Non-heart transplant surgical approaches with left ventricular restoration and mitral valve operation for advanced ischaemic cardiomyopathy

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Abstract

OBJECTIVES: The aim of this study was to assess long-term outcomes of non-heart transplant surgical approaches to advanced ischaemic cardiomyopathy (ICM), including left ventricular restoration (LVR) and mitral valve operation.

METHODS: Since September 2002, 102 consecutive patients (mean age 65, 18 females) with advanced ICM [ejection fraction (EF) <40%, left ventricular end-systolic volume index (LVESVI) > 60 ml/m²] were treated using non-heart transplant procedures. A total of 84 patients with asynergy of large scar exceeding 35% of left ventricular (LV) perimeter underwent LVR, and 30 patients with greater than or equal to moderate mitral regurgitation (MR) underwent mitral valve operation such as annuloplasty (n = 23) and valve replacement (n = 7). Patients were divided into four groups according to their interagency registry for mechanically assisted circulatory support (INTERMACS) profiles: Profile 1–2 (the highest levels of clinical compromise; n = 9), Profile 3–4 (n = 40), Profile 5–6 (n = 32) and Profile ≥7 (n = 21). We compared the four groups, looking at survival, major adverse cardiac and cerebrovascular event (MACCE), New York Heart Association (NYHA) status, LV volume and function.

RESULTS: The overall 8-year survival including 3 hospital deaths (2.9%) was 64.3% without sudden death due to arrhythmia. Ninety-nine survivors showed significant improvement in the mean NYHA status, from 2.9 to 1.4, and the mean EF (33.2–41.7%) (P < 0.0001). The mean LVESVI was significantly reduced from 104.1 to 61.4 ml/m² (41% volume reduction) (P < 0.0001). Seven-year survival in patients with Profiles 1–2, 3–4, 5–6 and ≥7 were 50.0, 57.2, 60.3 and 95.2%, respectively (P = 0.13). Freedom from MACCE at 5 years in patients with Profiles 1–2, 3–4, 5–6 and ≥7 were 29.6, 47.0, 67.2 and 95.2%, respectively (P = 0.0067). The improvements in NYHA status were significantly greater in patients with higher levels of clinical compromise (P < 0.0001), although, there was no significant difference in LV volume reduction and functional improvement among the four groups. Patients with Profile ≥7 had significantly better survival at 7 years (hazard ratio (HR), 0.11, P = 0.046) and freedom from MACCE at 5 years (HR: 0.053, P = 0.006) compared with patients with Profiles 1–2.

CONCLUSIONS: Our non-heart transplant surgical approaches using LVR and mitral valve operation for advanced ICM yielded excellent long-term outcomes in terms of survival and NYHA status, even in patients who are potential candidates for heart transplantation or LV assist devices; and are encouraging in a very particular situation where heart transplantation is limited due to organ storage.

Keywords: Non-heart transplant approaches • Left ventricular restoration • Mitral valve operation • INTERMACS profiles • Long-term outcomes

INTRODUCTION

Congestive heart failure is the ultimate consequence of ischaemic cardiomyopathy (ICM). It remains a major and growing public health problem, despite medical and surgical therapeutic advances [1]. Heart transplantation is the mainstay of treatment for patients with end-stage ICM, but the limitations of this approach, largely concerning organ storage, mean that the search for alternative treatments continues, particularly, in Japan where only 30 heart transplants were performed in 2011 [2].

Thus, non-heart transplant procedures such as left ventricular restoration (LVR) and mitral valve operation have gained popularity and reportedly attenuated left ventricular (LV) remodelling for patients with ICM, particularly those for whom there is no suitable heart donor [3–10]. A trial of surgical treatment for ischaemic heart failure (STICH) has, however, found that adding surgical ventricular reconstruction so as to reduce ventricular volume in coronary artery bypass grafting (CABG) does not improve symptoms or tolerance to exercise, and fails to reduce the death rate or
cardiac hospitalization [11]. Mitral valve operation that focuses on the down-sized ring annuloplasty was also found not to affect survival, although it is important to control mitral regurgitation (MR) that might ameliorate LV remodelling due to cardiomyopathy [12].

