

Review

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# Optimal timing of surgical revascularization in patients with acute myocardial infarction

Amin Zahrai<sup>1</sup>, Kenza Rahmouni<sup>1,2</sup>, Fraser D. Rubens<sup>1,2</sup> 

<sup>1</sup>School of Epidemiology and Public Health, University of Ottawa, Ottawa, ON K1G 5Z3, Canada.

<sup>2</sup>Division of Cardiac Surgery, University of Ottawa Heart Institute, Ottawa, ON K1Y 4W7, Canada.

**Correspondence to:** Prof. Fraser D. Rubens, Division of Cardiac Surgery, University of Ottawa Heart Institute, 40 Ruskin St, Ottawa, ON K1Y 4W7, Canada. E-mail: frubens@ottawaheart.ca

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## Abstract

Acute myocardial infarction (AMI) is the leading cause of cardiovascular mortality in developed countries. While primary percutaneous coronary intervention is the gold-standard first-line therapy for initial revascularization of a culprit vessel, coronary artery bypass grafting (CABG) surgery can allow for subsequent complete revascularization when additional high-risk coronary stenoses remain. The optimal timing of CABG after AMI remains controversial. Early surgery during the acute period can lead to a detrimental systemic inflammatory response and may be associated with a higher bleeding risk due to the use of antiplatelet and fibrinolytic agents. On the other hand, later surgery increases the risk of ischemic recurrence while waiting, with the potential for an irreversible decrease in myocardial function or death. This narrative review summarizes the evidence supporting decision-making for optimal timing of surgical revascularization in patients with AMI.

**Keywords:** Acute myocardial infarction, coronary artery bypass grafting, percutaneous coronary intervention, surgical timing optimization

## INTRODUCTION

Acute myocardial infarction (AMI) is among the leading causes of mortality in developed nations, with a prevalence of 3.8% in those younger than 60 years and 9.5% in those older than 60 years<sup>[1,2]</sup>. Preferred treatment options for AMI have evolved in the past 50 years, toggling between pharmacotherapeutic,



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catheter-based, and surgical management<sup>[3]</sup>. When treating AMI, clinicians need to decide on methods that lead to the least amount of harm to each unique patient.

AMI patients who have hemodynamic instability and/or ongoing ischemia, particularly in the presence of an ST-elevation myocardial infarction (STEMI), may be candidates for emergency revascularization<sup>[4]</sup>. A small proportion of STEMI patients may require emergency surgery due to mechanical complications of STEMI<sup>[5,6]</sup>. However, this review will focus on the larger group requiring intervention solely for revascularization. In particular, the strategies that have been proposed include complete revascularization to address all identified coronary stenoses, or a limited revascularization of the culprit vessel responsible for the acute event, with consideration given to revascularize any remaining areas of potential ischemic jeopardy at a later time. As discussed below, this review will focus on the data supporting the timing of surgery in the context of an AMI, particularly after percutaneous coronary intervention (PCI). When done too early, coronary artery bypass grafting (CABG) has been associated with injury from reperfusion and systemic inflammation, poor postoperative outcomes, and an increase in mortality<sup>[7,8]</sup>. On the other hand, delayed surgery may put the patient at risk for recurrent ischemia with the potential for myocardial loss and worsening left ventricular function<sup>[9,10]</sup>.

Recent studies have provided insight into the role that patient parameters, such as AMI type, left ventricular, pulmonary function, and others, could inform the process of surgical revascularization timing<sup>[10,11]</sup>. There also appears to be a scarcity of robust clinical trials studying AMI patients who do not respond successfully to initial PCI or who are eligible for first-line surgical revascularization. In this review, we summarize the current evidence to guide decision-making for the timing of surgical revascularization for AMI patients.

