ACD

Survival after myocardial revascularization for ischemic cardiomyopathy: A prospective ten-year follow-up study

Pallav J. Shah, MBBS, MS, McH[a]
David L. Hare, MBBS, DPM, FRACP[b]
Jai S. Raman, MBBS, MMed, FRACS, PhD[a]
Ian Gordon, MSc, PhD, AStat[c]
Robert K. Chan, MBBS, PhD, FRACP[b]
John D. Horowitz, MBBS, PhD, FRACP[d]
Alex Rosalion, MBBS, FRACS[a]
Brian F. Buxton, MB, MS, FRACS, FRCS, FRCS(C)[a]

Objective: The aim was to prospectively analyze all-cause mortality, predictors of survival, and late functional results after myocardial revascularization for ischemic cardiomyopathy over a 10-year follow-up.

Methods: We prospectively studied 57 patients with stable coronary artery disease and poor left ventricular ejection function (<35%), enrolled between 1989 and 1994. Stress thallium was analyzed in 37 patients to identify reversible ischemia. To avoid patients with a stunned myocardium, we excluded those with unstable angina or myocardial infarction within the previous 4 weeks. Mean age of the patients was 67 ± 8 years, and 93% of patients were men. Mean left ventricular ejection fraction was 0.28 ± 0.04, 50% were in Canadian Cardiovascular Society angina class III-IV, and 65% were in New York Heart Association functional class III-IV.

Results: Operative mortality was 1.7% (1/57). The mean left ventricular ejection fraction (0.30) at 15 months postoperatively did not change from before operation (0.28, P = .09). There were 8 deaths at 1 year and 42 deaths over the course of the study, producing a survival of 82.5% at 1 year, 55.7% at 5 years, and 23.9% at 10 years (95% confidence interval: 14.6%-39.1%). Symptom-free survival was 77.2% at 1 year and 20.3% at 10 years. The leading cause of death was heart failure in 29% (12/42). Multivariate analysis showed that large reversible defects on stress thallium were associated with improved left ventricular ejection fraction at 1 year (P = .01) but only male sex was associated with improved long-term survival (P = .036).

Conclusions: Myocardial revascularization for ischemic cardiomyopathy is associated with good functional relief from the symptoms of angina initially and, to a lesser extent, heart failure. Revascularization may have the advantage of preserving the remaining left ventricular function. However, the long-term mortality remains high.

From the Departments of Cardiac Surgery[a] and Cardiology,[b] Austin Hospital, Melbourne, Victoria, Australia; Statistical Consulting Centre,[c] University of Melbourne, Parkville, Victoria, Australia; and Department of Cardiology,[d] Queen Elizabeth Hospital, Adelaide, South Australia, Australia.

Received for publication Jan 8, 2003; revisions requested Feb 26, 2003; revisions received April 16, 2003; accepted for publication May 13, 2003.

Address for correspondence: Professor Brian F. Buxton, Director of Cardiac Surgery, Austin Hospital, Melbourne, Victoria, 3084 Australia (E-mail: brian.buxton@austin.org.au).

J Thorac Cardiovasc Surg 2003;126:1320-7

0022-5223/2003 $30.00 + 0

doi:10.1016/S0022-5223(03)00809-2

Patients with coronary artery disease and severe left ventricular (LV) dysfunction have a poor prognosis, with limited survival and functional improvement, when treated medically.[1-6] Transplantation is an effective treatment option but limited by availability of donors. It readily became apparent that a proportion of patients with end-stage ischemic heart disease could be offered myocardial revascularization with an early outcome comparable with transplantation.[5-9] Progress in the field of imaging and metabolic diagnostic techniques, as well as advances in intraoperative myocardial protection and postoperative care, have led to a significant decrease in operative risk over recent years.[10-13] However, there are few reports in the literature on long-term survival and symptomatic status in this group of patients.[14-16]

We have reported short-term outcomes for patients with severe LV dysfunction undergoing coronary artery bypass grafting (CABG).[12] This study reports the results of prospective 10-year follow-up on survival and relief from angina and heart failure in these patients.

Patients and Methods

Patients with stable coronary artery disease suitable for CABG and impaired LV function (LV ejection fraction [LVEF] $\leq$ 0.35 on radionuclide ventriculography [RNVG]) were prospectively entered into the study between June 1989 and June 1994. Patients with unstable angina, myocardial infarction, and other significant ischemic events within 4 weeks of surgery were specifically excluded. Those requiring repeat CABG or concomitant procedures (including valvular operation and aneurysmectomy) were also excluded. Patients with left main coronary artery stenosis of 50% or more were not included because of the risk involved from investigational stress testing. Of 1708 patients undergoing primary coronary surgery over the entry period, 234 patients fulfilled the above criteria and had impaired LV function on contrast left ventriculography. Of these, 57 patients had an LVEF 0.35 or less on RNVG and were enrolled in the study. The protocol was approved by the Austin Hospital Ethics Committee for Human Research. Written informed consent of all the enrolled patients was obtained including specific consent for thallium and RNVG studies.

