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## CLINICAL RESEARCH

# Long-term results of surgical treatment of secondary severe mitral regurgitation in patients with end-stage heart failure: Advantage of prosthesis insertion



*Résultats de la chirurgie de l'insuffisance mitrale secondaire chez des patients atteints d'insuffisance cardiaque terminale : intérêt du remplacement valvulaire*

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Received 16 March 2018; received in revised form 15 June 2018; accepted 5 September 2018  
Available online 29 December 2018

### KEYWORDS

Secondary mitral regurgitation;  
Mitral valve replacement;  
Mitral valve repair;  
Congestive heart failure;  
Surgery

### Summary

**Background.** — Surgical treatment of secondary mitral regurgitation (SMR) is controversial.  
**Aim.** — To analyse outcome after undersizing annuloplasty (UA) and mitral valve replacement (MVR).  
**Methods.** — Consecutive patients operated on for severe SMR, with left ventricular ejection fraction (LVEF) < 40% and refractory CHF, were included. Endpoints were in-hospital mortality, mid-term cardiovascular (CV) mortality, evolution of LV variables and recurrence of mitral regurgitation (MR).

**Abbreviations:** ACC, American College of Cardiology; AHA, American Heart Association; CABG, Coronary Artery Bypass Grafting; CHF, Congestive Heart Failure; CI, Confidence Interval; ERO, Effective Regurgitant Orifice; HR, Hazard Ratio; LVEF, Left Ventricular Ejection Fraction; LV, Left Ventricular; MR, Mitral Regurgitation; MVR, Mitral Valve Replacement; SMR, Secondary Mitral Regurgitation; sPAP, Systolic Pulmonary Artery Pressure; TTE, Transthoracic Echocardiography; UA, Undersizing Annuloplasty.

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<https://doi.org/10.1016/j.acvd.2018.09.006>

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**Results.** – 59 patients were included (mean age  $65 \pm 10$  years, preoperative LVEF  $36 \pm 6\%$ ; effective regurgitant orifice [ERO]  $41 \pm 17 \text{ mm}^2$ ), 41 with ischaemic disease: 12 underwent UA and 47 underwent MVR; only eight had concomitant coronary revascularization. In-hospital mortality was 3.3% (8.3% in UA group; 2.1% in MVR group). Eight-year CV mortality was  $39 \pm 13\%$  ( $40 \pm 18\%$  in UA group;  $27 \pm 10\%$  in MVR group). Older age (hazard ratio 1.14, 95% confidence interval 1.07 to 1.22;  $P < 0.001$ ) and LV end-systolic diameter (hazard ratio 1.18, 95% confidence interval 1.09 to 1.27;  $P < 0.001$ ) independently predicted CV mortality. LVEF did not change between the preoperative and follow-up transthoracic echocardiograms in the MVR group ( $36 \pm 6\%$  vs.  $35 \pm 10\%$ ;  $P = 0.6$ ) or the UA group ( $36 \pm 5\%$  vs.  $31 \pm 12\%$ ;  $P = 0.09$ ). Conversely, LV end-diastolic diameter decreased significantly in the MVR group ( $64 \pm 8 \text{ mm}$  to  $59 \pm 9 \text{ mm}$ ;  $P = 0.002$ ), but not in the UA group ( $61 \pm 7 \text{ mm}$  to  $64 \pm 10 \text{ mm}$ ;  $P = 0.2$ ). Recurrence of significant MR occurred in 81% of patients in the UA group (mean postoperative ERO  $19 \pm 6 \text{ mm}^2$ ) versus none in the MVR group.

**Conclusions.** – Surgical treatment of SMR can be performed with acceptable operative risk and mid-term survival in severe heart failure, even if there is no indication for revascularization. MVR is associated with significant reverse remodelling, and UA with prohibitive risk of MR recurrence.

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## MOTS CLÉS

Insuffisance mitrale secondaire ;  
Remplacement valvulaire mitral ;  
Réparation valvulaire mitrale ;  
Insuffisance cardiaque ;  
Chirurgie

## Résumé

**Contexte.** – Les indications et modalités de correction chirurgicale de l'insuffisance mitrale secondaire (IMS) sont controversées.

**Objectif.** – Déterminer l'impact pronostique de l'annuloplastie réductrice (AR) et du remplacement valvulaire mitral (RVM).

**Méthodes.** – Les patients opérés pour IMS avec FEVG  $< 40\%$  et insuffisance cardiaque réfractaire ont été inclus. La mortalité hospitalière, la mortalité cardiovasculaire (CV), l'évolution des paramètres VG et la récurrence d'IMS ont été analysés après RVM et AR.

