International Journal of Cardiology 168 (2013) 5316–5322

Contents lists available at ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

Coronary artery bypass grafting in patients with left ventricular dysfunction: Predictors of long-term survival and impact of surgical strategies

Jae Suk Yoo [1], Joon Bum Kim *,[1], Sung-Ho Jung [1], Suk Jung Choo [1], Cheol Hyun Chung [1], Jae Won Lee [1]

Department of Thoracic and Cardiovascular Surgery, Asan Medical Center, University of Ulsan College of Medicine, Seoul, South Korea

ARTICLE INFO

Article history:
Received 11 March 2013
Received in revised form 1 July 2013
Accepted 3 August 2013
Available online 15 August 2013

Keywords:
Ischemic heart disease
Ventricular function
Myocardial revascularization
Surgery
Prognosis

ABSTRACT

Background: In the surgical management of ischemic cardiomyopathy, factors associated with long-term prognosis after coronary artery bypass grafting (CABG) in patients with severe left ventricular (LV) dysfunction are poorly understood. This study aimed to determine predictors of clinical outcomes in patients with severe LV dysfunction undergoing CABG.

Methods: Out of 6084 patients who underwent CABG between 1997 and 2011, 476 patients (aged 62.6 ± 9.3 years, 100 females) were identified as having severe LV dysfunction (ejection fraction ≤ 35%), preoperatively. All-cause mortality and adverse cardiac events (myocardial infarction, repeat revascularization, stroke and hospitalization due to cardiovascular causes) were evaluated during a median follow-up period of 55.2 months (inter-quartile range: 26.4–94.8 months).

Results: During the follow-up, 187 patients (39.3%) died and 126 cardiac events occurred in 104 patients (21.8%). Five-year survival and event-free survival rates were 72.1 ± 2.2% and 61.3 ± 2.4%, respectively. On Cox-regression analysis, old age ($P < 0.001$), recent MI ($P < 0.001$), history of coronary stenting ($P = 0.023$), decreased glomerular filtration rate ($P < 0.001$), and presence of mitral regurgitation (≥moderate) ($P = 0.012$) or LV wall thinning ($P = 0.007$) emerged as significant and independent predictors of death. After adjustment for important covariates affecting outcomes, none of the pump strategy (off-pump vs. on-pump), concomitant mitral surgery or surgical ventricular reconstruction (SVR) affected survival or event-free survival ($P = 0.082$ to >0.99).

Conclusions: Long-term survival following CABG in patients with severe LV dysfunction was affected by age, renal function, recent MI, prior coronary stenting, and presence of mitral regurgitation or LV wall thinning. Neither concomitant mitral surgery nor SVR, however, had significant influence on clinical outcomes.

1. Introduction

Coronary artery disease is the most common cause of heart failure (HF) and has increased steadily with the growing incidence of associated mortality [1–3]. Along with these recent trends, the prevalence of severe left ventricular (LV) dysfunction in patients undergoing coronary artery bypass grafting (CABG) has also been growing [4]. Two thirds of ischemic LV dysfunction is known to be attributed to a dysfunctional but viable myocardium, and thus revascularization to the corresponding coronary lesions is believed to improve LV systolic function and clinical outcomes in patients with significant ischemic LV dysfunction [5,6].

Severe LV dysfunction, however, is known as a potent risk factor for mortality following CABG; therefore, there are still concerns that the risk of surgery may offset the potential benefits of coronary revascularization in this particular population. Although several observational studies have shown improved early outcomes following CABG in patients with severe LV dysfunction compared with older experiences [4,7], recent evidence has failed to demonstrate remarkable survival benefits in patients with severe LV dysfunction undergoing CABG compared to medical therapy alone [8,9]. As such, there is still a large amount of controversy and clinical uncertainty regarding this issue [3,10].

In these regards, understanding the prognosis and determinants of clinical outcomes following CABG in patients with severe LV dysfunction will be clinically important. However, previous studies have mainly focused on early operative outcomes, with limited data on the long-term outcomes in these patients. Very few studies have evaluated the long-term prognosis, taking into consideration baseline clinical variables as well as the various surgical strategies as potential predictors of outcome. Therefore, we sought to evaluate the long-term clinical outcomes and to identify predictors of such outcomes in patients with severe LV dysfunction undergoing CABG. In addition, we evaluated the impact of different surgical strategies, such as pump strategy (on-pump vs. off-pump), addition of surgical ventricular reconstruction (SVR), and concomitant correction of ischemic mitral regurgitation (MR) on clinical outcomes.

