Long-term influence of mild or moderate ischemic mitral regurgitation after off-pump coronary artery bypass surgery

Jong-Myeon Hong MD¹, Raymond Cartier MD², Michel Pellerin MD²,
Philippe Demers MD², Denis Bouchard MD², Pierre Couture MD³

J-M Hong, R Cartier, M Pellerin, P Demers, D Bouchard, P Couture. Long-term influence of mild or moderate ischemic mitral regurgitation after off-pump coronary artery bypass surgery. *Can J Cardiol* 2010;26(4):203-207.

BACKGROUND: The issue of mild to moderate ischemic mitral regurgitation (IMR) is controversial after conventional surgery, and has not been specifically studied after off-pump coronary artery bypass graft (OPCAB) surgery.

OBJECTIVE: To review the influence of mild or moderate IMR on long-term survival and recurrent cardiac events after OPCAB surgery.

METHODS: A total of 1000 consecutive and systematic OPCAB patients who underwent operations between September 1996 and March 2004 were prospectively followed. Sixty-seven patients (6.7%) had mild to moderate IMR at the time of surgery. Operative mortality, actuarial survival and major adverse cardiac event-free survival were studied to assess the effect of IMR.

RESULTS: The mean ($\pm$ SD) follow-up period was 66 ± 22 months and was completed in 97% of the cohort. IMR patients were older ($P < 0.001$), and had lower ejection fractions ($P < 0.001$) and more comorbidities. More female patients presented with IMR ($P = 0.002$). Operative mortality ($P = 0.25$) and prevalence of perioperative myocardial infarction ($P = 0.25$) were comparable for both groups. Eight-year survival was decreased in IMR patients ($P < 0.001$), but after adjusting for risk factors in the Cox regression model, mild to moderate IMR was not found to be a significant risk factor of long-term mortality ($P = 0.42$). Major adverse cardiac event-free survival at eight years was significantly lower in IMR patients ($P < 0.001$) and, more specifically, in patients with 2+ IMR. After adjusting for risk factors, IMR remained a significant cause of poor outcome (hazard ratio 2.09), especially for recurrent congestive heart failure and myocardial infarction.

CONCLUSIONS: OPCAB patients with preoperative mild or moderate IMR had a higher prevalence of preoperative risk factors than those without IMR. They had comparable perioperative mortality and morbidity but, over the long term, were found to be at risk for recurrent cardiac events.

Key Words: Coronary disease; Follow-up studies; Surgery

Influence à long terme de la régurgitation mitrale ischémique de légère à modérée après un pontage coronarien à cœur battant

HISTORIQUE : La question de la régurgitation mitrale ischémique (RMI) de légère à modérée reste controversée après la chirurgie classique et n'a pas été étudiée spécifiquement après le pontage coronarien à cœur battant.

OBJECTIF : Revoir l'influence de la RMI de légère à modérée sur la survie à long terme et la récurrence des événements cardiaques après un pontage à cœur battant.

MÉTHODE : En tout, 1 000 patients consécutifs ayant subi un pontage coronarien à cœur battant entre septembre 1996 et mars 2004 ont été suivis systématiquement de façon prospective. Soixante sept patients (6,7 %) présentaient une RMI de légère à modérée au moment de la chirurgie. La mortalité opératoire, la survie actuarielle et la survie sans événement cardiaque majeur ont été étudiées afin de mesurer l'effet de la RMI.

RÉSULTATS : La période de suivi médian ($\pm$ É. T.) a été de 66 ± 22 mois et a pu être complétée chez 97 % de la cohorte. Les patients atteints de RMI étaient plus âgés ($p < 0,001$) et présentaient des fractions d'éjection moindres ($p < 0,001$) et un plus grand nombre de comorbidités. Les femmes étaient plus nombreuses à souffrir de RMI ($p = 0,002$). La mortalité opératoire ($p = 0,25$) et la prévalence de l'infarctus du myocarde périopératoire ($p = 0,25$) ont été comparables dans les deux groupes. La survie à huit ans était plus faible chez les patients atteints de RMI ($p < 0,001$), mais après ajustement pour tenir compte des facteurs de risque selon le modèle de régression de Cox, la RMI de légère à modérée ne représentait pas un facteur de risque significatif de mortalité à long terme ($p = 0,42$). La survie sans événement cardiaque majeur à huit ans a été significativement moindre chez les patients qui souffraient de RMI ($p < 0,001$) et plus spécifiquement chez les patients qui présentaient une RMI 2+. Après ajustement pour tenir compte des facteurs de risque, la RMI est demeurée une cause significative de piètre pronostic (risque relatif 2,09), surtout dans les cas d'insuffisance cardiaque congestive et d'infarctus du myocarde récurrent.

