

Research paper

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# Sex-specific disparities in patients undergoing isolated CABG $^{\star}$



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#### A R T I C L E I N E O

## ABSTRACT

Keywords: CABG outcomes	Study objective: Examine sex-specific characteristics in patients undergoing coronary artery bypass grafting (CABG) at our institution.
Sex-disparities Ischemic heart disease	<i>Design</i> : Retrospective chart review was performed utilizing our institutional Society of Thoracic Surgeons (STS) database.
	Setting: An academic, quaternary care center from 2010 to 2021.
	Participants: 3163 females and 9573 males underwent isolated CABG.
	<i>Interventions:</i> The institutional STS database was queried for preoperative, intraoperative, and postoperative variables.
	Main outcome measures: Univariate comparisons between female and male groups were performed using chi-
	squared tests or fisher exact tests. Multivariate logistic regression was used to assess risk factors for 30-day mortality.
	Results: Females had more preoperative comorbidities than males, including hypertension, diabetes, peripheral
	arterial disease, cerebrovascular disease, renal failure, and prior myocardial infarction. Females more frequently
	underwent urgent (61 % vs. 58 %) or emergent CABG (5.8 % vs. 4.3 %) compared to males ( $p$ $<$ 0.0001). Females
	experienced longer total intensive care unit (ICU) hours (48.3 h vs. 43.5 h) ( $p < 0.0001$ ), were more frequently
	discharged to an extended care facility (13 $\%$ vs. 6.4 $\%$ ) (p < 0.0001) and prescribed less aspirin and beta blocker
	therapy at discharge than males. In-hospital mortality was higher in females (1.9 % vs. 1.2 %, $p = 0.002$ ), as was
	30-day mortality (2.7 % vs. 1.6 %, $p = 0.0001$ ). Female sex was an independent risk factor for 30-day mortality
	(odds ratio = 1.46, 95 % CI: 1.06, 2.03, p = 0.02).
	<i>Conclusion:</i> Over the past decade, females undergoing CABG had more preoperative comorbidities, urgent and emergent operations, longer postoperative ICU stay and a higher risk of mortality than their male counterparts.
	Further studies must investigate these disparities to improve outcomes for females undergoing CABG.

#### 1. Introduction

Cardiovascular disease remains a leading cause of death worldwide with nearly 17.9 million deaths annually, and the majority due to ischemic heart disease [1]. Our current management of ischemic heart disease involves medical therapy and revascularization with either percutaneous coronary interventions (PCI) or coronary artery bypass grafting (CABG). In multivessel coronary artery disease (CAD), or anatomy that is not conducive to PCI, CABG can provide restoration of coronary artery blood flow to jeopardized myocardium. CABG has consistently remained the most commonly performed cardiac surgery globally. Of the nearly 300,000 annual cardiac surgeries reported in the Society of Thoracic Surgeons (STS) adult cardiac surgery database in 2019, more than half were isolated CABG [2]. Despite the high frequency with which CABG is performed, several studies have demonstrated worse outcomes for females compared to males. A retrospective study of 3404 patients undergoing isolated CABG between 1995 and 1999 demonstrated that females were less likely to receive a left internal mammary artery (LIMA) graft and that female sex was an independent predictor of long-term adverse outcomes (HR = 1.18, p = 0.03) [3]. Additional research on 15,440 patients undergoing CABG across 31 midwestern hospitals from 1999 to 2000 also found female sex to be an independent predictor of perioperative mortality after accounting for all comorbidities including low BSA (risk-adjusted operative mortality:

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3.81 % for females, 2.43 % for males) [4]. In a more recent analysis of CABG outcomes among 1,042,506 patients between 2011 and 2018, female patients had higher odds of death compared with male patients (OR, 1.26; 95 % CI, 1.21 to 1.30) [5]. These findings of sex-disparate outcomes conflict with other studies that did not note any difference in mortality rates between females and males. Data from 1597 patients who underwent isolated CABG found that propensity matching females and males was challenging, with only 26 % of females able to be matched with males. In those patients that were well-matched, female sex was not associated with increased mortality [6]. Given the conflicting data on mortality outcomes between female and male patients undergoing isolated CABG, additional work is needed to define the barriers to improving outcomes for all patients with ischemic heart disease. Our study examines sex-specific characteristics in patients undergoing CABG at our institution to further address the gaps in our understanding of sex-specific disparities in care.

