Introduction

Ischemic heart disease is one of the most prevalent disorders in the heart, and various medical or surgical treatments had been already established. However, irreversible myocardial ischemia against adequate therapies results in functional and geometric alterations, including regional or global LV dysfunction, dilated LV dimension and functional mitral regurgitation (MR). In such situation, the most critical form is called ischemic cardiomyopathy (ICM), which is characterized by poor prognosis despite various treatments. Additionally, it was demonstrated that concomitant functional MR is one of the risk factors for long-term survival in ischemic heart disease. Thus, ICM with functional MR is the most critical combination and the definitive treatment is heart transplantation. However, heart transplantation would not be performed in all indicated patients due to the shortage of donor organs. Actually, they were treated by alternative treatments to heart transplantation in case with lack of allografts. When surgical treatment is considered as one of the alternatives, possible

Original Article

Prediction of Long-Term Survival in Patients with End-Stage Heart Failure Secondary to Ischemic Heart Disease: Surgical Correction and Volumetric Analysis

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Purpose: Ischemic heart disease (IHD) may result in lethal conditions such as ischemic cardiomyopathy (ICM) and mitral regurgitation (MR).

Methods: We hypothesized preoperative LV volume would be highly associated with long-term survival in such patients. We retrospectively evaluated effects of LV end-systolic volume index (LVESVI) on survival.

Results: Patients were divided into two groups according to LVESVI; Group S (n = 19, <100 ml/m²), and L (n = 55, >100 ml/m²). There were 74 patients (male 61, female 13; 61 ± 10 y.o.). There was no statistical significance in preoperative parameters, including ejection fraction (EF), severity of MR, severity of tricuspid regurgitation (TR), and right ventricular systolic pressure (RVSP). After operation, LVESVI and severity of MR were statistically reduced in both groups. However, EF, severity of TR and RVSP were not statistically alleviated in both groups. In Group S, 5- and 10-year survival rates were 93% and 48%. In Group L, 5- and 10-year survival rates were 50% and 29%. There was a statistical difference in long-term survival between two groups.

Conclusions: Preoperative LV volume would be one of the risk factors for long-term survival in patients with congestive heart failure secondary to IHD. Careful follow-up and optimal treatment should be recommended before LV dimension becomes too large.

Keywords: ischemic heart disease, mitral regurgitation, surgical ventricular restoration

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predictors for survival are beneficial to determine surgical indication. However, analysis of LV function would be difficult in patients with LV dysfunction and significant MR, especially in dilated LV.

We have treated patients with end-stage dilated cardiomyopathy (DCM) using three types of surgical ventricular restoration (SVR) and mitral valve surgery.\(^{10,11}\) A dilated LV with a focal akinetic lesion is a surgical indication for SVR, and the choice of procedure is determined by the location of the akinesis. Using this surgical strategy, we have treated critical patients with non-ischemic DCM such as muscular dystrophy and cardiac sarcoidosis, and demonstrated operative efficacies.\(^{12,13}\) In our surgical experience over 10 years, we had surgically treated 177 patients with ICM. When functional MR subsequently occurs in such patients, reliable predictors are required due to higher surgical risk and possible difficulties in analysis of LV function. Thus, we hypothesized that preoperative LV volume would be highly associated with postoperative survival for such patients and demonstrated retrospective analysis.

**Materials and Methods**

**Patients**

This study was approved by the Institutional Review Board and 177 patients with ICM were surgically treated between June 2000 and July 2012. Among them, 74 patients with ICM and functional MR who had completed the LV volume measurement before and after operation were involved in this study. Surgical cases for MR due to organic valvular changes such as prolapse were excluded in this series.

Patient characteristics were summarized in **Table 1**. The age ranged from 35 to 83 years old (mean, 61 ± 10 y.o.) and there were 61 men and 13 women. New York Heart Association (NYHA) functional class was class II in 0 (0%), III in 27 (36%), and IV in 47 patients (64%). Preoperatively, 38 patients (51%) depended on inotropes and intra-aortic balloon pumping was required in 14 patients (19%). Surgical risk was calculated by the risk model of EuroSCORE II. The elective operation was in 69 and emergent situation was in five patients.

