Influence of time elapsed between myocardial infarction and coronary artery bypass grafting surgery on operative mortality

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Abstract

Objective: Optimal timing for CABG surgery after myocardial infarction (MI) remains controversial. We examined the influence of patient age and time elapsed between MI and isolated CABG surgery on operative mortality.

Methods: Perioperative data of 13,545 patients who underwent isolated CABG surgery from 1991 to 2005 were reviewed. A previous MI was found in 7219 patients, classified among groups A—E whether they underwent surgery less than 6 h (A, n = 26), between 6 and 24 h (B, n = 51), between 1 and 7 days (C, n = 313), between 8 and 30 days (D, n = 917), or more than 30 days (E, n = 5912) after the event. Crude percentages and odds ratio estimates of operative mortality were calculated.

Results: In patients who had no history of MI, the mortality rate was 1.7%, while it was, respectively, 19.2, 9.8, 8.6, 3.2, and 2.4% in patients from groups A to E. Among 6589 patients over 65 years of age, 3027 had no history of MI. Their mortality was 2.4%, compared to, respectively, 35.7, 13.8, 11.3, 5.1, and 3.9% for those belonging to groups A—E. Overall odds ratio estimates of operative mortality were 3.92 (p = 0.19), 5.08 (p = 0.002), 4.33 (p = 0.0001), 1.50 (p = 0.08), and 1.18 (p = 0.24) for groups A—E, respectively.

Conclusions: Operative mortality is not influenced by a history of MI sustained more than 30 days prior to isolated CABG surgery, but is highly and most significantly increased between 6 h and 1 week after MI, especially in older patients. That critical period should be avoided whenever possible.

Keywords: Myocardial infarction; Coronary artery bypass grafting; Interval; Mortality

1. Introduction

With the findings of a recently published meta-analysis [1] including 23 randomized trials comparing primary coronary interventions (PCI) with thrombolysis that showed absolute reductions of 2% in mortality, 4% in non-fatal infarctions and 1% in strokes, cardiologists are sending more and more patients to the catheterization facility in the context of acute myocardial infarction (MI). This approach in turn identifies an increasing number of patients in the peri-infarction period who are candidates for surgical revascularization when PCI is not technically feasible or fails, or when the extent of their coronary artery disease (multivessel and/or left main disease, residual critical stenoses) warrants a surgical procedure. Coronary artery bypass grafting (CABG) surgery following MI has been associated with conflicting levels of risk, with mortality ranging between 5 and 30% historically [2]. Advocates of aggressive early surgical approaches [3,4] and proponents of safety waiting periods varying between 3 and 7 days before the intervention in such settings [5,6] have supported their suggested strategy with convincing data. Considering the increasing percentage of elderly patients in our surgical clientele and the impact of more frequent PCI for MI, we examined the influence of patient age and time elapsed between MI and CABG surgery on operative mortality in the contemporary experience of a high-volume single institution.

2. Materials and methods

2.1. Patients

Perioperative data of 13,545 consecutive patients undergoing first-operation isolated CABG surgery at Laval hospital between 1991 and 2005 were reviewed. All information regarding patients’ demographic data, medical history, operative procedures, and outcome was gathered prospectively in a data bank and analyzed retrospectively. The diagnosis of MI was based on clinical criteria including electrocardiographic evidence and characteristic elevation of serum myocardial enzymes, and no distinction was made...
between the transmural and subendocardial extent of the lesions. Perioperative mortality was defined as in-hospital death or death after discharge but prior to 30 days after surgery.

A previous MI was found in 7219 patients, classified among groups A–E whether they underwent surgery less than 6 h (group A, n = 26), between 6 and 24 h (group B, n = 51), between 1 and 7 days (group C, n = 313), between 8 and 30 days (group D, n = 917), or more than 30 days (group E, n = 5912) after the event. Among these 7219 patients, 3567 were less than 65 years of age while 3652 were older than 65 years. These patients were, respectively, classified in a similar manner, as follows: patients <65 years: group A, n = 12; group B, n = 22; group C, n = 145; group D, n = 424; and group E, n = 3054. Patients ≥65 years: group A, n = 14; group B, n = 29; group C, n = 168; group D, n = 493; and group E, n = 2858. Groups of patients with no history of MI were used as controls (all ages, n = 6326; patients <65 years, n = 3299; patients ≥65 years, n = 3027).

2.2. Data analysis

Data were expressed using mean ± standard deviation for continuous variable or as percentage for categorical data. Univariate comparisons between continuous variables were made with the Student’s t-test, while the Fisher exact test and chi-square test were used for discrete data. Variables with a P-value of less than 0.25 were entered into a stepwise logistic regression model for multivariate analysis. Significance was assumed if P-value was <0.05 and odds ratios are presented with 95% confidence intervals. Data were analyzed using the statistical package program SAS v8.2 (SAS Institute Inc., Cary, NC, USA).

