

# Does early coronary artery bypass surgery improve survival in non-ST acute myocardial infarction?

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## Abstract

A best evidence topic was written according to a structured protocol. Lack of evidence exists regarding the optimal timing for coronary artery bypass graft (CABG) surgery after non-ST myocardial infarction (NSTEMI). While some authors address the importance of the timing of surgery alone, others take into account the extent of myocardial damage. The question addressed was whether early or late CABG surgery improves hospital mortality and cardiovascular events after NSTEMI in stable patients. Using a designated search strategy, 459 articles were found, of which seven represented the best available evidence. All of these studies were level 3 (retrospective cohort studies). Studies could be divided into those which assessed CABG outcome based on preoperative cardiac troponin I (cTnI) level as a measure of the extent of myocardial damage and those which considered only the timing after myocardial infarction. Outcome measures included short-term survival, hospital mortality, length of hospital stay and major adverse cardiovascular events (MACEs). The biggest retrospective study analysing postoperative outcomes based on the timing of surgery after NSTEMI concluded that operative mortality is higher when surgery is performed within 6 h of the event. After 6 h, mortality is similar at any timepoint after 6h of NSTEMI. While other smaller studies agree that there are fewer postoperative complications when surgery is performed after 48 h of the event, no consensus is found regarding mortality between early (less than 48 h) and late CABG surgery. Taking into account preoperative cTnI values, CABG has a higher incidence of MACEs and hospital mortality in patients with cTnI >0.15 ng/ml. When surgery is performed within 24 h of symptoms, preoperative cTnI >0.72 ng/ml is associated with worse outcomes. In view of the methodological limitations and level of evidence of the studies included, it appears that surgery may be safely performed in NSTEMI patients at any time after the first 6 h of the event in patients with cTnI <0.15 ng/ml, whereas in those patients with higher values of cTnI, waiting for cTnI to reduce before considering surgery seems to be a wise option in order to decrease the incidence of MACEs and hospital mortality.

**Keywords:** Unstable angina • Myocardial infarction • Coronary artery bypass graft

## INTRODUCTION

A best evidence topic was constructed according to a structured protocol as described in ICVTS [1].

## THREE-PART QUESTION

In [patients with non-ST acute myocardial infarction (NSTEMI)] what is the [optimal timing for coronary artery bypass (CABG) surgery] regarding [survival and postoperative complications]?

## CLINICAL SCENARIO

A 65-year-old patient, with prior history of hypertension and tobacco use, was admitted 72 h ago to the intensive care unit due to unstable angina and a cardiac troponin I (cTnI) level of 0.88 ng/ml. Coronary angiography demonstrated severe proximal left anterior descending, mid-level circumflex and right coronary disease. The patient is stable, with no recurrent angina. The

surgical schedule for the next week is complete. You wonder whether it is advisable to change the surgical schedule in order to include this patient with NSTEMI and decrease the predicted mortality of late CABG. You resolve to review the literature.

## SEARCH STRATEGY

Medline (Pubmed interface), Cochrane library and Google Scholar databases were search for all studies between 1950 and October 2012 according to the following criteria: [exp\*Myocardial infarction/OR exp\*angina, Unstable/OR exp\*Acute coronary syndrome/] AND [exp\*Cardiac surgical procedures/OR Myocardial revascularization/OR exp\*Coronary artery bypass/OR exp\*coronary artery bypass, Off pump/] AND [exp\*Disease-free survival/OR exp\*Survival analysis/OR exp\*Survival/OR \*Hospital mortality/OR \*Mortality/OR \*Postoperative complications/]. The 'related articles' feature was used, and reference lists of all retrieved articles were reviewed to capture relevant articles.

