Preoperative Regional Left Ventricular Wall Thickening Determined by Quantitative Gated SPECT as a Predictor of Mid-Term Surgical Results for Ischemic and Nonischemic Cardiomyopathy

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Background: This study aimed to elucidate whether regional left ventricular wall thickening (LVWT) determined by quantitative gated SPECT (QGS) is useful in predicting surgical outcomes for ischemic (ICM) and nonischemic cardiomyopathy (NICM).

Methods and Results: The study group comprised 53 patients with either ICM (n=30, left ventricular ejection fraction (LVEF)=24.7±7.1%) or NICM (n=23, LVEF=24.0±6.3%) scheduled for surgical repair underwent preoperative QGS to evaluate regional LV function. LVWT of 20 segments derived from QGS was normalized by being divided by the normal value of each LV level. Normalized values of the segments were summed to be representative of each area. For 16 of the 30 patients with ICM and 17 of the 23 patients with NICM, surgical ventricular restoration and papillary muscle approximation (PMA) were performed for surgical repair and, for the rest, PMA alone was done for both ICM and NICM patients. Adjunctive coronary artery bypass grafting for ICM patients was added when necessary. Mean follow-up periods were 2.5±1.8 years for ICM and 2.2±2.4 years for NICM. Posterior regional LVWT in NICM (normalized sum value <0.61 n=7, ROC: AUC=0.80) predicted cardiac events (chronic heart failure and cardiac-caused death). The one-year cardiac event-free rates were 22.2% and 85.1% and the 2 years rates were 11.1% and 48.6% for the lower posterior WT group and higher posterior WT group respectively (P=0.003).

Conclusions: Posterior LVWT can be a predictor for postoperative cardiac events in patients with NICM. (Circ J 2013; 77: 2936–2941)

Key Words: Cardiomyopathy; Quantitative gated SPECT; Surgical results; Wall thickening

Surgical ventricular restoration (SVR) is performed for advanced heart failure (HF), especially that with ischemic cardiomyopathy (ICM). Although the report by Jones et al on the Surgical Treatment of Ischemic Heart Failure (STICH) trial suggested no additional effect of SVR on ICM, the effectiveness for the extremely dilated heart seems to be retained. The clinical relevance and advantages of SVR have been reported from many centers, indicating improvement in the New York Heart Association (NYHA) functional class and left ventricular (LV) volume. Various preoperative parameters have been assessed with several modalities to predict clinical outcomes prospectively. Echocardiography is used to derive indices of systolic and diastolic function for potential predictors of clinical results. Recently, magnetic resonance imaging (MRI) also has been increasingly applied to detect myocardial fibrosis, predicting postoperative outcomes in patients with ischemic HF. Indeed, similar approaches have been used with echocardiography, MRI, biopsy, and biochemical markers for nonischemic cardiomyopathy (NICM). The number of reports for NICM, however, is quite limited, particularly for patients after SVR. Moreover, assessments with quantitative gated SPECT (QGS) for NICM after SVR are scarce. We therefore attempted to investigate the predictors of clinical outcomes after surgical repair for NICM and ICM, focusing on QGS analysis of LV regional systolic function with wall thickening (WT).

Methods

Study Population
The study was approved by the hospital’s Institutional Review Board of and informed consent was given by the patients.
retrospectively examined patients with ICM or NICM scheduled for surgical repair from June 2004 to November 2011. Among them, all 53 patients who underwent preoperative QGS were included in this study. Patients who did not undergo preoperative QGS inspection because of time constraints, for instance, those with a preoperative emergency status, were naturally excluded.

**Table 1** shows the demographic data and LV volumes and functional measurements by QGS for the ICM (n=30) and NICM (n=23) groups. In the ICM group, 90% were male, as were 65% in the NICM group. Almost all the patients in the NICM group had an mitral regurgitation (MR) grade ≥3 (91%) and NYHA class ≥3 (96%); 5 of the 23 NICM patients were in a catecholamine-dependent condition when the surgical repair was performed.

Preoperative LV global function was assessed by QGS. The mean LV ejection fraction (LVEF) was 24.7±7.1% and 24.0±6.3% in the ICM and NICM groups, respectively. The LV was so dilated that the LV end-diastolic volume index reached 168±55 ml/m² in the ICM group and 212±63 ml/m² in the NICM group. After surgical repair, MR was significantly reduced in both groups (P<0.001). In addition, LV volume was extremely diminished in terms of LV end-diastolic volume, end-systolic volume and stroke volume (P<0.001). However, EF was significantly improved only in the ICM group and not in the NICM group (**Table 2**).

