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Differences in gender and outcomes following isolated coronary artery bypass graft (CABG) surgery

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Original Article

Abstract

BACKGROUND: Gender impacts pre-, intra-, and postoperative parameters and outcomes following coronary artery bypass graft (CABG) with conflicting results. This study aimed to identify differences in preoperative, intraoperative, and postoperative parameters. It also seeks to compare the postoperative complications and mortality between two genders who had CABG surgery.

METHODS: This prospective observational study included patients who had isolated CABG and were divided based on gender. Demographic information, underlying comorbidities, drug history, clinical and laboratory data at the time of referral, operative characteristics, postoperative variables, and mortality outcomes were tracked during hospitalization and six months after discharge.

RESULTS: Three hundred twenty patients were enrolled in the study during its duration. 71% were male. Women were older (62.40±9.03 vs. 59.99±9.81 years, p= 0.011) and had more dyslipidemia (p=0.003), hypertension (p=0.000), and diabetes (p=0.001), whereas men admitted with more myocardial infarction (MI) (p=0.011) and had lower Ejection fraction (EF) (p=0.001). They also had lower EF post-surgery and six months after discharge (p <0.001, 0.006). However, the number of vessels involved was not different between genders (p=0.589), but the number of grafts was higher in men (p=0.008).

There was no statistically significant difference in overall mortality rates between the two groups (4.42% and 6.38% in men and women, respectively, p= 0.464).

CONCLUSIONS: The women had more underlying comorbidities than men. Furthermore, there were some differences in the intra-operative parameters and postoperative complications between the two genders, but there was no difference in postoperative mortality in our setting.

Keywords: Coronary Artery Bypass, Gender Differences, Morbidity, Mortality, Survival

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Introduction

Coronary artery bypass graft (CABG) improves survival in patients with severe coronary artery disease who are at high risk for cardiovascular events, including those with left central coronary artery stenosis and three-vessel coronary artery diseases, particularly those with diabetes and higher SYNTAX score [1, 2].

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Age and comorbid conditions such as congestive heart failure (CHF), hypertension, peripheral vascular disease (PVD), renal disease, chronic lung disease, and metabolic syndrome are associated with poor outcomes after CABG [3-5]. Furthermore, socioeconomic background, medical services quality, environmental conditions, and other socio-cultural differences influence community CABG surgery outcomes [6-9]. According to some studies, the risk of mortality and morbidity after CABG surgery is higher in women than in men due to older age at the time of surgery, being at the acute stage of the disease, having smaller coronary arteries, and having a higher incidence of comorbid conditions [6, 10-13].

There have been studies on the disparity of CABG surgery outcomes between two genders in various populations. However, we designed this study to understand better the possible results of inequality between men and women following CABG [6, 11, 13, 14].

Our study aimed to identify differences in preoperative, intraoperative, and postoperative parameters between men and women undergoing CABG surgery. It also seeks to compare postoperative complications and mortality between the two genders.

Materials and Methods

Settings and Study population

From April 2018 to August 2021, this prospective observational study was conducted on adult patients who underwent isolated CABG surgery, either elective or emergent, at the Imam Hossein Medical Center, affiliated with Shahid Beheshti University of Medical Sciences (SBMU) in Tehran, Iran. The patients undergoing concurrent valve surgery or other cardiac procedures were excluded from this study.

The Institutional Review Boards of the Ethics Committee approved this study (IR.SBMU.RETECH.REC.1399.767) and written informed consent was obtained from each patient before enrollment in the study.

Assessments

The patients were divided into two groups based on gender. They were monitored during hospitalization and six months after discharge until they were removed from the study. The removal was due to death or the end of the follow-up period. Data were collected in six categories: demographic data, risk factors, drug history prior to admission, clinical and laboratory data at the time of referral, operative characteristics, postoperative variables, and mortality outcomes.

Demographic data

The demographic data for the patients include age, body mass index (BMI), physical activity level, education, income, and marital status.

The monthly income was recorded in Iranian Rials and, using the exchange rate at the time of this study, was presented in US dollars (USD). Using Iranian Central Bank data, the average USD to Iranian Rial exchange rate during the study was 169814 Iranian Rials. To report data in USD, we divided this parameter by 169814.

Risk factors and drug history before admission

The patients were evaluated for comorbid conditions that predict poor outcomes following CABG surgery and their drug history. These data were obtained from medical records or a primary evaluation during admission.