### 2. Materials and methods

Using our institutional STS database, we identified adult patients older than 18 years of age undergoing isolated CABG at Emory University in Atlanta, Georgia between 2010 and 2021. The study was approved by the Emory University Institutional Review Board. 12,736 total patients were identified. Demographic data collected included: patient characteristics (age, race, sex, body mass index, family history of premature CAD) and pertinent comorbidities (hypertension, diabetes, peripheral arterial disease, chronic lung disease, cerebrovascular disease, renal failure on hemodialysis, prior myocardial infarction, and heart failure). Additional preoperative variables collected included: preoperative creatinine, cardiogenic shock, previous cardiac intervention, previous PCI, previous cardiac surgery, previous CABG, and number of diseased vessels. Intraoperative variables collected included: operative status (elective, urgent, emergent, emergent salvage), use of cardiopulmonary bypass (CPB), time on CPB, aortic cross-clamp time, lowest temperature, intraoperative blood products, use of robot, number of distal vein anastomoses, and number of distal arterial anastomoses. Urgent operative status as defined by STS is described as surgery required during the same hospitalization in order to minimize chance of further clinical deterioration. Emergent operative status included patients with ongoing, refractory unrelenting cardiac compromise with or without hemodynamic instability and not responsive to any other therapy. The number of distal vein anastomoses were identified as number of vein grafts utilized, and the number of distal arterial anastomoses were identified as the number of grafts including internal mammary artery (IMA) or radial artery grafts. Postoperative variables collected included: total intensive care unit (ICU) hours, stroke, pneumonia, prolonged ventilator use (cumulative duration of 24 h or more of endotracheal intubation after transfer from operating room to ICU) [7], renal failure, need for dialysis at the time of discharge, in-hospital mortality, 30-day mortality, cardiac medications at the time of discharge, and discharge location. Patients within our cohort were consecutively identified and none were excluded from analysis. Any missing variables for individual patients were not included in the analysis. Statistical analysis was completed by statisticians within the Emory Department of Surgery. Univariate comparisons between female and male groups were performed using chi-squared tests or fisher exact tests. Multivariate logistic regression was used to assess risk factors for 30-day mortality. The pre-specified threshold for significance for each end point was a *p* value  $\leq$  0.02.

## 3. Results

We identified 3163 female and 9573 male adult patients undergoing isolated CABG at our institution between 2010 and 2021. The median age of the cohort was 66 years for females and 65 years for males. Median BMI was 29.3 for females and 28.5 for males. Females had

significantly more preoperative comorbidities than males, including hypertension (94 % vs. 91 %), diabetes (55 % vs. 44 %), peripheral arterial disease (17 % vs. 14 %), cerebrovascular disease (25 % vs. 19 %), renal failure on hemodialysis (4.6 % vs. 3 %), and prior myocardial infarction (MI) (57 % vs. 52 %) (all p < 0.0001) (Fig. 1). When examining severity of diabetes, females had a higher median hemoglobin A1C than males (6.2 vs. 6.0, p < 0.0001). Heart failure status was a notable missing variable in 53 % of patients in our cohort, but for those patients with data available (1548 patients), there was no significant difference between females and males with regard to presence of absence of heart failure (25 % vs. 26 %, p = 0.15), and median EF for both groups was 55 %. Females had a greater number of diseased vessels than males (4 vs. 3, p < 0.0001). Females and males had similar rates of cardiogenic shock (3.1 % vs. 2.8 %, p = 0.38), previous PCI (31 % vs. 31 %, p = 0.75), previous cardiac surgery (2.6 % vs. 2.7 %, p = 0.85), and previous CABG (2.1 % vs. 2.3 %, p = 0.67). Females had a higher median STS Predicted Morbidity and Mortality score (13.1 % vs. 9.2 %, p < 0.0001) and higher median STS Predicted Mortality score (1.5 % vs. 0.8 %, p < 0.0001) (Table 1).

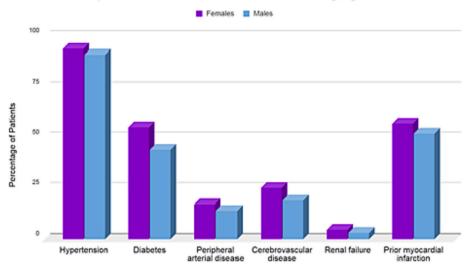
In terms of operative characteristics, females more frequently underwent urgent (61 % vs. 58 %) or emergent CABG (5.8 % vs. 4.3 %) compared to males (p < 0.0001) (Fig. 2). Females less frequently had on pump operations (41 % vs. 52 %, p < 0.0001) compared to males, but those who did undergo CPB had lower CPB time than males (94 min vs. 102 min, p < 0.0001). Aortic cross-clamp time was also lower in females (70 min vs. 78 min, p < 0.0001). Females were more likely than males to receive intraoperative blood products compared to males (39 % vs. 19 %, p < 0.0001) (Table 2). Females had fewer distal arterial anastomoses than males: 0 distal arterial anastomoses in 3.4 % females vs. 1.8 % in males (p < 0.0001) and 1 distal arterial anastomoses were performed in only 6.5 % females compared to 12 % males (p < 0.0001) (Table 3).

