Survival After Isolated Coronary Artery Bypass Grafting in Patients With Severe Left Ventricular Dysfunction

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Background. **The number of patients with severe left ventricular dysfunction referred for coronary artery bypass graft surgery (CABG) continues to increase. The aim of this study was to document the long-term survival in this group.**

Methods. **The 30-day mortality and long-term survival outcome of 162 patients with severely depressed left ventricular ejection fraction (LVEF [≤30%]) who had consecutive isolated CABG between 1996 and 2005 were compared with 661 patients who had impaired LVEF (31% to 59%) and 1,231 patients with normal LVEF (≥60%).**

Results. **The 30-day mortality for patients with severely depressed LVEF was 5.6%. The median survival for deceased patients was 3.4 years (interquartile range, 1.3 to 5.9). The risk of all-cause mortality attributable to severe left ventricular dysfunction was increased twofold compared with having normal LVEF (hazard ratio = 2.28; 95% confidence interval: 1.64 to 3.18; $p < 0.001$). Among the covariates, older age, emergency surgery, mitral incompetence, smoking history, respiratory disease, diabetes mellitus, cerebrovascular disease, intensive care unit intubation for 24 hours or more, postoperative renal failure, postoperative pleural effusion, and nonuse of left internal mammary artery were detected as significant predictors of increased mortality risk.**

Conclusions. **The mortality rate among CABG patients with severely depressed LVEF was comparable to that reported in other series. Severe left ventricular dysfunction carried more than a twofold increased mortality risk compared with patients who had an impaired LVEF, adjusted for traditional risk factors. These data suggest that LVEF has an impact on long-term patient survival even after preoperative covariates and postoperative morbidity outcomes are considered.**

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Heart failure (HF) is a worldwide public health problem, as highlighted by the American Heart Association Statistic Committee report in 2006 that revealed more than 5 million people have HF in the United States [1]. More than 1 million patients are hospitalized, and more than 50,000 patients die each year with HF as a primary diagnosis [1]. Coronary artery disease (CAD) is the most common cause of HF and is responsible for between 60% and 68% of HF etiology [2]. In ischemic coronary artery disease (CAD) without valvular lesion, HF is commonly caused by left ventricular systolic dysfunction.

Aggressive medical treatment of patients with severe left ventricular dysfunction (LVD) is unsatisfactory in terms of controlling symptoms and long-term survival, as reported in the Assessment of Treatment with Lisinopril and Survival (ATLAS) trial [3]. The ATLAS investigators reported that there were 717 cardiovascular deaths among 1,596 patients treated with low-dose lisinopril and 666 cardiovascular deaths from among 1,568 patients treated with high-dose lisinopril in patients with mild, moderate or severe HF at a median follow-up of 46 months. Favorable results with CABG in comparison with medical treatment alone make CABG a more attractive clinical option [4, 5]. However, high hospital mortality and morbidity makes CABG a surgical challenge among patients with severe LVD [6]. Previous reports have shown favorable short-term survival among severe LVD patients [7], although the long-term survival outcomes of patients with severe LVD undergoing CABG are not well defined in recent series with modern surgical techniques. In the present study, we compare the short- and long-term survival of patients with severe LVD, as ascertained by left ventricular ejection fraction (LVEF), with that of patients who have impaired and normal LVEF.

Patients and Methods

Patients

All patients having isolated CABG with cardiopulmonary bypass (CPB) performed at the Flinders Medical Centre from January 1, 1996, to December 31, 2005, were considered eligible for the study. Patients undergoing concom-

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Abbreviations and Acronyms

CABG = coronary artery bypass graft surgery
CAD = coronary artery disease
CCS = Canadian Cardiovascular Society
CI = confidence interval
CPB = cardiopulmonary bypass
HF = heart failure
HR = hazard ratio
ICU = intensive care unit
IABP = intra-aortic balloon pump
LIMA = left internal mammary artery
LVD = left ventricular dysfunction
LVEF = left ventricular ejection fraction
OR = odds ratio

itant procedures for mitral incompetence or aortic aneurysms were not considered eligible for this study. All data were collected prospectively at the time of operation by resident medical officers and entered into an electronic database. Identification of LVEF was based on either the preoperative echocardiography or cineangiography assessment performed by an independent cardiologist. Patient LVEF was stratified accordingly: severely impaired 30% or less, impaired 31% to 59%, and normal 60% or more.

