Downsizing of the mitral valve and coronary revascularization in severe ischemic mitral regurgitation results in reverse left ventricular and left atrial remodeling

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Received 9 January 2005; received in revised form 20 February 2005; accepted 28 February 2005; Available online 18 April 2005

Abstract

Objective: Data of combined mitral downsizing by restrictive prosthetic ring annuloplasty and coronary artery bypass grafting (CABG) in patients with ischemic cardiomyopathy and moderately severe to severe mitral regurgitation (MR) are rare, and little is known about the effect on reverse left ventricular (LV) and left atrial (LA) remodeling. Methods: Thirty-eight patients (70.6 ± 8.3 years) with coronary artery disease, ischemic cardiomyopathy (LV ejection fraction [LVEF] 31 ± 8%) and moderately severe to severe MR (grade 3.6 ± 0.5) underwent CABG and mitral downsizing by 2–4 ring sizes. Clinical follow-up and serial transthoracic echocardiographic studies were performed after surgery (discharge, 0.6 to 1.5 months, 0.5 months, 13 to 7 months) to assess survival, NYHA class, MR, leaflet coaptation height, LA and LV dimensions/volumes, fractional shortening (FS) and LVEF. Results: Early mortality (< 30 days) was 2.6%, survival at follow-up was 92 and 85%, respectively. NYHA class improved from 3.3 to 1.5 ± 0.6 (P < 0.001). Residual MR at discharge and at follow-up was grade 0.5 and 0.6, respectively (P < 0.001). Leaflet coaptation height was 8 ± 1 mm and did not change over time. LV end-diastolic, end-systolic and LA dimensions decreased from 60 ± 7 to 57 ± 8 mm, from 47 ± 9 to 42 ± 9 mm and from 51 ± 5 to 45 ± 4 mm, FS increased from 23 ± 9 to 28 ± 10% (P < 0.001); LV end-diastolic and end-systolic volumes decreased from 188 ± 33 to 171 ± 30 ml and from 129 ± 35 to 105 ± 33 ml, LVEF increased from 31 ± 8 to 39 ± 10% (P < 0.001). Conclusions: Combined mitral downsizing and CABG surgery was performed with excellent clinical results: only minimal residual MR, a significant reduction of LA dimension and an increase of LV contractility due to reverse remodeling were observed.

Keywords: Heart failure; Ischemic mitral regurgitation; Mitral valve repair; Reverse remodeling; Restrictive annuloplasty

1. Introduction

Coronary artery disease is the main reason for serious chronic heart failure [1,2]. In patients with coronary artery disease and concomitant ischemic left ventricular (LV) dysfunction, mitral regurgitation (MR) is frequently found with notably 30% presenting severe MR [3]. The surgical concept of mitral downsizing using ‘small’ undersized prosthetic rings analogous to restrictive mitral annuloplasty has been initially described as a feasible technique to improve the early outcome of patients with severe MR and end-stage cardiomyopathy [4], predominantly in cases without coronary artery disease. At present not much information is available on the feasibility and outcome of combined mitral downsizing and coronary artery bypass grafting (CABG) surgery. The effects on reverse LV and left atrial (LA) remodeling are still unknown. The presented data describe our experience with downsizing of the mitral valve (MV) and CABG in patients with ischemic cardiomyopathy and moderately severe to severe MR and the effect on survival, functional class and myocardial reverse remodeling.

2. Patients and methods

The population of this prospective study existed of 38 patients with chronic ischemic cardiomyopathy (LV ejection fraction [LVEF] ≤ 45%; range 17–45%) and moderately severe to severe MR (grades 3–4; 3.6 ± 0.5) which were scheduled for primary mitral downsizing and CABG between October 2001 and October 2004. Chronic ischemic MR was defined as follows: significant coronary artery disease (≥ 70% stenosis in at least one coronary branch), absence of organic MV disease (normal leaflet morphology) and chronic ischemic cardiomyopathy (reduced LV function with an LVEF of less than or equal to 45% and history of previous myocardial infarction not within the last 2 weeks). Patients with
Intrinsic MV disease (e.g. leafllet prolapse, papillary muscle rupture, severe MV thickening, annular calcification or vegetation) or MR grades 1-2+ were excluded from this study. All relevant data of patient characteristics are given in Table 1. In six cases concomitant surgery had to be performed (tricuspid valve [TV] repair: n=2; aortic valve [AV] replacement: n=1; both: n=3). All patients were managed medically before and after surgery with standard heart failure medications including beta-blocks, diuretics and angiotensin-converting enzyme inhibitors. Before surgery all patients were in stable sinus rhythm.