Implantable left ventricular assist devices (LVADs), developed for the treatment of patients with end-stage heart failure as a bridge-to-transplant, have been widely accepted as a destination therapy even in patients with lower levels of clinical compromise, and have yielded successful outcomes [13, 14].

We have routinely employed non-heart transplant approaches using LVR to aim total scar exclusion and mitral valve operation to completely regulate MR during the last decade for ICM, even in patients with cardiogenic shock due to progressive heart failure or in those who might be recommended LVADs for the bridge-to-transplantation or destination therapy. In the present study, we retrospectively analysed long-term outcomes of LVR and mitral valve operation for patients with ICM, looking especially at long-term outcomes of these non-heart transplant approaches for patients who might be candidates for heart transplantation or LVADs according to the interagency registry for mechanically assisted circulatory support (INTERMACS) profiles.

PATIENTS AND METHODS

Following approval from our Institution Ethics Committee/Institutional Review Board, a retrospective review was carried out on 102 consecutive patients (84 males and 18 females) having a mean age of 65 (±8) years, who underwent LVR and/or mitral valve operation for advanced ICM from September 2002 to December 2012. The advanced ICM was defined as an ejection fraction (EF) of <40% and a left ventricular end-systolic volume index (LVESVI) of >60 ml/m². These parameters were measured using either magnet resonance imaging (MRI) or LV angiography. Patients who required repair for mitral valve degeneration, ventriculot septal perforation or LV rupture were excluded from the study group.

Functional outcomes and follow-up

Follow-up information was obtained during patients’ visits. Preoperatively and during the mid-term follow-up, right heart catheterization was performed in order to assess pulmonary artery pressure (PAP). The EF and LVESVI were assessed at the same time using MRI or the monoplane method associated with LV angiography. Preoperative and postoperative variables were compared using the same modality. The primary end point was a major adverse cardiac and cerebrovascular event (MACCE) during follow-up, including death by any cause. This cerebrovascular event was taken as comprising focal neurological deficits of central origin lasting 72 h and resulting in permanent brain damage or body impairment.

Study groups

The INTERMACS profile groups patients with failing optimal medical therapy into seven profiles and provides convenient shorthand adjustment for preoperative risk and clarification of target populations for LVADs [18]. It was used to classify the study groups. The INTERMACS profile was defined after retrospective review by the cardiologists who were blinded to the study group. According to the INTERMACS profiles, we divided the study cohort into four groups as follows: (i) the highest level of clinical compromise requiring definitive intervention within hours or a few days, as Profiles 1–2 (n = 9, 8.8%); (ii) a high level of clinical compromise requiring definitive elective intervention, as Profiles 3–4 (n = 40, 39.2%); (iii) a low level of clinical compromise that might require intervention depending on maintenance, as Profiles 5–6 (n = 32, 31.4%) and (iv) the lowest level of clinical compromise as Profile ≥7 (n = 21, 21%). The present article focuses on long-term outcomes after LVR and/or mitral valve operation for patients with ICM who were classified as Profiles 1–2, 3–4, 5–6 and ≥7, based on the INTERMACS profiles.
Statistical analyses

Results are presented as mean (± standard deviation). Comparisons between the pre- and postoperative value for the entire group were performed using the paired t-test for normally distributed data, as confirmed by the Kolmogorov-Smirnoff test. Differences in preoperative value among the four INTERMACS profiles groups were analysed by one-way factorial analysis of variance (ANOVA). Categorical data were expressed as percentages. Preoperative proportions were analysed by \(\chi^2\) or the Fisher’s exact test, as appropriate. The difference between pre- and postoperative stages in the four different groups was evaluated by repeated measures ANOVA, followed by post hoc comparisons (when appropriate) with Dunnett’s test. Kaplan-Meier actuarial survival and event-free rate were calculated for the entire group and the four groups, and differences among the four groups were assessed using the log-rank test. A Cox proportional-hazards model was used to analyse the effects of the four INTERMACS profile groups on survival and MACCE, with LVR and/or mitral valve operation treated as a time-dependent covariate. A \(P\)-value of <0.05 was considered statistically significant. All statistical analyses were performed using IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY, USA: IBM Corp.

