Treatment of extensive ischemic cardiomyopathy: quality of life following two different surgical strategies

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Abstract

Objective: To review outcomes and quality of life following two surgical strategies for severe left ventricular dysfunction due to ischemic dilated cardiomyopathy. Methods: Hospital and follow-up records of 111 patients with extensive ischemic cardiomyopathy (mean age 57.3 ± 8.4) referring to our institution between January 1996 and December 2003 were reviewed. Group A included 42 patients (mean age 62.4 ± 7.9) with morphological and functional cardiac parameters allowing for ventricular restoration (including endoventricular circular patch plasty, coronary artery by-pass grafting, and, when needed, mitral surgery). Group B included 69 patients (mean age 54.3 ± 7.2), undergoing cardiac transplantation. Hospital mortality, treatment-related late mortality, incidence of cardiac events, freedom from cardiac failure, freedom from hospital re-admission, functional recovery at follow-up (3075.2 pts/months; 100% complete) and quality of life (WHOQOL test) were assessed. Results: Hospital mortality was 19% in group A and 8.7% in group B (\(P = 0.143\)). No treatment-related late deaths were observed in group A, while six deaths (9.5%) occurred in group B (\(P = 0.063\)). Incidence of cardiac events was comparable. At 60 months, freedom from cardiac failure was 93.5 ± 0.04 and 86.2 ± 0.05\%, respectively (\(P = 0.23\)), freedom from hospital re-admission was 93.5 ± 0.04 and 61.3 ± 0.07\% (\(P = 0.002\)). Exertion dyspnea was present in 40\% patients in group A versus 13\% in group B (\(P = 0.006\)). WHOQOL test showed a satisfying quality of life in both groups, although patients undergoing restoration reached higher scores in the psychological and social domains. Conclusions: Selected patients with ischemic cardiomyopathy, potentially eligible for transplantation, can be managed by ventricular restoration. In those patients post-operative quality of life is satisfactory, with comparable survival and low risk of re-hospitalization.

Keywords: Ischemic cardiomyopathy; Ventricular restoration; Heart transplantation; Quality of life

1. Introduction

Surgical treatment of ischemic left ventricular dysfunction continues to represent a challenge with an ever-increasing patient population presenting with congestive heart failure. Limitations in organ procurement severely restrict the use of heart transplantation, making listing criteria increasingly selective and supporting the development of new surgical approaches for selected patients. In those with viable myocardium revascularization effectively improves symptoms and quality of life. A growing body of knowledge supports the concept of surgical ventricular restoration, a strategy including various techniques that, since Dor’s pioneering experience [1], have been increasingly advocated whenever significant myocardial scarring has occurred. The relative merits, indication and durability of these procedures are under intense investigation. The evidence that the patient population corresponding to the diagnosis of ischemic cardiomyopathy, includes different subsets possibly amenable to different therapeutic strategies, has argued in our experience in favour of the development of a tailored approach. In particular, some patients present with echocardiographic and angiographic features allowing for ventricular restoration procedures, while others are judged to be treatable only with heart transplantation. In the present paper the results of a tailored approach to ischemic cardiomyopathy were reviewed, with special attention to post-operative quality of life parameters in patients who presented echocardiographic features allowing for ventricular restoration and in others undergoing heart transplantation.
2. Materials and methods

2.1. Study design

This is a single centre retrospective study analysing the experience over 7 years with surgical treatment of ischemic cardiomyopathy. From January 1996 and December 2003, 283 patients were operated on for ischemic cardiomyopathy at the Department of Cardio-Thoracic Sciences, Second University of Naples, ‘V. Monaldi’ Hospital. One hundred-seventy-two ischemic cardiomyopathy patients were excluded: 155 because they underwent only myocardial revascularisation with or without mitral surgery having an end systolic ventricular volume index (ESVI) <50 mL/m² and viable revascularizable myocardium; 17 because they underwent urgent heart transplantation or mechanical circulatory assistance. Inclusion criteria for the present study were end-stage ischemic cardiomyopathy, defined according to Burch and colleagues [2], ESVI of ≥50 mL/m² and an ejection fraction ≤35%. Patients with isolated lateral or posterior wall aneurysm were not considered in the definition of ischemic cardiomyopathy.