## HISTORY OF CORONARY REVASCULARIZATION IN AMI

Management of AMI has dramatically evolved owing to insights into the pathophysiology of coronary artery disease (CAD). In the mid-twentieth century, prolonged bedrest with oxygen and intravenous fluid therapy served as the principal treatment modality for AMI, often with fatal results<sup>[12]</sup>. Medical therapeutic interventions have included the introduction of coronary care units with improved monitoring and management of arrhythmias<sup>[13]</sup>, and the generalized use of aspirin as a potent platelet aggregation inhibitor<sup>[14-16]</sup>.

The recognition that AMI was a result of acute coronary thrombosis stimulated the introduction of thrombolysis with streptokinase as the first targeted revascularization approach in 1978, with moderate clinical success<sup>[12,17]</sup>. In parallel to this innovation, CABG was growing as a first-line revascularization therapy for CAD<sup>[18,19]</sup>. Investigations comparing surgical and non-surgical management of AMI patients included only nonrandomized data due to challenges with performing a clinical trial on surgical reperfusion<sup>[20,21]</sup>. This changed when Koshal *et al.* conducted the first randomized trial in 1988 to compare surgical revascularization with conventional medical methods (excluding thrombolysis) for treating AMI<sup>[22]</sup>. The authors discovered that urgent surgical reperfusion in AMI reduces early and late mortality compared to medical therapy.

PCI emerged in the 1970s when Andreas Gruentzig performed the first successful PCI in a 38-year-old with stable angina in 1977<sup>[23]</sup>. Two years later, Geoffrey Hartzler introduced primary angioplasty to treat AMI<sup>[24]</sup>. Several randomized trials and large registry studies subsequently compared primary angioplasty and thrombolysis, and a large meta-analysis of randomized trials including 7,739 patients confirmed the reduction in mortality, nonfatal reinfarction, and stroke with primary PCI, thereby justifying its wide use today<sup>[25]</sup>.

## CURRENT STATE OF AFFAIRS AND GUIDELINE REVIEW

The most recent American College of Cardiology/American Heart Association/Society of Cardiovascular Angiographic Interventions guidelines on the management of acute ST-Elevation Myocardial Infarction (STEMI) patients assigns a class 1 recommendation to primary PCI in patients with ischemic symptoms for < 12 h, to improve survival<sup>[26]</sup>. This recommendation is based on high-quality evidence, including the Primary Angioplasty in Myocardial Infarction (PAMI)<sup>[27]</sup> and the Global Use of Strategies to Open Occluded Coronary Artery in ACS (GUSTO IIb)<sup>[28]</sup> trials, both comparing primary percutaneous transluminal coronary angioplasty and thrombolysis. A sub-analysis of the GUSTO IIb study subsequently demonstrated that time to revascularization was intrinsically linked to mortality<sup>[29]</sup>. This led to the rise of the concept of “door-to-balloon” time, which should ideally be below 90 min and should not exceed 120 min from symptom onset<sup>[26]</sup>.

In patients with STEMI and multivessel CAD, revascularization of residual coronary artery stenoses can be achieved via surgical or percutaneous therapies, depending on patient factors (such as social situation, age, diabetes, and other comorbidities) and severity and complexity of the non-culprit coronary disease. Revascularization strategies include: multivessel PCI at the time of primary PCI, primary PCI followed by staged PCI, PCI on the culprit artery only, followed by an ischemia-guided PCI of the remaining vessels, and primary PCI followed by CABG. The option of primary PCI followed by staged PCI is endorsed by strong evidence, thereby justifying the class 1 recommendation for this strategy in the latest American guidelines on coronary revascularization<sup>[26]</sup>. In contrast, a class 2a recommendation was attributed to surgical revascularization in patients with residual complex multivessel non-culprit artery disease after successful primary PCI [Table 1]. This recommendation is largely based on the consensus of expert opinion rather than clinical data. Interestingly, in the 2021 American<sup>[26]</sup> and 2023 European<sup>[30]</sup> guidelines [Table 2], there is no mention of optimal timing for subsequent surgical revascularization in patients who undergo primary PCI for STEMI.