Coronary Revascularization

All patients underwent CABG under mild hypothermic (34°C) cardiopulmonary bypass using a membrane oxygenator. In all cases, distal anastomoses between the bypass grafts and native coronary arteries were performed under aortic crossclamping on a heart arrested by blood cardioplegic solution infused at room temperature. In the initial part of the study, cardioplegic solution was given antegradely. The proximal ends of vein grafts were then anastomosed to the aorta during partial exclusion. As retrograde coronary sinus cardioplegia became more popular, this technique was adopted in patients enrolled in the latter part of the study. All patients had proximal anastomoses completed during the single aortic crossclamp period. Patients were weaned from cardiopulmonary bypass and maintained on milrinone (loading dose: 0.5 μg/kg in 15 minutes; infusion: 0.125-0.5 $\mu g \cdot kg^{-1} \cdot min^{-1}$) for the first 12 hours postoperatively to maintain a cardiac index of 2.5 $L \cdot m^2 \cdot min$ or more in the latter part of the operative experience.

Patients received 1 to 6 coronary bypass grafts (mode of 3). Fifty-four patients (95%) had at least 1 internal thoracic artery used as a conduit, 8 of whom received bilateral internal thoracic artery grafts. The aortic crossclamp and cardiopulmonary bypass times were 61 $\pm$ 19 and 97 $\pm$ 27 minutes, respectively.

Radionuclide Ventriculography

Patients with an LVEF of 35% or less on RNVG, using isotope, were enrolled in the study. Approximately 12 months after the operation, 47 of the 49 surviving patients (96%) had RNVG for reassessment of LVEF performed in the same institution as the preoperative studies, using an identical protocol. All studies were reported by observers blinded to the clinical details and other investigational findings.

Thallium-201 Scintigraphy

All 57 patients underwent stress thallium-201 single-photon emission computed tomography (SPECT) before CABG. To provide uniform reporting, 2 independent nuclear medicine physicians reassessed all available studies during the first postoperative years. Twenty studies were not available or technically satisfactory, leaving 37 studies available for reanalysis. According to our previously published method to determine the presence and extent of ischemic myocardium,[12] 18 had large defects, 13 had defects of small to moderate size, and 6 had fixed perfusion defects.

Follow-up

All surviving patients were reviewed at 1 and 12 months postoperatively by an independent physician with no knowledge of preoperative clinical status. The surviving patients were assessed by clinical review or by telephone interview if they were unable to travel. Telephone interviews were conducted by an experienced research assistant. The clinical status, recurrence of symptoms, repeat hospitalization, and cause of death were carefully documented. For missing patients, the Australian National Death Index was used to track unrecorded deaths.

Outcome Assessment

The major end points of the study were all-cause mortality at 30 days, 12 months, and 10 years. These are expressed as "survival" and "event-free survival." Events were defined as: onset of Canadian Cardiovascular Society (CCS) and/or New York Heart Association (NYHA) class III-IV, hospitalization for cardiac reasons, and mitral valve surgery or transplantation. Functional class was also assessed at 30 days, 12 months, and 10 years, angina using CCS class and dyspnea using NYHA class. The effect of CABG on LV function was assessed comparing preoperative and 12-month RNVG measurements of LVEF.

Statistical Analysis

Continuous data were expressed as mean $\pm$ 1 SD. Survival was evaluated univariately by Kaplan-Meier analysis and multivariately by the Cox proportional hazards model. Variables considered for analysis in predicting survival were age, sex, diabetes, myocardial infarction, hypertension, peripheral vascular disease, chronic obstructive pulmonary disease, CCS angina class, NYHA functional class, LVEF, and perfusion defects on thallium scintigraphy.

Results

Fifty-seven patients entered the study, with the following statistics: age, 67 $\pm$ 8 years; LVEF, 0.28 $\pm$ 0.04 (range 0.17-0.35); male sex, 53 (93%); diabetes, 9 (16%); hypertension, 21 (37%); previous Q-wave myocardial infarction, 44 (77%); CCS class III-IV, 29 (50%); and NYHA class III-IV, 37 (65%).