The analysis included 111 patients of both sexes (85 males and 26 females), between 38 and 76 years of age (mean age 57.3 ± 8.4), divided into two groups. Group A included 42 patients (mean age 62.4 ± 7.9 years; 26 female) who were managed with ventricular restoration procedures (including endoventricular circular patch plasty, coronary artery by-pass grafting and mitral repair). Group B included 69 recipients of orthotopic cardiac transplantation (mean age 54.3 ± 7.2 years; 10 female).

2.2. Patient-procedure matching criteria

Choice of surgical treatment was based on morphological and functional cardiac parameters. In particular, as authoritatively outlined by Dor [3]: (a) severely depressed rightventricular function, (b) lack of ischemic areas suitable for revascularization, (c) lack of contraction improvement of basal segments during echo-dobutamine contraindicated surgical reshaping leaving transplantation as the only possible therapeutic option. Age proved a relative contraindication to heart transplantation given the shortage of organ disposition and the likelihood of decompensation during the waiting time.

2.3. Surgical procedures

All the restoration procedures were performed by means of a median sternotomy using a normothermic cardiopulmonary bypass, aortic cross clamp and myocardial protection by means of warm blood cardioplegia. The strategy included: (a) endoventricular patch plasty according to the Dor’s technique or its modified versions; (b) correction of mitral valve regurgitation by means of annuloplasty and/or valvuloplasty, according either to Bolling or Alfieri’s techniques (14.3%); (c) coronary bypass grafting, in order to achieve the maximal possible completeness of revascularization (38 patients: mean number of grafts 2.36 ± 0.67). In patients with preoperative ventricular arrhythmias (14.3% of the entire group), extensive circumferential endocardial resection according to Harken was performed without intraoperative mapping in the early phase of our experience, while since 2002, mapping-guided cryoablation was performed [4]. Prophylactic intra-aortic balloon counterpulsation was instituted soon before induction of anesthesia in those patients with more pronounced preoperative signs of congestive heart failure (23.8% of the entire group). Such approach aimed to grant hemodynamic stability during the early stages of the procedure and to prevent low postoperative cardiac output. Follow-up management was performed by our outpatient clinic physicians. Patients were maintained on an optimised regimen for treatment of heart failure that included use of β blockers and angiotensin-converting enzyme inhibitors.

As far as heart transplant procedure is concerned, donor heart procurement was performed with standard technique. Heart were protected with 2 L of cold (4–8 °C) Celsior solution and topical saline slush. Excised grafts were then immersed in 1 L of cold Celsior solution and stored under ice in closed cardiac storage container for transportation. All recipients underwent standard orthotopic transplantation using the atrial anastomotic technique. Principles of post-transplant care have been described elsewhere [5].

2.4. Quality of life assessment

All patients filled in a short Italian version of the World Health Organization Quality of Life Questionnaire [6]. The WHOQOL-BREF produces a quality of life profile. It is possible to derive four domain scores. There are also two items that are examined separately: question one asks about an individual’s overall perception of quality of life and question two asks about an individual’s overall perception of his/her health status. The four domain scores denote an individual’s perception of quality of life in each particular domain (physical, psychological, social, and environmental). Domain scores are scaled in a positive direction (i.e. higher scores denote higher quality of life). Raw scores were converted into a 0–100 scale according to the specific guidelines [7].

