Non-pharmacological heart failure therapies : evaluation by ventricular pressure-volume loops

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CHAPTER 9

Clinical efficacy of surgical ventricular restoration and restrictive mitral annuloplasty in patients with end-stage heart failure

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Submitted (J Heart Valve Disease)

Oral presentation at the third biennial meeting of the Society for Heart Valve Disease, June 17-20, 2005, Vancouver, Canada

ABSTRACT

Background. Surgical ventricular restoration (SVR) and restrictive mitral annuloplasty (RMA) are increasingly performed for end-stage heart failure. We studied their clinical efficacy in patients with end-stage heart failure.

Methods. We included 33 patients with NYHA class III/IV and left ventricular ejection fraction ≤ 35%. In this group, patients with moderate to severe mitral regurgitation (grade ≥ 2) underwent RMA and patients with anteroseptal aneurysm underwent SVR. A combined procedure (SVR and RMA) was performed in 12 patients, isolated SVR in 5 patients and isolated RMA in 16 patients. Additional coronary artery bypass grafting was done in 27 patients. Clinical parameters, including NYHA classification, Minnesota Quality of Life (QoL) questionnaire, and 6-minute walking distance, were assessed at baseline and 6 months after surgery.

Results. In the total group, operative mortality was 3% (n=1), in-hospital mortality was 9% (n=3), and there was no late mortality. Four patients (12%) needed post-operative intra-aortic balloon pump support. The median duration at intensive care was 4 days (range: 2-28) with a median hospital stay of 13 days (range: 7-49). All clinical parameters were significantly improved at 6 months follow-up ($p<0.001$); NYHA classification was improved from 3.4±0.5 to 1.5±0.5, QoL questionnaire score was improved from 44±22 to 16±12, and 6-minute walking distance was increased from 248±134 to 422±113 m.

Conclusions. Surgical treatment of end-stage heart failure by SVR and/or RMA was associated with 12% mortality at 6 months. Surviving patients showed a highly significant clinical improvement.

INTRODUCTION

Chronic heart failure is one of the major healthcare problems in the world both in terms of patient numbers, hospitalizations, and economic costs. In the United States, 4 to 5 million people have chronic heart failure, which leads to more than 2 million hospitalizations each year.[1] Despite optimal medical therapy, many patients remain severely symptomatic. In these patients, cardiac transplantation remains the most effective surgical therapy with 1-, 5- and 10-year survival rates of 94, 78, and 46%,

respectively.[2,3] Although effective, heart transplantation is importantly hindered by donor shortage, chronic rejection, and complications related to medication.

Given the limitations of medical therapy and cardiac transplantation, alternative surgical therapies such as surgical ventricular restoration (SVR) and restrictive mitral annuloplasty (RMA) have been introduced and are currently widely performed in patients with end-stage heart failure.[4,5] These therapies aim to correct frequently observed end-stage complications as left ventricular aneurysm and mitral regurgitation.[6,7] If not treated, these complications usually have important adverse effects on long-term morbidity and survival.[8-10]

A long-term study by the RESTORE-group has demonstrated that SVR is safe and highly effective in the treatment of ischemic cardiomyopathy with a reduction of end-systolic volume and a five-year survival of 69%.[11] Several studies reported promising results in patients with heart failure treated with RMA with one- and two-year survival rates of 86% and 84%, respectively.[12,13]

In the present study, clinical efficacy was evaluated six months after surgery in a cohort of patients with end-stage heart failure who underwent combined SVR and RMA, isolated SVR or isolated RMA.

METHODS

Patients

We included 33 patients with end-stage heart failure, NYHA classification III or IV with left ventricular ejection fraction ≤ 35%. These patients underwent heart failure surgery for anteroseptal aneurysm and/or moderate to severe mitral regurgitation. Twelve patients had both anteroseptal aneurysm and moderate to severe mitral regurgitation (grade ≥ 2) and they underwent combined SVR and RMA; 5 patients had an anteroseptal aneurysm and underwent isolated SVR (SVR group, n=17). Another 16 patients had severe mitral regurgitation (grade > 2) and no aneurysm and thus underwent isolated restrictive mitral annuloplasty (RMA group, n=16). All patients received stable medical therapy for chronic heart failure, including diuretics, spironolactone, β-blockers, and ACE-inhibitors. The institutional review board approved the study protocol and all patients provided informed consent. Patient characteristics are summarized in table 1.