**QGS Analysis**

99mTc SPECT was performed prior to surgical repair and the left ventricular wall thickening (LVWT) was analyzed for regional systolic function using QGS software, as previously reported when the wall function of the LV apical region was severely diminished. In brief, data were collected with a dual-head 90° camera after injection of 740 MBq of a 99mTc tetrofosmin tracer. The LV image was divided into 20 segments, including 6 circumferential myocardial segments each at the basal, middle and distal levels of the LV, and 2 segments of the apical region. For each individual, segmental LVWT, defined as systolic WT divided by diastolic WT, was automatically calculated using the QGS software. According to a robust database, normal WT values of each level differ, so to normalize the values, they were divided by the average WT of normal Japanese. As the next step, the normalized values of each segment in the same level or area were summed to represent each level or area (AS: anteroseptal, IS: inferoseptal, P: posterior, L: lateral).

**Surgical Indications and Procedures**

When the patient was in NYHA class 3 or more, or had a history of hemodynamic decompensation, surgical repair was considered. Our indications of SVR for ICM and NICM were LV diastolic dimension (LVDD) >65 mm and >70 mm, respectively. Papillary muscle approximation (PMA) was performed concomitantly or independently when the internal distance between the anterior and posterior papillary muscles was >30 mm and the mitral valve was tethered with functional MR of more than a mild grade.

Overlapping left ventriculoplasty (OLVP) was performed as previously reported when the wall function of the LV anteroseptal area was severely diminished. Briefly, a 10 cm-long incision was made longitudinally along the left anterior descending artery at the LV anterior wall. The separated left-hand margin was sutured to the septal wall, usually at the height of the lower two-thirds of it. The exact suture line was determined using an intraventricular cup sizer measuring 72 ml or 95 ml. After suturing of the lateral margin, the septal margin was then sutured onto the lateral wall slightly beyond the preceding suture line in ICM or onto the free LV wall in NICM, resulting in a layered overlap of the myocardial wall constructed in the anteroseptal lesion. In the PMA procedure, 2 or 3 pledgedt matress sutures were placed from the tip to the bottom along both the anterior and posterior papillary muscles that together formed the papillary muscle. A mitral annulus ring was placed (MAP) as part of mitral complex reconstruction, which was done with MAP and PMA.

**Table 1. Preoperative Characteristics of Patients With ICM or NICM**

<table>
<thead>
<tr>
<th></th>
<th>ICM (n=30)</th>
<th>NICM (n=23)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (average ±SD)</td>
<td>61±13</td>
<td>59±11</td>
<td></td>
</tr>
<tr>
<td>Male (%)</td>
<td>27 (90)</td>
<td>15 (65)</td>
<td></td>
</tr>
<tr>
<td>MR grade</td>
<td>2.5±1.3</td>
<td>3.6±0.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>&gt;3 (%)</td>
<td>14 (47)</td>
<td>21 (91)</td>
<td></td>
</tr>
<tr>
<td>NYHA class</td>
<td>3.0±0.7</td>
<td>3.3±0.6</td>
<td></td>
</tr>
<tr>
<td>&gt;3 (%)</td>
<td>24 (80)</td>
<td>22 (96)</td>
<td></td>
</tr>
<tr>
<td>CA depend (%)</td>
<td>2 (7)</td>
<td>5 (22)</td>
<td></td>
</tr>
</tbody>
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CA depend, catecholamine-dependent; ICM, ischemic; MR, mitral regurgitation; NYHA class, New York Heart Association classification; NICM, nonischemic cardiomyopathy.

**Table 2. Comparison of Pre- and Postoperative LV Parameters and Mitral Regurgitation in Patients With ICM or NICM**

<table>
<thead>
<tr>
<th></th>
<th>ICM (n=30)</th>
<th>NICM (n=23)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MR grade</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>QGS global</td>
<td></td>
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<tr>
<td>LVEDV (ml)</td>
<td>269±71</td>
<td>340±99</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LVEDVI (ml/m²)</td>
<td>168±55</td>
<td>212±63</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LVESV (ml)</td>
<td>204±61</td>
<td>260±83</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LVESVI (ml/m²)</td>
<td>127±48</td>
<td>162±53</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LVSV (ml)</td>
<td>66±22</td>
<td>80±29</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LVSVI (ml/m²)</td>
<td>40±14</td>
<td>50±17</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>24.7±7.1</td>
<td>24.0±6.3</td>
<td>NS</td>
</tr>
</tbody>
</table>

LV, left ventricular; LVEDV, left ventricular end-diastolic volume; LVEDVI, left ventricular end-diastolic volume index; LVEF, left ventricular ejection fraction; LVESV, left ventricular end-systolic volume; LVESVI, left ventricular end-systolic volume index; LVSV, left ventricular stroke volume; LVSVI, left ventricular stroke volume; MR grade, mitral regurgitation grade; ICM, ischemic cardiomyopathy; NICM, non-ischemic cardiomyopathy; NYHA class, New York Heart Association classification; QGS, quantitative gated SPECT. Other abbreviations as in Table 1.
Follow-up
The medical records of all patients were reviewed and patients were interviewed when the records were not sufficiently clear for the judgment of outcome. A cardiac event was defined as cardiac death or rehospitalization for HF or refractory arrhythmia. Follow-up was completed for all patients except those who died in the perioperative period.

