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Original article

Optimal coronary artery bypass graft timing in high-risk acute myocardial infarction with ST elevation

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Abstract: *Background* — Despite advances in surgical techniques, still tendency for waiting up to 6 weeks after myocardial infarction with ST segment elevation (STEMI). We aimed to evaluate optimal timing for coronary artery bypass graft (CABG) in stable patients with STEMI.
Material and Methods — Prospective, randomised study consisted of 30 patients with STEMI (age 57-78 years, 22 male) underwent on-pump CABG. According to the timing of CABG they were stratified as urgent (0-2 day) and late group (3 day and after). Transthoracic echocardiography and selective coronarography were done before surgery. Patients with ejection ftaction (EF) >50%, left main stenosis and/or multivessel coronary disease were included in the study. We excluded patients with mechanical complications, reduced EF, cerebrrovacular insult (CVI), renal failure or respiratory insufficiency.
Results — The primary endpoint for 30 days were adverse cardiac events (death, recurrent angina, prolonged mechanical ventilation/IABP insertion CVI, acute kidney injury, major bleeding). Eight (26.6%) patients underwent urgent CABG in first 48 h. due to haemodynamic instability/ongoing ischemia Three (37.5%) of them died and 6 (75%) had prolonged mechanical ventilation support and/or IABP. Twenty two (73.3%) patients in late group were operated after period of stabilization (10–14 day). They were discharged on 6-7 postoperative day.
Conclusion — Early surgery may be risky, but its delay also carries the risk of devastating complications. Stable patients operated on 10-14 day had similar outcomes as elective cases.

Keywords: acute myocardial infarction with ST elevation, coronary artery bypass graft, intraaortic balloon pump, mechanical ventilation

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Introduction

The myocardial infarction (MI) is the leading cause for death in industrial as well as in the developing countries. Contemporary non-surgical procedures, fibrinolytic therapy and primary percutaneous coronary intervention (PCI) in patients with acute myocardial infarction with ST segment elevation (STEMI), significantly reduce morbidity and mortality. Early surgical revascularization, coronary artery bypass graft (CABG), is reserved for left main and/or 3 vessel coronary disease, ongoing ischemia after successful or not PCI, coronary anatomy not adequate for PCI and mechanical complications of STEMI [1].

There was a trend in the early 70-ties for an urgent CABG in the patients with acute MI. But, retrospective studies showed an enormous mortality rate in comparison to elective surgery. The end of the 80-ties hypothesized the risk of hemorrhagic transformation from reperfusion and infarct extension, altered recovery and scar formation. Soon after, was introduced the practice to operate patients after 6 weeks of MI with Q wave. But after all these years, the optimal timing of CABG in hemodynamically stable STEMI patients remains controversial. There is a lack of prospective randomized study which compares the results of early versus late CABG in patients after MI [2].

Patients with hemodynamically stable STEMI, with indication for CABG, have a certain risk of serious complications, early and late, such as malignant arrhythmias, cardiogenic shock, pericarditis, embolism, mechanical complications (early), congestive heart failure, post MI syndrome or left ventricular aneurysm (late) [3].

Thus, if waiting too long for surgery carry the risk of complications, we hypothesize that shorten period of 4-6 weeks could be considered as an adequate. We aimed to evaluate optimal timing for bypass surgery in patients with STEMI.

Material and Methods

The study was prospective, randomised, open-labeled, consisted of 30 patients with STEMI. They presented with severe precordial pain, time onset more than 3 hours, and high myocardial enzyme activity (high sensitive cardiac troponin T, creatine kinase-MB). All patients underwent transthoracic echocardiography and selective coronarography. Inclusion criteria

were preserved systolic function (ejection ftaction >50%), left main stenosis and/or multivessel coronary disease. Mechanical complications, reduced ejection ftaction (EF) <50%, stroke, renal failure or respiratory insufficiency, were exclusion criteria.

The patients were prepared according to preoperative protocol and were stratified by the timing of CABG to urgent (0-2 day) and late group (day 3 and after).

On-pump CABG was performed under general anesthesia with endotracheal intubation, with standard surgical approach-median sternotomy. Left internal mammary artery (LIMA) was used to bypass the left anterior descending (LAD), right internal mammary artery (RIMA) to graft the left circumflex (LCx)/right coronary artery (RCA) and reversed saphenous vein grafts (SVGs) in case of multivessel coronary artery disease (CAD). Transesophageal echocardiography (TEE) was used during the surgery.

The primary endpoint at day 30 were death, chest pain, the dynamic of cardiac enzymes (cardiac troponin T, creatine kinase-MB), need of inotropic support, prolongs mechanical respiratory support, intra-aortic balloon pump (IABP) insertion, major bleeding, length of stay in intensive care unit (ICU) and overall hospitalization period as well as major bleeding, reinfarction, stroke and acute kidney Statistics

The statistical analyses were performed by using the commercial statistical package, Statistica for Windows, Version 6.0. Continuous parameters were expressed as mean with standard deviation (M+SD). The Mann–Whitney U-test was used to test the distribution for two independent variables and Wilcoxon Matched Pairs Test for two dependent samples. A $p<0.05$ was considered to indicate significance.

