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ORIGINAL RESEARCH

Sex-Based Differences in Outcomes Following Mitral Valve Surgery: A Contemporary Analysis From 2 Institutions

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BACKGROUND: Despite differences in operative characteristics in patients with mitral valve disease, it remains unclear if sex is an independent risk factor associated with perioperative mortality after mitral valve surgery.

METHODS: We performed a retrospective cohort study of 3313 adult patients who underwent mitral valve surgery between 2011 and 2024 at 2 academic institutions. Patients were stratified by sex, and the primary outcome was operative mortality. Multivariable logistic regression was used to identify independent predictors of operative mortality.

RESULTS: In our cohort, 44.5% were women. Women were older (63.9 versus 62.2 years, $P<0.0001$), more likely to have New York Heart Association class III (15.9% versus 7.6%) and IV (1.4 versus 1.1%) heart failure ($P<0.05$ for both), and less likely to undergo mitral valve repair (63.5% versus 80.0%, $P<0.0001$). Women had shorter cross-clamp times (101.1 versus 105.0 min, $P<0.01$). Although postoperative intensive care unit stay was longer for women (3.0 versus 2.3 days, $P<0.0001$), operative mortality did not differ significantly by sex (1.42% versus 0.92%, $P=0.32$). In multivariable regression, female sex was not significantly associated with mortality after adjusting for covariates (odds ratio [OR], 1.03 [95% CI, 0.39–2.77], $P=0.66$). Prolonged cardiopulmonary bypass time was significantly associated with an increased odds of postoperative mortality (OR, 1.01 per 10 minutes [95% CI, 1.01–1.02], $P=0.002$).

CONCLUSIONS: Despite differences in baseline characteristics and surgical approach, operative mortality did not differ significantly by sex. Female sex was not significantly associated with operative mortality after adjustment for clinical and operative factors in patients undergoing elective mitral valve surgery.

Key Words: mitral valve surgery ■ outcomes ■ postoperative outcomes ■ sex differences ■ valve repair

Prior studies have identified differences in the timing of surgical referral, procedural choice, and postoperative outcomes between men and women undergoing cardiovascular surgery.[1–3] Whether these disparities persist in mitral valve (MV) disease and how they affect perioperative outcomes remains uncertain.

Current evidence shows that women with degenerative mitral regurgitation are referred for surgery less frequently and often at more advanced stages of disease.[4,5] Additionally, women are less likely to receive guideline-recommended interventions and less likely to benefit from the normalization of life expectancy conferred upon patients after MV repair.[6,7] In our institutional experience, women presented to surgery with larger indexed left ventricular dimensions, more mitral annular calcification, and worse left atrial strain parameters, findings associated with longer intensive care unit (ICU) stays and greater need for mechanical support.[8] These differences appear driven by delayed presentation rather than sex itself, reflecting a combination of clinical and social factors such as access

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CLINICAL PERSPECTIVE

What Is New?

- In a contemporary 2-center cohort of >3300 isolated mitral valve surgeries, women were significantly less likely to undergo mitral valve repair yet had operative mortality equivalent to men after adjustment for comorbid and operative factors.

What Are the Clinical Implications?

- These findings suggest that sex-based differences in procedural selection (rather than sex itself) drive observed disparities, underscoring the need for earlier referral and equitable evaluation.
- Recognizing that women experience longer intensive care unit and hospital stays despite similar mortality highlights opportunities to tailor postoperative recovery pathways to improve outcomes.

Nonstandard Abbreviations and Acronyms

MV	mitral valve

to care, provider bias, and patient preferences.[9–11] Beyond short-term outcomes, a 2013 analysis of Medicare beneficiaries undergoing MV operations demonstrated that women had both worse in-hospital mortality and worse long-term survival compared with men after MV repair, with no differences noted after valve replacement.[12] In that analysis, which focused only on patients 65 years and older, the difference in long-term outcomes was again attributed to a worse preoperative profile for women.

Whether sex is significantly associated with adverse outcomes following MV surgery, after accounting for these preoperative factors, remains an important and clinically relevant question. Our current study seeks to build upon the findings of van Kampen et al., evaluating a broader cohort of patients undergoing MV surgery (both repair and replacement) for all indications beyond degenerative mitral disease. Specifically, we aim to evaluate whether female sex was significantly associated with higher operative mortality, as well as to identify other clinical and intraoperative differences in the management of men and women presenting with mitral valvular disease.

METHODS

Ethics Statement

The study was approved by the Mass General Brigham Institutional Review Board with a waiver of informed consent due to the retrospective nature of the study.