RESULTS

Figure 1 shows the survival curve and freedom from MACCE for the entire study group. The overall 8-year survival including 3 hospital deaths (2.9%) was 64.3% (Fig. 1A). One patient in the Profile 1–2 group, who underwent mitral annuloplasty, died of pneumonia. Two patients in the Profile 3–4 group who underwent LVR and LVR concomitant with mitral annuloplasty died of pneumonia and sepsis. There were 23 late deaths among the 99 operative survivors: due to pneumonia in 5 patients, neoplasms in 5, stroke in 4, cardiac death in 3, sepsis in 3, gastrointestinal bleeding in 2 and accident in 1. No sudden death due to ventricular tachycardia occurred in the same period. During follow-up, which extends to 10 years [mean 46 (±33) months], primary clinical end points were observed in 33 patients including hospital deaths. The overall freedom from MACCE at 7 years was 57.3% (Fig. 1B).

Figure 2 shows the preoperative baseline and postoperative values of New York Heart Association (NYHA) status, LVESVI, EF and PAP for 99 survivors. The NYHA status was significantly improved from 2.9 (±0.6) to 1.4 (±0.6) after the operation. \(P < 0.0001\) (Fig. 2A). The LVESVI was significantly reduced, from 104.1 (±37.4) ml/m\(^2\) to 61.4 (±21.9) ml/m\(^2\) (41% volume reduction) \(P < 0.0001\) (Fig. 2B). The mid-term changes in the LV function showed a significant increase in EF, from 32.1 (±8.5)% to 40.4 (±11.2)% \(P < 0.0001\) (Fig. 2C) and a significant reduction in PAP, from 34.5 (±13.2) mmHg to 27.3 (±8.2) mmHg \(P < 0.0001\) (Fig. 2D).

Table 1 sets out the preoperative and early postoperative clinical characteristics of patient in the INTERMACS profiled groups. A greater number of patients with higher levels of clinical compromise, such as INTERMACS profiles 1–2 and 3–4, had medically treated diabetes \((P = 0.073)\) and a history of ventricular tachycardia \((P = 0.056)\) than did patients with lower levels of clinical compromise, although the difference was not statistically significant. Upon looking at preoperative clinical characteristics, patients with higher levels of clinical compromise required (with statistically significance) inotropes, intra-aortic balloon pumping and mechanical ventilation \((P = 0.0001)\). The majority of the patients (67.5%) in the Profile 3–4 group revealed ‘Frequent Flyer’ of INTERMACS modifier who required frequent emergency visits or hospitalizations for cardiogenic events. The logistic EuroSCORE II was significantly greater in patients with higher levels of clinical compromise \((P < 0.0001)\). Fewer patients with higher levels of clinical compromise underwent concurrent CABG than patients with lower levels of clinical compromise \((P = 0.057)\). There was no significant difference among the four groups in procedural characteristics such as LVR and mitral valve operation. More patients with higher levels of clinical compromise required intra-aortic balloon pumping postoperatively than patients with lower levels of clinical compromise \((P = 0.0001)\). One patient (11.1%) with INTERMACS profiles 1–2 suffered postoperative stroke, and one (2.5%) with Profiles 3–4 required implantable cardioverter-defibrillator due to postoperative ventricular tachycardia.

Figure 3 shows preoperative baseline and postoperative values of NYHA status, LVESVI, EF and PAP for 99 survivors in the INTERMACS profiled groups. In the analysis for pre- and postoperative time-to-INTERMACS profiled group interaction, the postoperative improvements in NYHA status were significantly greater in patients with higher levels of clinical compromise than in patients with lower levels of clinical compromise \((P < 0.001)\), and following post hoc comparisons, there were also significant differences between two groups when compared with any other.
Figure 2: Changes in preoperative baseline and postoperative NYHA (A), LVESVI (B), EF (C) and PAP (D) of 99 operated survivors. Mean values are plotted and the error bars represent ±1 standard deviation. *P < 0.0001 versus preoperative value.

