Restrictive filling pattern in ischemic cardiomyopathy: Insights after surgical ventricular restoration

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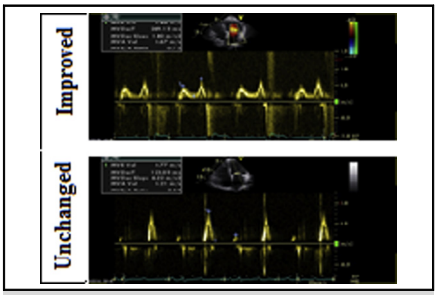
ABSTRACT

Objective: To examine factors possibly involved in the resolution or persistence of restrictive filling pattern (RFP) after surgical ventricular restoration (SVR) in a series of patients with ischemic cardiomyopathy (ICM) and RFP.

Methods: Echocardiography was performed at baseline (pre-SVR), discharge, and follow-up in 43 patients with ICM and RFP (E/A ratio $\geq$2). Patients were divided into 2 groups based on E/A ratio at discharge: improved (E/A ratio <2; 22 patients) and unchanged (E/A ratio $\geq$2; 21 patients).

Results: The improved group had a significantly increased mean deceleration time (from 137 $\pm$ 22 ms to 194 $\pm$ 68 ms; $P = .002$) and mean A wave velocity (from 43 $\pm$ 10 cm/s to 92 $\pm$ 37 cm/s; $P = .001$), and decreased E/e′ ratio (from 27.7 $\pm$ 9.5 to 19.2 $\pm$ 7.8; $P = .01$) after SVR. The unchanged group did not show any significant variations in diastolic parameters. The only significant differences at baseline between the two groups were thinner left ventricle posterior wall and lower relative wall thickness (RWT) in the unchanged group. RWT was the sole baseline parameter independently associated with persistent RFP.

Conclusions: RFP was reversed after SVR in 22 of our 43 patients with ICM with a response that remained stable over time, associated with improved New York Heart Association class. RWT was the sole baseline echocardiographic parameter significantly associated with the evolution of RFP after SVR. (J Thorac Cardiovasc Surg 2021;161:651-60)



Mitral flow in improved and unchanged RFP patients after SVR.

Central Message

A restrictive filling pattern (RFP) was reversed in approximately one-half of our patients with ischemic cardiomyopathy after surgical ventricular restoration (SVR). The response remained stable over time, and New York Heart Association class was improved. Relative wall thickness was the sole pre-SVR parameter associated with this evolution.

Perspective

Restrictive filling pattern (RFP) is a strong predictor of poor clinical outcome in patients with ischemic cardiomyopathy. It is generally considered irreversible; data on its evolution after surgical ventricular restoration (SVR) are scarce. We found that SVR, which involves incision of the pericardial sac and partial left ventricular (LV) excision, can reverse RFP. A baseline geometric pattern of LV "dilated" remodeling, indicated by very low relative wall thickness, was significantly associated with persistent RFP.

See Commentaries on pages 661, 662, and 664.

Left ventricular (LV) restrictive filling pattern (RFP) is an index of severe diastolic dysfunction in patients with ischemic cardiomyopathy (ICM).[1-3] It may become evident soon after myocardial infarction (MI) and has been shown to be a strong predictor of LV remodeling and adverse clinical outcomes, independent of age and LV

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Received for publication Feb 26, 2019; revisions received Sept 7, 2019; accepted for publication Sept 9, 2019; available ahead of print Oct 30, 2019.

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0022-5223/$36.00

https://doi.org/10.1016/j.jtcvs.2019.09.173

Abbreviations and Acronyms

DT = deceleration time
EDVI = end-diastolic volume index
ESVI = end-systolic volume index
ICM = ischemic cardiomyopathy
LVEF = left ventricular ejection fraction
LV = left ventricular
MI = myocardial infarction
NYHA = New York Heart Association
RFP = restrictive filling pattern
RWT = relative wall thickness
sPAP = systolic pulmonary artery pressure
SVR = surgical ventricular restoration
TDI = tissue Doppler index

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ejection fraction (LVEF).[4-8] Moreover, patients with ICM and baseline RFP have higher in-hospital mortality after surgical ventricular restoration (SVR) compared with patients with a nonrestrictive filling pattern.[9-13] Therefore, RFP is a key parameter in the risk stratification of patients with ICM, reduced systolic function, and/or signs of congestive heart failure.

The genesis of RFP is not fully understood, although some investigators have reported associations with infarct size, duration of ischemia, and myocardial viability.[14,15] Once it develops, RFP is usually persistent even with optimal medical treatment (pharmacologic), implantable devices (cardiac resynchronization therapy), and surgery that may achieve initial recovery of LV systolic function.[7,9-13] However, in our very small initial series of patients with ICM and baseline RFP subjected to SVR, we observed an improved filling pattern in some patients after surgery.[16] With a larger series of patients and a more stringent definition of RFP now available, we decided to conduct a retrospective analysis to evaluate RFP changes after SVR and investigate the eventual baseline characteristics and surgical factors involved.