Anesthetic, Surgical, and Cardiopulmonary Bypass Techniques

Anesthetic technique was standardized for all patients. For induction, midazolam, pancuronium, and fentanyl were used, and maintenance was with isofluorane or sevoflurane, and nitrous oxide or propofol, or both, as required. Before aortic cannulation, heparin was given at a dose of 300 IU/kg to achieve a target activated clotting time of 400 s or longer before commencement of CPB. On completion of all anastomoses and weaning of CPB, protamine was given to return the activating clotting time to preoperative levels.

After median sternotomy, and harvesting of arterial or venous conduit, CPB was instituted using an ascending aortic and either a two-stage right atrial or bicaval cannulation. Cardiopulmonary bypass was performed utilizing roller pumps; the circuit included a hard shell membrane oxygenator, PVC or biopassive tubing (SMARxT; Cobe Cardiovascular, Arvada, CO) and a 40 μm arterial line filter. Routine CPB protocol included nonpulsatile arterial flow rate of 1.8 to 2.4 lpm/m^2, alpha-stat pH management, gravity venous drainage, and tepid systemic temperature management (30° to 36°C). Myocardial protection was achieved by using intermittent antegrade hyperkalemic tepid blood cardioplegia (30° to 36°C). The initial or induction dose was given for 2 minutes (250 mL/min), then the maintenance dose was given approximately every 20 minutes as required through the grafting procedure. Attempts were made at all procedures to revascularize all vessels deemed operable by the respective surgeons. The heart was arrested, and the target coronary artery was opened; and distal anastomoses between the bypass graft and native coronary artery were performed using 7-0 or 6-0 polypropylene under aortic cross clamping. Proximal anastomoses were performed on beating heart and partial aortic clamping using 6-0 polypropylene. Gradual weaning from bypass started after completion of the proximal anastomoses. At the end of surgery, patients were transferred to the intensive care unit (ICU) and managed according to unit protocol.

Mortality Assessment

The study aim was to assess the 30-day mortality and long-term survival in severe LVD and compare them with the normal and impaired LVEF groups. Survival was ascertained by patient identification within the National Death Index provided to our institution by the Australian Institute of Health and Welfare for use in epidemiologic studies and medical research. National Death Index data provided all-cause mortality until December 31, 2006, and this date was taken as the censor date for patient survival. Eligible patients were operated on or before December 31, 2005, thus enabling a minimum 12-month follow-up on the cohort. Approval was granted by the Clinical Governance Committee of the Flinders Medical Centre to report these findings, waiving the need for patient consent for this study.

Statistical Analysis

Statistical analyses were performed using SPSS version 15.0 (SPSS, Chicago, IL) to compare the LVEF groups on demographic and surgical variables. Continuous data were analyzed with one-way analysis of variance. Categorical data were analyzed using the χ^2 statistic with Fisher's exact test where appropriate.

The primary endpoint of all-cause long-term mortality was analyzed using multivariable Cox proportional hazard modeling. Covariate selection was determined a priori from previous survival research [8, 9, 10]. Covariates adjusted for in multivariable analysis included the categorical variables of female sex, age (quartiles), angina (Canadian Cardiovascular Society [CCS] classification system) class II to IV versus I or none, diabetes mellitus, hypercholesterolemia, hypertension, renal disease, peripheral vascular disease, mitral incompetence, acute myocardial infarction 30 days or less, presence of cerebrovascular disease, tobacco-smoking history, respiratory disease, urgency of surgery (elective as the reference category versus urgent and emergency), use of left internal mammary artery (LIMA), ICU intra-aortic balloon pump (IABP), postoperative pleural effusion, postoperative renal failure, or ICU intubation for 24 hours or longer. Continuous variables adjusted for in multivariable analysis included the total cross-clamping time and the total number of anastomoses. All covariates described above were forced into the final adjusted hazard model in block fashion regardless of significance. The LVEF grouping variable was entered at the second step of the hazard model, with normal set as the reference category. During data screening, there were no outliers