Disclosure Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Study Design and Population

This was a multicenter, retrospective cohort study of adult patients (≥18 years) who underwent MV surgery between January 1, 2011 and December 31, 2024, at 2 large academic centers. Patients undergoing elective isolated MV surgery were identified from the institutional Society of Thoracic Surgeons Adult Cardiac Surgery Database. We excluded all redo cases and any patients who underwent concomitant nonmitral procedures such as coronary artery bypass grafting, aortic valve surgery, tricuspid procedures, or other major cardiac operations. Patients with missing data on sex and other key variables were also excluded.

Data Collection and Definitions

Patient demographic and clinical characteristics, including age, sex, race, body mass index, and comorbidities (diabetes, hypertension, chronic lung disease, prior myocardial infarction, peripheral artery disease, and dialysis) were compared. Operative characteristics, classified as procedure type (MV repair versus replacement), robotic approach, cross-clamp time, cardiopulmonary bypass time, and total operating time, were also assessed. Postoperative outcomes as defined by the Society of Thoracic Surgeons included operative mortality, stroke, prolonged ventilation, surgical site infection, renal failure, reoperation for bleeding, and 30-day readmission.

Outcome Measures

The primary outcome was operative mortality, defined as death during the index surgical hospitalization or death within 30 days of surgery. Secondary outcomes included stroke, prolonged ventilation, surgical site infection, postoperative renal failure, reoperation for bleeding, and 30-day readmission. Operative mortality and morbidity were assessed for the total cohort and stratified by sex. In secondary analyses, postoperative outcomes were additionally evaluated using covariate-adjusted regression models.

Statistical Analysis

Continuous variables were reported as mean±SD or median (interquartile range) and compared using Student's *t* test or Wilcoxon rank-sum test, as appropriate. Categorical variables were reported as counts and percentages and compared using chi-square or Fisher's exact test. Multivariable logistic regression was used to evaluate factors significantly associated with operative mortality after adjustment for covariates, with female sex as the primary exposure variable. The model adjusted for age, body mass index, race, diabetes, hypertension, prior myocardial infarction, peripheral artery disease, chronic lung disease, dialysis, prior coronary artery bypass grafting, MV repair versus replacement, and cardiopulmonary bypass time (per 10 minutes). Odds ratios (ORs) with 95% CIs were reported. To address potential overadjustment, we performed sensitivity analyses excluding cardiopulmonary bypass time and procedure type (repair versus replacement), given their potential role as mediators rather than confounders. Covariate-adjusted regression models were then performed with log-transformed linear regression for ICU and hospital length of stay, and logistic regression for binary outcomes. For rare events, Firth penalized logistic regression was used to reduce small-sample bias. Statistical significance was defined as a 2-tailed *P* value <0.05.

RESULTS

Baseline Characteristics and Intraoperative Variables

A total of 3313 patients underwent MV surgery during the study period, including 1475 (44.5%) women and 1838 (55.5%) men (Table 1). Women were significantly older than men (63.9 versus 62.2 years, *P*<0.0001) at the time of surgery and had a lower mean body mass index (26.3 versus 26.9 kg/m^2, *P*=0.001). Race and ethnicity distribution differed between sexes, with a higher proportion of Black and Hispanic patients among women compared with men (*P*=0.003). Comorbid conditions were generally similar between sexes, although women were more likely to have chronic lung disease (15.3% versus 11.3%, *P*=0.001), a history of stroke (6.4% versus 4.5%, *P*<0.001), and New York Heart Association functional class III (15.9% versus 7.6%) and IV (1.4% versus 1.1%) heart failure (*P*<0.05 for both).

Women were significantly less likely to undergo MV repair compared with men (63.5% versus 80.0%, *P*<0.0001), and a robotic approach for mitral surgery was also less commonly used in women (3.3% versus 5.3%, *P*=0.006). Women had shorter mean cross-clamp times (101.1 versus 105.0 minutes, *P*=0.010), shorter cardiopulmonary bypass times (146.1 versus 156.5 minutes, *P*<0.001), and shorter total operating times (363.7±81.0 versus 372.5±85.7 minutes, *P*=0.003) in our analysis.