Results

During the period of one year, 30 patients underwent on-pump CABG within 2 weeks of acute STEMI. They were at the age between 57 and 78 years, and 22 (73.3%) of them were male gender. Four patients (13.3%) got 2 bypasses, 25 (83.3%) got 3 bypasses and 1 patient (3.3%) got 4 bypass grafts. Demographic and clinical characteristics are given in *Table* 1.

In the urgent CABG group, 8 (26.6%) patients with persistent angina were operated in the first 48 h. One (12.5%) of them, due to hemodynamic instability (oxygen saturation (SaO_2) <98%, systolic blood pressure (SBP) <90 mmHg, mean arterial pressure (MAP) <60 mmHg) underwent CABG during the first night. The other 7 patients (87.5%) underwent open heart surgery on second day of admission.

Of the 8 patients operated in the first 48 hours, 3 died (37.5%) in the first and third day after the operation. One of them (female gender) was at the age of 78, with hemodynamic instability and cardiac arrest. The second, was 67 years old male, presented with hemodynamic instability first day after the CABG due to reinfarction, and acute abdomen second day after the surgery. The reason for acute abdomen was stress ulcer. He was underwent laparatomy to suture the ulcer and he died immediately after surgery.

The third patient was 71 year old female. First day after the surgery she become hemodynamically unstable (low blood pressure, low ejection fraction, high central venous pressure), and insertion of IABP was done. She died third day after surgery, due to low cardiac output.

Table 1. Demographic and clinical characteristics of the study patients

Parameters	*Urgent CABG group (n=8)*	*Late CABG group (n=22)*	*p*
Age, years, M±SD	71±4.5	71±4.2	NS
Male gender, no. (%)	6 (75%)	16 (73%)	NS
Hyperlipidemia, no. (%)	7 (87.5%)	13 (59%)	NS
Hypertension, no. (%)	6 (75%)	14 (63.6%)	NS
Diabetes, no. (%)	5 (62.5%)	13 (59%)	NS
Smoke, no. (%)	3 (25%)	8 (36.3%)	NS

Wilcoxon Matched Pairs Test did not shown statistically significant difference between groups. That means that both groups were homogeneous in terms of demographic and clinical parameters.

Table 2. The level of cardiac biomarkers troponin T and creatine kinase-MB (CK-MB) at 6 hours after the onset of STEMI

Parameters	*Urgent CABG group (n=8)*		*Late CABG group (n=22)*	
	M±SD	*Min – Max*	*M±SD*	*Min – Max*
Troponin T, ng/ml	11.0±7.1	0.7 – 20.0	3.1±2.7	0.5 – 8.0
CK-MB, IU/L	616±275	410 – 1200	595±151	410 – 950

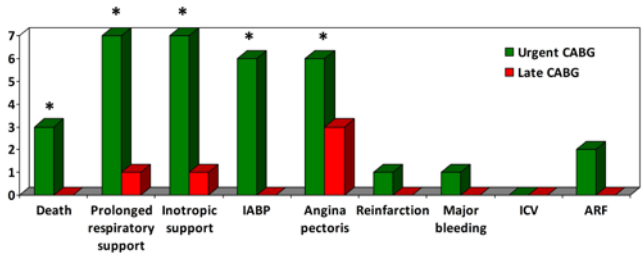

Figure 1. Adverse cardiac events.
Adverse cardiac events were dominant in urgent CABG group and Wilcoxon matched pairs test showed statically significant ($p<0.05$) differences between the groups (signed as *).
IABP, intra-aortic balloon pump; ICV, ischemic cardiovascular event; ARF, acute renal failure.

Two of the other 5 patients in urgent group had prolonged ICU stay to 10 and 15 days due to prolonged stay on the respiratory machine. The tracheotomies were performed and they were extubated after 1-2 weeks. The length of hospitalization was prolonged up to 20-27 days. No major complications were noted.

In the late CABG group, 22 (73.3%) patients were operated between 10 and 14 days after the onset of MI, stabilization and decrease in cardiac enzymes. There was no mortality or major intraoperative event. The patients were extubated without inotropic support. They left the hospital in good local and general condition, with normal laboratory findings, chest X rays and echocardiography, between 6 and 7 days after the surgery. Adverse cardiac events are shown in the *Figure* 1.

Regarding the enzyme activity, it was very high in all patients. The value of high sensitive cTnT reaching a peak of 20 ng/ml at 6 hours after the onset of MI. The level of creatine kinase-MB was also high (1,200 IU/L). In the urgent CABG group, there was continuous high level the myocardial biomarkers. In the late CABG group, we noted stabilization of their activity.

The level of cardiac biomarkers at 6 hours after the onset of STEMI is shown in *Table* 2.

The difference between the maximum activity of cardiac troponin T tested with Mann-Whitney U test showed statistical significance between two groups (U=145, p=0.007), but the

difference regarding creatine kinase-MB was not significant (U=71, p= 0.400).

