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1 Neochordae implantation versus leaflet resection in mitral valve posterior leaflet prolapse and dilated 2 left ventricle: a propensity score matching comparison with long-term follow-up 3 4 Benedetto Del Forno<sup>1</sup>, MD, Kevin Tavana<sup>1</sup>, MD, Claudio Ruffo<sup>1</sup>, MD, Davide Carino<sup>1</sup>, MD, Elisabetta 5 Lapenna<sup>1</sup>, MD, Guido Ascione<sup>1</sup>, MD, Arturo Bisogno<sup>1</sup>, MD, Igor Belluschi, MD, Maria Giovanna Scarale<sup>2</sup>, 6 Alessandro Nonis<sup>2</sup>, Fabrizio Monaco<sup>3</sup>, MD, Ottavio Alfieri<sup>1</sup>, MD, Alessandro Castiglioni<sup>1</sup>, MD, Francesco 7 Maisano<sup>1</sup>, MD and Michele De Bonis<sup>1</sup>, MD. 8 <sup>1</sup>Department of Cardiac Surgery, IRCCS San Raffaele Hospital, Vita-Salute San Raffaele University, Milan, 9 10 Italy. 11 <sup>2</sup> University Centre of Statistics in Biomedical Sciences (CUSSB), Vita-Salute San Raffaele University, Milan, 12 Italy. <sup>3</sup> Department of Anesthesiology, IRCCS San Raffaele Hospital, Vita-Salute San Raffaele University, Milan, 13 14 Italy. 15 Presented at the 36th EACTS Annual Meeting, 05-08 October 2022, Milan, Italy. 16 17 Text word count: 4473 18 19 Correspondence to: 20 Benedetto Del Forno, MD Department of Cardiac Surgery 21 22 **IRCCS San Raffaele Hospital** 23 "Vita-Salute" San Raffaele University 24 Via Olgettina 60 25 20132 Milano, Italy 26 Tel. +390226437102/7108 27 Fax. +390226437125 28 E-mail: delforno.benedetto@hsr.it

# 29 Visual Abstract

30 **Key question:** In patients with dilated left ventricle, what is the durability of neochordae as compared to 31 resections techniques?

32 Key findings: The long-term durability of neochordal repair is good and similar to resections techniques

33 Take-home message: even in dilated left ventricles neochoardae implantation ensures durability of the repair

- 34 and good left ventricular performance at follow-up.
- 35
- 36 Abstract
- 37 Background

38 Uncorrected severe mitral regurgitation due to posterior prolapse/flail leads to left ventricular dilatation. At 39 this stage, mitral valve repair becomes mandatory to avoid permanent myocardial injury. However, which 40 technique among neochoardae implantation and leaflet resection provides the best results in this scenario 41 remains unknown.

42 Methods

We selected 332 patients with left ventricular dilatation and severe degenerative mitral regurgitation due to posterior leaflet prolapse who underwent neochoardae implantation (85 patients) or posterior leaflet resection (247 patients) at our Institution between 2008 and 2020. A propensity score matching analysis was carried on to decrease the differences at baseline.

47 **Results** 

48 Matching yielded 85 neochordae implantations and 85 posterior leaflet resections. At 10-years, freedom from 49 cardiac death and freedom from mitral valve reoperation, was  $92.6 \pm 6.1\%$  vs  $97.8 \pm 2.1\%$  and  $97.7 \pm 2.2\%$  vs 50  $95\pm3\%$  in the neochordae group and in the posterior leaflet resection group respectively.

The mitral regurgitation  $\geq 2+$  recurrence rate was 23.9±10% in the neochordae group and 20.8 ± 5.8% in the posterior leaflet resection group (p=0.834) at 10-years. At last follow-up, neochordae group showed a higher reduction of left-ventricular end-diastolic diameter (44mm vs 48 mm; p=0.001) and a better ejection fraction (60% vs 55%; p <0.001) compared to posterior leaflet resection group.