**Résultats.** – 59 patients ont été inclus : 12 AR et 47 RVM. Âge moyen =  $65 \pm 10$  ans, FEVG préopératoire =  $36 \pm 6\%$  et SOR =  $41 \pm 17 \text{ mm}^2$ . Mortalité hospitalière = 3,3 % (8,3 % dans groupe AR ; 2,1 % dans groupe RVM). Mortalité cardiovasculaire à 8 ans =  $40 \pm 18\%$  après AR et  $27 \pm 10\%$  après RVM. L'âge (HR 1,14, IC95 % 1,07 à 1,22 ;  $P < 0,001$ ) et le DTSVG (HR 1,18, IC95 % 1,09 à 1,27 ;  $P < 0,001$ ) prédisaient de manière indépendante la mortalité CV. La FEVG restait stable entre la période préopératoire et le dernier suivi dans le groupe RVM ( $36 \pm 6\%$  vs  $35 \pm 10\%$  ;  $P = 0,6$ ) alors qu'elle tendait à diminuer dans le groupe AR ( $36 \pm 5\%$  vs  $31 \pm 12\%$  ;  $P = 0,09$ ). Le DTSVG diminuait significativement dans le groupe RVM ( $64 \pm 8 \text{ mm}$  à  $59 \pm 9 \text{ mm}$  ;  $P = 0,002$ ) mais restait stable dans le groupe AR ( $61 \pm 7 \text{ mm}$  à  $64 \pm 10 \text{ mm}$  ;  $P = 0,2$ ). Une récurrence d'IMS survenait chez 81 % des patients du groupe AR (SOR moyen =  $19 \pm 6 \text{ mm}^2$ ). Absence de récurrence d'IMS dans groupe RVM.

**Conclusions.** – Le traitement chirurgical de l'IMS peut être réalisé avec un risque opératoire acceptable et une survie satisfaisante même en cas de dysfonction systolique VG profonde et d'absence d'indication de revascularisation myocardique. Le RVM est associé à un remodelage VG inverse significatif alors que l'AR est associée à un risque réhibitoire de récurrence de la fuite.

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## Background

Secondary mitral regurgitation (SMR) is the consequence of left ventricular (LV) remodelling, systolic dysfunction and papillary muscle dyssynchrony despite normal leaflets and chordae [1,2]. SMR worsens the prognosis of patients with ischaemic or non-ischaemic heart failure [3], and is a strong risk factor for mortality and morbidity, independent of LV ejection fraction (LVEF) [4,5]. Therefore, in patients with severe and symptomatic SMR despite optimal medical

treatment, surgical correction is tempting to break the vicious circle between the leak and LV dysfunction. However, its modalities and indications are under debate, and percutaneous repair in this setting is not validated [6]. Undersizing annuloplasty (UA) was considered the gold standard for ischaemic SMR [7], but reports of high recurrence rates [8,9] raised doubts, and led to consideration of other modes of correction [6,10]. Besides innovative techniques not yet clinically validated [11–14], mitral valve replacement (MVR) with subvalvular structure preservation has recently

been considered as a possible alternative [8,15–17], particularly in case of extreme mitral deformation [18]. Indications for surgery are even more controversial in view of the increased surgical risk associated with LV dysfunction and the lack of outcome benefit reported so far, particularly in patients without option for revascularization. In such patients, with no indication for coronary artery bypass grafting (CABG) or with non-ischaemic SMR, European guidelines do not recommend surgery when LVEF is < 30%, whereas it is barely accepted as a class IIb indication in the most recent guidelines from the American College of Cardiology/American Heart Association (ACC/AHA) [6,10]. However, reports of low operative mortality despite a very severe clinical and echocardiographic presentation are encouraging, particularly in the context of organ shortage or in patients who are not candidates for a heart transplant [9,18–20].

Accordingly, we analysed the clinical and echocardiographic outcomes of patients operated on for very severe SMR, with severely depressed LV systolic function, congestive heart failure (CHF) symptoms refractory to optimal medical treatment and no indication for CABG (in most) or with non-ischaemic cardiomyopathy. We hypothesized that these patients incur acceptable operative mortality and mid-term postoperative prognosis, with a more favourable echocardiographic outcome after MVR than after UA.

## Methods

### Study design

The present study is a single-centre retrospective analysis of prospectively-collected data. All consecutive patients operated on between 1997 and 2015 for severe symptomatic SMR caused by ischaemic or non-ischaemic dilated cardiomyopathy were eligible for the study. Inclusion criteria were severe SMR [5], LVEF < 40% and severe CHF symptoms despite optimal medical treatment and resynchronization therapy when indicated. Exclusion criteria were presence of organic mitral disease, significant concomitant aortic valve disease or congenital disease, previous valve surgery, LVEF  $\geq$  40% and CABG as the main indication for surgery. Concomitant CABG was not an exclusion criterion when symptomatic SMR was the primary indication for surgery. Patients who denied authorization for the anonymous publication of their clinical data for research purposes were excluded. The study was conducted in accordance with institutional guidelines, national legal requirements and the revised Declaration of Helsinki.

### Clinical data

Cardiovascular history, baseline clinical and operative data and follow-up events were collected prospectively. All patients who were alive were seen as outpatients in our institution before follow-up closure. Surgical risk was assessed using EuroSCORE 1 [21]. During follow-up, patients were monitored by their personal physicians. Death certificates were consulted for determination of cause of death.

