Title: Repair of Mitral Prolapse: Comparison Of Thoracoscopic Minimally-invasive And Conventional Approaches.

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Visual abstract:

Key question: Can the same quality be obtained with minimally-invasive mitral valve repair in patients with degenerative mitral regurgitation?

Key findings: Thoracoscopic mitral repair associated shorter ventilation and ICU stay with less blood loss compared to the conventional approach

Take-home message: Thoracoscopic repair in degenerative mitral regurgitation showed excellent results, with similar repair rate and durability and facilitating recovery.

ABSTRACT:

Background and objectives: Surgical repair remains the best treatment for severe primary mitral regurgitation. Minimally-invasive mitral valve surgery is being increasingly performed, but there is a lack of solid evidence comparing thoracoscopic with conventional surgery. Our objective was to compare outcomes of both approaches for repair of leaflet prolapse.

Methods: All consecutive patients undergoing surgery for severe mitral regurgitation due to mitral prolapse from 2012 to 2020 were evaluated according to the approach used. Freedom from mortality, reoperation and recurrent severe mitral regurgitation were evaluated by Kaplan-Meier method. Differences in baseline characteristics were adjusted with propensity score matched analysis (1:1, nearest neighbor).

Results: 300 patients met inclusion criteria and were divided into thoracoscopic (N=188) and conventional (sternotomy; N=112) groups. Unmatched patients in the thoracoscopic group were younger and had lower body mass index, New York Heart Association class and EuroSCORE-II preoperatively. After matching, thoracoscopic group presented significantly shorter mechanical ventilation (9 vs.15h), shorter intensive care unit stay (41 vs. 65h) and higher postoperative hemoglobin levels (11 vs.10.2 mg/dL) despite longer bypass and cross-clamp times (+30 and +17min). There were no differences in mortality or mitral regurgitation grade at discharge between groups nor differences in survival, repair failures and reinterventions during follow-up.

Conclusions: Minimally-invasive mitral repair can be performed in the majority of patients with mitral prolapse, without compromising outcomes, repair rate or durability, while providing shorter mechanical ventilation and intensive care unit stay and less blood loss.

Word count: 238

KEY WORDS: mitral repair, mitral regurgitation, mitral prolapse, minimally-invasive surgery, perioperative outcomes.

ABBREVIATIONS:

AF - Atrial Fibrillation

BMI - Body Mass Index

CPB - Cardiopulmonary Bypass

ECMO - Extracorporeal Membrane Oxygenation

ICU - Intensive Care Unit

LV - Left Ventricle

MIMVS - Minimally-Invasive Mitral Valve Surgery

MR - Mitral Regurgitation

NYHA - New York Heart Association

PS - Propensity Score

SMD – Standardized mean difference

SARS-COV-2 - Severe Acute Respiratory Syndrome Coronavirus 2

TEE - Transesophageal Echocardiography

INTRODUCTION:

Primary mitral regurgitation (MR) is the most frequent type of mitral valve dysfunction in developed countries and, within this group, degenerative MR is the most common etiology[1]. Valve abnormalities in degenerative MR are in most cases amenable to successful surgical repair in centers with experience[2,3] with a class I recommendation by European and American Guidelines[4,5]. Furthermore, current guidelines advocate for surgical repair in patients with severe MR who present with a flail leaflet or left atrial enlargement, even if asymptomatic and left ventricular (LV) function remains normal, provided a successful repair could be expected with a low perioperative risk.

There is a wide variety of options for mitral repair, including the approach, the repair techniques or the annuloplasty devices used. Currently the gold-standard treatment implies performing the operation through a full median sternotomy. However, over the last 20 years minimally-invasive mitral surgery (MIMVS) techniques have been developed and increasingly performed[6]. Data from large series have shown that MIMVS provides excellent results, comparable to those of conventional surgery without a tradeoff in repair rate or durability, associated with less surgical trauma and a faster recovery[7,8,9]. However, some authors have reported an increased risk of neurological complications, aortic dissection and other complications with the vascular access used in MIMVS[10], but most of these studies were performed in the earlier experience with systematic use of endoaortic balloon-occlusion[11].

Our aim was to examine the contemporary early and mid-term results of mitral repair for degenerative MR according to the surgical approach used: minimally-invasive or median sternotomy.

