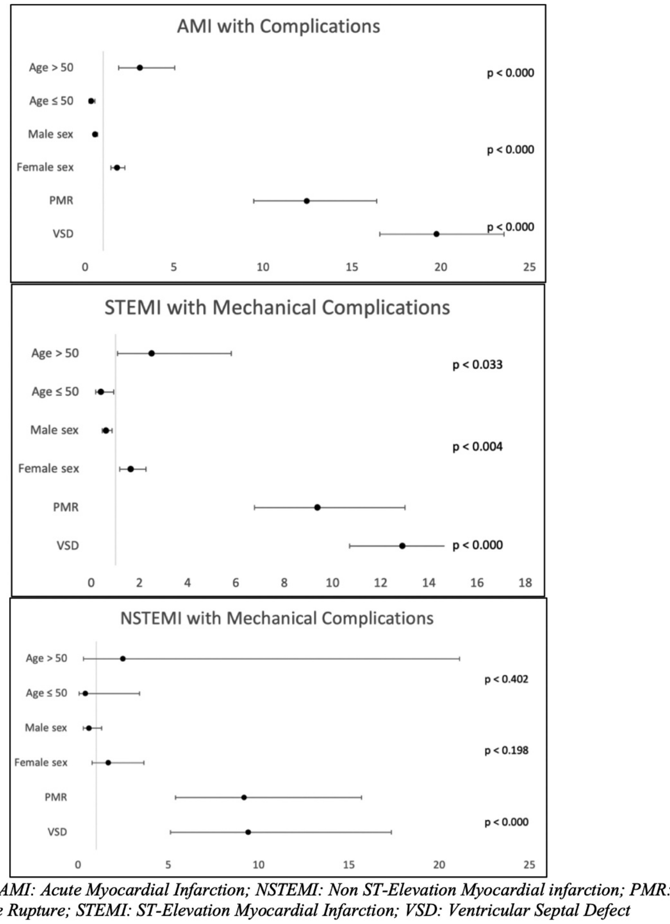

Figure 4. Subgroup analysis for in-hospital mortality in patients with ST-Segment elevation myocardial infarction, non-ST segment elevation myocardial infarction, and acute myocardial infarction who had mechanical complications according to age and sex.

Abbreviations: AMI: Acute Myocardial Infarction; NSTEMI: Non ST-Elevation Myocardial Infarction; PMR: Papillary Muscle Rupture; STEMI: ST-Elevation Myocardial Infarction; VSD: Ventricular Septal Defect.

Several factors including disparities in in-hospital care, higher prevalence of unfavorable comorbidities, and unique risk factors all contribute to an increased mortality rate in females with STEMI compared to males. As aforementioned, sex disparities in care for patients who had AMI has been established to exist for a long time. Females with STEMI receive suboptimal care than males despite multiple guidelines stating no difference in management [22,26,27]. For instance, females are less likely to undergo diagnostic catheterization and PCI than males [1,28–30]. We established that PMR and VSD were each associated with an increased risk for mortality ($p < 0.001$ and $p < 0.001$, respectively). Interestingly, a report from the Should we use emergently revascularize Occluded Coronaries in Cardiogenic Shock (SHOCK) Trial observed that females had a significantly higher incidence of MC post-AMI leading to cardiogenic shock (VSD: 7.7% in women vs. 3.5% in men, $p = 0.003$; severe MR: 11.4% in women vs. 7.1% in men, $p = 0.014$) [31,32]. The reduced collateral blood flow observed in women can lead to an increased incidence of complications during acute total coronary occlusion [31]. It is worth noting that whilst this is consistent with the literature cited, recently Giblett et al. found that amongst patients who had VSD from STEMI, there was no mortality difference between sexes when treated [33]. We found out that the majority of females with MC from STEMI had an anterior infarct. This is in contrast to women in the STEMI without MC cohort who mostly had inferior infarct. Findings from previous studies observed that anterior STEMI is associated with increased risk of FWR, PMR and VSD [34–37].

Studies have shown the existence of sex disparities in the performance of CABG among patients admitted for AMI [37–41]. In the 15-year retrospective study by Ashraf et al., they established that more men undergo CABG compared to women [42]. This was echoed by the findings of Bertoni et al. and Worrall-Carter et al., where they established that women were 25% to 40% less likely compared to men to receive CABG following AMI during the index admission [38,43]. Furthermore, utilizing the Swedish Coronary Angiography and Angioplasty Registry, Gudnadottir et al. established that among women with 2- or 3-vessel disease or left main stem stenosis, women were less likely to undergo CABG compared to men [44]. Not only does women receive less CABG but also suffer more adverse outcome after the procedure. Gupta et al. found that women who had CABG were 32% more likely to die compared with men. In addition, women had a higher rate of 30-day and 90-day readmission, aOR: 1.24, 95% CI: 1.21–1.28 and 1.25, 95% CI: 1.22–1.28, respectively [45]. This difference

