Original Article

Early Outcomes of Endoscopic Papillary Muscle Relocation for Secondary Mitral Regurgitation Type IIIb in Patients With Severe Left Ventricular Dysfunction

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Abstract

Objective: Subannular mitral valve (MV) repair techniques have been developed to address increased rates of recurrent mitral regurgitation (MR) in patients with secondary MR (SMR) type IIIb. Endoscopic papillary muscle relocation (PMR) is feasible via minithoracotomy. Nevertheless, the periprocedural outcome of patients with severe left ventricular (LV) dysfunction remains unknown. **Methods:** A total of 98 consecutive patients with SMR type IIIb underwent PMR at our institution. Due to concomitant coronary artery bypass grafting, 62 patients underwent sternotomy and were excluded from the current analysis, whereas 36 patients were treated by a minimally invasive technique using 3-dimensional endoscopy. Of these, 18 patients had severely depressed LV ejection fraction (LVEF) ≤35% (study group) and were compared to the remaining 18 patients with LVEF >35% (control group). Periprocedural outcome was retrospectively analyzed. **Results:** Although LVEF was significantly worse in the study group (30% ± 4% vs 43% ± 6%, $P < 0.001$), the severity of SMR and the degree of MV leaflet tethering were similar. The prevalence of concomitant procedures and the duration of surgery, cardiopulmonary bypass, and aortic cross-clamp were comparable. Periprocedural low cardiac output syndrome was favorably low in both groups (16.7% vs 5.6%, $P = 0.29$). Postoperative ventilation time (5.7 h [4.2 to 8.7 h] vs 6.0 h [4.6 to 9.8 h], $P = 0.43$) and duration of intensive care unit stay (2 days [1 to 3 days] vs 2 days [1 to 3 days], $P = 0.22$) were similar. There was no 30-day mortality in either group. **Conclusions:** Standardized endoscopic PMR resulted in favorable periprocedural outcomes in patients with severe LV dysfunction, suggesting that minimally invasive surgery can safely be extended to this patient population.

Keywords

minimally invasive surgery, endoscopic mitral valve repair, secondary mitral regurgitation, mitral leaflet tethering, subvalvular mitral valve repair, papillary muscle relocation

Central Message

Standardized endoscopic papillary muscle relocation (PMR), specifically addressing MV leaflet tethering, resulted in favorable periprocedural outcomes despite severe LV dysfunction. Minimally invasive PMR for patients with secondary MR type IIIb should be considered during routine inter-disciplinary heart team discussion.

Introduction

Secondary mitral regurgitation (SMR) with restricted leaflet motion during systole (type IIIb)[1] is a common sequela of chronic heart failure (HF) resulting from progressive left ventricular (LV) distortion caused by ischemic or dilated cardiomyopathy.[2] Instead of being a mere bystander of LV remodeling, SMR type IIIb is associated with worsening of HF symptoms and excessive mortality itself.[3,4] In symptomatic patients with SMR despite optimal medical therapy (OMT), percutaneous transcatheter edge-to-edge repair (TEER) represents a promising option for selected patients with suitable mitral valve (MV)

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anatomy.[5] Nevertheless, contradictory data regarding the prognostic benefit of TEER have been published.[5,6] Most notably, patients with advanced LV remodeling, such as the Cardiovascular Outcomes Assessment of the MitraClip Percutaneous Therapy for Heart Failure Patients With Functional Mitral Regurgitation (COAPT) trial exclusion criteria of LV ejection fraction (LVEF) <20% and LV end-diastolic diameter (LVEDD) >70 mm, might not benefit from TEER.[6–8]

Isolated mitral annuloplasty results in an increased prevalence of recurrent mitral regurgitation (MR)[9] and did not demonstrate any prognostic benefit in comparison to OMT or MV replacement (MVR).[10] Therefore, additional subannular repair strategies,[11] specifically addressing LV geometry and papillary muscle orientation, have been developed to improve long-term durability after MV repair.[12] Standardized papillary muscle relocation (PMR), in addition to ring annuloplasty,[13] is feasible in a minimally invasive MV surgery setting.[14] Nevertheless, the periprocedural outcomes of patients with severely depressed LVEF remains unknown.

