Surgical therapy for ischemic heart failure: Single-center experience with surgical anterior ventricular restoration

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Supplemental material is available online.

Objectives: Our objectives were (1) to report operative and long-term mortality in patients submitted to anterior surgical ventricular restoration, (2) to report changes in clinical and cardiac status induced by surgical ventricular restoration, and (3) to report predictors of death in a large cohort of patients operated on at San Donato Hospital, Milan, Italy.

Methods: A total of 1161 consecutive patients (83% men, 62 ± 10 years) had anterior surgical ventricular restoration with or without coronary artery bypass grafting and with or without mitral repair/replacement. A complete echocardiographic study was performed in 488 of 1161 patients operated on between January 1998 and October 2005 (study group). The indication for surgery was heart failure in 60% of patients, angina, and/or a combination of the two.

Results: Thirty-day cardiac mortality was 4.7% (55/1161) in the overall group and 4.9% (24/488) in the study group. Determinants of hospital mortality were mitral valve regurgitation and need for a mitral valve repair/replacement. Mitral regurgitation (>2+) associated with a New York Heart Association class greater than II and with diastolic dysfunction (early-to-late diastolic filling pressure >2) further increases mortality risk. Global systolic function improved postoperatively: ejection fraction improved from 33% ± 9% to 40% ± 10% ($P < .001$); end-diastolic and end-systolic volumes decreased from 211 ± 73 to 142 ± 50 and 145 ± 64 to 88 ± 40 mL, respectively ($P < .001$) early after surgery. New York Heart Association functional class improved from 2.7 ± 0.9 to 1.6 ± 0.7 ($P < .001$) late after surgery. Long-term survival in the overall population was 63% at 120 months.

Conclusions: Surgical ventricular restoration for ischemic heart failure reduces ventricular volumes, improves cardiac function and functional status, carries an acceptable operative mortality, and results in good long-term survival. Predictors of operative mortality are mitral regurgitation of 2+ or more, New York Heart Association class greater than II, and diastolic dysfunction (early-to-late diastolic filling pressure >2).

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Chronic ischemic heart failure (HF) is one of the major health care issues in the Western world in terms of increasing number of patients affected, rate of hospitalization, and costs.[1,2] Despite optimal medical treatment, mortality remains high in patients with ischemic HF and high functional class.[3] The increase

Abbreviations and Acronyms

AUC = area under the curve
CABG = coronary artery bypass grafting
E/A = early-to-late diastolic filling pressure
EF = ejection fraction
HF = heart failure
LV = left ventricular
MR = mitral regurgitation
NYHA = New York Heart Association
ROC = receiver operating characteristic
STICH = Surgical Treatment of IsChemic Heart failure (trial)
SVR = surgical ventricular restoration

in ventricular volume after myocardial infarction is a component of the remodeling process; when left ventricular (LV) volume has increased to a certain extent and geometry is markedly abnormal, HF progresses independently of neurohormonal activation, according to the biomechanical model of HF expressed by Mann and Bristow.[4] The concept of a biomechanical model of HF clearly introduces the need for therapies such as surgical ventricular restoration (SVR) that reduce LV volumes and restore geometry. SVR has proven to be effective in improving pump function, clinical status, and survival.[5-8] The technique, first described by Jatene[9] and Dor and associates,[10] applies not only to the classic aneurysm but also to ischemic dilated cardiomyopathy with akinesia or dyskinesia.[6]

SVR for patients with HF is increasingly performed, but the results are somewhat difficult to compare because the type of damage (ie, true aneurysm or dilated cardiomyopathy) is not well defined in the reported series.[11] Moreover, the reported studies are not randomized, and the question whether adding SVR to coronary artery bypass grafting (CABG) will improve survival and clinical status can only be answered by the ongoing STICH trial (Surgical Treatment of IsChemic Heart failure).[12]

In our center (San Donato Hospital, Milan, Italy), we have been performing SVR for ischemic cardiomyopathy since 1989, and a total of 1300 patients have been operated on. The majority (1161 patients aged 63 ± 10 years) had anterior ventricular repair; the remaining either had posterior repair (n = 108) or an associated procedure other than CABG or mitral repair (eg, ventricular septal defect closure, aortic replacement, or Bentall operation; n = 31). They are not included in the analysis because they deserve a separate description, and the aim of the present study is to describe as homogeneous a population as possible (ie, after anterior myocardial infarction).

The end points of this study are as follows: (1) operative cardiac and all causes long-term mortality in the consecutive series of 1161 patients having anterior SVR (1989–2005); (2) changes in LV volumes, ejection fraction (EF), and New York Heart Association (NYHA) functional class in 488 patients with a complete data set (1998-2005); and (3) predictors of operative mortality.

Patients and Methods

Patient Population

From June 1989 to October 2005, a total of 1300 patients were submitted to SVR at San Donato Hospital, Milan, Italy; 1161 patients had anterior SVR with or without CABG and with or without mitral repair/replacement.