## Echocardiographic methods

Baseline and follow-up transthoracic echocardiography (TTE) was performed during routine clinical practice. Diagnosis of SMR was based on presence of restrictive mitral regurgitation (MR), despite normal leaflets and chordae, in the context of LV remodelling and systolic dysfunction (Carpentier classification type IIIb) [1,10]. The degree of MR was assessed semiquantitatively initially, and subsequently using an integrative approach, including quantitative methods [22]. In patients with quantitative assessment, severe SMR was defined by an effective regurgitant orifice (ERO) area  $\geq$  20 mm<sup>2</sup> and a regurgitant volume  $\geq$  30 mL [5,10]. TTE was performed preoperatively and postoperatively before dismissal and at last follow-up in all patients who were alive.

## Surgical techniques

The decision to perform UA or MVR was left to the surgeon. When UA was performed, care was taken to realize a restrictive complete annuloplasty of less than two sizes compared with that used for degenerative MR [7]. When MVR was indicated, a triangular resection of anterior leaflet was performed, leaving all chords attached to the ventricular surface of the remnant anterior leaflet. Posterior leaflet and subvalvular apparatus were preserved, as suggested by the chordal sparing MVR technique [23].

## Statistical analysis

Baseline clinical and echocardiographic characteristics were described for the total population, and according to both subgroups. Primary endpoints were in-hospital death, cardiovascular mortality and hospitalization for postoperative CHF. Secondary endpoints were evolution of LV variables and recurrence of MR. The incidence of cardiovascular death was analysed by taking into account the specific framework of competing risks, death from non-cardiovascular causes being competitive with the endpoint. Univariate analyses were performed to assess the prognostic impact of various characteristics. Variables were considered as candidates for the multivariable analysis according to both the literature and the *P*-value in the univariate analysis (*P* < 0.20). A backward selection procedure was then applied to build final regression models. Subdistribution hazard ratios (HRs) and their 95% confidence intervals (CIs) were estimated using the Fine and Gray model. A multivariable model was built by including a priori selected variables according to literature data. Adjusted subdistribution HRs with their 95% CIs were estimated. The same strategy was used for the analysis of the incidence of CHF.

A two-way analysis of variance for repeated measures model was used to assess the effect of time and type of surgery on echocardiographic data, taking into account that echocardiographic variables were measured twice in the same patient. All analyses were performed using R software, version 3.0.3. All tests were performed two-sided, and for all analyses a *P*-value < 0.05 was considered statistically significant.

**Table 1** Baseline characteristics.

	Total population (n = 59)	UA (n = 12)	MVR (n = 47)	P
Age (years)	65 ± 10	61 ± 11	66 ± 9	0.1
Men	42 (71)	9 (75)	33 (70)	> 0.99
Ischaemic cardiac disease	41 (70)	7 (58)	34 (72)	0.4
Previous CABG	3 (5)	1 (8)	2 (4)	0.5
Diabetes	15 (25)	1 (8)	14 (29)	0.1
History of stroke	3 (5)	3 (6)	0	0.9
Atrial fibrillation	30 (50)	5 (41)	25 (53)	0.4
Creatinine concentration (μmol/L)	113 ± 45	109 ± 52	114 ± 44	0.3
ACEIs/ARBs	41 (70)	7 (58)	34 (79)	0.25
Beta-blockers	28 (47)	3 (25)	25 (55)	0.05
Diuretics	59 (100)	12 (100)	47 (100)	1
Resynchronization therapy	8 (13)	0 (0)	8 (17)	0.5
End-diastolic LV diameter (mm)	63 ± 8	61 ± 7	64 ± 8	0.7
End-systolic LV diameter (mm)	49 ± 9	45 ± 3	50 ± 9	0.5
End-diastolic LV volume (mL)	198 ± 69	187 ± 62	199 ± 71	0.7
End-systolic LV volume (mL)	122 ± 47	94 ± 46	123 ± 48	0.6
LVEF	36 ± 6	36 ± 5	36 ± 6	0.6
LVEF < 30% (% of total)	17 (29)	3 (25)	14 (29)	0.3
ERO area (mm <sup>2</sup> )	41 ± 17	46 ± 20	41 ± 15	0.9
Regurgitant volume (mL)	56 ± 23	65 ± 25	55 ± 20	0.5
sPAP (mmHg)	54 ± 15	51 ± 11	54 ± 16	0.5
EuroSCORE 1	7.5 ± 2.7	6.5 ± 2	7.7 ± 2	0.1

Data are expressed as mean ± standard deviation or number (%). ACEI: angiotensin-converting enzyme inhibitor; ARB: angiotensin receptor blocker; CABG: coronary artery bypass grafting; ERO: effective regurgitant orifice; LV: left ventricular; LVEF: left ventricular ejection fraction; MVR: mitral valve replacement; sPAP: systolic pulmonary artery pressure; UA: undersizing annuloplasty.

