#### **RESEARCH ARTICLE**

# Surgical Revascularization in Acute Coronary Syndrome

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## **ABSTRACT**

**Purpose**: This review evaluates surgical revascularization strategies in patients with acute coronary syndrome (ACS), focusing on optimal timing, patient selection criteria, and a comparative analysis with percutaneous coronary interventions (PCI). The study aims to provide a comprehensive overview of the indications, benefits, and limitations of surgical approaches in the context of multi-vessel disease and other complex ACS presentations.

**Methods**: A literature review was conducted, drawing from clinical trials, observational studies, and current guidelines on ACS management. Key studies examining outcomes of coronary artery bypass grafting (CABG) in ACS, including on-pump and off-pump techniques, were analyzed alongside PCI trials to assess the effectiveness and safety of these approaches.

Key Findings: Surgical revascularization, particularly CABG, offers advantages in selected ACS populations, such as those with multi-vessel disease or failed PCI, and is critical for patients with structural complications like ventricular septal rupture. Off-pump CABG (OPCAB) shows potential benefits in reducing systemic inflammation and perioperative complications, though patient selection remains essential. Guidelines recommend CABG for high SYNTAX score patients and in cases of left main disease, with emerging evidence supporting staged revascularization in multi-vessel disease to reduce adverse events. Comparatively, PCI offers rapid revascularization but may require repeat interventions, particularly in patients with complex coronary anatomy or comorbidities.

Conclusion: Surgical revascularization remains a crucial component of ACS management, particularly for complex cases where PCI is unsuitable or incomplete. This review underscores the importance of individualized patient assessment, the need for further comparative trials, and the role of the heart team approach in optimizing outcomes for ACS patients. Future research should focus on refining patient selection criteria and exploring hybrid revascularization approaches to improve clinical practice.

**Keywords:** Acute coronary syndrome, Urgent Revascularization, Coronary artery bypass surgery, Percutaneous coronary intervention, Anti thrombotics, Off pump CABG

# Introduction

The evolution of coronary revascularization over the past few decades has provided a range of therapeutic options for treating coronary artery disease (CAD). The first coronary artery bypass grafting (CABG) was performed by René Favaloro in 1967 at the Cleveland Clinic, using a saphenous vein graft (SVG) to bypass an occluded right coronary artery (RCA). A decade later, in 1977, Andreas Grüntzig pioneered percutaneous coronary intervention (PCI), expanding treatment possibilities for CAD. Early clinical trials compared CABG with medical therapy, including landmark studies like the VA Co-op trial (1972-74), the European Coronary Surgery Study (1973-76), and the CASS trial (1975-79). A meta-analysis by Yusuf etal<sup>1</sup>. in 1994 demonstrated the superior survival rates of CABG over medical therapy, especially in patients with multi-vessel disease, left main (LM) disease, or left ventricular (LV) dysfunction. The metaanalysis, which reviewed seven randomized clinical trials in patients with stable angina, found an operative mortality rate of 3.2% for CABG. Survival rates were significantly higher for CABG compared to medical therapy with higher mortality, on long term medical therapy at five years (CABG 10.2% vs. medical 15.8%), seven years (CABG 15.8% vs. medical 21.7%), and ten years (CABG 26.4% vs. medical 30.5%). Over the years, the technique of CABG has improved substantially, leading to a marked reduction in surgical mortality. Key advancements include enhanced myocardial protection, the use of arterial conduits for bypass, and improvements in peri-operative care. Additionally, the introduction of minimally invasive approaches, hybrid revascularization, and off-pump surgery have further optimized outcomes for patients undergoing coronary revascularization.

# Discussion

The debate over whether off-pump CABG (OPCAB) is as effective and safe as on-pump CABG remains unresolved, even after three randomized controlled trials—RCT<sup>2,3,4</sup>-ROOBY, CORONARY, and GOPCABE—failed to demonstrate a clear advantage for OPCAB over a five-year period. In terms of safety, OPCAB

