

Article

Female Gender in Cardiac Surgery: Is it Still a Significant Risk? A Retrospective Study in Saudi Arabia

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Abstract

Background: Female sex is considered an independent predictor for mortality and morbidity following cardiac surgery. This study is to review the outcomes of adult cardiac surgery between males and females in a Saudi tertiary referral hospital. **Method:** This was a retrospective study for 925 adult patients operated on for ischemic coronary artery disease and acquired aortic and mitral valvular heart disease from 2015 to August 2023. We analyzed patient characteristics, intraoperative data, and postoperative results to compare outcomes between males and females. **Results:** Preoperative risk factors were not significantly different in both groups. Postoperative outcomes showed gender-based differences. In univariable analysis, females, compared to males, had significantly greater odds of prolonged postoperative ventilation (>24 hours), 32.8% of females compared to 20.7% of males ($p < 0.001$). Also, sternal wound infection was notably higher among females (13.3%) ($p < 0.001$). Mortality also exhibited a significant association, with 14.2% of females experiencing mortality compared to 9.4% of males ($p = 0.049$). In the multivariable analysis for elevated postoperative troponin, the use of pre-operative intra-aortic balloon pump, urgent/emergent surgery, elevated pre-operative troponin and combined bypass grafting with valve surgery, were also predictive of higher post-operative troponin concentrations (beta = 0.43, 95% CI: 0.25 to 0.62, $p < 0.001$). **Conclusion:** Females in Saudi Arabia have an increased risk of short-term morbidity and mortality after cardiac surgery compared to males. Vague and delayed presentation and then the late diagnosis and referral are likely the main contributing factors. This highlights the need to implement preoperative measures to improve early diagnosis and referral to eliminate gender bias.

Keywords

females; coronary artery bypass; valvular cardiac surgery; morbidity; mortality

Introduction

Cardiovascular disease (CVD) is a significant public health issue and one of the leading causes of mortality worldwide. According to the World Health Organization (WHO), CVD accounted for 17.3 million fatalities per year in 2011, and this figure is anticipated to rise to more than 23.6 million by 2030 [1]. Ischemic heart disease has been identified as the major cause of mortality in the Middle East, particularly in Saudi Arabia. CVDs were found to be the cause of 42% of noncommunicable disease fatalities in Saudi Arabia in a 2010 study issued by the World Health Organization (WHO) and the Ministry of Health (MOH) Statistical Yearbook [1]. Society of Thoracic Surgeons (STS) and Euro score II, still recognize the extra perioperative risk to female patients [2]. Women tend to present later in their disease process and have poorer preoperative risk profiles than males [3]. Also, female anatomy is reported to be operatively more challenging with smaller, tortuous coronary arteries, and smaller diameter cardiac valves [4,5]. Other genetic and hormonal factors play a role in gender bias. The aim of this study was to know the differences in risk factors, postoperative complications, and mortality between females and males after coronary revascularization and valvular cardiac surgery within Saudi Arabia's current practice. The primary outcome was mortality. Secondary outcomes included short-term complications such as acute kidney injury, stroke, sternal wound infection, reoperation for bleeding, length of hospital stay, and duration of ventilation. A review in 2021 revealed that females are more likely to have residual disease and lower quality of life af-

ter surgery [6]. Men generally report higher post-coronary artery bypass grafting (CABG) physical functioning and emotional scores compared with women [7]. The reasons for these differences remain unclear but may be due to incomplete revascularization and late presentation. Moreover, a retrospective cohort following patients who underwent CABG from 2011 to 2020 showed that the (odds ratio) risk of female sex for operative mortality increased from 1.28 in 2011 to 1.41 in 2020 [8]. However, a study in India concluded that there are no significant differences between females and males in early postoperative composite outcomes [9]. The majority of the female gender research has been done in Western nations. The aim of this study is to identify the variations in outcomes between males and females after coronary revascularization and valvular cardiac surgery in King Abdulaziz University Hospital (KAUH), Jeddah, Saudi Arabia from January 2015 to August 2023.

Method and Materials

This study is a retrospective cohort study, the research was authorized by the Institutional Review Board of KAUH. The selection of patients was done using a non-probability convenient sampling technique. The patients included in the study were chosen from the list of individuals who underwent cardiac surgery at KAUH in Jeddah, Saudi Arabia. Informed consent was waived due to the retrospective nature of the study between January 2015 and August 2023. Our research involved the initial identification of a patient pool totaling 1892 individuals. This group included patients who had undergone cardiac procedures, including coronary artery bypass grafting (CABG), mitral valve replacement (MVR), aortic valve replacement (AVR), thoracic aortic repair, as well as combinations of these procedures including CABG and MVR, CABG and AVR, CABG combined with thoracic aortic repair, AVR combined with thoracic aortic repair, and CABG combined with MVR and AVR. However, we excluded patients who underwent cardiac surgeries for tumor removal, tricuspid valve repair (TVR), pulmonary valve repair (PVR), pediatric cardiac surgeries, and those with congenital heart defects (CHD). After applying these strict inclusion and exclusion criteria, our final study cohort consisted of 925 patients.