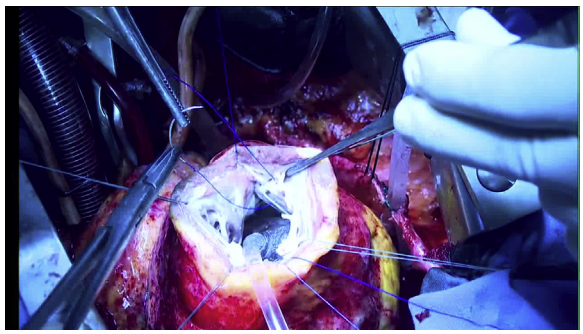
METHODS

This retrospective study was conducted using the database of the IRCCS Policlinico San Donato (July 2001 to date) for patients undergoing SVR. We enrolled patients with ICM who were referred to our institution for SVR, who presented with RFP on echocardiographic examination performed before surgery and completed echocardiographic examinations predischarge and at follow-up. Exclusion criteria were atrial fibrillation or other persistent cardiac rhythm alterations (n = 8), ventricular paced rhythm (n = 4), left bundle branch block (n = 4), any mitral or aortic valve stenosis (n = 3), previous valve repair or prosthetic valve implantation (n = 2), moderate to severe mitral regurgitation (n = 7), need for valve surgery (n = 8), cardiogenic shock or LV assist devices (n = 3), and a suboptimal echocardiographic examination (n = 6). Only 43 of the original 88 eligible patients with baseline RFP met all the criteria for inclusion in the present analysis. The outpatient follow-up included echocardiographic examination and thorough clinical examination. At 18 months, information on all patients was procured by telephone for clinical update (death and/or hospitalizations). The study was conducted in compliance with the Declaration of Helsinki, and the local Institutional Review Board approved the study protocol. All patients provided informed consent for the scientific analysis of their clinical data in an anonymous form.

Echocardiographic examination was done at baseline (pre-SVR), at discharge (post-SVR, 7-10 days after surgery), and at follow-up (7 months after SVR) using a GE Vivid 7 machine (GE Healthcare, Waukesha, Wisc). We registered the averages of measurements of 3 cardiac cycles for each patient. Electrocardiographic monitoring was performed using limb electrodes. A standard 2-dimensional (2D) echocardiographic study was performed for assessment of LV wall thickness and dimensions according to the American Society of Echocardiography/European Association of Echocardiography recommendations.[17] Diastolic and systolic LV internal diameters were measured from the parasternal long-axis view. Septal wall thickness and posterior wall thickness were measured in end-diastole. The relative wall thickness (RWT) was calculated as 2 times the posterior wall thickness divided by the LV diastolic diameter. The LV mass index was calculated using the modified Devereux equation.[17] The LV axes were measured from the 4- and 2-chamber apical views as the distance between the apex and the mitral plane for the long axis and at the middle level of the long axis for the short axis. The sphericity index was calculated as short/long axis ratio in diastole and systole. LV end-diastolic volume and end-systolic volume were measured from apical 4- and 2-chamber views applying the Simpson method and indexed for body surface area (EDVI and ESVI). LVEF and stroke volume index were derived from LV volumes. Left atrial volume was calculated using the biplane area-length formula and indexed for body surface area.[17] Systolic pulmonary artery pressure (sPAP) was calculated from the tricuspid regurgitation trace using continuous-wave Doppler.[17,18]

Measures of early (E) and peak late (A) filling velocities, E/A ratio, and E-velocity deceleration time (DT) were measured on the pulsed-wave Doppler mitral-inflow profile.[3] The tissue Doppler index was determined by placing the sample volume at the side of the medial (septal e′) and lateral annulus (lateral e′) from the apical 4-chamber view.[3] We used an average of the septal and the lateral e′ wave velocities (cm/sec) to calculate the ratio between mitral inflow E velocity and tissue Doppler index e′ (E/e′ ratio). Diastolic filling pattern was defined as restrictive with E/A ratio $\geq$2.[3]

Details of the surgical technique have been reported previously.[9,16,19] In brief, the procedure is conducted on arrested hearts with anterograde



VIDEO 1. The procedure of surgical ventricular restoration. Video available at: https://www.jtcvs.org/article/S0022-5223(19)32349-9/fulltext.