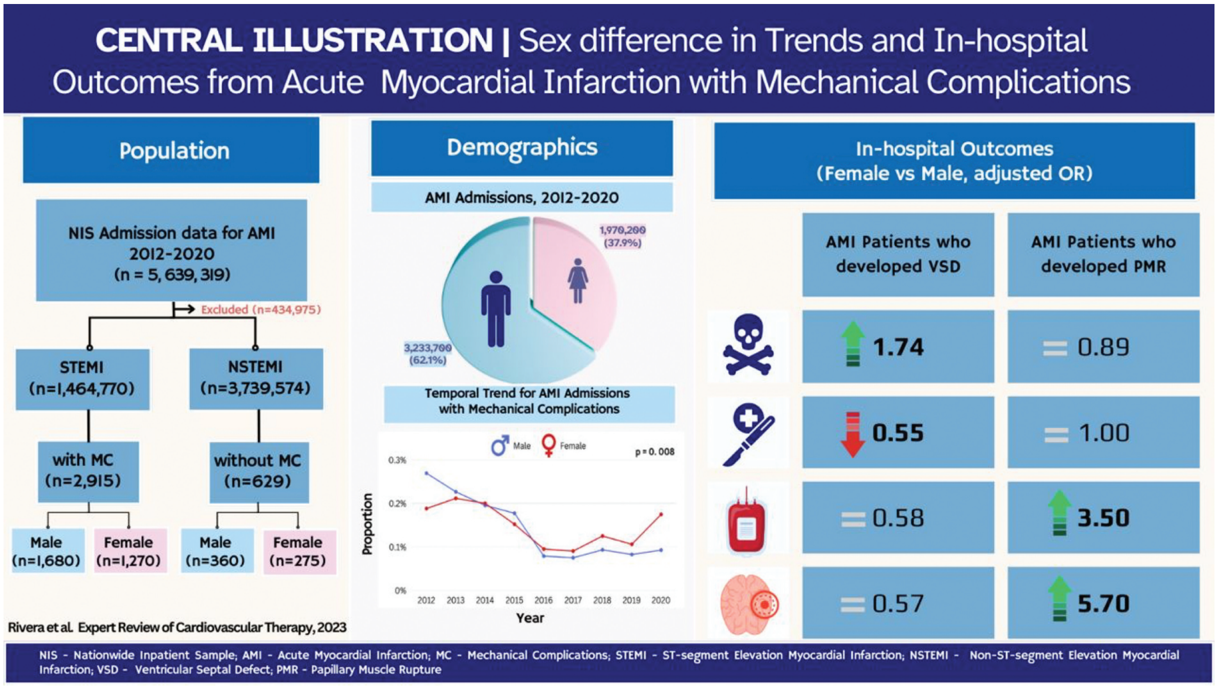

Figure 5. Central illustration.

in management between sexes is often attributed to knowledge-mediated bias especially in AMI where more females tend to present with additional symptoms which are often perceived as non-cardiac [46,47].

In the last decade, significant advances in the management of AMI have led to early diagnosis and management of related complications. Despite this, the gap in sex differences in in-hospital mortality still persist through decades highlighting a need for further action.

7. Strengths and limitations

To our knowledge, this is the first nationwide long-term retrospective study to specifically explore the sex difference among AMI patients presenting with MC. There are several limitations in our study. Being an administrative database utilizing ICD codes, the NIS is susceptible to documentation or coding errors which can lead to bias. Unsurprisingly, the results for the STEMI group mirror the NSTEMI group. In fact, for post infarct, VSD it is very likely that almost if not all the NSTEMI group are miscoded/misdiagnosed late STEMI cases since it requires transmural infarction. Moreover, the ICD-9 and 10 codes for left ventricular free wall rupture (FWR) lacks sensitivity and specificity hence we decided not to include it in our analysis. In addition, the absence of specific and deep data on MC subgroups regarding the role of sex in patients with MC is also a limitation of our study. Furthermore, the absence of deep data concerning surgery and outcomes after surgery gives an incomplete analysis of the sex differences issue. In addition, we combined all MCS modalities under the umbrella term ‘mechanical circulatory support’ hence lacking disaggregated data on the outcomes of each MCS. Lastly, the NIS represents hospitalization data; certain concomitant diagnoses may represent illnesses acquired outside the documented admission period. For similar reason, the NIS does not provide data on laboratory results and medications that patients were taking.

8. Conclusion

Although females were more likely to have MCs from AMI across the years, there is an overall decreasing trend in both sexes with regards to AMI admissions and the incidence of MCs arising from AMI. Among patients admitted for AMI, female sex and age >50 years were predictors of mortality, particularly in STEMI, regardless of the presence of MC. Significant sex disparities still exist in AMI treatment, as females were less likely to CABG and surgery for MCs. Further studies are needed to understand why females with AMI have a higher risk of MCs and less likely to life saving interventions. Factors such as delays in presentation and diagnosis, time from presentation to revascularization, troponin levels at presentation, and collateralization need to be evaluated.

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Ethic statement

Ethics approval for this paper is not required because this study is based exclusively on published literature. Patient consent was not needed as this study was based on publicly available data.

Data availability statement

All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

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