Early and late prognostic implications of coronary artery bypass timing after myocardial infarction

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Abstract

OBJECTIVES: The optimal timing of coronary artery bypass grafting (CABG) after myocardial infarction (MI) is still controversial. With advances in perioperative care and myocardial protection, CABG is not infrequently undertaken sooner. Although CABG soon after MI is associated with high morbidity and mortality, the impact of CABG timing on late survival is not clear.

METHODS: We analysed prospectively collected data for 8320 patients who underwent primary CABG from 1996 through 2010. Operative outcomes and late survival were compared between patient categories based on MI-to-CABG days: groups A (0–30, n = 658), B (31–60, n = 734), C (>90, n = 2698) and D (no MI, n = 4230). The effect of the timing of surgery on survival was determined using multivariate and Kaplan–Meier analyses.

RESULTS: As the MI-to-CABG interval increased, the frequency of urgent/emergency operations decreased and hospital mortality (A, 3.5% vs B, 2.6% vs C, 1.2%, vs D, 1.1%, P < 0.0001) steadily declined. In general, patients who had CABG within 90 days of MI had more cardiac morbidity and co-morbidities. Expectedly, therefore, postoperative organ system dysfunction (cardiac, renal, respiratory and neurological) was more frequent in these groups. Reoperation for bleeding was similar for all groups, but blood product transfusion decreased as the MI-to-CABG days increased. The 10-year survival improved with the MI-to-CABG interval (A, 72.2% vs B, 73.4% vs C, 75.8% vs D, 81.4%, P < 0.0001). By multivariate analysis, the MI-to-CABG interval was not a risk factor for operative or late mortality. However, less frequent were left internal mammary artery use, non-elective surgery and high blood transfusion rates; all more often associated with shorter MI-to-CABG intervals.

CONCLUSIONS: Early and late mortality risk for CABG declines with increasing interval from MI for reasons indirectly linked to the timing of surgery. Our findings emphasize the importance of preoperative organ system optimization and consistent left internal mammary artery use, regardless of the proximity of surgery to MI or the exigency of surgery.

Keywords: Myocardial infarction • Coronary artery bypass grafting • Outcomes—mortality and morbidity

INTRODUCTION

Acute myocardial infarction (MI) treated medically is associated with increased risk of further adverse cardiac events [1, 2]. The precipitating coronary artery lesions and/or the consequent morphological changes may require early surgical intervention. Although, according to the European System for Cardiac Operative Risk Evaluation [EuroSCORE] [4], which is widely used for risk stratification of cardiac surgery patients, the safe interval between MI and CABG is 90 days, controversy still exists about the optimal timing of CABG after MI [5, 6]. In current practice, it is not often possible to wait for this period of time without putting patients at greater risk for further adverse cardiac events. As a result, risk scoring systems such as the Global Registry of Acute Coronary Events (GRACE) score [7] have been devised not only to quantify the risk of such patients but also to recommend early surgical revascularization when necessary. More so, advances in perioperative care and myocardial protection including off-pump CABG have provided the impetus for surgical revascularization to be undertaken sooner, within the high-risk 90-day interval after MI. Even though the operative outcomes of CABG performed in the peri-infarct period have been well described, the late prognostic implications are not known.

The objectives of this retrospective study were, therefore, (i) to compare the operative outcomes of patients who underwent CABG at different intervals up to and beyond 90 days after MI with a contemporaneous group who did not have MI, (ii) to determine the late survival rates of these groups of patients and (iii) to investigate the impact of the MI-to-CABG interval on early and long-term survival.
MATERIALS AND METHODS

Patients

Clinical data, prospectively collected and stored in an internally validated database, for patients undergoing cardiac surgery at our university teaching hospital were retrieved for all primary isolated CABG from April 1996 through December 2010. Those who had prior MI were identified, and on the basis of the MI-to-CABG interval, patients were divided into three groups: group A (for an interval of 0–30 days), group B (31–90 days) and group C (>90 days). Patients with no history of MI constituted the control group, D.

Survival data were obtained using the National Health System tracking service in January 2011 and were 99.8% complete.

Study endpoints

The primary outcome measures of interest were operative and long-term survival. Operative survival is defined as surviving hospitalization after surgery and up to 30 days. Major postoperative complications in the form of organ system dysfunction were considered the secondary endpoint.

Statistical analysis

Baseline clinical characteristics and outcome measures were compared between the groups.