## Results

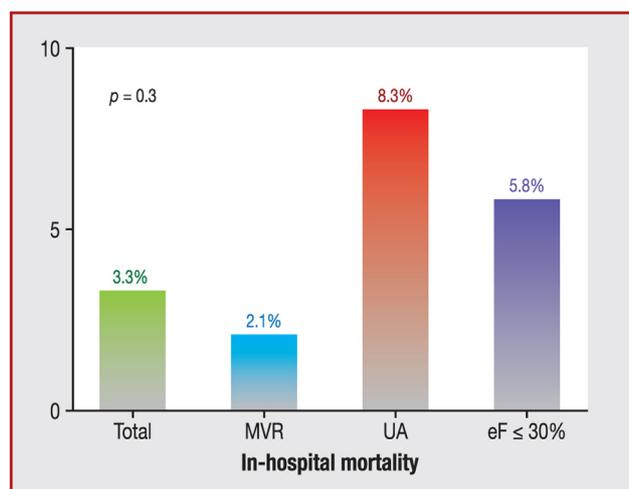
### Study population

Fifty-nine consecutive patients were included in the study: mean age was 65 ± 10 years, mean LVEF was 35 ± 6%, one third had an LVEF < 30% and one third had non-ischaemic cardiac disease. All patients had very severe SMR (mean ERO area 41 ± 17 mm<sup>2</sup> and mean regurgitant volume 56 ± 23 mL). All patients had been admitted for a recurrent episode of CHF in the 3 months preceding surgery.

Indication for surgery by study design was severe symptomatic SMR with recurrent CHF episodes despite optimal treatment in all patients. Patients with LVEF < 30% and refractory CHF were considered ineligible for heart transplantation because of age or co-morbidities; in these patients, mitral surgery was indicated after multidisciplinary discussion. Three patients were operated on while on inotropic support because of refractory CHF with massive MR (Table 1).

### Perioperative data

Twelve patients (20%) underwent UA with semirigid complete ring (mean ring size, 28 ± 1.2 mm). Forty-seven patients (80%) underwent MVR with preservation of subvalvular structures: 42 (89%) had a bioprosthesis. Eight patients (13%) had CABG, but in these patients severe



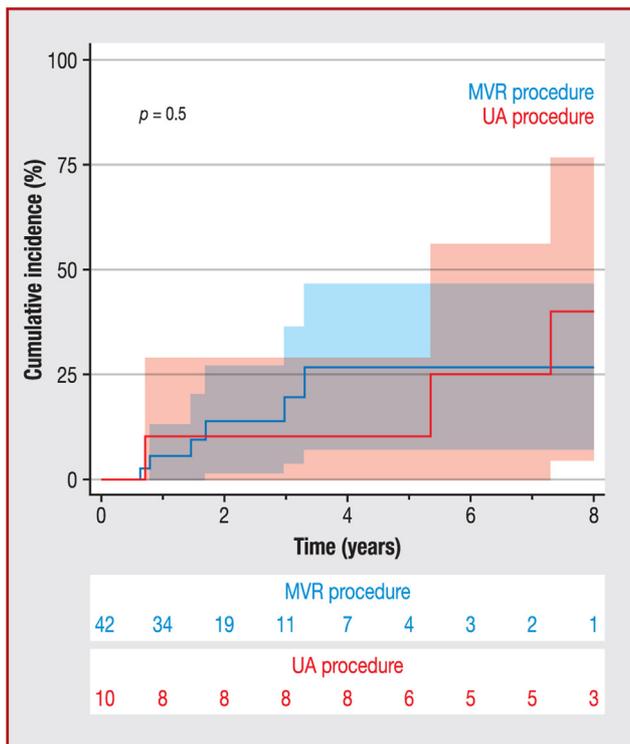
**Figure 1.** In-hospital mortality among 59 patients operated on for severe symptomatic secondary mitral regurgitation from 1997 to 2015. eF: left ventricular ejection fraction; MVR: mitral valve replacement; UA: undersizing annuloplasty.

symptomatic SMR remained the primary indication for surgery: four (33%) in the UA group and four (8%) in the MVR group ( $P=0.05$ ). Two patients died within 30 days of surgery (in-hospital mortality, 3.3%), one in each group (in-hospital mortality of 8.3% in the UA group vs. 2.1% in the MVR group) (Fig. 1); cause of death was cardiogenic shock and septic

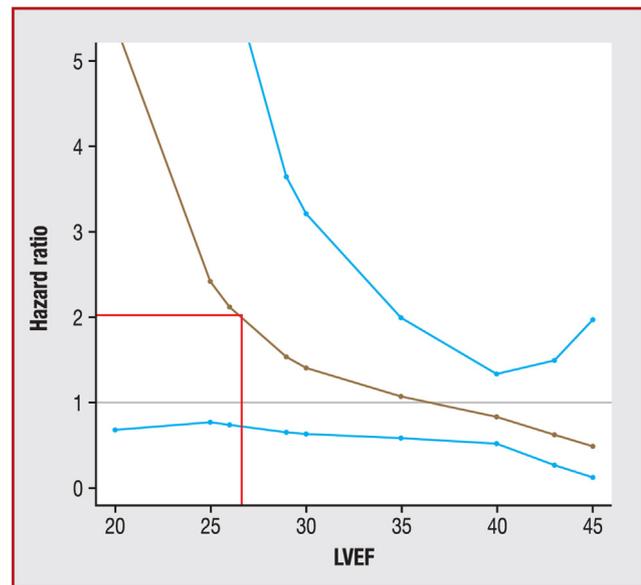
shock, respectively. These two patients had ischaemic cardiac disease, and LVEF was 35% and 30%, respectively. In-hospital mortality was therefore 5.8% in patients with LVEF  $\leq$  30%, but none of the patients with LVEF strictly  $<$  30% died within 30 days of surgery; nor did any of the three patients with inotropic support at the time of surgery.