Demographic, clinical, echocardiographic, and procedural data were collected on an Excel database, which has been approved by our local ethics committee. The study group consists of 488 patients (1998-2005) with complete clinical and echocardiographic data available for the analysis (LV volumes, EF, NYHA class, and degree of mitral regurgitation [MR]). Eighty-six were women and 402 men (63 ± 10 years). Main indications for surgery were symptoms of HF, angina, and/or a combination of the two.

Diastolic function was graded as follows: 0 = normal, 1 = abnormal relaxation, 2 = pseudonormal, and 3 = restrictive.

Echo assessment was made by transthoracic echocardiography preoperatively and before discharge (7 to 10 days after the operation); a late echo study has been performed 6 months to 2 years after the operation in patients who return to the hospital for clinical evaluation (n = 300).

Operative mortality was defined as 30-day mortality and late mortality as mortality that occurred at follow-up (time from surgery to death is available).

Follow-up was assessed by telephone interview with the patient, family, or family physicians; we contacted the regional death register if telephone interview failed.

Surgical Technique

The technique has been described previously.[7,13] In brief, the procedure is conducted on the arrested heart, with antegrade crystalloid or cold blood cardioplegia introduced in 2001. CABG is first performed, almost always on the left anterior descending coronary artery to preserve the upper part of the septum and to guarantee a complete revascularization. The mitral valve is repaired, when needed, through the ventricular opening with a double-armed stitch at the posterior annulus, from trigone to trigone, and the mitral orifice is undersized with a 24- to 26-mm Hegar sizer.[14]

Since July 2001 we have systematically introduced the use of a mannequin (TRISVR; Chase Medical, Richardson, Tex) filled at 50 to 60 mL/m^2 to optimize size and shape of the new ventricle. The technique is a refinement of the Dor technique and allows standardizing the procedure. The mannequin is useful when the ventricle is not very enlarged (to reduce the risk of too small a residual cavity) or when the infarcted region is not clearly demarcated, as occurs in dilated cardiomyopathy (type III silhouette, as described by Strobeck and associates[15]). In this circumstance, the transitional zone between scarred and nonscarred myocardium is not well defined and the mannequin allows rebuilding the ventricle in an elliptical way and avoiding sphericalization, which, besides the reduction in size, is the objective of the procedure.

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TABLE 1. Functional and cardiac status changes

	Preop (n = 488)	Early postop (n = 452)	Late postop (n = 300)
EDV (mL)	211 ± 73 (200)	142 ± 50 (136)*	167 ± 60 (153)*†
ESV (mL)	145 ± 64 (131)	88 ± 40 (81)*	104 ± 50 (94)*†
EF (%)	33 ± 10 (33)	40 ± 10 (39)*	39 ± 10 (39)*
MR grade (not repaired)	1.1 ± 0.8 (1)	0.7 ± 0.6 (1)*	1.3 ± 1.0 (1)
MR grade (repaired)	3.0 ± 1 (3)	0.7 ± 0.8 (1)*	1.5 ± 1.2 (1.5)*†
PAP (mm Hg)	36 ± 13 (34)	31 ± 10 (28)	34 ± 13 (30)
NYHA class	2.7 ± 0.9	n/a	1.6 ± 0.7 (1)*

Values are mean ± standard deviation (median). *EDV*, End-diastolic volume; *ESV*, end-systolic volume; *EF*, ejection fraction; *MR*, mitral regurgitation; *PAP*, systolic pulmonary artery pressure; *NYHA*, New York Heart Association; *n/a*, not applicable. *$P < .001$ vs preoperatively. †$P < .01$ vs early postoperatively.

Statistical Analysis

To determine the association between independent risk factors and hospital mortality, we applied the unpaired or paired Student *t* test, analysis of variance, or logistic regression analysis when appropriate. Predictability of the detected independent risk factors was tested by a receiver operating characteristics (ROC) analysis, considering an area under the curve (AUC) of at least 0.7 as predictive, and sensitivity-specificity testing for determination of cutoff values. Long-term survival was analyzed by Kaplan–Meier survival curves, and differences between curves have been tested with a log–rank test. Statistics have been performed with a computerized statistical package (SPSS 11.0; SPSS Inc, Chicago, Ill).

Results

Preoperatively, 278 (57%) of the 488 patients were in NYHA functional class III/IV and 107 (22%) in class IV. Overall, diastolic dysfunction was abnormal in the great majority of patients (96%), with a pattern of abnormal relaxation in 60% of patients, pseudonormal in 21%, and restrictive in 15%.

The great majority had coronary disease suitable for CABG; only 2.8% of the patients had nonsignificant coronary lesions resulting from previous percutaneous transluminal coronary angioplasty. Seventy-two percent had multivessel disease, and CABG was performed in 95% (mean number of anastomoses 2.8 ± 1.4); 92% received a thoracic artery graft on the left anterior descending coronary artery; 50% had patch reconstruction and 50% had a direct suture to close the ventricle. A Q-wave anterior myocardial infarction was present in 66% of patients. MR, graded 1 to 4+ at echo study, was present in 78% of patients; it was mild in the majority of patients and moderate to severe in 79 (18%) of 441; in 47 patients the degree of MR was not assessed. Mitral valve surgery (two mitral replacements) was performed in 18% (90/488); the indication to repair the valve was grade 3/4 regurgitation or grade 2+ regurgitation associated with annulus dilatation (≥40 mm).