## CLINICAL IMPACT OF TIMING OF SURGICAL REVASCULARIZATION AFTER PRIMARY PCI

The principal goal of optimizing the timing of CABG after primary PCI is to minimize surgical mortality and major cardiac and cerebrovascular events (MACCE). When emergent surgery is performed within 48 h of acute coronary syndrome (ACS), the mortality rate can reach 1,520%, compared to 4%-5% when surgery occurs after 48 h<sup>[31-33]</sup>. Table 3 provides a summary of the major studies that have addressed the timing of surgery in the context of ACS.

A recent systematic review and meta-analysis by Lang *et al.* further support the role of delayed surgery<sup>[34]</sup>. The authors analyzed 19 studies and 113,984 AMI participants who underwent staged CABG. Included studies assessed mortality and/or MACCE as a function of the timing of surgery. Early surgery was defined as CABG within 24-48 h of AMI, while late surgery occurred anytime thereafter. In-hospital mortality was significantly higher in patients who underwent CABG < 24 h, compared to those who had surgery > 24 h (OR 2.65; 95%CI: 1.96 to 3.58;  $P < 0.00001$ ). Similarly, patients who underwent CABG < 48 h had a significantly higher in-hospital mortality than those who underwent surgery > 48 h (OR 1.91; 95%CI: 1.11 to 3.29;  $P = 0.02$ ). There was no difference between early and late CABG with regards to perioperative MI (OR 1.38; 95%CI: 0.41 to 4.72;  $P = 0.60$ ) and cerebrovascular accidents (OR 1.31; 95%CI: 0.72 to 2.39;  $P = 0.38$ ).

**Table 1. Selected recommendations for revascularization of the infarct and non-infarct arteries in patients with STEMI from the 2021 ACC/AHA/SCAI guidelines<sup>[26]</sup>**

Class of recommendation	Level of evidence	Recommendation
<b>Recommendations for revascularization of the infarct artery in patients with STEMI</b>		
1	B	"In patients with STEMI and cardiogenic shock or hemodynamic instability, PCI or CABG (when PCI is not feasible) is indicated to improve survival, irrespective of the time delay from MI onset."
1	B	"In patients with STEMI who have mechanical complications (e.g. ventricular septal rupture, mitral valve insufficiency because of papillary muscle infarction or rupture, or free wall rupture), CABG is recommended at the time of surgery, with the goal of improving survival."
2a	B	"In patients with STEMI in whom PCI is not feasible or successful, with a large area of myocardium at risk, emergency or urgent CABG can be effective as a reperfusion modality to improve clinical outcomes."
3 (Harm)	C	"In patients with STEMI, emergency CABG should not be performed after failed primary PCI: -In the absence of ischemia or a large area of myocardium at risk, or -If surgical revascularization is not feasible because of a no-reflow state or poor distal targets."
<b>Recommendations for revascularization of the non-infarct artery in patients with STEMI</b>		
2a	C	"In selected patients with STEMI with complex multivessel non-infarct artery disease, after successful primary PCI, elective CABG is reasonable to reduce the risk of cardiac events."

STEMI: ST-Elevation myocardial infarction; PCI: percutaneous coronary intervention; CABG: coronary artery bypass grafting; MI: myocardial infarction.

**Table 2. Selected recommendations for revascularization of the infarct and non-infarct arteries in patients with Acute Coronary Syndromes from the 2023 ESC guidelines<sup>[30]</sup>**

Class of recommendation	Level of evidence	Recommendation
1	B	"Emergency CABG is recommended for ACS-related CS if PCI of the IRA is not feasible/unsuccessful."
2a	C	"Coronary artery bypass grafting should be considered in patients with an occluded IRA when PPCI is not feasible/unsuccessful and there is a large area of myocardium in jeopardy."
1	B	"It is recommended to base the revascularization strategy (IRA PCI, multivessel PCI/CABG) on the patient's clinical status and comorbidities, as well as their disease complexity, according to the principles of management of myocardial revascularization."
1	C	"If patients presenting with ACS stop DAPT to undergo CABG, it is recommended they resume DAPT after surgery for at least 12 months."