Table 1. Patient characteristics

Variable	N=33
Gender (M/F)	20/13
Age, yrs	64±12
Etiology (ischemic vs non-ischemic)	29/4
NYHA class	3.4±0.5
Duration of symptoms (median, months)	8 (2-62)
LVEF, %	27±8
Medication:	
- Diuretics/spironolactone	25 (76%)
- Nitrates	7 (21%)
- ACE-inhibitors/A-II antagonists	26 (79%)
- β-blockers	21 (64%)
- Anticoagulants/aspirin	22 (67%)

NYHA, New York Heart Association. LVEF, left ventricular ejection fraction, ACE, Angiotensin Converting Enzyme; A-II, Angiotensin II

Evaluation of mitral regurgitation

In patients with moderate to severe mitral regurgitation (grade ≥2) on transthoracic echocardiography (TTE), additional transesophageal echocardiography (TEE) was performed within 5 days before surgery. The TTE and TEE were performed without general anesthesia to avoid underestimation of the severity of mitral regurgitation. The severity of mitral regurgitation was graded semi-quantitatively from color-flow Doppler in the conventional parasternal long-axis and apical 4-chamber images. Mitral regurgitation was classified as: mild=1+ (jet area/atrial area <10%), moderate=2+ (jet area/atrial area 10-20%), moderately severe =3+ (jet area/atrial area 20-45%), and severe=4+ (jet area/atrial area >45%).[14,15] The severity and precise mechanism of mitral regurgitation was confirmed from the TEE images.

When the severity of mitral regurgitation was grade 2, an intraoperative loading test (as described previously) was performed.[16,17] Briefly, a preload test is performed by rapid infusion of volume through the aortic cannula until the pulmonary artery capillary wedge pressure increases by 15 mmHg. During this provocative test, the severity of mitral regurgitation is continuously monitored, and patients who deteriorated to grade 3 or 4 mitral regurgitation underwent RMA. Immediately after surgery, TEE was repeated to assess residual mitral regurgitation, transmitral diastolic gradient (determined from continuous-wave Doppler), and length of coaptation of the mitral leaflets.

Surgical procedures

SVR was performed by the endoventricular circular patch plasty as previously described by Dor.[18,19] Briefly, the left ventricle was opened through the infarcted area. An endocardial encircling suture (Fontan Stitch) was placed at the transitional zone between scarred and normal tissue. A balloon containing 55mL/m^2 body surface area saline was introduced into the left ventricle and the Fontan stitch was tightened to approximate the ventricular wall to the balloon. An oval dacron patch was tailored and used to close the residual orifice. The excluded scar tissue was closed over the patch to ensure hemostasis. Care was taken to eliminate all septal scar and to delineate a new apex with the goal to restore the normal elliptical shape.

Stringent restrictive mitral annuloplasty (2 sizes smaller than measured) was performed via an atrial transseptal approach using a Carpentier Edwards Physio ring (Edwards Lifesciences, USA) as previously described.[20] Additional coronary artery bypass grafting was performed, if indicated.

Clinical evaluation

Patients were evaluated at the outpatient clinic at baseline and at 6 months after surgery. Heart failure symptoms were classified using the NYHA score. Quality of Life score was assessed using the Minnesota Living with Heart Failure questionnaire.[21] This questionnaire contains 21 questions concerning the patient's perception of the effects of heart failure on daily life activities. Questions are scored from 0 to 5, resulting in a total score from 0 to 105, with the highest score reflecting the worst quality of life. Exercise tolerance was evaluated using 6-minute hall-walk tests at both visits.[22]

Statistics

Baseline and follow-up data were compared with paired t-tests. Statistical significance was assumed at $p < 0.05$. All data are presented as the mean value ± SD.

