

Optimal Timing of Surgical Revascularization for Myocardial Infarction and Left Ventricular Dysfunction

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Abstract

Background: The optimal timing of surgical revascularization for patients presenting with ST-segment elevation myocardial infarction (STEMI) and impaired left ventricular function is not well established. This study aimed to examine the timing of surgical revascularization after STEMI in patients with ischemic heart disease and left ventricular dysfunction (LVD) by comparing early and late results.

Methods: From January 2003 to December 2013, there were 2276 patients undergoing isolated coronary artery bypass grafting (CABG) in our institution. Two hundred and sixty-four (223 male, 41 females) patients with a history of STEMI and LVD were divided into early revascularization (ER, <3 weeks), mid-term revascularization (MR, 3 weeks to 3 months), and late revascularization (LR, >3 months) groups according to the time interval from STEMI to CABG. Mortality and complication rates were compared among the groups by Fisher's exact test. Cox regression analyses were performed to examine the effect of the time interval of surgery on long-term survival.

Results: No significant differences in 30-day mortality, long-term survival, freedom from all-cause death, and rehospitalization for heart failure existed among the groups ($P > 0.05$). More patients in the ER group (12.90%) had low cardiac output syndrome than those in the MR (2.89%) and LR (3.05%) groups ($P = 0.035$). The mean follow-up times were 46.72 ± 30.65 , 48.70 ± 32.74 , and 43.75 ± 32.43 months, respectively ($P = 0.716$). Cox regression analyses showed a severe preoperative condition (odds ratio = 7.13, 95% confidence interval 2.05–24.74, $P = 0.002$) rather than the time interval of CABG ($P > 0.05$) after myocardial infarction was a risk factor of long-term survival.

Conclusions: Surgical revascularization for patients with STEMI and LVD can be performed at different times after STEMI with comparable operative mortality and long-term survival. However, ER (<3 weeks) has a higher incidence of postoperative low cardiac output syndrome. A severe preoperative condition rather than the time interval of CABG after STEMI is a risk factor of long-term survival.

Key words: Ischemic Heart Disease; Left Ventricular Dysfunction; Myocardial Infarction; Surgical Revascularization

INTRODUCTION

Heart failure has become a worldwide health issue, which seriously affects quality of life and life expectancy, and ischemic heart disease (IHD) is the leading cause of this lethal problem.^[1-3] Acute ST-segment elevation myocardial infarction (STEMI) is the most critical illness among IHD with the worst prognostic results. Therefore, prompt and effective treatment of STEMI has always been one of the most challenging tasks in clinical practice.

With the wide use of thrombolytic therapy and primary percutaneous coronary intervention (PCI), surgical revascularization has become the second-line option for the treatment of STEMI.^[4,5] As prior studies have revealed, emergent coronary artery bypass grafting (CABG) was only performed as primary treatment in <5% of patients with

acute myocardial infarction (AMI) and as rescue treatment in another 5% of patients after failed PCI.^[6-9] However, with the extensive application of coronary angiography, nearly 50% of patients with an acute coronary syndrome were identified as having severe triple-vessel disease, and a considerable number of patients were not anatomically suitable for emergent PCI treatment.^[10-12] Thus, CABG plays an important role in the treatment of AMI.

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Controversy has been existed for a long time regarding the optimal timing of surgical revascularization after AMI.^[13-15] Although the latest American College of Cardiology (ACC)/American Heart Association guidelines for CABG surgery provided specific recommendations for surgical revascularization after STEMI, the optimal timing of CABG after AMI is still not well defined according to previous studies.^[16-19] Some studies recommended that an interval of at least 1 week between STEMI and surgical revascularization was relatively safe.^[20] However, other studies have demonstrated that CABG can be performed at any time after STEMI. These studies also considered that patients' preoperative risk factors rather than the time interval played a more important role in early results.^[21] For patients with left ventricular dysfunction (LVD) after STEMI, the issue about timing of surgical revascularization is even more complex because LVD is also an independent risk factor for operative mortality from CABG. At present, there is the dilemma that early revascularization (ER) may greatly enhance the surgical risk for this vulnerable patient group.^[21] Late revascularization (LR) may further aggravate ischemic damage, causing hibernating or stunned myocardium and worsened left ventricular (LV) function.^[17]

Therefore, we performed this retrospective study and analyzed the data of patients with LVD undergoing CABG at various times after STEMI. This study aimed to determine the optimal timing of surgical intervention and its effect on the short-term and long-term results of these patients.