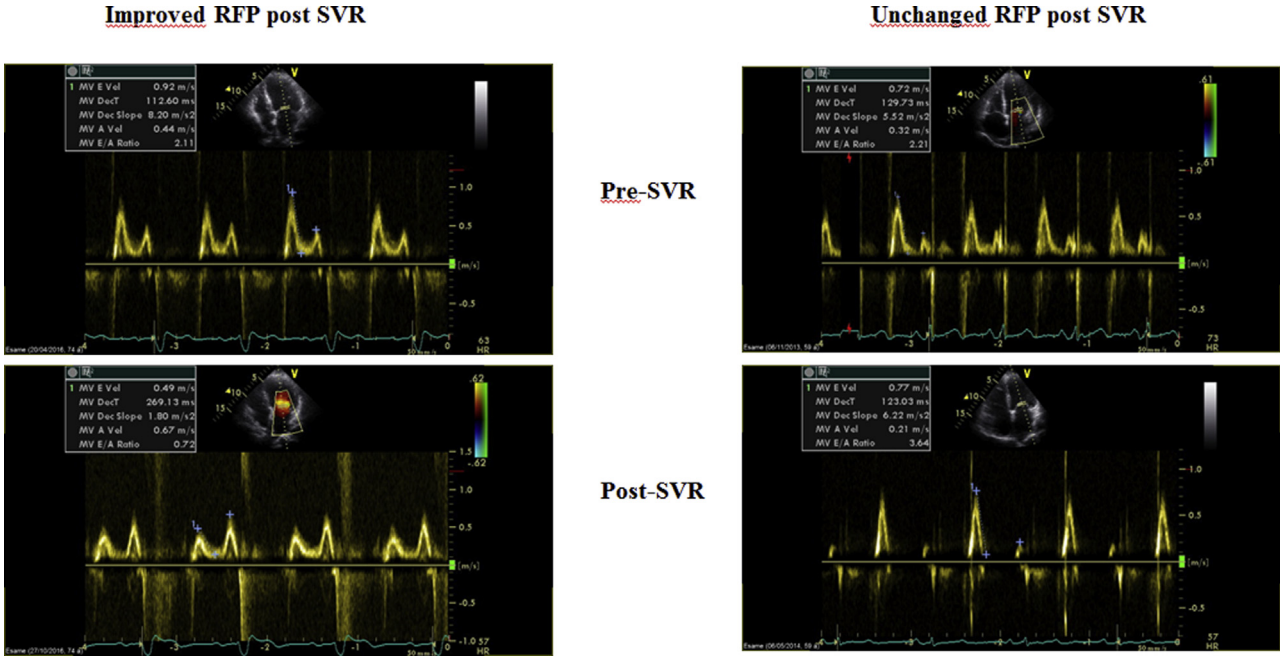


FIGURE 1. Doppler diastolic mitral flow tracing in 2 cases of ischemic cardiomyopathy with a restrictive filling pattern (*RFP*; E/A ratio $\geq$ 2): before surgical ventricular restoration *SVR* (pre-SVR) (*top*) and after SVR (post-SVR) (*bottom*). (*Left*) Improved diastolic mitral flow (E/A ratio = 0.72); (*right*) persistent RFP (E/A ratio = 3.64).

crystalloid or blood cold cardioplegia. First, complete coronary grafting is performed, and then the ventricle is opened and an intraventricular device (TRI-SVR Chase Medical, Richardson, Tex) is inserted and inflated (50-60 mL/m^2, based on body surface area), to resize and reshape the left ventricle. The new apex is remodeled around the shaper, which is removed before closure of the ventricle, with or without a patch (Video 1). The terms ''dilated LV remodeling'' and ''eccentric LV hypertrophy'' taken from the Gaasch classification[20] are used here for descriptive purposes only.

Statistical Methods

The 43 patients were divided into 2 groups based on the diastolic filling pattern at discharge (post-SVR): improved RFP (22 patients; E/A ratio <2) and unchanged RFP (21 patients; E/A ratio $\geq$2) (Figure 1). Variables were analysed for normal distribution using the Kolmogorov-Smirnov test. Categorical variables are presented as counts and percentages and compared using the χ^2 or Fisher's exact test. Continuous variables are summarized as mean $\pm$ standard deviation (SD) or median with interquartile range (IQR) and compared using the *t* test for normally distributed values; the Mann-Whitney *U* test was used alternatively. Repeated-measures analysis of variance was used to compare the echocardiographic parameter changes over time. Multiplicity issues resulting from the pairwise comparisons with respect to the baseline (pre-SVR) values were solved applying Bonferroni correction (yielding a significance threshold of 0.025). Unconditional logistic analysis was performed to identify the baseline variables significantly associated with predischarge (post-SVR) persisting RFP. The following baseline clinical and echocardiographic parameters were used for adjustment: age, RWT, EDVI, LVEF, and extent of coronary artery disease. The association is expressed as odds ratio with 95% confidence interval (CI). Both death and hospitalization for congestive heart failure within 18 months were included in the major cardiovascular events. The event-free survival curve at this follow-up was analyzed using the Kaplan-Meier method, and a Cox model was used to calculate the hazard ratio with 95% CI. A *P* value < .05 was considered significant (2-tailed test). All the analyses were carried out using Stata 12 software (StataCorp, College Station, Tex).

RESULTS

Table 1 presents clinical, laboratory, and surgical data for our study population (40 men; median age, 61 years; IQR, 51.5-67 years) divided into 2 groups: improved RFP after surgery and unchanged RFP after surgery. All patients had experienced a prior myocardial infarction (median time lapse from MI to SVR, 7.5 months; IQR, 4-41 months), and the majority were classified with advanced-stage heart disease (New York Heart Association [NYHA] class 3-4 in 70% of cases). In general, the 2 groups turned out to have very similar baseline clinical characteristics and surgical treatment.

Table 2 shows that both groups of patients presented a presurgical echocardiographic picture of typical ICM with severely reduced LVEF, increased LV-EDVI and ventricular mass, increased LA volume, high sPAP (>40 mm Hg), and high LV filling pressure (E/e′ ratio >20). The only statistically significant differences between the unchanged RFP and improved RFP groups at baseline (pre-SVR) were higher sPAP (58.6 mm Hg vs 45 mm Hg; $P = .009$), thinner posterior wall (8.95 mm vs 10.3 mm; $P = .01$), and lower RWT (0.27 vs 0.33; $P = .01$) in the unchanged RFP patients.