Methods

Patients

The local ethical committee approved the retrospective study, which complies with the Declaration of Helsinki. We herein analyzed the periprocedural outcome of 36 consecutive patients with SMR type IIIb who underwent minimally invasive standardized PMR at our institution between 2016 and 2021. According to preoperative transthoracic echocardiography, patients with severely reduced LVEF ≤35% (study group) were compared to patients with LVEF >35% (control group). After the evaluation and quantification of the severity of LV dysfunction and MR mechanism, all available therapeutic options, including TEER, transcatheter MV implantation (TMVI), surgical MV repair, and MVR, as well as LV assist device (LVAD) implantation and heart transplantation, were discussed in our institutional heart team.

Inclusion and Exclusion Criteria

Between 2016 and 2021, 98 consecutive patients with HF (LVEF <50%, LVEDD >55 mm) with symptomatic (New York Heart Association class ≥II) and severe (effective regurgitant orifice area [EROA] ≥0.2 cm^2) type IIIb SMR (i.e., tenting height >10 mm) despite OMT, who were suitable for MV surgery, underwent standardized PMR in addition to ring annuloplasty. Due to the need for simultaneous coronary artery bypass grafting, 62 patients underwent sternotomy and were excluded from the current analysis. The remaining 36 patients were treated by a minimally invasive technique using 3-dimensional (3D) endoscopy. Patients with mixed MV disease, primary MR, or those requiring emergency surgery were excluded.

Surgical Setup and Standardized PMR Technique

Minimally invasive MV surgery was performed in a standard operating room via right anterolateral minithoracotomy using a soft-tissue retractor and 3D endoscopic guidance. A limited skin incision (<4 cm) periareolar (in men) or submammary (in women) was used to enter the fourth intercostal space. Peripheral cardiopulmonary bypass (CPB) was established via direct femoral cannulation. Preoperative peripheral Doppler ultrasound determined adequacy of femoral vessels. Transthoracic Chitwood clamp was used for aortic cross-clamp, and antegrade cardioplegia (i.e., del Nido) was administered into the aortic root. After exposure of the MV using a left atrial access and intraoperative confirmation of SMR type IIIb, standardized PMR was performed in addition to conventional ring annuloplasty using an ETlogix ring (Edwards Lifesciences, Irvine, CA, USA).[13] Therefore, 2 pledgeted 3-0 polytetrafluorethylene sutures were placed through the trunks of both papillary muscles and subsequently passed through the posterior mitral annulus and the adjacent annuloplasty ring. After filling the LV with cold saline, stepwise traction was applied on both sutures until leaflet tethering disappeared. To create a stable distance between the papillary muscles and the mitral annulus, both sutures were tightly knotted on the annuloplasty ring, while keeping the constant traction (Fig. 1).
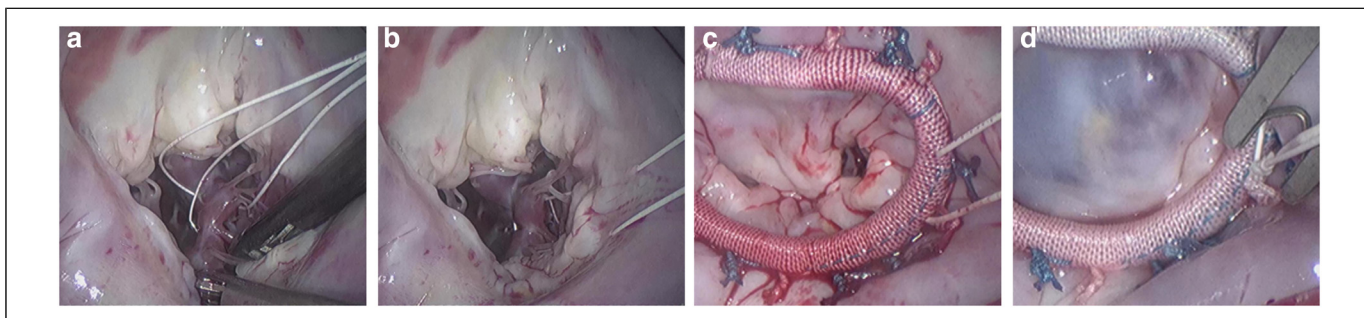
Fig. 1. Standardized endoscopic papillary muscle relocation. Two pledgeted 3-0 polytetrafluorethylene sutures were (a) placed through the trunks of both papillary muscles and subsequently passed through (b) the posterior mitral annulus and (c) the adjacent annuloplasty ring. After filling the left ventricle with cold saline, stepwise traction was applied on both sutures until leaflet tethering disappeared. (d) To create a stable distance between the papillary muscles and the mitral annulus, both sutures were tightly knotted on the annuloplasty ring while keeping the traction.