METHODS

Patients

From January 2003 to December 2013, 2276 patients underwent isolated CABG in our institution, 264 of whom were included in our study. Informed consent for this study was obtained from each patient and their family member, following the Institutional Review Board approval of this study. The inclusion criteria were as follows: (a) patients had a history of STEMI as determined by the presence of clinical, electrocardiographic, and biochemical results; (b) preoperative echocardiography showed an left ventricular ejection fraction (LVEF) <50%; and (c) severe coronary stenosis was identified by coronary angiography and isolated CABG was recommended in accordance with the 2004 and 2011 ACC/American Heart Association guidelines for CABG surgery. Patients were excluded from the study if they fulfilled any of the following criteria: (a) patients were diagnosed with non-STEMI before surgery; (b) LVEF >50%; (c) severe IHD requiring surgical revascularization with poor operative tolerance; and (d) any concomitant cardiac operation in addition to CABG, such as mitral valve or aortic valve replacement, or LV aneurysm resection. Patients were divided into the ER group ($n = 31$), mid-term revascularization group (MR, $n = 69$), and LR group ($n = 164$). This classification was performed according to whether the patients underwent surgery <3 weeks, between 3 weeks and 3 months, or more than 3 months after STEMI, respectively.

Methods

Surgical revascularization was performed with or without the use of cardiopulmonary bypass depending on the patient's condition and the surgeons' preference. All of the surgeries were performed by three experienced cardiac surgeons (>100 CABG procedures per year). The internal thoracic artery (ITA) was routinely applied for left anterior descending artery revascularization, and saphenous vein grafts were anastomosed to other target vessels. When on-pump CABG was selected, histidine-tryptophan-ketoglutarate cardioplegia or blood cardioplegia was used for myocardial protection. For off-pump CABG, the revascularization strategy included performing an LAD graft by ITA, followed by saphenous vein grafts to other target vessels. Graft flow was routinely assessed by Doppler transit time flowmetry (Medistim Butterfly Flowmeter; Medistim, Oslo, Norway) before weaning off cardiopulmonary bypass and closing the chest.

Patients' demographics and European System for Cardiac Operative Risk Evaluation II (EuroSCORE II) risk factors were obtained preoperatively. Short- and long-term clinical outcomes of the three groups were compared. The primary end points of short-term clinical outcomes were 30-day mortality and severe complications. These complications included low cardiac output syndrome, malignant ventricular arrhythmias, renal failure, surgical reexploration for bleeding, perioperative myocardial infarction (MI), deep wound infection, and stroke. The long-term end points were all-cause mortality and rehospitalization for heart failure.

Statistical analysis

Continuous data are expressed as mean \pm standard deviation (SD) and categorical variables as numbers and percentages. Comparisons of categorical variables between the groups were performed by the Chi-squared or Fisher's exact test. Comparisons of continuous variables between groups were analyzed by the unpaired Student's *t*-test. To identify the risk factors of long-term survival, baseline and imaging data as shown in Tables 1 and 2 were included in multivariable analysis using the cox proportional hazards model. In this mode, the entry criterion was $P = 0.05$ and stay criterion was $P = 0.1$. A value of $P < 0.05$ was considered statistically significant. Data analysis was performed with SPSS software version 13.0 (SPSS Inc., Chicago, IL, USA).

