Title: Effect of sex and surgical incision on survival after isolated primary mitral valve operations

Running title: Mitral valve surgery and sex differences

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Key question:
Does minimally-invasive mitral valve surgery (MIMVS) have impact on improving sex-specific survival compared to conventional mitral valve surgery (CS)?

Key findings:
A Cox model was fitted on 342 propensity score-matched pairs of MIMVS and CS patients and adjusted for propensity score. It showed no survival difference with surgical approach, sex or the interaction.

Take-home message:
MIMVS appears not to impact long-term survival either in women or men. However, it might aid the acceptance of earlier intervention with mitral surgery with its better cosmetic results.
Abstract

Objective: Multiple studies have suggested that women have worse outcomes than men following mitral valve surgery—most of those studies reported on conventional sternotomy mitral valve surgery (CS). Therefore, we aimed to explore whether or not the minimally invasive mitral valve surgery (MIMVS) approach might mitigate a worse survival in women following CS.

Methods: We identified patients with isolated primary mitral valve operations with or without tricuspid valve repair performed between 2007 and 2019. Patients were propensity score-matched across the MIMVS and CS surgical approaches. Sex was excluded from the matching process to discern whether female patients have a different likelihood of receiving minimally invasive surgery than males. A Cox proportional hazards model was fitted in the matched cohort and adjusted for the imbalance in baseline characteristics using the propensity score.

Results: Of 956 patients (417 MIMVS, 539 CS; 424 females), the matched set comprised 342 pairs (684 patients; 296 females) of patients who were well balanced across MIMVS and CS groups with regard to preoperative clinical characteristics. We observed a 47/53% female/male ratio in the CS and a 39/61% in the MIMVS group, p=0.054. In both matched groups, women were older than males. A Cox model adjusted for propensity scores showed no survival difference with sex, surgical type, or interaction.

Conclusions: Women present to the surgical team at an older age. They appear less likely to be considered for a MIMVS approach than men. Neither sex nor surgical approach was associated with survival in a matched sample.

Keywords: Gender; Minimally invasive surgery; Mitral valve; Outcomes; Techniques
**Introduction:**

Women are considered to have a greater risk for postoperative morbidity and mortality in cardiac surgery. Female sex remains an independent risk factor even after accounting for baseline imbalances in the risk profile.\(^1,2\) This is recognized by most perioperative, short-term risk cardiac surgery risk models, which give a higher score for the female sex. The original European System for Cardiac Operative Risk Evaluation (EuroSCORE) and the updated EuroSCORE II were predominantly based on patients undergoing coronary artery bypass grafting (CABG) and aortic valve surgery. Patients undergoing isolated mitral valve (MV) repair or replacement accounted for 9% and 18% of the databases,\(^3-5,\) thus rendering the predictive performance less precise for the MV population.\(^6\) The Society of Thoracic Surgeons recently released updated recalibrated short-term risk calculators, including stand-alone risk calculators for isolated mitral valve replacement and repair where female sex remained an independent risk factor for operative mortality.\(^7,8\) On the other hand, numerous reports show that the outcomes of sternotomy approach MV surgery are similar for women and men after risk adjustment.\(^9,10\)

The reasons which could explain the sex-based differences in MV operative risk are still elusive.\(^11,12\) Women tend to have smaller atria and ventricles than men, however more prominent when indexed to body surface area. Consequently, fewer women than men reach the classic surgical threshold of left ventricular diameter, which is an absolute rather than an indexed value.\(^13,14\) Women referred for MV surgery are older than men, with more advanced disease and more comorbidities.\(^15,16\) Women have markedly higher rates of rheumatic valve disease than men,\(^17\) and are more likely to undergo mitral valve replacement as opposed to repair, which has been shown to produce superior outcomes.\(^9,15,18-20\) Finally, women are less likely to experience postoperative left ventricular remodeling than men.\(^21\)

Notably, there is a paucity of data regarding the sex-based outcomes of minimally invasive mitral valve surgery (MIMVS). Therefore, it is unclear whether it provides females with a long-term survival advantage or not over the sternotomy approach. Furthermore, a recent report suggested that MIMVS did not offer any benefits over sternotomy in terms of in-hospital deaths or postoperative complications.\(^22\) We aimed to explore whether the effect of the surgical approach on long-term
survival varies by sex and to discern whether female patients had a different likelihood of receiving MIMVS than males with similar preoperative characteristics.

