The importance of grade 2 ischemic mitral regurgitation in coronary artery bypass grafting

Tina Rydén¹, Odd Bech-Hanssen², Gunnar Brandrup-Wognsen³, Folke Nilsson⁴, Sveneric Svensson⁴, Anders Jeppsson⁴,*

¹Department of Cardiothoracic Surgery Sahlgrenska University Hospital, Göteborg, Sweden
²Department of Clinical Physiology, Sahlgrenska University Hospital, Göteborg, Sweden

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Abstract

Objective: To study if grade 2 ischemic mitral regurgitation (MR) influences outcome after coronary artery bypass grafting (CABG).

Methods: Results of all CABG patients with grade 2/4 ischemic MR operated during 1995–1998 (n = 89) were compared with all CABG patients without MR (n = 4709) during the same period. To further evaluate patients with grade 2 ischemic MR, a case-control study focusing on functional status was performed. Control patients without MR (n = 89) were matched for age, gender and left ventricular ejection fraction. All patients were interviewed regarding angina symptoms and functional status. Results: Survival according to Kaplan–Meier at 1 and 3 years were inferior in the MR group compared to all CABG patients (91 vs 96% and 84 vs 92%, respectively (P < 0.0017). However, MR patients were older (68 ± 9 vs 65 ± 9 years (mean ± SD), P = 0.008) and had an inferior preoperative left ventricular ejection fraction (42 ± 14 vs 58 ± 14%, P < 0.0001). In the case-control study, New York Heart Association (NYHA) class and Higgins’ risk score differed preoperatively between the MR group and controls. Neither 30-day mortality (4.5% in both groups) nor survival at 1 (91 vs 93%) and 3 years (84 vs 88%) differed significantly. NYHA class and angina class (Canadian Cardiovascular Society, CCS) improved similarly in both groups. Postoperatively, 62% of the patients in the MR group had reduced, 36% unchanged and 2% increased MR.

Conclusions: CABG on patients with grade 2 ischemic MR reduces angina pectoris and improves functional status to the same extent as in CABG patients without MR. Postoperative morbidity and mortality do not differ significantly between the groups. Grade of MR is reduced or unchanged after CABG in patients with grade 2 ischemic MR. The study supports an operative strategy where grade 2 ischemic mitral regurgitation is treated by CABG alone but the result do not exclude that there might be individual patients that would benefit from a valvular or annular procedure in combination with CABG. How these patients should be identified remains unclear. © 2001 Elsevier Science B.V. All rights reserved.

Keywords: Coronary artery disease; Mitral regurgitation; Cardiac surgery; Echocardiography

1. Introduction

Mitral regurgitation (MR) from coronary artery disease, ischemic MR, is found in approximately 3% of all patients undergoing coronary angiography [1]. MR varies in severity and is judged by echocardiography on a four graded scale. The more severe forms of ischemic MR (grade 3 and 4) is generally treated with coronary artery bypass grafting (CABG) and a valve or annular procedure, while the milder forms (grade 1 and 2) are treated solely with CABG. This strategy is supported in the literature [2–5], although it has been questioned [6–9].

Ischemic MR is not an homogenous entity; at least three subgroups could be distinguished. First, coronary artery disease (CAD) with annular dilation, second CAD with ischemic or infarcted papillary muscles and third, CAD with chordal or leaflet pathology and prolapse in combination with annular dilation [3]. These subgroups may require different therapeutical strategies and make the interpretation of reports about ischemic MR as one entity difficult or even impossible.

The present investigation was undertaken to study the influence of grade 2 ischemic MR from CAD on outcome after CABG. For this purpose, we compared our results after CABG in patients with grade 2 ischemic MR with the results in patients without MR. It is possible that a grade 2 ischemic MR could indicate a more pronounced myocardial and/or valvular dysfunction, and therefore substantially influence
the results after CABG. If it is so, these patients may benefit from a changed surgical strategy including annuloplasty.

2. Materials and methods

2.1. Patients

During a 4-year period (1995–1998) 4798 patients underwent isolated first time CABG at Sahlgrenska University Hospital. All patients were screened for mitral regurgitation by left ventricular contrast injection during the coronary angiography or by echocardiography. All patients with suspected mitral regurgitation were investigated by transthoracic echocardiography and a group of CABG patients with grade 2/4 ischemic MR were identified. In this group, patients with MR from structural leaflet changes (prolapse) were excluded. Finally, there remained 89 patients with grade 2/4 ischemic MR from coronary artery disease (study group) corresponding to 1.8% of all CABG patients. Preoperative characteristics of the patients are given in Table 1.