To examine the effects of preoperative LV volume on long-term survival, patients were divided into two groups according to LV end-systolic volume index (LVESVI); Group S (n=19, LVESVI <100 ml/m\(^2\)), and Group L (n = 55, LVESVI <100 ml/m\(^2\)).

**Assessment of cardiac geometry and functional MR**

Two-dimensional echocardiography was used to evaluate cardiac geometry, including dimensions and LV volume, valvular morphology, and the subvalvular apparatus. LV volume was calculated by modified Simpson method, i.e., LVESVI and LV end-diastolic volume index (LVEDVI). To determine the location of akinetic or dyskinetic lesion to exclude, regional LV strain was assessed by speckle-tracking echocardiography under normal and dobutamine-stress conditions.\(^{14}\)

**Surgical procedures**

Details of SVR and mitral valve surgery were described in our previous reports.\(^{10,11}\) We used three types of SVR, including endoventricular circular patch plasty (EVCPP) for the antero-apical lesion, SAVE for the broad anterior lesion, and posterior restoration procedure (PRP) for the posterior lesion. In addition to SVR, cryoablation was performed for incision line to prevent postoperative ventricular arrhythmia. Ischemic myocardial lesion was concomitantly treated by coronary artery bypass grafting.
Prediction of Survival in ICM

(CABG) prior to SVR and mitral valve surgery. Functional MR was corrected by mitral valve plasty (MVP) including mitral annuloplasty with a one-undersized rigid annuloplasty ring, chordal cutting of the basal chordae, papillary muscle approximation, and chordal translocation. In the early period of the series, MVR was indicated for limited cases.

Statistical analysis

Results are expressed as means ± SEM. An analysis was performed by paired or unpaired Student’s t test and Chi-square test to compare the data. The Kaplan-Meier survival method was used to estimate survival. The criterion for statistical significance was set at a value of p <0.05.

Table 2 Surgical procedures

<table>
<thead>
<tr>
<th></th>
<th>Total (n = 74)</th>
<th>Group S (n = 19)</th>
<th>Group L (n = 55)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MVP/MVR</td>
<td>66/8</td>
<td>18/1</td>
<td>48/7</td>
<td>0.3664</td>
</tr>
<tr>
<td>SVR</td>
<td>74</td>
<td>19</td>
<td>55</td>
<td>0.1940</td>
</tr>
<tr>
<td>EVCPP</td>
<td>17</td>
<td>5</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>SAVE</td>
<td>40</td>
<td>9</td>
<td>37</td>
<td></td>
</tr>
<tr>
<td>PRP</td>
<td>11</td>
<td>5</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>CABG</td>
<td>59</td>
<td>18</td>
<td>40*</td>
<td>0.0445</td>
</tr>
<tr>
<td>No. of distal anastomoses</td>
<td>2.8 ± 1.3</td>
<td>3.2 ± 1.3</td>
<td>2.5 ± 1.3*</td>
<td>0.0353</td>
</tr>
<tr>
<td>TAP</td>
<td>21</td>
<td>5</td>
<td>16</td>
<td>0.8771</td>
</tr>
<tr>
<td>MAZE</td>
<td>8</td>
<td>1</td>
<td>7</td>
<td>0.3664</td>
</tr>
<tr>
<td>ACC time (min)</td>
<td>85 ± 38</td>
<td>84 ± 34</td>
<td>85 ± 39</td>
<td>0.4478</td>
</tr>
<tr>
<td>CPB time (min)</td>
<td>149 ± 37</td>
<td>151 ± 25</td>
<td>148 ± 40</td>
<td>0.3759</td>
</tr>
</tbody>
</table>

MVP: mitral valve plasty; MVR: mitral valve replacement; SVR: surgical ventricular restoration; EVCPP: endo-ventricular circular patch plasty; SAVE: septal anterior ventricular exclusion; PRP: posterior restoration procedure; CABG: coronary artery bypass grafting; TAP: tricuspid valve annuloplasty; MAZE: Maze operation; ACC: aortic-cross clamping; CPB: cardiopulmonary bypass. *p <0.05 vs. Group L. Values are expressed as means ± SEM.