CONCLUSION : Chez les patients ayant subi un pontage coronarien à cœur battant qui présentaient une RMI préopératoire de légère à modérée, la prévalence des facteurs de risque préopératoires était plus élevée que chez les sujets indemnes de RMI et ils présentaient une mortalité et une morbidité périopératoires comparables, mais à long terme, se sont révélés exposés à un risque de récurrence d'événements cardiaques.

The coexistence of functional ischemic mitral regurgitation (IMR) in patients undergoing coronary artery bypass grafting (CABG) is often associated with poor operative and long-term outcomes (1-3). There is general agreement among cardiac surgeons that severe IMR should be corrected at the time of CABG, and that

trace to mild IMR can be left alone when treating isolated CABG. However, the optimal management of moderate IMR still remains controversial. There have been pros and cons about concurrent mitral valve reparative procedures at the time of CABG in managing IMR patients (1,2,4-8).

¹Department of Thoracic and Cardiovascular Surgery, College of Medicine, Chungbuk National University, Cheongju, South Korea; ²Department of Surgery; ³Department of Anesthesiology, Montreal Heart Institute, Université de Montréal, Montreal, Quebec

Correspondence: Dr Raymond Cartier, Department of Surgery, Montreal Heart Institute, 5000 Belanger Street, Montreal, Quebec H3T 1C8.

Telephone 514-376-3330 ext 3715, fax 514-593-2157, e-mail rc2910@aol.com

Received for publication June 25, 2008. Accepted October 11, 2008

TABLE 1
Demographic data and preoperative risk factors

Characteristics	No IMR (n=933)	IMR (n=67)	P
Age, years	63.88±10.11	69.42±7.62	<0.0001
Women	198 (21.22)	25 (37.31)	0.0022
Diabetes	251 (26.90)	26 (38.81)	0.0355
Hypertension	492 (52.73)	48 (71.64)	0.0016
Smoking	277 (29.69)	11 (16.42)	0.0240
COPD	107 (11.47)	11 (16.42)	0.2060
Atrial fibrillation	32 (3.43)	5 (7.46)	0.0916
PVD	166 (17.79)	18 (26.87)	0.0641
Carotid stenosis	146 (15.65)	15 (22.39)	0.1471
LMCA	272 (29.15)	24 (35.82)	0.2482
Renal insufficiency	39 (4.18)	9 (13.43)	0.0006
LVEF, %	0.54±0.12	0.45±0.13	<0.0001
CHF	71 (7.61)	17 (25.37)	<0.0001
Old MI (>30 days)	367 (39.34)	31 (46.27)	0.2628
Recent MI (≤30 days)	170 (18.22)	27 (40.30)	<0.0001
Unstable angina	636 (68.17)	56 (83.58)	0.0083
IABP (preoperative)	62 (6.65)	12 (17.91)	0.0007
Reoperation	66 (7.07)	3 (4.48)	0.4180
Emergency	44 (4.72)	10 (14.93)	0.0003
PHT	75 (8.04)	19 (28.36)	<0.0001
Diseased coronaries, n	2.68±0.57	2.78±0.45	0.2089
Parsonnet score	11.0±8.2	19.7±8.3	0.001

Data presented as n (%) or mean ± SD. CHF Congestive heart failure; COPD Chronic obstructive pulmonary disease; IABP Intra-aortic balloon pump; IMR Ischemic mitral regurgitation; LMCA Left main coronary artery stenosis; LVEF Left ventricular ejection fraction; MI Myocardial infarction; PHT Pulmonary hypertension; PVD Peripheral vascular disease

Nowadays, the safety and advantages of off-pump CABG (OPCAB) have been clearly established by many centres, especially in patients with many associated comorbidities (9). However, performing OPCAB in a patient with severe functional IMR may induce ischemia and aggravate mitral regurgitation, causing severe hemodynamic instability and unwanted conversion to on-pump bypass. Consequently, patients presenting with severe IMR are generally referred for conventional revascularization surgery with mitral valve repair or replacement. The issue of patients with preoperative mild to moderate IMR has not been specifically studied. The purpose of the present study was to evaluate the influence of preoperative mild to moderate IMR on long-term survival and recurrent cardiac-related events after isolated OPCAB surgery.