Clinical Data

Patient data was methodically collected from the hospital's medical records using Microsoft Excel. This extensive dataset spanned a wide spectrum of patient details and clinical variables, including demographic information, comorbidities, and risk factors. It also covered preoperative, intraoperative, and postoperative variables. Moreover, it encompassed data related to postoperative complications, including bleeding, sternal wound infections, acute

kidney injuries, strokes, postoperative myocardial infarctions, mortality, arrhythmias, heart failures, and recurrent laryngeal injuries.

Statistical Analysis

Statistical analysis in the current study was performed using RStudio (R version 4.3.0, RStudio, Inc., Boston, MA, USA). We expressed variables using frequencies and percentages (for categorical data) or median and interquartile range (IQR) for continuous data. Inferential analyses were carried out to assess the differences between males and females in terms of preoperative, operative, and postoperative variables. This was performed using a Pearson's Chi-squared test or a Fisher's exact test for categorical variables and a Wilcoxon rank sum test for continuous variables. Risk factors for postoperative outcomes were investigated by initially constructing univariable logistic regression model (for categorical variables) or univariable generalized linear model (for continuous variables). Each primary outcome was entered as a dependent variable and patients' variables as an independent variable. Subsequently, variables showing a significant association were used as independent variables in a multivariable model to assess the independent risk factors for the outcome under investigation. Results of the regression model were presented as odds ratios (for logistic regression models) or beta coefficients (for linear regression models), and the 95% confidence intervals (95% CIs) were demonstrated along with the main effects. Statistical significance was deemed at $p < 0.05$.

Results

Preoperative Characteristics

The current study included an analysis of 925 patients. Males represented more than three-quarters of the population under study (78.7%), whereas 21.3% of patients were females. The majority of patients were of non-Saudi nationality (60.3%). Risk factors, including diabetes (64.0%), hypertension (67.6%), and dyslipidemia (25.7%) were prevalent among the patients. Smoking was noted in 36.6% of cases, while endocarditis was observed in 3.3% of patients (Table 1). Almost one-third of patients had severe left ventricular (LV) dysfunction (Ejection fraction (EF) $< 30\%$) (35.4%). A significant difference in nationality distribution was observed, with a higher proportion of non-Saudi females (67.5%) compared to non-Saudi males (58.3%, $p = 0.019$). Height and weight also displayed significant gender-based differences, with females having a median height of 155.0 cm and a median weight of 66.0 kg, while males had a median height of 167.0 cm and a median weight of 74.5 kg ($p < 0.001$ for both). However, body mass index (BMI) did not show a significant difference between males

Table 1. Preoperative characteristics of patients.

Characteristic	Overall	Male	Female	<i>p</i> -value
	N = 925	N = 728	N = 197	
Age (year)	56.0 (49.0–64.0)	56.0 (49.8–64.0)	58.0 (49.0–64.0)	0.783
Nationality				0.019
Saudi	367 (39.7%)	303 (41.7%)	64 (32.5%)	
Non-Saudi	557 (60.3%)	424 (58.3%)	133 (67.5%)	
Height (cm)	164.0 (158.0–170.0)	167.0 (162.0–172.0)	155.0 (150.0–159.0)	<0.001
Weight (kg)	73.0 (65.0–82.6)	74.5 (66.0–84.0)	66.0 (57.0–75.0)	<0.001
BMI	27.0 (24.2–30.2)	26.8 (24.2–29.7)	27.8 (23.8–32.3)	0.110
Risk factors				0.036
None	83 (9.5%)	58 (8.4%)	25 (13.4%)	
Present	795 (90.5%)	634 (91.6%)	161 (86.6%)	
Diabetes	591 (64.0%)	453 (62.4%)	138 (70.1%)	0.047
HTN	624 (67.6%)	484 (66.7%)	140 (71.1%)	0.242
Dyslipidemia	237 (25.7%)	202 (27.8%)	35 (17.8%)	0.004
Smoking	231 (36.6%)	220 (44.4%)	11 (8.0%)	<0.001
COPD	5 (0.5%)	4 (0.6%)	1 (0.5%)	>0.999
Old stroke	44 (4.8%)	34 (4.7%)	10 (5.1%)	0.807
Endocarditis	19 (3.3%)	11 (2.4%)	8 (6.2%)	0.047
Pre-operative EF				0.097
Normal	213 (43.3%)	158 (41.1%)	55 (50.9%)	
Borderline	105 (21.3%)	89 (23.2%)	16 (14.8%)	
Severe	174 (35.4%)	137 (35.7%)	37 (34.3%)	
Pre-operative IABP use	30 (3.3%)	24 (3.3%)	6 (3.1%)	0.858
Pre-operative troponin	0.1 (0.0–2.1)	0.1 (0.0–2.2)	0.1 (0.0–1.3)	0.258

N (%); Median (IQR). Pearson's Chi-squared test; Fisher's exact test; Wilcoxon rank sum test. BMI, body mass index; HTN, Hypertension; COPD, chronic obstructive pulmonary disease; IABP, intra-aortic balloon pump; EF, %, Ejection fraction, %.

and females. The prevalence of risk factors, such as diabetes (70.1% in females vs. 62.4% in males, $p = 0.047$), dyslipidemia (27.8% in males vs. 17.8% in females, $p = 0.004$), and smoking (44.4% in males vs. 8.0% in females, $p < 0.001$), exhibited significant gender-related disparities. Furthermore, the presence of endocarditis was significantly higher in females (6.2%) compared to males (2.4%) ($p = 0.047$).