After surgery (post-SVR), both groups of patients presented with a noticeable reduction in LV volume and an increase in LVEF, which was most evident in the improved RFP patients (Table 2). The unchanged RFP patients did not show any significant changes in the

TABLE 1. Patient characteristics

Characteristic	Improved RFP post-SVR (N = 22)	Unchanged RFP post-SVR (N = 21)	*P* value
Age, y, median (IQR)	60.5 (51-67)	61 (52-67)	.83
Male sex, n (%)	19 (86)	21 (100)	.08
Smoker, n (%)	15 (68)	17 (81)	.62
Family history of CVD, n (%)	8 (36)	12 (57)	.17
Hypertension, n (%)	15 (68)	10 (48)	.17
Diabetes mellitus, n (%)	7 (32)	3 (14.3)	.13
Dyslipidemia, n (%)	14 (64)	10 (48)	.29
Hemoglobin, mg/dL, mean ± SD	12.4 ± 1.8	12.6 ± 1.3	.63
Creatinine, mg/dL, mean ± SD	1.09 ± 0.29	1.15 ± 0.28	.49
Delay from MI, mo, median (IQR)	7 (2-56)	8 (4-31)	.41
Anterior MI, n (%)	20 (91)	19 (90.5)	.98
QRS length, msec, median (IQR)	103 (98-131)	108 (103-144)	.28
Angina CCS grade ≥3, n (%)	2 (9)	3 (14)	.58
Ventricular arrhythmias, n (%)	5 (23)	8 (38)	.66
NYHA class, n (%)			.81
2	6 (27)	7 (33)	
3	14 (64)	13 (62)	
4	2 (9)	1 (4.8)	
Multivessel CAD, n (%)	17 (77)	11 (52)	.13
Pharmacologic treatment, n (%)			
Aspirin	21 (95)	20 (95)	.57
Nitrates	5 (23)	3 (14)	.48
Diuretics	21 (95)	20 (95)	.97
Beta-blockers	20 (91)	16 (76)	.19
ACE inhibitors/ARBs	19 (86)	17 (81)	.63
Amiodarone	2 (9)	4 (19)	.21
Statins	17 (77)	18 (86)	.47
Warfarin	—	3 (14)	.07
Surgical data			
0/1 grafts, n (%)	6 (27)	10 (48)	.29
≥2 grafts, n (%)	16 (73)	11 (52)	.29
LIMA graft to LAD, n (%)	17 (77)	12 (57)	.16
Patch implantation, n (%)	5 (23)	8 (38)	.51

RFP, Restrictive filling pattern; *SVR*, surgical ventricular restoration; *IQR*, interquartile range; *CVD*, cardiovascular disease; *MI*, myocardial infarction; *CCS*, Canadian Cardiovascular Society; *NYHA*, New York Heart Association; *CAD*, coronary artery disease; *ACE*, angiotensin-converting enzyme; *ARB*, angiotensin II receptor blocker; *LIMA*, left internal mammary artery; *LAD*, left anterior descending artery.

echocardiographic parameters of diastolic function (E/A ratio and DT) and LA volume index. They also presented with a significant reduction in sPAP, but an increase in the E/e′ ratio compared with baseline. Finally, the sphericity index was slightly increased post-SVR. The improved RFP patients presented with noticeable changes in post-SVR echocardiographic parameters of diastolic function: significantly decreased E/A ratio, significantly increased peak A velocity, and prolonged DT. The overall amelioration of diastolic profile was accompanied by consistent improvement in hemodynamic balance with reduced LV filling pressure evidenced by decreased sPAP and E/e′ ratio.

It is interesting to note that over time, echocardiographic measures remained stable in both groups from discharge to the outpatient follow-up (median interval of 7 months, IQR, 6.8-7.18 months) (Table 2). The only noticeable changes were minor increases in LV volume index and EF in the improved patients, who also showed an increase in peak E, resulting in a very slight increase in E/A ratio. DT continued with a slow but not significant increase, confirming the maintenance of an improved diastolic filling pattern. None of the improved patients showed signs of relapse (no diastolic dysfunction grade 3 or 4).

Stratifying the population into 3 groups according to tertiles of baseline RWT (≥0.32, <0.32 to ≥ 0.25, and

TABLE 2. Echocardiographic data at baseline (pre-SVR), predischarge (post-SVR), and follow-up