Early Outcome

Operative cardiac mortality was 4.7% (55/1161) in the overall consecutive series and 4.9% in the study group (24/488). The main determinants of hospital mortality were severity of MR and the need for mitral valve repair/replacement. Severity of MR (graded 0–4) was significantly associated with hospital mortality at a logistic regression analysis ($P < .001$), and its predictivity was confirmed by a ROC analysis (AUC of 0.81). Patients requiring mitral valve repair/replacement had a significantly higher (13% vs 3.0%; $P < .001$) operative mortality rate.

Cardiac function improved postoperatively and the degree of MR significantly decreased (Table 1).

Late Outcome

Clinical follow-up was completed in 95% of the entire population (average follow-up 56 ± 48 months). Figure E1 shows Kaplan–Meier long-term survival curve.

NYHA class improved from 2.7 ± 0.9 to 1.6 ± 0.7 ($P < .001$). Repaired moderate-to-severe MR (>2+) decreased significantly ($P < .001$) from 3.0 ± 1 to 0.7 ± 0.8 and to 1.5 ± 1.2 at follow-up (time from surgery 6 months to 2 years; Table 1).

Figure 1 shows long-term survival stratified by preoperative characteristics of the study group.

Recent experience (2001–2005). A subgroup of 254 patients (65 ± 9 years) operated on in recent years was prospectively collected and received a comprehensive echo assessment before and after the operation, including risk factors, medical treatment, diastolic function parameters (early-to-late diastolic filling pressure [E/A] ratio, isovolumic relaxation time, and deceleration time), rate of hospitalization, cardiac events, and procedures after surgery.

Cardiac operative mortality in this subgroup was 7.0% (18/254), not significantly different from that of the early experience. Preoperative factors being associated with hospital mortality at univariate analysis are listed in Table 2.

Owing to the relatively low number of events, we tested for predictivity the various factors being associated with hospital mortality at the univariate analysis using a ROC analysis and assuming as cutoff value for predictivity an AUC less than 0.7.

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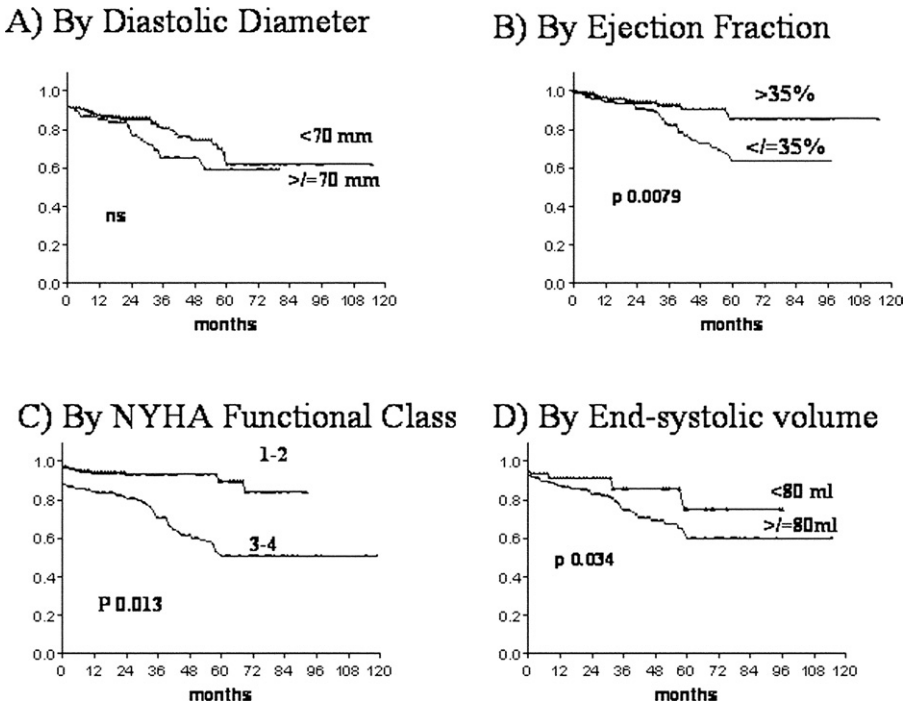

Figure 1. Kaplan–Meier survival curve in patients stratified by preoperative characteristics. A, Diastolic diameter (≥70 mm. <70 mm). B, Preoperative ejection fraction (>35%; ≤35%). C, Preoperative New York Heart Association *(NYHA)* classes I/II and III/IV. D, Preoperative end-systolic volume (>80 mL; ≤80 mL).

The results of this analysis are reported in Table E1. Five variables demonstrated an acceptable level of predictivity: NYHA class, EF, left atrial diameter, E/A ratio, and MR severity. However, we could not determine an adequate cutoff value for EF, which is evidently associated with the hospital mortality risk in a continuous fashion; the left atrial diameter was strongly dependent on the MR severity; finally, the E/A ratio cutoff was settled at a value of 2.0, to avoid the problem of distinguishing between impaired relaxation profiles and pseudonormal patterns. As a result, we maintained in our model three predictive factors for in-hospital mortality: an NYHA class of III/IV, an E/A ratio greater than 2.0, and an MR grade 2 or more. MR alone does not significantly increase operative mortality risk; conversely, if associated with NYHA class III/IV, it determines a significant ($P = .03$) increase of the mortality risk; if a severe diastolic dysfunction is also present, the risk is further ($P < .001$) increased (Figure 2).