In the first study, the results after CABG in the study group were compared to the results of all CABG patients. The comparison of the two groups revealed substantial preoperative differences (Table 1) and therefore a second study with a case control design was performed. In this part, the study group was matched to a control group consisting of 89 CABG patients without evidence of MR on echocardiography or angiography. The groups were matched regarding sex, age, and left ventricular ejection fraction and due to the relative short follow-up period, to month of operation.

We searched for each study patient a control subject among all CABG patients without mitral regurgitation operated during the same period. The control should unconditionally have the same gender and when it comes to age, left ventricular ejection fraction and operation month we used a computerized matching system which gave us the best match (= minimize the maximum difference divided by the corresponding standard deviation) to a study subject.

Mean follow-up time was 28 ± 15 months (mean ± SD) and was 100% complete regarding survival and 98.4% complete regarding postoperative angina and function.

2.2. Echocardiography

Echocardiography was performed using an Acuson Computed Sonograh (Acuson, Mountain View, CA, USA) or Vingmed Ultrasound equipment (Vingmed Sound AS, Horten, Norway). M-mode measurements were made according to the recommendations of the American Society of Echocardiography [10]). The ejection fraction was calculated either from M-mode according to Teichholtz [11], or from two-dimensional recordings according to Simpson’s rule [12].

All the patients were investigated by color Doppler, as well as by pulsed and continuous wave Doppler. Mitral flow was recorded at the tips of the mitral leaflets in the four-chamber view. Pulmonary venous flow velocities were obtained by placing the sample volume at the orifice of the upper right pulmonary vein. Peak velocity during systole (S) and diastole (D) was measured. Continuous wave Doppler signals were recorded by a 2 MHz non-imaging probe to obtain an optimal signal-to-noise ratio and multiple windows were used.

The assessment of mitral regurgitation severity was based on a number of variables: color Doppler jet characteristics including jet width and area [13,14], continuous wave Doppler intensity and shape of the spectral recording, mitral inflow [15] and pulmonary vein flow pattern by pulsed wave Doppler [16], left atrial size, left ventricular dimensions and pulmonary artery pressure. These variables are either directly influenced by mitral regurgitation severity or related to compensatory changes in the heart. All patients were graded on a four graded scale. Grade 1 regurgitation was characterized by a weak holosystolic continuous wave

Table 1

<table>
<thead>
<tr>
<th>Patient characteristicsa</th>
<th>CAD + MR 2 (n = 89)</th>
<th>Control group (n = 89)</th>
<th>All CABG patients (n = 4709)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>68 ± 8.7**</td>
<td>67 ± 8.2</td>
<td>65 ± 9.3</td>
</tr>
<tr>
<td>Male sex (%)</td>
<td>63***</td>
<td>63</td>
<td>79</td>
</tr>
<tr>
<td>BMI</td>
<td>26 ± 3.4</td>
<td>26 ± 3.2</td>
<td>26 ± 4.5</td>
</tr>
<tr>
<td>Previous stroke (%)</td>
<td>5.6</td>
<td>5.6</td>
<td>4.6</td>
</tr>
<tr>
<td>Obstructive pulmonary disease (%)</td>
<td>8.9*</td>
<td>5.6</td>
<td>4.7</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>44</td>
<td>39</td>
<td>38</td>
</tr>
<tr>
<td>Diabetes (%)</td>
<td>26*</td>
<td>19</td>
<td>17</td>
</tr>
<tr>
<td>Unstable angina (%)</td>
<td>24</td>
<td>29</td>
<td>21</td>
</tr>
<tr>
<td>Ejection fraction (%)</td>
<td>42 ± 14***</td>
<td>44 ± 12</td>
<td>58 ± 14</td>
</tr>
<tr>
<td>Left main stenosis (%)</td>
<td>21</td>
<td>18</td>
<td>19</td>
</tr>
<tr>
<td>S-creatinine (μmol/l)</td>
<td>107 ± 33</td>
<td>105 ± 65</td>
<td>103 ± 51</td>
</tr>
<tr>
<td>Higgins’ risk score</td>
<td>3.3 ± 2.4**</td>
<td>2.3 ± 1.8</td>
<td>1.8 ± 1.8</td>
</tr>
</tbody>
</table>

a Key: BMI, body mass index, CABG, coronary artery bypass grafting. CAD, coronary artery disease. MR, mitral regurgitation. *P ˂ 0.05 study group vs all CABG patients; **P ˂ 0.01 study group vs all CABG patients; ***P ˂ 0.001 study group vs all CABG patients. §P ˂ 0.01 study group vs control group.
Doppler signal and a small color Doppler area. Grade 2 regurgitation was characterized by a continuous wave Doppler signal with intermediate intensity, normal pulmonary vein flow pattern and no marked increase in the mitral inflow velocity. Left ventricular and atrial enlargement, high continuous Doppler intensity, large color Doppler area, high mitral inflow velocity, blunted or reversed systolic pulmonary vein flow and pulmonary artery hypertension characterizes grade 3 and 4 mitral regurgitation.