In terms of postoperative characteristics, females experienced longer total intensive care unit (ICU) hours (48.3 h vs. 43.5 h, p < 0.0001). Females more frequently had prolonged ventilation (13 % vs. 8.5 %, p < 0.0001). Females more often experienced in-hospital post-operative stroke (2.3 % vs. 1.4 %, p = 0.0004). Females were more frequently discharged to an extended care facility (13 % vs. 6.4 %, p < 0.0001). On review of discharge medications, females were less frequently discharged on aspirin (97 % vs. 98 %, p = 0.0001) and beta-blocker (95 % vs. 96 %, p = 0.01). However, females were more frequently discharged on a statin (99 % vs. 98 %, p = 0.0004). In-hospital mortality was higher in females (1.9 % vs. 1.2 %, p = 0.002), as was 30-day mortality (2.7 % vs. 1.6 %, p = 0.0001) (Fig. 3) (Table 4).

Multivariable logistic regression model demonstrated several independent risk factors for 30-day mortality. Female sex was an independent risk factor for 30-day mortality (OR = 1.46, 95 % CI: 1.06, 2.03, p = 0.02). Additional independent risk factors included age (OR = 1.04, 95 % CI: 1.02, 1.05, p < 0.0001), presence of renal failure on hemodialysis (OR = 2.11, 95 % CI: 1.16, 3.84, p = 0.01), prior MI (OR = 1.79, 95 % CI: 1.25, 2.58, p = 0.002), cardiogenic shock (OR = 11.37, 95 % CI: 7.71, 16.77, p < 0.0001), and previous CABG (OR = 5.92, 95 % CI: 3.54, 9.90, p < 0.0001) (Table 5).

#### 4. Discussion

We examined the sex-specific characteristics in adult patients undergoing isolated CABG at our institution and compared preoperative, intraoperative, and postoperative variables between females and males. The major findings of our study were that females undergoing CABG over the past decade had more preoperative comorbidities, more frequent urgent and emergent operations, longer postoperative ICU stay, and a higher risk of mortality than their male counterparts. Furthermore, female sex was an independent risk factor for 30-day mortality. Our findings are consistent with those published in a retrospective cohort study of 1,297,204 patients from the STS Database who Preoperative Comorbidities in Females vs. Males Undergoing CABG



**Fig. 1.** Preoperative comorbidities in females vs. males undergoing CABG. Females had more preoperative comorbidities than males (all p < 0.0001).

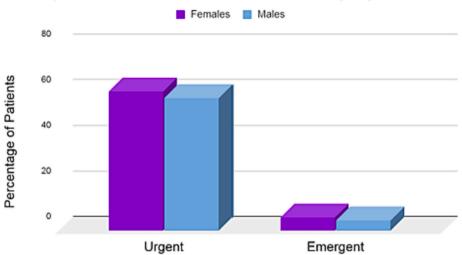
Table 1
Demographics and preoperative characteristics in patients undergoing CABG.