2.1. Surgical procedure

Surgery was performed on cardiopulmonary bypass (CPB) with antegrade Bretschneider cardioplegia. After median sternotomy distal anastomoses for conventional CABG were performed. Then the LA was opened by standard left sternotomy distal anastomoses for conventional CABG. Proximal LA and LV dimensions were determined from parasternal M-mode acquisitions. Severity of MR was graded from color-flow Doppler in the parasternal long-axis and apical 4-chamber images. MR was quantified by the maximal jet area/left atrial area and vena contracta [7,8].

2.2. Functional status, echocardiography and design of the protocol

Functional status was assessed to the New York Heart Association (NYHA) criteria within 1 week before surgery, transthoracic (TTE) and transesophageal (TEE) echocardiography were performed within 3 days before surgery using a Vingmed Vivid 5 (General Electric-Vingmed) system. LV and LA dimensions were determined from parasternal M-mode acquisitions. Severity of MR was graded from color-flow Doppler in the parasternal long-axis and apical 4-chamber images. MR was quantified by the maximal jet area/left atrial area and vena contracta [7,8]. MR was characterized as mild, moderate, moderately severe and severe (grades 1-4+) according to jet area/left atrial area (<10, 10-20, 21-45 and >45%) and vena contracta (4-5, 6-7 and >7 mm). For MR measurement an average of three cardiac cycles was taken; when the severity of MR was less than grade 3+, a standard provocative test was performed. Preoperative LVEF was assessed as mean value of angiographic and echocardiographic data. After CPB, TEE was performed to assess residual MR, leafllet coaptation height and MV area using a Vingmed Vivid 3 (General Electric-Vingmed) system. Residual MR of less than or equal to grade 1+, leafllet coaptation of ≥5 mm and MV area of ≥2 cm² was assessed as good result of MV repair. Clinical follow-up and serial TTE studies were performed after surgery (at discharge, at 3 ± 0.5 months [early follow-up; range 2-4 months] and at 13 ± 7 months [late follow-up; range 6-29 months]) to assess survival, NYHA class, MR, leafllet coaptation height, LA and LV dimensions (LA-diameter, LV end-diastolic [LVEDD] and end-systolic dimension [LVESD]) and fractional shortening (FS), which was evaluated as follows: FS = 100 × [(LVEDD− LVESD)/LVEDD]. LV volumes (LV end-diastolic [LVEDV] and end-systolic volume [LVESV]) were calculated using the biplane Simpson method from the apical 4- and 2-chamber views; postoperative LVEF was evaluated as follows: LVEF = 100 × [(LVEDV− LVESV)/LVEDV]. All postoperative TTEs were analyzed in random order by experienced cardiologists using a Vingmed Vivid 5 system, blinded to TTE-timing and the precise clinical and surgical data (e.g. annuloplasty ring size, number of grafts, previous LA and LV dimensions/ volumes and functional status). According to the protocol CPB time, aortic cross-clamping (ACC) time and total operation time were documented. Further pre- and postoperative cardiac rhythm, the need for intra-aortic balloon pumping (IABP), intensive/intermediate care unit stay and the following complications were noted: cardiac and non-cardiac death, perioperative myocardial infarction, reoperation for bleeding, cerebrovascular events, pneumonia and wound infection. At early and late follow-up the following events were noted: cardiac and non-cardiac death, myocardial infarction, endocarditis and reoperation for recurrent MR.

Table 1

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
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<tbody>
<tr>
<td>Age, years</td>
<td>70.6 ± 8.3</td>
</tr>
<tr>
<td>Gender, M/F</td>
<td>23/15</td>
</tr>
<tr>
<td>NYHA</td>
<td>3.3 ± 0.6</td>
</tr>
<tr>
<td>LVEF, %</td>
<td>31 ± 8</td>
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<tr>
<td>Euro-Score</td>
<td>8 ± 2.3</td>
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NYHA, New York Heart association; LVEF, left ventricular ejection fraction; CABG, coronary artery bypass grafting; PTCA, percutaneous transluminal coronary angioplasty.
2.3. Statistical analysis

Continuous data were expressed as mean and standard deviation. Changes of echocardiographic and functional parameters were investigated using univariate repeated measures analysis. Significances were calculated by overall multivariate F tests on the follow-up times, based on exact F-values. P-values were interpreted nominally, i.e. not further adjusted for multiple comparisons on the data set and considered to be statistically significant when lower than 0.05. Analysis was performed with SPSS for Windows 11.5.1.