Table 1: Preoperative and early postoperative clinical characteristics of patient in the INTERMACS profiled groups

<table>
<thead>
<tr>
<th></th>
<th>Profiles 1–2 (n = 9)</th>
<th>Profiles 3–4 (n = 40)</th>
<th>Profiles 5–6 (n = 32)</th>
<th>Profile ≥ 7 (n = 21)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>69.7 (±5.8)</td>
<td>63.9 (±9.2)</td>
<td>66.5 (±7.6)</td>
<td>65.2 (±10.1)</td>
<td>0.17</td>
</tr>
<tr>
<td>Male</td>
<td>6 (66.7%)</td>
<td>34 (85.0%)</td>
<td>24 (75.0%)</td>
<td>20 (95.2%)</td>
<td>0.15</td>
</tr>
<tr>
<td>Preoperative NYHA status</td>
<td>3.6 (±0.5)</td>
<td>2.8 (±0.4)</td>
<td>3.0 (±2.0)</td>
<td>2.1 (±0.4)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>6 (66.7%)</td>
<td>13 (65.0%)</td>
<td>26 (66.7%)</td>
<td>27 (66.7%)</td>
<td>0.73</td>
</tr>
<tr>
<td>Preoperative haemodialysis</td>
<td>1 (11.1%)</td>
<td>3 (9.4%)</td>
<td>1 (4.8%)</td>
<td>1 (4.8%)</td>
<td>0.33</td>
</tr>
<tr>
<td>Prior cardiac surgery</td>
<td>2 (22.2%)</td>
<td>5 (12.5%)</td>
<td>2 (6.3%)</td>
<td>2 (6.3%)</td>
<td>0.56</td>
</tr>
<tr>
<td>Prior ventricular tachycardia</td>
<td>0 (0%)</td>
<td>9 (22.5%)</td>
<td>2 (6.3%)</td>
<td>2 (6.3%)</td>
<td>0.065</td>
</tr>
<tr>
<td>Preoperative inotropes</td>
<td>8 (88.9%)</td>
<td>9 (22.5%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Preoperative IABP</td>
<td>8 (88.9%)</td>
<td>4 (10.0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Preoperative respirator</td>
<td>7 (77.8%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Frequent Flyer (INTERMACS)</td>
<td>0 (0%)</td>
<td>27 (67.5%)</td>
<td>2 (6.3%)</td>
<td>0 (0%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Logistic EuroSCORE II</td>
<td>28.8 (±29.9)</td>
<td>11.7 (±9.8)</td>
<td>5.9 (±3.4)</td>
<td>3.5 (±1.9)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Left ventricular restoration</td>
<td>6 (66.7%)</td>
<td>26 (65.0%)</td>
<td>22 (68.8%)</td>
<td>18 (85.7%)</td>
<td>0.62</td>
</tr>
<tr>
<td>Left ventricular restoration + mitral annuloplasty</td>
<td>1 (11.1%)</td>
<td>7 (17.5%)</td>
<td>4 (10.0%)</td>
<td>0 (0%)</td>
<td>0.66</td>
</tr>
<tr>
<td>Dor</td>
<td>7 (77.8%)</td>
<td>22 (55.0%)</td>
<td>18 (56.3%)</td>
<td>11 (52.4%)</td>
<td>0.29</td>
</tr>
<tr>
<td>Linear closure</td>
<td>0 (0%)</td>
<td>11 (27.5%)</td>
<td>8 (25.0%)</td>
<td>7 (33.3%)</td>
<td>0.29</td>
</tr>
<tr>
<td>Concomitant endocardectomy</td>
<td>3 (33.3%)</td>
<td>23 (57.5%)</td>
<td>19 (59.4%)</td>
<td>13 (72.2%)</td>
<td>0.47</td>
</tr>
<tr>
<td>Mitral valve replacement</td>
<td>1 (11.1%)</td>
<td>3 (7.5%)</td>
<td>3 (9.4%)</td>
<td>0 (0%)</td>
<td>0.66</td>
</tr>
<tr>
<td>Mitral annuloplasty</td>
<td>1 (11.1%)</td>
<td>4 (10.0%)</td>
<td>3 (9.4%)</td>
<td>3 (14.3%)</td>
<td>0.66</td>
</tr>
<tr>
<td>Concomitant CABG</td>
<td>4 (44.4%)</td>
<td>33 (82.5%)</td>
<td>26 (81.3%)</td>
<td>34 (85.7%)</td>
<td>0.057</td>
</tr>
<tr>
<td>Required IABP</td>
<td>8 (88.9%)</td>
<td>17 (42.5%)</td>
<td>3 (9.4%)</td>
<td>1 (4.8%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Postoperative tachycardia</td>
<td>0 (0%)</td>
<td>1 (2.5%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0.67</td>
</tr>
<tr>
<td>Postoperative stroke</td>
<td>1 (11.1%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0.015</td>
</tr>
<tr>
<td>Mortality</td>
<td>1 (11.1%)</td>
<td>2 (5.0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0.23</td>
</tr>
</tbody>
</table>