Clinical and laboratory data at the referral time

We evaluated severe symptoms, hemodynamic, echocardiographic, angiographic findings, and laboratory data at the admission time in this category. Drugs prescribed during the admission period were also recorded for all patients.

Operative characteristics

This category included operative details and any complications that arose during the operation.

Postoperative variables

Paraclinical and laboratory data and

complications following surgery were tracked during the hospitalization and six months after discharge. The intensive care unit (ICU) and hospital length of stay were also recorded. The total cost of hospitalization was reported in USD.

Mortality outcomes

This category was divided into two subdivisions: mortality during hospitalization and six months follow-up after discharge. Furthermore, the survival probability for each gender was estimated.

Statistical analysis

The Kolmogorov-Smirnov test was used to determine the normality of distributions. Then the unpaired student's *t*-test and Mann-Whitney U test were used to compare normal and non-normal distribution data. For comparing the frequency of categories variables between groups based on the frequency of variables, the fisher exact test or chi-square test was used. The quantitative data were presented as mean ±standard deviation (SD) or median (percentile, Q1, Q3) for normal and non-normal distributions and n(%) for qualitative data. SPSS for Windows was used to perform all statistical analyses (Version 21.0; SPSS Inc., Chicago, IL, USA). Also, the Kaplan-Meier method was used to estimate survival probability, and the log-rank test was used to calculate p-values for comparing survival curves. *Statistical significance* was defined as a two-sided p-value less than 0.05.

Results

Demographic data

Three hundred twenty patients were included in the study.

Table 1. Participants' demographic data based on gender

		Male	Female	p-value [a]
Total number		226 (71)	94 (29)	-
Age (year)		59.99±9.81	62.40±9.03	0.011
Body mass index (BMI)		26.55±4.12	26.21±4.68	0.259
Physical activity level [b] M(180), F(80)	0-1 day/week	46(25.5)	34(42.5)	<0.001
	2-5 days/week	81(45)	42(52.5)	
	≥ 5 days/week	53(29.4)	4(5)	
Educational status	Half-educated (lower than 12 years of compulsory education)	14(6.19)	21(22.34)	<0.001
	High school diploma (up to 12 years of compulsory education)	181(80.08)	72(76.59)	
	University education	31(13.71)	1(1.06)	
Marital status	Married	224(99.11)	78(82.97)	<0.001
	Single	2(0.88)	16(17.02)	
Income [c] M(178), F(76)	Below 176.6	2(1.12)	14(18.42)	<0.001
	Between 176.6 to 588.8	157(88.20)	61(80.26)	
	Above 588.8	19(10.67)	1(1.31)	

a, unpaired student's t test, Mann-Whitney U test ,chi-square test based on the data; b, defined at least 30 minutes of moderate-intensity physical activity on one day; c, based on US dollar(USD), per month. Data presented as the n (%) or mean±SD based on the parameters

The majority of patients, 226 (71%), were men, while 29% were women. Women were older than men (62.40±9.03 vs. 59.99±9.81 years, p= 0.011). Because we could not collect information on physical activity level and income for all included patients, we mentioned the number of patients in front of the data in Table 1. Furthermore, the level of physical activity, education, marital status, and income were statistically different between the two groups (p<0.001). Table 1 provides the demographic data of the participants.

Risk factors and drug history before admission

Table 2 provides all related data. Female patients had a higher prevalence of dyslipidemia (24.46% vs. 11.5%, p=0.003), hypertension (85.10% vs. 48.67%, p<0.001), and diabetes (65.95% vs. 44.69%, p=0.001). Meanwhile, the prevalence of dialysis-dependent renal failure was statistically significant in male patients (54.54% vs. 0%, p=0.022). Men had a higher rate of current smoking (51.76% vs. 7.44%, p<0.001), whereas females had a statistically significant higher rate of past smoking (18.08% vs. 9.73%, p=0.038). In addition, women were significantly more likely to use antiplatelet therapy (62.76% vs. 51.32%, p<0.001 for ASA, 34.04% vs. 20.35%, p=0.009 for Clopidogrel, and 31.91% vs. 19.02%, p= 0.012 for dual antiplatelet therapy (DAPT)).