3. Results

All relevant surgical and early postoperative clinical data are given in Table 2, echocardiographic data are outlined in Table 3. Intraoperative TEE demonstrated successful MV repair in all cases. Early mortality (<30 days) was 2.6% (1 cardiac death). Thirty-seven patients were discharged in stable sinus rhythm and without relevant MR. Survival was 92% at early follow-up (35 of 38 patients; total deaths: 2 cardiac and 1 non-cardiac) and 85% at late follow-up (29 of 34 patients, total deaths: 3 cardiac, 2 non-cardiac). NYHA class improved from 3.3 ± 0.6 to 1.5 ± 0.6 (P < 0.001), 11 patients had an improvement of 1 class, 14 of 2 classes and 4 of 3 classes. Ninety-three percent (27 of 29 patients) were in NYHA class I or II at late follow-up. Residual MR at early (late) follow-up was grade 0.6 (0.6), respectively. At late follow-up 15 of 29 patients had no MR (52%), nine patients had MR grade 1 (31%) and five patients had MR grade 2 (17%). LVEDD, LVESD and LA-diameter decreased from 60 ± 7 to 57 ± 8 mm (P < 0.001), from 47 ± 9 to 42 ± 9 mm (P < 0.001) and from 51 ± 5 to 45 ± 4 mm (P < 0.001). FS increased from 23 ± 9 to 28 ± 10% (P = 0.001; Table 3). LVEDV and LVESV decreased from 188 ± 33 to 171 ± 30 ml (P < 0.001) and from 129 ± 35 to 105 ± 33 ml (P < 0.001), LVEF increased from 31 ± 8 to 39 ± 10% (P < 0.001; Table 3).

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Thirty-eight, 47, 62 and 71% of patients demonstrated at least 10% improvement of LVEDD, LVESD, LA-diameters and FS values compared to prior to surgery, even cases with excessive LV enlargement/dysfunction (2 of 4 patients with LVEDD ≥ 70 mm; 2 of 3 with LVESD ≥ 60 mm and 6 of 7 with FS ≤ 15%). After discharge, there was no further LVEDD improvement; 48, 86 and 69% of patients demonstrated at least 10% improvement of LVEDV, LVESV and LVEF values compared to prior to surgery. In general after discharge, there was no significant further improvement of LVEDV values. An influence of annuloplasty ring type (flexible [n=8] vs. semi-rigid [n=30]) on the outcome regarding survival and postoperative functional class could not be demonstrated. During the late follow-up period there was neither any case of myocardial infarction or endocarditis, nor reoperation because of recurrent MR.

4. Discussion

Mitral regurgitation is frequently found in patients with coronary artery disease, concomitant ischemic cardiomyopathy and left ventricular dysfunction [3]. In these cases...
the prognosis directly relates to the severity of MR [9]. Conservative therapy in patients with combined severe ischemic MR and heart failure syndrome has a very poor prognosis with a 1-year survival of only 30-40% [3,10,11]. Compared to medical therapy or CABG alone, improved survival after combined MV and CABG surgery has been demonstrated [10-12]. Particularly prosthetic ring annuloplasty has been described as a therapeutic surgical approach to preserve all MV structures and to relieve ischemic MR [5,13,14]; by reducing the anterior-posterior dimensions and the valve area both mitral leaflets are brought in apposition again. This procedure of repair was recently described to be superior to valve replacement in terms of perioperative morbidity and mortality and long-term survival in patients with ischemic cardiac disease [15]. Even if the usefulness in cases of mild to moderate MR in patients undergoing CABG surgery alone was recently doubted [16] and revascularization alone was described to be a sufficient therapy even in patients with mild to moderate MR and advanced ischemic cardiomyopathy [17], the initial benefit of ring annuloplasty in cases of ischemic MR grades 3-4+ is undoubted [5,11,14,15].

As MR recurrence after prosthetic ring annuloplasty due to progressive LV remodeling (a disease that is possibly not directly addressed by annuloplasty) has been described particularly when ‘normal’ sized rings or bovine pericardial annuloplasty were used [14,15,18,19], mitral downsizing combined with CABG might be an improvement of conventional annuloplasty and may influence myocardial function in sense of reverse remodeling. An implantation of undersized ‘small’ annuloplasty rings has been initially described as a feasible technique to improve the prognosis of patients with severe MR and end-stage cardiomyopathy [4]. This method was performed within the meaning of downsizing the mitral annulus to influence leaflet coaptation, LV ventricular geometry and mitral orifice area as well. However, the grade of downsizing, particularly the precise choice of the prosthetic ring and its size remained entirely empirical and dependent on the surgeons’ assessment of the mitral valve and myocardial function. A downsizing of two ring sizes (e.g. from 30 to 26 [Carpentier-Edwards Physio-ring]; from 31 to 27 [Duran-Medtronic Flexible-ring]) was recommended as a concept of recent practice [20]. But even if the feasibility and an initial benefit for the outcome have been documented [4], precise data on the effect on reverse LV and LA remodeling are scarce. In the current literature this item is discussed controversially: whereas the group of Leiden University Medical Center recently documented LV reverse remodeling in a study group of 51 patients (1.5-year follow-up), Hung et al. reported on a retrospective analysis of 30 patients (4-year follow-up) with recurrent MR after CABG and ring annuloplasty [18,20]. The conclusion was that LV remodeling in these patients might be a progressive ventricular problem, which cannot be treated by annuloplasty [18]. However, in that study annuloplasty had not been routinely performed in a restrictive fashion.