RESULTS

The preoperative characteristics of the three groups are shown in Table 1. The EuroSCORE II risk factors (including female, dyspraxia, severe preoperative severe condition [e.g., cardiogenic shock, intra-aortic balloon pump support, etc.],^[16] MI within 3 months, and emergent surgery [within 24 h]^[16]) were significantly higher in the ER group than those in MR and LR groups. The number of diseased vessels, incidence of left main disease, proportion of off-pump CABG, number of anastomoses, and incidence of perioperative intra-aortic balloon pump implantation were equally distributed in

Table 1: Baseline demographics in three groups

Characteristics	Early operative group (<21 days)	Mid-term operative group (21–90 days)	Late operative group (>90 days)	F/ χ^2	P
	n = 31	n = 69	n = 164		
Age (years)	62.97 ± 9.69	62.97 ± 7.96	62.32 ± 9.43	0.160	0.852
Gender (female), %	29.03 (9)	21.74 (15)*	10.37 (17)* [†]	9.670	0.008
Renal insufficiency, %	51.61 (16)	68.12 (47)	70.12 (115)	7.233	0.124
Peripheral vascular disease, %	3.23 (1)	8.69 (6)	6.71 (11)	1.016	0.602
Mobility impairment, %	9.68 (3)	1.45 (1)*	1.83 (3)*	6.744	0.034
Prior cardiac surgery, %	0 (0)	0 (0)	0.61 (1)	0.612	0.736
Chronic obstructive pulmonary disease, %	0 (0)	1.45 (1)	2.44 (4/64)	0.934	0.627
Acute endocarditis, %	0 (0)	0 (0)	0 (0)	–	–
Preoperative severe condition, %	19.35 (6)	7.25 (5)*	6.10 (10)*	6.322	0.042
Diabetes, %	19.35 (6)	8.70 (6)	19.51 (32)	4.274	0.118
NYHA (III/IV), %	19.35 (6)	59.42 (41)	12.20 (20)	2.104	0.124
CCS Class IV, %	58.07 (18)	56.52 (39)	60.98 (100)	2.547	0.636
LVEF (%)	42.19 ± 5.50	41.41 ± 6.05	41.77 ± 6.17	0.190	0.827
Previous MI within 3 months, %	100 (31)	100 (69)	23.17 (38)* [†]	135.514	0.000
PAP	30.90 ± 12.25	29.84 ± 10.48	28.89 ± 11.92	0.407	0.666
Emergent surgery, %	25.81 (8)	5.79 (4)*	7.32 (12)*	12.011	0.002
EuroSCORE II [‡]	0.06 ± 0.090	0.048 ± 0.182	0.032 ± 0.127	0.556	0.574

*Compared with early operative group (<21 days); [†]Compared with mid-term operative group (21–90 days); [‡]The definition referred to reference 16. All data were expressed as mean ± SD or % (n). NYHA: New York Heart Association; CCS: Canadian Cardiovascular Society; LVEF: Left ventricular ejection fraction; PAP: Pulmonary artery pressure; EuroSCORE II: European System for Cardiac Operative Risk Evaluation II; SD: Standard deviation.

Table 2: Preoperative echocardiographic and angiographic characteristics of patients undergoing CABG after MI

Items	Early operative group (<21 days)	Mid-term operative group (21–90 days)	Late operative group (>90 days)	F/ χ^2	P
	n = 31	n = 69	n = 164		
LVEDD	51.00 ± 5.37	53.41 ± 5.32*	54.99 ± 6.35*	6.437	0.002
LVEF	41.94 ± 5.30	41.55 ± 5.91	41.76 ± 6.10	0.051	0.950
Mild-to moderate MR, %	58.1 (18)	55.1 (38)	49.4 (81)	9.765	0.283
Left main disease, %	41.9 (13)	33.3 (23)	29.2 (43)	3.589	0.166
Multivessel disease, %	93.55 (29)	91.30 (63)	93.29 (153)	0.317	0.854

*Compared with early operative group (<21 days). All data were expressed as mean ± SD or % (n). LVEDD: Left ventricular end-diastolic dimension; LVEF: Left ventricular ejection fraction; MR: Mitral regurgitation; SD: Standard deviation; CABG: Coronary artery bypass grafting; MI: Myocardial infarction.