Follow-up (20 ± 10 months) was 100% complete in this subset of patients. Forty-four patients (18%) of 232 survivors had cardiac hospitalization during the entire period of follow-up. The most frequent causes of hospitalization were progressive HF (18/44), cardiac arrhythmias (8/44), unstable angina (3/44), and stroke (1/44). Five (2.3%) of 215 patients (for whom procedures during hospitalization were available) had implantation of an internal cardioverter device, coupled with biventricular pacing in 2; 4 more patients had biventricular pacing alone, for a total of 6 (2.8%) patients with biventricular pacing; 3 patients received percutaneous transluminal coronary angioplasty. Overall, 82% of patients did not need hospitalization after surgery.

TABLE 2. Factors associated with hospital mortality at the univariate analysis (subgroup of 254 patients)

Factor	Survived	Dead	*t*	*P* value
QRS duration (ms)	110 ± 25	129 ± 33	3.04	.003
Hemoglobin value (mg/dL)	13.4 ± 1.6	12.4 ± 1.9	2.71	.007
NYHA class	2.4 ± 0.7	3.0 ± 0.6	3.89	<.001
Ejection fraction	0.33 ± 0.08	0.27 ± 0.1	3.13	<.002
Left atrial diameter (mm)	43 ± 8	50 ± 5	2.82	<.005
Mitral flow E/A ratio	1.1 ± 0.7	2.1 ± 1.4	4.25	<.001
Diastolic pattern (graded 0–3)	1.4 ± 0.7	1.9 ± 1.1	2.07	<.04
Mitral regurgitation (graded 0–4)	1.3 ± 1.2	2.5 ± 1.3	4.11	<.001

NYHA, New York Heart Association; *E/A*, early-to-late diastolic filling pressure.

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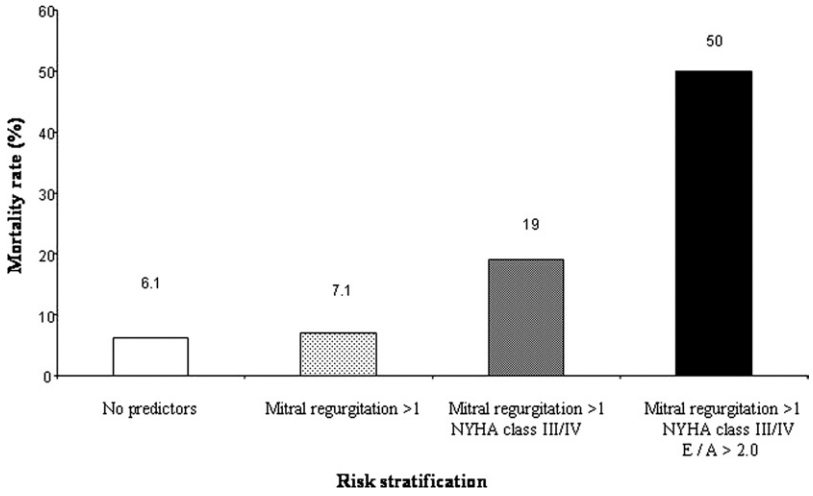

Figure 2. Risk stratification for operative mortality based on our predictive model (see text). *NYHA*, New York Heart Association; *E/A*, early-to-late diastolic filling pressure.

Patients with depressed LV function. A group of 301 (62%) of the 488 patients had a preoperative EF of 35% or less; baseline clinical and hemodynamic characteristics are reported in Table E2.

Cardiac operative mortality was 6.6% (20/301). Causes of operative cardiac death were low cardiac output in 14, intractable ventricular arrhythmias in 4, sudden death during rehabilitation in 1, and acute thrombosis of the graft in 1. Table 3 shows cardiac function and clinical status before, early postoperatively, and late postoperatively. Volume, EF, and NYHA class improved significantly after surgery; the degree of preoperative moderate-to-severe MR decreased significantly. We compared this group of patients with failing ventricles with the 187 patients with LV dilatation (end-diastolic volume index = 100 ± 36 mL/m^2; end-systolic volume index = 58 ± 20 mL/m^2) and preoperative EF greater than 35% whose main indication for surgery was need for coronary revascularization. We found that patients with better pump function benefit less from SVR: EF was 43% ± 6% preoperatively and changed to 45% ± 10% early postoperatively ($P < .02$) and to 44% ± 8% late after surgery ($P < .10$). Operative cardiac mortality rate was 2.1% (4/187) (χ^2 test $P < .02$).

Discussion

The present article describes the largest single-center series of patients with anterior SVR, and it is the largest that extends follow-up observation beyond 5 years.