ACS: Acute coronary syndrome; CABG: coronary artery bypass grafting; CS: cardiogenic shock; DAPT: dual-antiplatelet therapy; PCI: percutaneous coronary intervention; IRA: infarct-related artery.

Bernard *et al.* performed a large single-center retrospective cohort study to evaluate the impact of the timing of surgical revascularization on mortality in 477 stable patients after myocardial infarction<sup>[31]</sup>. The overall 30-day mortality of the cohort was 7%, and it was significantly higher (14%) in patients who underwent surgery within 4 days of the initial presentation. Risk factors for mortality in this study included older age, pre-operative renal failure, peripheral vascular disease, and pre-operative ischemic recurrence. Left ventricular function, type of AMI, and perioperative transfusions were not linked with mortality. These

**Table 3. Summary of the studies included**

First author (year)	Study design	MI type	Number of patients	Intervention(s)	Mean age ± SD (years)	Time to CABG (days)	Primary outcome(s)	Main results
Sintek <i>et al.</i> (1994) <sup>[41]</sup>	Retrospective cohort	STEMI, NSTEMI	2,175 (1,013 STEMI, # of NSTEMI not specified)	Isolated CABG	63.4 (Range 32-85)	< 1 1-2 2-3 3-7 7-30	30-day operative mortality	Timing of surgery was not significantly associated with operative mortality
Thielmann <i>et al.</i> (2007) <sup>[39]</sup>	Retrospective cohort	STEMI	138	Primary isolated CABG	65.6 ± 10.8	< 0.25 0.25-1 1-3 4-7 8-14	All-cause in-hospital mortality	Patients who underwent CABG between 7-23 h (after symptom onset) had significantly higher mortality rate than those in the 4-7 days [vs. 7-23 h group: OR = 0.5 (95% CI 0.3-0.8)] or 8-14 days groups [7-23 h vs. 8-14 days: OR = 3.4 (1.7-21.3)]
Weiss <i>et al.</i> (2008) <sup>[7]</sup>	Retrospective cohort	AMI type not specified	9,476	CABG of any type	67.6 ± 11.0	< 2 > 2	All-cause hospital mortality	Early CABG (0-2 days) was an independent predictor of hospital mortality (OR = 1.40, 95% CI: 1.12-1.74)  Surgical delay beyond 3 days did not provide any further survival benefit
Parikh <i>et al.</i> (2010) <sup>[45]</sup>	Retrospective cohort	NSTEMI	2,647	CABG of any type	64.0	< 2 > 2	Composite of death, MI, cardiogenic shock, or congestive heart failure	NSTEMI patients undergoing early and late CABG had similar in-hospital mortality (OR = 1.12, 95% CI: 0.71-1.78) and composite outcome (OR = 0.94, 0.69-1.28) occurrences
Chen <i>et al.</i> (2014) <sup>[33]</sup>	Meta-analysis of 12 studies	STEMI (3 studies)  NSTEMI (1 study)  STEMI/NSTEMI (8 studies)	100,048	CABG of any type	Not specified	Many sub-divisions ranging from < 0.25 to > 43	In-hospital mortality between different CABG time intervals after AMI	There was an increase in in-hospital mortality of 0.950 (95% CI 0.936-0.964) for each day delay to CABG after acute MI and 0.774 (95% CI 0.719-0.834) for each 5 day increase
Lemaire <i>et al.</i> (2020) <sup>[37]</sup>	Retrospective	STEMI	5,963	CABG of any type	63.1 ± 11.1	< 1	Postoperative	