Postoperative Outcomes

Postoperative outcomes are summarized in Table 2. Operative mortality did not differ significantly between women and men (1.42% versus 0.92%, *P*=0.32). Rates of postoperative stroke (0.75% versus 0.54%, *P*=0.33), prolonged ventilation (6.1% versus 4.5%, *P*=0.09), surgical site infection (0.34% versus 0.22%, *P*=0.79), and postoperative renal failure (1.69% versus 1.74%, *P*=0.34) were also similar between sexes. Women had significantly longer ICU) stays (3.0 versus 2.3 days, *P*<0.0001) and longer average hospital length of stay (length of stay) (8.4 versus 7.1 days, *P*<0.0001) compared with men but had a lower unadjusted 30-day readmission rate (4.2% versus 6.4%, *P*=0.002). After covariate-adjusted analyses (Table S1), female sex remained associated with longer ICU/hospital length of stay and lower odds of reoperation for bleeding (adjusted OR, 0.47 [95% CI, 0.27–0.81], *P*=0.007), but with higher odds of 30-day readmission (adjusted OR, 1.43 [95% CI, 1.09–1.87], *P*=0.01). Adjusted associations with postoperative stroke, prolonged ventilation, surgical site infection, and renal failure were not statistically significant.

Multivariable Regression Analysis

In the multivariable logistic regression model for operative mortality, female sex was not significantly associated with mortality after adjusting for covariates (OR, 1.03 [95% CI, 0.39–2.77], *P*=0.66). Prolonged cardiopulmonary bypass time was significantly associated with an increased odds of postoperative mortality after adjustment (OR, 1.01 per 10 minutes [95% CI, 1.01–1.02], *P*=0.002). Age, body mass index, race, diabetes, hypertension, prior myocardial infarction, chronic lung disease, peripheral artery disease, and MV procedure type (repair versus replacement) were not significantly associated with mortality after adjusting for covariates (Figure). Sensitivity analyses excluding cross-clamp time, and separately, procedure type from the model yielded similar results, with female sex remaining nonsignificantly associated with operative mortality (adjusted ORs, 1.05–1.09, *P*>0.5 for all). In secondary analyses stratified by institution, the association between female sex and operative mortality remained nonsignificant at both institutions (Table S2).

DISCUSSION

This study provides a contemporary analysis of sex-based differences in patients undergoing MV surgery for all indications at 2 centers. Our findings demonstrate that women undergoing MV surgery are significantly older at the time of surgery and are more likely to present to surgery with severely advanced and symptomatic New York Heart Association class III/IV heart failure. In our cohort, which spanned from 2011 to 2024, women were also less likely to undergo MV repair instead of replacement. Despite these baseline differences, female sex was not significantly associated with operative mortality after adjustment for demographic, comorbid, and operative variables on multivariable analysis. This suggests that the observed differences in baseline characteristics and procedural approaches do not directly

Table 1. Baseline Characteristics and Operative Variables

Characteristics	Total (n=3313)	Female patients (n=1475)	Male patients (n=1838)	*P* value
Age, y, mean±SD	63.0±12.3	63.9±12.8	62.2±11.8	<0.0001
Body mass index, kg/m^2, mean±SD	26.6±5.3	26.3±6.1	26.9±4.5	0.001
Race or ethnicity				0.003
White	3039 (91.7%)	1324 (89.8%)	1715 (93.3%)	
Black	84 (2.5%)	49 (3.3%)	35 (1.9%)	
Hispanic	45 (1.4%)	29 (1.9%)	16 (0.87%)	
Asian	61 (1.8%)	34 (2.31%)	27 (1.47%)	
Other*	29 (0.88%)	13 (0.88%)	16 (0.87%)	
Prior myocardial infarction	148 (4.5%)	69 (4.68%)	79 (4.3%)	0.590
Atrial fibrillation				0.640
Paroxysmal	380 (11.5%)	171 (11.6%)	209 (11.4%)	
Persistent	559 (16.9%)	262 (17.8%)	297 (16.2%)	
Chronic lung disease	433 (13.1%)	225 (15.3%)	208 (11.3%)	0.001
Hypertension	1888 (57.0%)	817 (55.4%)	1071 (58.3%)	0.190
Dialysis	16 (0.48%)	7 (0.47%)	9 (0.49)	0.950
History of diabetes	252 (7.6%)	125 (8.5%)	127 (6.9%)	0.128
History of stroke	177 (5.3%)	94 (6.37%)	83 (4.5%)	<0.001
History of smoking	1015 (30.6%)	451 (30.6%)	564 (30.7%)	0.760
Peripheral artery disease	98 (2.96%)	44 (2.98%)	54 (2.94%)	0.670
Heart failure				<0.001
NYHA class III	373 (11.3%)	234 (15.9%)	139 (7.6%)	
NYHA class IV	40 (1.2%)	20 (1.4%)	20 (1.1%)	
LVEF %, mean±SD	61.5±7.7	62.0±7.7	61.1±7.7	0.006
LVEF <40%	38 (1.6%)	17 (1.61%)	21 (1.62%)	0.99
Intraoperative variables				
Mitral valve repair	2406 (72.6%)	936 (63.5%)	1470 (80.0%)	<0.0001
Mitral valve replacement	907 (27.4%)	539 (36.5%)	368 (20.0%)	<0.0001
Mitral repair attempted	126 (3.8%)	60 (4.1%)	66 (3.60%)	<0.0001
Robotic approach	146 (4.4%)	49 (3.3%)	97 (5.3%)	0.006
Mitral implant type				<0.0001
Mechanical	238 (7.2%)	152 (10.3%)	86 (4.7%)	
Bioprosthetic	459 (13.9%)	249 (16.9%)	210 (11.4%)	
Annuloplasty ring	1918 (57.9%)	745 (50.5%)	1173 (63.8%)	
Atrial fibrillation procedure performed	758 (22.9%)	350 (23.7%)	408 (22.2%)	0.360
Cross-clamp time, min, mean±SD	103.2±40.6	101.1±40.5	105.0±40.6	0.010
Cardiopulmonary bypass time, min, mean±SD	151.9±56.7	146.1±54.8	156.5±57.8	<0.001
Total operating time, min, mean±SD	368.6±83.7	363.7±81.0	372.5±85.7	0.003