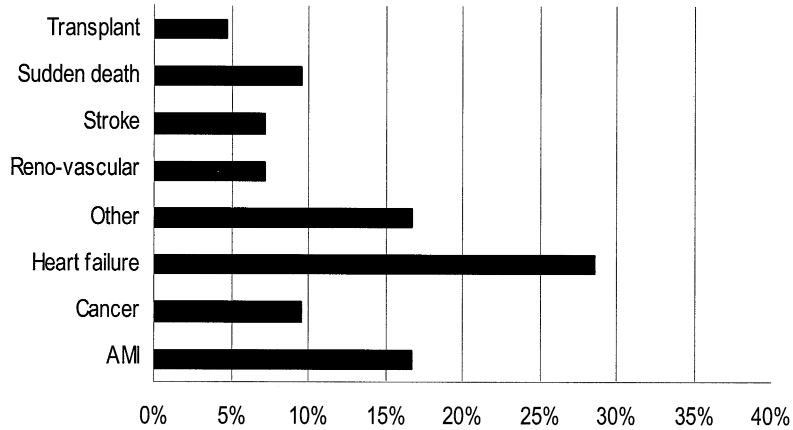

Figure 1. Bar graph illustrating distribution of causes of death among 42 events (40 deaths, 2 transplants) over the course of 10 years in 57 patients undergoing myocardial revascularization for ischemic cardiomyopathy. *AMI*, acute myocardial infarction.

Surgical Complications

All but 1 patient survived the operation and hospital admission, yielding an operative (inpatient 30-day) mortality of 1.7%. None of the patients had perioperative Q-wave myocardial infarction. Three patients (5%) required insertion of an intra-aortic balloon pump during the perioperative period due to low cardiac output.

LV Function

Of the 49 patients who survived beyond 12 months after the operation, 47 underwent repeat RNVG at a mean of 15 ± 3 months postoperatively. Their mean LVEF postoperatively (0.30 ± 0.09) did not differ significantly from that before operation (0.28 ± 0.04; $P = .09$). In a subgroup of patients who had large areas of reversible ischemia on thallium, the LVEF improved by 0.1 ± 0.04 (range: 0.05-0.21), rising from 0.30 ± 0.03 preoperatively to 0.40 ± 0.05 postoperatively ($P = .01$).

Early Postoperative Outcome

Severe preoperative angina and heart failure symptoms (classes III and IV), age at operation, presence of pathologic Q-waves on surface electrocardiograms, and cardiothoracic ratio on chest roentgenograms were examined in all patients. Findings of preoperative stress thallium-201 SPECT were available in 37 patients.

By multivariate analyses, the adjusted odds ratio for large reversible perfusion defects on preoperative stress thallium-201 SPECT, for improved outcome for survival and event-free survival at 15 months, was found to be 15 (95% confidence interval, 1.6-140, $P = .03$), indicating it to be an independent predictor of an early outcome. None of the other clinical variables were shown to have any predictive value.

All-Cause Mortality

During the course of study over 10 years, there were 42 events (40 deaths and 2 transplants). The main causes of death were heart failure in 12 (29%) patients, acute myocardial infarction in 7 (17%), sudden death in 4 (10%), and stroke in 3 (7%) (Figure 1). The survival in our study was 82.5% at 1 year, 55.7% at 5 years, and 23.9% at 10 years (Figure 2).

According to the Cox proportional hazards model (Table 1), only male sex predicted improved long-term survival ($P = .04$). NYHA class III-IV showed a trend toward reduced long-term survival (Figure 3). Age, diabetes, and preoperative myocardial infarction did not affect survival. EF did not affect long-term survival (Figure 4). CCS class III-IV (Figure 5) did not affect long-term survival. Large areas of reversible ischemia on thallium, which is a predictor of improved early outcome, did not affect survival (Figure 6).

Symptom-Free Survival

The overall symptom-free survival in our study population was 77.2% at 1 year and 20.3% at 10 years. Preoperatively, 50% of patients were in CCS class III-IV; at 12 months, 94% (46/49) of the surviving patients were in CCS class 0-I. At 10 years all the 11 surviving patients were in CCS class 0-I. Preoperatively, 65% of patients were in NYHA class III-IV; at 12 months, 71% (35/49) of the survivors were in NYHA class I. At 10 years all 11 surviving patients were in class II.

Discussion

This is one of a handful of studies reported in the literature examining the 10-year outcome of patients undergoing myocardial revascularization for ischemic cardiomyopathy and the only one that has been conducted prospectively.