55 Conclusions

57 the repair in the long-term. Neochordae implantation might have a better effect on dilated left ventricle.

58

# 59 Abstract word count: 246

60

61 Key words: mitral valve repair, neochoardae implantation, posterior leaflet resection, dilated left ventricle,

- 62 reverse remodelling
- 63

# 64 Introduction

65 Surgical mitral valve (MV) repair represents the treatment of choice to address severe degenerative mitral 66 regurgitation (MR). In this context, posterior leaflet (PL) prolapse is the most common lesion and it is usually

- 67 treated by leaflet resection or neochordae implantation [1].
- Resection techniques, either triangular and quadrangular, often associated to sliding or folding plasty, have
  been introduced and popularized by *Alain Carpentier* in the early 80s [2]. These techniques have been widely
  adopted and greatly stood the test of time [3,4].
- adopted and greatry stood the test of time [5,4].

71 Conversely, based on the early work of *Robert Frater* [5], David et al. started using PTFE sutures for 72 neochordae replacement with excellent early and long-term results [6,7]. More recently, *Patrick Perier* 73 proposed the so called "respect approach" mainly based to avoid removal of leaflet tissue and to implant PTFE 74 neochorde to restore the physiological motion of the valve [8].

The comparison between these two repair strategies is still object of ongoing debate, but no clear differencesin results have been observed [9,10].

Indeed, if not timely corrected, the persistent volume overload leads to left ventricular (LV) dilatation and remodelling [11]. Although LV reverse remodelling can occur after surgical correction of MR, it is unclear whether this process is related to the surgical technique and does have an impact on the long-term durability of the repair. In particular, it remains unknown the effect of significant LV reverse remodelling on implanted chordal length and its consequences on MR recurrence. 82 The aim of this study was to compare the early and long-term clinical and echocardiographic outcomes of 83 resection techniques versus artificial chordae implantation, specifically in patients with posterior leaflet 84 prolapse and dilated left ventricle.

85

### 86 Patients and Methods

87 *Ethical statement* 

The Ethical Committee of the San Raffaele Hospital approved the study (115/INT/2022) and waived the
individual informed consent for this retrospective anonymous analysis.

90

91 Study Population

92 From January 2008 to December 2020, 856 patients with LV dilatation and severe degenerative MR due to PL

93 prolapse underwent MV repair at San Raffaele University Hospital, Milan, Italy.

We included in this study patients with LV dilatation defined as a left ventricular end-diastolic diameter (LVEDD)  $\geq$ 58 mm in male and  $\geq$ 53 mm in female, according to the position paper of the American Society of Echocardiography and the European Association of Cardiovascular Imaging [12].

For the purpose of the study and to minimize all possible confounding factors, we selected patients who 97 underwent neochordae implantation or PL resection techniques, namely triangular resection or quadrangular 98 99 resection associated to folding plasty. Therefore, we excluded 416 patients who were treated with different repair techniques such as quadrangular resection associated to sliding plasty or annular plication, central or 100 101 commissural edge-to-edge, chordal transposition and "butterfly" technique. Moreover, we excluded 108 patients with one of the following conditions: severe LV dysfunction, urgent or emergency operation, 102 103 concomitant infective endocarditis, previous mediastinal radiation therapy or hypertrophic obstructive 104 cardiomyopathy.

Finally, 332 patients were selected and represented the overall cohort of the study. Neochordae implantation
was performed in 85 patients whereas PL resection in 247 patients.