cohort									
						2-3		complications; in-hospital mortality	Patients who underwent CABG within 24 h were more likely to develop any complications compared to those in 2-3 and 4-7 days groups, respectively (OR = 1.22, 95% CI 1.05-1.41, and OR = 1.18, 95% CI 1.01-1.36, respectively). Differences in complications between 2-3 and 4-7 days groups were not statistically significant (OR = 0.97, 95% CI 0.85-1.11)
						4-7			Odds of in-hospital mortality was higher in the < 1 day, compared to 2-3 days group (OR = 1.85, 95% CI 1.52-2.25) and 4-7 days group (OR = 2.21, 95% CI 1.82-2.68). The latter two groups did not differ in terms of in-hospital mortality
Liakopoulos <i>et al.</i> (2020) <sup>[38]</sup>	Prospective registry cohort	STEMI, NSTEMI	618 STEMI 1,218 NSTEMI	CABG of any type	STEMI: 68.3 ± 10.3 NSTEMI: 66.6 ± 11.3	< 1 1-3 > 3		In-hospital all-cause mortality	In-hospital mortality occurred two-fold higher in STEMI patients who had CABG < 24 h compared both to those who had CABG > 72 h and to those between 24-72 h  CABG timing did not affect the in-hospital mortality of patients with unstable angina or those with NSTEMI
Bianco <i>et al.</i> (2021) <sup>[40]</sup>	Retrospective cohort	STEMI NSTEMI	368 STEMI 1,690 NSTEMI	Isolated CABG	66.0 (Range 58.0-74.0)	< 1 > 1		All-cause mortality	All-cause mortality postop was significantly higher < 1 day, compared to the > 1 day group [Hazard ratio (HR) (95% CI) = 0.63 (0.42-0.97)]. After risk factor adjustments, there was no difference in terms of mortality (4.15% vs. 4.58%, P = 0.62). Timing of CABG did not impact mortality in either STEMI (HR = 0.57 (0.25-1.29) or NSTEMI (HR = 0.99 (0.56-1.76)) groups
Lang <i>et al.</i> (2022) <sup>[34]</sup>	Systematic review and meta-analysis	STEMI NSTEMI Undefined STEMI/NSTEMI	38,469 STEMI 3,405 NSTEMI 72,675 Undefined STEMI/NSTEMI	CABG of any type	STEMI: 63.7 NSTEMI: 67.2 Undefined STEMI/NSTEMI: 65.9	Many subdivisions ranging from < 0.25 to 15-30 (STEMI) < 1 to 3-21 (NSTEMI) < 2 to > 42 (Undefined STEMI/NSTEMI)		In-hospital mortality	OR between < 24 h CABG and > 24 h CABG groups was 2.65 (95% CI: 1.96-3.58). This was 3.88 (2.69-5.60) for undefined STEMI/NSTEMI, 2.62 (1.58-4.35) for STEMI, and 1.24 (0.83-1.85) for NSTEMI groups  OR between < 48 h CABG and > 48 h

								CABG groups was 1.91 (95% CI: 1.11-3.29). This was 2.84 (1.31-6.14) for undefined STEMI/NSTEMI and 0.96 (0.62-1.48) for the NSTEMI groups
Kite <i>et al.</i> (2022) <sup>[46]</sup>	Systematic review and meta-analysis	NSTE-ACS	10,209 received either an early or late invasive strategy procedure (either PCI, CABG, or optimal medical therapy; 605 received early CABG and 642 received late CABG)	Invasive coronary angiography strategies	Not provided	Cut-off times for early and late procedures were not defined by authors. Authors extracted this data for each study. Pooled median time to angiography across the included studies was found to be 3.43 h (1.47-5.40 h) in the early strategy group and 41.3 h (29.3-53.2 h) in the delayed strategy group	All-cause mortality	No significant differences were observed in the risk of all-cause mortality (risk ratio = 0.90, 95% CI 0.78-1.04)
Bernard <i>et al.</i> (2023) <sup>[31]</sup>	Retrospective cohort	Undefined STEMI/NSTEMI	477 STEMI: 162 NSTEMI 315	CABG, either as a first-line treatment or after angioplasty failure	67 ± 12	< 4 5-10 ≥ 11	30-day mortality  Postoperative complications (LCOS, stroke, cardiogenic shock, cardiac arrest, surgical re-exploration)	Mortality was significantly higher for patients who underwent CABG < 4 days compared to 5-10 days and ≥ 11 days (14% vs. 4.0% vs. 8.6%; <i>P</i> < 0.01)  No difference between groups for postoperative complications