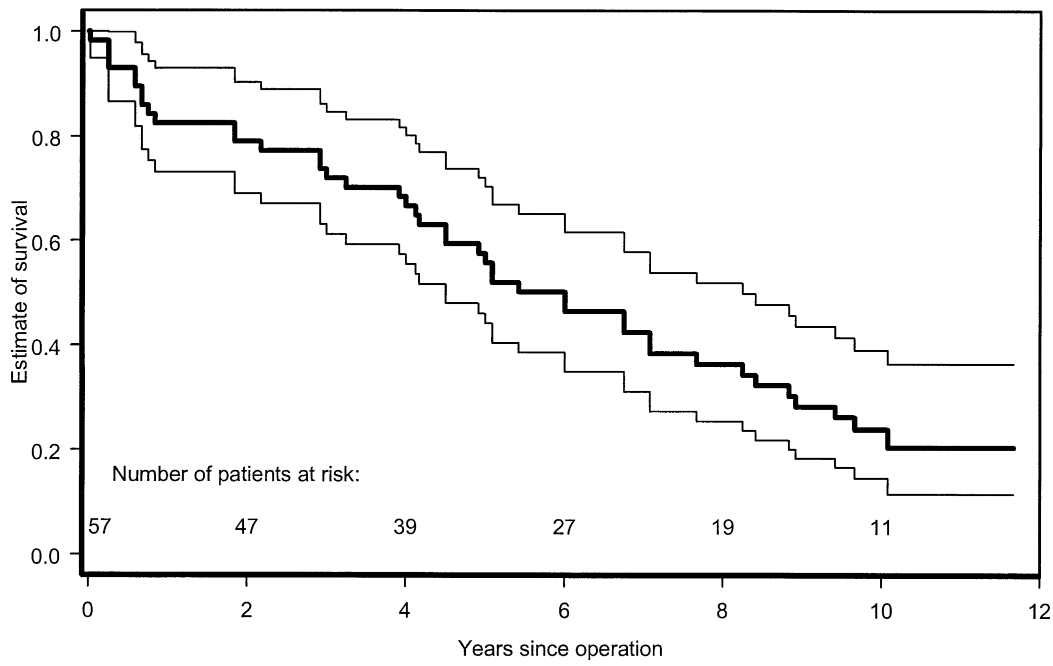

Figure 2. Survival and 95% confidence limits of 57 patients.

TABLE 1. Predictors of survival: Cox proportional hazards model

Variables	Rate ratio	95% CI	*P* value
Sex (male versus female)	0.54	0.31-0.96	.04
Age (*x* versus *x* − 10 years)*	0.76	0.49-1.19	.2
Diabetes	0.79	0.30-2.10	.6
Previous MI	0.41	0.15-1.16	.2
Hypertension	0.60	0.28-1.32	.2
PVD	0.33	0.06-1.69	.2
COPD	1.12	0.28-4.38	.9
CCS angina class (3/4 versus 1/2)	1.15	0.81-1.62	.4
NYHA functional class (3/4 versus 1/2)	1.42	0.97-2.07	.07
LVEF % (*x* versus *x* − 10)*	1.17	0.56-2.44	.7
>5 viable segments on thallium	0.45	0.17-1.18	.1

CI, Confidence interval; *MI,* myocardial infarction; *PVD,* peripheral vascular disease; *COPD,* chronic obstructive pulmonary disease; *CCS,* Canedian Cardiovascular Society; *NYHA,* New York Heart Association; *LVEF,* left ventricular ejection fraction.
*x versus $x - 10$ years compares actual number versus actual number minus 10.

Patients with unstable angina, myocardial infarction, and other significant ischemic events within 4 weeks of the study were specifically excluded. This was to minimize the effects of myocardial stunning on postoperative changes in contractile function.

Medical treatment alone for patients with coronary artery disease and LV dysfunction has been associated with poor results. Louie and colleagues[5] reported 3-year survival of 25% in 54 patients (mean EF 22%), and Luciani and colleagues[6] reported 5-year survival of 28% in 72 patients (mean EF 21%). Currently end-stage ischemic heart disease is one of the primary indications for heart transplantation and accounts for 40% to 50% of procedures performed. Only 10% of eligible patients undergo transplantation and many die on the waiting list[17] because of limited donor availability.[18] The present study demonstrates that myocardial revascularization can be offered to patients with ischemic LV dysfunction at a low operative risk (1.7%) but is associated with poor long-term survival.