Result

Operative procedures are summarized in Table 2. MVP and MVR were performed in all patients (MVP vs. MVR, 66 vs. 8). SVR was also performed in all patients, and the procedures included EVCPP in 17, SAVE in 46 and PRP in 11. CABG was performed in 59 patients. Tricuspid annuloplasty (TAP) was performed in 21 patients, and MAZE operation was performed in 8 patients. Although there was no statistical significance in operative time between two groups, proportion of CABG in Group S was higher than Group L.

In this series, 30 days mortality was 1% (1/74), and the patient died of low cardiac output (LOS) was involved in Group L. During a follow-up period of 40 ± 35 months, 30 patients were died of fatal ventricular arrhythmia in 14 (1 vs. 13), LOS in 14 (Group S vs. L; 3 vs. 11), and non-cardiac causes in two patients (0 vs. 2).

As a long-term surgical result, survival was estimated by the Kaplan-Meier survival method (Fig. 1). The 5-year and 10-year survival rates in overall patients were 60% and 34%, respectively. In Group S, the 5-year and 10-year survival rates were 93% and 48%, respectively. In Group L, the 5-year and 10-year survival rates were 50% and 29%, respectively. There was a statistical difference in long-term survival between two groups (p = 0.0471).
Table 3 Geometric and functional data of the left ventricle

<table>
<thead>
<tr>
<th></th>
<th>Group S (n = 51)</th>
<th>Group L (n = 60)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVEDD (mm)</td>
<td>Preoperative</td>
<td>63 ± 6</td>
<td>70 ± 11*</td>
</tr>
<tr>
<td></td>
<td>Postoperative</td>
<td>57 ± 8</td>
<td>63 ± 8</td>
</tr>
<tr>
<td>LVESD (mm)</td>
<td>Preoperative</td>
<td>51 ± 10</td>
<td>60 ± 13*</td>
</tr>
<tr>
<td></td>
<td>Postoperative</td>
<td>49 ± 11</td>
<td>55 ± 9</td>
</tr>
<tr>
<td>LVEDVI (ml/m²)</td>
<td>Preoperative</td>
<td>129 ± 17</td>
<td>200 ± 52*</td>
</tr>
<tr>
<td></td>
<td>Postoperative</td>
<td>89 ± 24</td>
<td>141 ± 38*</td>
</tr>
<tr>
<td>LVESVI (ml/m²)</td>
<td>Preoperative</td>
<td>85 ± 15</td>
<td>159 ± 49*</td>
</tr>
<tr>
<td></td>
<td>Postoperative</td>
<td>61 ± 19</td>
<td>108 ± 40*</td>
</tr>
<tr>
<td>EF (%)</td>
<td>Preoperative</td>
<td>26 ± 6</td>
<td>24 ± 7</td>
</tr>
<tr>
<td></td>
<td>Postoperative</td>
<td>24 ± 7</td>
<td>22 ± 5</td>
</tr>
<tr>
<td>Severity of MR</td>
<td>Preoperative</td>
<td>2.9 ± 0.9</td>
<td>2.5 ± 1.0</td>
</tr>
<tr>
<td></td>
<td>Postoperative</td>
<td>0.9 ± 1.6</td>
<td>0.4 ± 0.6</td>
</tr>
<tr>
<td>Severity of TR</td>
<td>Preoperative</td>
<td>0.6 ± 0.9</td>
<td>0.7 ± 0.9</td>
</tr>
<tr>
<td></td>
<td>Postoperative</td>
<td>0.5 ± 0.8</td>
<td>0.4 ± 0.5</td>
</tr>
<tr>
<td>RVSP (mm Hg)</td>
<td>Preoperative</td>
<td>41 ± 19</td>
<td>39 ± 16</td>
</tr>
<tr>
<td></td>
<td>Postoperative</td>
<td>33 ± 8</td>
<td>32 ± 13</td>
</tr>
</tbody>
</table>