METHODS

The present review was approved by the Montreal Heart Institutional Board on May 27, 2008. Informed consent was waived by the Board for the present study.

Patient population

A total of 1000 consecutive and systematic OPCAB patients operated on by one surgeon between September 1996 and March 2004 at the Montreal Heart Institute (Montreal, Quebec) were prospectively followed, representing more than 95% of the entire patient cohort who underwent an operation for coronary revascularization during the same time frame.

Early and midterm outcomes of these series have already been published (10). Among these patients, 67 were preoperatively identified as having mild to moderate IMR at the time of the surgery and will be the main topic of the present report. Follow-up was completed in 97% of the patients. The grade of IMR was based on the pre- and postoperative transthoracic echocardiograms, and the 2006 American College of Cardiology/American Heart Association guidelines (11). In brief,

1+ and 2+ mitral insufficiency were defined as small central jets with Doppler vena contractas of less than 0.3 cm and 0.7 cm, respectively, or regurgitant orifice areas of less than 0.2 cm² and 0.4 cm², respectively. Vena contracta superior to 0.7 cm or a regurgitant fraction above 0.4 cm², or any reversed flow in the pulmonary veins, was considered to be 3+ IMR.

Surgical technique

The surgical technique used has been consistent over the years and has been described in previous reports (10). In summary, median sternotomy was used in more than 99% of the patients, and all procedures since 2000 were performed under general anesthesia with continuous pulmonary artery pressure and transeophageal echocardiography monitoring. A compression-type stabilizer (Cor-Vasc retractor-stabilizer; CoroNéo Inc, Canada) was used in all cases. Postoperatively, patients were maintained on oral acetylsalicylic acid (80 mg/day) and subcutaneous heparin (5000 kIU, three times per day) throughout the entire hospital stay. Since August 2002, clopidogrel (75 mg/day) has been added to the post-operative medication for the first three months.

Clinical follow-up

All perioperative data were prospectively gathered. Clinical follow-up was completed through regular outpatient clinic visits, telephone interviews by the attending surgeon and/or chart reviews whenever applicable (such as in the case of emergency room visits or rehospitalization). For cases in which patients were admitted to other hospitals, the reasons for the visit and subsequent findings were obtained from the attending physician. All information collected was systematically entered into a computer database (SPSS 13.0; SPSS Inc, USA).

A major adverse cardiac event (MACE) during the follow-up period was defined as one of the following: cardiac death or death of unknown cause, rehospitalization for congestive heart failure (CHF), myocardial infarction (MI), recurrent unstable angina or repeat revascularization (surgical or percutaneous coronary intervention [PCI]).

The completeness of revascularization was defined according to the original Coronary Artery Surgery Study (CASS) (12), defined as all three major vessels receiving a bypass graft in patients with triple-vessel disease.

Statistical analysis

Data are presented as mean ± SD for continuous variables, while categorical variables are presented as frequencies and percentages. Patient population characteristics and outcomes were compared between diabetic and nondiabetic patients using the χ^2 test for categorical variables, while continuous variables were compared using Student's *t* test or the Mann-Whitney U test if distributional assumptions were not met. Time to mortality was presented using adjusted survival curves and compared between groups (diabetic versus nondiabetic) using the log-rank test. Cox regression analysis was used to analyze the effect of diabetes on mortality adjusted for the risk factors that were significant at a 0.20 level in the univariate analysis. The interaction between each risk factor and group (diabetic versus nondiabetic) was tested at a 0.05 level to evaluate whether the effect of a given risk factor was the same in the diabetic group versus the nondiabetic group. Nonsignificant interactions were dropped from the model. Statistical analyses were performed using SPSS software and conducted at a 0.05 significance level. Univariate analysis was performed to evaluate the impact of patient characteristics and risk factors, as defined in Table 1, on long-term outcomes. All patients were considered as 'intention to treat'. No more than one variable for 10 events was considered for multivariate analysis purposes. For long-term end points, independent risk factor analyses are presented as hazard ratios (HRs) with 95% CIs. Actuarial survival was obtained using the Kaplan-Meier method. Probability values were defined using log-rank analysis, and *P*<0.05 was considered to be statistically significant.