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	Total	Male	Female	p-Value
	( <i>n</i> =	( <i>n</i> =	(n = 3163)	•
	12,736)	9573)		
Age, years	65 (57, 72)	65 (57,	66 (58, 73)	< 0.0001
		71)		
Race				
White	9035 (71)	7039 (74)	1946 (62)	< 0.0001
Black/African American	2612 (21)	1600 (17)	1012 (32)	< 0.0001
Asian	545 (4.3)	438 (4.6)	107 (3.4)	0.004
American Indian or	47 (0.4)	39 (0.4)	8 (0.3)	0.21
Alaskan Native				
Native Hawaiian or	29 (0.2)	25 (0.3)	4 (0.1)	0.17
Pacific Islander				
Other	424 (3.3)	346 (3.6)	78 (2.5)	0.002
BMI	28.7 (25.5,	28.5	29.3 (25.2,	< 0.0001
	32.6)	(25.5,	33.9)	
		32.1)		
Hypertension	11,653	8689 (91)	2964 (94)	< 0.0001
	(92)			
Diabetes	5918 (46)	4175 (44)	1743 (55)	< 0.0001
HbA1c	6.1 (5.5,	6.0 (5.5,	6.2 (5.6,	< 0.0001
	7.3)	7.2)	7.6)	
Peripheral arterial disease	1842 (14)	1319 (14)	523 (17)	0.0001
Chronic lung disease	3276 (26)	2387 (25)	889 (7.0)	0.0004
Cerebrovascular disease	2604 (20)	1802 (19)	802 (25)	< 0.0001
Prior stroke	1158 (9.1)	793 (8.3)	365 (11.6)	< 0.0001
Family history of	2845 (22)	2017 (21)	828 (26)	< 0.0001
premature CAD				
Renal failure on HD	433 (3.4)	289 (3.0)	144 (4.6)	< 0.0001
Preoperative creatinine	1.0 (0.8,	1.0 (0.9,	0.9 (0.7,	< 0.0001
	1.2)	1.2)	1.1)	
Prior MI	6785 (53)	4993 (52)	1792 (57)	< 0.0001
Cardiogenic shock	362 (2.8)	265 (2.8)	97 (3.1)	0.38
Previous cardiac	4440 (35)	3404 (36)	1036 (35)	0.56
intervention	1110 (00)	0101(00)	1000 (00)	0.00
Previous PCI	3897 (31)	2983 (31)	914 (31)	0.75
Previous cardiac surgery	336 (2.6)	254 (2.7)	82 (2.6)	0.85
Previous CABG	282 (2.2)	215 (2.3)	67 (2.1)	0.67
Number of diseased vessels	3 (2,3)	3 (2, 3)	4 (3, 4)	< 0.0001
STS predicted morbidity	10.0 (6.4,	9.2 (6.0,	13.1 (8.3,	< 0.0001
and mortality (%)	17.2)	15.7)	22.4)	20.0001
STS predicted mortality	17.2)	0.8 (0.5,	1.5 (0.8,	< 0.0001
(%)			3.1)	0.0001
(%)	2.0)	1.6)	3.1)	

underwent isolated CABG from 2011 to 2020. The attributable risk of female sex for operative mortality varied from 1.28 in 2011 to 1.41 in 2020 (p = 0.38) and there was no significant change over the study period [8]. Sex-disparate outcomes have also been found in patients undergoing revascularization with PCI. In a study of 18,334 patients with CAD treated with PCI, females remained at a higher risk of a composite of cardiac mortality, MI or stroke up to three years after PCI than males [9].

It remains unclear as to why females appear to have worse outcomes than males. Outcomes may be linked to an older age at presentation, driven by the declining estrogen levels of menopause that can serve as an additional risk factor. Late presentation of coronary disease may alternatively be due to unrecognized symptoms of angina, such as dyspnea, fatigue, nausea and jaw or back pain, that result in delayed diagnosis and treatment [10]. Other posited procedural considerations that may contribute to worse outcomes in females relative to males include small coronary artery diameter [11]. Given the established superior patency of arterial anastomoses over venous grafts, our finding that there were overall fewer distal arterial anastomoses performed in females than males offers insight into another potential factor contributing to worse outcomes in female patients [12]. The lower CPB time that we found in females relative to males (94 min vs. 102 min, p < 0.0001) likely reflects the fewer bypass grafts that were performed in female patients. The lack of any distal arterial anastomoses in more female than male patients (3.4 % females vs. 1.8 % in males, p < 0.0001) is particularly concerning as absence of an IMA graft is known to be linked to worse survival [12]. The higher use of intraoperative blood products in females compared to males may also play a role in increased risk of mortality. Surgical literature indicates that intra-operative transfusion can be associated with at least a three-fold increased risk of 30-day mortality and underscores the importance of addressing anemia preoperatively when able [13].

The higher burden of preoperative comorbidities in females that composed our cohort may also confer increased complexity of disease and poorer outcomes. Our finding that females have more comorbid illnesses at the time of CABG is similar to prior studies that describe more baseline diabetes, peripheral vascular disease, and renal dysfunction compared to male patients [14,15]. Our data also showed higher median hemoglobin A1C values in females, indicating poorer disease control relative to male counterparts. A study by Gulbins et al. suggested that diabetes increased the risk in females significantly more than males, which in combination with older age at presentation, may



## Operative Status in Females vs. Males Undergoing CABG

Fig. 2. Operative status in females vs. males undergoing CABG. Females more frequently underwent urgent or emergent CABG compared to males (all p < 0.0001).