Table 3: Operative variables and operative outcome in patients after CABG

Items	Early operative group (<21 days)	Mid-term operative group (21–90 days)	Late operative group (>90 days)	F/ χ^2	P
	n = 31	n = 69	n = 164		
Off-pump CABG, %	22.58 (7)	21.74 (15)	24.39 (40)	0.206	0.902
Number of anastomoses	2.94 ± 0.73	3.06 ± 0.80	2.95 ± 0.80	0.532	0.558
Postoperative IABP, %	19.36 (6)	8.69 (6)	10.37 (17)	2.655	0.265
Surgery-mortality, %	6.45 (2)	0 (0)	2.44 (4)	4.062	0.131
Malignant ventricular arrhythmias, %	6.45 (2)	4.35 (3)	4.27 (7)	0.295	0.863
Perioperative MI, %	3.23 (1)	1.45 (1)	0.61 (1)	1.670	0.434
Re-exploration for bleeding, %	0 (0)	0 (0)	1.22 (2)	1.217	0.544
Postoperative renal failure, %	6.45 (2)	7.25 (5)	3.05 (5)	2.266	0.322
Mediastinal infection, %	0 (0)	0 (0)	0 (0)	–	–
Low cardiac output syndrome, %	12.90 (4)	2.89 (2)*	3.05 (5)*	6.717	0.035
Stroke, %	3.23 (1)	1.45 (1)	3.66 (6)	0.811	0.667

*Compared with early operative group (<21 days). All data were expressed as mean ± SD or % (n). CABG: Coronary artery bypass grafting; MI: Myocardial infarction; IABP: Intra-aortic balloon pump; SD: Standard deviation.

the three groups [Tables 2 and 3]. Six (2.3%) deaths occurred within 30 days after surgery, and there was no significant difference for 30-day mortality among the three groups. The incidence of low cardiac output syndrome was significantly higher in the ER group compared with the MR and LR groups. None of the other postoperative adverse events were significantly different among the groups [Table 3]. The mean follow-up time of the 264 patients was 45.36 ± 32.25 months, and twenty patients were lost during follow-up. The follow-up rates of ER, MR, and LR groups were 93.55%, 91.40%, and 92.68%, respectively, with no significant difference among the three groups. The overall 5-year survival rate was 82.8%. The Kaplan-Meier curves at 5 years showed no significant difference in survival rate among the three groups ([Figure 1], $\chi^2 = 0.668$, $P = 0.716$). Rates of freedom from all-cause death or rehospitalization for heart failure in ER, MR, and LR groups were 54.5%, 67.2%, and 62.3%, respectively, with no significant difference among the groups ([Figure 2], $\chi^2 = 0.878$, $P = 0.645$). Multivariate analyses showed that a severe preoperative condition rather than the time interval of CABG after MI was a risk factor of long-term survival [Table 4].

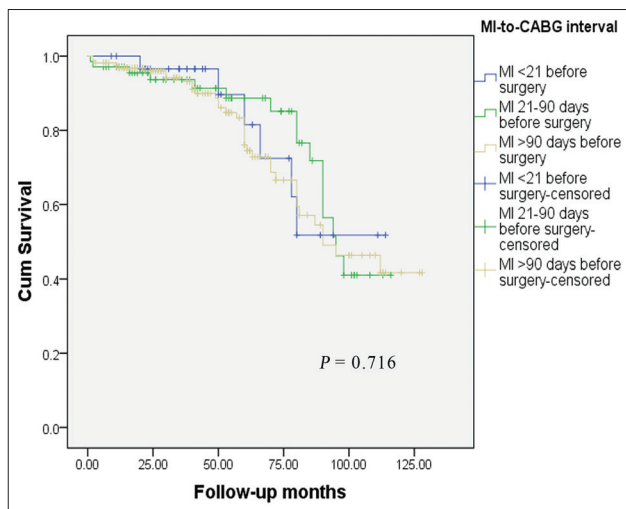


Figure 1: The Kaplan-Meier curves at 5 years showed no significant difference in survival rates among the three groups (82.2%, 82.5%, and 79.7%; $\chi^2 = 0.668$, $P = 0.716$).