Standardized PMR was implemented within our institutional clinical routine, and a group of 5 experienced MV surgeons performed the operations accordingly. Concomitant procedures such as atrial fibrillation (AF) ablation, left atrial appendage (LAA) closure, and tricuspid valve repair were performed according to our institutional standard without major changes during the study period.

Statistical Analysis

Baseline and follow-up data were retrospectively analyzed. Normally distributed continuous variables are presented as mean values and standard deviations. Otherwise, medians and interquartile ranges are used for continuous variables and absolute numbers and percentages for categorical variables. Unpaired t tests were used for between-group comparison of normally distributed numeric variables. Chi-squared tests were used for between-group comparison of categorial variables if the minimum expected cell size was at least 5. Otherwise, Fisher's exact tests and Mann-Whitney U tests were used. Results were considered statistically significant if the P value was <0.05. IBM SPSS Statistics for Windows, Version 26.0 (IBM Corp., Armonk, NY, USA) was used for all statistical analyses. The data underlying this article will be shared on reasonable request to the corresponding author.

Results

Study Sample

A total of 98 consecutive patients with symptomatic type IIIb SMR (Fig. 2) despite OMT underwent surgical MV repair including standardized PMR at our institution between 2016 and 2021. Out of 36 patients, who we treated minimally invasively via right-sided minithoracotomy under 3D endoscopic guidance, 18 patients showed a severely reduced LVEF ≤35% (study group) and were compared to 18 patients with an LVEF >35% (control group).

Median age at the time of surgery was 63 (53 to 72) years in the whole cohort, and 61% of patients (22 of 36) were male (Table 1). Prevalence of ischemic cardiomyopathy was similar in both study and control groups (33.3% vs 44.4%, $P = 0.31$). Nevertheless, preoperative coronary angiogram confirmed no further need for coronary revascularization in all patients. Despite more severe impairment of LVEF (30% ± 4% vs 43% ± 6%, $P < 0.001$) and tricuspid annular systolic excursion (TAPSE; 18 ± 3 mm vs 23 ± 5 mm, $P = 0.001$), the severity of SMR indicated by EROA (0.28 ± 0.1 cm^2 vs 0.33 ± 0.1 cm^2, $P = 0.084$) and the degree of MV leaflet tethering indicated by tenting height (12 ± 3 mm vs 12 ± 1 mm, $P = 0.60$) and tenting area (309 ± 61 mm^2 vs 301 ± 85 mm^2, $P = 0.84$) were similar in the study and control groups. In addition, systolic pulmonary artery pressure (sPAP) and the prevalence of concomitant tricuspid regurgitation were comparable. Furthermore, no significant differences were present in the study versus control groups regarding patient demographics or prevalence of other outcome-relevant risk factors. Most patients were New York Heart Association functional class ≥III in both groups (89% vs 67%, $P = 0.28$) and had similar serum levels of creatinine and natriuretic peptide at baseline (Table 1).

Table 1. Preoperative Patient Characteristics and Echocardiographic Parameters.