Statistical Analysis
All data are expressed as mean ± standard deviation. Student’s t test was used to compare means of continuous variables. The relations among variables were investigated with a multivariate logistic regression model. Receiver-operating characteristic (ROC) curves were used to determine the accuracy and optimal thresholds of significant variables predicting cardiac events. The Kaplan-Meier method was used to evaluate the incidence of cardiac events and 2 groups were compared by the log-rank test. P<0.05 was considered statistically significant. SPSS Statistics version 19 (SPSS Inc, Chicago, IL, USA) was used for all statistical analyses.

Results
Operative Data
In total, 16 of the 30 ICM patients (53%) and 17 of the 23 NICM patients (74%) underwent SVR. OLVP was applied for SVR in all patients except the one in each group who underwent partial ventriculoplasty. All of the patients in the NICM group and 27 of the 30 patients (90%) in the ICM group had MAP with a semirigid or rigid ring. Aortic valve replacement and tricuspid ring annuloplasty were also added when necessary. Adjunctive coronary artery bypass grafting (GABG) was performed in 27 patients (90%) with ICM (Table 3).

Early Outcomes
The 30-day mortality rate was 6.7% (2 cases) for the ICM group and 8.7% (1 case) for the NICM group. The cause of both deaths in the ICM group was low-output syndrome following the operation. The single NICM death was of a patient who had percutaneous cardiopulmonary support prior to the SVR operation and died of low-output syndrome 16 days after an emergency operation. There were 2 hospital deaths in the ICM group and 4 in the NICM group, all caused by low-output syndrome.

Mid-Term Outcomes
The mean follow-up periods were 2.5±1.8 years for ICM and 2.2±2.4 years for NICM. Cardiac events necessitating readmission occurred in 8 ICM patients and 12 NICM patients. There was acute exacerbation of HF in 6 and 11 patients, and refractory arrhythmia in 1 and 2 patients in the NICM and ICM groups, respectively.

Relation Between Preoperative Regional LVWT and Postoperative Cardiac Events
Univariate and multivariate analyses of LVWT in those with cardiac events (CE+ group) and those without (CE− group) are shown in Table 4. The analyses revealed that deterioration of posterior LVWT was significantly associated with CE in NICM (P<0.05). There was no difference between the CE+ and CE− groups at any level or area in ICM patients.

Figure 1 shows the ROC curve of posterior LVWT for prediction of CE. It revealed that the cutoff value of 0.61, determined by the Youden index method, would predict cardiac events after surgery with sensitivity and specificity of 56.3% and 100%, respectively. The area under the curve was 0.80 (95% confidence interval 0.61–0.98, P=0.027).

Kaplan-Meier plots depicted freedom from cardiac death after surgery stratified according to posterior LVWT (WT≥0.61 vs. <0.61). The rates of freedom from cardiac death at 1 year were 92.9% and 66.7%, and at 2 years 83.6% and 22.2% in the ≥0.61 and <0.61 groups, respectively. Log-rank statistics showed a significantly better outcome in the greater posterior LVWT
Regional LVWT Predicts Surgical Outcome

This report demonstrates that deterioration of posterior LVWT determined using QGS can be a predictor for cardiac events after surgery for patients who undergo surgical repair for NICM based on our surgical treatment strategy. Our surgical strategy for cardiomyopathy patients can be summarized as follows. SVR is considered when the LVDd is >65 mm for ICM and >70 mm for NICM, and our original procedure called OLVP is used when the anteroseptal wall function of LV is diminished, which is evaluated using echocardiography and MRI and/or acetate positron emission tomography. Adjunctively, PMA with mitral ring annuloplasty is performed when the internal distance between the anterior and posterior papillary muscles reaches 30 mm and functional MR of more than a mild grade with tethering is also detected. The main concept of surgical repair for the severely dilated heart is reducing LV wall shear stress caused by reducing the LV cavity size and also eliminating MR. However, the crucial factor for the prognosis after surgical intervention may be the remaining LV function, which is hard to measure in advance. One of the reasons for this measurement difficulty is that the myocardium with NICM becomes progressively worse.