**Table 1:** Best evidence papers discussing CABG timing for NSTEMI

Author (date), journal, country, Study type, level of evidence	Patient group	Outcomes	Key results	Comments
Braxton <i>et al.</i> (1995) <i>Circulation</i> , USA [2] Retrospective study (level 3 evidence)	368 patients undergoing CABG with no MI (252 patients) and with previous Q and non-Q MI (116 patients). Patients were divided into <48 h, 3–5 days and 6–42 days from admission to CABG	Hospital mortality  Requirement for vasopressors, IABP, hospital stay  Perioperative MI	Non-Q wave MI patients showed similar overall mortality (3.4%) to non-MI patients (2.4%)  No differences were found at any of the studied time points with regard to need of vasopressors, IABP or hospital stay  Perioperative MI was higher in the <48 h group compared with non-MI patients	Non-Q wave MI patients may receive CABG surgery at any time with similar outcomes to non-MI patients. Nonetheless, there was no comparison regarding mortality between different time points in the non-Q wave MI patients
Deek <i>et al.</i> (1998) <i>Am J Surg</i> , USA [3] Retrospective study (level 3 evidence)	214 patients undergoing CABG with no MI (155 patients, group I), non-transmural MI (39 patients, group II) and transmural MI (20 patients, group III)	Time from MI or admission to CABG  Hospital mortality, length of stay	Group I were operated after a mean of 2.3 days, group II 4.2 days and group III 5.2 days  No difference in hospital mortality nor length of stay	A waiting period of 3–5 days after non-transmural MI produces similar postoperative outcomes to those in non-MI CABG patients. There was no comparison between patients with non-transmural MI operated at different time points
Lee <i>et al.</i> (2001) <i>Ann Thorac Surg</i> , USA [4] Retrospective study (level 3 evidence)	21 382 patients with non-transmural acute MI received CABG at different time points after acute MI: <6 h, 6–23 h, 1–7 days, 8–14 days, ≥15 days	Hospital mortality  Predictors of hospital mortality	Hospital mortality was higher when CABG was done <6 h from MI (11.5%) than 6–23 h (6.2%) or 1–7 days (3.5%) or 8–14 days (2.5%) or ≥15 days (2.5%)  CABG <6 h from MI was an independent predictor of hospital mortality	Hospital mortality after CABG peaks in the first 6 h after MI, being stable thereafter
Parikh <i>et al.</i> (2010) <i>JACC Cardiovasc Interv</i> , USA [5] Retrospective study (level 3 evidence)	2647 NSTEMI patients who received early (<48 h; 825 patients) and late CABG (>48 h; 1822 patients)	Hospital mortality, MI, stroke, congestive heart failure  Length of stay, transfusion	Hospital mortality, stroke, MI and congestive heart failure were similar in both groups  Late CABG patients received more red blood cell transfusion and had longer in-hospital stay	Patients with late CABG were older, with more hypertension, diabetes, peripheral artery disease, prior MI, prior CABG, prior heart failure, prior stroke, higher creatinine value and lower haematocrit  There was no difference in hospital mortality, MI and stroke between early and late CABG
Paparella <i>et al.</i> (2010) <i>Ann Thorac Surg</i> , Italy [6] Retrospective study (level 3 evidence)	184 patients with recent (onset <21 days) acute MI were divided into two groups based on cTnI values: 117 with <0.15 ng/ml and 67 with >0.15 ng/ml	Postoperative complications (ventilation time, IABP use, atrial fibrillation)  6 month survival	Patients with cTnI >0.15 ng/ml had longer ventilation time, more IABP use, higher incidence of atrial fibrillation  The 6-month survival was worse in patients with cTnI >0.15 ng/ml	The 6-month mortality rate was lower in patients operated on during the second week after acute MI, but the difference was not statistically significant
Thielmann <i>et al.</i> (2006) <i>Circulation</i> , Germany [7] Retrospective study (level 3 evidence)	197 NSTEMI patients operated within 24 h of symptom onset. cTnI was measured before surgery	Hospital mortality and MACE	cTnI levels were independent predictors of hospital mortality and MACE. A cut-off value of 0.72 ng/ml was determined for cTnI and hospital mortality	Although the timing of CABG was considered, preoperative cTnI values were found to be stronger predictors of hospital mortality than EuroSCORE
Thielmann <i>et al.</i> (2005) <i>Chest</i> , Germany [8] Retrospective study (level 3 evidence)	NSTEMI patients were grouped as preoperative cTnI 0.1–1.5 ng/ml (265 patients) or cTnI >0.15 ng/ml (121 patients)	Perioperative MI, hospital mortality and MACE	Perioperative MI, hospital mortality and MACE were higher in patients with cTnI >0.15 ng/ml at the time of surgery	Preoperative cTnI was a strong predictor of hospital mortality in these patients

CABG: coronary artery bypass graft; cTnI: cardiac troponin I; EF: ejection fraction; IABP: Intra-aortic balloon pump; MACE: major adverse cardiovascular event; MI: myocardial infarction; NSTEMI: non-ST myocardial infarction.

## SEARCH OUTCOME

A total of 459 papers were identified, of which only 31 were found to be related to our search after reading the title. From these, the abstract was read, and only seven were strictly related to our question, for which the full text was retrieved and analysed (Table 1). Papers in which patients received surgery due to unstable conditions after coronary angiography were not included.

## RESULTS

Braxton *et al.* [2] evaluated the timing of CABG after non-Q wave myocardial infarction (MI), considering the need for vasopressors, use of a balloon to separate from bypass and hospital mortality compared with a control group, which included patients with no MI. Patients were divided into the following three groups according to the time from admission to CABG: less than 48 h, 3–5 and 6–42 days. Mortality was similar between groups at every time point. Perioperative MI was greater in the non-Q wave MI group compared with the control group when surgery was performed less than 48 h from admission.

Deeik *et al.* [3] evaluated patients with NSTEMI or ST elevation myocardial infarction (STEMI) and patients who required CABG but had not had a recent MI (control group). The mean time from admission to surgery was 2.3 days for the control group, 4.2 days for the NSTEMI group and 5.2 days for STEMI group. No differences were found regarding hospital mortality and length of stay in the three groups.