Variable	Study group ($n = 18$)	Control group ($n = 18$)	P value
Age, y	57.8 (50.3–70.5)	67.5 (58.3–73.8)	0.29
Male	11 (61.1)	11 (61.1)	1.00
BMI, kg/m^2	26.0 (23.5–28.1)	26.9 ± 3.3	0.26
Diabetes mellitus	4 (22.2)	4 (22.2)	1.00
COPD > GOLD class I	3 (16.7)	5 (27.8)	0.69
Atrial fibrillation	7 (38.9)	4 (22.2)	0.28
Coronary artery disease	6 (33.3)	8 (44.4)	0.31
Serum creatinine level, mg/dL	1.2 (0.9–1.4)	1.3 (1.0–1.6)	0.33
NYHA class ≥III	16 (88.9)	12 (66.7)	0.28
NT-proBNP, pg/dL	1,916 (1,204–5,132)	1,351 (1,023–2,935)	0.53
LVEF, %	29.8 ± 4.4	42.8 ± 5.8	<0.001
LVEDD, mm	65.4 ± 10.6	57.0 ± 8.7	0.10
EROA, cm^2	0.28 ± 0.1	0.33 ± 0.1	0.084
Tenting area, mm^2	309 ± 61	301 ± 85	0.84
Tenting height, mm	12.3 ± 2.7	11.7 ± 1.3	0.60
LA volume, mL	91 (74–121)	93 (75–118)	0.93
TAPSE, mm	17.8 ± 2.5	22.8 ± 5.0	0.001
sPAP, mm Hg	52.5 ± 15.3	55.1 ± 13.1	0.66
Tricuspid regurgitation ≥2	4 (22.2)	3 (16.7)	0.67

Abbreviations: BMI, body mass index; COPD, chronic obstructive pulmonary disease; EROA, effective regurgitant orifice area; GOLD, Global Initiative for Chronic Obstructive Lung Disease; LA, left atrial; LVEDD, left ventricular end-diastolic diameter; LVEF, left ventricular ejection fraction; NT-proBNP, N-terminal proB-type natriuretic peptide; NYHA, New York Heart Association; PCI, percutaneous coronary intervention; sPAP, systolic pulmonary artery pressure; TAPSE, tricuspid annular plane systolic excursion.
Data presented as median (interquartile range), mean ± SD, or n (%).

Periprocedural Outcomes

Conversion to sternotomy was required due to excessive pleural adhesions in 1 patient in each group. The prevalence of concomitant tricuspid valve repair, AF ablation, and LAA closure was similar in the study and control groups. Rigid complete annuloplasty rings, with similar median of manufacturer given ring sizes (28 mm [28 to 30 mm]), were used in all patients (IMR ETlogix annuloplasty ring). The duration of surgery, CPB, and cross-clamp were similar (Table 2). Of note, there was no need for perioperative extracorporeal membrane oxygenation (ECMO) support in either group. However, intra-aortic balloon pump was inserted in 1 patient in each group due to high periprocedural pharmacological inotropic support. Rethoracotomy for bleeding and rates of postoperative pacemaker implantation were similar between groups. Furthermore, there was no difference in postoperative mechanical ventilation time (5.7 vs 6.0 h, $P = 0.43$; Table 2). The incidence of low cardiac output syndrome, as well as length of intensive care unit stay, was similar in both groups. In-hospital and 30-day survival was 100% in both groups.

Outcome Parameters at Discharge

One patient in the study group with severe preoperative LV dysfunction (LVEF <20%, LVEDD >75 mm) and excessive MV leaflet tethering required reoperation and chordal-sparing MVR due to persistent MR during the same hospital stay. In all remaining patients, no residual MR greater than mild was found at discharge. Residual MV tethering (tenting height and tenting area) at discharge was significantly reduced in comparison to baseline values in both groups (Table 3). No functional mitral stenosis or reduced MV orifice area were identified in any patient postoperatively. Postoperative right ventricular function, measured as TAPSE, was comparable in both groups (13.3 ± 3.9 mm vs 15.1 ± 3.1 mm, $P = 0.14$), although systolic LV function remained significantly reduced in the study group versus the control group ($P = 0.001$; Table 3).