SD: Standard deviation; ACS: acute coronary syndrome; AMI: acute myocardial infarction; CABG: coronary artery bypass grafting; LCOS: low-cardiac output syndrome; NSTEMI: non-ST-segment elevation myocardial infarction; OR: odds ratio; PCI: percutaneous coronary intervention; STEMI: ST-segment elevation myocardial infarction. Standard deviations have been provided where available.

findings suggest that early revascularization may be detrimental to patients with non-cardiac comorbidities, conferring a higher surgical risk. A large cohort study from Maganti *et al.* and a national retrospective study by Klempfner *et al.* similarly demonstrated the benefit of delaying surgical revascularization, particularly in high-risk patients. This is consistent with the findings of a study by Lemaire *et al.* in which patients who underwent surgical revascularization within 24 h were more likely to develop cardiac, renal, respiratory, and bleeding complications<sup>[35-37]</sup>.

Most of the literature on the optimal timing of surgical revascularization in patients with acute myocardial infarction has been derived from nonrandomized data. Therefore, the burden of selection bias in these cohorts of patients is high. In other words, patients who required a surgical intervention earlier were more likely to have a greater extent of ischemia and hemodynamic instability than those who could tolerate and survive a pre-operative waiting phase of a few days.

### STEMI VERSUS NON-STEMI

The timing of surgery after AMI has also been evaluated relative to the type of myocardial infarction at presentation. The clinical course and treatment strategies for STEMI and NSTEMI are often distinct, which may influence the optimal timing of surgical revascularization. In STEMI patients, there seems to



be a clinical benefit in delaying surgery by 24-48 h, whereas this difference in outcomes may not be present in patients with NSTEMI. A systematic review and meta-analysis of 113,984 AMI patients undergoing CABG treatment found that early intervention (within 24 or 48 h from AMI occurrence) in the STEMI group was associated with a higher risk of mortality compared to late intervention, while early versus late timing of CABG did not significantly impact mortality in NSTEMI patients<sup>[34]</sup>. Results from registry and retrospective cohort studies suggest that in the absence of an absolute need for urgent surgery, delay may be considered for STEMI patients due to the mortality risk of earlier operations<sup>[37-39]</sup>. Some studies have identified early surgical intervention as a predictor of increased mortality in ACS patients<sup>[7]</sup>, while others have demonstrated no association between the time of surgical revascularization and mortality or periprocedural complications<sup>[40,41]</sup>.

The transmural infarction seen in STEMI may be a factor resulting in increased inflammatory markers, the levels of which may be further elevated with early CABG procedures after AMI and potentially impact myocardial function, and can lead to a profound systemic inflammatory response, a well-known risk factor for perioperative mortality<sup>[34,41-43]</sup>. For example, levels of the inflammatory marker C-reactive protein can be demonstrated to be significantly increased after a transmural MI<sup>[43,44]</sup>. CABG is also associated with profound increases in these markers, suggesting that these inflammatory changes may be compounded<sup>[44]</sup>. On the other hand, studies have not found significant differences in postoperative outcomes of NSTEMI patients who undergo early versus late surgical revascularization; delayed surgery may therefore increase resource use without considerably improving patient outcomes<sup>[45,46]</sup>.

Patients with acute STEMI and multivessel CAD who require surgical revascularization are at a higher risk of death than STEMI patients with an isolated single culprit lesion<sup>[47]</sup>. These patients may be considered for other interventions, for example, primary PCI using balloon angioplasty of the culprit lesion and medical management of the non-culprit lesions without risk of further angina or MI<sup>[48,49]</sup>. Other options include primary PCI and later staged PCIs to treat the non-culprit lesions, or ad-hoc PCI procedures during the primary PCI. This group of patients, especially if they have cardiogenic shock or ischemia after treating the culprit lesion, would require complete revascularization<sup>[50]</sup>. On the other hand, hemodynamically stable patients can benefit from primary-staged PCIs and multivessel PCIs<sup>[51,52]</sup>.