Operative Characteristics

In terms of procedure type, CABG procedures were the most common (84.1%). There were significant differences in the distribution between males and females. Notably, a higher proportion of males underwent CABG (87.9%) compared to females (70.1%, $p < 0.001$), while MVR was more common among females (15.2%) than males (3.4%, $p < 0.001$). Furthermore, the use of inotropes during surgery displayed a significant gender-related difference, with 54.1% of females receiving inotropes compared to 45.0% of males ($p = 0.023$). Blood transfusions also showed a substantial gender-based variation, with 79.0% of females receiving blood transfusions compared to 49.8% of males ($p < 0.001$, Table 2).

Postoperative Outcomes

A significant difference was observed in postoperative ventilation, with 32.8% of females requiring prolonged ventilation (>24 hours) compared to 20.7% of males ($p < 0.001$). Additionally, the occurrence of sternal wound infection was significantly higher among females (13.3%) compared to males (5.9%, $p < 0.001$). Mortality also exhibited a significant association, with 14.2% of females experiencing mortality compared to 9.4% of males ($p = 0.049$, Table 3).

Predictors of Postoperative Outcomes

Risk factors for a prolonged postoperative ventilation included operation urgency, with emergent cases having a significantly higher risk (odds ratio (OR) = 2.19, 95% CI: 1.14 to 4.15, $p = 0.017$). Inotrope's usage was also strongly associated with prolonged postoperative ventilation (OR = 2.43, 95% CI: 1.44 to 4.15, $p < 0.001$), as was the use of an intra-aortic balloon pump (IABP) (OR = 20.6, 95% CI: 7.16 to 76.4, $p < 0.001$). Additionally, intraoperative complications were significantly linked to prolonged ventilation (OR = 2.57, 95% CI: 1.25 to 5.26, $p = 0.010$). A shorter

Table 2. Operative characteristics.

Characteristic	Overall	Male	Female	<i>p</i> -value
	N = 925	N = 728	N = 197	
Procedure type				
CABG	778 (84.1%)	640 (87.9%)	138 (70.1%)	<0.001
MVR	55 (5.9%)	25 (3.4%)	30 (15.2%)	<0.001
AVR	48 (5.2%)	33 (4.5%)	15 (7.6%)	0.084
Thoracic aortic repair	8 (0.9%)	6 (0.8%)	2 (1.0%)	0.681
CABG+MVR	16 (1.7%)	10 (1.4%)	6 (3.0%)	0.124
CABG+AVR	10 (1.1%)	9 (1.2%)	1 (0.5%)	0.698
CABG+thoracic aortic repair	1 (0.1%)	1 (0.1%)	0 (0.0%)	>0.999
MVR+AVR	18 (1.9%)	11 (1.5%)	7 (3.6%)	0.080
AVR+thoracic aortic repair	5 (0.5%)	3 (0.4%)	2 (1.0%)	0.289
CABG+MVR+AVR	2 (0.2%)	2 (0.3%)	0 (0.0%)	>0.999
Operation urgency				
Emergent	239 (25.8%)	190 (26.1%)	49 (24.9%)	0.727
Elective	686 (74.2%)	538 (73.9%)	148 (75.1%)	
Cardiopulmonary bypass time	115.0 (93.0–147.3)	113.5 (93.0–144.0)	120.0 (96.5–156.0)	0.245
Aortic cross clamp time	71.5 (56.0–94.0)	69.0 (56.0–93.8)	77.5 (58.5–95.8)	0.101
Inotropes	431 (46.9%)	325 (45.0%)	106 (54.1%)	0.023
Use of IABP	90 (9.8%)	71 (9.8%)	19 (9.6%)	0.950
Blood loss (mL)	300.0 (200.0–400.0)	300.0 (200.0–400.0)	300.0 (200.0–500.0)	0.352
Blood transfusion	310 (56.1%)	216 (49.8%)	94 (79.0%)	<0.001
Duration of operation in minutes	260.0 (221.0–302.0)	258.0 (222.0–300.0)	267.0 (207.0–319.0)	0.763

N (%); Median (IQR). Pearson's Chi-squared test; Fisher's exact test; Wilcoxon rank sum test. CABG, coronary artery bypass grafting; MVR, mitral valve replacement; AVR, aortic valve replacement.

Table 3. Postoperative outcomes among patients.