METHODS:

Ethical Statement

This study was approved by the Institutional Ethics Committee of the Hospital Clínic of Barcelona, Spain, (HCB/2021/0248) on 03/02/2021. The need for individual written informed consent was waived.

Study Population

We evaluated all consecutive patients treated in our center from November-2011 to November-2020 with 4+ primary MR secondary to degenerative disease who underwent surgical intervention, regardless of the planned procedure. We excluded patients with previous interventions and those requiring additional concomitant procedures other than atrial fibrillation ablation or closure of patent *foramen ovale*, to facilitate direct comparisons of both approaches. Also, patients with contraindications for MIMVS were excluded: severe aorto-iliac disease (contraindication for femoral cannulation and retrograde perfusion), ascending aorta aneurysm (>45mm), a severely calcified mitral annulus, >2+ aortic regurgitation or previous surgery on the right chest. The choice of the approach was at the discretion of the attending surgeon.

Surgical Techniques

Mitral repair strategy included a large variety of standardized techniques, but basically consisted in leaflet resection and/or chordal replacement to treat the prolapse of the posterior leaflet and chordal replacement to treat anterior leaflet prolapse. A small number of patients, with more complex forms of the disease, needed additional techniques such as chordal transposition, chordal shortening, papillary muscle repositioning and commissural plication. The choice of annuloplasty devices was made at the discretion of the attending surgeon and included a variety of flexible bands and complete, rigid or semirigid rings. All patients were operated under normothermic extracorporeal circulation and using intermittent antegrade cold blood-cardioplegia.

MIMVS was performed using specifically-designed, long-shafted endoscopic instruments inserted through a working port created with a right lateral mini-thoracotomy (3-4cm) in the fourth or fifth intercostal space, or with a periareolar incision in a minority of selected cases (Figure 1). Two additional 5mm ports were placed in the right hemithorax for a 5mm-30º videocamera and continuous CO_2 insufflation (3rd/4th intercostal space, mid-axillary line) and for the left atrial retractor (4th/5th intercostal space, midclavicular line). Finally, a 10mm port was placed for venting the left chambers and to introduce a pleural drain after the intervention (6^{th} right intercostal space, anterior axillary line). Our routine approach to perform these procedures involves cannulation of the right common femoral artery and vein using single femoral venous cannulation, thus avoiding placing a second jugular cannula. Direct transthoracic aortic clamping and antegrade blood-cardioplegia infusion directly in the aortic root was performed in all cases for cardioplegic arrest and myocardial protection, similarly to the conventional approach through median sternotomy. All procedures were performed through a left atriotomy.

Outcomes and Sources of Data

The primary outcomes of this study were mitral repair rate, mortality and mayor complications (stroke, acute renal failure) rates. Secondary outcomes were all other postoperative complications, transfusion and blood loss and duration of mechanical ventilation, and ICU & hospital stay. Time-related follow-up outcomes included survival, freedom form reoperation and from mitral replacement and freedom from recurrent MR. Data on patient demographics, baseline characteristics, perioperative outcomes, follow-up and vital status were obtained from our institutional databases. All patients had a comprehensive preoperative transthoracic echocardiography, intraoperative transesophageal echocardiographic monitoring and a complete transthoracic echocardiography before hospital discharge. Patients were followed in our outpatient clinic with annual echocardiography. MR was graded following current recommendations[12]. Follow-up data gathering was completed (and the dataset closed) on November 2022.

Statistical Analysis

Descriptive statistics for categorical variables were reported as frequency and percentage, and comparisons performed using a chi-squared test or the Fisher's exact test. Continuous variables were reported as mean/standard deviation or as median/interquartile range depending on normality and comparisons were performed using the Wilcoxon-Mann-Whitney test. The Kaplan-Meier method was used to calculate survival time-related events and comparisons were performed using Cox regression. All comparisons were performed on an intention-to-treat basis.