Percentages are reported for categorical variables and compared between the groups using the chi-squared test, whereas the mean ± standard deviation or median and interquartile range are presented for continuous variables and compared between the groups using analysis of variance or Kruskal–Wallis test, as appropriate. In order to identify the predictors of operative mortality, the baseline variables in Table 1 and operative factors in Table 2 (operation details and blood product use) were inputted into a multifactorial stepwise backward logistic regression model. Long-term survival was determined using the Kaplan–Meier method and compared between the groups using the log-rank test. The determinants of late mortality were identified using the Cox proportional hazards model, inclusive of all the variables referred to the above. Statistical significance was set at two-tailed P-value less than 0.05. The Statistical Package for the Social Sciences (SPSS) version 20.0 for Windows (SPSS Inc. 2011, Chicago, IL, USA) was utilized for the analysis.

RESULTS

Baseline characteristics

Out of a total of 8320 patients, 658 (7.9%) had surgery within 30 days of an acute MI (group A), 734 (8.8%) between 31 and 90 days (group B), 2698 (32.4%) more than 90 days after an MI (group C) and 4230 (50.8%) had no prior MI (group D). There were vast differences in the baseline characteristics between the groups, as shown in Table 1. Patients in groups A and B were older with higher prevalence rates for cardiac morbidity such as triple vessel and left main coronary artery disease, left ventricular ejection fraction less than 0.30 and co-morbidities such as diabetes, impairment of renal function and chronic obstructive pulmonary disease.

As the distribution of severe symptoms indicates, the timing of surgery was not symptom-driven.

Operative and postoperative parameters

As expected, the majority of patients in groups A and B had their operation in urgent or emergency settings (Table 2). Cardiopulmonary bypass was used for most of the patients regardless of the interval between MI and CABG, with significantly longer times for group A patients but similar ischaemic times for all groups. In general, the use of left internal mammary artery was common for all the patients, but, by comparison, significantly less in group A patients. There was no difference in the mean numbers of diseased vessels, 2.8, 2.8, 2.7 and 2.7 for groups A, B, C and D, and the corresponding numbers of bypass grafts, 3.2, 3.3, 3.2 and 3.2, respectively. Although the median blood loss in first 24 h after surgery was less for groups A and B, the rates of blood product transfusion were higher for group A. There was no difference between the groups for reopening for bleeding and/or tamponade. Perioperative use of intra-aortic balloon pump counterpulsation and inotropes were more frequent among group A and B patients. Not surprisingly, group A patients, who had more co-morbidities, experienced higher rates of postoperative organ system dysfunction (Table 2).

The operative mortality decreased from group A to D as the interval between MI and surgical revascularization increased (Fig. 1). The predictors for operative mortality by multivariate analysis were age in years [odds ratio (OR) 1.07, 95% confidence interval (CI) 1.04–1.09, P < 0.0001], New York Heart Association functional class III/IV (OR 1.66, 95% CI 1.07–2.59, P = 0.02), left ventricular ejection fraction of 0.30–0.50 (OR 1.97, 95% CI 1.21–3.20, P = 0.006), left ventricular ejection fraction less than 0.30 (OR 3.57, 95% CI 1.78–7.14, P < 0.0001), emergent/salvage operative priority (OR 6.35, 95% CI 3.37–11.98, P = 0.004), cardiopulmonary bypass time in minutes (OR 1.01, 95% CI 1.00–1.01, P < 0.0001), transfusion of packed red blood cells (OR 3.09, 95% CI 1.90–5.03, P < 0.0001) and platelets (OR 2.54, 95% CI 1.42–4.54, P = 0.002). The use of left internal mammary artery graft reduced the risk of operative mortality by more than half (OR 0.39, 95% CI 0.20–0.79, P = 0.009). The MI-to-CABG interval did not exhibit any direct influence on operative mortality: 0–30 days (OR 1.04, 95% CI 0.52–2.10, P = 0.91), 31–90 days (OR 1.66, 95% CI 0.85–3.23, P = 0.14) and >90 days (OR 0.82, 95% CI 0.48–1.38, P = 0.45).

Late survival

The Kaplan–Meier survival rates at 5 (group A 85.5%, group B 85.2%, group C 89.3% and group D 92.1%) and 10 years (group A 72.1%, group B 73.4%, group C 75.8% and group D 81.4%) were substantially lower for the groups of patients who had surgery within 90 days of MI (P < 0.0001), as shown in Fig. 2. However, multivariate analysis revealed that the MI-to-CABG interval did not directly influence late mortality, but co-morbidities predominant in these groups of patients and the exigency of surgery were the predictors of late death (Table 3). The use of left internal mammary artery graft reduced the probability of late death for all patients.
DISCUSSION

CABG soon after acute MI is associated with high operative mortality and morbidity. The present study shows that factors related, but not directly linked, to the duration of the intervening period between MI and surgery contribute to this risk. Technical operative difficulties encountered during CABG soon after MI usually due to oedema, induration and fragility of myocardial...
tissue may partly explain this finding. In this setting, cardiac trauma with abrasive injury can occur even with gentle handling, and visualization of target vessel and arteriotomy can be challenging, making precision of coronary anastomoses even more demanding. There is also the risk of reperfusion injury after successful revascularization of territories related to the infarct area [8].