has shown benefits such as reduced systemic inflammatory response, lower risk of bleeding, stroke, and surgical mortality. Despite this, OPCAB is currently preferred by a limited number of cardiac surgeons and only for selected patient groups. Minimally invasive direct coronary artery bypass (MIDCAB) techniques, including left minithoracotomy and subxiphoid approaches, can be performed with or without thoracoscopic assistance. For multi-vessel coronary artery disease (CAD), total endoscopic coronary artery bypass (TECAB) provides a minimally invasive option. Hybrid coronary revascularization, which involves grafting the left internal mammary artery (LIMA) to the left anterior descending artery (LAD) via surgery while treating other coronary obstructions with PCI, is another feasible approach. This strategy is based on the long-term patency of the LIMA, which is central to the benefits of CABG. The superiority of CABG over PCI with drug-eluting stents (DES) in multi-vessel disease, particularly in diabetic patients with high SYNTAX scores, has been established in trials such as SYNTAXES, BEST, and ASCERT. Current ACC-AHA and ESC guidelines provide Class I recommendation and level of evidence B for CABG in patients with multi-vessel disease. For left main disease, meta-analyses of randomized controlled trials<sup>5,6</sup> (NOBLE, EXCEL) and high-quality observational data indicate that CABG is preferable to PCI, especially in patients with high SYNTAX scores.

A pooled analysis of four RCTs—SYNTAX, <sup>7</sup>PRECOMBAT, NOBLE, and EXCEL—compared PCI (with DES) and CABG in patients with LMCA disease, with and without ACS, who were equally suited for either approach (low and intermediate SYNTAX scores).

The results were as follows:

- Patients with ACS experienced higher early mortality rates compared to those with stable CAD.
- ii) All-cause mortality rates over five years were similar between PCI and CABG, with comparable outcomes extending to ten years.

iii) The relative benefits of PCI (lower stroke rates, reduced early mortality) and CABG (lower long-term risk of spontaneous MI and repeat revascularization) were consistent, regardless of ACS status. These findings suggest that both PCI and CABG are viable options for patients with ACS and LMCA requiring urgent revascularization.

Complete revascularization is a key goal in treating symptomatic CAD patients, as long-term MACE is inversely related to the extent of non-revascularized territories. The residual SYNTAX score (quantifying anatomical complexity) and the revascularization index (percentage of re-vascularized area) help assess this. A <sup>8</sup>residual SYNTAX score of less than 8 and a revascularization index over 80% are associated with favorable long-term outcomes in terms of MACE.

It is important to note that ischemia is only one of three major factors influencing long-term disease progression, and it can be measured using both invasive and non-invasive tests. The other two factors, plaque burden and plaque vulnerability, are often under-assessed by clinicians, yet they significantly affect the clinical manifestation of CAD. This was highlighted in the BARI trial, which showed that an increase in angina recurrence at five years was linked to the progression of previously untreated coronary vessels, underscoring the importance of GDMT in CAD management. The SYNTAX<sup>9</sup> score II, which incorporates clinical factors such as diabetes, CKD, and LV dysfunction, indirectly accounts for plaque burden and vulnerability.

Long-term outcomes of coronary artery disease (CAD) are influenced by the severity of ischemia, plaque burden, plaque vulnerability, and the type and completeness of revascularization, along with appropriate guideline-directed medical therapy (GDMT) to prevent further disease progression.

The management of acute myocardial infarction (AMI) has advanced over the decades due to a deeper understanding of the disease pathophysiology and the development of more therapeutic options.

Thrombolysis was first introduced in 1978, and primary percutaneous coronary intervention (PCI) was pioneered by Geoffrey Hartzler<sup>10</sup> in 1979. In 1998, <sup>11</sup>Koshal and colleagues conducted the first randomized controlled trial (RCT) comparing surgical revascularization in AMI with medical therapy (excluding thrombolysis). The study demonstrated a reduction in both early and late mortality with surgical intervention compared to medical therapy alone.

Optimal timing for coronary artery bypass grafting (CABG) in AMI patients has not yet been firmly established by any RCT. To address this, a nationwide retrospective study from <sup>12</sup>Korea analyzed data from the National Health Insurance database, focusing on 1,705,843 adult AMI patients hospitalized between 2007 and 2018 who underwent CABG within one year of diagnosis. Patients were categorized into five groups based on the timing of surgery relative to their AMI diagnosis: Group I (<1 day), Group II (1-2 days), Group III (3-7 days), Group IV (8-21 days), and Group V (>21 days). The study found that only 1.18% of AMI patients received CABG. It concluded that performing CABG within 24 hours of AMI effectively minimized myocardial damage and improved clinical outcomes. When surgery within this time frame was not feasible, waiting more than three days was associated with reduced major adverse cardiac and cerebrovascular events (MACCE). However, a significant limitation of the study was the lack of differentiation between STEMI and NSTEMI. Perioperative use of aspirin has been associated with a significant reduction in 30-day mortality without a substantial increase in bleeding risk.