## BLEEDING RISK CONSIDERATIONS

Anticoagulation and antiplatelet therapy (and sometimes fibrinolytic agents) are vital in the management of ACS. While significantly decreasing the risk of ischemic recurrence, these agents increase the surgical risk due to bleeding<sup>[31,53]</sup>. Patients with coagulopathy and prolonged bleeding times suffer from longer surgical time, higher transfusion rate, and higher risk of re-exploration. This is well-known and was one of the major drawbacks in several large randomized control trials evaluating the use of antiplatelet therapy in ACS, including the CURE<sup>[54]</sup> and the TRITON-TIMI 38<sup>[55]</sup> CABG substudies.

The 2017 European Society of Cardiology focused update on dual antiplatelet therapy in coronary artery disease<sup>[56]</sup> and the 2018 Canadian Cardiovascular Society Guidelines for the use of antiplatelet therapy<sup>[57]</sup> provide specific recommendations for a timeline of discontinuation of antiplatelet therapy prior to CABG, to minimize this risk [Table 4]. This information must be considered to derive the risk and benefit ratio of early versus late surgery shortly after the administration of antiplatelet agents to individualize care for each patient.

In patients with an ACS requiring urgent CABG after administration of antiplatelet agents, certain strategies exist for clinicians to mitigate the bleeding risk. When possible, performing off-pump surgery may be



**Table 4. European and Canadian recommendations for timing of discontinuation of antiplatelet agents prior to coronary artery bypass grafting. Class or strength of recommendation are in parentheses**

Aspirin	Ticagrelor	Clopidogrel	Prasugrel
<b>European society of cardiology (2017)<sup>[56]</sup></b>			
No discontinuation (Class 1)	3 days (Class 2a)	5 days (Class 2a)	7 days (Class 2a)
<b>Canadian cardiovascular society (2018)<sup>[57]</sup></b>			
No discontinuation (Strong)	Minimum: 48-72 h (Weak) Ideal: 5 days (Strong)	Minimum: 48-72 h (Weak) Ideal: 5 days (Strong)	Minimum: 5 days (Weak) Ideal: 7 days (Strong)

favorable to decrease bleeding risk, as the use of cardiopulmonary bypass may exacerbate the deleterious effect of antiplatelet therapy on hemostasis<sup>[58]</sup>. Furthermore, the use of platelet function testing, such as rotational thromboelastometry assays and genotyping, may be used to guide decision-making for antiplatelet therapy de-escalation and for optimal timing of surgical intervention<sup>[59,60]</sup>. In addition, antiplatelet reversal agents are currently being investigated for clinical use. In an experimental study by Bhatt *et al.*, intravenous administration of the monoclonal antibody PB2452 in healthy volunteers resulted in immediate and persistent reversal of the antiplatelet effects of ticagrelor<sup>[61]</sup>. These findings have been further supported in a prospective study evaluating the use of this drug in 150 ticagrelor-treated patients who required urgent surgery or who were suffering from a major hemorrhage. Platelet-function testing confirmed the rapid reversal of ticagrelor-mediated platelet dysfunction within five to ten min. Hemostasis was achieved in over 90% of the patients<sup>[62]</sup>. This drug is currently not available for routine use but is being tested in REVERSE-IT, an international multicentre trial (ClinicalTrials.gov ID NCT04286438), in cardiac surgery patients.