2.5. Follow-up and statistical analysis

All preoperative and hospital data of patients undergoing surgical procedures in our department have been recorded prospectively in a computerized archive since 1990. Information regarding follow-up was obtained for all hospital survivors and was 100% complete. Data were collected either through outpatients clinic reports (100% for the heart transplant recipient group; about 80% for the ventricular restoration group) or by telephone interview with the patients or the referring physician. Hospital mortality was defined as death within the 30th post-operative day. Treatment-related late mortality was defined as cardiac death in the restoration group and cardiac deaths (due to acute or chronic rejection) or immunosuppressive therapy related deaths (infections, PTLD and malignancies). In group A post-operative angina or acute myocardial infarction along with major arrhythmias and cardiac decompensation represented major cardiac events. Acute rejection >2 and clinically significant graft vasculopathy represented major
cardiac events in group B. SPSS software (version 10.1; Chicago, IL, USA) was employed for statistical analysis. Data were expressed as mean ± SD or counts and percentages when appropriate. Differences in categorical variables were compared by means of the χ² Pearson’s test or Fisher’s exact test. Continuous variables were analyzed with two-tailed Student’s t-test. Incidence of post-operative events were presented as absolute frequencies and linearized rates (%/pts/months) and compared with the likelihood ratio test. Actuarial survival, freedom from re-hospitalisation and from cardiac failure were calculated with the product-limit method. Comparisons between groups were performed with the log-rank test. Statistical significance was defined as P < 0.05.

3. Results

3.1. Preoperative clinical characteristics

Table 1 presents the preoperative clinical and demographic features of patients population. Those offered orthotopic transplantation proved significantly younger, reflecting the age restriction of transplant candidacy. Study groups proved homogeneous as regards sex, NYHA class, left ventricular ejection fraction, ventricular dimensions, presence and degree of mitral regurgitation along with mean time from diagnosis to surgery, incidence of diabetes and peripheral vascular disease and percentage of prior myocardial revascularization.

3.2. Post-operative clinical data and hospital mortality

Table 2 presents early post-operative clinical data and outcomes. A significant difference emerged as to mean post-operative intensive care length of stay and IABP support, with more complicated perioperative course in the restoration group (see incidences of low cardiac output syndrome). No significant differences between the groups emerged in terms of incidence of renal failure, prolonged mechanical ventilatory support and revision for bleeding. Hospital mortality, despite the relevantly higher incidence in the restoration group, did not show statistically significant differences between the two treatments. Causes of death after ventricular restoration were: low cardiac output in 4 patients, refractory ventricular arrhythmias in 4 patients (all had been operated on before the introduction of intra-operative mapping). Post-transplant deaths were due to acute graft failure in 3 patients, multiorgan failure in 1, pneumonia in 1 and encephalitis in 1.

3.3. Delayed outcomes

Mean follow-up time was 31.7 ± 24.8 months (range 2–90.5) without inter-group differences (group A: 33.1 ± 27, group B: 30.9 ± 23.7). Actuarial survival is shown in Fig. 1. Five-year survival was 87.5 ± 0.11% in group A, 79.4 ± 0.07% in group B (P = NS). No death for treatment-related causes was observed in group A (Table 3), while 6 treatment-related deaths (9.5%) were detected in group B (P = 0.063). Indeed 1 ventricular restoration patient died for...
cyrrhosis. Deaths in the transplant group were due to acute rejection (1 case), chronic rejection (1 case), pancreatitis (1 case) and infections (3 cases); as regards nontreatment-related deaths, 1 was due to cyrrhosis, 1 to stroke. Total number of cardiac events was comparable with a linearised rate of 0.35%/pts/months in group A and 0.41%/pts/months in group B (P < 0.894). At 60 months, freedom from cardiac failure (Fig. 2) was 93.5 ± 0.04 and 86.2 ± 0.05%, respectively, in group A and B (P < 0.23), while freedom from hospital re-admission (Fig. 3) was 93.5 ± 0.04 and 61.3 ± 0.07% (P < 0.002).