Major findings from our results are as follow: (1) Significant volume reduction and improvement in EF are observed at the predischarge echo evaluation, and this improvement is still significant at late follow-up, despite a slight but significant increase in volumes and in MR, in respect to early after surgery. The late increase in volume could be ascribed to loading conditions that are lower when the patient is hospitalized, at rest. (2) Clinical status, as evaluated by NYHA functional class, is significantly improved. (3) Eighty-two percent of patients are free from cardiac rehospitalization. (4) Very few patients required an internal cardioverter device and biventricular pacing implantation. (5) Long-term survival is promising also in patients with depressed cardiac function and high functional class.

The Biomechanical Model of HF

In a recent article Mann and Bristow[4] described the concept of a biomechanical model for HF to explain the progression

TABLE 3. Preoperative and postoperative (early and late after surgery) hemodynamic and functional data in patients with preoperative EF ≤ 35% (median)

	Preop	Early postop	Late postop	*P* vs basal	*P* vs postop
Diast Diam (mm)	66 ± 9 (67)	61 ± 9 (62)	64 ± 10 (65)	.0001	.004
Syst Diam (mm)	54 ± 11 (55)	51 ± 10 (52)	52 ± 12 (52)	.0003	NS
EDV (ml)	235 ± 73 (224)	154 ± 52 (146)	180 ± 67 (169)	.0001	.001
ESV (ml)	173 ± 62 (161)	100 ± 41 (93)	117 ± 45 (112)	.0001	.0002
EF (%)	27 ± 6 (28)	36 ± 9 (36)	36 ± 9 (35)	.0001	NS
NYHA class	2.8 ± 0.8 (3)	n/a	1.6 ± 0.6 (2)	.0001	—
Degree of MR (≥3+)	3.6 ± 0.5 (4)	0.8 ± 0.9 (1)	1.7 ± 1.2 (1)	.0001	.0001

EF, Ejection fraction; *Diast Diam*, diastolic diameter; *Syst Diam*, systolic diameter; *EDV*, end-diastolic volume; *ESV*, end-systolic volume; *NYHA*, New York Heart Association; *MR*, mitral regurgitation; *n/a*, not available; *NS*, not significant.

of HF independently of the neurohormonal status of the patient. According to these authors, our current neurohormonal models fail to completely explain disease progression in HF. Current medical therapy acting against neurohormonal activation tends to slow progression but fails to arrest the process of remodeling. In addition, many types of neurohormonal inhibition proved to be ineffective or even harmful in patients with HF.[16] To explain failure of neurohormonal antagonism, the authors focus on LV size and geometry abnormalities as responsible for progression of the disease. Geometric changes lead to structural abnormalities of the myocytes and of the myocardium, which worsen cardiac function and increase neurohormonal activation; this may make the cardiovascular system less responsive to normal homeostatic control mechanisms.

Therapeutic strategies designed to interrupt the vicious cycle will favorably affect the HF phenotype and the natural history of HF progression according to Mann and Bristow.[4] SVR is a surgical strategy that reduces LV volume, improves geometry, and relieves ischemia.[5-7,11,13]

Our patients are left on HF medical therapy after surgery (94% are receiving diuretics, 81% angiotensin-converting enzyme inhibitors, 34% beta-blockers, and almost all are receiving acetylsalicylic acid). In our common practice it is frequent to observe that some patients do clinically better than could be expected from cardiac function status, and this mismatch could be explained on the basis of the biomechanical model of HF in that SVR may not only revert the remodeling process but also may make the cardiovascular system more responsive to treatment and to neurohormonal activation, once dimensions and geometry have improved.

Aneurysm Repair or HF Surgical Therapy?

SVR as described by Dor and associates[10] was developed as a more physiologic repair of LV aneurysm, compared with simple linear repair,[9,17] but along with time and experience it was applied also to dilated ischemic cardiomyopathy, without the classic signs of the true aneurysm, that is, a severe distortion of the chamber with a discrete lesion, most often dyskinetic. In ischemic dilated cardiomyopathy, the demarcation of the ischemic/necrotic lesion is no longer present and the curvature of the ventricle is flattened not only at the apical level but also at the basal portions.[15] In our early experience we mainly treated patients with true aneurysm, but more recently, ventricles that exhibit dilated ischemic cardiomyopathy are more frequently encountered. Ischemic dilated cardiomyopathy is the result of more severe damage of the entire chamber, including damage in the remote zones, as the remodeling process progresses and is associated with more severe hemodynamic abnormalities (higher pulmonary pressure, higher volumes, lower EF, more frequent MR). Moreover, in our more recent experience, patients are significantly older and have more comorbidities, and we have increased the number of mitral repairs (it was 5% in the early experience and it is now 18%), which translates into higher risk patients.

It has been known for many years that a true aneurysm can be successfully treated with surgery, and the European guidelines for diagnosis and treatment of HF give indication for LV aneurysmectomy in patients with large, discrete LV aneurysm in whom HF develops.[18] However, the new challenge is to treat patients with dilated ischemic cardiomyopathy, and we think that SVR should be regarded as a viable option in modern interventional treatment of HF and not only as an aneurysm repair technique.