3. Results

A total of 13,545 patients underwent first-operation isolated coronary artery bypass grafting surgery at our institution during the study period. Overall operative mortality was 2.3% (318 patients). Among 7219 patients with a history of prior MI, perioperative mortality was 2.9% (210 patients), compared with 1.7% (108 patients) from the remaining 6326 patients (P < 0.001).

Results of multivariate analysis of risk factors of perioperative mortality in patients with a history of MI are shown in Table 1. Apart from classical risk factors appearing in the upper third of the table, further descriptions of the effects of age as well as time elapsed between MI and surgery are presented. As shown in Fig. 1, perioperative mortality was, respectively, 19.2% (5/26), 9.8% (5/51), 8.6% (27/313), 3.2% (29/917), and 2.4% (144/5912) for patients from groups A to E. Significant differences compared to the control group of patients with no history of MI were found in all groups except group E, where surgery was performed more than 30 days after the event, and group A where clinically important odds ratio of 3.92 did not reach statistical significance because of a limited number of patients.

Analysis of patients’ age at the time of surgery reveals a different pattern of influence of the time elapsed between MI and surgery on perioperative mortality, which is significantly increased in patients over 65 years. In fact, a little more than half of the patients of the cohort were under 65 years of age (6956 patients), while 6589 patients were 65 years or older. In the latter group of patients, overall operative mortality was 3.6% (237/6589), significantly higher in patients who had suffered a prior MI (4.6%; 165/3652) than those who had not (2.4%; 72/3027, P < 0.001). Contrastingly, in the former group or younger patients, overall mortality was 1.2% (81/6956) and was not affected by a history of prior MI (perioperative mortality 1.2% (45/3652) vs 1.1% (36/3299) in patients with no MI history). The results of multivariate analysis of risk factors of perioperative mortality for those subgroups of patients are displayed in Table 2. Significant risk factors in patients of 65 years or more included a previous stroke, renal failure, peripheral vascular disease, and advanced CCS angina class (Table 2A). In that group, perioperative mortality decreased as time elapsed between MI and surgery increased, as further illustrated in Fig. 2.
In patients under 65 years of age (Table 2B), risk factors of perioperative mortality after a MI were a left ventricular ejection fraction lower than 40%, chronic pulmonary obstructive disease and renal failure. The only time frame after MI where operative mortality was significantly increased in that group was between 1 and 7 days (Fig. 3).

4. Discussion

Optimal timing for surgical revascularization after MI remains a matter of debate. Conflicting results with operative mortality ranging from 5 to 30% have been reported [2,7—9]. Theoretical advantages or early intervention include limitation of both infarct expansion and adverse ventricular remodeling [2,10], as well as avoidance of an unnecessary waiting period. During delay for CABG following MI, cardiac events are frequent and tend to occur early, and the associated morbidity and mortality are related to left ventricular dysfunction, heart failure, and time [11]. On the other hand, ischemia—reperfusion injury leading to hemorrhagic infarction and additional myocardial damage constitute possible complications of early surgery [12], as well as exacerbation of the acute systemic inflammatory response [5]. The goal is thus to determine the best window for intervention at a time safe from infarct extension and prior to remodeling, in order to limit myocardial damage while maintaining structural integrity [3,13]. This is especially true in the era of rapid catheterization for ongoing acute MI with the identification of an increasing number of surgical candidates diagnosed in that clinical setting [14]. Newer techniques such as off-pump CABG and better myocardial protection strategies (ante/retrograde perfusion, blood cardioplegia) with intensified hemodynamic support [15,16] as well as improved comprehensive use of intra-aortic balloon pumps [17] have contributed to widen our arsenal for facing early revascularization complications. Other groups have addressed the issue of optimal timing for intervention, but many studies were conducted at a time where surgical techniques did not benefit from the actual developments or were flawed by small number of patients [6,18,19], while others were multicenter-based and prone to bias from heterogeneity in surgical practices.

Results from our contemporary series of patients from a single high-volume institution corroborate previously reported increased overall perioperative mortality for surgical revascularization in the early phase following MI. In contrast with findings from a recent multicenter retrospective study using a large database [5] suggesting that surgical revascularization is safe as early as 3 days after MI, perioperative mortality in our cohort was still significantly increased in the group undergoing surgery between 8 and 30 days following the event and only returned to a level comparable to that of the no-MI control group after that period. However, the risk ratio of 1.5 for mortality in patients operated on during this 8—30 days interval, found in the multivariate analysis, did not reach statistical significance.
The usual risk factors for increased mortality were identified and are presented in Table 1.