**Methods**

**ETHICS STATEMENT**

The study was approved by the Research Ethics Committee - Health Research Authority (HRA), and in line with other retrospective studies, the need for informed consent was waived (study ID 278325; reference number 20/HRA/3772). The database was anonymized before analysis.

**STUDY POPULATION AND STUDY DESIGN**

We conducted a longitudinal, observational, retrospective cohort study in a tertiary care cardiothoracic center in North West England, UK, of all consecutive patients undergoing mitral valve surgery between January 2007 and December 2019 who met the following criteria: first mitral valve surgery, either conventional (via sternotomy) (CS) or minimally invasive (MIMVS) with or without tricuspid valve surgery or procedures for atrial fibrillation. Patients with previous mitral valve surgery, concomitant coronary artery bypass graft surgery, simultaneous aortic valve repair/replacement or surgery on ascending aorta, emergency (operation before the beginning of the next working day after the decision to operate) or salvage procedure (patients requiring cardiopulmonary resuscitation en route to the operating theatre or prior to induction of anaesthesia), and those younger than 18 were excluded. Demographic and preoperative information, operative data, and in-hospital postoperative outcomes for all patients were retrieved from the institutional database maintained and validated for the purpose of outcome reporting to The National Adult Cardiac Surgery Audit managed by the National Institute for Cardiovascular Outcomes Research (NICOR). The study outcome measure was time to all-cause mortality. Information on vital status and date of death was obtained from our Institution’s Patient Administration System linked to the UK’s Office for National Statistics. It was up-to-date as of May 14, 2020.
For all analyses, a 2-sided \( p < 0.05 \) was considered statistically significant. All data were processed using R v. 4.1.2. The normality assumption for continuous variables was evaluated with the Shapiro–Wilk test. Continuous variables are presented as median [interquartile range (IQR)] and compared using the Kruskal–Wallis H test. Categorical variables are presented as counts and percentages and compared with Fisher's exact test.

The sample of patients was propensity-matched across MIMVS and CS surgical types, using a logistic model to derive propensity scores with the following predictor variables: age, body mass index (BMI), arterial hypertension, pulmonary hypertension (defined as systolic pulmonary artery pressure > 60 mmHg), diabetes mellitus, New York Heart Association (NYHA) functional class 3 or 4, chronic pulmonary disease, recent myocardial infarction (within 90 days), left ventricular ejection fraction category (poor 30% or less, fair 31-50% or good > 50%), poor mobility, serum creatinine > 200 \( \mu \text{mol/L} \), operative urgency (elective vs urgent), previous cardiac surgery, critical preoperative status as per the EuroSCORE definition (ventricular tachycardia or ventricular fibrillation or aborted sudden death, preoperative cardiac massage, preoperative ventilation before anaesthetic room, preoperative inotropes or intra-aortic balloon pump, preoperative acute renal failure), concomitant tricuspid valve surgery, and underlying mitral valve pathology (categorized as degenerative, functional, rheumatic, infective endocarditis or other).

Sex was excluded from the matching process to discern whether female patients have a different likelihood of receiving minimally invasive surgery than males with similar preoperative characteristics. We did not use EuroSCORE itself as a predictor variable as the majority of its components were individually used in the matching process.

Propensity score matching was conducted using the MatchIt package with a greedy "nearest neighbour" algorithm and a caliper 0.2 times the standard deviation of propensity scores. MIMVS and CS patients were paired 1:1 and without replacement.

Survival for the matched set was visualized using a plot of Kaplan–Meier estimates. A Cox proportional hazards model was fitted to explore whether the effect of surgical type varies by sex.
using an interaction between surgery and sex while adjusting for the imbalance in baseline characteristics between sexes using the propensity score.

Results

BASELINE CHARACTERISTICS

We included 956 patients undergoing their first mitral valve surgery, 539 (56.4%) had surgery via a conventional approach (sternotomy), and 417 (43.6%) via a minimally invasive approach (Supplementary Figure S1). Twelve patients (2.9%) had surgical access intraoperatively converted from minimally invasive to conventional. There were 275 females and 287 males in the CS approach and 158 females and 259 males in the MIMVS approach, whose baseline characteristics are presented in Table 1. At first mitral valve surgery, the median age was 68 years (IQR 58–75), range 19–92, and 424 (44.4%) were females. The median survival for the whole sample was 4.9 years (IQR 2.3 – 8.2); 197 (20.1%) patients died during the study period.