Surgical Technique

SVR is not a standardized technique. According to Dor and colleagues,[19] the use of a patch is mandatory, and more recently they introduced the use of a sizer; Caldeira and McCarthy[20] use a double purse-string suture technique; Mickleborough and associates[8] use a linear closure and septoplasty, sometimes with a patch, and it is difficult to say which other ways of rebuilding the LV are in the hands of surgeons. We think that the technique should be standardized to compare the results and to find the best way to treat patients with HF. We have been using a sizer and shaper since 2001 in all our patients, and we think that the device is helpful to standardize the procedure, reducing the risk of restriction and of sphericalization of LV chamber.

Mitral Repair

Functional MR is frequently associated with postischemic ventricular dilatation, and its presence worsens prognosis.[21] At present, it has not been established whether, when, and how the mitral valve should be repaired during SVR. The presence of moderate-to-severe MR and its surgical repair carries a higher operative risk in our study group. It is difficult to distinguish whether the higher mortality is due to the surgical procedure per sè, because patients with MR have worse clinical and hemodynamic conditions. In the most recent series, MR alone (≥2+) did not increase the in-hospital mortality risk; conversely, if associated with NYHA class III/IV and with severe diastolic dysfunction, the risk is significantly increased. Our interpretation is that MR becomes a true predictor of hospital mortality only when the LV end-diastolic pressure, and therefore the left atrial pressure, are severely increased (as occurs whenever the E/A ratio exceeds 2.0), leading to congestive HF and severe functional impairment (NYHA class III/IV).

- On the basis of this experience, we consider the following to be the indications for SVR:
- Previous anterior myocardial infarction (either Q or non-Q) as evaluated by electrocardiogram or cardiac magnetic resonance.

- LV dysfunction with dilatation of the ventricle and regional asynergy (either akinetic or dyskinetic). When LV asynergy is severe and diffuse, SVR can be performed only if regions remote from the scar have some degree of contraction detectable at rest or under inotropic stimulus (like dobutamine test).
- HF symptoms are the first indication for SVR, but also patients presenting with ventricular arrhythmias and/or angina who need surgical revascularization represent an indication for SVR (if the previous conditions are present) to avoid further dilatation.
- For patients who are asymptomatic despite postinfarction LV dysfunction, we suggest that serial echocardiographic studies be performed to detect the first signs of deterioration (ie, LV progressive enlargement or decline in EF).

The following are contraindications:

- Severe right ventricular dysfunction (biventricular dilated cardiomyopathy) (absolute).
- Severe pulmonary hypertension not associated with MR (relative).
- Severe regional asynergy without LV dilatation (absolute).
- Restrictive diastolic pattern associated with high functional class and MR (absolute).

When patients have relative or absolute contraindications or when cardiac dysfunction is severe and diffuse, we perform a stress echo dobutamine test. If contractility improves, we perform SVR; if it does not improve and other options such as transplantation are available, heart transplant should be done. However, in some elderly patients when full medical therapy and other devices fail to improve clinical status, SVR can be the only treatment option and both patients and surgeons should be aware of an increased mortality risk.

Conclusions

Our study is observational and not randomized. Collection of data is not uniform, being prospective in a minority of our population, which remains the largest reported until now. The severity of HF was based on NYHA functional class, which has limitations; we did not estimate quality of life, which is critical in this kind of patient with severe HF. We expect the STICH trial to answer all these critical questions.

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Discussion

Dr Andrew S. Wechsler *(Philadelphia, Pa).* This and Vincent Dor's series comprise the two largest observational series from single centers on this operative procedure, at least to my knowledge. Your results in this very challenging group of patients are excellent. I have four questions for you.

First, when I read the manuscript I noted that you used patch closure only in about 50% of the patients. Should I take away the implication that many of these ventricles were not severely dilated, or perhaps that you did the SVR as an incidental procedure when the primary operation was in fact coronary revascularization?

My second question, and I have asked Dr Dor this same question on several occasions, is this. When I did the calculations based on your own data, although there was an important increase in EF, I found little or no increase in stroke volume. Are you

surprised that despite a reduction in end-diastolic volume, there is no increase in stroke volume? Do you think this implies that the primary benefit of the procedure is, in fact, in reducing myocardial oxygen consumption at the same external work level, or is it possible that after the surgery there is, in fact, restricted filling of the ventricles owing to a change in diastolic properties?

I noted that you indicated that pulmonary artery pressure greater than 60 mm Hg was a warning sign to you and that you tended not to operate on those patients, but I did not see within your data any actual calculation of pulmonary artery pressure as a continuous variable associated with enhanced mortality. Maybe you could comment on that.

Finally, in your analysis, MR and increased end-systolic volume both turn out to be predictors of poor outcome and mortality. Did you analyze these as discrete variables, or is the MR just a marker of a more severely dilated ventricle and not really different from ventricular size as a risk factor?

Dr Menicanti. Dr Wechsler, thank you very much for your questions, which are really crucial in this type of procedure. The first question concerns the type of closure that we have to employ. The decision to use or not use the patch is determined by the anatomic characteristic of the ventricle. If the volume of the ventricle is not too big or the transitional zone is distal, the probability to close the ventricle without a patch is high. By contrast, if you have a very big ventricle or if you have calcification of the septum or if the walls of the LV are thick, this condition normally implied the use of a patch. I think that the patch is related to the real anatomic situation of the ventricle. That is an important tool in the decision-making to use a sizer. In effect, since we have started to use the sizer, the number of patches has increased.