Continuous data are presented as mean (± standard deviation).
CABG: coronary artery bypass grafting; IABP: intra-aortic balloon pumping; INTERMACS: interagency registry for mechanically assisted circulatory support.
INTERMACS profiled group ($P < 0.05$) (Fig. 3A). There was no significant difference in the mid-term LV volume reduction ($P = 0.35$) (Fig. 3B) and LV functional improvement, in terms of EF ($P = 0.40$) (Fig. 3C) and PAP ($P = 0.19$) (Fig. 3D), among the four groups.

Figure 4 shows the survival curves for the four INTERMACS profiled groups. Three cardiac deaths occurred during follow-up (2 patients with Profiles 3–4 and 1 with Profiles 5–6). The survival was 66.7% at 3 years and 50.0% at 7 years for patients with INTERMACS profiles 1–2; 74.9% at 3 years and 57.2% at 7 years for patients with Profiles 3–4; 79.5% at 3 years and 60.3% at 7 years for patients with Profiles 5–6; and 95.2% at 3 years and 95.2% at 7 years for patients with Profiles ≥7. There was no significant difference among the four groups ($P = 0.13$). Patients with Profiles ≥7 had significantly better survival than patients with Profiles 1–2 (hazard ratio [HR]: 0.11, $P = 0.046$).

Table 2 sets out the primary clinical endpoints in MACCE for patients in the INTERMACS profiled groups. During follow-up, MACCE occurred significantly more often in patients with higher levels of clinical compromise than in those with lower clinical compromise ($P = 0.0042$). Freedom from MACCE was 44.4% at 3 years and 29.6% at 5 years for patients with INTERMACS profiles 1–2; 66.7% at 3 years and 47.0% at 5 years for patients with Profiles 3–4; 72.8% at 3 years and 67.2% at 5 years for patients with Profiles 5–6 and 95.2% at 3 years and 95.2% at 5 years for patients with Profile ≥7 ($P = 0.0067$) (Fig. 5). Patients with Profile ≥7 experienced significantly better freedom from MACCE than patients with Profiles 1–2 (HR: 0.053, $P = 0.0066$).

**DISCUSSION**

Our non-heart transplant surgical approaches for ICM with LVR and mitral valve operation, such as mitral valve annuloplasty and mitral valve replacement, led to a significant LV volume reduction (41%) to the mean LVESVI value of 61.4 ml/m². Isomura et al. [19] from the RESTORE group found that LVR was most effective in promoting long-term survival when a volume reduction rate of >33% was able to achieve a LVESVI of <90 ml/m². These postoperative results confirmed an improved LV systolic function as reflected in an increase in global EF and a decrease in PAP. Late improvement in NYHA status with excellent 64.3% survival at 8 years and 57.3% freedom from MACCE at 7 years was observed after the LVR and/or mitral valve operation.

We also set out the findings of our single-institution study examining long-term outcomes after non-heart transplant surgical treatment for patients with ICM, who were classified into the four groups according to the INTERMACS profiles. According to preoperative data, more patients with higher levels of clinical compromise had medically treated diabetes and history of ventricular tachycardia than patients with lower levels of clinical compromise. The same applied to patients whose baseline PAP was significantly higher and LVESVI was greater. These data confirmed that the logistic EuroSCORE in patients with higher levels of clinical compromise was significantly greater than in patients with lower levels of clinical compromise. However, there was no significant difference in the mid-term LV volume reduction and LV functional...
improvement, in terms of EF and PAP, among the four groups (Fig. 3). It is surprising that the improvements in NYHA status after LVR and/or mitral valve operation were significantly greater in patients with higher levels of clinical compromise than in patients with lower levels of clinical compromise (Fig. 3A). Furthermore, the 7-year survival in the patients with Profiles 1–2, 3–4, 5–6 and ≥7 (respectively 50.0, 57.2, 60.3 and 95.2%, respectively (P = 0.13) showed no significant difference (Fig. 4). These outcomes indicate that our non-heart transplant approaches could ameliorate LV remodelling in ICM, with excellent long-term survival and quality-of-life, in terms of NYHA status, even in patients with higher levels of clinical compromise who might be candidates for heart transplantation or LVADs. Our data also provide a benchmark against which long-term outcomes of the destination therapy with LVADs can be compared.