107 In general practice, the surgeon's preference played the major role for the choice of the reparative technique.

108 To mitigate this selection bias and to obtain two balanced groups of patients, a propensity score matching was

109 used. This methodology allowed us to achieve two similar groups (85 patients each), with respect to the

- 110 preoperative characteristics, that have then been used for the analysis.
- 111 Pre-operative, intra-operative and post-operative data were collected through our hospital database.
- 112
- 113 Surgical Techniques

114 The operations were carried out through both conventional median sternotomy or right-sided anterolateral

- 115 minithoracotomy, with moderately hypothermic cardiopulmonary bypass and cold crystalloid cardioplegia.
- 116 The mitral valve was exposed through a conventional left atrial incision, parallel to the interatrial groove. 117 According to the inclusion criteria of the study, in the PL resection group the technique of repair was a triangular resection of the central scallop of the posterior leaflet (P2) (47 patients, 55%) or a limited 118 119 quadrangular resection with folding plasty (38 patients, 45%). Conversely, in the neochordae group, artificial PTFE neochordae were implanted to address the P2 lesion. In our series, 50 patients (59%) underwent standard 120 121 "hand adjusted" neochordae implantation (median number of neochordae implanted: 2) and 35 patients (41%) underwent premeasured loops technique (median number of loops implanted: 3; median loops length: 14 mm). 122 123 In all patients a prosthetic annuloplasty was associated.
- 124 Concomitant procedures such as tricuspid valve repair, coronary artery bypass grafting and atrial fibrillation
  125 ablation, were associated whenever indicated.
- 126
- 127 Statistical Analyses

Propensity score matching was performed using exclusively all the complete variables such as sex, age, body surface area (BSA), hypertension, pre-operative atrial fibrillation (AF), NYHA functional class, pre-operative left ventricular ejection fraction (LVEF), pre-operative LVEDD and planned associated procedures. The matching was used to randomly select the subgroup of patients undergoing PL resection to be compared to the group of patients undergoing neochordae implantation. Patients were weighted according to the propensity score and the samples were matched at 1:1 ratio without replacement. Standardized mean differences (SMD) have been used to evaluate the quality of the matching (Figure 1) [13].

135 Continuous variables were reported as median and interquartile range [IQR 25th percentile; 75th percentile],

136 whereas categorical variables were reported as total frequencies and percentages. Two-sided *p*-values for

137 continuous variables refer to Kruskal-Wallis test. Two-sided *p*-values for categorical variables refer to Fisher

138 Exact test when appropriated.

- Kaplan-Meier method was used to estimate overall survival, freedom from cardiac death and freedom fromMV reintervention for each group of intervention.
- 141 According to *Peduzzi et al.*, we decided to not compute inferential comparison between neochordae group and
- 142 PL resection group for overall survival, freedom from cardiac death and freedom from MV reoperation because
- 143 of the low number of events (<10) in each outcome [14].
- 144 The main outcome was MR recurrence  $\geq 2$ . Competing risks proportional-hazards regression model, following

145 the Fine-Gray model, for time to  $MR \ge 2$  with death as competing risk was performed. Cumulative incidence

146 function (CIF) for time to MR  $\geq 2$  with death as competing risk was calculated.

- Risks were reported as hazard ratios (HRs) along with their 95% confidence intervals (CIs). A P value <0.05 was considered significant. All analyses were performed using R statistical software (version 4.0.4; https://cran.r-project.org/index.html). The R package Matchlt was used to implement propensity score matching. The R packages survival and cmprsk were used to perform survival and competing risk analyses.</p>
- 151

### 152 Echocardiographic evaluation

All patients underwent preoperative transesophageal echocardiography focused to confirm the severity of the 153 MR and to identify and better define the characteristic of PL lesions. In this cohort, all patients showed an 154 isolated prolapse or flail of the central portion of the PL (P2). A transesophageal echocardiography was 155 routinely repeated immediately after weaning from cardiopulmonary bypass. A transthoracic 156 echocardiography examination was performed in all patients before hospital discharge, and was available in 157 158 all patients alive and who were not lost at follow-up. To evaluate the recurrence of MR, an integrative approach 159 was used to define MR severity. A non-linear 4-grade scale was adopted to define MR as mild (1+/4+), mild-160 to-moderate (2+/4+), moderate-to-severe (3+/4+) and severe (4+/4+).