3.4. Functional recovery and quality of life

In the ventricular restoration group, there was a significant improvement in all of the left ventricular geometric and functional parameters. No moderate or severe mitral insufficiency was echocardiographically detected in the restoration group. Echocardiographically detected post-transplant graft function was satisfactory, while moderate to severe tricuspid insufficiency emerged in 3.6% of the subset. At the time of follow-up 48 (87.3%) transplanted patients were in NYHA class I, 7 (12.7%) in NYHA class II, while 20 patients (60.6%) from group A were in NYHA class I, 13 in II (39.4%) (P < 0.005). Quality of life assessment through the WHOQOL-BREF was performed in all the survivors. Score analysis indicates that both approaches imply a significant benefit, even though patients undergoing restoration seem to perform better. Indeed orthotopic heart transplantation patients generated higher scores only in the domain of physical capacity, while ventricular reshaping patients in the psychological and social relationship domains. The two strategies provided similar environmental benefits. Table 4 summarises quality of life analysis.

4. Discussion

This retrospective review aiming to assess outcomes and quality of life of patients affected by ischemic cardiomyopathy treated either with heart transplantation or left ventricular restoration strongly supports the evidence that a variety of surgical strategies are available, that are comparably effective for treatment of ischemic cardiomyopathy. Indeed, the most important findings of this study are: (a) better hospital outcomes in the transplantation group, as expected; (b) low rates of treatment-related deaths in the follow-up and gratifying freedom from re-hospitalisation in survivors from the ventricular restoration group; (c) a stable functional recovery leading to a good quality of life in both groups.

Due to the aging of population and the successfulness of emergency interventions, the burden of ischemic dilated cardiomyopathy is emerging as the major etiologic factor in the increasing public health problem of heart failure. Cardiac transplantation continues to be an extraordinarily important therapeutic option for selected patients. Nonetheless, limitations with organ supply, along with medical and social issues restrict the use of this strategy. The improvement in the medical management and in the outcomes of other surgical procedures have changed

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Table 3

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>Group A</th>
<th>Group B</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean follow-up time (months)</td>
<td>31.7 ± 24.8 (range 2-90.5)</td>
<td>33.1 ± 27 (range 2.8-90.5)</td>
<td>30.9 ± 23.7 (range 2-86.6)</td>
<td>NS</td>
</tr>
<tr>
<td>Total follow-up time (months)</td>
<td>3075.20</td>
<td>1130.34</td>
<td>1944.86</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total deaths</td>
<td>9/97 (9.3%)</td>
<td>1/34 (2.9%)</td>
<td>8/63 (12.7%)</td>
<td>0.063</td>
</tr>
<tr>
<td>Treatment-related deaths</td>
<td>6 (12.4%)</td>
<td>6 (9.9%)</td>
<td>0.063</td>
<td></td>
</tr>
<tr>
<td>Sudden</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Acute rejection</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Chronic rejection</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Neoplasm</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Infection</td>
<td>3</td>
<td>3</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Others</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Not treatment-related deaths</td>
<td>3</td>
<td>1</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Total cardiac events</td>
<td>12 (0.39%/pt/month)</td>
<td>4 (0.35%/pt/month)</td>
<td>8 (0.41%/pt/month)</td>
<td>NS</td>
</tr>
<tr>
<td>Recurrence of angina</td>
<td>2</td>
<td>2</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Recurrence of CHF</td>
<td>2</td>
<td>2</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Late OTx</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Acute rejection</td>
<td>7</td>
<td>7</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Chronic rejection</td>
<td>1</td>
<td>1</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Re-OTx</td>
<td>-</td>
<td>-</td>
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</tbody>
</table>
the scenario and the therapeutic challenge today is to choose the most appropriate strategy for each patient.