Your second question is really more complicated. My idea, and surely I can be wrong, is that there are two possibilities. First, in some patients we have seen, with magnetic resonance imaging, with echo, and with angiograms, that the basal portion presents an increased contractility. Thus there is a hyperkinesia. When we reduce the volume, this portion goes to a normal contractility, and consequently the stroke volume does not change in this particular case. The other possibility is that there is a direct relationship between stroke volume and the preload. This relation is called the *cardiac functional relationship*. The curve increases up to a certain level: at this point, increasing the preload does not increase the stroke volume, and this point represents the limit of the maximal preload reserve. If we decrease the preload, decreasing the volume of the LV cavity, the stroke volume does not change because we are moving in the upper part of the curve. What has changed is the preload reserve; the patient now has a preload reserve. This I think is the reason why the patients do better, because finally they regain preload reserve. In this situation we have improved mechanical efficiency with reduced oxygen consumption for the same external work.

Pulmonary hypertension, as you rightly stated, is not considered as a predictive factor in our analysis. This is determined by the fact that we did not achieve statistical evidence, because for this value in our database there are several missing data. Clinically, we consider pulmonary hypertension a very important predictor of complication after the intervention, but unfortunately we were unable to prove it statistically. We hope that by collecting data in a prospective way in the past 5 years we finally have the data to demonstrate this aspect statistically.

According to MR and dimension, Marisa Di Donato in the American College of Cardiology meeting in 2003 demonstrated a clear relationship between the degree of MR and ventricular end-diastolic volume and shape. Particularly, there is a strict correlation between the transverse diameter and MR. I think MR is the effect of a bigger ventricle, and particularly of a large ventricle that presents an involvement of the inferolateral wall determined either by an extension of an anterior infarction or by a second infarction in this region. This is particularly true when we treat patients who have a double-sided myocardial infarction, an anterior and an inferior. This type of patient, because the distance between the papillary muscles is increased in a very important way, very frequently has MR. This group of patients is very difficult to treat because the quality of the remote myocardium is poor.

Dr John V. Conte, Jr *(Baltimore, Md).* As one of the many surgeons you have allowed to visit you in Milan and to watch you operate, I want to thank you for sharing your wealth of experience. I know I have benefited from it greatly.

My question has to do with the role of ventricular restoration and transplantation in the treatment of end-stage heart disease. Where do you see transplantation in those patients who were in class III or class IV, the highest risk populations, who are potentially candidates for each operation? Probably half of the patients that I operate on are candidates for either operation. When we discuss the risks and benefits and alternatives, it is hard sometimes to provide a good black-and-white answer regarding what operation is appropriate. Can you give us any insight as to how you address that?

Dr Menicanti. Thank you very much. You are perfectly right. If we have a patient who has diastolic dysfunction, MR, NYHA class III or IV, and pulmonary hypertension, we know for sure that our mortality in this group of patients is high, 20% to 25%. It is very difficult to propose a surgical procedure like that to the patient. There is no question that the heart transplant is the best choice. The problem is that the great majority of these patients are at an age that is not suitable for heart transplant. The mean age of our group in the past 5 years is 65 years. Last year 300 transplants were performed in Italy—very few. If the patient is young, there is no question that you have to send them to heart transplant. If the patient is old with comorbidities, I think that this procedure is the only choice that we have.

Dr Robert A. E. Dion *(Leiden, The Netherlands).* We try to follow your example in Leiden, and last year we performed as many as 50 SVRs according to Dor. I just have a short question about the sizing of the residual cavity in the LV. I hear that you recommend sometimes 50, sometimes 60 mL/m 2. I think it is a very important topic because it is probably a determining factor for diastolic function. Could you elaborate on your thoughts about that? When are you using a smaller volume, when are you using a higher volume, and why?

Dr Menicanti. That is a very nice question and not so easy to answer. From a very practical point of view, we use a small volume (ie, 50 mL/m^2) when the basal portion of the ventricle is normal, so that the transverse diameter is almost in the range of normality. When we have a more important dilatation or global dilatation with dilatation also of the basal portion, with the idea to

try to keep the longitudinal diameter more or less double the transverse diameter, we use a bigger size, 60 or 65 mL/m^2 sometimes. The choice of a bigger balloon is determined by dilatation of the basal portion.

Dr David H. Adams *(New York, NY).* Dr Menicanti, can you tell us a little bit more about this mitral valve subgroup in the sense of what percent had primary anterior infarction, how you dealt with that, did you see an increased mortality with replacement versus repair, and did you use annuloplasty or repair all of these from inside the ventricle?