Parameter	Improved RFP post-SVR (N = 22)				Unchanged RFP post-SVR (N = 21)				Improved vs unchanged comparison *P* values†		
	Pre-SVR	Post-SVR	FU	*P* value*	Pre-SVR	Post-SVR	FU	*P* value*	Pre-SVR	Post-SVR	FU
2D study, mean ± SD											
PWT, mm	10.3 ± 1.8	10.6 ± 1.4	9.8 ± 1.9	.45	8.95 ± 1.5	9.5 ± 1.07	9.2 ± 1.3	.48	.01	.01	.31
SWT, mm	9.7 ± 2	9.9 ± 2.2	9.3 ± 2	.83	9.1 ± 1.8	9.2 ± 1.4	8.6 ± 1.6	.65	.33	.29	.34
DD, mm	65 ± 10	63 ± 7.2	64 ± 7.5	.64	68 ± 8	66 ± 6	66 ± 5.4	.48	.35	.18	.34
SD, mm	51 ± 11	52 ± 8.2	51 ± 9.6	.99	55 ± 7	53 ± 7.3	53 ± 4.6	.62	.26	.54	.27
Mass/BSA, g/m^2	163 ± 34	164 ± 26	157 ± 41	.07	158 ± 52	159 ± 28	153 ± 24	.68	.9	.52	.59
RWT	0.33 ± 0.09	0.32 ± 0.11	0.32 ± 0.09	.53	0.27 ± 0.05	0.29 ± 0.03	0.28 ± 0.05	.08	.01	.01	.21
DSI	0.64 ± 0.15	0.67 ± 0.09	0.70 ± 0.11	.36	0.64 ± 0.07	0.70 ± 0.06	0.72 ± 0.08	.012§	.98	.37	.65
SSI	0.58 ± 0.17	0.59 ± 0.1	0.59 ± 0.1	.68	0.57 ± 0.08	0.62 ± 0.04	0.65 ± 0.05	.005§	.95	.35	.25
EDVI, mL/m^2	123 ± 33	82 ± 18	91 ± 27	.0001‡,§	122 ± 23	92 ± 12	93 ± 18	.0001‡,§	.88	.051	.87
ESVI, mL/m^2	85 ± 29	52 ± 13	56 ± 19	.0001‡,§	84 ± 20	61 ± 12	62 ± 17	.0001‡,§	.95	.03	.35
SVI, mL/m^2	38 ± 11	28 ± 12	28 ± 18	.027	37 ± 7	31.3 ± 5	27 ± 11	.001‡,§	.72	.37	.36
EF, %	31.5 ± 7.5	37.4 ± 6.9	39.7 ± 9	.004‡,§	31 ± 5	34.3 ± 6.2	34 ± 8	.15	.74	.14	.053
LAV/BSA, mL/m^2	53 ± 15	44 ± 15	49 ± 13	.26	58 ± 17	51 ± 13	52 ± 16	.42	.35	.09	.59
Doppler/TDI, mean ± SD											
E/A ratio	2.8 ± 0.51	1.07 ± 0.4	1.28 ± 0.7	.0001‡,§	3.1 ± 0.57	3.14 ± 0.8	3.2 ± 1.6	.96	.07	.0001	.001
Peak E, cm/s	115 ± 16	97 ± 23	115 ± 41	.18	104 ± 19	124 ± 30	114 ± 37	.21	.09	.02	.9
Peak A, cm/s	43 ± 10	92 ± 37	93 ± 32	.0001‡,§	34 ± 6	40 ± 10	39 ± 18	.37	.01	.0002	.0001
DT, ms	137 ± 22	194 ± 68	221 ± 84	.001‡,§	131 ± 21	145 ± 40	141 ± 68	.81	.36	.01	.009
E/e′ ratio	27.7 ± 9.5	19.2 ± 7.8	22.7 ± 11	.09	23 ± 9.02	30.6 ± 13	23 ± 9	.25	.15	.03	.97
sPAP, mm Hg	45 ± 10	31 ± 6	36 ± 12	.003‡	58.6 ± 19	43.4 ± 11	44 ± 17	.021‡,§	.01	.006	.18
Post-SVR vs Pre-SVR changes											
EDVI, mL, median (IQR)		−34 (−25 to −49)				−24 (−20 to −35)				.06	
ESVI, mL, median (IQR)		−26 (−20 to −40)				−24 (−13 to −28)				.21	
EDVI, %, mean ± SD		−32 ± 13				−22 ± 7				.007	
ESVI, %, mean ± SD		−37 ± 15				−29 ± 19				.13	
EF, %, median (IQR)		19 (10 to 35)				19 (−2.7 to 26)				.29	

RFP, Restrictive filling pattern; *SVR*, surgical ventricular restoration; *FU*, follow-up; *PWT*, posterior wall thickness; *SWT*, septal wall thickness; *DD*, diastolic diameter; *SD*, systolic diameter; *BSA*, body surface area; *RWT*, relative wall thickness; *DSI*, diastolic sphericity index; *SSI*, systolic sphericity index; *EDVI*, end-diastolic volume index; *ESVI*, end-systolic volume index; *SVI*, stroke volume index; *EF*, ejection fraction; *LAV*, left atrial volume; *TDI*, tissue Doppler imaging; *DT*, deceleration time; *sPAP*, systolic pulmonary artery pressure; *IQR*, interquartile range. *Intragroup comparison *P* values calculated with analysis of variance adjusted with Bonferroni correction ($P < .025$). †Intergroup comparisons (improved RFP vs unchanged RFP) at the 3 time points (pre-SVR, post-SVR, and FU) were assessed with analysis of variance. ‡Post-SVR vs pre-SVR values. §Follow-up vs pre-SVR.

<0.25), the incidence of persistent RFP after SVR increased progressively from 23% in the first tertile to 57% in the second tertile and 72% in the third tertile (*P* for trend = .037) (Figure 2). In a logistic model that also includes age, severity of coronary artery disease, LVEF, and EDVI, RWT <0.32 (second and third tertiles) was the only baseline parameter significantly associated with persistent RFP (odds ratio, 18; 95% CI, 2.27-143; $P = .006$).

At the outpatient follow-up, no patients were classified as NYHA class 4; patients in the improved RFP group had overall higher NYHA class compared with the unchanged RFP patients (Figure 3). There were no significant differences between the 2 groups in the occurrence of major adverse cardiovascular events at 18 months (Table 3).

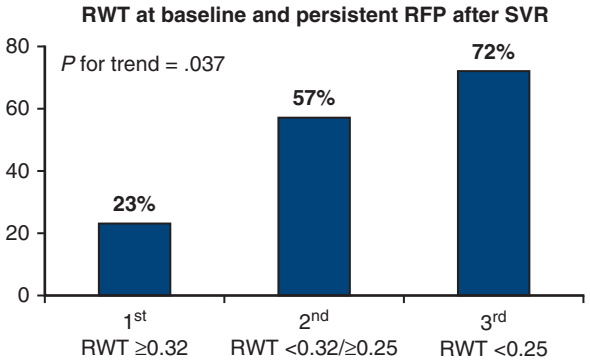


FIGURE 2. Incidence of persistent diastolic restrictive filling pattern (*RFP*) after surgical ventricular restoration (*SVR*) in patients divided into tertiles of baseline relative wall thickness (*RWT*).

Figure 4 shows the event-free survival curves at 18 months (death or rehospitalization for congestive heart failure).