### Mid-term cardiovascular mortality

Median follow-up (complete in all patients) was  $88 \pm 51$  months in the total population,  $97 \pm 64$  months in the UA group and  $51 \pm 40$  months in the MVR group ( $P=0.4$ ). Sixteen patients died during follow-up, 13 from a cardiovascular cause (intractable CHF), two from cancer and one from chronic renal insufficiency. Twelve deaths occurred in the MVR group and four in the UA group. The 8-year mortality rate was  $48 \pm 17\%$  in the UA group and  $43 \pm 12\%$  in the MVR group. The 8-year cardiovascular mortality rate was  $39 \pm 13\%$  in the overall population,  $40 \pm 18\%$  in the UA group and  $27 \pm 10\%$  in the MVR group (Figs. 2 and 3). Two different models of multivariable analysis were used. In the first, older age (HR 1.14, 95% CI 1.07 to 1.22;  $P < 0.001$ ) and preoperative LV end-systolic diameter (HR 1.18, 95% CI 1.09 to 1.27;  $P < 0.001$ ) independently predicted cardiovascular mortality. In the second model, older age (HR 1.07, 95% CI 1.02 to 1.12;  $P=0.003$ ) and preoperative LVEF (HR 0.90, 95% CI 0.83 to 0.98;  $P=0.01$ ) independently predicted cardiovascular mortality. Type of surgery was not associated with cardiovascular mortality (HR 1.5, 95% CI 0.4 to 5.6;  $P=0.5$  for UA versus MVR) (Table 2).



**Figure 2.** Mid-term cardiovascular mortality according to type of surgery among 59 patients operated on for severe symptomatic secondary mitral regurgitation. MVR: mitral valve replacement; UA: undersizing annuloplasty.



**Figure 3.** Spline curve analysis showing the relationship between mid-term cardiovascular mortality and left ventricular ejection fraction (LVEF) in 59 patients operated on for severe symptomatic secondary mitral regurgitation.

**Table 2** Determinants of mid-term cardiovascular mortality by two models of multivariable analysis among 57 patients who survived an operation for severe symptomatic secondary mitral regurgitation.

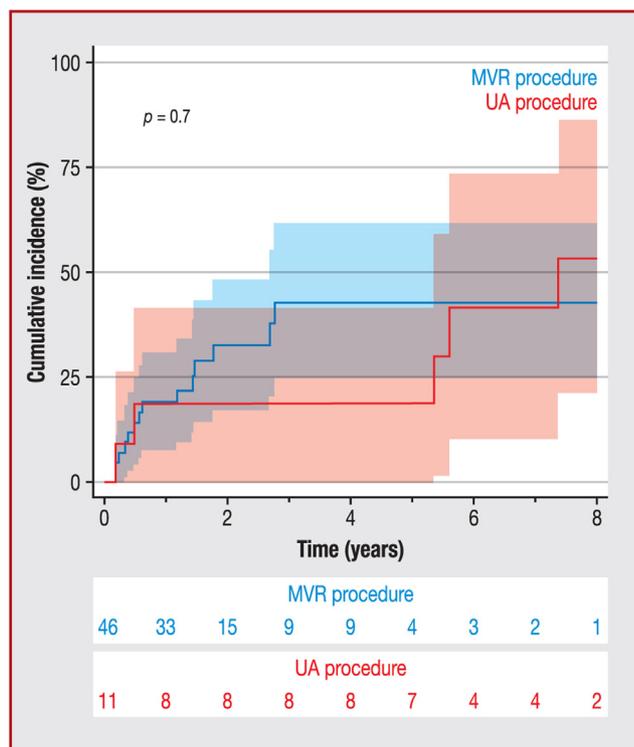
	Multivariable analysis		
	Hazard ratio	95% CI	<i>P</i>
Model 1			
Age	1.14	1.07 to 1.22	$< 0.001$
Preoperative LVESD	1.18	1.09 to 1.27	$< 0.001$
Model 2			
Age	1.07	1.02 to 1.12	0.003
Preoperative LVEF	0.90	0.83 to 0.98	0.018

CI: confidence interval; LVEF: left ventricular ejection fraction; LVESD: left ventricular end-systolic diameter.

### Mid-term incidence of postoperative CHF

During follow-up, 21 patients (37% of patients who survived surgery) experienced at least one episode of CHF requiring hospitalization: five in the UA group (45% of UA patients alive after surgery) and 16 in the MVR group (35% of MVR patients alive after surgery). Among patients without postoperative CHF ( $n=36$ ), four remained asymptomatic, all from the MVR group, and the remaining 32 were in New York Heart Association class II, without recurrence of CHF symptoms, six in the UA group and 26 in the MVR group.