Table 2. Risk factors and drug history before admission, based on sex

	Male (N=226)	Female (N=94)	p-value [a]
Comorbid risk factors			
Dyslipidemia	26(11.5)	23(24.46)	0.003
Hypertension	110(48.67)	80(85.10)	<0.001
Diabetes	101(44.69)	62(65.95)	0.001
Insulin-dependent diabetes	20(19.8)	14(22.58)	0.672
Renal failure	11(4.86)	7(7.44)	0.362
Dialysis-dependent renal failure	6(54.54)	0	0.022
Peripheral artery disease (PAD)	6(2.65)	4(4.25)	0.487
Chronic obstructive pulmonary disease (COPD)	23(10.17)	9(9.57)	0.870
Previous myocardial infarction (MI)	38(16.81)	12(12.76)	0.364
History of coronary artery bypass (CABG) surgery	2(0.88)	0	0.498
History of percutaneous coronary intervention (PCI)	28(12.38)	18(19.14)	0.116
Heart failure (HF)	10(4.42)	4(4.25)	0.606
Cerebral vascular accidents (CVA)	13(5.75)	4(4.25)	0.786
Family history of coronary artery disease (CAD)	37(16.37)	15(15.95)	0.927
Current smoking	117(51.76)	7(7.44)	<0.001
Past smoking	22(9.73)	17(18.08)	0.038
Drug history			
ASA	116(51.32)	59(62.76)	<0.001
Clopidogrel	46(20.35)	32(34.04)	0.009
Dual antiplatelet therapy (DAPT)	43(19.02)	30(31.91)	0.012
Statin	91(40.26)	48(51.06)	0.076
Beta-blockers	77(34.07)	42(44.68)	0.074

a, chi-square test, fisher exact test based on the data. Data presented as the n (%)

Table 3. Clinical and laboratory data of patients in admission time, based on sex

		Male (N=226)	Female (N=94)	p-value [a]
Severe symptoms				
Pulmonary edema		3(1.32)	0	0.558
Cardiogenic shock		1(0.44)	0	0.706
Cardiogenic syncope		4(1.76)	0	0.325
Heart failure (HF)		8(3.53)	6(6.38)	0.257
Myocardial infarction (MI)		81(35.84)	20(21.27)	0.011
Hemodynamic finding				
Systolic blood pressure (mmHg)		125.1±20.84	133.04±22.52	0.001
Diastolic blood pressure (mmHg)		75.49±11.53	80.49±12.63	0.001
Heart rate (beats/min)		78.57±12.27	78.77±10.06	0.941
Echocardiographic findings				
Ejection fraction (EF) (%)		43.67±9.73	47.18±8.72	0.001
Pulmonary artery pressure (PAP)(mmHg)		26.63±7.71	26.67±7.7	0.759
laboratory data				
Hemoglobin (Hgb)(g/dl)		13.30±1.74	12.70±1.70	<0.001
Serum creatinine (Scr), (mg/dl)		1.29±0.82	1.08±0.32	0.001
Fasting blood sugar (FBS) (mg/dl)		134.75±51.51	142.44±48.02	0.046
Hgb A1C (%)		7.72±2.18	8.19±1.97	0.040
LDL-C (mg/dl)		93.09±29.63	100.41±35.79	0.097
HDL-C (mg/dl)		34.31±7.34	36.53±9.27	0.061
TG (mg/dl)		136.23±85.32	140.31±70.03	0.328
Cholesterol (mg/dl)		151.33±40.75	163.23±42.57	0.048
Prescribe drugs in admission				
ASA		223(98.23)	93(98.93)	0.847
Clopidogrel		113(50)	48(51.06)	0.862
Dual antiplatelet therapy (DAPT)		113(50)	48(51.06)	0.862
Glycoprotein IIb/IIIa inhibitors		17(7.52)	8(8.51)	0.764
Statin		226(100)	94(100)	-
Beta-blockers		201(88.93)	89(94.68)	0.108
Angiographic findings				
Number of vessel involvement	One vessel	11(4.86)	7(7.44)	0.589
	Two vessels	30(13.27)	14(14.89)	
	Three vessels	185(81.85)	73(77.65)	
Left main diseases		43(19.02)	10(10.63)	0.066

a, unpaired student's t test, Mann-Whitney U test, chi-square test, fisher exact test based on the data. Data presented as the n (%) or mean±SD based on the parameters