TABLE 2
Perioperative data

Characteristics	No IMR (n=933)	IMR (n=67)	P
Operative mortality	15 (1.6)	2 (3)	0.25
Grafts, n	3.2±0.9	3.3±0.9	0.41
Complete revascularization	882 (95)	61 (91)	0.71
Conversion to CPB	3 (0.3)	1 (1.5)	0.24
Perioperative MI	31 (3.3)	7 (10.45)	0.26
Intensive care unit stay, h	64±56	88.06±118	0.003
Hospital stay, days	6.5±5.8	7.78±8.89	0.1
Infection	27 (2.9)	4 (6.0)	0.58
Atrial fibrillation	245 (26)	22 (33)	0.13
Intra-aortic balloon pump	6 (0.6)	1 (1.5)	0.38
Bleeding	36 (3.9)	5 (7.6)	0.18

Data presented as n (%) or mean ± SD. CPB Cardiopulmonary bypass; IMR Ischemic mitral regurgitation; MI Myocardial infarction

TABLE 3
Long-term survival by Cox logistic regression analysis

	P	Hazard ratio	95% CI
Age	<0.001	1.07	1.05–1.09
Congestive heart failure	0.04	1.82	1.18–2.81
Peripheral vascular disease	0.01	1.63	1.12–2.35
Cerebral atherosclerosis	0.03	1.53	1.06–1.23
Left ventricular ejection fraction	0.002	0.13	0.04–0.46
Incomplete revascularization	0.002	2.23	1.43–3.60
Renal insufficiency	0.01	1.97	1.17–3.31
Ischemic mitral regurgitation	0.42		

RESULTS

Patient characteristics and preoperative risk factors

Patient demographics and preoperative risk factors are displayed in Table 1. Among the 67 patients who presented with IMR, 38 had 1+ IMR, 26 had 2+ IMR and three had 3+ IMR. IMR patients were an average of five years older, had lower ejection fractions (EFs), and had a higher prevalence of diabetes, hypertension, chronic renal insufficiency, CHF, recent MI, unstable angina, preoperative intra-aortic balloon pump and emergency surgery, and higher Parsonnet risk scores than patients without IMR. Female patients also presented with IMR (37.31%) more frequently than men (21.22%).

Perioperative data (Table 2)

The operative mortality rate was 3.0% (two deaths) in IMR patients and 1.6% (15 deaths) in non-IMR patients ($P=0.25$). On average, the number of bypass grafts, and the percentage of complete revascularizations performed, conversion to cardiopulmonary bypass and the perioperative MI were similar for both groups. Intensive care unit stay, however, was longer in IMR patients.

Long-term results

The long-term survival rate was significantly decreased in IMR patients compared with those without IMR at one year ($94.0\pm2.9\%$ versus $97.0\pm0.6\%$), five years ($78.0\pm6.8\%$ versus $88.0\pm1.0\%$) and eight years ($42.0\pm11.3\%$ versus $77\pm2.1\%$) ($P<0.001$). Following Cox logistic regression analysis, only age at the time of operation, a history of CHF, peripheral and cerebral vascular diseases, low EF, incomplete revascularization, and renal insufficiency were significant risk factors for the long-term survival (Table 3). After correcting for risk factors, IMR (1+ and 2+) patients had a survival rate comparable with non-IMR patients (Figure 1). For the purpose of estimating the effect of mild to moderate IMR, 3+ IMR was excluded for long-term results.

MACE-free survival was also decreased in IMR patients at one year ($86\pm4\%$ versus $97.0\pm0.7\%$), five years ($69\pm8\%$ versus $88.0\pm1\%$) and

Figure 1) Survival curve comparing patients with (1+ and 2+) and without ischemic mitral regurgitation (IMR) after correcting for risk factors. Cumulative

TABLE 4
Major cardiac adverse event-free survival by Cox logistic regression analysis

	P	Hazard ratio	95% CI
COPD	0.01	1.70	1.14–2.55
Peripheral vascular disease	<0.001	1.93	1.37–2.72
Previous PCI	0.02	1.69	1.09–2.61
Chronic renal insufficiency	0.003	2.27	1.33–3.88
Incomplete revascularization	0.02	1.84	1.10–3.06
Left ventricular ejection fraction	0.05	0.32	0.10–0.99
Emergency	0.06	1.69	0.97–2.94
Ischemic mitral regurgitation	0.007	2.09	1.22–3.57