The low operative mortality (1.7%) is in line with the estimates from other authors.[13,19-21] Early cardiac morbidity was low with no perioperative myocardial infarction and

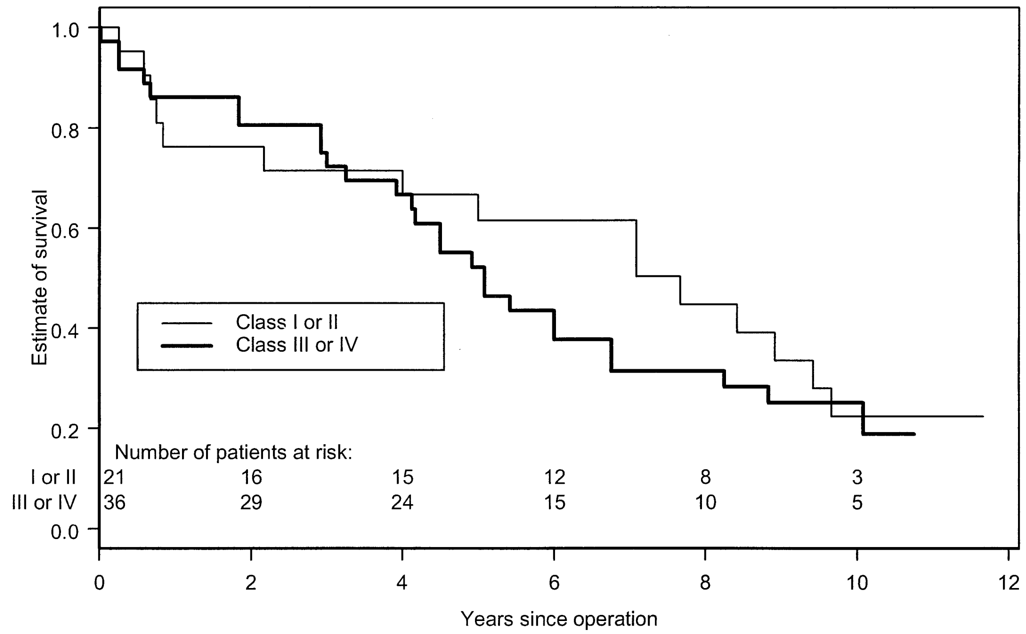

Figure 3. Baseline NYHA class III-IV versus I-II and survival.

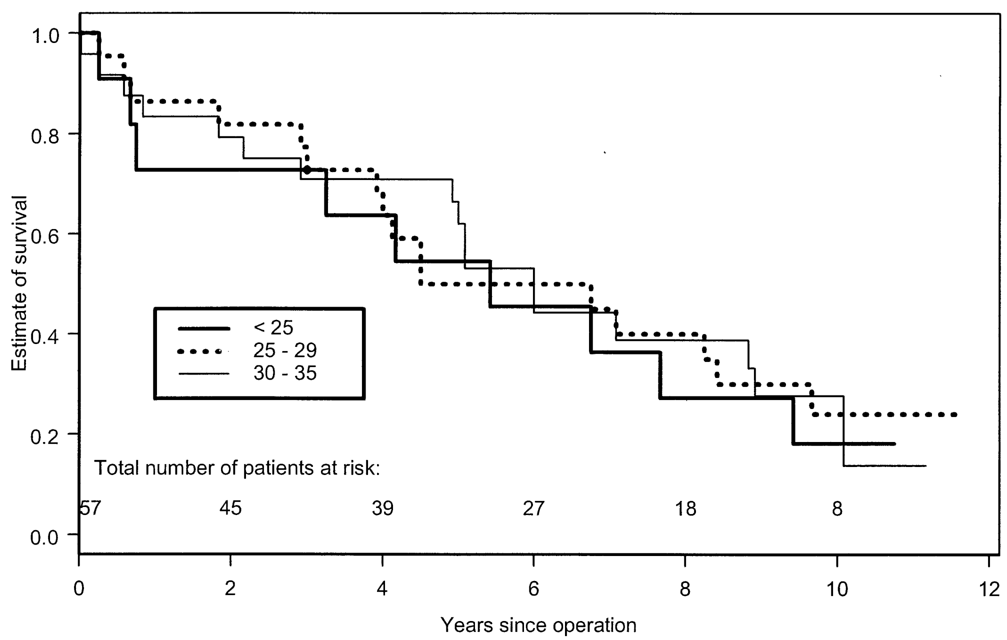

Figure 4. Baseline ejection fraction (<25%, 25%-29%, and 30%-35%) and survival.

use of intra-aortic balloon pumping in only 5% of patients. Other recent developments such as off-pump surgery or pump-assisted CABG might improve perioperative outcomes in this high-risk group of patients.[22]

