Current Results of Combined Coronary Artery Bypass Grafting and Mitral Annuloplasty in Patients with Moderate Ischemic Mitral Regurgitation

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Background and aim of the study: **Combined coronary artery bypass grafting (CABG) and mitral annuloplasty for ischemic mitral regurgitation (MR) is historically associated with high operative mortality, and remains controversial in the setting of moderate ischemic MR. Herein, operative mortality rates in patients undergoing combined CABG and mitral annuloplasty for moderate ischemic MR were examined.**

Methods: **Between January 1992 and August 1999, 108 patients with moderate (grade 3+) ischemic MR and coronary artery disease underwent combined CABG and mitral annuloplasty. Univariable analysis was used to identify perioperative risk factors associated with operative mortality in patients undergoing surgery during two different time periods (1992-95 versus 1996-99). Bivariable logistic regression was used to evaluate the possible effect of era on operative mortality, while controlling for potential confounders.**

Results: **The overall operative mortality was 6.4%. During 1992-95 the operative mortality was 14% (4/28), but fell to 3.7% (3/80) during 1996-99 (p = 0.07). Patients from the earlier period were more likely to have unstable angina, worse NYHA functional class, and preoperative atrial fibrillation. Patients from the latter period were more likely to have peripheral vascular disease and chronic obstructive pulmonary disease. The unadjusted odds ratio (OR) for operative mortality associated with the earlier era was 4.3 (95% CI 9-20.8; p = 0.07). In the bivariable logistic regression models, where patient characteristics that potentially were responsible for the difference in mortality were added, the OR for operative mortality associated with the 1992-95 era ranged from 3.4 to 6.7. None of the patient characteristics appreciably reduced this risk.**

Conclusion: **Recent decreased operative mortality in combined CABG and mitral annuloplasty for moderate ischemic MR suggests that a more liberal application of this approach may be warranted.**

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The results of recent studies have identified an increased incidence of ischemic mitral regurgitation (MR), and 10-15% of patients now referred for mitral valve surgery present with an ischemic etiology. The standard treatment for severe ischemic MR is combined coronary artery bypass grafting (CABG) and mitral valve repair or replacement. Historically, this procedure was associated with a considerably high operative mortality of 30-40% (1,2), but more recently an improvement in outcome has been reported, with operative mortality rates of between 9% and 15% (3-7). Despite improving results, an extension of the indication for a combined procedure to patients with moderate (grade 3+) MR remains controversial. Some groups have recommended isolated CABG, without any attempt being made surgically to correct concomitant MR (8-10). One rationale for this approach is the potential regression of MR in patients following myocardial revascularization, whilst another rationale is that residual MR does not have any clinical significance. Finally, some investigators have argued that the operative mortality of a combined CABG and mitral annuloplasty outweighs the potential benefits of the procedure.

Other reports have advocated a combined CABG and mitral annuloplasty in the setting of moderate ischemic MR based on the fact that CABG alone does not correct ischemic MR (11), and the deleterious effect of the latter on both early and late survival (12-14). Another argument for a combined approach is the

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complexity of performing late mitral valve repair (15,16) after previous CABG, where operative mortality rates remain high (16).

In recent years, the present authors have increasingly utilized combined myocardial revascularization and mitral annuloplasty in patients with moderate ischemic MR. The present retrospective study was designed to analyze the outcome of this approach in subgroups of patients with moderate ischemic MR operated on during two time periods, namely 1992 to 1995, and 1996 to 1999.

Clinical material and methods

Patients

A computer-based registry of all cardiac surgery patients at Brigham and Women's Hospital was used to identify patients undergoing primary combined coronary artery revascularization and mitral annuloplasty between January 1992 and August 1999. Patient records were reviewed retrospectively to identify those in whom the mitral valves were regurgitant on the basis of an ischemic etiology. Ischemic MR was defined as: (i) a documented history of significant myocardial ischemia or myocardial infarction; (ii) an absence of history of degenerative mitral valve disease, rheumatic fever, endocarditis, and dilated cardiomyopathy; and (iii) an absence of structural valve abnormalities and/or extensive mitral annular calcification on preoperative echocardiography and during the valve exploration (11).

Preoperative investigations

Preoperative two-dimensional (2-D) transthoracic echocardiography (TTE) was performed in all patients to detect any wall motion abnormalities, to calculate the left ventricular ejection fraction, and to determine the mechanism of MR according to Carpentier's functional classification (17). The degree of MR was determined by assessing jet geometry and area in multiple views; the severity of MR was graded on a scale from 1+ to 4+, with 1+ representing trace, 2+ mild, 3+ moderate, and 4+ severe MR with systolic flow reversal in the pulmonary vein.