DISCUSSION

The present retrospective study shows that (1) a restrictive LV filling pattern can be reversed by SVR in patients with advanced ICM, with an "all-or-nothing" response; (2) when it is improved after SVR, the diastolic filling pattern remains stable over time and is associated with better clinical prognosis; and (3) a baseline geometric pattern of LV "dilated" remodeling, indicated by very low RWT, is significantly associated with persistent RFP after SVR. The graphical abstract (Figure 5) shows a pre-SVR mitral inflow Doppler profile and 2D image in a patient with ICM with RFP. The SVR procedure reduces LV volume, resulting in an improved diastolic filling pattern in 50% of cases, as evidenced by the post-SVR Doppler profile. Pre-SVR RWT values were found to be predictive of post-SVR outcome.

The effects of SVR on LV function have been amply studied.[21-23] Of all the changes produced by SVR, a reduction in EDVI certainly has the most significant impact on the mechanics of LV contraction.[22] The impact of SVR on diastolic function has been less widely investigated.[9,10,13] LV chamber enlargement characteristic of ICM leads to increased wall stress (Laplace's law). Because the pressure-volume relation is exponential, diastolic filling occurs in the steeper part of the curve, resulting in reduced LV compliance. We do know that SVR can improve LV compliance by influencing the pressure–volume relationship; the marked decrease in LV volume induced by SVR, associated with a significant decrease in filling pressure, can lead to LV filling in a more favorable portion of the curve.[21,22] Although diastolic dysfunction is relatively common after MI, only a minority of patients present with a severe degree of LV diastolic dysfunction (ie, RFP).[4,24,25] Once established, RFP appears to be refractory to pharmacologic intervention, device implantation, and surgery.[7,9-13] In many cases, even when EDVI is reduced by SVR, there are no significant changes in this specific LV filling pattern.[9,25]

The findings of the present study, based strictly on patients with severe ICM and RFP, show primarily a surprising "all-or-nothing" response to SVR in terms of LV filling pattern. After SVR, the improved group showed a general amelioration in diastolic function, associated with evident improvement of the hemodynamic picture, whereas the unchanged group showed no significant

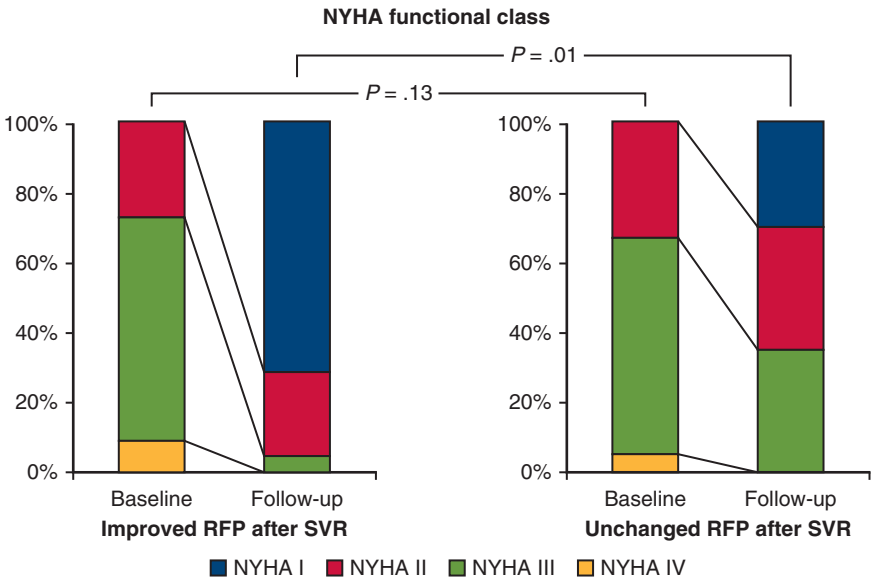


FIGURE 3. Distribution of New York Heart Association (*NYHA*) functional classes at baseline and follow-up (approximately 7 months after surgical ventricular restoration [*SVR*]) in patients with improved and unchanged restrictive filling pattern (*RFP*) after surgery.

TABLE 3. Adverse clinical events at 18 months

Event	Improved RFP post-SVR (N = 22)	Unchanged RFP post-SVR (N = 21)	*P* value*
Cardiac death, n (%)	1 (4.5)	2 (9.5)	.61
Non cardiac death, n (%)	1 (4.5)	—	—
Hospitalization for CHF, n (%)	3 (13.6)	6 (28.6)	.28
Hospitalization for ventricular arrhythmia, n (%)	1 (4.5)	2 (9.5)	.61
ICD/CRT implantation, n (%)	1 (4.5)	3 (14.3)	.34

RFP, Restrictive filling pattern; *SVR*, surgical ventricular restoration; *CHF*, cardiac heart failure; *ICD/CRT*, implantable cardioverter defibrillator/cardiac resynchronization therapy. *Fisher's exact test.

changes in diastolic pattern and only marginal improvements in systolic function. We note that these 2 different responses occurred using the same surgical technique (number of coronary grafts and patch implants) in the 2 groups (Table 1). If RFP depended only on structural alterations of the LV wall (mainly interstitial fibrosis and scarring) common in advanced stages of ICM, it would be difficult to explain the rapid diastolic changes (only 10 days from surgery to first post-SVR echocardiographic examination) seen in the improved patients.[26] Moreover, these patients did not present with signs of diastolic relapse at follow-up (7-month echocardiographic checkup) and they even exhibited further prolongation of DT.