2.3. Study variables

All pre- and peroperative variables were registered prospectively. Mortality after the hospital stay was collected from the county’s database. Postoperative heart failure was defined as the need for IABP and/or inotropic support postoperatively. Higgins’ risk score was used for preoperative risk evaluation [17]. Follow-up in surviving patients in the study group and the matched control group was obtained by telephone interview. Predefined inquiries were made regarding level of physical activity that could be performed without causing angina, dyspnea or fatigue. Angina was graded according to the New York Heart Association, NYHA [19]. Postoperative echocardiography was performed only when indicated, as determined by the patient’s cardiologist. The echocardiographic investigations were performed either at Sahlgrenska University Hospital or at the local hospital. The same criteria for mitral regurgitation grading was used by all investigators. In the study group, postoperative echocardiogram was available in 40 patients (45%) 346 ± 78 days (range 8–1114) after surgery.

2.4. Statistics

All continuous data are given as mean ± standard deviation. Unpaired t-test or Mann–Whitney U-test (abnormally distributed data) were used to compare continuous variables and Fisher’s exact test to compare categorical data between the groups. To compare changes in NYHA and CCS class, Fisher’s test for paired comparisons [20], was used within the groups and Fisher’s permutation test [21] between the groups. Survival curves were calculated according to Kaplan–Meier, followed by Log-Rank test to compare the groups. A P-value of ≤0.05 was considered significant.

3. Results

3.1. Study group vs all CABG patients (Study 1)

3.1.1. Preoperative data (Table 1)

When patients with MR grade 2 were compared to all CABG patients, the study patients were older and a greater proportion were females. Study patients had a higher incidence of previous stroke, obstructive pulmonary disease and diabetes. The study group had also inferior LVEF (P < 0.0001), higher Higgins’ risk score (P < 0.0001) and inferior preoperative functional status (P < 0.0001).

3.2. Early postoperative parameters (Table 2)

Mean number of anastomoses was higher and extracorporeal circulation time and aortic cross clamp time were longer in the study group compared to all CABG patients. In addition, postoperative heart failure and postoperative myocardial infarction were more common in the study group. Thirty-day mortality tended to be higher in the study (4.5 vs 2.2%) but did not reach statistical significance.

3.3. Survival

Survival according to Kaplan–Meier during the follow-up period differed significantly between the two groups (P = 0.0017). One-year survival was 91% in the study group and 96% among all CABG patients and 3-year survival 84 and 92%, respectively.

3.4. Case-control study (Study 2)

3.4.1. Preoperative parameters (Table 1)

When the study group was compared to a matched population, the study group had preoperatively higher Higgins'
risk score and inferior functional status (Fig. 1), while all other preoperative variables were comparable.

3.4.2. Per- and early postoperative results (Table 2)

Thirty-day mortality was identical between the groups (4.5% in both groups). There were no significant differences in early morbidity even though the data indicate a more complicated postoperative course for the study group.

3.5. Follow-up

Survival curves are given in Fig. 2. Survival did not differ significantly between the groups ($P = 0.21$). One-year survival for the study group and the control group was 91 and 93%, respectively. Three-year survival was 84 and 88%, respectively.

CABG reduced angina symptoms similarly in both groups (Fig. 3). Functional status improved in both groups (Fig. 1) but the improvement reached statistical significance only in the study group.

Postoperative echocardiogram was obtained in 40 patients in the study group and 63% had reduced MR, 35% had unchanged MR (grade 2) and one patient (2%) had increased MR, grade 3 (Fig. 4). Postoperative LVEF was unchanged compared to the preoperative value ($42 \pm 15$ vs $42 \pm 13\%$, $P = ns$).

4. Discussion

The main findings of the study are (1) CABG on patients with grade 2 MR reduces angina pectoris and improves functional status to the same extent as in CABG patients without MR. (2) Morbidity and mortality are comparable in CABG patients with or without grade 2 MR. (3) Grade of MR is reduced or unchanged in CABG patients with grade 2 MR after CABG alone.