COPD Chronic obstructive pulmonary disease; PCI Percutaneous coronary intervention

eight years ($54\pm11\%$ versus $76\pm2\%$) ($P<0.001$). After correcting for risk factors, IMR emerged as a cause of MACE occurrence (HR 2.09) at follow-up (Table 4). After excluding 3+ IMR, 2+ IMR but not 1+ IMR was found to affect MACE occurrence (Figure 2). By specifically breaking down each MACE by type, IMR (HR 2.54, 95% CI 1.06 to 2.54) remained a significant factor of rehospitalization for CHF, along with a history of left ventricular (LV) EF and chronic renal insufficiency. Rehospitalization for new MI was also more frequent in IMR patients but remained at the limit of clinical significance ($P=0.06$). The small number of events did not allow for differentiation between 1+ and 2+ IMR.

DISCUSSION

Patients who present with MI complicated by IMR have a significantly worse outcome than those without IMR (5,13-15). Lamas et al (13) demonstrated that the presence of angiographic mild IMR after MI, often clinically unrecognized, was a marker of a geometrically distorted LV and is associated with a significant increase in subsequent cardiac death. These patients also showed a higher prevalence of cardiovascular mortality, severe heart failure and recurrent MI. Grigioni et al (3) showed that in the chronic phase of an MI, the presence of IMR was associated with excess mortality, independent of baseline characteristics and severe ventricular dysfunction. Risk of death was directly related to the importance of IMR (3). In patients undergoing primary PCI in the setup of an acute MI (16), Pellizzony et al (17) showed that survival was markedly reduced in patients with IMR at both 30 days and one year, and was correlated with the severity of mitral regurgitation. Even the

Figure 2) Major cardiac adverse event-free survival curve comparing patients with (1+ or 2+) and without ischemic mitral regurgitation (IMR) after correcting for risk factors. Cum Cumulative

presence of mild IMR at baseline has been recognized as an independent predictor of reduced survival after PCI (18).

Authors have questioned whether the presence of moderate IMR is simply a marker of high-risk patients or whether it is a true risk factor of mortality at the time of a CABG procedure. Lam et al (8) reported that CABG patients with nonsurgically repaired IMR at the time of surgery had reduced survival compared with patients without IMR, and that moderate IMR was an independent risk factor of mortality. Paparella et al (19) reported similar observations in patients with poor LV function. However, in their study, the independent predictors of poor survival were mainly advanced age, LV dysfunction, heart failure, diabetes, previous stroke, peripheral vascular disease and nonuse of the internal mammary artery. IMR was not an independent predictor of long-term mortality. The authors could not conclude whether the poorer outcomes in these patients were related to the dysfunctional valvular status or the presence of more extensive comorbidities such as ventricular dysfunction. It has been suggested that the LV morpho-functional status (LV regurgitation) might be a more important feature than the mitral regurgitation itself (20).

In IMR patients, the operative strategies aim to improve late survival and functional status as well as late quality of life without increasing perioperative morbidity and mortality (7). There is no clear consensus on the surgical indication for correcting moderate IMR, as well as a lack of consistency regarding the grading of mitral regurgitation based on ventriculography or echocardiography (transthoracic or transesophageal). In the current study, preoperative transthoracic echocardiographic evaluation was performed according to the American College of Cardiology/American Heart Association guidelines (11). The great majority of our patients had an IMR grade of 2+ or less, which normally does not require surgical correction in our institution.

Some authors have favoured concurrent mitral valve repair at the time of CABG (2,5,7,9), whereas others have not (1,6,8,21). The rationale for a conservative approach is that revascularization of the ischemic region will improve regional wall motion and correct the IMR. Even if some residual IMR persists, several studies suggest that long-term survival or functional status will not be affected. Mitral valve repair always has the potential to increase the surgical risk of the procedure (1,6,20,22-24). The rationale for aggressive mitral repair is to decrease the risk of recurrent CHF, especially in patients with previous CHF symptoms associated with an enlarged left atrium (5). In this specific group, CABG alone may not correct moderate IMR. Significant residual IMR affects quality of life and may decrease long-term survival. Interestingly, ischemic patients who undergo surgical correction

of IMR have been associated with diminished survival compared with those without IMR or degenerative mitral regurgitation due to an increased operative mortality (22-24). As a result, patients with IMR have been more reluctantly referred for surgery than patients without IMR. However, the question remains whether the adverse outcome observed after repair of IMR is due to the more advanced ischemic status of the myocardium or is simply a reflection of a higher prevalence of preoperative risk factors.