The matched set comprised 342 pairs (684 patients) of patients who are well balanced across MIMVS and CS groups (Figures 1 & 2 & 3, Table 2). Balance was assessed using standardized mean differences (SMD) between surgical groups, with an SMD lower than 0.1 deemed satisfactory balance; Figure 2 shows the between-group SMD of preoperative characteristics in the whole sample and in the matched sub-sample.

The matched set described a subset of the observed cohort: the group of patients with a small probability of receiving MIMVS given their baseline characteristics, shown by the first local mode coloured pink in Figure 1, were largely discarded during the matching process. Table 2 suggests that patients in the whole sample receiving conventional surgery were much more likely to be tricuspid valve surgery patients and showed higher rates of hypertension, diabetes and dyspnoea than the conventional sternotomy patients remaining in the matched sample. Therefore, conclusions drawn from this analysis relate to those patients described in the matched sample for whom both operative approaches were viable options for their surgery.
The 342-pair matched sample showed some imbalance in the mitral valve pathology category; however, this was much improved from the whole, unmatched sample and was likely due to small numbers split across many (five) categories. In addition, the Fisher's exact test of independence for the mitral valve pathology variable in the matched sample was non-significant with \( p=0.45 \), which gives some confidence that the remaining imbalance should not significantly affect conclusions.

The matched set described a set of patients with very similar preoperative clinical characteristics. A substantially higher proportion of the MIMVS group were male than in the CS group (61% vs 53% male, \( p=0.054 \), SMD 0.154), suggesting that females were under-represented in the MIMVS group despite the two surgical groups being clinically similar in all other relevant preoperative characteristics.

When exploring matching in more detail, we observed that males had much higher propensity scores (likelihood of MIMVS) than females, regardless of whether they received MIMVS or CS (Figure 3). In the matched cohort across MIMVS and CS, we showed that in the CS group, women were older (66.7 vs 63.6 years, SMD=0.227) and sicker than men (NYHA 3 or 4: 58.4% vs 43.1%, SMD=0.309), in MIMVS women were older (67.4 vs 62.0 years, pairwise SMD=0.417) but comparably sick (NYHA 3 or 4: 51.1% vs 45.9%, pairwise SMD=0.105) (Supplementary Table S1).

Kaplan–Meier survival estimates of the matched set showed no difference in survival between the treatment groups (Figure 4, log-rank test \( p=0.72 \)). Also, Kaplan–Meier curves in a four-way sex/treatment variable showed no significant difference in survival (Supplementary Figure S2, log-rank test \( p=0.21 \)).

A Cox proportional hazard model adjusted for surgical type, sex, the interaction of surgical type and sex, and the propensity score (as a measure of preoperative imbalance) showed no survival difference with any covariate once sex baseline imbalance is accounted for (Table 3). This model satisfied the assumption of proportional hazards (global \( p=0.63 \)).
Discussion

We present for the first time results on long-term sex-based differences in survival after isolated mitral valve surgery relative to the surgical approach. Of 956 patients included, 44% were women. Several notable baseline differences were discovered based on sample division by sex and surgical approach. First, there were significant differences in age at the time of surgery; females were older than men in CS, and MIMVS approaches. While our observations corroborate evidence concerning age discrepancy in conventional MVR, the differences in MIMVS have not been shown before.\textsuperscript{15,16} In terms of the NYHA class, women undergoing sternotomy had a higher degree of dyspnoea than those with MIMVS. In our population, females had a higher incidence of rheumatic valve disease, whereas males had more degenerative valve disease. That may explain why females were more likely to receive a replacement than males.\textsuperscript{9,14,15,18-20,24}

MIMVS is perceived to cause less pain to the patient and superior cosmetic results. There is evidence in aortic valve surgery that leaving the pericardium intact in minimally invasive surgery as opposed to leaving it open in sternotomy results in the right ventricular (RV) function being less affected.\textsuperscript{25} Previous studies also showed that there is less need for blood transfusion in MIMVS vs CS and MIMVS results in shorter postoperative stay compared to CS. In contrast, the cumulative bypass and cross-clamp times are longer in MIMVS.\textsuperscript{26} However, the long-term effects of MIMVS appear to be on par with CS.\textsuperscript{26,27} The debate between these two approaches is still ongoing as a UK-based randomized trial of minimally invasive techniques versus sternotomy for mitral valve surgery is currently underway with a primary outcome of functional recovery after surgery.\textsuperscript{28} Noteworthy, the UK’s mini-mitral trial excludes patients with previous cardiac surgery and those who required mitral valve replacement. Our data show that patients meeting the above criteria constituted approximately one-third of all comers, of whom one-third had MIMVR and two-thirds had a sternotomy. We also showed that unmatched patients receiving the conventional surgery were much more likely to need tricuspid valve surgery and had higher rates of hypertension, diabetes, and NYHA class than the conventional surgery patients remaining in the matched sample. Notably, the inference based on the
matched sub-cohort only goes as far as the patient types included in the matched population, and a randomized controlled trial is warranted to exclude the bias inherent to observational data.