Table 2
Operative characteristics in patients undergoing CABG.

	Total (n = 12,736)	Male (n = 9573)	Female (n = 3163)	p-Value
Status				< 0.0001
Elective	4664 (37)	3630 (38)	1034 (33)	
Urgent	7464 (59)	5522 (58)	1942 (61)	
Emergent	593 (4.6)	410 (4.3)	183 (5.8)	
Emergent salvage	15 (0.1)	11 (0.1)	4 (0.1)	
Cardiopulmonary	6032 (50)	5017 (52)	1015 (41)	< 0.0001
bypass				
CPB time	100 (81,	102 (83,	94 (75, 117)	< 0.0001
	123)	124)		
Aortic cross-clamp time	76 (60, 94)	78 (61, 95)	70 (55, 88)	< 0.0001
Lowest temperature	34.2 (33.9,	34.2 (33.8,	34.3 (34.0,	0.002
	35.5)	35.8)	35.6)	
Intraoperative blood products	3013 (24)	1780 (19)	1233 (39)	< 0.0001
Robot used	1401 (11)	1063 (11)	338 (11)	0.51

#### Table 3

Distal anastomoses in patients undergoing CABG.

	Total (n = 12,736)	Male (n = 9573)	Female (n = 3163)	p-Value
Distal vein anastomoses	2 (1,2)	2 (1, 2)	2 (1, 2)	<0.0001
Distal arterial anastomoses	1 (1,1)	1 (1, 1)	1 (1, 1)	<0.0001
0	270 (2.2)	166 (1.8)	104 (3.4)	
1	10,461 (85)	7742 (84)	2719 (89)	
2	1315 (11)	1118 (12)	197 (6.5)	
3	171 (1.4)	152 (1.7)	19 (0.6)	
4	21 (0.2)	20 (0.2)	1 (0.03)	

result in the overall higher mortality observed in female patients [16]. The consistent findings of females presenting for CABG with more comorbid disease and more severe disease demands earlier and more aggressive interventions to address cardiac risk factors prior to surgery. Diabetes and hypertension in particular are well-described preoperative risk factors with strong correlation to mortality and morbidity rates after CABG, and optimizing management of these conditions has the potential to positively impact postoperative outcomes [17]. A limitation in our understanding of the preoperative condition of the patients in this study includes the lack of data on heart failure status and EF in about half of our cohort. Our analysis was also limited by missing data regarding details of the subtype of myocardial infarction (MI) and timing of any prior PCI patients underwent prior to undergoing CABG. Given the important role depression as a risk factor for cardiovascular morbidity and mortality and the higher prevalence in females relative to males, mental health comorbidities are another preoperative condition not examined in our cohort that may be an important factor to address with future research.

In terms of postoperative events following CABG, the findings of our study are similar to prior work demonstrating the increased rate of postoperative MI and stroke in female patients [18]. Interestingly, our postoperative outcomes also highlighted that females were more often discharged to extended care facilities than males. Although decisions regarding discharge destination depend on a multitude of factors including the patient's condition, burden of comorbidities, available support system, and the quality of care in different settings, the higher rates of postoperative complications in female patients after CABG may increase the need for aid offered by an extended care facility. Furthermore, given the significant benefits associated with participation in and completion of cardiac rehabilitation programs, emphasis should be placed on active attendance in cardiac rehab upon discharge. Sexspecific disparities have been observed in cardiac rehab referral, enrollment and completion, with studies of registry data demonstrating that females are 12 % less likely to be referred, 9 % less likely to enroll, and 13 % less likely to complete cardiac rehab programs as compared to males [19,20]. Although cardiac rehab participation data was not available to us in this study, this is an important area of future study.

Our review of differences in discharge medications between females and males also revealed that females received less aspirin and beta blocker use at the time of discharge. This reflects a similar pattern observed in several studies showing that females are less likely than males to receive guideline-based primary and secondary prevention for coronary artery disease despite well documented efficacy in both sexes [21]. The differences observed in discharge location and discharge medications and their potential impact on 30-day mortality warrant further investigation.

#### 5. Conclusion

We present a decade of data on comparative outcomes in CABG between genders at a single institution and highlight the increased

## Postoperative Outcomes in Females vs. Males Undergoing CABG

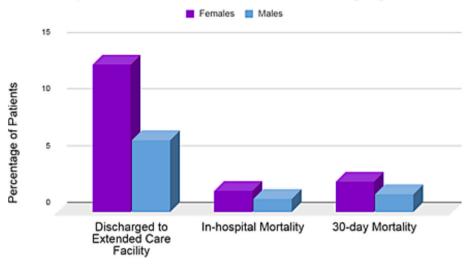


Fig. 3. Postoperative outcomes in females vs. males undergoing CABG.