Characteristic	Overall	Male	Female	<i>p</i> -value
	N = 925	N = 728	N = 197	
Post op ventilation				
Normal (<24 hours)	704 (76.7%)	573 (79.3%)	131 (67.2%)	<0.001
Prolonged (>24 hours)	214 (23.3%)	150 (20.7%)	64 (32.8%)	
Ejection fraction				
>50	136 (43.2%)	94 (40.2%)	42 (51.9%)	0.056
41 to 49	51 (16.2%)	44 (18.8%)	7 (8.6%)	
<40	128 (40.6%)	96 (41.0%)	32 (39.5%)	
Troponin	13.3 (7.3–27.2)	13.2 (7.2–27.2)	14.4 (9.3–26.8)	0.322
Length of ICU stay	3.0 (2.0–5.0)	3.0 (2.0–5.0)	3.0 (2.0–5.0)	0.504
Length of cardiac ward stay	4.0 (2.0–6.0)	4.0 (2.0–5.0)	4.0 (2.0–7.0)	0.047
Post op complications				
Bleeding	122 (13.2%)	92 (12.7%)	30 (15.3%)	0.334
Sternal wound infection	69 (7.5%)	43 (5.9%)	26 (13.3%)	<0.001
Acute kidney injury	76 (8.2%)	56 (7.7%)	20 (10.2%)	0.258
Stroke	33 (3.6%)	30 (4.1%)	3 (1.5%)	0.082
Myocardial infarction	44 (4.8%)	32 (4.4%)	12 (6.1%)	0.320
Mortality	96 (10.4%)	68 (9.4%)	28 (14.2%)	0.049
Arrhythmia	145 (15.7%)	109 (15.0%)	36 (18.4%)	0.256
Recurrent laryngeal nerve injury	3 (0.5%)	1 (0.2%)	2 (1.6%)	0.125
Heart failure	31 (5.4%)	22 (4.9%)	9 (7.0%)	0.342

ICU, intensive care unit.

cardiopulmonary bypass time was independently associated with a lower likelihood of prolonged ventilation (OR = 0.99,

95% CI: 0.98 to 0.99, *p* = 0.001) whereas the duration of operation (OR = 1.01, 95% CI: 1.01 to 1.02, *p* < 0.001) was

identified as a significant risk factor of prolonged postoperative ventilation (Table 4). Regarding bleeding, female gender was not found to be a risk factor. Smoking was strongly associated with an increased risk of bleeding (OR = 0.37, 95% CI: 0.21 to 0.62, $p < 0.001$). For sternal wound infection, female gender was a strong predictor (OR = 2.34, 95% CI: 1.37 to 3.92, $p = 0.002$) as well as diabetes (OR = 4.38, 95% CI: 2.19 to 10.1, $p < 0.001$, Tables 5,6). Notably, the use of IABP was the sole risk factor for acute kidney injury (OR = 4.35, 95% CI: 1.64 to 11.3, $p = 0.003$), and stroke (OR = 5.29, 95% CI: 1.79 to 15.3, $p = 0.002$). The existence of intraoperative complications was a risk factor for myocardial infarction (OR = 4.96, 95% CI: 1.39 to 15.8, $p = 0.008$). Regarding mortality, female patients with a history of chronic obstructive pulmonary disease (COPD) had a substantially higher risk (OR = 23.1, 95% CI: 1.55 to 671, $p = 0.028$), emergency surgery (OR = 2.84, 95% CI: 1.11 to 6.98, $p = 0.025$), bleeding intra and postoperatively (OR = 1.00, 95% CI: 1.00 to 1.00, $p = 0.021$) and the use of an intra-aortic balloon pump (IABP) were significant risk factors for mortality (OR = 6.13, 95% CI: 2.25 to 17.3, $p < 0.001$). Notably, the use of inotropes was associated with an increased risk of arrhythmia (OR = 3.21, 95% CI: 1.83 to 5.85, $p < 0.001$). In the multivariable linear regression analysis of risk factors for elevated troponin concentrations following cardiac surgery, several variables displayed significant associations ($p < 0.05$). The use of pre-operative intra-aortic balloon pump (IABP) was strongly associated with higher troponin concentrations (beta = 27.6, 95% CI: 9.28 to 45.8, $p = 0.003$). Elevated pre-operative troponin levels were also predictive of higher post-operative troponin concentrations (beta = 0.43, 95% CI: 0.25 to 0.62, $p < 0.001$). Urgent/emergent surgery was linked to increased troponin concentrations (beta = 15.8, 95% CI: 7.54 to 24.0, $p < 0.001$). The combined procedure of CABG+AVR was associated with higher troponin levels (beta = 22.0, 95% CI: 1.15 to 42.8, $p = 0.039$). The use of inotropes (beta = 6.44, 95% CI: 0.46 to 12.4, $p = 0.035$) and intraoperative complications (beta = 16.2, 95% CI: 6.84 to 25.5, $p < 0.001$) were also associated with higher troponin levels. Finally, the use of IABP (beta = 1.61, 95% CI: 0.24 to 2.98, $p = 0.022$) and inotropes (beta = 1.32, 95% CI: 0.58 to 2.07, $p < 0.001$) were independently associated with a longer intensive care unit (ICU) stay.

Discussion

Over the past 20 years, observational, risk-adjusted, and propensity-matched studies have documented increased mortality after CABG in women compared with men [4,10,11]. Our research findings have indicated that, from a preoperative risk factor perspective, there isn't a substantial divergence between females and males. However, it is noteworthy that the number of female patients in