In agreement with our findings, previous studies have demonstrated that short and long-term results of MIMVS and CS are equivalent if experienced surgeons undertake minimally invasive surgery in large volumes like in our center. After adjusting for propensity scores, no difference in survival was noted between sex, surgical approach and their interaction term. Our long-term findings are concordant with the recent study looking at in-hospital mortality following minimally invasive and sternotomy isolated aortic and mitral valve operations where no significant interaction was found between sex and surgical approach in neither aortic nor mitral valve subgroups after adjusting for confounders. The advantage of our analysis was the robust and complete data for post-discharge survival. Additionally, in the matched samples across surgical types, we have shown that females were less likely than males to receive MIMVS, and we found no apparent reason for this since survival appeared unrelated to treatment type or sex. This potential discrepancy in access to minimally invasive mitral valve surgery warrants further exploration, emphasizing referral pathways and a broader decision-making process. We found that women are older than males and with higher NYHA class at the surgery. Further studies are needed to evaluate the psychological impact of the scar that may be in play when women consider sternotomy surgery. We hope that our results will highlight the sex gap in minimally invasive mitral surgery and help persuade women to consider heart surgery earlier in the course of the mitral valve disease.

LIMITATIONS

This study is a retrospective review of patients with all inherent limitations. We have only analyzed data that were available for all the subjects; we did not include information on atrial fibrillation history, relevant echocardiographic parameters, or the degree of mitral annular calcification due to missing data. A single-center setting limits the generalisability of study findings. In addition, the treatment allocation was likely confounded by the surgical risk profile and patient and surgeon preference. However, to counterbalance the non-experimental study design, we propensity score-matched patients across the two types of surgical approaches. The matched set is matched entirely,
but the subgroups of male and female patients are not directly matched. A four-way matched solution was not able to be found. Deriving propensity scores for sex is not clinically useful (sex is pre-determined and cannot be randomly assigned pre-operatively). While propensity scores for treatment allocation could then be used to match males and females within each surgical type separately, these groups were no longer matched across treatment allocation.

This may mean we still do not have all the answers as to whether there is a sex-by-surgery difference. However, we can conclude this far that given all relevant baseline covariates (of which sex is just one) for this matched sub-cohort, there appears to be no difference in survival by surgery type, by sex or by the interaction of both.

In contrast to using Cox models without matching first, the present method adds (a) description of the cohort who are viable and comparable MIMVS candidates and (b) the result that females appear to be disadvantaged with respect to access to MIMVS without apparent cause.

Conclusions

In a matched sub-cohort across conventional and minimally invasive mitral valve surgery without using sex as a predictor variable, we show that females are less likely to be offered minimally invasive mitral valve surgery in our centre. After adjusting for surgical access, sex, the interaction of surgical access and sex, and the propensity score (as a measure of preoperative imbalance), there appears to be no difference in survival by surgery type, by sex or by the interaction of both.

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Conflict of interest: JZ receives Proctoring Fees from Edwards Lifesciences, Abbott, Cryolife and Medtronic. VV receives payment or honoraria for lectures, presentations, speakers bureaus or
educational events from Medtronic, Novartis and Astra Zeneca. Other authors declare no conflict of interest.

Author contributions: MD, RT, and JZ had full access to all the data in the study. RT conducted a formal analysis. MD and RT wrote the manuscript draft and take responsibility for the data integrity and the accuracy of the results. JZ provided mentorship and oversight over the administration and management of the research project. VV provided supervision and assisted in the study design. All authors critically revised the manuscript and approved the final version.

Acknowledgements: We thank Mrs Catherine Malpas for her assistance in data curation.

Data availability statement: The data underlying this article will be shared on reasonable request to the corresponding author.