The most common cause of death was heart failure, similar to other recent studies,[16,18,19,21] and over half the deaths were due to noncardiac causes. The 5-year survival of 55% is slightly lower than those in other studies.[13,19,21] The differences may be due to estimated survivals used in the other studies. No previous studies have described complete 10-year survival results.[15] A 20-year survival study from the Emory group showed that low ejection fractions independently predicted poor long-term survival after CABG despite good relief of angina.[23]

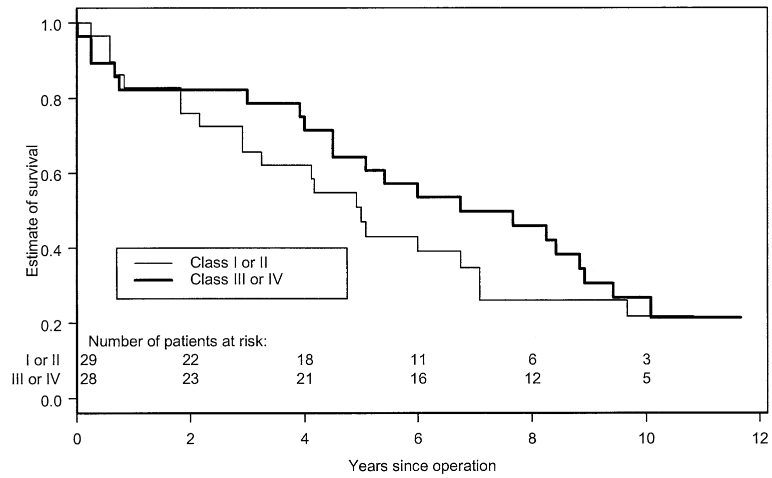

Figure 5. Baseline CCS class III-IV versus I-II and survival.

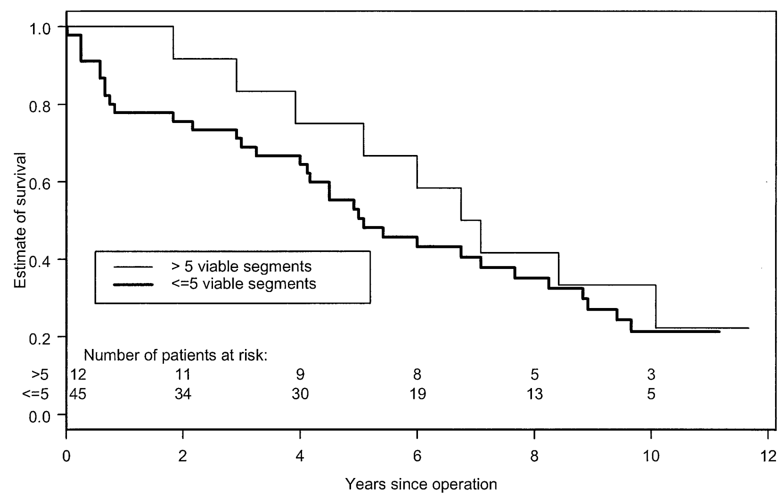

Figure 6. Relationship between viability on preoperative thallium-201 scintigraphy and survival.

Male sex was the only variable associated with good long-term survival similar to another report.[19] Age and NYHA class did not affect long-term survival, unlike other studies.[16,18,19,21] NYHA class III-IV did show a trend toward poor long-term survival. CCS class III-IV was associated with a trend toward better survival throughout the course of study, although not statistically significant. This could be explained by higher CCS class, possibly being associated with larger areas of reversible ischemic myocardium.

Few studies have provided details of functional outcomes after operation. In patients with chronic heart failure, functional capacity has very little relationship to LVEF.[4] Early reports of revascularization have suggested that improvement in LVEF might be an index of successful functional outcome.[5,6,11,24-26] However, more recent reports clearly show that an increase in LVEF is not necessarily associated with clinical improvement as measured by NYHA, exercise capacity, or quality-of-life scores.[12,27-30] Our study also showed no significant increase in LVEF at a mean of 15 months postoperatively, except in a subgroup of patients with large areas of viable myocardium on thallium. However, extensive preoperative reversible ischemia did not predict a greater improvement in functional class at 15 months, despite the prediction of improved survival and event-free survival.

Symptom-free survival (from heart failure symptoms) of 20% at 10 years is low. The de novo appearance, recurrence, or persistence of heart failure symptoms may indicate the relentless progress toward LV insufficiency. Most of our patients were free from angina during the course of study, similar to recently reported studies,[20,22] and compared favorably to the studies by Trachiotis and colleagues[13] (40% at 5.8 years) and Kaul and coworkers[10] (35% at 3.6 years). One of the important outcomes was that nearly all the 10-year survivors were symptom-free.