161

## 162 Follow-Up

Follow-up data were obtained by means of outpatient visit and transthoracic echocardiography performed in
our Institution in 75% of the cases. In the remaining patients, the follow-up data were acquired with telephone

165 interview with the patients and referring cardiologists. We focused on survival, causes of death, incidence of 166 MV reoperation, recurrence of MR  $\geq 2+$ , clinical status, symptoms and echocardiographic parameters. When 167 the transthoracic echocardiography was performed in a different institution, the report was collected for review. 168 Transthoracic echocardiography data regarding the degree of MR, LVEF and LVEDD were available for all 169 the patients alive and who were not lost at follow-up. We conducted follow-up examinations in the same period 170 for all patients, irrespective of the time since the operation occurred (common closing date method). The cause 171 of death was determined from death certificates or from information from the physician who was caring for 172 the patient at that time. Follow-up was 96% complete. The median clinical and echocardiographic follow-up 173 time was 5.97 years [4.49-9.61] with a maximum follow-up time of 13.76 years.

174

### 175 **Results**

176 Among 332 overall patients, 85 (25.6%) underwent neochordae implantation and 247 (74.4%) underwent PL resection. Matching yielded 85 neochordae implantation and 85 PL resections. Matched groups were well 177 balanced and there were no significant differences in both groups with regard to the preoperative clinical 178 characteristics (Table 1). The median age was 63 years [IQR 52-70] in the neochordae group and 63 years 179 [IQR 53-69.3] in the PL resection group (p=0.875). Eleven patients (12.9%) in the neochordae group and 14 180 181 patients (16.5%) in the PL resection group were in New York Heart Association (NYHA) functional class III or IV (p=0.326). The median LVEF was 64% [IQR 60-68] in the neochordae group and 65% [IQR 60.0-69.0] 182 in the PL resection group (p=0.727) and the median LVEDD was 61 mm [IQR 57-63] in the neochordae group 183 and 61 mm [IQR 59.0-64.0] in the PL resection group (p=0.433). 184

185

# 186 In-hospital outcomes

Operative characteristics of the matched population are shown in Table 2. Only one in-hospital death (1.2%) occurred in neochordae group whereas no patient died in the PL resection group. Right minithoracotomy approach was performed in 21 patients (24.7%) of the neochordae group and in 15 patients (17.6%) of the PL resection group (p= 0.348). The median ring size was 35 mm [IQR 33-36] in the neochordae group and 35 mm [IQR 33-35] in the PL resection group (p=0.954). CPB time was 82 minutes [IQR 68-100] in the neochordae group and 74 minutes [IQR 66-90] in the PL resection group (p=0.013) whereas aortic cross-clamp time was 193 62 minutes [IQR 52-78] in the neochordae group and 55 minutes [IQR 48-68] in the PL resection group (p= 194 0.019). Four patients (4.7%) in the neochordae group and three patients (3.5%) in the PL resection group 195 needed intra-aortic balloon pump (IABP) (p = 1.0). Sixteen patients (19.0%) in the neochordae group and 19 196 patients (22.9%) in the PL resection group developed AF during postoperative hospitalization (p=0.674). 197 Echocardiography performed at hospital discharge showed residual MR 2+ in two patients (2.4%) in the 198 neochordae group and in five patients (6.2%) in the PL resection group (p=0.623). All other patients of both 199 groups presented mild (1+) or no residual postoperative MR.

- 200
- 201 Follow-up outcomes

During follow-up of the matched population, seven patients (4%) in the neochordae group and two patients (1%) in the PL resection group died. Five deaths (3%) were cardiac-related: four in the neochordae group and one in the PL resection group. The 10-years overall survival was  $84.6\pm7.6\%$  in the neochordae group and 96.6±2.4% in the PL resection group. At 10-years, the freedom from cardiac death was  $92.6\pm6.1\%$  in the neochordae group and  $97.8\pm2.1\%$  in the PL resection group (Figure 2).

Moreover, five patients required re-operation: two patients (1%) of the neochordae group and three patients (2%) of the PL resection group. The freedom from MV reoperation, was  $97.7\pm2.2\%$  in the neochordae group and  $95\pm3\%$  in the PL resection group at 10-years (Figure 3).