Freedom from MACCE at 5 years in the Profile 1–2 group, Profile 3–4 group, Profile 5–6 group and Profile ≥7 group were 29.6, 47.0, 67.2 95.2%, respectively (P = 0.0067) (Fig. 5). Perhaps our results are comparable with those of LVAD-supported patients, of whom 28–29% have a risk of mortality and morbidity due to LVAD-related complications such as stroke, haemorrhage and infection [20]. Patient with Profile ≥7 had significantly better freedom from MACCE (HR: 0.053, P = 0.006) as well as survival (HR: 0.11, P = 0.046) than patients with Profiles 1–2. Risk factor analysis points to earlier surgical approach, particularly for patients with lower levels of clinical compromise such as those with INTERMACS profile ≥7.

The LVR was first described by Dor et al. [3] as an endoventricular circular patch plasty that can totally exclude the akinetic or dyskinetic scar of LV, and reshape the LV with the Fontan stitch encircling the transitional zone between the contractile and non-contractile myocardium, then re-establish optimal ventricular volume using the circular patch. However, the late change occurring after LVR, particularly after the Dor procedure, has been reported to induce the increased sphericity of the LV which might adversely affect both LV systolic and diastolic function, and late MR [21, 22]. To deal with this problem, a rubber balloon that is inflated to the theoretical physiological diastolic LV volume (i.e. ~60 m/m²) could be used when excessive volume reduction is estimated after total scar exclusion. Furthermore, the flattened-out elliptical patch closure could reduce the LV volume without losing elliptical shape [4, 5, 16]. With minor modifications, and other techniques such as the tailored linear closure technique, septal anterior ventricular exclusion [23] and overlapping procedures [24], the LVR has been found to abort or reverse remodelling, diminish heart failure and improve survival even in patients with advanced ICM who could be candidates for heart transplantation or LV assist devices [5–8, 15–17, 19].

The STICH trial concluded that adding surgical ventricular reconstruction so as to reduce LV volume to CABG does not improve symptoms or tolerance to exercise, and fails to lower the death rate or cardiac hospitalization [11]. However, that trial had enrolled patients with invalid echocardiographic volume evaluations; and viability measurements, which should show regional non-viability of >35% asynergy, were not documented in the report [25]. A precise and feasible methodology for viability and scar evaluation in the MRI could provide a benchmark for preoperative evaluation [15]. Furthermore, in the trial LVESVI at 4 months after surgical ventricular reconstruction, there was only a 19% volume reduction in the 33% of patients who might have an inadequate end point. The RESTORE group reported that LVR achieved no benefit if <15% volume reduction retained a residual LVESVI of > 90 ml/m² [19]. Consequently, we are in disagreement with the STICH report, because investigators failed to demonstrate an accurate scar evaluation and to achieve optimal LV volume. That trial also excluded patients with cardiogenic shock requiring mechanical support, combined anterior and inferior asynergy, and diseased arteries not amenable to CABG, who should be able to receive the benefits of LVR if adequate volume reduction is performed.

In our series, down-sized mitral valve annuloplasty was performed for moderate or moderate-to-severe ischaemic MR using the saddle-shaped rigid ring to regulate both the non-planarity angle and the antero-posterior diameter. Mitral valve replacement was performed on patients with greater than or equal to

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**Table 2:** Primary clinical end points in MACCE among patients in the INTERMACS profiled groups