RFP can occur early after MI either due to altered passive elastic properties of the LV wall or as a consequence of ischemic damage to LV geometry and mechanics.[4-6] Acute MI can cause a rapid increase in EDVI, especially when the extension of the remote zones is associated with expansion of the area of necrosis.[27] Ventricular dilatation not only influences the pressure–volume relationship, but also is hindered by an insufficiently compliant pericardial sac. The result would be an altered content–container relationship. Given the third principle of dynamics (ie, for every action there is an equal and opposite reaction),[28] in this context the effect would be indistinguishable from that of LV "constriction."[29] Such a mechanism was hypothesized 3 decades ago and verified experimentally in the elegant studies by Lavine and colleagues,[30-32] who showed that pericardiectomy resolved RFP in dogs with advanced heart failure and LV dysfunction. SVR comports incision of the pericardial sac together with partial LV excision. This eliminates pericardial constraint and reduces EDVI, leading to a "reset" toward a pre-MI default diastolic pattern. This could explain the distribution of LV filling later in diastole with a more prominent A wave and prolonged DT of the E wave, evident in our patients who showed improvement after SVR.

In contrast, failure of regression or even slight improvement of LV filling pattern in the unchanged RFP patients may be due to their greater degree of pre-SVR LV remodeling and loss of pericardial elasticity. Structural and functional alterations after MI (eg, scarring, loss of viable myocardium, exuberant inflammatory response, neurohormonal activation) can render the LV wall less distensible, shifting the pressure–volume relationship to the left. This condition affects also remote, noninfarcted LV regions,

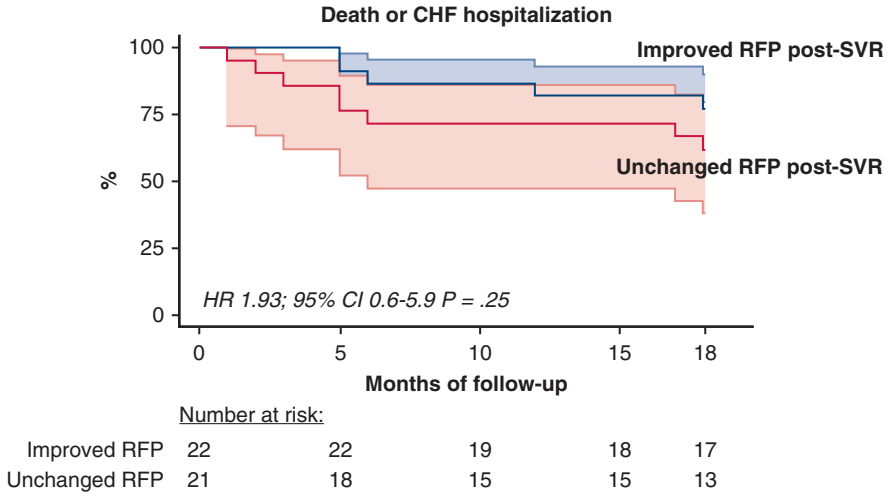


FIGURE 4. Kaplan-Meier survival curve of all-cause death or hospitalization for congestive heart failure (*CHF*) within 18 months of follow-up in patients with improved and unchanged restrictive filling pattern (*RFP*) after surgery. Colored areas represent the 95% confidence limits. *HR*, Hazard ratio; *CI*, confidence interval; *SVR*, surgical ventricular restoration.