The CIF of MR recurrence  $\geq 2^+$ , with death as competing risk, was  $23.9\pm10\%$  in the neochordae group and 20.8  $\pm$  5.8% in the PL resection group (p=0.834) at 10-years (Figure 4). Specifically, nine patients in the neochordae group and 15 patients in the PL resection group had this event. MR  $\geq 1^+$  at discharge (HR 2.71, 95% CI [1.10-6.67], p=0.030) was the only predictor of MR recurrence  $\geq 2^+$  in the long-term. At the last followup, only one patient (1.3%) in the neochordae group and three patients (3.7%) in the PL resection group had MR 3+.

At last follow-up, 11 patients (14.1%) in the neochordae group and 21 patients (31%) in the PL resection group were affected by AF (p=0.032). The median LVEDD was 44 mm [IQR 42-47] in the neochordae group and 48 mm [IQR 43.7-50] in the PL resection group (p=0.001).

In the neochordae group, 41 patients (54.7%) were in NYHA Class I, 33 patients (44%) were NYHA Class II

and one patient (1.3%) was in NYHA Class III whereas in the PL resection group, 25 patients (35.7%) were

in NYHA Class I, 43 patients (61.4%) were NYHA Class II and two patients (2.9%) were in NYHA Class III

(p=0.05). The median EF was 60% [IQR 58-63] in neochordae group and 55% [IQR 55-60] in PL resection
 group (p <0.001).</li>

224

### 225 Discussion

- 226 The findings of this retrospective propensity score matching analysis showed that neochordae implantation
- and PL resection provide similar excellent results in terms of survival and durability of the repair in patients
- 228 with severe MR and dilated left ventricle.
- This kind of patients represent a specific subgroup in whom the continuous LV volume overload due to the uncorrected chronic MR results in a progressive overstretching of cardiomyocytes and consequent enlargement of the left ventricle. At this stage, MV repair becomes mandatory as well as the choice of the most appropriate reparative technique. The aim of surgery is both to interrupt the vicious cycle before irreversible myocardial damage occurs and to promote LV reverse remodeling.
- After MV repair, LV reverse remodeling happens in two distinct phases. In the first stage there is a decrease in LV end-diastolic volume with no change in LV end-systolic volume, leading to a decrease in LVEF. The second stage of reverse remodeling is characterized by an improvement in systolic function, due to the decrease in LV end-systolic volume and consequent improvement of LVEF [15].
- In the context of PL pathology, PL resection and neochordae implantation have been the most adoptedtechniques over the last four decades.
- Generally speaking, MV repair aims to restore physiological leaflet motion, create a sufficient surface of coaptation with adequate orifice area and stabilize the mitral annulus. Although resection techniques have provided durable and hemodynamically satisfactory results with excellent freedom from reoperation, when performed in dedicated centers, partial resection of the PL alters its geometry and its physiological motion. Moreover, when those techniques are associated to annular plication and sliding plasty, the crimping of the posterior annulus can lead to a detrimental effect on LV performance [6].
- 246 On the other hand, neochordae implantation follows the main principles of reparative MV surgery providing
- 247 largest orifice area and surface of coaptation and better preservation of the ventriculo-annular continuity.
- 248 Based on this hypothesis, neochordae implantation might be the most appropriate technique, especially in

patient with altered LV geometry. However, it remains unknown if the subsequent LV reverse remodelling after MR correction does influence the length of the implanted neochoardae potentially resulting in recurrent PL prolapse. Neochordal repair can be performed by either using "hand adjusted" PTFE neochordae or premeasured loops. It is noteworthy that in our series both these techniques have been used.

With respect to cardiac death and rate of MV reoperation, both groups showed excellent results although we cannot provide inferential comparison given the low number of events. Regarding MR recurrence, remarkably only one patient in the neochordae group and three patients in PL resection group had MR 3+ at the last followup. At 10-years, the CIF of MR recurrence  $\geq 2+$ , with death as competing risk, was similar between the two groups. The *Fine and Gray* confirmed that achieving an immediate optimal result is the best predictor of the durability of the repair.