RESULTS

Mean cardiopulmonary bypass (CPB)-time was 192±64 minutes with a mean aortic cross-clamp time of 132±49 minutes. Weaning from CPB was uneventful in almost all patients. However, in one case a patient developed an irreversible vasoplegic shock after weaning from CPB and died during surgery (3% operative mortality) and four patients

(12%) needed post-operative intra-aortic balloon pump support. There were no peri-operative myocardial infarctions. Three additional patients died in the hospital (9%); one patient who underwent combined SVR/RMA died 30 days postoperatively due to a cerebrovascular accident, one patient (isolated SVR) died 5h postoperatively due to left ventricular failure, and one patient (isolated RMA) died 7 days postoperatively due to left ventricular failure. Early non-fatal complications consisted of postoperative atrial fibrillation (3 patients), cerebrovascular accidents (1 patient), and renal failure (1 patient). One patient developed postoperative sepsis with an empyema in the pleural space, which required surgical evacuation and this patient stayed 54 days at ICU with a total hospital stay of 66 days. For the remaining patients, the median duration at intensive care was 4 days (range: 2-28) with a median hospital stay of 13 days (range: 7-49). In the total group, we had no late mortality during the 6 months follow-up period. Thus, overall mortality in our patient group was 12% at 6 months and complete clinical assessment was performed in the 29 surviving patients.

Mitral regurgitation

The mean grade of mitral regurgitation at baseline in the patients who underwent RMA was 3.0±0.6. The length of the anterior mitral leaflet (AML) was 2.88±0.30 cm with a mean mitral annular diameter (MAD) of 4.08±0.55 cm (mean ratio MAD/AML 1.42±0.18). After surgery, no recurrence of mitral regurgitation was observed in these patients (0.3±0.4) with restored length of leaflet coaptation of 0.82±0.19 cm and a mean gradient of 2.9±1.3 mmHg.

NYHA score

In the total group, the mean NYHA score improved from 3.4±0.5 at baseline to 1.5±0.5 at 6 months follow-up ($p< 0.001$) (Figure 1). In both the RMA and SVR patients the improvements in NYHA score was similar; in the RMA patients NYHA score improved from 3.4±0.5 at baseline to 1.5±0.5 at 6 months follow-up ($p< 0.001$) and in the SVR patients NYHA score improved from 3.5±0.5 at baseline to 1.5±0.5 at 6 months follow-up ($p< 0.001$).

Quality-of-Life Minnesota score

Quality of Life score in the total group at baseline was 44±22 and decreased by 64% to 16±12 at 6 months follow-up ($p< 0.001$) (Figure 1). The change in the total group was

similar to changes in the RMA (-63%) and SVR (-65%) subgroups. In the RMA patients Quality of Life score was decreased from 48±23 at baseline to 18±11 at 6 months follow-up ($p< 0.001$) and this score was decreased from 40±21 at baseline to 14±12 at 6 months follow-up ($p=0.002$) in the SVR patients.

Six-minute hall-walk test

The mean walking distance in the total group of patients was 248±134 m at baseline and improved by 70% to a mean walking distance of 422±113 m at 6 months follow-up ($p< 0.001$) (Figure 1). In the RMA patients the mean distance walked was 238±151 m at baseline and improved significantly ($p <0.001$) to 438±110 m at 6 months follow-up. In the SVR patients, the mean walking distance increased from 258±120 m at baseline to 406±117 m at 6 months follow-up ($p< 0.001$).