Propensity Score matching: the propensity scores (PS) for undergoing surgery using the MIMVS approach were estimated by means of a logistic regression model. Bias reduction and balance between the groups was assessed with standardized difference of covariates. Based on the logit scores obtained and using the nearest neighbor method (1:1, without replacement, without caliper), a cohort of 103 pairs was selected to perform unbiassed comparisons between both surgical approaches. Table S1 and Figures S1 and S2 on the supplemental material provide a full description of the variables before and after propensity score matching and the standardized bias reduction accomplished. Two-sided *p* values <0.05 were considered significant and standardized mean differences (SMD) were calculated for all comparisons. All survival analyses were stratified by matched pairs and using robust variance-covariance matrix estimation, with the Cox proportional hazards model. All analyses were performed using STATA® (StataCorp, USA).

RESULTS:

Preoperative characteristics:

300 consecutive patients met the selection criteria during the study period and were included. Of those, 188 patients underwent a minimally-invasive thoracoscopic mitral repair (MIMVS group;63%) and 112 had surgery through a median sternotomy (Conventional group;37%). Detailed data on volume and distribution of cases is shown in Figure 2. Baseline characteristics are shown in Table 1. MIMVS patients were younger (59vs.64 years; p<0.01), and had lower

BMI (25vs.26; p=0.02), and EuroSCORE II (1.61vs.2.28%; p<0.01), less chronic renal disease (2.5vs.8%; p<0.05) and a higher percentage was in NYHA class I or II (75vs.52.5%; p<0.01). All preoperative characteristics were balanced after PS adjustment with no significant differences between groups at baseline in the matched cohort. All patients had 4+ degenerative MR and the prevalence of more complex morphologies (anterior, commissural or bileaflet prolapse) was high, accounting for more than one third of cases, with the same proportion in both groups (Table 1).

Cardiac intervention:

A successful mitral repair was achieved in 295 patients (>98%), with only 5 patients requiring mitral replacement, one in the MIMVS group and four in the Conventional group (99.5vs.96.5%; p=0.07). Among the MIMVS group, there was only one conversion to median sternotomy (0.5%).

Multiple repair techniques were used on both groups, with no significant differences between them (Table 2). Concomitant AF ablation was performed in 36 patients with similar frequency in both groups (11vs.13.5%; p=0.58).

In the overall population, operative times were significantly longer in the MIMVS group compared to the Conventional group, (+25 min on CPB and +15 min on cross-clamp duration; p<0.01). Similar differences were also found after matching, where patients in the MIMVS group required a longer CPB (+30 min, SMD=-0.70) and cross-clamp (+17 min,SMD=-0.54).

Perioperative clinical outcomes:

There were no significant differences in major postoperative complications, including stroke (<1%), permanent pacemaker implantation (3%), postoperative renal failure (2%), reintervention (5.4%) and tamponade (1.3%). Detailed information is presented in Table 3.

In the entire cohort, there were no significant differences in first 24 hours chest tube output, nor in the amount of blood products transfused. However, hemoglobin levels on the fifth day after surgery were significantly higher in the MIMVS group (11 mg/dLvs.10.2 mg/dL; p<0.01). This difference persisted significant in the PS-matched cohort (10.9 mg/dLvs.10.2 mg/dL;SMD=-0.47). Also, patients on the MIMVS group had less incidence of *de novo* postoperative AF compared to the open group in the entire cohort (24%vs.37%; p=0.02). This finding was also seen after PS matching, although not statistically significant (29%vs.39%; SMD=0.21).

Compared to the Conventional group and despite longer CPB times, the MIMVS group required a significantly shorter median duration of mechanical ventilation (6vs.14h; p<0.01), probably explained by a higher proportion of patients extubated in the operating room (60vs.17%, p<0.01). These differences persisted after matching. Median ICU and hospital stay were significantly shorter in the MIMVS group (all patients in the study were discharged home and not to other care facilities). The significant reduction in ICU stay was also seen in the PS-matched cohort (1.7dvs.2.7d; SMD=0.32). Five patients (4 MIMVS/1 Conventional) underwent reoperation before hospital discharge due to unsatisfactory mitral valve function at the postoperative echocardiographic control. All patients were successfully re-repaired using the same original approach. Details of these cases are described in Table S2.

Lastly, there were four postoperative deaths during the study period, two in each group (1.1vs.1.8%; p=0.63). In the conventional group one patient died because of an intraoperative atrioventricular groove rupture and another with severe preoperative tracheal stenosis was unable to wean from invasive respiratory support. In the MIMVS group one patient died due to severe pulmonary distress requiring ECMO support and another patient died due to intercurrent postoperative SARS-CoV-2 infection.