our study cohort is significantly smaller than that of males. Additionally, the majority of included patients were postmenopausal women, so the absence of the protective cardiovascular effect of estrogen could be an explanation for increased risk in female than male. This disparity may potentially be attributed to, or indicative of, delayed diagnosis and referral practices for female patients. Addressing this issue of delayed diagnosis and referral is paramount in bridging the gender-based gap in outcomes following cardiac surgery. The underrepresentation of smaller female populations in our study and in recent cardiac research studies highlights an ongoing gender bias that often leads to delayed diagnosis and referral for women with cardiac issues. This delay can be attributed to differences in symptom presentation, which may include atypical cardiac symptoms not immediately recognized as heart-related, contributing to diagnostic delays. Moreover, their underrepresentation in clinical trials has resulted in a lack of gender-specific knowledge, potentially hindering timely intervention. Healthcare provider bias can further underestimate cardiovascular risk in female patients, leading to delayed referrals to cardiac specialists. Such delays can have adverse effects on post-cardiac surgery outcomes, as more advanced diseases at the time of surgery may result in increased complications and poorer long-term results [12]. Our results showed higher incidence of prolonged postoperative ventilation in females post cardiac surgery in Table 3. Predictors of delayed extubation in our study included operation urgency, with emergent cases having a significantly higher risk of prolonged ventilation. Intraoperative complications, use of high inotropes and prolonged bypass time also affect the length of postoperative ventilation. Wong and colleagues [13] studied the length of ventilation post CABG on 885 patients and reported that female gender, inotropes, and excessive bleeding are risk factors for delayed extubation. Our findings are consistent with a previous study that also found no correlation between body mass index (BMI) and delayed extubating [14]. Some studies suggest that both low BMI and high BMI can be considered risk factors for prolonged mechanical ventilation [15]. The female gender is protective against bleeding as shown in another research and confirmed in our study [16]. Hormonal, mainly estrogen, and genetic factors, causing a reduced antiplatelet effect to aspirin, thus increasing thrombogenicity, may be implicated in the pathophysiology of decreased post-operative bleeding in females [17]. Significant risk factors for bleeding in our study were smoking, use of IABP, inotropes, and the presence of intraoperative complications. The findings presented in Table 3 of our study indicate a higher mortality rate among females following cardiac surgery. Risk factors also include comorbidities like COPD, emergency surgery, surgical complications, and the use of IABP. Female surgical challenges include anatomical factors of smaller valve areas, smaller and thinner coronary artery targets for grafting, narrower conduits, and more diffuse patterns of coro-

Table 4. Predictors and Analysis of the risk factors for a prolonged postoperative ventilation.

Characteristic	Univariable			Multivariable		
	OR	95% CI	<i>p</i> -value	OR	95% CI	<i>p</i> -value
Female	1.87	1.31, 2.64	<0.001	1.42	0.78, 2.58	0.249
Non-Saudi	1.42	1.03, 1.96	0.033	1.13	0.60, 2.18	0.716
Diabetes mellitus	1.49	1.07, 2.08	0.019			
Hypertension	1.49	1.06, 2.11	0.024	1.44	0.83, 2.53	0.199
Pre-operative IABP	2.61	1.22, 5.45	0.011	0.27	0.05, 1.25	0.105
Emergency	1.80	1.29, 2.50	<0.001	2.19	1.14, 4.15	0.017
CABG	0.56	0.38, 0.83	0.003	0.74	0.34, 1.70	0.466
MVR	2.03	1.13, 3.58	0.016	1.21	0.44, 3.36	0.707
CABG+MVR	4.37	1.61, 12.4	0.004	1.41	0.30, 6.68	0.660
Cardiopulmonary bypass time (more than 2 hours)	1.01	1.00, 1.01	0.011	0.99	0.98, 0.99	0.001
Inotropes	4.03	2.90, 5.66	<0.001	2.43	1.44, 4.15	<0.001
Postop IABP	9.15	5.70, 15.0	<0.001	20.6	7.16, 76.4	<0.001
Complications	3.34	1.99, 5.60	<0.001	2.57	1.25, 5.26	0.010
Duration of operation (more than 6 hours)	1.01	1.00, 1.01	<0.001	1.01	1.01, 1.02	<0.001

OR, odds ratio.

Table 5. Predictors and analysis of the risk factors for bleeding.

Characteristic	Uni and multivariable					
	OR	95% CI	<i>p</i> -value	OR	95% CI	<i>p</i> -value
Female	1.25	0.79, 1.93	0.335			
Non-Saudi	0.62	0.42, 0.91	0.015	2.08	0.45, 18.8	0.423
Smoking	0.37	0.21, 0.62	<0.001			
Cardiopulmonary bypass time (>2 hours)	1.01	1.00, 1.01	0.002	0.99	0.97, 1.02	0.539
Aortic cross-clamp time (>90 min)	1.01	1.00, 1.02	0.032	1.01	0.98, 1.04	0.485
Inotropes	2.14	1.45, 3.21	<0.001	2.36	0.79, 8.01	0.137
Use of IABP	3.35	1.99, 5.51	<0.001	0.68	0.12, 2.87	0.624
Intraoperative complications	3.11	1.54, 5.99	<0.001	2.72	0.76, 8.80	0.105
Duration of operation (>6 hours)	1.01	1.00, 1.01	0.002	1.00	0.99, 1.01	0.548

nary disease [18,19]. These all will increase the risk of perioperative MI and postoperative low cardiac output [20]. More studies are needed on to study the role of off-pump and hybrid cardiac surgery on females to see their effect on gender bias in outcome [21–23]. Gender disparities also exist in valvular heart disease outcomes. The full mechanisms behind why women may have worse outcomes compared to men following aortic valve replacement (AVR) are not yet fully understood. However, several factors have been implicated in this disparity. Females with similar degrees of aortic stenosis tend to have higher transvalvular pressure gradients, thicker ventricle walls, and smaller end-systolic and end-diastolic chamber sizes compared to males. In addition, women, on average, receive smaller-sized valves during AVR, which can cause patient-prosthesis mismatch. Females are more likely to require additional aortic annular enlargement procedures compared to males. This procedure carries its own operative risks, which can contribute to an increased overall risk for female patients undergoing AVR [24]. Dixon and colleagues [23] reported that women frequently receive smaller valves, which could po-