Figure legends:
Central Image. Key messages, the standardized mean difference of preoperative characteristics in the whole and matched samples and a Cox proportional hazards model on the matched set.

Figure 1. Distributional balance of propensity scores.

Figure 2. A standardized mean difference of preoperative characteristics in the whole and matched samples.

Figure 3. Propensity scores for males and females.

Figure 4. Kaplan–Meier survival curves for the matched set, split by surgery type. CS=conventional sternotomy, MI=minimally invasive mitral valve surgery. A log-rank p-value is given.
Table 1: Treatment by sex differences in preoperative and operative clinical characteristics for all data, n=956. Global differences between the four groups are tested using the Kruskal–Wallis H test (continuous variables) or Fisher's exact test (categorical variables). SMD=standardised mean difference; mean-averaged across all pairwise SMD. IE=infective endocarditis; NYHA=New York Heart Association. Previous cardiac surgery was coronary artery bypass grafting (CABG) in 26 pts, CABG and aortic valve surgery (AVS) in 13 pts, AVS in 40 pts, and other heart surgery, including congenital heart disease correction in 7 pts.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Conventional</th>
<th>Minimally Invasive</th>
<th>Global test of group difference</th>
<th>Average SMD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Female, n=266</td>
<td>Male, n=273</td>
<td>Female, n=158</td>
<td>Male, n=259</td>
</tr>
<tr>
<td>Age, years</td>
<td>71 [63-76]</td>
<td>67 [58-75]</td>
<td>70 [61-76]</td>
<td>64 [52-71]</td>
</tr>
<tr>
<td>Hypertension</td>
<td>Yes</td>
<td>155 (58.3)</td>
<td>39 (50.9)</td>
<td>81 (51.3)</td>
</tr>
<tr>
<td>Pulmonary hypertension</td>
<td>Severe</td>
<td>71 (26.7)</td>
<td>66 (24.2)</td>
<td>36 (22.8)</td>
</tr>
<tr>
<td>Poor mobility</td>
<td>Yes</td>
<td>31 (11.7)</td>
<td>16 (5.9)</td>
<td>19 (12.0)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>Yes</td>
<td>34 (12.8)</td>
<td>19 (7.0)</td>
<td>7 (4.4)</td>
</tr>
<tr>
<td>Dyspnoea</td>
<td>NYHA class 3 or 4</td>
<td>166 (62.4)</td>
<td>136 (49.8)</td>
<td>82 (51.9)</td>
</tr>
<tr>
<td>Previous cardiac surgery</td>
<td>Yes</td>
<td>22 (8.3)</td>
<td>18 (6.6)</td>
<td>19 (12.0)</td>
</tr>
<tr>
<td>Chronic lung disease</td>
<td>Yes</td>
<td>38 (14.3)</td>
<td>28 (10.3)</td>
<td>18 (11.4)</td>
</tr>
<tr>
<td>Creatinine</td>
<td>&gt;200 µmol/L</td>
<td>1 (0.4)</td>
<td>7 (2.6)</td>
<td>0</td>
</tr>
<tr>
<td>Recent myocardial infarction</td>
<td>Yes</td>
<td>5 (1.9)</td>
<td>3 (1.1)</td>
<td>0</td>
</tr>
<tr>
<td>Left ventricular ejection fraction</td>
<td>Poor (≤30%)</td>
<td>5 (1.9)</td>
<td>8 (2.9)</td>
<td>3 (1.9)</td>
</tr>
<tr>
<td></td>
<td>Fair (31-50%)</td>
<td>44 (16.5)</td>
<td>41 (15.0)</td>
<td>15 (9.5)</td>
</tr>
<tr>
<td></td>
<td>Good (&gt;50%)</td>
<td>217 (81.6)</td>
<td>224 (82.1)</td>
<td>140 (88.6)</td>
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<td>Operative priority</td>
<td>Urgent</td>
<td>35 (13.2)</td>
<td>35 (12.8)</td>
<td>9 (5.7)</td>
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<tr>
<td>Critical pre-operative state</td>
<td>Yes</td>
<td>3 (1.1)</td>
<td>3 (1.1)</td>
<td>0</td>
</tr>
<tr>
<td>----------------------------</td>
<td>-----</td>
<td>---------</td>
<td>---------</td>
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</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td></td>
<td>26.4 [23.7-30.0]</td>
<td>25.9 [23.6-28.7]</td>
<td>24.9 [21.9-28.8]</td>
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<td>Mitral valve pathology</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td>Degenerative</td>
<td></td>
<td>152 (57.1)</td>
<td>202 (74.0)</td>
<td>97 (61.4)</td>
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<tr>
<td>Functional</td>
<td></td>
<td>28 (10.5)</td>
<td>36 (13.2)</td>
<td>27 (17.1)</td>
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<tr>
<td>IE</td>
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<td>4 (1.5)</td>
<td>7 (2.6)</td>
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<td>Rheumatic</td>
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<td>70 (26.3)</td>
