Baseline Left Ventricular Volume and Shape as Determinants of Reverse Remodeling Induced by Surgical Ventricular Reconstruction

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Background. Early postoperative data show that surgical ventricular reconstruction (SVR) induces reverse remodeling (RR) in dilated ischemic cardiomyopathy. The stability of these results at follow-up is debated. This retrospective study determined whether RR was stable at follow-up and the role, if any, of preoperative left ventricle volume and shape on SVR-induced changes.

Methods. The study group comprised 220 patients (age, 64 ± 9 years) with an echocardiography study at baseline, discharge, and at follow-up. RR was defined as a reduction of left ventricular end-systolic volume index (ESVI) at follow-up exceeding 15% vs baseline.

Results. Reverse remodelling occurred in 162 patients (74%); the ESVI at follow-up in the remaining 58 (26%) was equal to or greater than at baseline (no-RR). At baseline, the no-RR patients had lower volumes and higher ejection fraction; at the 1-week post-SVR evaluation, all patients reached significant ESV reduction, but at follow-up, the no-RR patients had dilated and showed significantly higher volumes and lower ejection fraction vs patients with RR. New York Heart Association class improved in both groups (2.6 ± 0.6 to 1.6 ± 0.5 and 2.5 ± 0.8 to 1.8 ± 0.7, respectively, p = 0.0001). Baseline ESVI less than 73 mL/m², apical axis less than 4.35 cm, and conicity index less than 0.759 were predictors of no-RR.

Conclusions. A relatively small ESVI and a more physiologic apical shape (conical) are predictors of no-RR after SVR. Despite lack of RR, the ESV at follow-up is not severely enlarged, which explains the good survival rate in these patients.

Study Population and Study Design

Patient and operative information was reviewed from the computerized SVR database that is collected prospectively for all patients. We retrospectively analyzed data for the 468 postinfarction patients who underwent SVR between July 2001 and 2009 at the Istituto di Ricovero e Cura a Carattere Scientifico Policlinico S. Donato. We included patients from this population who had undergone a complete echocardiographic evaluation at baseline, 1 week, and at follow-up, which was a minimum of 3 months after SVR. The flow chart (Fig 1) shows the selection of the study group and the excluded cohort.

Definitions

Reverse remodelling was defined as a reduction of LV end-systolic volume index (ESVI) at follow-up greater than 15%, according to the definition of responders to cardiac resynchronization therapy [1, 2, 9–11]. No reverse remodelling (no-RR) was defined as an ESVI reduction at follow-up of 15% or less compared with baseline.

Echocardiographic Evaluation

Echocardiographic images were obtained with a 3.5-MHz transducer in the left lateral decubitus position using a commercially available system (Vivid Seven, General Electric, Milwaukee, WI). Standard 2-dimensional and color Doppler data, triggered to the QRS complex, were recorded before the operation, at discharge (10 days after SVR), and at follow-up (minimum, 3 months).

The LV end-diastolic volume (EDV) and ESV were calculated using the Simpson biplane method, and LV EF was derived. Several functional and geometric variables were measured at the three intervals (Table 1) [12]. The severity of mitral regurgitation was graded 0 to 4 using the apical 4-chamber views from the color-flow Doppler images.

Follow-Up

Long-term survival, defined as time from SVR to death, was conducted by telephone contact with the patients, their relatives, or family doctors, and was 100% complete. If the telephone interview was not possible, we contacted the national registry of death.

Surgical Technique

Details of the surgical technique have been previously reported [6, 7, 13–15]. In brief, the procedure was conducted on the arrested heart with antegrade cold blood cardioplegia. Complete coronary artery revascularization by bypass grafting (CABG) was performed first, almost always with the left internal mammary artery on left anterior descending artery and sequential venous grafts on the right and circumflex arteries, when needed.