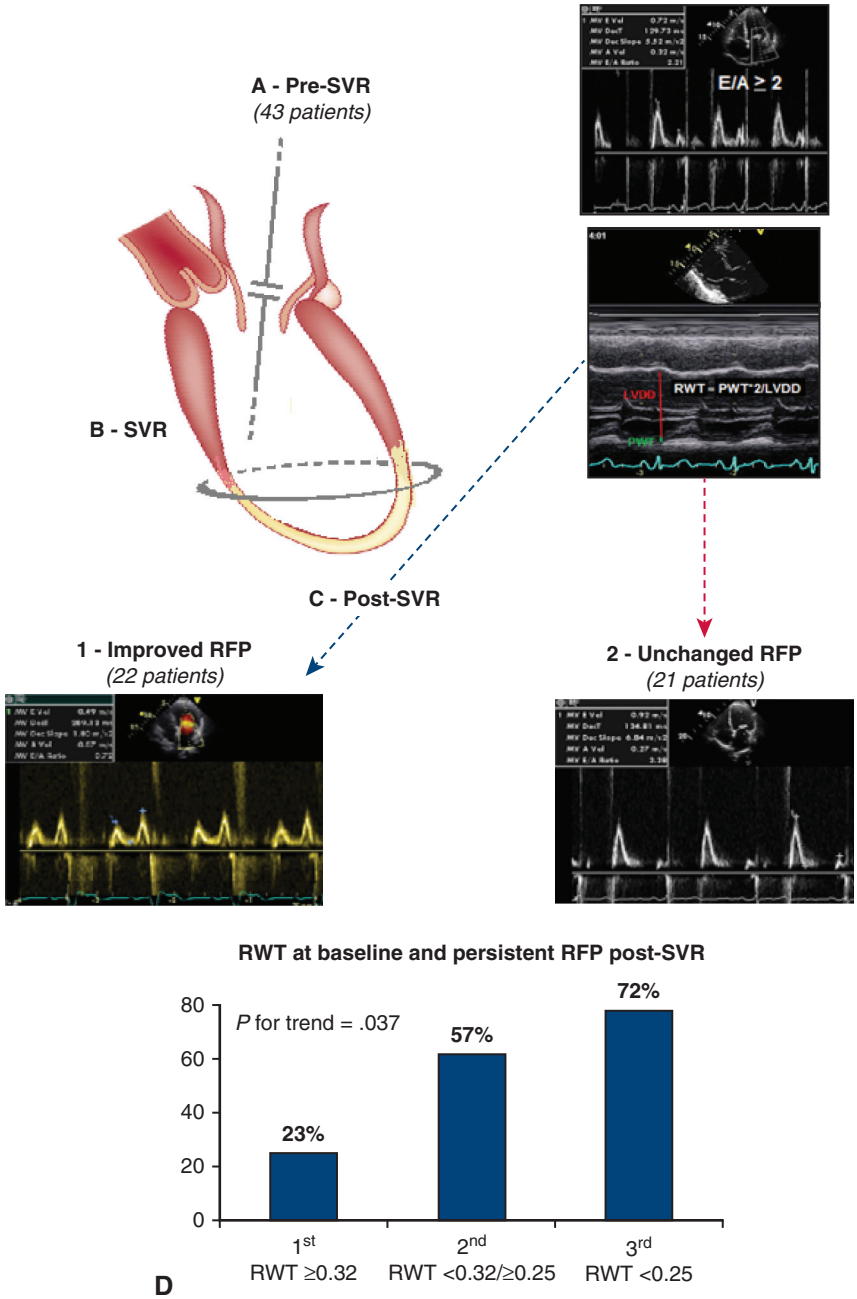


FIGURE 5. Pre–surgical ventricular restoration (*SVR*) mitral inflow Doppler profile and 2D image in a patient with ischemic cardiomyopathy (*ICM*) with a restrictive filling pattern (*RFP*). The SVR surgical procedure reduces left ventricular (*LV*) volume, resulting in an improved diastolic filling pattern in 50% of cases, as evidenced by the post-SVR Doppler profile. Pre-SVR relative wall thickness (*RWT*) values were found to be predictive of post-SVR outcome. A, Baseline (pre-SVR) echocardiographic evaluation of patients with ICM with an RFP defined by an E/A ratio ≥2 based on the Doppler mitral flow (*top*) and RWT is 2 times the posterior wall thickness (*PWT*) divided by the LV diastolic diameter (*LVDD*) (*bottom*). B, SVR with partial LV excision. C, Doppler images of mitral flow in improved RFP post-SVR (1) and of mitral flow in unchanged RFP post-SVR (2). D, Relationship between baseline RWT and persistent RFP post-SVR. The 43 patients were divided into tertiles of baseline RWT (≥0.32, <0.32 to ≥0.25, and <0.25).

possibly triggering myocardial interstitial and replacement fibrosis. This process is common in postinfarction dilated ICM, where the increased LV radius provokes elevated abnormal stress on the relatively thinner LV wall.[27] The significantly lower RWT and thinner posterior wall of our unchanged RFP patients at baseline represent a relatively more dilated pattern of LV remodeling somewhat similar to that seen in dilated cardiomyopathy, whereas the improved patients show a pattern similar to that of Gaasch's eccentric remodeling.[20] We note that the Gaasch

classification as such cannot be applied to patients with ICM who have nonuniform wall thickness. More advanced imaging techniques, such as cardiac magnetic resonance imaging, might provide more precise details regarding LV structure (eg, scarring, hypertrophy) and dimensions in these ICM patients. Furthermore, baseline RWT was the sole baseline parameter associated with persistent RFP after SVR in this series of patients in a logistic model that included age, severity of coronary artery disease, LVEF, and EDVI. The subsequent absence of significant variations in LV filling in the unchanged group at the 7-month follow-up indicates that once it presents, ''structural'' RFP accompanies the clinical evolution of ''advanced'' ICM.

Although our series is small, we note that the echocardiographic picture post-SVR is reflected in the clinical findings at follow-up when patients with improved RFP showed a significantly better NYHA functional class and a trend toward fewer adverse clinical events compared with the unchanged RFP patients. Larger series of patients must be investigated to establish whether the reversal of RFP after SVR comports medium- and long-term favorable prognostic impacts in patients with ICM.

Study Limitations

This study has several limitations. It is a very small, strictly selected patient series with a preponderance of male subjects. Doppler-derived LV filling pattern can be influenced by multiple factors, including heart rate, paced rhythm, loading conditions, and left-sided valvular disease. We excluded patients with moderate-to-severe mitral regurgitation or aortic stenosis and those with a pacemaker. Heart rate and blood pressure data were not collected. Moreover, we did not evaluate respirophasic- or Valsalva maneuver–related changes in pulsed-wave Doppler findings useful in differentiating pericardial constriction and myocardial restriction.[3,29] The lack of cardiac magnetic resonance imaging data made it impossible to investigate the eventual relationship between RFP changes after SVR and the extent of baseline ischemia and replacement fibrosis. The small size of our series made it unfeasible to investigate potential connections between LV volume changes and RFP persistence after SVR.

CONCLUSIONS

In our ICM patients with RFP subjected to SVR, an improvement in diastolic filling pattern was seen in approximately 50% of cases. These improved patients showed a remarkable and prompt improvement in hemodynamic balance as well. These immediate findings that persisted over time were reflected in better clinical outcome, based on NYHA class. A specific baseline LV remodeling phenotype was seen in patients with persistent RFP after SVR.

Conflict of Interest Statement

Authors have nothing to disclose with regard to commercial support.

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Key Words: restrictive filling pattern, surgical ventricular restoration, ischemic cardiomyopathy

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