DISCUSSION

In this cohort of patients with STEMI and LVD undergoing surgical revascularization, we found that time interval from STEMI to surgery was not associated with a significantly increased risk of operative and long-term mortality. Nonetheless, there was a trend toward higher incidence of postoperative low cardiac output syndrome when CABG was performed within 3 weeks after STEMI. On long-term follow-up of over 5 years, preoperative severe condition rather than time interval of CABG after STEMI had a significant influence on mortality.

Our study showed that the incidence of low cardiac output syndrome in the ER group (within 3 weeks) was significantly higher than that in the other two groups. However, the operative mortality rate showed no significant difference among the three groups. This result showed the importance of meticulous perioperative management, which significantly decreased hospital mortality caused by low cardiac output syndrome and led to an insignificant difference in hospital mortality among the three groups. With regard to the

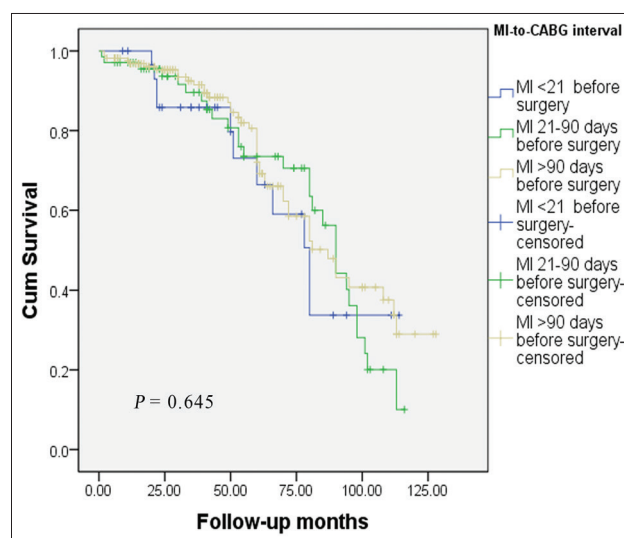


Figure 2: The Kaplan-Meier curves at 5 years showed no significant difference in freedom from all-cause death or readmission for heart failure among the three groups (54.5%, 67.2%, and 62.3%; $\chi^2 = 0.878$, $P = 0.645$).

Table 4: Risk factors for late mortality after CABG in the study population

Items	B	SE	Wald	df	Significant	Exp(B)	95% CI for Exp(B)	
							Lower	Upper
Preoperative severe condition	1.964	0.635	9.562	1	0.002	7.125	2.052	24.737
LVEF	-0.044	0.026	2.811	1	0.094	0.957	0.909	1.007
Emergent surgery	1.394	0.758	3.377	1	0.066	4.030	0.911	17.817
MI (days)								
<21			2.087	2	0.352			
21-90	0.621	0.654	0.901	1	0.343	1.860	0.516	6.704
>90	1.179	0.823	2.050	1	0.152	3.251	0.647	16.329

CABG: Coronary artery bypass grafting; MI: Myocardial infarction; SE: Standard deviation; CI: Confidence interval; LVEF: left ventricular ejection fraction.

long-term results, the present study showed no significant difference in long-term survival or freedom from all-cause death/rehospitalization for heart failure among the three groups. Moreover, cox regression multivariate analyses showed that a severe preoperative condition and emergent surgery (nearly reaching statistical significance) rather than the time interval of CABG after STEMI were risk factors of long-term survival. This finding is consistent with the findings of Ngaage *et al.* and Ladeira *et al.*^[17,18] These investigators prospectively analyzed 4090 patients who underwent CABG after MI and divided them into three groups based on the MI-to-CABG intervals of 0–30 days, 31–90 days, and >90 days. Their 5-year survival rates were 85.5%, 85.2%, and 89.3%, respectively, with no significant difference among the three groups. Their multivariate analysis also showed that the MI-to-CABG interval did not directly affect late mortality. However, comorbidities that were predominant in these groups of patients and the urgency of surgery were predictors of late death. The difference in the 5-year survival rate between our study and that of Ngaage *et al.* may be attributed to the proportion of patients with impaired LV function, which was 100% in our study and only 35% in their study.^[17]