Echocardiographic results at hospital discharge:

98.6% of repaired patients were discharged with ≦1+ MR, without significant differences between approaches (99vs.98%; p=0.61). Detailed are presented in Table 3.

Follow-up results:

The median clinical follow-up time was 4.0 years (range:0.1-8.9years). Survival at 1, 3 and 5 years after the operation was 99%, 98% and 95%, respectively (Table 4; Figure 3). The predominant cause of death in the follow-up period was non-cardiovascular (67%). Follow-up index for patients in both groups [median(IQR)] were: MIMVS: 0.90(0.82-0.94), Conventional:0.92(0.85-0.95).

Freedom from recurrent 4+ MR after 1, 3 and 5 years in the entire cohort was 98%, 94% and 93%, respectively (Table 4; Figure 3). Freedom from reoperation was 98%, 95% and 94%, whereas freedom from mitral replacement was 98%, 96% and 96%, respectively. None of these outcomes showed significant differences in the PS-matched cohort.

16 patients (5.3%) required reoperation during follow-up (median:1year; range 1month – 7years). Of these, 10 had undergone MIMVS (5.3%) and 6 (5.4%) a Conventional repair. There were no cases of mitral stenosis or infective endocarditis. The rate of successful mitral re-repair was 62.5% (80% after MIMVS and 33% after Conventional surgery). Table S3 provides detailed information on all the reinterventions performed during follow-up.

DISCUSSION:

Our study describes and compares the contemporary early and mid-term results of conventional and MIMVS repair for mitral prolapse over the last decade. Using statistical methods to adjust for baseline characteristics, we could demonstrate that MIMVS offers a safe and effective alternative to conventional open surgery, with comparable repair rates and even providing advantages on key clinical outcomes.

Noteworthy, our study included all consecutive patients with MR due to leaflet prolapse referred for surgery, regardless of the planned procedure and operation performed. This unselected population provides the most realistic measure of repair rate, which was very high in both groups, exceeding 98%. The minimally-invasive approach did not compromise the possibility of using a wide range of surgical techniques and concomitant AF ablation, and did not affect repair quality or durability.

Despite requiring longer operative times, MIMVS was not associated with a negative impact on postoperative outcomes, in accordance with other large series of mitral repair using a similar approach[13,9,14,15,]. On the contrary, MIMVS was associated with significantly shorter median duration of mechanical ventilation and ICU stay, in line with some previous reports[10,16,17]. Patients in the MIMVS group presented significantly higher hemoglobin levels, with similar transfusion requirements in both groups. Serum hemoglobin after cardiac surgery decreases due to blood loss, the need for fluid resuscitation in the early postoperative period, and the inflammatory effects of the surgical manipulation and CPB. Hemoglobin after cardiac surgery tend to drift down, reaching a nadir around postoperative day 4 and recovering partially in most patients over the following days[18]. Hemoglobin level on postoperative day 5 provides typically a good indication of total blood loss and the maximal anemic state after cardiac surgery.

Our goal was to leave the operating room without residual MR, as it has a negative impact on late outcomes[19]. All cases were performed under TEE control and underwent a comprehensive transthoracic echocardiogram before discharge. In the presence of residual MR greater than the observed at the end of the operation, we were proactive taking back the patient to the operating room, particularly if the mechanism was technical. Noteworthy, the valves were successfully re-repaired in all cases, and all reinterventions were performed using the approach initially used, thus maintaining the benefits of MIMVS.

Finally, mid-term outcomes of our cohort showed no differences between groups in terms of survival, freedom from reoperation, valve replacement or recurrent 4+ MR, which is consistent with some previous reports[16,20,21,22]. Compared to previous publications[20,23,24], our study shows a higher survival rate at 5 years of follow-up for both groups and a higher repair rate. It should be noted that, unlike these referenced series, our study is focused on one type of mitral dysfunction (mitral prolapse) instead of on the procedure performed (“mitral intervention” in both registries) and comes from a single center where MIMVS is the most frequent approach (63% MIMVS cases vs. 29 and 27% for the Netherlands and UK registries, respectively). This provides a different and valuable information on the outcomes that can be achieved in the most frequent type of patients with mitral regurgitation in a dedicated program, although these might not be directly extrapolated to other causes of MR and centers. In our study, there were no differences in MR recurrence when comparing the surgical approach used or the complexity of mitral lesions (isolated posterior vs. anterior or bileaflet prolapse), reinforcing that MIMVS can be used with excellent results in all the disease spectrum, comparable to other large series using a conventional approach[25,26].