LVEF indicates left ventricular ejection fraction; and NYHA, New York Heart Association.
*Other denotes race or ethnicity that is not listed.

translate to worse short-term postoperative outcomes for women after MV surgery at our institutions.

Although operative mortality did not differ by sex, our study identified important differences in postoperative recovery and morbidity. Even after covariate-adjusted analysis, women had longer ICU and total hospital stays, suggesting more prolonged recovery with greater postoperative resource use. Recognizing these differences should yield an intense examination of surgical management patterns and an acknowledgement that sex-based differences extend beyond mortality. Our findings align with some previous studies that have reported sex disparities in the natural history and management of MV disease in women, including lower rates of MV repair.[5] Prior research has suggested that women are referred for surgery at a more advanced stage of disease, potentially due to delayed referral, differences in symptom recognition, or provider

Table 2. Postoperative Outcomes by Sex

Outcomes	Female patients (n=1475)	Male patients (n=1838)	*P* value
Postoperative length of stay, d, mean±SD	8.4±6.2	7.1±6.0	<0.0001
Intensive care unit length of stay, d, mean±SD	3.0±4.6	2.3±3.6	<0.0001
Operative mortality (%)	21 (1.42%)	17 (0.92%)	0.32
Postoperative stroke (%)	11 (0.75%)	10 (0.54%)	0.33
Prolonged ventilation (%)	90 (6.1%)	83 (4.5%)	0.09
Surgical site infection (%)	5 (0.34%)	4 (0.22%)	0.79
Postoperative renal failure (%)	25 (1.69%)	32 (1.74%)	0.34
Reoperation for bleeding (%)	21 (1.42%)	46 (2.50%)	0.02
30-d readmission (%)	139 (4.2%)	118 (6.4%)	0.002

biases.[13–15] However, lower repair rates in women may also reflect anatomic and technical considerations, including smaller annular dimensions, greater prevalence of mitral annular calcification, or more complex leaflet pathology, which can limit repair options. A 2024 analysis by van Kampen et al. suggested that nonindexed left ventricular dimension cutoffs may also contribute to late referral of women to surgery.[8] Specifically, European and North American guidelines currently recommend a left ventricular end-systolic diameter ≥40 mm as a potential indication to operate on asymptomatic patients with degenerative mitral disease.[16,17] However, this cutoff value was created from studies dominated by male patients and may not be appropriate for female patients when indexed by body surface area.[18,19] Of note, women in our cohort had longer ICU stays and longer hospital stays, which also aligns with existing data suggesting that women experience more prolonged postoperative recovery after cardiac surgery.[15,20,21]

The lack of a significant association between female sex and operative mortality in our study is consistent with prior studies focused on short-term outcomes after MV surgery.[8,22] Although women are known to experience worse outcomes in other cardiac operations such as coronary artery bypass grafting and thoracic aortic surgery, our findings suggest that sex does not significantly drive adverse outcomes in MV surgery.[21,23–26] Instead, sex may serve as a proxy for other risk-enhancing factors such as delayed referral, more advanced heart failure at presentation, and lower