# ACS - Multi vessel disease

Around 50% of patients with STEMI and 60% of patients with NSTEMI have multivessel disease, putting them at a higher risk for cardiovascular events. The long-term benefit of complete revascularization over culprit vessel angioplasty has been supported by both ESC and ACC/AHA guidelines. The optimal timing of complete revascularization in ACS patients

—either during the index event or as a staged procedure—has been studied in the <sup>13</sup>MULTISTARS-AMI and <sup>14</sup>BIOVASC trials. These trials were designed to compare multivessel PCI performed during the index procedure with staged procedures, done within six weeks in the BIOVASC trial or within 19-45 days in the MULTISTARS-AMI trial.

Immediate multi-vessel PCI in acute cardiogenic shock has shown higher rates of death and renal failure compared to culprit vessel PCI alone. Assessing non-culprit vessels in ACS is important in making therapeutic decisions regarding CAD. In acute STEMI, coronary vasoconstriction due to alpha-adrenergic stimulation can lead to a 10% overestimation of lesion severity, resulting in overtreatment. Physiological assessment of non-culprit lesions (NCL) in ACS is considered safe and reliable, but it is important to understand the underestimation of severity by FFR and overestimation by IFR. The role of intravascular imaging such as IVUS or OCT in guiding clinical decisions during ACS is not yet established.

In general, there is no data to support PCI of bystander chronic total occlusions (CTO) during the acute phase of ACS, particularly following the results of the COMPLETE trial, which demonstrated that the benefit of complete revascularization was consistent whether performed during the index hospitalization or after discharge. Therefore, all ACS patients, except those in cardiogenic shock, should be offered complete revascularization by PCI either during the index procedure, before discharge, or at least within one month, if coronary anatomy allows. The choice between PCI and surgery should be based on the complexity of coronary anatomy, patientspecific factors (such as risk factors and comorbidities), and patient preferences. In complex cases, involving a 'Heart Team' approach is advisable.

In patients with STEMI and multi-vessel CAD, revascularization of residual CAD after primary PCI can be achieved either percutaneously or surgically via CABG. The choice between these methods depends on the severity and complexity of the non-culprit lesions, as well as factors such as age, diabetes,

and patient preference. Regardless of the method chosen, complete revascularization—whether staged or simultaneous is critical for better long-term outcomes, including reduced MACCE.

The timing of CABG after primary PCI is crucial to minimizing surgical mortality and adverse events. Emergency surgery performed within 48 hours of a cardiac event carries a mortality risk of up to 20%, compared to 4-5% when performed after 48 hours. A meta-analysis by Lang et al. of <sup>15</sup>19 studies involving 113,984 AMI patients found higher mortality rates for CABG performed within 24 hours (OR: 2.65, 95% CI 1.96-3.58, P=<0.00001) compared to surgeries performed after 24 hours. However, there was no significant difference in perioperative MI or stroke between early and delayed CABG. Bernard et al. reached similar conclusions in a single-center retrospective study of 477 stable post-MI patients, where those undergoing surgery within four days had significantly higher mortality (14%) compared to those with delayed surgery (>4 days). These studies suggest that early CABG may be harmful in AMI, possibly due to non-cardiac comorbidities. In contrast, the timing of CABG in NSTEMI does not appear to significantly affect mortality, potentially due to differences in the inflammatory response in STEMI, where surgery may exacerbate a systemic inflammatory response, increasing operative risk.

Anticoagulation and antiplatelet therapy are key in ACS management, significantly reducing the risk of ischemic recurrence in both STEMI and NSTEMI. However, these medications must be stopped before surgery due to increased bleeding risk, leading to longer surgical times, higher transfusion rates, and a greater risk of re-exploration. Managing bleeding complications in patients treated with potent antiplatelet agents is a major challenge during CABG. In cases requiring urgent CABG after antiplatelet administration, strategies to mitigate bleeding include platelet function testing for de-escalation of antiplatelet therapy and performing off-pump CABG (OPCAB) without the use of cardiopulmonary bypass, which can further affect platelet function and hemostasis.

Monoclonal antibodies targeting ticagrelor have been tested in clinical trials, including the <sup>16</sup>REVERSE-IT trial, to immediately reverse antiplatelet effects in cardiac surgery patients. Additionally, CYTOSORB absorber technology has been used during cardiopulmonary bypass to reduce ticagrelor levels,

potentially decreasing postoperative bleeding. Platelet transfusion has been explored as a strategy, though it may be effective against prasugrel but not ticagrelor, which binds reversibly to platelet ADP receptors and blocks freshly transfused platelets. Further results from ongoing studies are awaited.