Discussion

SMR type IIIb, which is prevalent in about one-third of patients with advanced HF,[15] is associated with a dismal outcome and remains a promising therapeutic target.[16] Despite contradictory data regarding the prognostic effect of TEER in patients with HF who have concomitant SMR,[5,6] TEER was upgraded in the current guidelines for the management of valvular heart disease.[17] Accordingly, in symptomatic patients despite OMT, who have no indication for coronary revascularization and exhibit appropriate anatomical features (LVEF between 20% and 50%, LV end-systolic diameter <70 mm, sPAP <70 mm Hg), TEER is reasonable (Class IIa, Level B). In contrast, MV surgery has only a Class IIb, Level C indication in the clinical setting described above.[17] Due to an excellent periprocedural safety profile and less invasiveness as compared to conventional open heart surgery, TEER emerges to be the first-line treatment option for SMR in patients with HF.

Isolated mitral annuloplasty is associated with an unacceptably high rate of recurrent SMR up to 60%[9] and does not show any beneficial prognostic effect in comparison to OMT.[10] To improve repair durability and to avoid the drawbacks of MVR, subannular repair

Table 2. Periprocedural Outcomes.

Variable	Study group ($n = 18$)	Control group ($n = 18$)	P value
Sternotomy	1 (5.6)	1 (5.6)	1.00
Additional TV repair	1 (5.6)	1 (5.6)	1.00
LAA occlusion	8 (44.4)	8 (44.4)	1.00
Atrial fibrillation ablation	6 (33.3)	4 (22.2)	0.46
Duration of surgery, min	219 ± 33	239 ± 51	0.18
Cardiopulmonary bypass time, min	158 ± 24	171 ± 38	0.41
Cross-clamp time, min	86 ± 19	93 ± 24	0.42
ECMO support	0	0	—
IABP support	1 (5.6)	1 (5.6)	1.00
Rethoracotomy for bleeding	2 (11.1)	0	0.49
Reoperation and MVR	1 (5.6)	0	0.31
Postoperative low-output syndrome	3 (16.7)	1 (5.6)	0.29
Postoperative temporary hemodialysis	0	0	—
Permanent pacemaker implantation	1 (5.6)	0	0.31
Postoperative ventilation time, h	5.7 (4.2–8.7)	6.0 (4.6–9.8)	0.43
ICU stay, d	2.0 (1.0–3.0)	2.0 (1.0–2.8)	0.21
Hospital stay, d	10.5 (7.0–14.0)	7.5 (7.0–10.0)	0.085
In-hospital mortality	0	0	—
30-day mortality	0	0	—