After CABG was completed, the LV was opened with an incision parallel to the left anterior descending artery, extending from the apex to the middle scarred region. The LV cavity was inspected, and any thrombi were

Table 1. Echocardiographic Variables Evaluated at Baseline, at Discharge, and at Follow-Up

- End-diastolic and end-systolic volume (mL/m²), indexed by body surface area.
- Ejection fraction using the biplane Simpson technique
- Long axis in 4-chamber view measured as the distance between the apex and the mitral plane (mm)
- Short axis in 4-chamber view measured as the septal-lateral dimensions at the midlevel of the long axis (mm)
- Sphericity index calculated as short-axis/long-axis ratio in diastole and systole
- Conicity index calculated as the ratio between the apical and the short axis to assess the shape of the apex (see Di Donato and colleagues [12]).
removed. Each papillary muscle head was identified, and the mitral valve apparatus was evaluated.

Surgical ventricular reconstruction was performed using the TRISVR Mannequin (Chase Medical, Richardson, TX) filled at 50 to 60 mL/m² to optimize the size and shape of the new ventricle. Mitral repair was performed if the degree of mitral regurgitation was severe (grade 3 to 4+) or at grade 2+ with dilated mitral annulus or with severely depressed pump function, or both. The mitral valve repair was performed through the ventricular opening. The technique consists in a double arm stitch at the posterior annulus, from trigone to trigone. The suture is tightened on a 26-mm Hegar sizer device to obtain an over-reduction of the mitral area.

**Statistical Analysis**

Continuous variables are expressed as median or mean ± standard deviation and categoric variables as frequencies and percentage. Statistical analysis included the analysis of variance with Bonferroni within-group comparison, and an independent variables Student t test for comparison between two groups (continuous variables) or a Pearson χ² (categoric variables).

The univariate association of potential risk factors (preoperative and operation-related) with no-RR at follow-up was explored with a logistic regression analysis for continuous variables and a Pearson χ² with relative risk analysis for categoric variables. A receiver operating characteristics (ROC) analysis was used to identify cutoff values at the highest value of sensitivity and specificity. The multivariable risk analysis was based on a multivariate stepwise forward logistic regression analysis. Survival was explored with Kaplan-Meier actuarial curves as time from SVR to death. For all the statistical tests, a value of p < .05 was considered significant. Statistical calculations were performed using SPSS 11.0 software (SPSS Inc, Chicago, IL).

**Results**

The study population consisted of 220 patients (30 women, aged 64 ± 9 years) who underwent SVR. The SVR in 204 patients (93%) was associated with coronary artery bypass grafting (CABG). Mitral repair was performed in 61 (27.7%).

The median time from operation to echocardiography at follow-up was 11 months, with a minimum of 3 months from SVR (average time, 16 ± 17 months). Median survival was 38 months (mean, 40 ± 24 months) from operation to death. Excluded patients, as indicated in the flow chart, did not differ significantly from the study group in baseline and discharge variables, except for the following: patients in New York Heart Association class III and IV were monitored more frequently at follow-up than those in class I and II (72% vs 52%, p = 0.019) as well as patients taking full medications (64% vs 48%, p = 0.023). ESVI was significantly reduced in all patients early after SVR (median, – 41%). At follow-up, RR occurred in 162 patients (74%) but 58 did not have RR (no-RR). In 33 of 58, ESVI at follow-up was equal to or greater than the preoperative ESVI (no responders), and in 25, it was reduced less than 15% (poor responders). The average

![Fig 2. Left ventricular volume changes after surgical ventricular reconstruction (SVR) at three intervals in patients with (squares) and without (diamonds) reverse remodeling. Median values are reported. (EDVI = end-diastolic volume index; EF = ejection fraction; ESVI = end-systolic volume index; FUP = follow-up; SVI = stroke volume index.) **p = 0.05. ***p = 0.01.](image-url)
ESVI reduction at follow-up was \(-38\% \pm 17\%\) in RR and \(8\% \pm 20\%\) in no-RR. Figure 2 shows median hemodynamic changes in patients with RR compared with no-RR patients.