Clinical and laboratory data at the referral time

Men were more likely than women to have a myocardial infarction (MI) at the time of referral (35.84% vs. 21.27%, p=0.011). Male patients had lower systolic and diastolic blood pressure (SBP and DBP) and ejection fraction (EF) (SBP: 125.1±20.84 vs. 133.04±22.52 mmHg, DBP: 75.49±11.53 vs. 80.49±12.63 mmHg, p= 0.001, and EF: 43.67±9.73 vs. 47.18±8.72 %, p=0.001), but higher serum creatinine (Scr) (1.29±0.82 vs. 1.08±0.32 mg/dl, p=0.001). Women had higher fasting blood glucose (FBS), HgbA1C, and cholesterol levels than men (142.44±48.02 vs. 134.75±51.51 mg/dl, p=0.046 for FBS, 8.19±1.97% vs. 7.72±2.18 %, p=0.040 for HgbA1C, and 163.23±42.57 vs. 151.33±40.75 mg/dl, p=0.048 for cholesterol). In addition, the female had lower hemoglobin (Hgb) levels (12.70±1.70 vs. 13.30±1.74 mg/dl, p<0.001). Table 3 depicts the disparity between the two study arms.

Operative characteristics

There was no statistically significant difference in operative characteristics between men and women, except for the unit of packed red blood cells transfused during surgery, which was higher in female patients (3(2-4) vs. 2(2-4), p=0.041), and the number of grafts, which was higher in men (men vs. women, 3(3,4) vs. 3(2,4), p=0.008) (Table 4).

Postoperative variables

Except for re-percutaneous coronary intervention (PCI), which was more common in women (2.22% vs. 0%, p=0.032), there was no statistically significant difference in postoperative complications between the two arms of the study. Table 5 displays the data.EF was significantly lower in men during hospitalization (post-surgery and before discharge) and six months after discharge (43.40±9.98% vs. 48.02±7.46%, p<0.001 post-surgery and 43.18±11.89% vs. 49.52±8.79%, p= 0.006 after six months). Serum creatinine (Scr) was higher in men (1.49±1.07 vs. 1.28±0.6 mg/dl post-surgery and 1.32±1.03 vs. 1.02±0.32mg/dl before discharge, p<0.001) while hemoglobin (Hgb) was lower in women (8.78±1.37 vs. 9.36±1.83 mg/dl, p=0.009 post-surgery and 9.93±1.09 vs. 10.28±1.33 mg/dl, p=0.046 before discharge).

Mortality outcomes

During the study period, the overall mortality rate in our setting was 4.42% and 6.38% in men and women, with no statistically significant difference between the two groups (p= 0.464).

Table 4. Operative characteristics of patients, based on sex

	Male (N=226)	Female (N=94)	p-value [a]
Emergent CABG	11(4.86)	1(1.06)	0.118
Off-pump procedure	19(8.40)	11(11.70)	0.357
Cardiopulmonary bypass time,(min)	117.38±44.99	112.74±45.4	0.515
Aortic cross-clamp time (min)	71.61±28.3	71.04±24.56	0.624
Number of grafts	3(3,4)	3(2,4)	0.008
Blood transfusion	200(88.49)	87(92.55)	0.277
Units of packed red blood cells transfused	2(2,4)	3(2,4)	0.041
Repeated sternotomy	2(0.88)	3(3.19)	0.078

a, unpaired student's t test, Mann-Whitney U test, chi-square test, fisher exact test based on the data based on the data. Data presented as the n (%), mean±SD or median (Q1, Q2) based on the parameters