tentially elevate the risk of patient-prosthesis mismatch and associated complications. These factors contribute to the technical difficulties associated with performing surgical AVR in women [25]. Strategic Solutions for this gender bias include developing guidelines for tailored valve selection specifically for female patients, advancements in valve technology to provide a wider range of valve sizes suitable for women, optimizing surgical techniques to minimize complications associated with aortic annular enlargement procedures, and implementing comprehensive preoperative evaluation to identify high-risk female patients who may benefit from additional interventions or alternative treatment approaches. Recent technical advancements in cardiac surgery including minimally invasive aortic valve replacement and trans aortic valve implantation (TAVI) are promising [26]. Our study also showed a significant risk of sternal wound complications in females. In our analysis, diabetes mellitus (DM), smoking, and dyslipidemia were the two most prevalent risk factors. Barts Surgical Infection Risk Score, developed in the United Kingdom, identifies the female sex as one of the six independent predictors

Table 6. Analysis of the risk factors for sternal wound infection.

Characteristic	OR	95% CI	p-value	OR	95% CI	p-value
Age (year)	1.01	0.99, 1.03	0.400			
Gender						
Female	2.43	1.44, 4.05	<0.001	2.34	1.37, 3.92	0.002
BMI	1.00		0.890			
Diabetes	4.57	2.29, 10.5	<0.001	4.38	2.19, 10.1	<0.001
Smoking	0.49	0.23, 0.98	0.054			
Dyslipidemia	0.00		0.984			
Old stroke	0.94	0.22, 2.67	0.915			
Endocarditis	1.53	0.24, 5.58	0.581			
Pre-operative EF						
Normal	Ref	Ref				
Borderline	0.62	0.17, 1.79	0.406			
Severe	1.78	0.85, 3.81	0.130			
Pre-operative IABP use						
No	Ref	Ref				
Yes	1.94	0.56, 5.16	0.232			
Pre-operative troponin	1.00	0.96, 1.01	0.676			
Operation urgency						
Elective	Ref	Ref				
Emergent	0.86	0.47, 1.50	0.608			
CABG	1.74	0.83, 4.24	0.177			
MVR	0.97	0.29, 2.47	0.953			
AVR	0.25	0.01, 1.18	0.177			
Thoracic aortic repair	0.00		0.980			
CABG+MVR	0.82	0.05, 4.15	0.851			
CABG+AVR	3.16	0.47, 12.9	0.151			
Cardiopulmonary bypass time	1.00	0.99, 1.00	0.437			
Aortic cross clamp time	1.00	0.98, 1.01	0.378			
Inotropes	1.53	0.93, 2.52	0.094			
Use of IABP	1.07	0.44, 2.27	0.865			
Blood transfusion						
Blood transfusion (>2 units)	1.02	0.53, 1.99	0.955			
Duration of operation (>6 hours)	1.00	0.99, 1.00	0.750			

Ref, Reference of normal value which is more than 50% in our study.

of surgical site infection after cardiac surgery. The score considers other factors such as a BMI greater than 30, diabetes, left ventricular ejection fraction below 45%, and peripheral vascular disease [27]. To minimize the risk of sternal wound complications in both male and female patients undergoing CABG surgery, several strategies can be implemented. Preoperative optimization of comorbidities such as DM and dyslipidemia is essential, as these conditions can impair wound healing and increase susceptibility to infections. Moreover, strict adherence to infection prevention measures, including thorough hand hygiene, proper sterilization of surgical instruments, and appropriate use of prophylactic antibiotics, are important [27–29]. Patient education on wound care and postoperative hygiene is important to ensure early detection of complications. Weight management strategies, encouraging a healthy BMI through lifestyle modifications, should be implemented [28]. The

implementation of surgical guidelines in cardiac surgery helps in the management of preventable surgical complications like bleeding, sternal wound infection and acute kidney injury [30]. Multidisciplinary care involving surgeons, nurses, infectious disease specialists, and wound care specialists is vital for comprehensive evaluation and management.

Recommendations for Future Research

Ongoing research is necessary to further understand the relationship between gender and sternal wound complications and develop targeted interventions. Implementation of strategies aiming at improved symptom recognition, preoperative evaluation, specialized surgical decision-making, multidisciplinary collaboration, and continuous

quality improvement can reduce mortality risk, optimize outcomes, and ensure equitable healthcare for all cardiac surgery patients. Establishment of Centers of specialization for women's health applying advanced intraoperative techniques like the use of arterial grafts, complete revascularization, and minimally invasive coronary, mitral, and aortic procedures may help to close the gender bias gap in cardiac surgery outcome.

Study Limitation

Study limitations include: (1) It is a retrospective single center experience and we think that a control group would provide a better basis for comparison. (2) Poor documentation of data was also a limitation of this study. (3) It focuses on our institute in Saudi tertiary referral hospital, which may limit the generalizability of the findings to other cardiac surgery settings, so the specific factors unique to this hospital and Saudi Arabia may influence the effects of female gender as an independent risk factor. (4) It does not thoroughly address potential confounding factors that could contribute to the observed gender-based differences in outcomes.