At 8-year follow-up, the cumulative incidence of CHF was  $52.5 \pm 10.1\%$  for the overall population,  $42.7 \pm 9.6\%$  for the



**Figure 4.** Eight-year cumulative incidence of hospitalization for postoperative heart failure according to type of surgery among patients operated on for severe symptomatic secondary mitral regurgitation. MVR: mitral valve replacement; UA: undersizing annuloplasty.

MVR group and  $53.2 \pm 16.7\%$  for the UA group. In the multi-variable analysis, lower preoperative LVEF (HR 1.1, 95% CI 1.05 to 1.15;  $P=0.0001$ ) was the only variable independently associated with recurrent CHF after surgery, while type of surgery was not (HR 1.1, 95% CI 0.4 to 2.6;  $P=0.7$  for UA versus MVR) (Fig. 4).

### Postoperative echocardiographic data

Median time between preoperative and last follow-up TTE was 578 days in the total population, 588 days in the UA group and 568 days in the MVR group ( $P=0.8$ ).

### Postoperative LVEF (Fig. 5)

Early postoperative LVEF evaluated at discharge was  $35 \pm 7\%$  vs.  $36 \pm 6\%$  preoperatively for the overall population ( $P=0.6$ ),  $34 \pm 8\%$  vs.  $36 \pm 5\%$  in the UA group and  $35 \pm 7\%$  vs.  $36 \pm 6\%$  in the MVR group ( $P=0.6$ ). At last follow-up TTE, LVEF was  $34 \pm 11\%$  for the overall population ( $P=0.6$  for comparison between preoperative and last follow-up LVEF),  $31 \pm 12\%$  in the UA group and  $35 \pm 10\%$  in the MVR group.

### LV diameters (Fig. 5)

At last follow-up TTE, end-diastolic LV diameter had significantly decreased versus the preoperative value in the total population ( $60 \pm 10$  mm vs.  $63 \pm 8$  mm;  $P=0.02$ ) and in the MVR group ( $59 \pm 9$  mm vs.  $64 \pm 8$  mm;  $P=0.002$ ), but tended to increase in the UA group ( $64 \pm 10$  mm vs.  $61 \pm 7$  mm;  $P=0.2$ ). End-systolic LV diameter remained stable versus

preoperative values in the total population ( $49 \pm 9$  mm vs.  $49 \pm 9$  mm;  $P=0.9$ ) and in the MVR group ( $49 \pm 10$  mm vs.  $50 \pm 9$  mm;  $P=0.3$ ), but tended to increase in the UA group ( $48 \pm 6$  mm vs.  $45 \pm 3$  mm;  $P=0.3$ ).

### Postoperative systolic pulmonary artery pressure (sPAP) (Fig. 5)

At last follow-up TTE, sPAP had significantly decreased versus preoperative values in the total population ( $40 \pm 11\%$  vs.  $53 \pm 15\%$ ;  $P<0.01$ ) and in the MVR group ( $39 \pm 11\%$  vs.  $54 \pm 16\%$ ;  $P<0.01$ ), but had not changed in the UA group ( $47 \pm 11\%$  vs.  $50 \pm 11\%$ ;  $P=0.5$ ).

### Postoperative recurrence of MR

No prosthetic leak was observed in the MVR group. Nine patients from the UA group (81% of the patients alive in the UA group) presented recurrence of significant MR during follow-up (mean postoperative ERO area,  $19 \pm 6$  mm<sup>2</sup>), including six patients (55%) with severe SMR. Among these patients, four were hospitalized for a recurrence of CHF, and three deaths occurred.

### Impact of time and type of surgical correction on evolution of TTE variables

By using two-way analysis of variance for repeated measures method, time from baseline TTE to last follow-up TTE did not affect LVEF significantly (HR  $-1.6$ , 95% CI  $-4.1$  to  $0.9$ ;  $P=0.2$ ), but it affected significantly the evolution of end-diastolic LV diameter (HR  $-4.0$ , 95% CI  $-6.7$  to  $-1.4$ ;  $P=0.004$ ) and sPAP (HR  $-12.2$ , 95% CI  $-17.2$  to  $-7.1$ ;  $P<0.001$ ).