Discussion

Advances in surgical techniques and strategy for pre and postoperative management, did not resoved the dilemma about optimal timing for CABG in stable patients with STEMI. The hypothesis that the early reperfusion results in hemorrhagic transformation, which ends with infarct extension, delayed healing and scar formation is the reason for delaying the CABG in STEMI patients. Current 2013 ACC/AHA guidelines for the management of patients with ST-elevation myocardial infarction clearly defined Class I recommendation for urgent CABG in patients with STEMI and coronary anatomy not amenable to PCI who have ongoing/recurrent ischemia, cardiogenic shock, congestive heart falure or other high-risk features. They have given Class II recommenaton for emergency CABG within 6 hours of symptom onset may be considered in patients with STEMI who do not have cardiogenic shock and are not candidates for PCI or fibrinolytic therapy [4].

Also, there is a large discrepancy among studies, between early surgery post-MI, some as early as 6 hours and others up to eight days.

In our study, we tried to evaluate timing of surgery after acute MI and postoperative adverse cardiac events. We had patients underwent CABG in first 48 hours and patients operated between 10 and 14 day.

Among the patients in the early group, 2 were hemodynamic instable, and the others had persistent precordial pain despite the conservative therapy. The remaining 22 patients were stable, the cardiac biomarkers were decreased, and we operated them between the 10 and 14 day.

Several retrospective studies about the indication and optimal timing for operation in stable post MI patients, mostly suggest that early reperfusion may lead to increased mortality, and also report benefit from delayed surgical treatment in stable post MI patients [5].

The most recent guidelines 2014 ESC/EACTS Guidelines on myocardial revascularization: state that in patients who have had an ST-segment elevation MI (STEMI), CABG mortality is elevated for the first three to seven days after infarction, and the benefit of revascularization must be balanced against this increased risk [6].

Comparing the adverse cardiac events between early and late group, we had 3 (37.5%) lethal events in early group and none in late group. Our study is comparative to the other studies. Braxton et al. have 50% mortality in the early group (in first 48 hours) followed with 11,6% intrahospital mortality, and almost the same score with the elective surgery in Deeik study (between 5 and 7 day) [7, 8].

We did not have a patient with major bleeding and renal dysfunction prior surgery, while 2 of our patients after surgery had renal impairment which worsened the prognosis. One of them ended lethally, and the second one, had a prolonged stay on the respiratory machine. We did few dialyses while in ICU resulting in renal function improvement. While having relatively selected group, we would conclude that the time of surgery, age and female gender was the leading cause of death. The complications and delayed recovery were also in relation to the time of surgery.

These results arises the question how long we may postpone the surgery, knowing that poor perfused myocardium is at risk of remodeling and new MI?

2014 ESC/EACTS Guidelines on myocardial revascularization state that in patients with STEMI suggests that in patients with reduced left ventricular systolic function CABG should be performd within 6 weeks, to allow myocardial recovery to occur. The data suggest poor quality of life in patients waiting long time for surgery, and in addition, higher costs for hospitalization. Also, other factors that influence early mortality are unstable angina, previous surgery (CABG), preoperative hypertension, non-elective surgery, previous cardiac arrest and female gender. Zaroff et al. in his study [9] with defined model of risk prediction stated that the mortality in patients with STEMI operated urgently is still higher than in elective (5.5%). Fifty-five percent of the patients have mortality between 4-13%, compared with elective, with 1 to 3% mortality rate. Despite female gender, the most important risk factor is age (75 years) and anamnesis of previous MI.

The most important process in these patients is LV remodeling after MI. It is a result of changed ventricular geometry and function because of MI. It is a compensatory mechanism aimed to increase the stroke volume in conditions where the ejection fraction is reduced. This leads to left ventricle dilatation and heart failure, a state that directly depends on the infarct size and the left ventricular wall stress. Factors, such as thrombolysis, angiotensin-converting-enzyme (ACE) inhibitors, angioplasty and CABG, may influence the remodeling. Theoretically, these patients have great benefit from the early revascularization while there is not irreversible necrosis and left ventricular dysfunction.

From the other side, the time of transformation from hibernation to irreversible dysfunction is not known. We would say that there is no way to predict the transformation and to operate in the moment when it is still not late. Delaying the surgery would be helpful to estimate the optimal timing for operation from one side, but we have to estimate the safety of waiting as well. There is data that conclude severe preoperative and postoperative complications while waiting longer, such as mortality. But also, the incidence of perioperative MI, permanent cerebrovascular events and atrial fibrillation are most frequent between the patients that are surgically revascularized right after the MI [10].

The same authors refer to quality of life after the revascularization in patients operated within 3 months and after 3 months of MI. The last, have significant reduction in physical activity, vitality, social function and the health in general. Also, the expenses for the hospitalization are greater.

Conclusion

We may conclude that patients with STEMI with clear indication for surgery should not wait too long, but if there is a possibility to wait at least 10 days after MI, and the CABG is in the first 2 weeks, the result could be the same as in elective patients.

Conflict of interest

The authors declared that they have no conflict of interest.

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