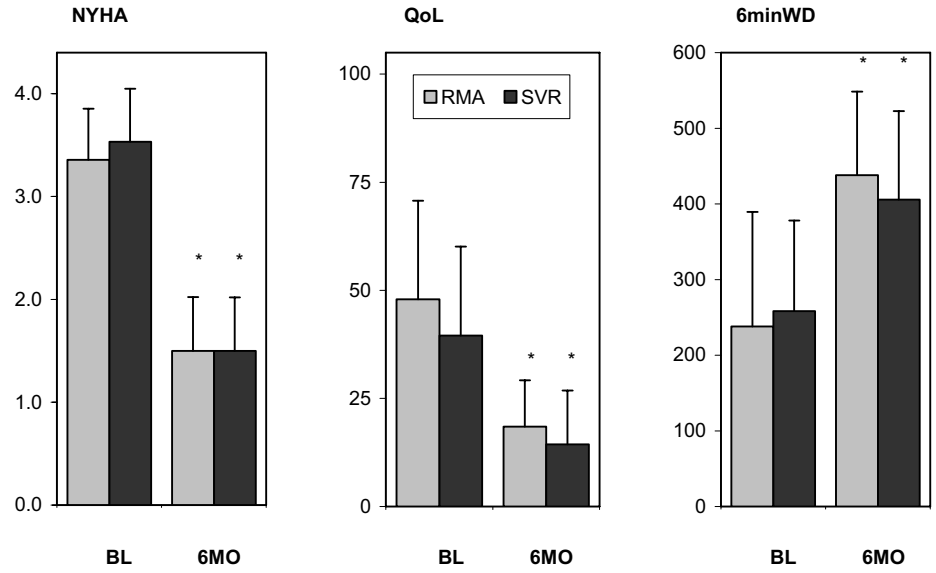

*Figure 1. NYHA classification, quality-of-life (QoL) score, and 6-minute walking distance (6minWD) at baseline (BL) and at 6 months follow-up (6MO) for the RMA and the SVR groups. Significant improvements were observed in all parameters at 6 months follow-up in both groups. No significant differences were found between groups. * p < 0.002 versus baseline*

DISCUSSION

Heart transplantation is now considered standard treatment for select patients with end-stage heart disease; but it is only applicable to a small number of patients. In an effort to address this problem, alternative surgical therapies are evolving, including SVR and

RMA, and other approaches. These operative techniques to alter the shape of the left ventricle, in combination with optimal medical management for heart failure, may improve survival. In some patients it may even avoid or postpone transplantation.

The purpose of the present study was to evaluate the clinical efficacy of these treatments using NYHA classification, Minnesota Living with Heart failure questionnaire, and 6-minute hall-walk test in a cohort of patients with end-stage heart failure who underwent SVR and/or RMA at our institution.

We found that the surgical treatment was associated with 12% mortality at 6 months and resulted in an improvement in symptoms (NYHA class), accompanied by improvement in 6-minute walking distance and Quality of Life score. Our results regarding mortality are in line with the results of Dor et al. who reported 12% operative mortality in 835 patients with end-stage heart failure.[23] Earlier studies by Di Donato et al. indicated a 19% in-hospital mortality and 26% mortality at one-year follow-up.[24] However, the mean left ventricular ejection fraction in Di Donato's group was 17±3%, while the mean ejection fraction in our series was 27±8% and in Dor's group only about 10% of the patients had an left ventricular ejection fraction < 20%. More recently, Qin et al. reported a lower rate of mortality at six months follow-up of 5% in 60 patients who underwent SVR with or without mitral valve repair.[25] Similar findings were reported by the RESTORE group with a 30-day mortality after SVR of 5.3% (8.7% with mitral repair vs. 4.0% without repair).[11] However, in this large patient population, also patients with NYHA classification I/II were included. In all these previous studies, a significant improvement in NYHA classification has been observed at long-term follow-up, which was similar to the improvement found in our series.

The aim of alternative surgical interventions (SVR and RMA) in patients with end-stage heart failure is to reduce left ventricular wall stress leading to reduced oxygen demand, improved mechanical dyssynchrony and mechanical efficiency. These effects may result in improvement of global and intrinsic systolic function. These theoretical assumptions were recently confirmed by hemodynamic studies in patients with end-stage heart failure.[26,27] Operative mortality of both SVR and RMA are acceptable, however long-term results are limited to survival rates, NYHA classification and hemodynamic parameters.[11,12,28] Therefore, it is still relatively unknown whether these therapies lead to improvement of clinical status of the patient. Although previous studies indicate improvement in NYHA classification, to our best knowledge, our study is the first to show that these interventions lead to clinical improvement using 6-minute walking distance and Quality of Life score at 6-months follow-up. Our study did not include a

control group. However, previous epidemiological studies indicate that 1-year mortality rate in class III/IV heart failure patients is around 50%. [29] In comparison, the clinical efficacy of our surgical approach in terms of Quality of Life and 6-minute walking distance appears to be similar to the outcome after biventricular pacing in patients with end-stage heart failure.[30-32]

Limitations

This study represents a single-center experience in a relatively small cohort of patients with a combined surgical approach of SVR and/or RMA. Subgroup analysis did not show statistical differences, but the groups were relatively small and treatment obviously was not randomized. Moreover, this comparison should be taken with caution because, despite similar baseline clinical parameters, the etiology was different between groups.

In conclusion, surgical treatment of end-stage heart failure by SVR and RMA seems relatively safe and surviving patients have clear clinical benefit at six months follow-up. Long-term prospective clinical randomized trials should be performed to assess benefit over optimal medical therapy.

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