A total of 108 patients presented with moderate (3+) ischemic MR and underwent a combined primary CABG and mitral annuloplasty. These patients were divided into two groups, based on the year of surgical procedure. Group A comprised 28 patients (26%) treated between 1992 and 1995, while group B comprised 80 patients (74%) treated between 1996 and 1999. Patient characteristics are listed in Table I. The median age was 73 years (range: 46 to 85 years) in group A, and 70.5 years (range: 58 to 81 years) in group B; 57% and

Table I: Description of perioperative patient characteristics (%) by era and operative mortality.

Characteristic	Era		p-value	Operative death		p-value
	1992-95 (n = 28)	1996-99 (n = 80)		Yes (n = 7)	No (n = 101)	
1992-95 era	-	-	-	57	24	0.07
Operative death	14	3.7	0.07	-	-	-
Age >70 years	21	28	0.36	14	27	0.42
Male gender	57	61	0.44	86	58	0.15
Diabetes mellitus	46	45	0.53	57	45	0.40
Renal failure	32	23	0.22	29	25	0.56
PVD	14	31	0.06	14	29	0.39
COPD	7	21	0.09	29	17	0.36
Atrial fibrillation	25	5	0.006	29	9	0.15
NYHA class III/IV	93	68	0.006	100	72	0.12
CHF	78	78	0.60	100	76	0.16
EF <30%	21	30	0.27	71	25	0.02
MI	81	74	0.33	86	75	0.45
Unstable angina	43	28	0.10	43	31	0.39
Three-vessel disease	86	94	0.18	100	91	0.53
Urgent surgery	71	55	0.10	71	58	0.40
IABP	39	41	0.52	86	38	0.02
Cross-clamp time >90 min	64	60	0.43	57	61	0.56
CPB time >120 min	71	65	0.35	57	67	0.43

CHF: Congestive heart failure; COPD: Chronic obstructive pulmonary disease; CPB: Cardiopulmonary bypass; EF: Ejection fraction; IABP: Intra-aortic balloon pump; MI: Myocardial infarction; PVD: Peripheral vascular disease.

Table II: Catheterization data.

Group (Era)	One-vessel disease (n)	Two-vessel disease (n)	Three-vessel disease (n)
A (1992-95)	1 (3)*	3 (11)	24 (86)
B (1996-99)	1 (1)*	4 (5)	75 (94)

Values in parentheses are percentages.
*In patients with one-vessel disease, the lesion was located in a dominant right coronary artery.

61% of group A and B respectively were males. Seven patients (25%) in group A, and four patients (5%) in group B, presented with atrial fibrillation (p = 0.006). Among patients, 26 (94%) in group A and 54 (68%) in group B were in NYHA classes III and IV (p = 0.006).

Preoperative 2-D TTE identified severe inferoposterior hypokinesis or akinesis in 89% of patients in group A, and in 87% of those in group B. Additional moderate to severe anterior hypokinesis was observed in 53% of group A patients, and in 52% of group B patients. The median ejection fraction was 35% (range: 15 to 70%) in group A, and 37.5% (range: 20 to 65%) in group B. The mechanism of MR (according to Carpentier's functional classification) was type I (annular dilatation) or IIIb (posterior leaflet restriction) in all patients. Details of preoperative cardiac catheterization procedures are summarized in Table II.

Operative technique

Intraoperative transesophageal echocardiography (TEE) was performed on all patients. Because afterload reduction secondary to general anesthesia downgrades the degree of MR, TEE was not used to assess MR severity (18,19). The TEE was a key element in assessing left ventricular function, in studying the quality of repair, and deairing of the cardiac cavities.