Tests of the preoperative demographic, clinical, geometric, and operative variables to assess differences that can distinguish between the RR and no-RR groups showed that the no-RR patients had significantly smaller LV volumes, higher EF, smaller apical axis, and a lower conicity index. An interesting finding was that the RR and no-RR groups had the same EDV index (EDVI) and ESVI early after SVR as measured by an intraventricular sizer device, but the no-RR patients had dilated further at follow-up and showed significantly higher volumes and lower EF compared with the RR patients.

Among operative variables, patients with no-RR more frequently had no-patch surgical reconstruction (71% vs 43% with patch, \(p = 0.0001\)) and more frequent grade 3 or 4 mitral insufficiency (36% vs 20% in RR, \(p = 0.03\)) and had mitral repair more frequently as consequence (37% vs 24%, \(p = 0.06\)). Diabetes was more frequent in no-RR patients than in the RR patients (32% vs 19%, \(p = 0.04\)).

Figure 3 shows single ESVI changes from baseline to follow-up in RR and no-RR patients. Figure 4 shows ESVI changes from baseline to discharge to follow-up according to the time from SVR to the follow-up echocardiography study. Four categories at different times from SVR to echocardiography were identified. No differences in volume changes by time to echocardiography were observed.

At follow-up, 108 patients (67%) had an ESVI reduction of greater than 30%. New York Heart Association class improved significantly, from 2.6 ± 0.6 to 1.6 ± 0.5 in RR patients and from 2.5 ± 0.8 to 1.8 ± 0.7 in no-RR patients (\(p = 0.0001\)).

Multivariate analysis showed that significant predictors of no-RR were baseline ESVI, apical axis, and the conicity index in systole. The ROC analysis (Fig 5) showed ESVI, apical axis, and conicity index were able to predict no-RR.

Respective cutoff values are reported. This analysis indicates that if preoperative ESVI is not large enough (< 73 mL/m²), the apical axis is less than 4.35 cm, and the apex is not enlarged and rounded (conicity index <
SVR may induce a poor response and can even be uselessness because the LV volume returns to basal values. By combining a conicity index of less than 0.759 and the ESVI of less than 73 mL/m² (shape and size) in one index (shape-volume index), the ROC analysis to predict no-RR shows a very high sensitivity and specificity with an area under the curve of 0.896 (confidence interval, 0.870 to 1.002; \( p \leq 0.0001 \); Fig 6). No-RR patients, either poor or no-responders, have a good survival rate, as shown in the survival curves for both groups (Fig 7).

Comment

Our findings can be summarized as follows: SVR induces reverse remodeling in all patients at discharge with a median ESVI reduction of 41%, and RR is maintained at follow-up in 74% of patients. No-RR occurred in 26% of patients, of whom 15% had poor response and 11% had no response. Preoperative significant differences between the RR and no-RR groups indicate that LV morphology and size as well as clinical characteristics (diabetes and severe mitral regurgitation) influence SVR-induced changes. Among operative variables, the minor incidence of patch reconstruction in patients with further remodelling can be explained by our center’s policy to use a patch only in very dilated ventricles.

Baseline predictors of no-RR were an ESVI of less than 73 mL/m², an apical axis shorter than 4.35 cm, and a conicity index of less than 0.759 in systole. When we combined small ventricular size with more conical apical shape, the probability was high that SVR would induce a poor response or would even be uselessness and that the LV would tend to return to baseline values.

Surgical Ventricular Reconstruction

Surgical ventricular reconstruction is a well-established treatment for ischemic postinfarction dilated cardiomyopathy. Results with SVR have been reported in several large retrospective studies, overall representing almost 5000 patients. The consistent findings in all of the major retrospective studies include an improvement in EF of between 0.10 and 0.20, a reduction in LV volumes of about 40%, an improvement in New York Heart Association functional class, and survival rates superior to those of medically treated patients [16–18].

Survival in heart failure patients with ischemic cardiomyopathy is highly affected by LV size and residual LV function [19, 20]. Survival is also affected by revascularization of viable, nonfunctional myocardium [21] and preservation of LV geometry [22]; however, revascularization alone may not be as effective in the presence of extensive LV remodeling [11].