Study Limitations

The main limitation of this study is the limited sample size, its unicenter nature and the absence of randomization, which implies a risk of selection bias. Patients in the MIMVS group were operated only by two surgeons, although these same two surgeons were also performing the majority of the cases in the conventional group (61%). A second analysis excluding the patients operated by surgeons other than the two performing MIMVS showed same conclusions for all our defined outcomes. In our cohort however, MIMVS was the most frequent approach used and we had been performing MIMVS long before the period of the study, so the learning curve of MIMVS is not included[24]. Nevertheless, to minimize the potential risk of selection bias, we performed a sensitivity analysis on a PS-matched cohort obtained from the complete population, thus balancing all preoperative variables. We had enough patients in all risk strata in both groups to effectively balance all variables. This method provides proven, excellent control of selection bias related with the variables included in the regression model but, unlike randomization, does not control for other factors that were not measured. Finally, we performed all MIMVS procedures using a standardized fully-thoracoscopic approach. There are other different surgical approaches to repair the mitral valve that could be considered to be minimally-invasive, and thus, the results reported might not be extrapolated to other techniques. Larger series and multicenter studies could provide valuable confirmatory data on these issues in the future.

CONCLUSIONS:

MIMVS surgery for mitral prolapse is a safe and effective procedure and can be accomplished with excellent results by expert teams. Under this premise, it can be offered to most of these patients, regardless of the complexity of the lesions, with equivalent quality and advantages in key postoperative results as compared with conventional repair through a median sternotomy.

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Data availability statement: Data would be available on request.

FIGURE LEGENDS:

Central Image: Kaplan-Meier curve showing excellent repair rates with both the minimally-invasive and the conventional approaches, with 93% of the patients free from severe MR at 5 years of follow up, after comparing these two groups using a propensity score matched analysis.

Figure 1: A: Landmarks required for surgical set-up. **B:** Set-up during transareolar approach. The arrow demonstrates the videocamera used during this endoscopic procedure using long-shafted instruments (asterisk). Result after a minithoracotomy (**C**) or a periareolar approach (**D**).

Figure 2: Yearly volume (yellow line, right axis) and proportional distribution (left axis) of MIMVS (blue) and Conventional (red) cases throughout the study. Year 2012 includes patients from the incomplete contiguous year (asterisk). Year 2020 is not shown in this graph due to the decreased in the number of cases per year secondary to COVID-19 restrictions (n=24).

Figure 3: Clinical follow-up data of matched patients (**A**,**B**,**C**)

Figure 4: Echocardiographic follow-up. Freedom from recurrent 4+ mitral regurgitation: for the entire cohort (**A**); for isolated posterior prolapse (yellow line) and more complex forms (green line) (**B**); for different approaches in the entire cohort (**C**) and in the matched groups (**D**).

Table 1. Preoperative Data.