Following a median sternotomy, cardiopulmonary bypass (CPB) was instituted between the ascending aorta and superior and inferior vena cava with moderate systemic hypothermia. Myocardial protection was achieved with antegrade or a combined antegrade and retrograde cold blood high-potassium cardioplegia. Distal anastomoses were performed first, with a median of three grafts (range: one to five grafts) being performed in both groups. The left internal thoracic artery was anastomosed to the left anterior descending artery in 32% of patients in group A (n = 9) and in 34% of group B (n = 27) (p = 0.54). Among 99 patients with three-vessel disease, a minimum of three grafts was constructed in 91 cases (92%). The remaining eight patients (one in group A, seven in group B) had only two grafts. A third bypass could not be performed because of: (i) a small-caliber coronary artery; (ii) a heavily calcified artery; and (iii) no viable territory because of a prior history of myocardial infarction and akinesis on echocardiography. The mitral valve was exposed through Sondergaard's groove. Segmental valve analysis confirmed the preoperative echocardiographic data. Structural valve abnormalities were not observed in any patients. All patients presented with a type I or type IIIb mitral valve dysfunction. Ring annuloplasty was the only procedure performed to restore leaflet coaptation and valve competency. After correct sizing, as described previously (17), a flexible ring annuloplasty was performed. Unlike patients with myxomatous MR, in whom there is a tendency to oversize the ring, the present authors' approach with ischemic MR was to use a true-sized or down-sized ring. The ring size was ≥30 mm in 11% of group A patients (3/28), and in 12% (10/80) of group B patients (p = 0.54), but the majority of patients received a ring of 26 or 28 mm. When the ring had been secured to the mitral annulus, a saline test was performed to confirm mitral valve competency. Finally, the proximal anastomoses were constructed using the single clamp technique (20), and the patients were weaned from CPB. Post-bypass TEE did not show any significant residual MR in any patients. The median CPB time was 136 min (range: 81 to 408 min) in group A patients, and 145 min (range: 85 to 267 min) in group B (p = 0.12). The median cross-clamp time was not significantly different between groups A and B (97 min (range: 52 to 200 min) versus 106 min (range: 64 to 219 min), respectively (p = 0.66).

Statistical analysis

Fisher's exact test was used to evaluate potential confounders of the relationship between operative era (1992-95 versus 1996-99) and operative mortality. A variable was considered a potential confounder if it was related to both era and operative death with a p-value <0.4, though variables with a p-value >0.4 were also deemed clinically relevant. Multivariable analyses could not be performed due to the small number of deaths in the series. Bivariable logistic regression was used to predict the risk of operative mortality associated with the 1992-95 era, while controlling for one potential confounder at a time. Statistical analyses

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Table III: Odds ratio (OR) for operative mortality in early era using univariable and bivariable logistic regression models.

Parameter	OR	95% CI	p-value
Era (1992-95)*	4.3	0.9, 20	0.07
Era+	4.2	0.9, 20	0.08
Age >70 years	0.5	0.06, 4.4	0.53
Era+	4.7	0.95, 23	0.06
Male	4.8	0.5, 42	0.16
Era+	5.7	1.1, 31	0.04
COPD	3.2	0.5, 21	0.23
Era+	3.4	0.7, 18	0.14
Atrial fibrillation	2.5	0.4, 17	0.35
Era+	6.7	1.2, 38	0.03
EF <30%	10.8	1.7, 67	0.01
Era+	4.1	0.8, 20	0.08
Unstable angina	1.4	0.3, 6.8	0.70
Era+	4.1	0.8, 20	0.08
Urgent surgery	1.4	0.3, 8.1	0.68
Era+	4.5	0.9, 22	0.06
CPB time >120 min	0.6	0.1, 2.8	0.49

*Unadjusted OR.
+Adjusted OR (95% CI, p-value) for operative mortality of early era by bivariable analysis while controlling for one significant perioperative characteristic (p <0.4) at a time.

were carried out using Stata Version 7 (Stata Corporation, College Station, Texas, USA).

Results

Operative mortality

The overall operative mortality was 6.4% (7/108), with all deaths being of cardiac origin. During the period 1992-95, the operative mortality was 14% (4/28), and this fell to 3.7% (3/80) during 1996-99 (p = 0.07) (Table I). Patients who died were more likely to have an ejection fraction <30% (71% in group A versus 25% in group B; p = 0.02) and to have had an intra-aortic balloon counterpulsation (86% versus 38% respectively; p = 0.02) (Table I). Patients operated on during the earlier era were more likely to present with unstable angina, NYHA class III/IV, and atrial fibrillation. Patients who presented during the later era were more likely to have peripheral vascular disease and chronic obstructive pulmonary disease (COPD).

Potential confounders of the relationship between operative mortality and the era of surgery included age >70 years, male gender, COPD, atrial fibrillation, ejection fraction <30%, unstable angina, urgent surgery, and CPB time >120 min. Because NYHA class III/IV was a predictor of operative mortality, it was excluded from further statistical analyses. The unadjusted (univariable) odds ratio (OR) for operative mortality associated with the earlier era was 4.3 (95% CI 0.9-20; p = 0.07) (Table III). In the bivariable logistic regression models, where patient characteristics were added that potentially might be responsible for the difference in mortality, the OR for operative mortality associated with the 1992-95 era ranged from 3.4 to 6.7. None of the patient characteristics appreciably reduced this risk.