The comparison on reoperation rate has been objected by several studies. *Pfanimueller et al.* recently reported their results in a large cohort of patients undergoing minimally invasive MV repair with neochordae implantation by using premeasured loops or resection techniques. At 10-years, they showed an excellent freedom from MV reoperation in both group (total 96.7%) without statistically significant difference between the two groups [16]. *Lange et al.* showed similar freedom from MV-related reoperation between patients undergoing standard "hand adjusted" chordal replacement or PL resection at 4-years. At last follow-up they observed that 94% of patients had no or mild MR without difference between the two groups [10].

Another finding of our research is that a significant reduction in LVEDD was observed in both groups. This occurrence did not impact the performance of the nechordae implantation repair, thus confirming that this technique can be adopted even in patients with dilated left ventricles.

269 Moreover, in our series neochordae group showed a better LVEF and a smaller LVEDD as compared to the 270 resection group at the latest follow-up. In a large meta-analysis, Mazine et al. also reported higher 271 postoperative LVEF in patients undergoing chordal replacement technique [17]. This conclusion is mainly 272 based on the results of the research by *Imasaka* and colleagues, who analysed the hemodynamic performance 273 of 72 patients who underwent neochoardae implantation or PL resection. One month after surgery, they 274 observed a better improvement of LVEF in the neochoardae group. The researchers theorized that preservation 275 of the ventriculo-annular continuity could be a possible explanation for their findings [18]. Conversely, van 276 Wijngaarden et al. investigated the LV function using LV global longitudinal strain in patients undergoing chordal replacement or PL resection. They reported similar LV performances both at post-operative evaluationand at two-years follow-up [19].

With respect to the evolution of the LVEDD, a recent sub-analysis of the CAMRA Trial showed no differences in term of reduction of the LVEDD and LV end-diastolic volume at 12-month follow-up. The authors concluded that the mitral valve repair techniques did not influence the post-operative LV reverse remodelling [20].

Our research differs from previous ones in two main aspects. First of all, we analysed exclusively patients with dilated left ventricle. Secondly, we observed these patients at longer follow-up. In our opinion, these two points could explain our different results. Probably, in patients with dilated left ventricle, the benefit due to the better preservation of the ventriculo-annular continuity are more evident.

287

# 288 Study limitations

First of all, this is a retrospective single center report and therefore subject to the inherent weaknesses of a 289 290 retrospective analysis. Secondly, to define the left ventricle dilatation, we could just use the LVEDD and not the LV end-diastolic volume which was not available in all patients. Thirdly, we used a common closing date 291 method to acquire follow-up data. This methodology may have generated differences in the follow-up period 292 293 between the two groups, which could have an impact on the results. Fourthly, in Kaplan-Meier analysis for 294 overall survival, freedom from cardiac death and freedom from MV reoperation, we were not able to provide an inferential comparison between the two groups given the low numbers of events. Finally, after the first 295 296 echocardiogram (within 30 days), only 75% of the patients had their exams performed at our Institutions, while 297 the remaining patients were followed by the referring cardiologist and therefore, we could just acquire the 298 echocardiogram reports.

299

## 300 Conclusion

301 In patients with dilated left ventricle and severe MR due to PL prolapse, both leaflet resection and neochordae

302 implantation provide excellent long-term results in terms of survival and durability of the repair.

303 Neochoardae implantation might result in a higher reduction of LVEDD and a better LVEF as compared to

304 leaflet resection. In our series, the reduction of LVEDD after chordal implantation does not lead to higher

305 recurrence of PL prolapse and mitral regurgitation.