Further the Cleveland Clinic group recently reported on recurrent mitral regurgitation (grades 3-4+) in 28% of patients after MV annuloplasty and CABG (n=585) for functional ischemic MR [19]. But in contrast to our investigation and the data of the Leiden University Medical Center group in that study in close to 80% of patients for MV repair either a flexible band or bovine pericardium had been used, and most echocardiograms were performed very early after surgery (median 8 days) and only 17% at 1 year or beyond; however, ‘small’ annuloplasty size did not influence postoperative regurgitation grade, moreover annuloplasty type of MV repair was not associated with survival.

In contrast to these data and other research in our prospective investigation mitral downsizing was performed in a dynamic fashion (2, 3 or 4 ring sizes) dependent from cardiac function to prevent recurrent MR even in patients without further LV improvement with the result of a satisfactory early outcome after surgery. Our data are in line with other research [14,20,21]: early mortality was low (2.6%) and survival at 3 and 13 months of 92 and 85% was satisfactory. However, the criteria for downsizing were still empiric, because there is possibly no direct relation between LVEF and the degree of tethering of the MV. Perhaps a more rational approach would have been to downsize progressively according to the greater degree of tethering.

Another surgical technique described recently in chronic ischemic MR and localized tethering is patch enlargement of a restricted posterior leaflet (segment P2, posterior commissure and particularly segment P3) using autologous or bovine pericardium with a width of approximately 14 mm to restore both, the normal extend of mitral leaflet coaptation and posterior leaflet motion [22]. This technique considers the fact of valve asymmetry caused by localized posterior leaflet restriction. However, the long-term effects of this technique, particularly in patients with severe reduced left ventricular function, are still unknown and data of large series are still not available; possibly the problem of an asymmetric posterior leaflet restriction could be solved with a specific asymmetric three-dimensional annuloplasty ring design, what should be subject of further research.

In the literature surgical approaches including LV restoration procedures in patients with chronic ischemic cardiomyopathy and MR have been proposed recently [23,24]. Even if operative mortality was almost 20% in these series, reduction of LV wall tension by decreasing LV size may be of advantage in patients with large transmural myocardial infarction and large akinesia. However, in the series of Isomura et al. [24] only 38 of 92 patients (41%) had MR grades 3-4+, only 31 of these underwent CABG and a high proportion had MV replacement, what makes it difficult to compare these data with our series. Further, in contrast to our study group, all 46 patients of the series of Menicanti et al. [23] had a large anterior transmural infarction, but only 69% had MR grades 3-4+. In congruity with the data of others all surviving patients in our series had an improved NYHA class with 93% of patients in classes I and II [20]. MR was corrected without any case of reoperation because of recurrent MR.

In contrast to other research our data also obtain a complete TTE series of the first week after surgery, which notably demonstrated that LV end-diastolic dimensions/volumes did already improve very early (before discharge), whereas further decrease could not be documented. In contrast LV end-systolic dimensions/volumes (and secondary FS/LVEF), and also LA dimension as well, improved over...
time; significant improvement with the meaning of reverse LV remodeling appeared over time mainly by reduction of LV end-systolic dimension/volume. As described from Bax et al., the left atrium also exhibited reverse remodeling [20]. In patients with idiopathic dilated and ischemic cardiomyopathy LA enlargement (which is generally known to be the consequence of LA pressure/overload predominantly in MV disease) has been described as an independent risk factor for reduced long-term prognosis [25]. The phenomenon of continuous LA size reduction after surgery might be a consequence of reliable MV sufficiency after surgery, what has been documented in this series over a period of mean 13 months in all cases.

We interpret our results of functional status and echocardiographic data after surgery on the basic experience of others [4,5,19,20]. Combined mitral downsizing and CABG surgery represents a reliable and sufficient option to cure patients with coronary artery disease, ischemic cardiomyopathy, reduced functional status and moderately severe to severe MR from significant insufficiency with low risk and significant reverse myocardial remodeling during a period of mean 13 months. However, further investigations are required to confirm these early results over a longer period in large patient populations.

5. Limitations

The study was designed for patients with ischemic cardiomyopathy and MR grades 3–4+. To evaluate the precise influence of revascularization on the myocardium may further optimize selection of the patients and help to evaluate the precise influence of revascularization on the results.

6. Conclusions

In patients with coronary artery disease and moderately severe to severe mitral insufficiency combined mitral downsizing and CABG surgery corrected MR in all patients with low early and late mortality. A significant reduction of LA dimension and an increase of LV contractility due to reverse remodeling were observed.

References