Dr Menicanti. All patients that we are describing in this group had an anterior myocardial infarction. Now, 20% of the patients who are operated on are also operated on for a mitral plasty. I think the mortality in this group of patients is higher because the extension of the infarction is really very important and because the basal portion in this group of patients is not normal. Sometimes there is another infarction in that portion, sometimes there is fibrosis because this situation lasts for such a long time and the myocytes can be transformed into a fibroblast. The fact that we have increased mortality depends, in my opinion, and I can be wrong, on the fact that in this group of patients the residual contractile myocardium is not so good as in the other situation. We have 13% mortality when the mitral valve is approached. In the past 2 years this mortality has decreased, probably because we are just a little better, but it is around 10%. I think that is determined by the quality of tissue that we have. We approach the mitral valve in the great majority of the cases (95%) through the ventricle. When the opening of the ventricle is small and it is difficult to see the valve, we approach through the left atrium, but normally the ventricle that presents MR is a big one.

Dr Robert H. Jones *(Durham, NC).* I congratulate Dr Menicanti, Dr Di Donato, and the others at San Donato on a beautiful observational study, remarkable for including all of your patients and well describing their outcomes into subgroups. One subgroup you did not mention was the 22 patients that during the past 3 years you did choose to randomize into the STICH trial, and you are adding also to the other hypothesis comparing the value of CABG added to medicine in this cohort. Would you share with us, first of all, the differences that made you at equipoise in those 22 patients compared with the others? How did you deal with telling the families and the referring physicians that, on one hand, you are doing the standard operation but in another situation you are willing to randomize? You have taught many of us how to do this operation. We in North America, as we are facing the opportunity to put together a network to do more randomized clinical studies, need to learn from our European colleagues, who enroll more patients into the STICH trial than we have in North America, how to deal with this latter problem. Could you share your insight, please?

Dr Menicanti. Thank you, Dr Jones. This is really a problem for us, because we believe in this procedure. The idea to randomize the patients is sometimes very, very difficult. But what we did is a very simple issue. We know that this procedure is absolutely fantastic when there is a good or a relatively good basal portion, and we know the surgical mortality is really very low. So these are the patients whom I did not randomize. Those whom I randomized were the patients with globally dilated cardiomyopathy, as we have seen in the echo in the beginning of my presentation, in whom I know that the mortality is increased and in whom I have some doubt about the outcome in terms of life expectancy. I randomize patients if I am not sure they are not good candidates. And I explain that to them. Normally, they are in a very bad functional class, all are in full medical therapy, and they understand that their life expectancy is not long. They understand that we are trying to do something to help, and they accept being randomized.

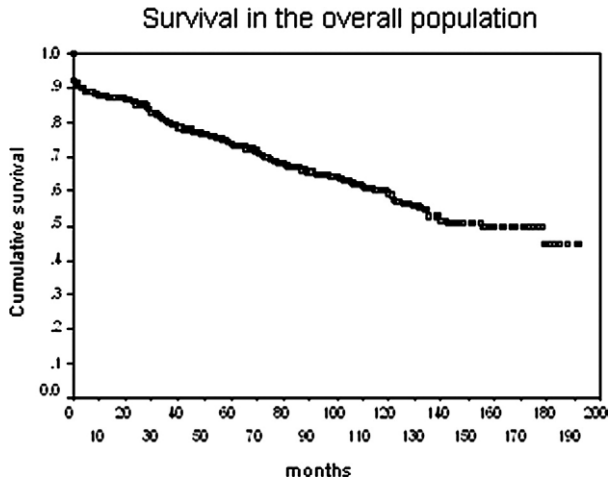

Figure E1. Kaplan–Meier survival curve in the whole population.

TABLE E1. ROC analysis for the factors being associated with hospital mortality at the univariate analysis

Factor	AUC	Cutoff value	Sensitivity	Specificity
QRS duration	0.65	—	—	—
Hemoglobin value	0.65	—	—	—
NYHA class	0.71	3	70%	70%
Ejection fraction	0.72	—	—	—
Left atrial diameter	0.74	50	60%	80%
E/A ratio	0.72	2.0	50%	90%
Diastolic pattern	0.63	—	—	—
Mitral regurgitation	0.74	2	60%	80%

ROC, Receiver operating characteristics; *AUC*, area under the curve; *NYHA*, New York Heart Association; *E/A*, early-to-late diastolic filling pressure.

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TABLE E2. Baseline clinical and hemodynamic characteristics in patients with preoperative EF ≤ 35% (n = 301)

	Count (%)
Age	63 ± 10
M/F	244/57
NYHA class	
I	12 (4)
II	85 (28)
III	132 (44)
IV	69 (23)
Mitral regurgitation	
None or trace	41 (16)
Mild (≤2+)	160 (63)
Moderate (3+)	22 (9)
Severe (4+)	31 (12)
Not assessed	47
LVEF (%)	
N	301
Median	28
Mean ± SD	27 ± 6
LVESV (mL)	
N	229
Median	161
Mean ± SD	173 ± 62
LVEDV (mL)	
N	229
Median	224
Mean ± SD	235 ± 73

LVEF, Left ventricular ejection fraction; *LVESV*, left ventricular end-systolic volume; *LVEDV*, left ventricular end-diastolic volume; *NYHA*, New York Heart Association; *SD*, standard deviation.

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Surgical therapy for ischemic heart failure: Single-center experience with surgical anterior ventricular restoration

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