The largest cohort study regarding the timing of CABG in NSTEMI patients has been reported by Lee *et al.* [4]. They included 21 382 patients with NSTEMI. Surgery <6 h from the acute event was an independent predictor of mortality. Although this is not a focused analysis of NSTEMI patients, we can conclude from their results that surgery can be safely performed at any time point after 6 h of the event without increasing hospital mortality.

Parikh *et al.* [5] used the CRUSADE (Can Rapid Risk Stratification of Unstable Angina Patients Suppress Adverse Outcomes with Early Implementation of the American College of Cardiology/American Heart Association Guidelines) and ACTION Registry–GWTG (Acute Coronary Treatment and Intervention Outcomes Network Registry–Get With The Guidelines) databases to evaluate timing of in-hospital CABG for NSTEMI and in-hospital outcomes. They reviewed 2647 patients and divided them into the following two groups: less than 48 h and after 48 h. Patients operated more than 48 h after the acute event had a higher risk profile. Hospital mortality, stroke, MI and congestive heart failure were similar between both groups. Late CABG patients received more red blood cell transfusions and had a longer hospital stay. This last result is probably due to the higher risk profile of the late CABG group.

Paparella *et al.* [6] tackle the timing of CABG after MI from a pathophysiological perspective, taking into account the release of cTnI. Comparing postoperative major complications and 6 month survival after CABG in stable acute MI patients, they

report that those patients with cTnI >0.15 ng/ml at the time of surgery had more complications and worse survival than patients with cTnI <0.15 ng/ml. This was irrespective of the duration in days from the MI to the CABG.

Thielmann *et al.* [7, 8] provide interesting pathophysiological evidence regarding the timing of CABG in NSTEMI patients. For patients operated within 24 h of symptom onset, cTnI >0.77 ng/ml was found to be an independent predictor of hospital mortality [7]. In patients undergoing elective surgery, cTnI values >0.15 ng/ml at the time of surgery were associated with a higher incidence of major adverse cardiovascular events and hospital mortality [8].

## CLINICAL BOTTOM LINE

Taking into consideration the evidence, patients with NSTEMI who are stable should be operated after 6 h from the acute event. Those patients with cTnI >0.15 ng/ml should wait until cardiac biomarkers descend below this value, in order to decrease the risk of hospital mortality and major adverse cardiovascular events. The optimal strategy for our clinical scenario patient should be to wait until cTnI descends below 0.15 ng/ml and then schedule surgery in the next available slot.

**Conflict of interest:** none declared.

## REFERENCES

- [1] Dunning J, Prendergast B, Mackway-Jones K. Towards evidence-based medicine in cardiothoracic surgery: best BETS. *Interact CardioVasc Thorac Surg* 2003;2:405–9.
- [2] Braxton JH, Hammond GL, Letsou GV, Franco KL, Kopf GS, Elefteriades JA *et al.* Optimal timing of coronary artery bypass graft surgery after acute myocardial infarction. *Circulation* 1995;92:66–8.
- [3] Deeik RK, Schmitt TM, Ihrig TG, Sugimoto JT. Appropriate timing of elective coronary artery bypass graft surgery following acute myocardial infarction. *Am J Surg* 1998;176:581–5.
- [4] Lee DC, Oz MC, Weinberg AD, Lin SX, Ting W. Optimal timing of revascularization: transmural versus nontransmural myocardial infarction. *Ann Thorac Surg* 2001;71:1197–202; discussion 1202–4.
- [5] Parikh SV, de Lemos JA, Jessen ME, Brilakis ES, Ohman M, Chen AY *et al.* Timing of in-hospital coronary artery bypass graft surgery for non-ST segment elevation myocardial infarction patients: Results From the National Cardiovascular Data Registry ACTION Registry–GWTG (Acute Coronary Treatment and Intervention Outcomes Network Registry–Get With The Guidelines). *JACC Cardiovasc Interv* 2010;3:419–27.
- [6] Paparella D, Scarscia G, Paramythiotis A, Guida P, Magari V, Malvindi PG *et al.* Preoperative cardiac troponin I to assess midterm risks of coronary bypass grafting operations in patients with recent myocardial infarction. *Ann Thorac Surg* 2010;89:696–702.
- [7] Thielmann M, Massoudy P, Neuhäuser M, Tsagakis K, Marggraf G, Kamler M *et al.* Prognostic value of preoperative cardiac troponin I in patients undergoing emergency coronary artery bypass surgery with non-ST-elevation or ST-elevation acute coronary syndromes. *Circulation* 2006;114(1 Suppl): I448–53.
- [8] Thielmann M, Massoudy P, Neuhäuser M, Knipp S, Kamler M, Piotrowski J *et al.* Prognostic value of preoperative cardiac troponin I in patients with non-ST-segment elevation acute coronary syndromes undergoing coronary artery bypass surgery. *Chest* 2005;128:3526–36.