LVEDD: left ventricular end-diastolic diameter; LVESD: left ventricular end-systolic diameter; LVEDVI: left ventricular end-diastolic volume index; LVESVI: left ventricular end-systolic volume index; EF: ejection fraction; MR: mitral regurgitation; TR: tricuspid regurgitation; RVSP: right ventricular systolic pressure. *p <0.05 vs. Preoperative values. Pre and postoperative values are expressed as means ± SEM.

Geometric and functional data are summarized in Table 3. Between two groups, there were statistical significances in preoperative parameters such as LVEDD (63 ± 6 vs. 70 ± 11 mm; p = 0.0486), LVESD (51 ± 10 vs. 60 ± 13 mm; p = 0.0431), LVEDVI (129 ± 17 vs. 200 ± 52 ml/m²; p <0.0001), and LVESVI (85 ± 15 vs. 159 ± 49 ml/m²; p <0.0001). In contrast, there was no statistical significances in preoperative parameters, including EF (26 ± 6 vs. 24 ± 7%; p = 0.0623), severity of MR (2.9 ± 0.9 vs. 2.5 ± 1.0; p = 0.1694), severity of tricuspid regurgitation (TR) (0.6 ± 0.9 vs. 0.7 ± 0.9; p = 0.3398), and right ventricular systolic pressure (RVSP) (41 ± 19 vs. 39 ± 16 mm Hg; p = 0.3819). In both groups, LVESVI was statistically reduced after the operation (Group S: 85 ± 15 vs. 61 ± 19 ml/m²; p <0.0001, Group L: 159 ± 49 vs. 108 ± 40 ml/m²; p <0.0001).

Although EF was reduced after the operation, there was no statistical significance in both groups (Group S: 26 ± 6 vs. 24 ± 7%; p = 0.0698, Group L: 24 ± 7 vs. 22 ± 5%; p = 0.1495). In contrast, severity of MR was significantly reduced by the operation in both groups (Group S: 2.9 ± 0.9 vs. 0.9 ± 1.6, p = 0.0064, Group L: 2.5 ± 1.0 vs. 0.4 ± 0.6, p <0.0001). Severity of TR was unchanged by the operation in both groups (Group S: 0.6 ± 0.9 vs. 0.5 ± 0.8, p = 0.4213, Group L: 0.7 ± 0.9 vs. 0.4 ± 0.5, p = 0.0535). Similarly, RVSP was also unchanged after the operation (Group S: 41 ± 19 vs. 33 ± 8 mm Hg, p = 0.1559, Group L: 39 ± 16 vs. 32 ± 13 mm Hg, p = 0.0663).

Discussion

We have surgically treated patients with end-stage heart failure secondary to ischemic heart disease using three types of SVR. Concomitant functional MR was surgically repaired and successful outcome was obtained by our strategy. Furthermore, potential effect of preoperative LV volume on survival was demonstrated by retrospective analysis. Although early survival outcome was not affected by preoperative volume, long-term survival in patients with smaller LV volume was significantly better than those with larger volume. Accordingly, preoperative LV volume would be one of the possible predictors for long-term survival in patients with end-stage heart failure caused by ischemia.