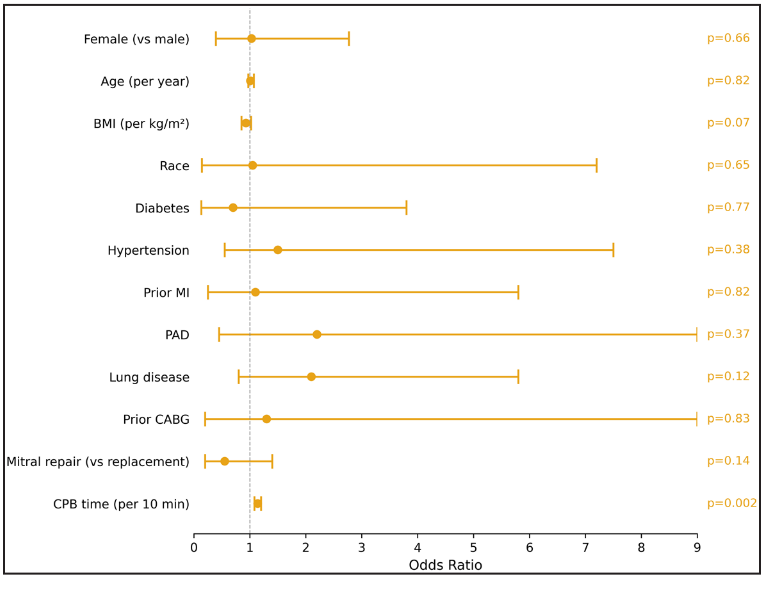

Figure Adjusted odds ratios for operative mortality after mitral valve surgery.
Forest plot demonstrating multivariable-adjusted odds ratios (ORs) and 95% CIs for operative mortality following mitral valve surgery. Estimates are derived from a multivariable logistic regression model adjusting for demographic characteristics, comorbid conditions, and operative variables included in the primary analysis. BMI indicates body mass index; CABG, coronary artery bypass graft; CPB, cardiopulmonary bypass; MI, myocardial infarction; and PAD, peripheral artery disease.

likelihood of undergoing MV repair.[8,12,27,28] The finding that women experienced longer ICU and hospital length of stay despite fewer reoperations for bleeding suggests that prolonged hospitalization was not driven by excess major surgical complications. Instead, these findings may reflect the aforementioned elevated baseline risk, yielding a greater need for postoperative monitoring and delayed readiness for discharge. Although women remained hospitalized longer, they nonetheless demonstrated higher adjusted odds of 30-day readmission, indicating that extended inpatient stays may not fully mitigate their postdischarge risk. Additionally, the lower rate of MV repair and lower rates of robotic operations raise concerns about potential disparities in procedural approach. Further investigation is needed to determine whether these differences reflect appropriate patient selection or unrecognized biases.

This study has several strengths, including its large cohort size and contemporary analysis, accounting for era biases and evolving management strategies. However, it is not without limitations. As a retrospective study at our institutions, the findings may not be generalizable to other institutions. Our findings reflect the experience of 2 academic centers with unique referral patterns, access to subspecialty care, and perioperative resources that may mitigate sex-based disparities differently compared with other settings. Next, because detailed echocardiographic data were not available, we could not determine whether lower repair rates in women primarily reflected anatomic complexity or surgical decision-making differences. Additionally, the institutional Society of Thoracic Surgeons database does not include Synergy Between PCI [Percutaneous Coronary Intervention] With Taxus and Cardiac Surgery scores or angiographic data. However, because our study was restricted to isolated MV operations, patients with significant coronary artery disease requiring coronary artery bypass grafting were excluded, minimizing the likelihood that coronary artery disease complexity confounded our findings. Finally, because procedure type may represent a mediator of sex-based disparities rather than a pure confounder, adjustment for this variable could partially attenuate any underlying association between sex and outcomes. However, sensitivity analyses excluding procedure type did not alter our findings.

CONCLUSIONS

In this cohort of patients undergoing MV surgery, women were significantly less likely to undergo MV repair. Our analyses show that sex is not significantly associated with mortality after adjusting for covariates. Although operative mortality was similar between sexes, differences in postoperative recovery highlight opportunities to tailor perioperative management and recovery strategies to improve outcomes for both women and men undergoing MV surgery. Further research is needed to explore the reasons for sex-based differences in procedural selection and to develop strategies to optimize outcomes for all patients.

ARTICLE INFORMATION

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Supplemental Material

Tables S1–S2.

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