Other studies have recently focused on the critical role of decision making in end-stage coronary artery disease and compared outcomes of heart transplantation and conventional approaches [8]. Cope and co-workers, comparing in-hospital costs and early outcome, concluded that non-transplant surgery yields comparable early outcomes, being markedly less expensive. In addition they noted that transplantation does not confer any long-term survival benefit in patients with ischemic cardiomyopathy [9]. In our experience, the risk of hospital mortality in the restoration group resulted to be more than twice the risk in the other group, although this difference did not result significant, due to the low numbers. This is partly explained by the older mean age of group A patients. It has been already found that longer time to surgery after myocardial infarction, its posterior location, lower preoperative left ventricular ejection fraction, higher pulmonary artery occlusive pressures, and significant mitral regurgitation negatively affect left ventricular remodelling, the possibility for successful surgical restoration, and clinical outcomes [10–13]. In this perspective, the high hospital mortality rates in this series may also reflect a selection bias, as well as the ‘learning curve effect’ of our staff. However, treatment-related complications and deaths in the follow-up occurred in the transplant group at higher rates than in patients undergoing ventricular restoration. All in all, at mid-term follow-up the survival benefit offered to the two patient groups seems nearly equal. Lower post-operative morbidity and mortality in patients undergoing ventricular restoration is expected when a more aggressive approach is adopted, with respect to surgical timing and use of associated procedures for arrhythmias and secondary mitral regurgitation [1,3,10]. In-depth knowledge of the multifactorial pathophysiology of post-ischemic remodelling has stressed the need for a tailored surgical approach suggesting that a combination of multiple techniques fare better than isolated procedures and that adequate post-operative medical therapy is a main stem [14,15]. Long term fate of survivors in the restoration group may be strongly influenced by concomitant revascularization procedures, that, when feasible, was routinely a part of the strategy in this study.

Several studies addressed the long term outcomes of heart transplant in the setting of ischemic cardiomyopathy as compared to other aetiologies [16,17]. Actuarial survival for this patient subset proved poorer and this discrepancy increased with time after transplant. More, ischemic recipients were more functionally impaired, displayed an higher NYHA status, and experienced a significantly higher incidence of transplant coronary disease, also reflecting in higher risk of 1 and 5-year mortality [18]. In the present study, among post-operative outcomes of transplantation, chronic rejection was defined as clinical manifestation of coronary allograft vasculopathy with moderate-severe functional impairment, excluding early signs of graft vasculopathy without cardiac failure. This accounts for the relatively low incidence of total cardiac events after transplantation for a group of ischemic cardiomyopathy patients, 36 and 10% of whom had, respectively, diabetes and peripheral vascular disease.

Although the two surgical strategies compared in the present study are not actually ‘alternative’, since patients undergoing transplant were considered unsuitable for any other surgical therapy, almost all patients receiving ventricular restoration could have been offered heart transplant as well. After the present study’s results, it is expected that they would have not experienced markedly better results in terms of clinical outcomes and of quality of life. Although medical therapy can nowadays allow for a prolonged pre-operative period of relative compensation, clinical outcomes of ventricular restoration could further improve, provided earlier surgical indications will be considered [1,10]. Given the above mentioned shortage of donors and the greater sanitary burden entailed by transplantation, the resulting message is that a tailored approach seems rationally justified, implying accurate screening of patients with ischemic cardiomyopathy with focus on features indicating ventricular restoration.

### Table 4

<table>
<thead>
<tr>
<th>WHO domain</th>
<th>Group A</th>
<th>Group B</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical capacity</td>
<td>56 ± 10</td>
<td>63 ± 5</td>
<td>0.01</td>
</tr>
<tr>
<td>Psychological</td>
<td>58 ± 6</td>
<td>55 ± 11</td>
<td>0.02</td>
</tr>
<tr>
<td>Social relationship</td>
<td>63 ± 10</td>
<td>57 ± 8</td>
<td>0.007</td>
</tr>
<tr>
<td>Environmental</td>
<td>65 ± 5</td>
<td>63 ± 10</td>
<td>NS</td>
</tr>
</tbody>
</table>

Fig. 2. Actuarial freedom from cardiac failure in the follow-up in patients with ischemic cardiomyopathy undergoing ventricular restoration (group A) and in those undergoing heart transplantation (group B).