* Corresponding author at: Department of Thoracic and Cardiovascular Surgery, Asan Medical Center, University of Ulsan College of Medicine, 388-1 Pungnap-dong Songpa-gu, Seoul 138-736, South Korea. Tel.: +82 2 3010 5416; fax: +82 2 3010 6966.
E-mail address: jbkim1975@amc.seoul.kr (J.B. Kim).

[1] These authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

0167-5273/$ – see front matter. Crown Copyright © 2013 Published by Elsevier Ireland Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.ijcard.2013.08.009

2. Materials and methods

2.1. Patients

From January 1997 to October 2011, a total of 6084 patients underwent CABG at the Asan Medical Center, Seoul, Korea. Among them, we identified 547 patients who had LV ejection fraction (EF) of 35% or less on preoperative echocardiographic evaluations. Patients with concomitant aortic valve or aorta replacement (n = 50), ventricular septal defect secondary to myocardial infarction (MI) (n = 3), a history of prior major cardiac surgery (n = 9), and organic MV dysfunction (n = 9) were excluded from this study. Finally, 476 subject patients (aged 62.6 ± 9.3 years, 100 females) were selected. This study was approved by our institutional Ethics Committee/Review Board, which waived the requirement for informed patient consent because of the retrospective nature of the study.

2.2. Surgical procedures

All patients were operated through a median sternotomy. Each surgery was conducted by one of the five cardiac surgeons. Each surgeon adopted a different surgical strategies for CABG regarding the institution of cardiopulmonary bypass (CPB) (off-pump vs. conventional on-pump vs. on-pump beating), methods of internal mammary artery harvesting technique (skeletonization vs. pedicled harvesting), preference on second or third conduits (arterial vs. venous conduits) for target vessel revascularization, and the use of the Y-composite or sequential bypassing techniques.

Arterial conduits were prepared by topical application of diluted solution of papaverine after harvesting. For patients undergoing conventional on-pump CABG, myocardial protection during surgery was achieved by intermittent, antegrade blood cardioplegia (28 °C–32 °C) infusions. Although the method of CPB was determined by the attending surgeon's preference and by other concomitant procedures, on-pump beating CABG was preferred in patients with unstable hemodynamics when performed by surgeons who were accustomed to off-pump CABG.

2.3. Definitions and data collection

The primary outcome of interest was all-cause mortality. All-cause death rather than cardiac death was chosen as one of the primary end points because it is the most robust and unbiased index, requiring no adjudication to avoid inaccurate or biased documentation and clinical assessments. Secondary outcomes included MI, repeat revascularization, stroke, and hospitalization due to cardiovascular causes.

Data were obtained through August 2012 during six-month interval regular visits to the outpatient clinic or by telephone interviews. For validation of complete information on mortality, data on vital status, and dates and causes of death were obtained through August 2012, from the Korean National Registry of Vital Statistics. All deaths were considered of cardiac origin unless a non-cardiac origin was established.

2.4. Statistics

Categorical variables, presented as frequencies and percentages, were compared using the Chi-square test or Fisher's exact test. Continuous variables, expressed as mean ± SD or median with range, were compared using Student's unpaired *t*-test or the Mann–Whitney *U* test, as appropriate. For multivariable analyses, the Cox proportional hazards models were used to determine the risk factors of mortality. Baseline and procedural variables listed in Tables 1 and 2 were evaluated in the models, and those with a P value ≤0.20 in univariate analysis were candidates for the multivariable Cox models. Multivariable analyses involved a backward elimination technique and only variables with a P value ≤0.10 were used in the final model. Final models were validated in 1000 bootstrap samples. To calculate the risk-adjusted hazard ratio of clinical outcomes of several additional surgical procedures (i.e., MV repair and SVR), each procedural factor was incorporated into the Cox-regression model as a covariate along with important risk covariates that had significant effects ($P < 0.1$) on clinical outcomes.