	Entire Unmatched Cohort				Propensity Score-matched Cohort			
	Total (n=300)	**MIMVS (n=188)**	**Open (n=112)**	***p***	**MIMVS (n=103)**	**Open (n=103)**	***p***	***SMD***
Age (years)	61 (±12)	59 (±13)	64 (±11)	<0.01	62 (±12)	64 (±12)	0.42	0.11
Male gender (%)	202 (68)	126 (68)	76 (69)	0.80	71 (69)	69 (67)	0.88	0.04
Weight (Kg)	73 (±14)	73 (±14)	74 (±13)	0.26	74 (±14)	74 (±13)	0.81	-0.01
Height (cm)	169 (±9)	169 (±9)	168 (±9)	0.26	168 (±9)	168 (±9)	0.37	-0.09
Body mass index (Kg/m^2)	25.7 (±4)	25 (±4)	26 (±4)	0.02	26 (±4)	26 (±4)	0.46	0.04
Creatinine (mg/dL)	0.95 (±0.30)	0.93 (±0.29)	0.98 (±0.31)	0.11	0.97 (±0.35)	0.98 (±0.32)	0.63	0.04
Chronic Renal Disease	14 (5)	5 (2.5)	9 (8)	0.05	4 (4)	8 (8)	0.37	0.16
Smoking (%)	69 (23)	44 (23)	25 (22)	0.89	22 (21)	23 (22)	1.00	0.02
Ischemic cardiopathy (%)	10 (3.3)	5 (2.5)	5 (4)	0.51	3 (3)	4 (4)	1.00	0.05
Hypertension (%)	126 (42)	77 (41)	49 (44)	0.72	41 (40)	42 (41)	1.00	0.02
Dyslipidemia (%)	82 (27)	45 (24)	37 (33)	0.11	33 (32)	34 (33)	1.00	0.02
Diabetes (%)	29 (6.7)	10 (5)	10 (9)	0.24	8 (8)	9 (9)	1.00	0.04
Prior stroke (%)	14 (5)	9 (5)	5 (4.5)	0.44	5 (5)	5 (5)	1.00	0.04
Prior atrial fibrillation (%)	87 (29)	48 (25)	39 (35)	0.09	33 (32)	36 (35)	0.77	0.06
COPD (%)	16 (5)	8 (4)	8 (7)	0.30	8 (8)	7 (7)	1.00	0.04
Peripheral vascular disease (%)	6 (2)	3 (1.5)	3 (2.5)	0.67	2 (2)	2 (2)	1.00	<0.01
Hypothyroidism (%)	21 (7)	12 (6)	9 (8)	0.64	11 (11)	8 (8)	0.63	0.10
NYHA (%)								
I-II	198 (66.5)	140 (75)	58 (52.5)	0.00	63 (61)	53 (52)	0.23	0.20
III-IV	100 (33.5)	47 (25)	53 (47.5)		40 (39)	50 (48)		
Prolapse (%):				0.92			0.59	
Posterior	192 (64)	119 (63)	73 (65)		62 (60)	67 (65)		
Anterior	24 (8)	16 (8.5)	8 (7)		11 (11)	7 (7)		0.10
Bileaflet	84 (28)	53 (28)	31 (28)		30 (29)	29 (28)		
LVEF (%)	61 (±7)	61 (±6.5)	60 (±8)	0.52	60 (±7)	60 (±8)	0.73	0.03
EDD (mm)	57 (±7)	57 (±7)	57 (±6)	0.54	57 (±7)	57 (±6)	0.44	0.10
ESD (mm)	35 (±6)	35 (±6)	35.5 (±6)	0.32	35.5 (±6)	35.5 (±6)	0.70	0.01
sPAP (mmHg)	39 (±13)	38 (±12)	41 (±15)	0.04	40 (±13)	42 (±15)	0.58	0.13
LAD (mm)	45.7 (±7.3)	45.3 (±7.3)	46.3 (±7.4)	0.37	45.7 (±8.2)	46.0 (±7.6)	0.83	0.04
TR grade	0.63 (±0.6)	0.64 (±0.6)	0.62 (±0.6)	1.00	0.65 (±0.6)	0.60 (±0.6)	0.71	-0.09
EuroSCORE II	1.87 (±2.10)	1.61 (±1.84)	2.28 (±2.40)	<0.01	1.96 (±2.20)	2.31 (±2.45)	0.43	0.15

Continuous variables are expressed as mean (± standard deviation).
MIMVS: minimally-invasive mitral valve surgery, SMD: standardized mean difference, NYHA: New York Heart Association, LVEF: left ventricular ejection fraction, EDD: end-diastolic diameter, ESD: end-systolic diameter, sPAP: systolic pulmonary artery pressure, LAD: left atrium diameter, TR: tricuspid regurgitation).

Table 2. Intraoperative Data.