Abbreviations: CABG, coronary artery bypass grafting; ECMO, extracorporeal membrane oxygenation; IABP, intra-aortic balloon pump; ICU, intensive care unit; LAA, left atrial appendage; MVR, mitral valve replacement; TV, tricuspid valve.
Data presented as median (interquartile range), mean ± SD, or n (%).
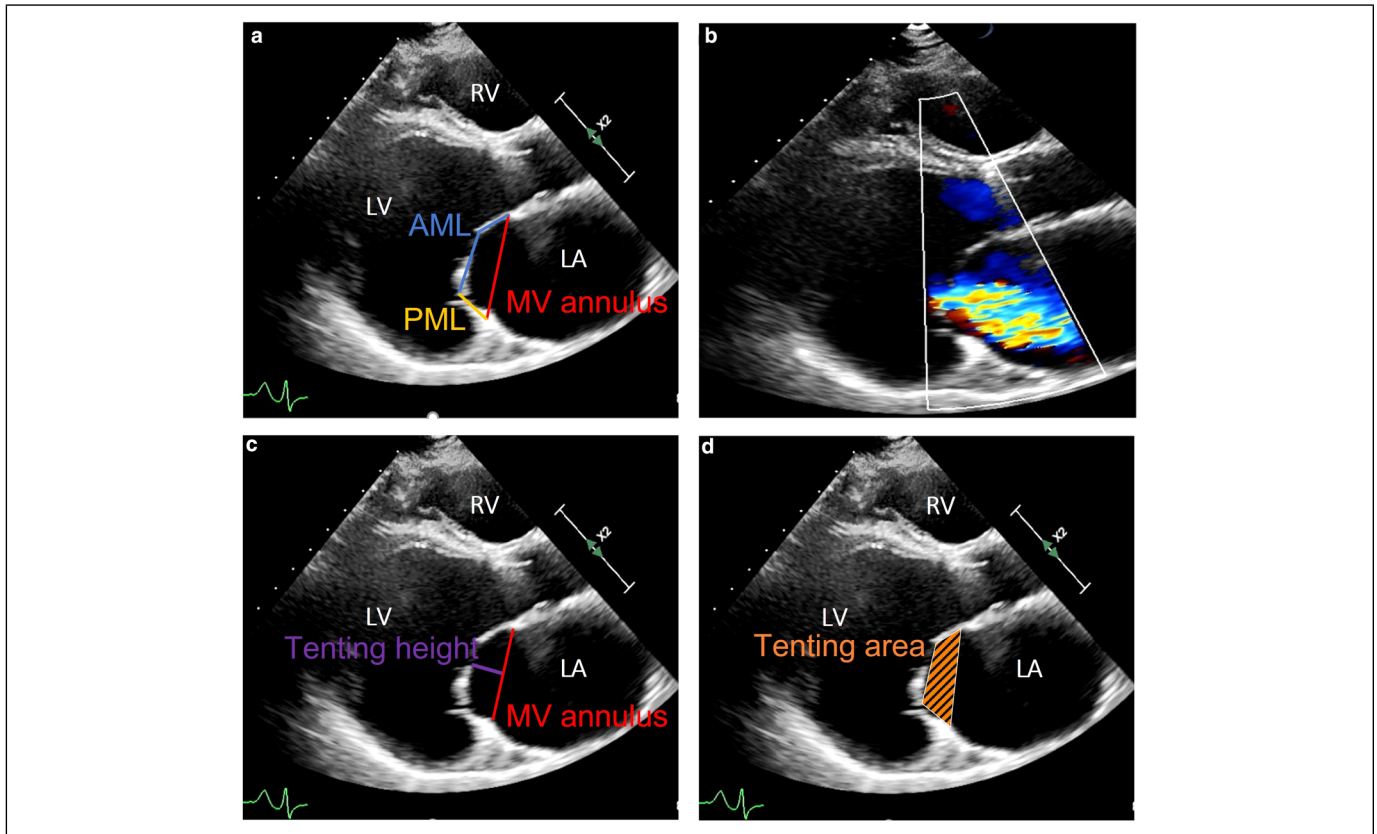
Fig. 2. Advanced LV remodeling resulting in severe secondary mitral regurgitation type IIIb. (a) Preoperative echocardiography parasternal long axis view (AML, blue; PML, yellow; MV annular plane, red). (b) Color Doppler echocardiography reveals severe secondary mitral regurgitation type IIIb (effective regurgitant orifice area = 0.38 cm^2) in parasternal long-axis view. Severe tethering of both mitral leaflets with (c) tenting height in purple (14 mm) and (d) tenting area in orange (3.2 cm^2) in parasternal long axis view. AML, anterior mitral leaflet; LA, left atrium; LV, left ventricle; MV, mitral valve; PML, posterior mitral leaflet; RV, right ventricle.

strategies have been established. In particular, standardized PMR is feasible in a minimally invasive MV surgery setting, although the periprocedural outcome of patients with severely depressed LVEF remains unknown.

Study Population

We aimed to compare the periprocedural outcome of minimally invasive standardized PMR in patients with HF who have LVEF ≤35% and LVEF >35% in the treatment of symptomatic SMR type IIIb. After echocardiographic and clinical assessment, all symptomatic patients with SMR type IIIb were discussed in our institutional interdisciplinary heart team, including the evaluation of TEER, TMVI, surgical MV repair, and MVR strategies, as well as LVAD implantation and heart transplantation. Despite the obvious differences in the severity of LV dysfunction, baseline patient characteristics including comorbidities, as well as mitral leaflet tethering parameters, were similar in both groups.