Conclusion

Despite advances in cardiac surgery, females in Saudi Arabia have an increased risk of short-term morbidity and mortality after cardiac surgery compared to males. Vague and delayed presentation and then the late diagnosis and referral are likely the main contributing factors. This highlights the need to implement preoperative measures to improve early diagnosis, focus on understanding the causes behind these disparities and follow sex-specific strategies and innovative procedures to improve the outcomes of females undergoing cardiac surgery.

Abbreviations

CABG, Coronary artery bypass surgery; AVR, Aortic valve replacement; MVR, Mitral valve replacement; CVD, Cardiovascular diseases; TVR, Tricuspid valve replacement; PVR, Pulmonary valve replacement; CHD, Congenital heart disease; BMI, Body mass index; TAVI, Transaortic valve implantation; DM, Diabetes mellitus; HTN, Hypertension.

Availability of Data and Materials

Datasets used and/or analyzed for this study are available from the corresponding author upon appropriate request.

Author Contributions

Idea and study design by KEAE and AAE. Collecting data by SAAlbi, AMA and RAA. Statistics done by NFA, LAA, SSA and MMA. The acquisition, analysis, and interpretation of data by AHB, MAF, SAAlbu and AKA. Revision by KEAE and AAE. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

Ethics were approved by King Abdulaziz University, Faculty of Medicine, Unit of biomedical ethics, Research Ethics Committee (REC), ethics approval number: (521-23). Participates were waived regarding consent because the study is a retrospective data analysis.

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Conflict of Interest

The authors declare no conflict of interest.

References

- [1] Alamri HM, Alotaibi TO, Alghatani AA, Alharthy TF, Sufyani AM, Alharthi AM, *et al*. Effect of Gender on Postoperative Outcome and Duration of Ventilation After Coronary Artery Bypass Grafting (CABG). *Cureus*. 2023; 15: e37717.
- [2] Gaudino M, Samadashvili Z, Hameed I, Chikwe J, Girardi LN, Hannan EL. Differences in Long-term Outcomes After Coronary Artery Bypass Grafting Using Single vs Multiple Arterial Grafts and the Association With Sex. *JAMA Cardiology*. 2020; 6: 10.1001/jamacardio.2020.6585.
- [3] El-Andari R, Bozso SJ, Fialka NM, Kang JJH, Nagendran J. Does sex impact outcomes after mitral valve surgery? A systematic review and meta-analysis. *Scandinavian Journal of Surgery: SJS: Official Organ for the Finnish Surgical Society and the Scandinavian Surgical Society*. 2022; 111: 99–109.
- [4] Dixon LK, Dimagli A, Di Tommaso E, Sinha S, Fudulu DP, Sandhu M, *et al*. Females have an increased risk of short-term mortality after cardiac surgery compared to males: Insights from