<table>
<thead>
<tr>
<th></th>
<th>Profiles 1–2 (n = 9)</th>
<th>Profiles 3–4 (n = 40)</th>
<th>Profiles 5–6 (n = 32)</th>
<th>Profile ≥7 (n = 21)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>3 (33.3%)</td>
<td>8 (20.0%)</td>
<td>5 (15.6%)</td>
<td>1 (4.8%)</td>
<td>0.23</td>
</tr>
<tr>
<td>CHF</td>
<td>2 (22.2%)</td>
<td>5 (12.5%)</td>
<td>2 (6.3%)</td>
<td>0 (0%)</td>
<td>0.17</td>
</tr>
<tr>
<td>VT</td>
<td>0 (0%)</td>
<td>1 (2.5%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0.67</td>
</tr>
<tr>
<td>Stroke</td>
<td>1 (11.1%)</td>
<td>2 (5.0%)</td>
<td>3 (9.4%)</td>
<td>0 (0%)</td>
<td>0.47</td>
</tr>
<tr>
<td>MACCE</td>
<td>6 (66.7%)</td>
<td>16 (40.0%)</td>
<td>10 (31.3%)</td>
<td>1 (4.8%)</td>
<td>0.0042</td>
</tr>
</tbody>
</table>

CHF: chronic heart failure; MACCE: major adverse cardiac and cerebrovascular events; VT: ventricular tachycardia.
severe (≥severe) MR in echocardiography. We also recommend mitral valve replacement associated with LVR for patients with moderate or moderate-to-severe MR whose LV scar could not be totally excluded after LVR, although there was no such patient in the present series. We believe that, since residual scar and residual MR could be a cause, as well as a consequence, of LV redilatation, non-heart transplant approaches should aim to totally exclude the scarred ventricle and to completely control MR.

Papillary muscle approximation combined with LVR in the patients with dilated cardiomyopathy and functional MR has been demonstrated to give excellent results in mitral valve function [10, 24]. We nevertheless believe that, in the Dor procedure, the Fontan stitch, located along the transitional zone, can move the posterior papillary muscle towards the LV base and septum, which thereby reduce mitral valve tethering. Furthermore, the tailored linear closure technique applied for postero-lateral lesion, which excludes the large scar between both papillary muscles, can reduce the papillary muscle distance. We, therefore, do not perform any intervention that manipulates the mitral subvalvular apparatus such as papillary muscle approximation or relocation.

We operated on the mitral valve when the MR grade was greater than or equal to moderate. A Japanese surgical ventricular reconstruction group [6] reported that preoperative higher MR grade was significantly associated with poor prognosis in survival after LVR for the patients with ICM. The mechanism of the functional MR might be complex and more difficult to detect clinically. Modalities are not sensitive to functional MR, and this could be missed or the grade might be underestimated, particularly in extremely dilated ventricles. The small sample precludes any further comment on this peculiar subset of patients; however, a more aggressive approach and adequate MR control is called for.

The main limitation of this study is its retrospective nature and and the fact that it describes a mixed population with heart failure symptoms. There are relatively small number of patients in cardiogenic shock (9 patients in the Profiles 1–2) and patients in stable condition at rest (21 patients in the Profile ≥7). However, they were consecutive patients with advanced ICM whose EF was <40% and LVESVI >60 ml/m². Preoperative clinical characteristics among the four INTERMACS profiled groups could be very different depending on the sequence of the LV remodelling process.

Another issue is the lack of outcomes of patients who received LVADs. Our study was not designed to assert that non-heart transplant approaches are superior to destination therapy with implantable LVADs. We nevertheless believe that our excellent long-term outcomes after LVR and/or mitral valve operation for patients with ICM imply that physicians would do well to determine the optimal treatment for whom might be assigned to the INTERMACS registry for heart transplantation or destination therapy with LVADs. Our data also encourage non-heart transplant approaches, particularly in Japan where heart transplantation is limited due to organ storage.

Further limitations are also the variety of surgical procedures ranging from LVR alone to mitral valve operation alone, LVR plus mitral valve operation with or without CABG and the size of the patient cohort who underwent mitral valve operation, which is small compared to the LVR. However, we have been employing non-heart transplant surgeries as appropriate under strict indications. LVRs and mitral valve operations were homogeneously distributed during the study period, and the pattern of techniques did not depend on the preferences of individual operating surgeons.

CONCLUSIONS

Our non-heart transplant surgical approaches with LVR and mitral valve operation for advanced ICM show excellent long-term survival and quality-of-life, in terms of NYHA status, even in patients with higher level of clinical compromise who might be candidates for heart transplantation or LVADs. Risk factor analyses for survival and MACCE recommend earlier surgical approach, particularly for patients with lower levels of clinical compromise such as INTERMACS profile ≥7. Our data encourage non-heart transplant approaches in a very particular situation where heart transplantation is limited due to organ storage, and also provide a benchmark against which long-term outcomes of destination therapy with LVADs can be compared.