Also, a short MI-to-CABG interval constrains the ability to optimally correct deranged physiological parameters, control cardiac morbidities, manage co-morbidities and alter preoperative medications appropriately. Although some of the predictive factors of operative mortality are modifiable by preoperative interventions, intraoperative strategies and/or postoperative measures, these are not often achieved before non-elective surgery is performed. For example, not discontinuing multiple anti-platelet therapy, as is often the case when CABG is performed soon after MI, has been shown to increase the postoperative morbidity and mortality [9–11]. Our study clearly shows that operative mortality declines with delaying the timing of CABG after MI. In a large retrospective study, Parikh et al. [6] examined the influence of CABG timing after non-ST elevation MI on operative outcomes in 2647 patients from the ACTION registry—GWTG (Acute Coronary Treatment and Intervention Outcomes Network Registry—Get With The Guidelines) database. Using a 48 h time cut-off, they classified the timing of CABG as early (≤48 h, n = 825, 31.2%) or late (>48 h, n = 1822, 68.8%) and found no significant survival differences between the groups after controlling for significant differences in baseline characteristics. On the contrary, other workers [12, 13] have also demonstrated an early survival advantage when CABG is appropriately timed as far away from MI as it is possible. Weiss et al. [13] reported an average operative mortality of 4.7% for CABG performed within 28 days of MI: a nadir of 3.0% was observed on days 3–5 and, interestingly, a peak of 12.5% occurred between 14 and 28 days after MI. That study which examined 9476 patients from the California registry did not have a control group without prior MI to compare their results with. The findings of that study, which compares with our operative mortality of 3.5% for patients who had CABG within 30 days of MI, suggest that the operative risk within the 30-day time frame is still higher than for patients operated later and/or those without prior MI.

The interval between MI and CABG has an indirect bearing on late mortality as well. This is a notable finding not reported previously. The early survival benefit of longer MI-to-CABG intervals was sustained into the long term in our study patients. A possible contributory factor is the significantly higher rate of internal mammary artery use in patients with longer MI-to-CABG intervals. Perhaps, also, the technical difficulties encountered in patients with short MI-to-CABG intervals and reperfusion injury may result in a suboptimal revascularization with adverse long-term consequences. Despite the fact that the MI-to-CABG interval per se did not influence late survival, other factors more frequent in patients with shorter intervals between MI and CABG,
such as urgent and emergency operation, preoperative organ dysfunction (cardiac, renal and pulmonary) and blood transfusion, exhibited adverse effects on long-term survival.

The ideal duration of the wait after an MI before CABG is undertaken remains controversial. Although short MI-to-CABG intervals are associated with poor early and late operative outcomes, it has to be emphasized that long intervals place post-infarct patients at risk of further adverse cardiac events, which could be fatal. The timing of surgery should consider a balance between the risks and the benefits and focus on multi-organ optimization of the patient, developing a well thought-out intra-operative strategy, the insistent use of the internal mammary artery and the conduct of surgery under elective conditions.

### Study limitations

The study design lends itself to the inherent limitations of a retrospective study. We have not made a distinction between non-ST elevation and ST elevation MI in this large retrospective study because the difference was not indicated in the database. However, while population-based studies [14] have reported a declining frequency of ST elevation MI, clinical management trials [15] have shown similarities in the prognostic of both types of MI. Perhaps, the level of troponin rise may be more relevant for future studies. Also, the infarcted territories were not specified. Whether this has an independent prognostic impact, separate from the influence of the resultant impairment of left ventricular function, is uncertain.

The study findings and the clinical implications should be appreciated in the context of the fairly long MI-to-CABG intervals used in this study, which have been widely and repeatedly validated in the EuroSCORE.

### Conclusion

Our study suggests that prognostic implications may have indirect associations with the timing of CABG after an MI. We found that patients who had CABG after short intervals from an MI experienced inferior early and late survivals for several reasons indirectly linked to the duration of the intervening period. It is worthy of note that the use of left internal mammary artery graft, which had both early and late survival benefits was less frequent in patients who had surgery after short MI-to-CABG intervals, while organ system dysfunction and blood transfusion were more common for short MI-to-CABG intervals which negatively impacted survival. As patients undergoing CABG after short intervals from MI often have more cardiac morbidities and co-morbidities, our findings support due diligence in preoperative multi-organ optimization and a consistent use of the left internal mammary artery whenever possible, regardless of the proximity of surgery to MI or the exigency of surgery.

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### Conflict of interest

none declared.

### REFERENCES