By comparing ischemic and nonischemic patients with mitral regurgitation, Glower et al (22) showed that long-term survival was more dependent on baseline patient characteristics and comorbidity than the ischemic nature of the mitral regurgitation. Other studies by Dalberg et al (23) at the Mayo Clinic (USA) and Gillinov et al (24) at the Cleveland Clinic (USA) reached similar conclusions, confirming that survival after mitral valve surgery and CABG was better determined by the extent of coronary artery disease and LV dysfunction than the etiology of the mitral disease. Our study obtained a very similar result in excluding IMR as a significant factor of long-term mortality.

There are very few reports concerning OPCAB and residual IMR. Harris et al (5) reported that 17 of 989 OPCAB patients presented preoperatively with moderate to moderately severe IMR. Among them, there were 11 men and six women. The three-year survival rate for these patients was 62%, which was comparable with a historically matched group operated on for routine CABG under cardiopulmonary bypass.

In our study, OPCAB patients with mild to moderate functional IMR were definitely sicker than those with normal mitral function. They were older, with more women presenting with IMR than without, and had more risk factors, which clinically translated into a higher Parsonnet score. However, they had comparable operative mortalities and morbidities. After correction for risk factors, their long-term survival was comparable with the survival of those without IMR. However, regression analysis established that IMR patients were at a higher risk of rehospitalization for cardiac failure and, to a lesser extent, new MI confirming the higher ischemic and dysfunctional status of the heart. In this aspect, our data led us to the same conclusion as those of Glower et al (22) at Duke University (USA), Dalberg et al (23) at the Mayo Clinic and Gillinov et al (24) at the Cleveland Clinic.

Limitations

The present study had several limitations. There was only a small number of OPCAB patients with IMR, which limited statistical analysis. Echocardiographic assessments were not systematically performed for the first 300 patients and no specific echographic follow-ups were performed on IMR patients postoperatively to determine whether the residual IMR was persistent. Consequently, no direct correlation with persistent residual IMR and cardiac evolution could be established.

CONCLUSION

Our results suggest that patients with mild to moderate IMR undergoing OPCAB surgery are at a higher risk for developing CHF at follow-up. Further studies are required to examine the need for additional mitral procedures at the time of OPCAB in patients with mild or moderate IMR.

DISCLOSURE: Dr Cartier is a senior advisor for CoroNéo Inc, Montreal, Quebec.

ACKNOWLEDGEMENTS: The authors thank Sylvie Levesque for her kind support of the statistical analysis.

REFERENCES

1. Kang DH, Kim MJ, Kang SJ, et al. Mitral valve repair versus revascularization alone in the treatment of ischemic mitral regurgitation. *Circulation* 2006;114(Suppl 1):I499-503.
2. Grossi EA, Crooke GA, DiGiorgi PL, et al. Impact of moderate functional mitral insufficiency in patients undergoing surgical revascularization. *Circulation* 2006;114(Suppl 1):I573-6.