Surgical ventricular reconstruction is designed to counteract the effects of LV postinfarction remodeling and the Surgical Treatment for Ischemic Heart Failure (STICH) trial was designed to assess whether adding SVR to CABG in ischemic cardiomyopathy improved survival free of hospitalization [23]. Hypothesis 2 of the trial was supposed to help us understand the role of SVR.
in this respect. The average volume reduction after SVR according to published studies from a variety of centers with experience in performing SVR varies from 30% to almost 60% [24]. This wide variation depends on when measurements are taken (1 week or 6 months to 1 year after SVR), on patient selection, and on surgical technique (whether an intraventricular sizer device is used).

**Insight Into the STICH Trial**

The recently released STICH results [25] showed an average ESVI reduction of 19%, which is far below the reported values that have been published, and a postoperative median ESVI of 67 mL/m² at 4 months after SVR that is a large enough value to qualify for the trial. The STICH results have raised concern on the adequacy of the procedure, and because STICH data at discharge are not available, the progression of remodeling that might have occurred at 4 months is also a concern.

Our results show that all patients had an appropriate LV reduction at discharge (ESVI, –41%) and that RR was maintained in most patients for a long time. The lack of RR after SVR is due to baseline characteristics, including a volume not enough enlarged and a shape not truly deformed. These findings may help in evaluating the appropriateness of patient selection for SVR.

Our data show that the conicity index, which reflects regional apical shape, affects reverse remodeling after SVR and also survival. We can conclude that patients with relatively small ventricles, without enlargement and flattening of the apex, are not appropriate candidates for SVR.

The STICH subanalysis presented at 2010 American College of Cardiology meeting showed that almost one-third of the enrolled population who had paired volume data had a baseline ESVI of 60 mL/m². These patients had no ESVI change at 4 months with CABG or SVR. Patients with a baseline ESVI of less than 90 mL/m² showed a greater and more uniform reduction of 76 ± 8 to 58 ± 17 mL/m² with SVR compared with 73 ± 10 to 70 ± 25 mL/m² for CABG. This subanalysis showed SVR patients with a basal ESVI of less than 90 mL/m² (also including very small ventricles) had a better survival rate, confirming the effect of ESVI on outcome. It is not known, yet, how many STICH patients reached the expected 30% reduction after SVR and, more important, how many patients reached a postoperative ESVI of less than 60 mL/m². It will be extremely important to assess whether, once obtained, an appropriate indication to SVR and an appropriate reduction of ESVI, SVR adds benefit to CABG. Until this information is available, the results of hypothesis 2 of the STICH trial will not improve the state of the art of SVR, as correctly pointed out by Conte in his recent editorial [24].

In conclusion, patients with a large LV volume at baseline who undergo SVR operations have sustained RR at follow-up. They have improvement in clinical status and a good survival rate; however, the present data show that patients with no-RR also do clinically well because they have a relatively small ESVI and a more physiologic apical shape at baseline, and even though ESVI returns to baseline, it is still relatively small—the smaller, the better. These data highlight the importance of measuring LV volumes to give an appropriate surgical indication.
References


INVITED COMMENTARY

Dr Di Donato and coworkers presented a large observational clinical study examining outcomes of patients with ischemic cardiomyopathy who underwent surgical ventricular restoration (SVR) [1]. Responders were defined as those who had greater than 15% reduction in left ventricular end-systolic volume index (LVEF), whereas nonresponders had LVEF reduction of less than 15%. Survival in both groups was similar. Small end-systolic volume and a more physiologic apical shape were predictors of poor response to SVR. The authors concluded that small ventricular size and preserved conical shape serve as predictors of adverse remodeling. The fact that poor responders had clinical outcomes that were as good as those of responders was attributed to the small ventricular size and better ejection fraction at the time of operation in these patients.

The effectiveness of surgical ventricular restoration has been the focus of numerous articles and countless debates at national meetings. This study attempted to address the issue of long-term clinical benefits of reverse remodeling after SVR. Unfortunately the findings of this study add even more ambiguity to our understanding of the clinical effects of SVR. The authors found that nonresponders had outcomes better than or similar to those