<td>14 (5.1)</td>
<td>26 (16.5)</td>
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<td>Other</td>
<td></td>
<td>12 (4.5)</td>
<td>14 (5.1)</td>
<td>8 (5.1)</td>
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<tr>
<td>Tricuspid valve surgery</td>
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<td></td>
<td></td>
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<td>Yes</td>
<td></td>
<td>128 (48.1)</td>
<td>111 (40.7)</td>
<td>39 (24.7)</td>
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</table>
Table 2: Preoperative patient characteristics, before and after propensity matching. Age and body mass index are given as mean and standard deviation, all others as frequency and percentage. SMD = standardized mean difference. IE = infective endocarditis; NYHA = New York Heart Association.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Whole sample, n=956</th>
<th>Matched sample, n=684</th>
<th>SMD</th>
<th>Conventional, n=539</th>
<th>Minimally invasive, n=417</th>
<th>SMD</th>
<th>Conventional, n=342</th>
<th>Minimally invasive, n=342</th>
<th>SMD</th>
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<tr>
<td><strong>Matching covariates:</strong></td>
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<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Age, years</td>
<td>70 [60-76]</td>
<td>66 [55-74]</td>
<td>0.249</td>
<td>68 [58-75]</td>
<td>67 [56-74]</td>
<td>0.081</td>
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<td>Hypertension</td>
<td>Yes</td>
<td>294 (55)</td>
<td>0.171</td>
<td>192 (46)</td>
<td>169 (49)</td>
<td>0.041</td>
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<td>Pulmonary hypertension</td>
<td>Severe</td>
<td>137 (25)</td>
<td>0.120</td>
<td>85 (20)</td>
<td>75 (22)</td>
<td>0.036</td>
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<td>Poor mobility</td>
<td>Yes</td>
<td>47 (9)</td>
<td>0.003</td>
<td>36 (9)</td>
<td>29 (9)</td>
<td>0.041</td>
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<td>Diabetes</td>
<td>Yes</td>
<td>53 (10)</td>
<td>0.184</td>
<td>21 (8)</td>
<td>23 (7)</td>
<td>0.062</td>
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<td>Dyspnoea</td>
<td>NYHA class 3 or 4</td>
<td>302 (56)</td>
<td>0.177</td>
<td>197 (47)</td>
<td>172 (50)</td>
<td>0.047</td>
<td></td>
<td></td>
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<td>Previous cardiac surgery</td>
<td>Yes</td>
<td>40 (7)</td>
<td>0.125</td>
<td>46 (11)</td>
<td>30 (9)</td>
<td>0.030</td>
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<td>Chronic lung disease</td>
<td>Yes</td>
<td>66 (12)</td>
<td>&lt;0.001</td>
<td>51 (12)</td>
<td>42 (12)</td>
<td>0.009</td>
<td></td>
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<td>Creatinine</td>
<td>&gt;200 µmol/L</td>
<td>8 (2)</td>
<td>0.025</td>
<td>5 (1)</td>
<td>6 (2)</td>
<td>0.077</td>
<td></td>
<td></td>
<td></td>
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<td>Recent myocardial infarction</td>
<td>Yes</td>
<td>8 (2)</td>
<td>0.174</td>
<td>0</td>
<td>0</td>
<td>&lt;0.001</td>
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<tr>
<td>Left ventricular ejection fraction</td>
<td>Poor (≤30%)</td>
<td>13 (2)</td>
<td>0.043</td>
<td>9 (2)</td>
<td>6 (2)</td>
<td>0.075</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Fair (31-50%)</td>
<td>85 (16)</td>
<td></td>
<td>60 (14)</td>
<td>42 (12)</td>
<td>49 (14)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Good (&gt;50%)</td>
<td>441 (82)</td>
<td></td>
<td>348 (84)</td>
<td>294 (86)</td>
<td>285 (83)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Operative priority</td>
<td>Urgent</td>
<td>70 (13)</td>
<td>0.231</td>
<td>26 (6)</td>
<td>24 (7)</td>
<td>0.011</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Critical pre-operative state</td>
<td>Yes</td>
<td>6 (1)</td>
<td>0.107</td>
<td>1 (0.2)</td>
<td>0</td>
<td>0.077</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>26.1 [23.6-29.4]</td>
<td>25.8 [22.8-28.9]</td>
<td>0.090</td>
<td>26.0 [23.8-29.4]</td>
<td>25.8 [22.7-28.9]</td>
<td>0.086</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Mitral valve pathology