Twenty years ago, Yamaguchi et al. demonstrated that preoperative LVESVI less than 100 ml/m² was a predictor for better postoperative status and survival in patients with ICM. Although the cut off value of the study was similar to our study, there are obvious differences in patient background between two studies, i.e., presence of MR. In patients with MR, functional assessment would be very
difficult because the LV volume depends on the extent of mitral regurgitant volume. To our knowledge, this is the first report, suggesting that preoperative LV volume was highly associated with long-term survival in patients with ICM and MR. Earlier clinical reports demonstrated that there were various preoperative risk factors including low EF and severity of MR in patients with ICM.\textsuperscript{17,18} However, the results would not be fairly compared due to uneven patient background. Additionally, surgical risk in our series would be much higher than that in Yamaguchi’s report, because the severity of MR would be apparently greater in our patients. Although it is very difficult to compare with earlier results due to these reasons, larger preoperative LV volume would be one of the risk factors for long-term survival in patients with ICM and MR.

Coronary revascularization is the definitive treatment for patients with ICM and EF was increased by CABG after the operation.\textsuperscript{19} According to the report, the extent of hibernating myocardium would be highly associated with preoperative LVESVI and patients with preoperative LVESVI less than 100 ml/m\textsuperscript{2} responded to the operation, resulting in increase of postoperative EF. However, in our series, EF was not improved in patients with preoperative LVESVI less than 100 ml/m\textsuperscript{2}. The existence of MR may affect the difference in this result, and the possible mechanism of early decline in EF had been already reported.\textsuperscript{19} In this report, the early decrease in EF is more pronounced in patients with larger LV volume, depressed preoperative EF and advanced symptoms preoperatively. These conditions are completely applicable to patients in our study. Accordingly, functional effects on the LV by mitral valve surgery would be more pronounced postoperatively compared with those by coronary revascularization in patients with ICM and MR.

In this series, dilated LV was repaired with SVR to exclude akinetic and/or dyskinetic area.\textsuperscript{10,11} The purpose of SVR includes two major reasons such as reduction of LV volume and subvalvular procedures for functional MR. Earlier reports demonstrated that functional MR may result from dilation of the mitral annulus, laterally displaced papillary muscles, and enhanced tethering force of the valve leaflets in the hearts with dilated LV.\textsuperscript{20,21} Thus, the distance between both papillary muscles was approximated through the left ventriculotomy of the antero-apical LV wall during SAVE and EVCPP procedure. In contrast, the posterior LV wall between both papillary muscles was directly closed and approximated during PRP procedure. In regard to volume reduction, reduction rate of Group S and L were 28\% and 32\%, respectively. Although the reduction rates were almost similar to each other, long-term survival was different between two groups with different preoperative LVESVI. We demonstrated that long-term survival rate in patients with smaller postoperative LVESVI was much higher compared with those with larger LV volume.\textsuperscript{10,11} Additionally, another report also demonstrated that lower postoperative LVESVI was highly associated with midterm survival.\textsuperscript{22,23} Thus, LVESVI less than 100 ml/m\textsuperscript{2} would be one of possible predictors for long-term survival in patients with ICM and MR, despite the timing of the operation (preoperative and postoperative).

There are several limitations to this study. First, there was a difference in proportion of surgical procedure of CABG between two groups. Although there was no significance in surgical risk calculated by EuroSCORE II between two groups, the percentage of CABG in Group L (73\%) was significantly lower than that in Group S (95\%). The reason may be explained by the inclusion of patients with irreversible myocardial change into Group L, who do not require surgical revascularization. Second, this series may include heterogeneity of patient population who had treated with various procedures such as MVP, CABG and SVR. Due to a small number of this series, it would be very difficult to analyze under even patient background. Third, we preferably used both SAVE and PRP compared with EVCPP to obtain the elliptical shape of the LV. However, selection of SVR and with or without subvalvular procedures may affect volumetric and functional parameters of the LV. Fourth, our results were obtained from retrospective analysis with a small number. Further cases would be required to validate these data.

**Conclusion**

Preoperative LV volume would be highly associated with surgical outcome in patients with ICM and MR, especially for long-term survival. Thus, careful follow-up and optimal treatment should be recommended for such patients before the LV dimension becomes too large.

**Disclosure Statement**

There is no financial disclosure in all authors.

**References**