Analysis of the effect of patients’ age revealed an increasing mortality risk as patients got older, but patients less than 65 years of age had no statistically significant increase of overall perioperative mortality after MI compared to their control group without a history of prior MI. When a separate analysis of patients below and over 65 years was performed, an increase in perioperative mortality in the former group could be found only after a waiting period comprised between 1 and 7 days. Because of the small number of patients undergoing surgical revascularization less than 24 h after MI in that group, the clinically relevant increased risk ratio of 2.14 in that period did not reach statistical significance. Contrastingly, perioperative mortality in the older group was increased at all time points following MI, and the risk was particularly increased in the earlier phases up to 7 days post-MI. Perioperative mortality in that group was also still significantly increased even after a 30-day waiting period when compared to that of patients with no prior MI. However, it was not significantly different than the perioperative mortality observed in the subgroup of patients who underwent surgery between 8 and 30 days after MI, suggesting that there is no added benefit of extending the waiting period beyond 7 days in patients over 65 years of age. As suggested by others [20,21], early revascularization could thus probably be safely performed in selected patients with the potential benefit of avoiding unnecessary delays and their associated complications.

This study bears important limitations. No difference was made between transmural and non-transmural MIs, while there is evidence that the latter are associated with a better prognosis and different response patterns with respect to timing of operation [22]. Details about the urgency of interventions, mostly those performed in the earlier phases, were not accounted for. This has a significant clinical impact since patients who were directed to such an early procedure were more prone to be unstable and have a poorer prognosis, but at the same time represent a population where a conservative approach is not conceivable. However, it is difficult to derive any statistically significant information when these very few patients are excluded.

Despite these limitations, our study underlines the importance of global risk assessment integrating multiple individual factors with the timing of intervention in order to determine the optimal treatment strategy for specific subgroups of patients. Especially over the last 10 years, the surgical literature reports important efforts to circumcribe with more and more precision the safety window for surgical intervention in the context of acute MI. Earlier studies have also identified potential subgroups of patients with better outcome after early revascularization following MI, such as younger [23] male [24] patients, in the absence of the left main involvement [24], with preserved left ventricular function or having suffered a subendocardial instead of transmural MI [18,25]. The results of our study may bring more questions than answers in this regard and illustrate quite clearly that an important inter-individual variability is present. Probably more than the recency of MI, the co-morbidities and the clinical status of the patients (hemodynamic stability, ongoing ischemia with residual angina) constitute significant determinants of perioperative mortality. This emphasizes the importance of a tailored approach for each subgroup of patients and even each patient individually, as well as the need for additional large, contemporary, and randomized studies to further characterize the risk factors for operative mortality after recent MI. This is especially true in the evolving era of rapid catheterization for patients suffering MI, where unwarranted delays in the surgical treatment of lower risk patients need to be avoided.

References

Appendix A. Conference discussion

Dr K. Higuchi (Chiba, Japan): I agree with your opinion. I had better to avoid the operation during a first week after AMI. But if we have patients with left main stenosis and they’re hemodynamically unstable, what can I do? When I have to wait for one week in our institute, I put an IABP and then operate. So what do you think?

Dr Voisine: I think it’s a very good strategy. There are different approaches to this problem reported in the literature. Some people are very aggressive in performing very early revascularization and support their strategy with very good results. Others, as you mentioned, favor medical stabilization of the patient, trying to postpone the surgery to a later period, deemed safer.

It’s difficult to tell anything from this study of our patients because there was a very small number of patients who were operated in the very early period, between 0 and 24 h. It is thus hard to take out the patients who were unstable hemodynamically and who were at an immediate risk for their life without surgery. Whatever the bias they introduce into the analysis, their exclusion from the statistical analysis results in a number of patients too small to allow any significant conclusion to be drawn.

The take-home message of our study is that there will be more and more patients that will be directed towards surgery because cardiologists found earlier that they have an anatomy that warrants a surgical procedure early on in the course of their myocardial infarct, because they send them earlier to the cath lab.

What we realize is that a better categorization of the patients with an appropriate break down of the risk factors, such as age in this instance, the influence of the recency of the MI may not be significant in terms of mortality for all subgroups. So I think that we have to rethink our strategies for treating these patients. Although it’s probably very secure to stabilize the patients and wait before performing the surgery, in very low-risk patients the delay itself in treatment, which is also associated with risk, may not be warranted.

Dr R. Schistek (Salzburg, Austria): What do you think is the reason that the patients that are operated early on die? Is it a coagulation problem or is it due to the damaged myocardium?

Dr Voisine: There are many possibilities. It could be the very systemic inflammatory state in which the patients are. It could be ischemia/reperfusion. It could be the instability of the myocardium and its incapacity to recuperate in this acute setting. It’s hard to tell.

But at the time we presented the abstract, we had data from 1991 to 2003. And since then we have added patients from the last 2 years, which have been presented here. When I looked at the differences between these two groups of patients, it became obvious that there was a very significant decrease in mortality over the last years. So now the next thing we are going to do is break down this group of patients into the last 7 or 8 years and compare them to the 7 or 8 years before.

There was actually, I think, 35 patients operated on within the first 24 h after the infarct in the last 2 years and there was no perioperative death in that group. I believe that with the improving surgical techniques and myocardial protection strategies, we can achieve good results even in the earlier phases.