<table>
<thead>
<tr>
<th>Category</th>
<th>Degenerative</th>
<th>Functional</th>
<th>IE</th>
<th>Rheumatic</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>354 (66)</td>
<td>278 (67)</td>
<td>240 (70)</td>
<td>236 (69)</td>
<td></td>
</tr>
<tr>
<td>P</td>
<td>0.332</td>
<td>0.143</td>
<td>0.143</td>
<td>0.143</td>
<td></td>
</tr>
</tbody>
</table>

### Tricuspid valve surgery

<table>
<thead>
<tr>
<th>Category</th>
<th>Yes</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>239 (44)</td>
</tr>
<tr>
<td>P</td>
<td>0.661</td>
</tr>
</tbody>
</table>

### Covariates not matched for:

- **Sex**
  - Male: 273 (51)
  - Female: 259 (62)
  - P: 0.233

- **Type of mitral valve surgery**
  - Replacement: 185 (34.3)
  - Other: 93 (22.3)
  - P: 0.269

- **Need for blood transfusion**
  - Yes: 109 (20.2)
  - No: 28 (6.7)
  - P: 0.404

- **Postprocedural length of stay, days**
  - Median: 9 [7-14]
  - P: 0.480

- **Cumulative bypass time, min**
  - Median: 132 [110-166]
  - P: 0.606

- **Cumulative cross-clamp time, min**
  - Median: 98 [80-125]
  - P: 0.139

- **Logistic EuroSCORE**
  - Median: 5.8 [3.3-10.2]
  - P: 0.129

- **Additive EuroSCORE**
  - Median: 6 [5-8]
  - P: 0.278
Table 3: Cox model on matched set, n=684. HR=hazard ratio. CI=confidence interval.

<table>
<thead>
<tr>
<th>Covariate</th>
<th>HR (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MIMVS</td>
<td>1.15 (0.70, 1.88)</td>
<td>0.58</td>
</tr>
<tr>
<td>Male sex</td>
<td>0.75 (0.47, 1.20)</td>
<td>0.23</td>
</tr>
<tr>
<td>MIMVS and male sex (interaction)</td>
<td>0.95 (0.47, 1.92)</td>
<td>0.89</td>
</tr>
<tr>
<td>Propensity score</td>
<td>0.54 (0.17, 1.67)</td>
<td>0.28</td>
</tr>
</tbody>
</table>
References


Distributional balance of propensity scores

Unmatched

Matched

Surgery type

CS

MIMVS

Density

Propensity score
Variable SMD between procedure groups before and after propensity score matching

- Tricuspid valve surgery
- Mitral valve pathology (Ref: degenerative)
- Age
- Sex (Ref: female)
- Urgent procedure
- Diabetes
- NYHA 3 or 4
- Recent myocardial infarction
- Hypertension
- Previous cardiac surgery
- Pulmonary hypertension
- Critical peri-operative state
- Body mass index
- Left ventricular ejection fraction (Ref: poor [<30%])
- Creatinine >200µmol/L
- Poor mobility
- Chronic obstructive pulmonary disease
- Matched sample
- Whole sample

Standardised Mean Difference (SMD)
Survival probability

Time

Surgery type

CS

MI

Number at risk

0 2.5 5 7.5 10 12.5

Time

Surgery type

CS

MI

p = 0.72
Does minimally-invasive mitral valve surgery (MIMVS) have impact on improving sex-specific survival compared to conventional mitral valve surgery (CS)?

A Cox model was fitted on 342 propensity score-matched pairs of MIMVS and CS patients and adjusted for propensity score. It showed no survival difference with surgical approach, sex or the interaction.

MIMVS appears not to impact long-term survival either in women or men. However, it might aid the acceptance of earlier intervention with mitral surgery with its better cosmetic results.