Morbidity

Among the survivors, low cardiac output was the most common complication, occurring in 25% and 21% of group A and group B patients, respectively (p = NS). Other important postoperative complications are listed in Table IV.

Discussion

During the past decade, many experimental investigations have contributed to a better understanding of

Table IV: Postoperative morbidity.

Complication	Group A (1992-95) (n)	Group B (1996-99) (n)
Stroke	1 (4)	4 (5)
Low cardiac output*	6 (25)	16 (21)
Renal failure (dialysis)*	0	4 (5)
Pneumonia*	5 (20)	8 (10)
Reoperation for bleeding*	1 (4)	3 (4)

Values in parentheses are percentages.
*p = Not significant.

the pathophysiology of ischemic MR (21-28). Several anatomic and physiological changes are associated with the pathogenesis of this complex process, including left ventricular remodeling after myocardial infarction, left ventricular wall motion abnormalities, papillary muscle infarction, and mitral annulus dilatation. Both, Carpentier (17) and Llaneras et al. (22) have shown that ischemic MR occurs after a combination of papillary muscle infarction and left ventricular wall dyskinesia, but neither of these conditions alone is sufficient to produce MR. following myocardial infarction, left ventricular remodeling converts the ventricular shape from ellipsoidal to spherical. This process results in geometric changes in papillary muscle orientation and displacement of the free edges of the leaflets toward the apex. This displacement in turn causes a restriction of leaflet motion during the systole, mainly the posterior leaflet, which significantly reduces the leaflet coaptation surface and leads to the onset of MR (Carpentier's functional class IIIb). In some patients, further ventricular dilatation causes a secondary annular dilatation, and this may contribute to worsening MR. Carpentier's type IIIb is the most common form of ischemic MR, and in a study of the condition reported by Hendren et al. (3), restrictive leaflet motion was present in 60% of the patients. Later, Dion et al. reported similar results and identified leaflet restriction in 41.5% of patients and isolated annular dilatation in 24.4% (5).

Historically, the operative mortality of combined CABG and mitral valve annuloplasty for ischemic MR has been high. A review of the present authors' single institution experience showed the operative mortality to be 14% (4/28) during the period 1992-95, and this was similar to results reported by others during the same period. For example, Czer et al. (29) and Dion et al. (5) reported operative mortalities of 18.5% and 14.8% respectively for combined CABG and mitral valve repair (including annuloplasty) in patients with grade 3+ or 4+ ischemic MR.

At the present authors' institution, the operative mortality for combined CABG and mitral annuloplasty in the setting of ischemic MR was markedly decreased, to 3.7%, between 1996 and 1999. Duarte et al. reported an operative mortality of 3.4% for a population of 58 patients with moderate MR and coronary artery disease who had isolated CABG (8), though it should be noted that the etiology of MR was not ischemic in 26% of the patients in that series. Likewise, Christenson et al. reported an operative mortality of 3.6% among a cohort of 56 patients with mild to moderate ischemic MR and poor left ventricular function (9). Among these patients, only six (11%) presented with grade 3+ MR, while the others presented with grade 1 or 2. Interestingly, in terms of operative mortality the present authors' recent results with a combined approach compared favorably with their own experience with isolated CABG in patients with moderate ischemic MR (11).

The primary goal of the present analysis was to document the most recent outcome with CABG and mitral annuloplasty in the setting of moderate ischemic MR in order to further clarify surgical decision-making. In order to better understand these improved results, a bivariable analysis of individual perioperative risk factors in patients in successive time periods was performed. The results of this analysis revealed that the earlier era remained a strong predictor of increased operative mortality, irrespective of all perioperative risk factors except for NYHA class III/IV. NYHA functional class could not be eliminated as a potential confounder because all deaths in both time periods occurred in patients of NYHA class III or IV. Although the exact cause of the decreased mortality in the later era remains undetermined, it is likely that cumulative experience and improved perioperative care contributed to the improved results.

In conclusion, with an observed operative mortality rate of less than 4% in recent years, it seems reasonable to correct moderate ischemic MR at the time of coronary artery revascularization. It remains to be determined whether or not the addition of annuloplasty to

CABG will result in improved long-term survival or freedom from adverse events such as heart failure. A prospective randomized trial comparing CABG alone with CABG plus mitral annuloplasty is needed to define the potential benefit of concomitant mitral annuloplasty in the setting of moderate ischemic MR.

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