Mitral regurgitation may be degenerative, rheumatic or
ischemic in origin [3]. It is difficult to distinguish between different forms of MR and combinations are probably common. Ischemic MR in itself is complex with different mechanisms resulting in regurgitation. Thus, results from studies where different definitions of ischemic MR have been used are difficult to compare and should be interpreted with caution. In addition, different grading systems, based on either angiography or echocardiography, have been used and there is also a lack of consistency in the terminology. In some papers a grade 2 MR is referred to as moderate [4,8,22] and in some papers as mild [6,7,9] which further increases the degree of difficulty to read and interpret previous studies. Therefore, in the present paper we chose to use only the term ‘grade 2 MR’ exclusively based on echocardiography.

In the present study, we included only patients with significant coronary disease and MR grade 2 while patients with prolapse were excluded. This was done to receive an as homogenous study population as possible and therefore simplify interpretation. It is appreciated that the selection restricts the validity of our conclusions to the same patient category.

At our institution, patients with grade 2 ischemic MR is treated with CABG alone while patients with more severe ischemic MR (grade 3 and 4) are treated with CABG and annuloplasty. According to published reports [2–5], this is the most widespread strategy. However, it has been questioned both by those who advocate a more aggressive attitude towards annuloplasty [9] in patients with less severe forms of ischemic MR (after intra-operative dynamic testing) and those who have a more conservative attitude and treat patient with severe MR by CABG alone [6–8]. Connolly et al. [2] showed significantly inferior survival for CABG patients with grade 3 ischemic MR than CABG patients without MR and suggested that MR grade 3 and 4 should be corrected at the time for CABG. On the other hand, Arcidi et al. [6] presented 1988 results indicating that patients with grade 3 ischemic MR undergoing CABG alone had comparable results to patients undergoing CABG and valve replacement/annuloplasty. Christenson et al. [7] in 1995, reported good survival and functional improvement after CABG alone in patients with MR grade 1 to 3 in combination with poor ventricular function. Recently, Duarte reported that long time survival is comparable in CABG patients with or without grade 3 MR, 20 years after the operation [8]. However, none of these studies are randomized and therefore differences in patient selection may explain the results.

In the present study, we compared outcome after CABG in patients with ischemic MR grade 2 with CABG patients without MR. We reasoned that if the results in the CABG + MR grade 2 group were equivalent to those obtained in comparable patients without MR, this would indicate that CABG alone in patients with ischemic MR grade 2 is justified, while other operative strategies may be considered if the results were evidently inferior.

When the results in the study group were compared with those in the whole CABG population, there was an obvious difference in outcome. However, when the preoperative parameters were analyzed, it became evident that we did not have comparable groups. It was a marked discrepancy between the groups in, among others, age, gender and LVEF. Therefore, we chose to make a case control study with controls matched for age, gender and LVEF.

In the case-control study, morbidity and mortality were comparable in both groups, which not is surprising given that the MR was reduced postoperatively in the majority of the study patients. In addition, both groups improved similarly after CABG in functional status. The results imply that a grade 2 ischemic MR from annular dilation does not substantially influence the results after CABG. Therefore, the results suggest that the present operational strategy is appropriate, but it should be emphasized that the follow-up period is short and there is a tendency towards a more complicated postoperative course and decreased long-time survival in the study group, which may be more evident after a longer follow-up period. On the other hand, in spite of the efforts to match the groups, it appears that the groups were not completely comparable. Preoperatively, the study group had significantly higher risk score (Table 1) and worse functional status (Fig. 3) compared to the control group. Thus, a more complicated postoperative course could be expected in the study population and in fact, the absence of significant differences in postoperative morbidity and mortality argues for the present surgical strategy.

Echocardiography demonstrated that grade 2 MR decreased or remained unchanged postoperatively which is in accordance with Christensen et al.’s findings [7]. However, postoperative echo was only performed when the treating cardiologist found it indicated and therefore only about 45% of the patients had been examined at different time points after the operation. Of course, this restricts the validity of the findings considerably. On the other hand, one may speculate that the cardiologists only examined patients when they, from physical examination, suspected impaired cardiac function and/or worsened mitral regurgitation. Subsequently this indicates that only the patients with more severe symptoms were investigated and that the reported improvement of MR may be underestimated.

In the present study, all patients with ischemic MR grade 2 was treated by CABG solely. Even though the majority of patients had less severe MR and improved their functional status postoperatively, does the result not exclude that there might be patients that would benefit from a valvular or annular procedure in combination with CABG. The present study gives no information about this issue. An open question remain, how should these patients be identified. It is possible that dynamic testing as suggested by Dion et al. [9] can be one alternative.

In summary, the results of the study support a surgical strategy where grade 2 ischemic MR from annular dilation is treated solely with CABG.
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References


Appendix A. Conference discussion