	Entire Unmatched Cohort				Propensity Score-matched Cohort			
	Total (n=300)	**MIMVS (n=188)**	**Open (n=112)**	***p***	**MIMVS (n=103)**	**Open (n=103)**	***p***	***SMD***
Prosthetic mitral replacement (%)	5 (1.7)	1 (0.5)	4 (3.5)	0.07	0	3 (3)	0.25	0.24
Annuloplasty* (%)	294 (99.7)	184 (100)	107 (99.1)	0.35	103 (100)	99 (99)	1.00	0.14
Leaflet resection* (%):				0.98			0.89	0.05
Triangular	102 (35)	65 (35)	37 (35)		38 (37)	33 (34)		
Quadrangular	35 (12)	23 (12)	12 (11)		10 (10)	10 (10)		
Neochordae (%)	144 (48.6)	86 (46)	58 (54)	0.23	46 (44)	56 (56)	0.12	0.23
Atrial fibrillation ablation (%)	36 (12)	21 (11)	15 (13.5)	0.58	14 (14)	15 (15)	0.84	0.03
Cardiopulmonary bypass time (min)	115 (85-134)	124 (94-141)	99 (77-112)	<0.01	128 (95-146)	98 (77-112)	<0.01	-0.70
Aortic cross-clamp time (min)	88 (64-105)	93 (69-112)	78 (61-88)	<0.01	95 (70-114)	78 (61-88)	<0.01	-0.54
Coaptation length (mm)	9 (7.5-10)	10 (8-10)	8 (7-10)	0.44	10 (10-14)	8 (7-10)	0.10	-1.53
Patients extubated in the OR (%)	132 (44)	113 (60)	19 (17)	<0.01	56 (54)	17 (17)	<0.01	0.86

Continuous variables expressed as median (interquartile range).
*After removing the patients who had a valve replacement.
MIMVS: minimally-invasive mitral valve surgery, SMD: standardized mean difference.

Table 3. Perioperative Data.

	Entire Unmatched Cohort				Propensity Score-matched Cohort			
	Total (n=300)	**MIMVS (n=188)**	**Open (n=112)**	***p***	**MIMVS (n=103)**	**Open (n=103)**	***p***	***SMD***
Drainage in 24h (mL)	380 (±280)	380 (±289)	380 (±267)	0.89	437 (±325)	396 (±269)	0.52	-0.14
Patients transfused (%)	84 (28)	51 (27)	33 (29)	0.69	36 (35)	32 (31)	0.66	0.08
PRBC transfused (units)	0.71 (±2.4)	0.70 (±2.8)	0.72 (±1.5)	0.18	0.97 (±3.7)	0.78 (±1.6)	0.57	-0.07
Hemoglobin at 5th day (mg/dL)	10.7 (±1.5)	11.0 (±1.5)	10.2 (±1.4)	<0.01	10.9 (±1.5)	10.2 (±1.4)	<0.01	-0.47
Mechanical ventilation duration (h, IQR)	9 (0-7)	6 (0-5)	14 (4-10)	<0.01	9 (0-7)	15 (4-10)	<0.01	0.11
de novo Postoperative AF (%)	86 (29)	45 (24)	41 (37)	0.02	30 (29)	40 (39)	0.14	0.21
Permanent pacemaker (%)	9 (3)	4 (2)	5 (4.5)	0.30	3 (3)	5 (5)	0.49	0.10
Pericarditis (%)	9 (3)	7 (4)	2 (2)	0.49	5 (5)	2 (2)	0.44	0.16
Permanent stroke (%)	2 (0.67)	1 (0.5)	1 (0.9)	1.00	1 (1)	1 (1)	1.00	<0.01
AKI (%)	6 (2)	4 (2)	2 (2)	1.00	3 (3)	2 (2)	0.68	0.07
Re-intervention (%)	16 (5.4)	12 (6)	4 (3.6)	0.43	6 (6)	4 (4)	0.75	0.09
Infection (%)	15 (5)	11 (6)	4 (3.6)	0.58	7 (7)	4 (4)	0.54	0.13
ICU stay (days)	2 (1-2)	1.6 (1-2)	2.7 (1-3)	<0.01	1.7 (1-2)	2.7 (1-3)	<0.01	0.32
Hospital stay (days)	9 (6-10)	8.5 (6-9.5)	10 (6-11)	0.01	10 (6-12)	10 (7-11)	0.93	0.01
In-hospital mortality (%)	4 (1.3)	2 (1)	2 (2)	0.63	2 (2)	2 (2)	1.00	<0.01
Echocardiographic MR at discharge (%)	n=292*	n=185*	n=107*	0.61	n=101*	n=97*	0.61	0.09
0-1+	288 (98.6)	183 (99)	105 (98)		100 (99)	95 (98)		
2+	4 (1.4)	2 (1)	2 (2)		1 (1)	2 (2)		
3-4+	0	0	0		0	0		