Weiss *et al.* suggested that CABG should be deferred for 3–7 days after AMI in nonurgent cases to reduce perioperative mortality and complications.^[9] Another study by Assmann *et al.* also concluded that CABG performed <10 days after AMI was accompanied by significantly increased mortality.^[10] However, Caceres and Weiman found that only seven of 18 retrospective studies reported an independent association between early CABG and an increased mortality rate, while no independent association was identified in another 11 reports.^[11] Another finding of these investigations was that early surgical intervention was only associated with higher mortality in high-risk patients (age older than 65 years, ongoing ischemia before the operation, impaired LV function, and myocardial enzyme elevation). By contrast, there was no significant difference in mortality in low-risk patients at various times of surgical intervention. Therefore, the authors considered that the high mortality rate was related to the severity of the clinical conditions rather than the time interval before operation after AMI.^[22]

LVD is an adverse outcome secondary to STEMI and is one of the major predictors of mortality for surgical revascularization. A subgroup study of the HORIZONS-AMI trial^[23] reported that of 2648 patients with STEMI undergoing emergency PCI and evaluation of LV function, 23.3% had impaired LV function (LVEF \leq 50%). Of these, 8.27% were severely impaired (LVEF \leq 40%) and 14.94% were moderately impaired. This study showed that patients with severely impaired LV function who were treated by emergency PCI after STEMI had an increased rate of adverse outcomes compared to those with normal LV function. Assmann *et al.* and Ngaage *et al.* also reported that impaired LV function after MI was an independent predictor

of mortality after CABG.^[10,17] To date, there has been only one study, with a small sample, that analyzed the optimal timing of surgical intervention for patients with impaired LV function after STEMI. This study suggested that the operation be deferred, as far as possible, to 1 month after STEMI. In addition, regarding risk stratification in European and American risk score systems, less than a 3-month time interval after AMI was identified as a risk factor for CABG.^[24,25] Based on these findings, we divided the patients in our study into three groups according to the time interval of surgical intervention after STEMI: ER group (<3 weeks), MR group (3 weeks to 3 months), and LR group (>3 months).

There are several distinct differences between our study and previous studies. First, all of the patients in our study had a definitive diagnosis of STEMI whereas previous studies did not clearly distinguish STEMI from non-STEMI.^[26,27] Second, all of our patients had impaired LV function (LVEF \leq 50%) whereas most patients in previous studies had normal LV function.^[28,29] Third, short- and long-term outcomes of surgical revascularization, which was performed at different times, were observed in our study whereas only one long-term result was reported in a previous series.^[30,31]

Our study has some limitations inherent to single-center and retrospective studies, such as a small sample size, unmatched baseline characteristics, and sample inequality among groups. Thus, the insignificant difference of surgery mortality results between the three groups may also due to the small number of each group. Although a prospective, randomized, controlled trial of CABG is unlikely to be conducted in hemodynamically unstable patients, a retrospective, multicenter analysis of a large database is warranted to help draw reliable conclusions regarding the optimal timing of CABG after MI.

In conclusion, surgical revascularization for patients with STEMI and LVD can be performed at different times after STEMI with comparable operative mortality and long-term survival. However, early intervention (within 3 weeks after STEMI) has a high incidence of low cardiac output syndrome postoperatively. Thereafter, meticulous perioperative management is a prerequisite for implementation of early surgical revascularization. A severe preoperative condition rather than the time interval of CABG after STEMI is a risk factor of long-term survival.

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Conflicts of interest

There are no conflicts of interest.

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