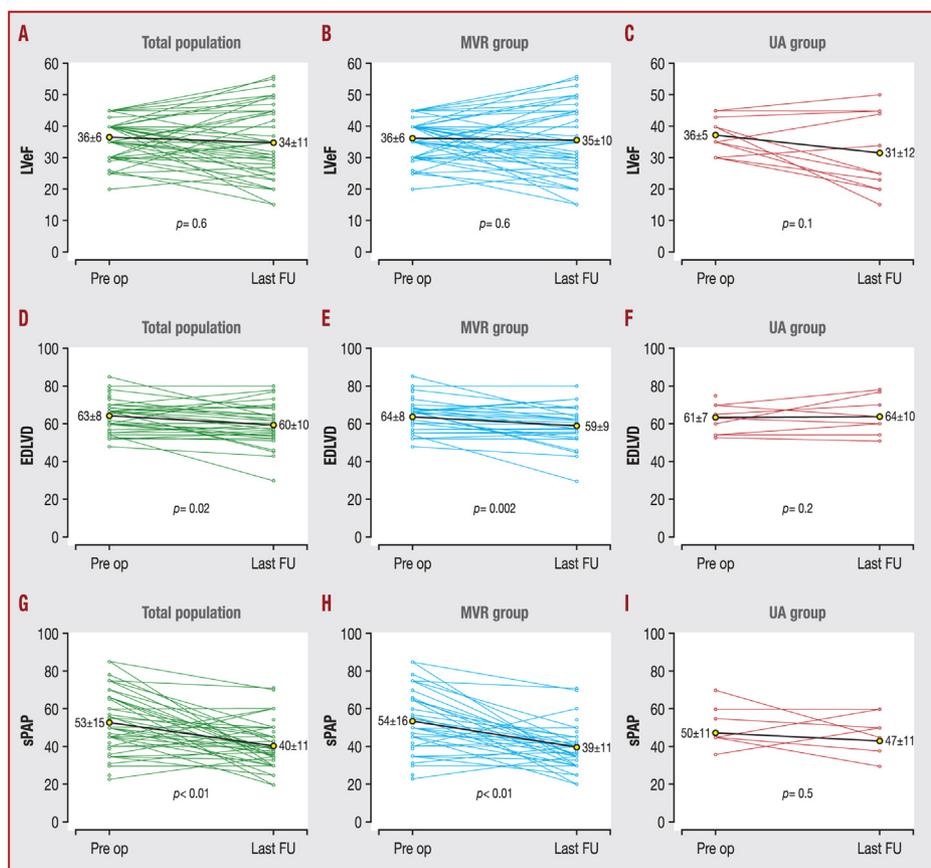
The type of surgical correction did not affect any of these three variables: HR 1.4, 95% CI  $-3.5$  to  $6.3$  ( $P=0.6$ ) for LVEF; HR  $-1.6$ , 95% CI  $-7.3$  to  $4.1$  ( $P=0.6$ ) for end-diastolic LV diameter; and HR 2.0, 95% CI  $-6.2$  to  $10.3$  ( $P=0.6$ ) for sPAP.

## Discussion

The present study, including 59 consecutive patients operated on for severe symptomatic MR secondary to severe LV dysfunction, shows that:

- surgical correction can be performed in such patients with low in-hospital mortality despite absence of revascularization in most;
- mid-term clinical outcome is acceptable despite very severe clinical and echocardiographic presentation and absence of revascularization in most;
- LVEF does not decrease after surgical correction of SMR regardless of the mode of correction, in neither the short-term nor the mid-term postoperatively;
- MVR is associated with favourable echocardiographic outcome without exposing patients to MR recurrence, which is particularly frequent after UA.

Occurrence of SMR in the course of LV systolic dysfunction has been reported as the main determinant of pulmonary hypertension [24], and as an independent risk factor for higher mortality and morbidity, in both ischaemic disease [4] and non-ischaemic disease [3]. Medical treatment of LV dysfunction and resynchronization therapy can decrease



**Figure 5.** Comparison of left ventricular ejection fraction (LVEF), end-diastolic left ventricular diameter (EDLVD) and systolic pulmonary artery pressure (sPAP) between preoperative evaluation (Pre op) and last follow-up echocardiogram (FU) in both subgroups. MVR: mitral valve replacement; UA: undersizing annuloplasty.

MR through LV reverse remodelling, an increase in closing forces and pacemaker resynchronization [25]. Conversely, in case of underlying ischaemic LV dysfunction, revascularization alone was reported to be insufficient to allow sustained decrease in ischaemic SMR [26]. Therefore, in patients with persistent severe SMR despite optimal medical treatment, surgical correction of MR with specific mitral procedure is appealing in view of its impact on clinical outcome [3,4].

However, crippling operative risk as a result of LV dysfunction was the first hindrance, based on historical series reporting operative mortality rates as high as 12%, whereas in more recent series operative mortality was reported as being between 2 and 5% [9,19], or even as low as 1.3% in a recent randomized trial [27]. Our series, despite including patients with very severe presentation at surgery, is in line with this acceptable operative risk, with in-hospital mortality of 2% in the MVR group and no in-hospital death in patients with LVEF < 30% or with inotropic support at the time of surgery.

The second historical concern was the fear of an acute postoperative fall in LVEF by closing the ERO, which has been seen in the past as a way of discharging the overloaded ventricle. This concern was not confirmed by recent data [27], including ours, as LVEF did not drop postoperatively in either group, neither at discharge nor at last follow-up. Stabilization of LVEF in such patients could even be seen as a favourable consequence of MR correction, suggesting

that SMR could affect outcome through worsening of systolic dysfunction.