Limitations

The current study does not have a parallel control group of patients treated medically to determine which fared better. The symptomatic follow-up was incomplete between 12 months and 10 years. Nearly all patients were operated on more than 10 years ago and hence the possible additional effects of newly evolving surgical procedures, such as LV reconstructive surgery and mitral valve repair, were unknown. During the progress of this study, there have been major advances in medical management of chronic heart failure, especially blockade of renin-angiotension and sympathetic nervous system.[3,31,32] In the absence of regular RNVG to assess LVEF and regular coronary angiograms to access graft patency, it is difficult to determine whether the poor late outcome was a result of progressive LV dysfunction, bypass graft disease, or other factors.

Conclusion

Myocardial revascularization for ischemic cardiomyopathy can be performed relatively safely with low operative mortality. It has the advantage of preserving the LV function at 15 months. It is associated with good functional relief, especially from angina and, to a lesser extent, from heart failure symptoms. However, long-term mortality still remains high. It is possible that additional strategies such as LV reconstructive surgery and current optimal medical therapy could further improve this outlook.

We acknowledge the help of Meg Storer, RN, BN(Hons), GrdCert (Cardio Thoracic).

References

1. Pigott JD, Kouchoukos NT, Oberman A, Cutter GR. Late results of surgical and medical therapy for patients with coronary artery disease and depressed left ventricular function. *J Am Coll Cardiol*. 1985;5: 1036-45.
2. Franciosa JA, Wilen M, Ziesche S, Cohn JN. Survival in men with severe chronic left ventricular failure due to either coronary heart disease or idiopathic dilated cardiomyopathy. *Am J Cardiol*. 1983;51: 831-6.
3. The SOLVD Investigators. Effect of enalapril on survival in patients with reduced left ventricular ejection fraction and congestive heart failure. *N Engl J Med*. 1991;325:293-302.
4. Cohn JN, Johnson GR, Shabeti R, et al. Ejection fraction, peak exercise oxygen consumption, cardiothoracic ratio, ventricular arrhythmias, and plasma norepinephrine as determinants of prognosis in heart failure. *Circulation*. 1993;87(Suppl VI):VI5-16.
5. Louie HW, Laks H, Milgalter E, et al. Ischemic cardiomyopathy. Criteria for coronary revascularization and cardiac transplantation. *Circulation*. 1991;84:SIII290-5.
6. Luciani GB, Faggian G, Razzolini R, Livi U, Bortolotti U, Mazzucco A. Severe ischemic left ventricular failure: coronary operation or heart transplantation? *Ann Thorac Surg*. 1993;55:719-23.
7. Kron IL, Flanagan TL, Blackbourne LH, Schroeder RA, Nolon SP. Coronary revascularization rather than cardiac transplantation for chronic ischemic cardiomyopathy. *Ann Surg*. 1989;210:348-54.
8. Blakeman BM, Pifarré R, Sullivan H, Castanzo-Nordin MR, Zucker MJ. High-risk heart surgery in the heart transplant candidate. *J Heart Transplant*. 1990;9:468-72.
9. Sanchez JA, Smith CR, Drusin RE, Reison DS, Malm JR, Rose EA. High-risk reparative surgery. A neglected alternative to heart transplantation. *Circulation*. 1990;82(Suppl 4):302-5.
10. Kaul TK, Agnihotri AK, Fields BL, Riggins LS, Wyatt DA, Jones CR. Coronary artery bypass grafting in patients with an ejection fraction of twenty percent or less. *J Thorac Cardiovasc Surg*. 1996;111:1001-12.
11. Dreyfus GD, Duboc D, Blasco A, et al. Myocardial viability assessment in ischemic cardiomyopathy: benefits of coronary revascularization. *Ann Thorac Surg*. 1994;57:1402-8.
12. Chan RK, Raman J, Lee KJ, et al. Prediction of outcome after revascularization in patients with poor left ventricular function. *Ann Thorac Surg*. 1996;61:1428-34.
13. Trachiotis GD, Weintraub WS, Johnston TS, Jones EL, Guyton RA, Craver JM. Coronary artery bypass grafting in patients with advanced left ventricular dysfunction. *Ann Thorac Surg*. 1998;66:1632-9.
14. Carr AJ, Haithcock BE, Paone G, Barnabei AF, Siverman NA. Long-term outcome after coronary artery bypass grafting in patients with severe left ventricular dysfunction. *Ann Thorac Surg*. 2002;74:1531-6.