Table 5. Postoperative variables and mortality outcome, based on sex

	Male (N=226)	Female (N=94)	p-value [a]
Para clinical and laboratory data			
Pulmonary artery pressure (PAP) post-surgery (mmHg)	26.41±7.03	26.39±6.06	0.636
Ejection fraction (EF) post-surgery (%)	43.40±9.98	48.02±7.46	<0.001
Ejection fraction (EF) after six months (%)	43.18±11.89	49.52±8.79	0.006
Differences in EF before and post-surgery (%)	0 (-5,0)	0 (0,5)	0.258
Differences in EF post-surgery and after six months (%)	0 (-5,5)	0 (0,2.5)	0.888
Hemoglobin (Hgb) post-surgery(g/dl)	9.36±1.83	8.78±1.37	0.009
Hemoglobin (Hgb) before discharge (g/dl)	10.28±1.33	9.93±1.09	0.046
Serum creatinine (Scr), post-surgery (mg/dl)	1.49±1.07	1.28±0.6	<0.001
Serum creatinine (Scr), before discharge (mg/dl)	1.32±1.03	1.02±0.32	<0.001
Complications during hospitalization			
	Male (N=226)	**Female (N=94)**	**p-value [a]**
Recurrent myocardial infarction (MI)	1(0.44)	0	0.709
Cerebral vascular attack	7(3.09)	2(2.12)	0.478
Gastrointestinal (GI) bleeding	0	0	-
Intracranial hemorrhage (ICH)	0	0	-
Complications after six months			
	Male (N=220)	**Female (N=90)**	
Cerebral vascular attack	1(0.45)	0	0.711
Gastrointestinal (GI) bleeding	2(0.90)	0	0.505
Re-angiography	3(1.36)	4(4.44)	0.416
Re-percutaneous coronary intervention (PCI)	0	2(2.22)	0.032
Re-coronary artery bypass (CABG) surgery	0	0	-
Hospital assessment			
	Male (N=226)	**Female (N=94)**	
Intensive care unit(ICU) length of stay (day)	6.06±3.17	5.56±2.01	0.411
Hospital length of stay(day)	14.47±9.39	14.41±5.53	0.591
Total Hospitalization costs [b]	1655.3±550.8	1641.3±447.8	0.666
Mortality outcome			
	Male (N=226)	**Female (N=94)**	**p-value [a]**
During hospitalization	6(2.65)	4(4.25)	0.545
	Male (N=220)	**Female (N=90)**	
After six months	4(1.81)	2(2.22)	0.557
	Male (N=226)	**Female (N=94)**	
Overall mortality	10(4.42)	6(6.38)	0.464

a, unpaired student's t test, Mann-Whitney U test, chi-square test, fisher exact test based on the data based on the data. Data presented as the n (%), mean±SD or median (Q1, Q2) based on the parameters. b, based on US dollar (USD)