The third limitation for surgical correction comes from uncertainties about the postoperative benefit of surgery, which leaves the underlying LV dysfunction untreated, particularly in case of no indication for concomitant CABG or in non-ischaemic cardiomyopathy. Indeed, no outcome benefit was reported after surgical correction of SMR, mostly ischaemic versus medical treatment alone, in a non-randomized study, after propensity score matching [20]. Similarly, no survival advantage was reported in patients with MR correction at the time of CABG versus CABG alone, in a non-randomized series [9] and in two randomized trials [19,27]. These disappointing results could reflect a non-relevant target, as MR remains the consequence and not the cause of LV dysfunction; they may also relate to an imperfect surgical technique, as all above-mentioned surgical series relieved SMR using UA, which was considered for a long time to be the gold standard for surgical correction of SMR. The rationale for UA is disputable in view of the physiology of the leak, and its accuracy was largely questioned in the last ACC/AHA guidelines [6]. Actually, high rates of MR recurrence have been reported, in both observational series [8,9] and randomized trials [15,27,28], reaching 33% of patients at 1 year and 60% at 2 years [15,28], which is concerning in view of its logical association with postoperative excess mortality and recurrence of CHF [29].

Our results in the UA group are consistent, by reporting more than half of the patients as having severe MR after UA, and a mean postoperative ERO close to the threshold of severity [5]. Continued LV remodeling despite ring insertion is a reasonable explanation for postoperative MR recurrence [30]. In addition, UA, by displacing anteriorly the posterior annulus, could subsequently worsen the outward projection of papillary muscles, enhancing tethering of the posterior leaflet, which subsequently cannot achieve normal coaptation [30]. The inability of UA to restore mitral competence appears particularly relevant in patients with more pronounced leaflet deformation and tenting [16], and in patients with the largest ventricles, who represented the majority of our study population [7].

At variance with organic MR correction, which aims to restore normal life expectancy through repair, surgical correction of SMR cannot have such an ambition because of pre-existing LV dysfunction, which jeopardizes prognosis per se. Therefore, MVR by bioprosthesis insertion with total chordal sparing [16] appears to be an acceptable alternative, as the durability of prostheses will likely exceed patient life expectancy. Besides, observational studies [8,17] and one randomized trial [15,30] reported no survival advantage for UA over replacement in patients with ischaemic SMR, most of whom had CABG at the time of MR correction. The present study is in line with these data, but our study population differed substantially from previous series [8,17,27] by including patients with both ischaemic and non-ischaemic disease, very depressed systolic function and massive SMR as the primary indication for surgery, with few cases of concurrent CABG. Surgical indication in such patients is barely a class IIb indication in the ACC/AHA guidelines [6], and is decided upon after multidisciplinary evaluation because of refractory CHF with no other therapeutic option. Despite such a severe presentation, mid-term postoperative functional status and survival, with >50% of patients alive at 8 years in both groups, appears acceptable, with a trend favouring MVR. Even if proper evaluation against natural history is not possible, this postoperative prognosis compares well with the spontaneous outcome of patients with severe ischaemic MR [4,5]. Spline curve analysis and multivariable models have suggested, however, that surgical correction of SMR should be considered before extreme LV remodelling and systolic dysfunction. Echocardiographic outcome was also satisfactory, particularly after MVR, with stabilization of LVEF and a decrease in end-diastolic LV diameter and sPAP. Such favourable echocardiographic evolution was not observed in patients with UA, possibly because of the prohibitive rate of MR recurrence in this group. Nevertheless, it was not possible to make a formal comparison between groups because of the low number of patients in the UA group.

### Study limitations

The present series was an observational non-randomized study, but is in line with other observational series and a recent randomized trial [15], extending their conclusions to patients with very severe SMR and no concomitant CABG. The choice between UA and MVR was left to the surgeon, but baseline comparison between the two groups showed no difference in terms of main outcome risk factors,

particularly LVEF. The asymmetrical patient numbers in the two groups comes from the observed high rates of MR recurrence after UA with time, favouring systematic use of MVR in our institution most recently. In our series, post-repair coaptation height was not available in most patients, and ring insertion was used as an isolated procedure, limiting the conclusion to isolated UA. One series did report superiority of repair over replacement in terms of postoperative survival [18], but 25% in the repair group had an edge-to-edge procedure combined with UA. In addition, in this series, patients from the replacement group were considered unsuitable for repair because of extreme tenting, limiting the use of repair to patients with little leaflet deformation [18]. Evolution of end-diastolic LV diameter and sPAP seemed more favourable in the MVR group than in the UA group, but it appeared that time lag between preoperative and last follow-up TTE had more impact on this improvement than the type of surgery. However, the high recurrence rate of MR with UA versus MR could ultimately turn into a significantly less favourable outcome with longer follow-up. Lastly, percutaneous repair of SMR is an attractive alternative in such patients at increased surgical risk. However, results of ongoing trials are pending.

### Conclusions

In patients with very severe SMR, very low LVEF and recurrent CHF symptoms despite optimal medical treatment, surgical correction of MR can be performed with acceptable operative risk and mid-term outcome, even in the absence of an indication for CABG. In our series, MVR was associated with significant reverse LV remodelling, and isolated UA with prohibitive rates of MR recurrence.

### Sources of funding

None.

### Disclosure of interest

The authors declare that they have no competing interest.

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