To further evaluate the effects of SVR on echocardiographic parameters, we determined propensity score-matched groups (SVR vs. non-SVR groups). The propensity scores were estimated without considering outcome variables by multiple logistic regression analysis. A propensity score model was developed that included all the variables shown in Table 1. Propensity score-matched pairs without replacement (a 1:1 match) were determined using the greedy 5-to-1 digit match algorithm. After propensity score matching, the echocardiographic parameters of the two groups were compared using paired *t*-tests. Trends in each parameter over time were investigated using repeated-measures ANOVAs. All reported P values were two-sided, and a value of $P < 0.05$ was considered statistically significant. SPSS software version 18.0 (SPSS Inc., IBM Company, Chicago, IL, USA) was used for statistical analyses.

3. Results

3.1. Baseline characteristics

Table 1 describes the baseline characteristics of all patients. In summary, mean LV EF was 28.9 ± 4.9%. Twenty-six patients (5.5%) required emergent or urgent operations, and 58 patients (12.2) were critically ill. MR was observed in most patients (n = 408, 85.7%), with 115 (24.2%) patients showing moderate or greater MR. Twenty-seven patients (5.7%) had definite aneurysm of the LV whereas 231 patients (48.5%) showed thinning of the LV without definite aneurysm formation.

Table 1
Baseline characteristics of patients (n = 476).

Variables	Values
Age, year	62.6 ± 9.3
Female gender, n (%)	100 (21.0)
Diabetes mellitus, n (%)	162 (34.0)
Hypertension, n (%)	99 (20.8)
Stroke, n (%)	37 (7.8)
Chronic renal failure, n (%)	52 (10.9)
Prior coronary stenting, n (%)	31 (6.5)
Chronic lung disease, n (%)	9 (1.9)
Extracardiac arteriopathy, n (%)	22 (4.6)
Recent myocardial infarction, n (%)	83 (17.4)
Critical status, n (%)	58 (12.2)
Urgent/emergent surgery, n (%)	26 (5.5)
Atrial fibrillation, n (%)	33 (6.9)
eGFR, mL/min/1.73 m^2	62.6 ± 26.9
Coronary anatomy	
No. of vessels with stenosis of ≥50%, n (%)	
One	5 (1.1)
Two	65 (13.6)
Three	406 (85.3)
Left main disease, n(%)	92 (19.3)
Echocardiographic findings	
LV systolic dimension, mm	51.3 ± 25.7
LV diastolic dimension, mm	61.9 ± 7.5
LV ejection fraction, %	28.9 ± 4.9
End-systolic volume mL	119.4 ± 40.9
End-diastolic volume, mL	166.7 ± 51.1
Left atrial dimension, mm	45.1 ± 6.0
E/E′ ratio	21.8 ± 11.5
Mitral regurgitation grade, n (%)	
None	68 (14.3)
Mild	293 (61.6)
Moderate	90 (18.9)
Severe	25 (5.3)
Tricuspid regurgitation grade, n (%)	
None	211 (44.3)
Mild	249 (52.3)
Moderate	10 (2.1)
Severe	6 (1.3)
Peak pressure gradient of tricuspid regurgitation, mm Hg	29.5 ± 13.4
LV wall abnormality, n (%)	238 (50.0)
Aneurysm	27 (5.7)
Thinning	231 (48.5)

eGFR, estimated glomerular filtration rate; LV, left ventricle.

Table 2
Surgical procedures (n = 476).

Surgical procedures	Values, n (%)
Initial CPB strategy	
Conventional on-pump	246 (51.7)
On-pump beating	94 (19.7)
Off-pump	136 (28.6)[a]
No. of distal anastomosis (median: 3, range: 1–7)	
One	24 (5.0)
Two	95 (20.0)
Three	150 (31.5)
≥Four	234 (43.5)
Left ventricular reconstruction	63 (13.2)
Aneurysmectomy	22 (4.6)
Endo-ventricular patch reconstruction	41 (8.6)
Mitral valve surgery	77 (16.2)
Repair	72 (15.1)
Replacement	5 (1.1)
Mechanical valves	2
Bioprosthetic valves	3
Tricuspid valve repair	14 (2.9)
Maze procedure	8 (1.7)

CPB, cardiopulmonary bypass.
[a] These include four patients who were converted from off-pump to on-pump surgery.