3. Grigioni F, Enriquez-Sarano M, Zehr KJ, Bailey KR, Tajik AJ. Ischemic mitral regurgitation long-term outcome and prognostic implication with quantitative Doppler assessment. *Circulation* 2001;103:1759-64.
4. Aklog L, Filsoufi F, Flores KQ, et al. Does coronary artery bypass grafting alone correct moderate ischemic mitral regurgitation? *Circulation* 2001;104(Suppl 1):I68-75.
5. Harris KM, Reddy A, Aeppli D, Wilson B, Emery RW. Initial report of off-pump coronary artery bypass surgery as sole therapy for moderate ischemic mitral regurgitation: Operative and intermediate-term outcome. *Heart Surg Forum* 2005;8:E89-93.
6. Mallidi HR, Pellerier MP, Lamb J, et al. Late outcomes in patients with uncorrected mild to moderate mitral regurgitation at the time of isolated coronary artery bypass grafting. *J Thorac Cardiovasc Surg* 2004;127:636-44.
7. Trichon BH, Glower DD, Shaw LK, et al. Survival after coronary revascularization, with and without mitral valve surgery, in patients with ischemic mitral regurgitation. *Circulation* 2003;108(Suppl II):II103-10.
8. Lam BK, Gillinov AM, Blackstone EH, et al. Importance of moderate ischemic mitral regurgitation. *Ann Thorac Surg* 2005;79:462-70.
9. Stamou SC, Jablonski KA, Hill PC. Coronary revascularization without cardiopulmonary bypass versus the conventional approach in high-risk patients. *Ann Thorac Surg* 2005;79:552-7.
10. El-Hamamsy I, Cartier R, Demers P, Bouchard D, Pellerin M. Long-term results after systematic off-pump coronary artery bypass graft surgery in 1000 consecutive patients. *Circulation* 2006;114(Suppl 1):I486-91.
11. Bonow RO, Carabello BA, Kanu C, et al. ACC/AHA 2006 guidelines for the management of patients with valvular heart disease. *Circulation* 2006;114:e84-231.
12. Coronary Artery Surgery Study (CASS): A randomized trial of coronary artery bypass surgery. Survival data. *Circulation* 1983;68:939-50.
13. Lamas GA, Mitchell GF, Flaker, et al. Clinical significance of mitral regurgitation after acute myocardial infarction. Survival and Ventricular Enlargement Investigators. *Circulation* 1997;96:827-33.
14. Sutton MSJ, Pfeffer MA, Plappert T, et al. Quantitative two-dimensional echocardiographic measurements are major predictors of adverse cardiovascular events after acute myocardial infarction. *Circulation* 1994;89:68-75.
15. Sutton MSJ, Pfeffer MA, Moye LA, et al. Cardiovascular death and left ventricular remodelling two years after myocardial infarction: Baseline predictors and impact of long-term use of captopril: Information from the Survival and Ventricular Enlargement (SAVE) trial. *Circulation* 1997;96:3294-9.
16. Heuser RR, Maddoux GL, Goss JE, Ramo BW, Ruff GL, Shadoff N. Coronary angioplasty for acute mitral regurgitation due to myocardial infarction. *Ann Intern Med* 1987;107:852-5.
17. Pellizzony GG, Grines CL, Cox DA, et al. Importance of mitral regurgitation in patients undergoing percutaneous coronary intervention for acute myocardial infarction. *J Am Coll Cardiol* 2004;43:1368-74.
18. Ellis SG, Whitlow PL, Raymond RE, Schneider JP. Impact of mitral regurgitation on long-term survival after percutaneous coronary intervention. *Am J Cardiol* 2002;89:315-8.
19. Paparella D, Mickleborough LL, Carson S, Ivanov J. Mild to moderate mitral regurgitation in patients undergoing coronary bypass grafting: Effects on operative mortality and long-term significance. *Ann Thorac Surg* 2003;76:1094-100.
20. Wu AH, Aaronson KD, Bolling SF, Pagani FD, Welch K, Koelling TM. Impact of mitral valve annuloplasty on mortality risk in patients with mitral regurgitation and left ventricular systolic dysfunction. *J Am Coll Cardiol* 2005;45:381-7.
21. Tolis GA, Korkolis DP, Kopf GS, Elefteriades JA. Revascularization alone (without mitral valve repair) suffices in patients with advanced ischemic cardiomyopathy and mild-to-moderate mitral regurgitation. *Ann Thorac Surg* 2002;74:1476-81.
22. Glower DD, Tuttle RH, Shaw LK, Orozco RE, Rankin JS. Patient survival characteristics after routine mitral valve repair for ischemic mitral regurgitation. *J Thorac Cardiovasc Surg* 2005;129:860-8.
23. Dalberg PS, Orszulak TA, Mullany CJ, Daly RC, Enriquez-Sarano M, Schaff HV. Late outcome of mitral valve surgery for patients with coronary artery disease. *Ann Thorac Surg* 2003;76:1539-47; discussion 47-8.
24. Gillinov AM, Blackstone EH, Rajeswaran J, et al. Ischemic versus degenerative mitral regurgitation: Does etiology affect survival? *Ann Thorac Surg* 2005;80:811-9.