Fig. 3. Actuarial freedom from new hospital admissions in the follow-up in patients with ischemic cardiomyopathy undergoing ventricular restoration (group A) and in those undergoing heart transplantation (group B).
Indeed, a significantly higher number of patients in group A were in NYHA class II when compared to group B, even though the finding of post-operative functional class improvement was a constant observation also in the restoration group. However, NYHA class is an incomplete, subjective and scarcely reproducible parameter for quality of life assessment. The lower freedom from re-admission to hospital in the transplant group clearly reflects the higher incidence of early acute events requiring specialist assistance, when compared to ventricular restoration patients, who generally require more cardiologic medical therapy, but only ambulatory consultations. One of the most important indicators of the success of a therapeutic intervention for the failing heart is its impact on the patients’ quality of life. Indeed, together with outcome measures of survival, morbidity and physiologic response, quality-of-life benefits have to be factored in the decision making phase of surgical management. The WHOQOL-BREF has good discriminative capacity, content validity, internal consistency and test-retest reliability. It has been validated in other studies of chronic illness as well as in comparing heart transplantation to alternative surgical strategies [19]. In the present series, both the approaches effectively improved perceived quality of life in properly selected patients. Better physical scores in the transplant recipients confirm the major and more uniform increase in functional status reported above. Drawbacks of the substitutive strategy (namely higher psychological stress, deteriorated self image, and anxiety) affect the psychological and social relation scores. The comparable results in the environmental domain are to be considered gratifying, in the light of the significantly older age in the restoration group.

4.1. Study limitations

Present study suffers from the potential limitations of any retrospective analysis and from the smallness of the two unbalanced sample groups. Nevertheless, the retrospective nature of the study limited the uniformity of the reported series only in terms of surgeons’ technical experience and knowledge of the correct indications and contraindications, that was still an ongoing issue. On the contrary, nonrandomized design is maybe obligatory in this setting: patients eligible for heart transplantation strongly differ from those susceptible of surgical restoration as to stage of the disease and echocardiographic preoperative features. Beside the defining criteria of ventricular end diastolic volume and ejection fraction, as stated in the method section, other factors, such as viability of basal segments and potential for remodelling differentiated one group from the other and those differences could not have been ignored even in an hypothetical prospective trial, for the sake of the intention to treat.

4.2. Conclusions

Ventricular restoration procedures proved in a mid-term follow-up a valuable tool in the treatment of patients with extensive ischemic cardiomyopathy. If treated by heart transplantation, these patients are likely to experience higher rates of re-hospitalization, even though with a risk of hospital mortality that is by trend lower. In the mid-term ventricular restoration provides a significant improvement in cardiac function allowing for a satisfactory quality of life. A comprehensive surgical approach combining multiple techniques tailored to address all pathophysiologic factors of the individual patient is crucial.

References

Appendix A. Conference discussion

Dr L. Menicanti (Segrate, Italy): I think that this is a really very interesting paper that demonstrates that the restoration of the left ventricle in terms of life expectancy and quality of life can challenge the heart transplant that was considered the gold standard for this type of patient. Surely, as Professor Cotrufo stressed, the hospital mortality is higher, but the age of the two groups is very different. So I think that this paper forces us into thinking very, very hard to increasing our indications for this type of procedure, particularly in the patients who are not suitable for heart transplant.

Would you comment on the heart transplant situation in our country, in Italy. Do you know what number of patients are transplanted in Italy?

Dr Cotrufo: Every year?

Dr Menicanti: Yes.

Dr Cotrufo: About 300 patients are transplanted every year, and almost the same number are dying because the organs are not available. So I agree with you that really every case should be studied in order to verify if there are any options other than transplant.