306

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- 309

### 310 Data Availability Statement

311 The datasets analysed in the current study are available from the corresponding author on reasonable request

MANUS

- 312
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- 315
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- 317 None.
- 318
- **319 Author contribution statement**

Benedetto Del Forno: conceptualization, data curation, methodology, writing – original draft; Kevin Tavana:
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formal analysis; Alessandro Nonis: formal analysis; Fabrizio Monaco: visualization; Ottavio Alfieri:
supervision; Alessandro Castiglioni: supervision; Francesco Maisano: supervision; Michele De Bonis:
project administration, supervision, validation, review & editing.

327

# 328 Figure legends

329 Central Image. Long-term performance of neochordal implantation and posterior leaflet resection in the

330 matched population.

- **Figure 1.** Love plot displaying covariate balance pre and post matching. Vertical dotted lines at ±0.25 indicate
- the acceptability bounds. After matching all variables stand within the acceptability threshold [13].
- **Figure 2.** Ten-years Kaplan-Meyer freedom from cardiac death for both groups.
- **Figure 3.** Ten-years Kaplan-Meyer freedom from mitral valve reoperation for both groups.
- **Figure 4.** Cumulative incidence function of mitral regurgitation recurrence  $\geq 2+$  with death as competing risk
- in both groups.

## **337** Table 1: Pre-operative features (unmatched and matched groups)

- 338 Given its layout, Table 1 is provided as additional .docx file.
- 339

## **340** Table 2: Operative and postoperative data (matched groups)

	S			
Variables	Neochordae Group	PL Resection Group	p-value	
	85 patients	85 patients		
Ring size, mm (median, IQR)	35 [33-36]	35 [33-35]	0.954	
Right minithoracotomy (n,%)	21 (24.7%)	15 (17.6%)	0.348	
CPB time, min (median, IQR)	82 [68-100]	74 [66-90]	0.013	
Aortic cross-clamp time, min (median, IQR)	62 [52-78]	55 [48-68]	0.019	
Coronary artery bypass grafting (n,%)	7 (8.2)	9 (10.6)	0.433	
Tricuspid valve repair (n,%)	21 (24.7)	16 (19)	0.479	
Atrial fibrillation ablation (n,%)	10 (11.7)	6 (7)	0.37	
IABP (n,%)	4 (4.7)	3 (3.5)	1	
Post-operative atrial fibrillation (n,%)	16 (19.0)	19 (22.9)	0.674	
MR at discharge			0.623	
• grade 0 (n,%)	42 (49.4)	43 (50.6)		
• grade 1 (n,%)	41 (48.2)	37 (43.5)		
• grade 2 (n,%)	2 (2.3)	5 (6.2)		
Hospital stay (median, IQR)	5 [4-6]	5 [4-7]	0.528	

- 341
  342 IQR: interquartile range; CBP: cardiopulmonary bypass; IABP: intra-aortic balloon pump; MR: mitral
  343 regurgitation.
- 344

# 345 Table 3. Predictors of mitral regurgitation recurrence ≥2+ (Fine–Gray model)

346

	Univariable			Multivariable		
	HR	p-value	95% CI	HR	p-value	95% CI
Matched groups comparison	0.91	0.834	0.39-2.13	(	- X -	
Age	1.02	0.068	1.00-1.03	1.01	0.223	0.99-1.03
LVEF	0.97	0.215	0.93-1.02	5		
Female sex	0.63	0.254	0.28-1.4			
IABP	1.64	0.493	0.40-6.79			
Planned associated procedures	1.38	0.441	0.61-3.15			
sPAP	1.0	0.963	0.97-1.03			
AF	1.69	0.297	0.63-4.53			
MR at discharge ≥1	2.15	0.070	0.94-4.93	2.71	0.030	1.10-6.67
NYHA class ≥2	3.76	0.031	1.13-12.56	3.47	0.064	0.99-1.03

- 347 HR: hazard ratio; LVEF: left ventricular ejection fraction; IABP: intra-aortic balloon pump; sPAP: systolic
  348 pulmonary artery pressure; AF: atrial fibrillation; MR: mitral regurgitation. NYHA: New York Heart
  349 Association.
- 350
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