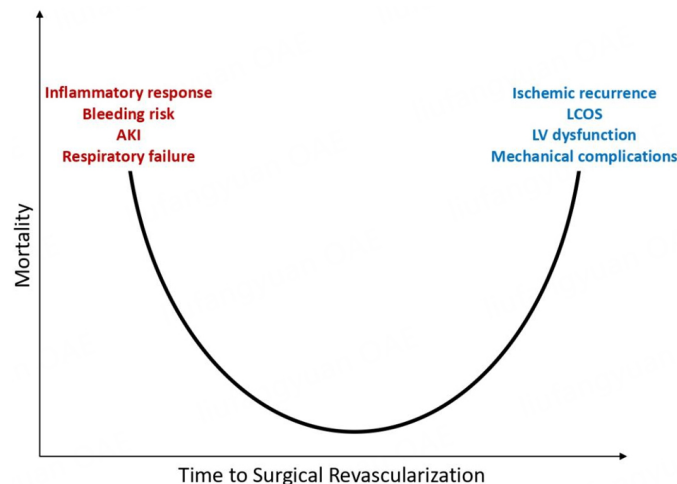
Most in-hospital patients awaiting surgery after a STEMI are treated with parenteral anticoagulation. Whereas unfractionated heparin (UFH) can be continued up to induction in the operating theatre, most other forms of anticoagulation should be stopped well in advance as they cannot effectively be reversed with protamine at the end of cardiopulmonary bypass. It is currently recommended that low molecular weight heparin (LMWH) be stopped a minimum of 18 h prior to surgery<sup>[63]</sup> or longer, depending on renal function. In patients treated with the synthetic pentasaccharide fondaparinux, the drug should be stopped for at least 3 full days as anticoagulant activity may persist even in the presence of normal renal function<sup>[64]</sup>.

## SPECIAL CONSIDERATIONS

In certain cases, the presence of an indication for emergent surgery, such as structural complications and ongoing ischemia with hemodynamic instability, overrides the risks of early surgery in AMI patients<sup>[34,37]</sup>. In the 2021 ACC/AHA/SCAI guidelines [Table 2], a class 1 indication is attributed for CABG in patients with STEMI who have mechanical complications (e.g., ventricular septal rupture, mitral insufficiency secondary to papillary muscle infarction or rupture, or free wall rupture)<sup>[26]</sup>. Similarly, emergent revascularization - whether with CABG or PCI - is recommended as a class 1 indication in patients with cardiogenic shock and hemodynamic instability<sup>[26,65]</sup>.

## CONCLUSION

While some studies have shown an association between early CABG and surgical mortality following ACS treated with primary PCI, the optimal timing of CABG remains to be elucidated. Chen and Liu proposed a U-shaped distribution in mortality depending on the timing of surgery from AMI [Figure 1]<sup>[33]</sup>. This concept supports the idea that the lowest mortality can be achieved after the hyperacute phase of systemic inflammation and before the development of irreversible complications from myocardial injury. Ultimately,



**Figure 1.** U-shaped distribution of the surgical mortality as a function of timing of coronary artery bypass grafting in patients with acute myocardial infarction. The lowest mortality can be achieved after the hyperacute phase of systemic inflammation and before the development of irreversible complications from myocardial injury. AKI: Acute kidney injury; LCOS: low cardiac output syndrome; LV: left ventricle.

individual decisions regarding the optimal timing of complete revascularization for patients who suffer from an ACS should be made with a multidisciplinary Heart Team<sup>[26]</sup>. There seems to be a benefit in delaying surgery by 48 h after initial ACS presentation; however, there is a paucity of data on the additional value of further postponing surgery to a few weeks after the index event. Higher quality studies with standardized patient selection criteria and randomized treatment assignment are required to better guide decision-making for appropriate timing of surgical revascularization in patients who underwent primary PCI for ACS.

## DECLARATIONS

### Authors contributions

Made substantial contributions to the conception and design of the study and performed all data analysis and interpretation: Zahrai A, Rahmouni K, Rubens FD

### Availability of data and materials

Not applicable.

### Financial Support and Sponsorship

None.

### Conflicts of Interest

All authors declared that there are no conflicts of interest.

### Ethical approval and consent to participate

Not applicable.

### Consent for publication

Not applicable.

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