Females were more frequently discharged to an extended care facility (p < 0.0001). In-hospital mortality was higher in females (p = 0.002), as was 30-day mortality (p = 0.0001).

Table 4	
Postoperative characteristics in	patients undergoing CABG.

	Total (n = 12,736)	Male (n = 9573)	Female (n = 3163)	p-Value
Total ICU hours	44.9 (24.9,	43.5 (24.5,	48.3 (26.4,	< 0.0001
	72.2)	70.5)	84.8)	
In-hospital events	5884 (46)	4379 (46)	1505 (48)	0.07
Stroke	185 (1.6)	113 (1.4)	72 (2.3)	0.0004
Pneumonia	324 (2.5)	234 (2.4)	90 (2.9)	0.21
Prolonged ventilation	1219 (9.6)	814 (8.5)	405 (13)	<0.0001
Renal failure	268 (2.1)	186 (1.9)	82 (2.6)	0.03
Requiring	150 (1.2)	106 (1.1)	44 (1.4)	0.20
dialysis				
Dialysis at	35 (0.3)	23 (0.2)	12 (0.4)	0.20
discharge				
In-hospital	176 (1.4)	115 (1.2)	61 (1.9)	0.002
mortality				
30-day mortality	232 (1.9)	149 (1.6)	83 (2.7)	0.0001
Discharge				
medication				
Aspirin	11,979 (98)	9260 (98)	2719 (97)	0.0001
Statin	7732 (98)	4665 (98)	3067 (99)	0.0004
Beta-blocker	11,744 (96)	9075 (96)	2669 (95)	0.01
Discharge location				< 0.0001
Home	11,361 (90)	8730 (92)	2631 (85)	
Extended care	1015 (8.1)	608 (6.4)	407 (13)	
facility				
Other acute care	72 (0.6)	48 (0.5)	24 (0.8)	
hospital				
Nursing home	83 (0.7)	47 (0.5)	36 (0.2)	
Hospice	12 (0.1)	7 (0.1)	5 (0.2)	
Other	15 (0.1)	15 (0.2)	0 (0)	

#### Table 5

Risk factors for 30-day mortality by multivariable logistic model.

Risk factor	Odds ratio [95 % confidence interval]	p-Value
Sex, female	1.46 [1.06, 2.03]	0.02
Age	1.04 [1.02, 1.05]	< 0.0001
Diabetes	1.32 [0.96, 1.81]	0.08
Prior stroke	1.57 [1.03, 2.40]	0.04
Renal failure on dialysis	2.11 [1.16, 3.84]	0.01
Prior MI	1.79 [1.25, 2.58]	0.002
Cardiogenic shock	11.37 [7.71, 16.77]	< 0.0001
Previous CABG	5.92 [3.54, 9.90]	< 0.0001

mortality that impacts female patients. A limitation of our study is that our data comes from a single institution and may not be representative of the general population. Despite this, our relatively large sample size as a high-volume center provides insight into the current state of sexspecific disparities in outcomes post-CABG. Despite improvement in outcomes after cardiac surgery observed over time due to advancements in care, disparities in outcomes persist. Over the past decade, females undergoing CABG had higher morbidity and mortality than their male counterparts, indicating the ongoing need to better understand and address sex-specific disparities in care.

#### Ethical statement

Ethical Statement for "Sex-Specific Disparities in Patients Undergoing Isolated CABG".

I, Maya Dassanayake, consciously assure that for the manuscript "Sex-Specific Disparities in Patients Undergoing Isolated CABG" the following is fulfilled:

- 1) This material is the authors' own original work, which has not been previously published elsewhere.
- 2) The paper is not currently being considered for publication elsewhere.
- 3) The paper reflects the authors' own research and analysis in a truthful and complete manner.
- 4) The paper properly credits the meaningful contributions of coauthors and co-researchers.
- 5) The results are appropriately placed in the context of prior and existing research.
- 6) All sources used are properly disclosed (correct citation).
- 7) All authors have been personally and actively involved in substantial work leading to the paper, and will take public responsibility for its content.

I agree with the above statements and declare that this submission follows the policies of American Heart Journal Plus: Cardiology Research and Practice as outlined in the Guide for Authors.

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#### Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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