- a national database. *Journal of Cardiac Surgery*. 2022; 37: 3507–3519.
- [5] Cho L, Kibbe MR, Bakaeen F, Aggarwal NR, Davis MB, Karmalou T, *et al*. Cardiac Surgery in Women in the Current Era: What Are the Gaps in Care? *Circulation*. 2021; 144: 1172–1185.
- [6] Perrotti A, Ecarnot F, Monaco F, Dorigo E, Monteleone P, Besch G, *et al*. Quality of life 10 years after cardiac surgery in adults: a long-term follow-up study. *Health and Quality of Life Outcomes*. 2019; 17: 88.
- [7] Al-Ebrahim KE, Albishri SA, Alotaibi SW, Alsayegh LA, Almufarriji EM, Babader RB, *et al*. The Quality of Life in Patients with Valve Prosthesis After Undergoing Surgery for Valvular Heart Diseases. *Cureus*. 2023; 15: e43030.
- [8] Gaudino M, Chadow D, Rahouma M, Soletti GJ, Sandner S, Perezgrovas-Olaria R, *et al*. Operative Outcomes of Women Undergoing Coronary Artery Bypass Surgery in the US, 2011 to 2020. *JAMA Surgery*. 2023; 158: 494–502.
- [9] Sajja LR, Mannam G, Kamtam DN, Balakrishna N. Female gender does not have any significant impact on the early postoperative outcomes after coronary artery bypass grafting: a propensity-matched analysis. *Indian Journal of Thoracic and Cardiovascular Surgery*. 2023; 39: 231–237.
- [10] Murthy SC, Arroliga AC, Walts PA, Feng J, Yared JP, Lytle BW, *et al*. Ventilatory dependency after cardiovascular surgery. *The Journal of Thoracic and Cardiovascular Surgery*. 2007; 134: 484–490.
- [11] Madhu Krishna NR, Nagaraja PS, Singh NG, Nanjappa SN, Kumar KN, Prabhakar V, *et al*. Evaluation of risk scores in predicting perioperative blood transfusions in adult cardiac surgery. *Annals of Cardiac Anaesthesia*. 2019; 22: 73–78.
- [12] Lichtman JH, Leifheit EC, Safdar B, Bao H, Krumholz HM, Lorenze NP, *et al*. Sex Differences in the Presentation and Perception of Symptoms Among Young Patients With Myocardial Infarction: Evidence from the VIRGO Study (Variation in Recovery: Role of Gender on Outcomes of Young AMI Patients). *Circulation*. 2018; 137: 781–790.
- [13] Wong DT, Cheng DC, Kustra R, Tibshirani R, Karski J, Carroll-Munro J, *et al*. Risk factors of delayed extubation, prolonged length of stay in the intensive care unit, and mortality in patients undergoing coronary artery bypass graft with fast-track cardiac anesthesia: a new cardiac risk score. *Anesthesiology*. 1999; 91: 936–944.
- [14] Almramhi K, Aljehani M, Bamuflih M, Alghamdi S, Banser S, Almousa A, *et al*. Frequency and Risk Factors of Unplanned 30-Day Readmission After Open Heart Surgeries: A Retrospective Study in a Tertiary Care Center. *The Heart Surgery Forum*. 2022; 25: E608–E615.
- [15] Al-Ebrahim K, Alsheikh A, Ramadan SA, Alshehri A, Aljohani B, Rami A, *et al*. Sternal Wound Infection Following Open Heart Surgery: Incidence, Risk Factor, Pathogen, and Mortality. *The Heart Surgery Forum*. 2023; 26: E134–E140.
- [16] Ellassal AA, Al-Ebrahim KE, Debis RS, Ragab ES, Faden MS, Fatani MA, *et al*. Re-exploration for bleeding after cardiac surgery: reevaluation of urgency and factors promoting low rate. *Journal of Cardiothoracic Surgery*. 2021; 16: 166.
- [17] Zuern CS, Lindemann S, Gawaz M. Platelet function and response to aspirin: gender-specific features and implications for female thrombotic risk and management. *Seminars in Thrombosis and Hemostasis*. 2009; 35: 295–306.
- [18] Dalén M, Nielsen S, Ivert T, Holzmann MJ, Sartipy U. Coronary Artery Bypass Grafting in Women 50 Years or Younger. *Journal of the American Heart Association*. 2019; 8: e013211.
- [19] Swaminathan RV, Feldman DN, Pashun RA, Patil RK, Shah T, Geleris JD, *et al*. Gender Differences in In-Hospital Outcomes After Coronary Artery Bypass Grafting. *The American Journal of Cardiology*. 2016; 118: 362–368.
- [20] Hessian R, Jabagi H, Ngu JMC, Rubens FD. Coronary Surgery in Women and the Challenges We Face. *The Canadian Journal of Cardiology*. 2018; 34: 413–421.
- [21] Al-Ebrahim EK, Madani TA, Al-Ebrahim KE. Future of cardiac surgery, introducing the interventional surgeon. *Journal of Cardiac Surgery*. 2022; 37: 88–92.
- [22] Ellassal AA, Al-Ebrahim K, Makhdoom AM, Fatani M, Ibrahim M. Hybrid Coronary Revascularization: Perspective Current State After 25 Years of Start. *The Heart Surgery Forum*. 2021; 24: E392–E401.
- [23] Dixon LK, Di Tommaso E, Dimagli A, Sinha S, Sandhu M, Benedetto U, *et al*. Impact of sex on outcomes after cardiac surgery: A systematic review and meta-analysis. *International Journal of Cardiology*. 2021; 343: 27–34.
- [24] Kaier K, von Zur Mühlen C, Zirlik A, Schmoor C, Roth K, Bothe W, *et al*. Sex-Specific Differences in Outcome of Transcatheter or Surgical Aortic Valve Replacement. *The Canadian Journal of Cardiology*. 2018; 34: 992–998.
- [25] Chaker Z, Badhwar V, Alqahtani F, Aljohani S, Zack CJ, Holmes DR, *et al*. Sex Differences in the Utilization and Outcomes of Surgical Aortic Valve Replacement for Severe Aortic Stenosis. *Journal of the American Heart Association*. 2017; 6: e006370.
- [26] Mikhles MM, Soloukey Tbalvandany S, Siregar S, Versteegh MIM, Noyez L, van Putte B, *et al*. Male-female differences in aortic valve and combined aortic valve/coronary surgery: a national cohort study in the Netherlands. *Open Heart*. 2018; 5: e000868.
- [27] Alebrahim K, Al-Ebrahim E. Prevention, Classification and Management Review of Deep Sternal Wound Infection. *The Heart Surgery Forum*. 2020; 23: E652–E657.
- [28] Lazar HL, Salm TV, Engelman R, Orgill D, Gordon S. Prevention and management of sternal wound infections. *The Journal of Thoracic and Cardiovascular Surgery*. 2016; 152: 962–972.
- [29] Magboo R, Drey N, Cooper J, Byers H, Shipolini A, Sanders J. Predicting cardiac surgical site infection: development and validation of the Barts Surgical Infection Risk tool. *Journal of Clinical Epidemiology*. 2020; 128: 57–65.
- [30] Alghamdi AA, Aqeeli MO, Alshammari FK, Altalhi SM, Bajebair AM, Al-Ebrahim Frcsc KE. Cardiac Surgery-Associated Acute Kidney Injury (CSA-AKI) in Adults and Pediatrics; Prevention is the Optimal Management. *The Heart Surgery Forum*. 2022; 25: E504–E509.