Conflict of interest: none declared.

REFERENCES


APPENDIX. CONFERENCE DISCUSSION

Dr L. Menicanti (Milan, Italy): This is an interesting paper, reporting on patients with ischemic cardiomyopathy in accordance with INTERMACS classification, which includes a really wide variety of clinical presentation. We have patients in cardiogenic shock and patients in Class III NYHA. So in my understanding of the data that you present to us, this population can be divided into two big groups, one with INTERMACS more than 4 and the other one with INTERMACS less than 4. If you consider the mortality of these two groups, when you have more than 4, there is no surgical mortality, is that correct?

Dr Cho: Yes, that’s correct.

Dr Menicanti: And in the other group, the mortality is relevant. In your paper, mitral surgery – repair or replacement – plus SVR is more frequent, almost double than in patients with INTERMACS less than 4. So it’s really difficult to know if the mitral surgery impacts on the outcome of these patients or whether the prognosis of these patients is determined by the quality of the ventricle that is beneath. What is your indication for treating the mitral valve, and what is your feeling about the presence of mitral regurgitation?

Dr Cho: We operate on the mitral valve when the MR grade reaches moderate, and MVR is applied for greater than severe MR or when we fail to achieve total scar exclusion by LVR because residual scar causes further dilation of the LV.

So the mechanism of ischaemic MR might be complex and more difficult to detect clinically because the modalities are not sensitive to functional MR, and this could be missed, or the grade might be underestimated particularly in an extremely dilated ventricle. So we speculate that a more aggressive approach for adequate MR control is called for.

Dr Menicanti: And the other thing that I would like to outline is that the surgical results in patients in INTERMACS 7, are outstanding. So do you advocate treating these patients early before reaching a lower INTERMACS class? This is a very important issue because a surgical procedure sometimes is postponed to avoid an increased surgical risk, in the hope of stabilizing the clinical situation. But probably we are wrong, and we have to do something sooner.

Dr Cho: As for the second question, we believe that total scar exclusion is most important for the long-term outcomes of the LVR. So we are now doing LVR not to achieve volume reduction but to achieve total scar exclusion. So we speculate that our results were achieved by detecting the scar area earlier by MRI and excluding it as totally as possible. However, our indication for LVR is the same as the RESTORE groups.

Dr A. Basu (Chennai, India): This is a general question to all the previous speakers regarding postoperative care. Do almost all patients require an IABP or ECMO? What is the duration of ICU stay? And how hard do you try to save the patient if things go wrong because many of them are not transplant candidates?

Dr Cho: We have no patient who required ECMO or LVAD perioperatively. In our series, we’ve never failed a patient for the LVAD after non-heart transplant approaches.

Dr M. Zembala (Zabrze, Poland): Zero mortality in INTERMACS Class 1 is indeed a very special result. Do you have a VAD programme, a mechanical circulatory support programme in your institution?

Dr Cho: No.

Dr Zembala: What about ECMO and so on - no?

Dr Cho: No, not in my series. We had no patients.

Dr Zembala: Not in your series, but generally you do use it?

Dr Cho: Generally I use it, yes, just in case we fail.

Dr Zembala: What were the criteria for this series of INTERMACS 1? Nine, eight patients, very sick patients, you still did not use anything except a balloon and then surgery. What was the main indication?

Dr Cho: An extremely dilated heart without asynergy. That’s the indication for VAD, LVAD.

Dr Zembala: You lost one patient in INTERMACS 1, yes?

Dr Cho: Yes, yes, I lost one patient.

Dr Zembala: Just one?

Dr Cho: Yes. In INTERMACS profile 2.

Dr Basu: Postop IABP, intra-aortic balloon pump, and the length of ICU stay ventilation, just a rough idea?

Dr Zembala: How long was the postoperative course, ICU stay?

Dr Cho: The mean ICU stay is between four days and five days.

Dr L. Menicanti: And do you use the balloon pump in all of your patients?

Dr Cho: Not all patients, about 30% in my series.

Dr Menicanti: And do you use ECMO in INTERMACS 1, 2, 3?

Dr Cho: No patient required ECMO after operation.