In-Hospital Outcomes

Except for 2 patients who underwent conversion to sternotomy due to excessive pleural adhesions, all remaining patients were

Table 3. Discharge Outcomes.

Variable	Study group	Control group	P value
Serum creatinine level, mg/dL	0.9 (0.9–1.2)	1.1 (0.9–1.6)	0.33
LVEF, %	26.2 ± 10.7	37.7 ± 7.7	0.001
LVEDD, mm	64.1 ± 13.0	59.3 ± 6.7	0.23
TAPSE, mm	13.3 ± 3.9	15.1 ± 3.1	0.14
LA volume, mL	82 (60–93)	85 (69–99)	0.89
sPAP, mm Hg	44.7 ± 8.7	48.4 ± 9.7	0.32
Mean transmitral pressure gradient, mm Hg	4.0 ± 2.3	4.5 ± 1.6	0.26
Tenting area, mm^2	147 ± 47	133 ± 53	0.59
Tenting height, mm	7.5 ± 1.5	7.0 ± 1.5	0.66

Abbreviations: LA, left atrial; LVEDD, left ventricular end-diastolic diameter; LVEF, left ventricular ejection fraction; sPAP, systolic pulmonary artery pressure; TAPSE, tricuspid annular plane systolic excursion.
Data presented as median (interquartile range), mean ± SD, or n (%).

successfully treated minimally invasively via right-sided mini-thoracotomy under 3D endoscopic guidance. Concomitant procedures, procedural duration times, and CPB and cross-clamp times were similar in both groups. Our data demonstrate that

in contrast to other described subannular MV repair strategies (e.g., papillary muscle approximation or the "ring plus string" technique),[18,19] standardized PMR can be reproducibly performed in a minimally invasive MV surgery setting, independent of the severity of LV dysfunction. Periprocedural complication rates were comparably low in both groups. Of note, despite the severe degree of LV dysfunction, there was no weaning failure from CPB or need for perioperative ECMO support. This finding underlines the importance of a thorough heart team discussion, to select appropriate surgical candidates. Obviously, a reasonable comparison with previously published TEER cohorts is quite limited due to methodological issues because patients enrolled in the COAPT and Multicentre Study of Percutaneous Mitral Valve Repair MitraClip Device in Patients With Severe Secondary Mitral Regurgitation (MITRA-FR) trials were either inoperable or at very high surgical risk. Nonetheless, procedural safety and in-hospital mortality in our series seem to be lower as compared to previously published surgically treated SMR cohorts.[9,20,21]

Apart from cosmetic advantages, patients with HF who have severe LV dysfunction might particularly benefit from rapid extubation protocols, decreased transfusion rates, and the absence of sternal wound infections after endoscopic MV repair.[22,23] In addition, all further surgical interventions that might be required due to advancing HF (i.e., LVAD implantation, heart transplantation) are technically less challenging after previous minimally invasive surgery as compared to conventional sternotomy. Furthermore, due to the implementation of enhanced recovery after cardiac surgery protocols,[24] as well as the adaption of advanced percutaneous cannulation techniques,[25] perioperative complication rates after minimally invasive MV surgery will potentially further decrease.

Although long-term durability of endoscopic PMR is yet to be established, very favorable periprocedural results might suggest that minimally invasive MV surgery can safely be extended to patients with HF who have severe LV dysfunction.

Study Limitations

This is a limited-size single-center study with a nonrandomized study design. Furthermore, only perioperative outcomes were addressed. We included no additional control group of patients with SMR after TEER or OMT alone, which would be required for a more extensive comparison. Therefore, the comparability of our results with the alternative SMR treatment modalities is limited.

Conclusions

Standardized endoscopic PMR results in favorable periprocedural outcomes, even in patients with severe LV dysfunction. Compared to patients with less severe LV dysfunction, the perioperative results were similar, suggesting that minimally invasive surgery can be safely extended to this patient population. Further studies with an increased follow-up period in a larger patient population are needed to evaluate the future role of

minimally invasive standardized PMR as a treatment option for patients with HR who have SMR type IIIb.

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