Continuous variables are expressed as mean (± standard deviation) or median (IQR).
Blood products: Rate of patients with one or more blood product transfused during or after surgery.
SMD: standardized mean difference, AF: atrial fibrillation; AKI: acute kidney insufficiency that meets the STS criteria (>3x increase from preoperative creatinine, Cr>4mg/dL [with a minimum increase >0.5mg/dL] or requirement of CRRT/Hemodialysis) for acute renal failure; ICU: intensive care unit; IQR: interquartile range; MIMVS: minimally-invasive mitral valve surgery; PRBC: packed red blood cell (transfused during all hospital admission).
*After removing the patients who had a valve replacement or died during postoperative period.

Table 4. Follow-up Data.

	Unmatched Cohort				Propensity Score-matched Cohort			
Clinical Follow-Up Median (IQR): 4.0 years (2.1-5.8) Range: 0.1-8.9 years	**1 year**	**3 years**	**5 years**	***p***	**1 year**	**3 years**	**5 years**	***p***
Survival (%):								
Overall	99	98	95		99	98	95	
MIMVS	98	97	94	0.19	98	97	91	0.01
Conventional	99	99	97		99	99	99	
Freedom from Reoperation (%):								
Overall	98	95	94		98	94	92	
MIMVS	98	95	93	0.90	98	94	90	0.38
Conventional	98	95	95		98	94	94	
Freedom from Mitral Replacement (%):								
Overall	98	96	96		98	96	96	
MIMVS	99	98	98	0.03	100	98	98	0.13
Conventional	95	93	93		96	94	94	
Echocardiographic Follow-Up Median (IQR): 3.5 years (1.6-5.6) Range: 0.7-9.5 years	**1 year**	**3 years**	**5 years**	***p***	**1 year**	**3 years**	**5 years**	***p***
Freedom from Severe (4+) MR (%):								
Overall	98	94	93		98	93	91	
MIMVS	99	95	93	0.34	100	93	90	0.16
Conventional	97	92	92		97	92	92	
Freedom from ≥ Moderate (2+) MR (%):								
Overall	95	89	86		95	89	85	
MIMVS	95	88	84	0.71	95	87	80	0.12
Conventional	96	91	89		95	91	89	

Echocardiographic measures at 1 year:

	Entire Unmatched Cohort			Propensity Score-matched Cohort		
	MIMVS (n=188)	**Open (n=112)**	**p**	**MIMVS (n=103)**	**Open (n=103)**	**SMD**
LAD (mm)	41.1(±7.5)	42.9(±7.9)	0.15	41.5(±7.8)	42.9(±8.1)	0.17
EDD (mm)	42.8(±11.1)	44.3(±9.8)	0.49	42.7(±11.9)	44.1(±10.0)	0.13
ESD (mm)	38.3(±10.7)	40.3 (±10.9)	0.23	39.2(±10.9)	40.7(±10.9)	0.14
sPAP (mmHg)	28.1(±7.3)	31.6(±9.5)	0.18	28.6(±7.8)	31.2(±9.7)	0.30
Mean transmitral gradient (mmHg)	3.2(±1.7)	3.2(±1.9)	0.29	3(2-4)	3 (2-4)	-0.10
Mean TR grade	0.50(±0.5)	0.56(±0.6)	0.65	0.48(±0.5)	0.54(±0.6)	0.11

Continuous variables are expressed as mean (± standard deviation) or median (IQR).
IQR: interquartile range, SMD: standardized mean difference, MIMVS: minimally-invasive mitral valve surgery, MR: mitral regurgitation, LAD: left atrium diameter, ESD:left ventricular end-systolic diameter, EDD:left ventricle end-diastolic diameter, sPAP: systolic pulmonary arterial pressure, TR: .
* In 275 patients, after removing the patients who had a valve replacement.

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