15. O'Connor CM, Velazquez EJ, Gardner LH, et al. Comparison of coronary artery bypass grafting versus medical therapy on long-term outcome in patients with ischemic cardiomyopathy (a 25-year experience from the Duke Cardiovascular Disease Databank). *Am J Cardiol*. 2002;90:101-7.
16. Hausmann H, Siniawski H, Meyer R, et al. Coronary artery bypass grafting in patients with highly impaired ventricular function. Long-term outcome. *Dtsch Med Wochenschr*. 2002;127:2503-7.
17. Evans RW, Manninen DL, Garrison LP Jr, Maier AM. Donor availability as the primary determinant of the future of heart transplantation. *JAMA*. 1986;255:1892-8.
18. Kaye MP. The Registry of the International Society for Heart and Lung Transplantation: Ninth Official Report—1992. *J Heart Lung Transplant*. 1992;11:599-606.
19. Luciani GB, Montalbano G, Casali G, Mazzucco A. Predicting long-term functional results after myocardial revascularization in ischemic cardiomyopathy. *J Thorac Cardiovasc Surg*. 2000;120:478-89.
20. Christakis GT, Weisel RD, Fremes SE, et al. Coronary artery bypass grafting in patients with poor left ventricular function. *J Thorac Cardiovasc Surg*. 1992;103:1083-92.
21. Mickleborough LL, Carson S, Tamariz M, Ivanov J. Results of revascularization in patients with severe left ventricular dysfunction. *J Thorac Cardiovasc Surg*. 2000;119:550-7.
22. Antunes PE, de Oliveira JM, Antunes MJ. Coronary surgery with non-cardioplegic methods in patients with advanced left ventricular dysfunction: immediate and long-term results. *Heart*. 2003;89:427-31.
23. Weintraub WS, Clements SD Jr, Cricso LV. Twenty-year survival after coronary artery surgery: an institutional perspective from Emory University. *Circulation*. 2003;107:1271-8.
24. Cigarroa CG, De Filippi CR, Brickner ME, Alvarez LG, Wait MA, Grayburn PA. Dobutamine stress echocardiography identifies hibernating myocardium and predicts recovery of left ventricular function after coronary revascularization. *Circulation*. 1993;88:430-6.
25. Bonow RO, Dilsiziam V, Cuocolo A, Bacharach SL. Identification of viable myocardium in patients with chronic coronary artery disease and left ventricular dysfunction. Comparison of thallium scintigraphy with rejection and PET imaging with 18F-fluorodeoxyglucose. *Circulation*. 1991;83:26-37.
26. Elefteriades JA, Tolis G Jr, Levi E, Mills LK, Zaret BL. Coronary artery bypass grafting in severe left ventricular dysfunction: excellent survival with improved ejection fraction and functional status. *J Am Coll Cardiol*. 1993;22:1411-7.
27. Townend JN, Pagano D, Allen SM, et al. Results of surgical revascularization in ischemic heart failure without angina. *Eur J Cardiothorac Surg*. 1995;9:507-13.
28. Pagano D, Townend JN, Littler WA, Horton R, Camici PG, Bonser RS. Coronary artery bypass surgery as treatment for ischemic heart

failure: the predictive value of viability assessment with quantitative positron emission tomography for symptomatic and functional outcome. *J Thorac Cardiovasc Surg*. 1998;115:791-9.
29. Bax JJ, Poldermans D, Elhendy A, et al. Improvement of left ventricular ejection fraction, heart failure symptoms and prognosis after revascularization in patients with chronic coronary artery disease and viable myocardium detected by dobutamine stress echocardiography. *J Am Coll Cardiol*. 1999;34:163-9.
30. Marwick TH, Zuchowski C, Lauer MS, Secknus MA, Williams J, Lytle BW. Functional status and quality of life in patients with heart failure undergoing coronary bypass surgery after assessment of myocardial viability. *J Am Coll Cardiol*. 1999;33:750-8.
31. Cohn JN, Johnson G, Ziesche S, Cobb F, Francis G, Tristani F. A comparison of enalapril with hydralazine-isosorbide dinitrate in the treatment of chronic congestive heart failure. *N Engl J Med*. 1991; 325:303-10.
32. Packer M, Bristow MR, Cohn JN, et al. The effect of carvedilol on morbidity and mortality in patients with chronic heart failure: U.S. Carvedilol Heart Failure Study Group. *N Engl J Med*. 1996;334:1349-55.