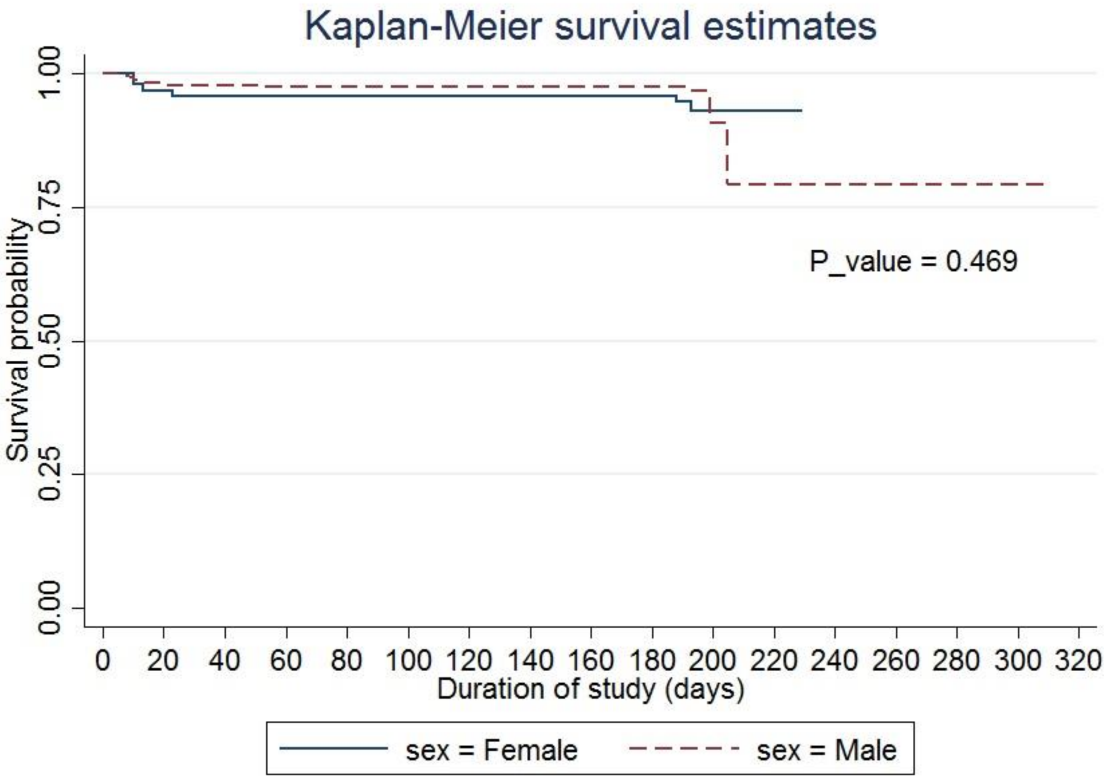

Table 1. Demographic data of participation, based on sex

Furthermore, there were no statistically significant differences between genders regarding in-hospital and six-months-after-discharge mortality (p=0.545 for in-hospital mortality and p=0.557 for six months after discharge). Table 5 summarizes the findings. Figure 1 depicts the survival probability during the study period. Survival probability was 0.92 (95%CI, 0.84 – 0.96) and 0.79 (95%CI, 0.46 – 0.93) in females and males, respectively, with no statistically significant difference between genders according to the Log Ranks test (p= 0.469). In addition, the total survival probability was 0.83 (95% CI, 0.60 – 0.93).

Discussion

Several studies have been conducted to assess sex differences in outcomes following CABG surgery [6, 11-15]. As a result, ours is not the first study, but it is one of the few conducted on the Iranian population [16-18].

Women who presented for cardiac surgery were older than men, and the onset of symptomatic coronary artery diseases (CAD) was delayed in females [11-14, 19]. Female patients were also older in this study. Possible explanations for this finding include the delayed onset of CAD after menopause and delayed diagnosis and treatment of CAD in women compared to men [19]. As in previous studies [11, 13, 14, 19], the incidence of comorbid conditions, such as dyslipidemia, hypertension, and diabetes, was significantly higher in females in our study. Women had higher fasting blood glucose (FBS) and HgbA1C levels, indicating that the incidence of diabetes was more significant in females. In contrast, men were more likely to have MI and had lower EF in our study.

In contrast to other studies, there was no statistically significant difference between the two genders in comorbidities such as chronic lung disease, PVD, cerebral vascular diseases, CHF, previous MI, and cardiac surgery [11-13]. Females received more units of packed red blood cells transfused, according to statistics. A higher incidence of anemia in women and lower preoperative Hgb levels could explain this disparity. In line with our findings, deNeto et al. investigated postoperative complications following CABG surgery and concluded that the rate of transfusion in the operating room is significantly higher in women [14].

In our study, the male gender had a high incidence of dialysis-dependent renal failure and a higher serum creatinine level at referral time. However, this finding contradicts a previous study conducted in the Iranian population, which found lower mean creatinine clearance in women at the referral time. Additionally, unlike the mentioned study, there was no difference in our study's incidence of previous MI [16].

Other studies did not evaluate income, educational and marital status, and physical activity level. However, we did evaluate and find statistical differences between the two groups. These findings revealed socioeconomic differences between the two genders. In the study conducted by Bagheri et al. [16], there was no difference in operative variables. However, this study showed a statistical difference in the units of packed red blood cells transfused, with females receiving more. Differences could explain this result in surgeon experience, and socioeconomic status among Iranian populations admitted to different hospitals.

The impact of gender on early and long-term mortality after CABG yields contradictory results. According to observational studies, the female gender is an independent risk factor for morbidity and mortality after CABG [6, 11-13, 20]. Women's gender differences in outcomes after CABG surgery are explained by older age, smaller body size and coronary artery diameters, a higher incidence of comorbid complications, a more frequent need for postoperative inotropic support, preoperative blood transfusions, and longer lengths of hospital stay [6, 11, 12, 21].

However, despite differences in pre, during, and postoperative variables, there was no difference in mortality between the two genders in other studies [14, 22]. We found no significant difference between the study's two arms.

Because the risk of mortality following CABG surgery depends on multiple risk factors, such as comorbid diseases, postoperative complications, and the hospital and surgeon experience, differences in these factors in various communities may be associated with this confounding results about the mortality. We also acknowledge the study's potential limitations. First, the current study had an unequal number of two groups, which could limit group comparability. Second, because our hospital is one of the crucial public referral centers for low socioeconomic status patients, it may possess biased effects as a confounding factor on the patient's selection and the study results.

In conclusion, there were some differences in the preoperative, intra-operative, and postoperative CABG parameters between the two genders, but there was no difference in postoperative mortality in our setting.

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Authors' Contribution

RM and RS designed the study, and MS. RH and RS conducted the research and drafted the proposal. NK and RS assisted in data collection. RH examined the data. RS, RH, and MS were responsible for data interpretation and original draft preparation. The preparation was reviewed and edited by RH, MS, and RS. All authors contributed to the manuscript's improvement and finalization of the article for publication.

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