Many reports have attempted to predict recurrence of functional MR. However, there are few concerning the surgical results after considering the preoperative parameters of NICM patients. We reported here that posterior LVWT might be a predictor of CE in NICM patients. On the other hand, we could not identify any predictor for ICM in terms of LVWT. CABG was adjunctively performed in anticipation of myocardial recovery among hibernating areas with coronary revascularization. Regional wall function in patients with ICM after surgical repair will be affected not only by SVR but also by revascularization. Therefore, it makes sense that there is a certain limit to determining predictors prior to surgery for ICM.

Why is the posterior wall a predictor but not the lateral wall? We speculate that the posterior wall is very susceptible to damage, but why? To consider this question, the concept of the helical ventricular myocardial band, proposed by Torrent-Guasp et al. and expanded by Buckberg et al., is informative. According to this concept, the LV wall consists of crossed double layers that have different strips of myocardial fibers except at the posterior and inferior walls. These areas are not lined with...
another layer, resulting in a constructional weakness. When the myocardium becomes diseased, the posterior wall tends to functionally deteriorate. Furthermore, there have been several reports of regional contractile heterogeneity in NICM patients. Uematsu et al measured peak myocardial velocity gradients by 2-D tissue Doppler echocardiography and found lower velocity gradients in the anteroseptal segments than in the posterior segments. Moreover, Young et al detected septal dysfunction and relatively normal lateral wall function by magnetic resonance tissue tagging. They reported circumferential heterogeneity with a consistent pattern in dilated cardiomyopathy (DCM) patients. Meanwhile, Suma et al showed heterogeneity of myocardial fibrosis with several patterns in DCM patients. They demonstrated that fibrosis was dominant in the septum in some cases and also dominant in the lateral wall in some cases. Likewise, diversity of circumferential heterogeneity of LV wall function may exist. In our current study, NICM patients (n=21) could be classified into 3 types based on the area of deteriorated WT, including the anteroseptal type (6 patients), posterior type (5 patients) and other (10 patients: inferior relatively reduced). All 5 patients with the posterior type were categorized as posterior LVWT <0.61 and 4 of them had a CE during follow-up.

Based on our surgical strategy, SVR was performed for a severely dilated LV. Moreover, in most cases, OLV was the procedure because anteroseptal wall function was restricted to a certain degree, as is often the case with NICM. When posterior wall deterioration also existed, it was obvious that remaining global LV function was diminished, leading to a poor prognosis. When posterior wall function was not so damaged, global LV function was maintained, leading to a better prognosis. The distance between the internal papillary muscles was so wide that PMA was necessary to correct the mitral valve tethering for all of the NICM patients. PMA is a procedure that joins both muscles together without resection or exclusion of the posterior wall between them. Therefore, it causes no reduction or increase of posterior WT when preoperative and postoperative WT are compared, as we reported previously. Thus, there is a possibility that a direct procedure for the posterior wall, where PMA cannot reach, might improve the surgical results for patients with deteriorated posterior LVWT. If it is able to additionally reduce the LV volume after the usual SVR, an adjunctive procedure for posterior wall exclusion, such as partial left ventriculectomy or posterior wall plication, might be considered if posterior LVWT is extremely diminished.

QGS is a very useful modality for assessing regional cardiac function in DCM. It is not prohibited in patients with CRT or pacemaker as is MRI, or by renal insufficiency as is enhanced computed tomography (CT). Moreover, LVWT as regional LV wall function can be obtained automatically with the commercially supplied software. LV wall motion, indeed, can be provided by cardiac cine MRI or CT and also by echocardiography. However, we believe that WT is crucial for evaluating regional LV function. In NICM, delayed enhancement typically at the mid-layer of the LV wall is characteristic for contrast-enhanced cardiac MRI. When we examined the preoperative cardiac MRI of 11 out of the 23 NICM patients in this study, the distribution of delayed enhancement in the LV wall did not relate to their postoperative CE as a surgical result. We think that QGS study has extensive application and facility to assess LV regional wall function.

Study Limitations
First, this study was retrospective. Second, in both groups the number of patients was small. Lastly, surgical procedures were not the same in all patients of each group, as there were patients with and without OLVP and so on. Therefore, it is difficult to determine the main cause of the effect on the surgical outcome. Despite these limitations, all the patients were treated using a consistent surgical strategy.

Conclusion
Posterior LVWT can be a predictor for postoperative cardiac events in patients with NICM.

Disclosures
Conflict of interest: none declared.

References

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