# Anti-platelet drugs – discontinuation – prior to CABG<sup>17</sup>

Drug	ESC 2017 Guidelines	Canadian Cardiovascular Society 2018 Guidelines
Aspirin	No discontinuation	No discontinuation
Ticagrelor	Discontinue 3 days before surgery	Minimum 48-72 hours; Ideal 5 days before surgery
Clopidogrel	Discontinue 5 days before surgery	Minimum 48-72 hours; Ideal 5 days before surgery
Prasugrel	Discontinue 7 days before surgery	Minimum 48-72 hours; Ideal 7 days before surgery

Anticoagulants such as unfractionated heparin (UFH) and Low-molecular-weight heparin (LMWH) are used alongside antiplatelets in ACS patients to reduce ischemic episodes. UFH can be continued until the induction of anesthesia, as it can be reversed with protamine at the end of cardiopulmonary bypass. In contrast, LMWH must be stopped at least 12 hours before surgery, and Fondaparinux needs to be discontinued at least three days prior due to its prolonged anticoagulant activity.

ST-Elevation Myocardial Infarction is often treated with PCI as the primary therapy or after thrombolysis (pharmaco-invasive strategy) when a patient presents at a hospital without a cath lab. The management of residual CAD, whether by PCI or CABG, depends on the complexity of the coronary artery disease and the presence of comorbidities such as diabetes, chronic kidney disease, peripheral artery disease, and cerebrovascular disease.

Coronary artery bypass surgery is rarely indicated in AMI but may be necessary when complicated by structural abnormalities, such as ventricular septal rupture, papillary mscule rupture, free wall rupture. In such cases, this indication may outweigh the high mortality risk associated with early CABG.

Most ACS patients are treated with PCI or drug therapy, while CABG is reserved for specific subgroups, including those with left main coronary artery disease combined with triple vessel disease, complex coronary anatomy unsuitable for PCI (such as those with very high SYNTAX scores), or failed PCI. There are different methods of performing CABG, including on-pump CABG (on CPB with arrested heart), OPCAB (off-pump, on a beating heart without CPB), and On-pump Beating Heart CABG (ON-BH-CABG). These approaches aim to reduce the systemic inflammatory response induced by cardiopulmonary bypass (CPB) while maintaining myocardial protection by preserving coronary flow and avoiding reperfusion injury. However, the beating-heart approach is technically more demanding, which may impact the completeness of revascularization and long-term patency, and there is high morbidity and mortality associated with emergent conversion from OPCAB to on-pump CABG.

A network meta-analysis of 19 studies<sup>18</sup> comparing on-pump CABG, OPCAB, and on-pump beating heart CABG in ACS patients suggests that OPCAB may provide a mortality benefit over on-pump CABG, particularly in AMI patients, by avoiding inflammatory and ischemic injury. A <sup>19</sup>multi-center surgical registry from North Rhine-Westphalia, Germany, further highlighted that emergency CABG remains an important treatment option in the contemporary PCI era. This study involved 2,432

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patients who underwent CABG for ACS between January 2010 and December 2017, with 25% presenting with unstable angina, 50% with NSTEMI, and 25% with STEMI. Hospital mortality was 12.6%, and the incidence of MACCE (major adverse cardiac and cerebral events) was 28.5%, with the highest rates observed in STEMI patients. Unstable angina had the lowest hospital mortality (4.2%) and MACCE (7.9%).

A second study on revascularization in ACS was a retrospective analysis of 45,439 patients with AMI (38.7% STEMI, 61.3% NSTEMI) who underwent either PCI or surgical revascularization in the USA. Single-vessel revascularization was performed in 67.8% of cases, while multi-vessel revascularization was done in 32.2%. This study found that PCI was associated with higher in-hospital mortality but lower morbidity and shorter hospital stays. The mortality benefit of surgical revascularization was observed

primarily in multi-vessel revascularization, not in single-vessel disease.

Patients with STEMI/ACS and failed PCI who are referred for emergency CABG, especially in cardiogenic shock, are at very high risk of mortality.

The benefit of early revascularization in evolving AMI is well established in improving clinical outcomes and left ventricular function. While PCI and thrombolysis can restore blood flow in a timely manner, CABG is associated with a time delay and is used in less than 10% of patients as a primary mode of therapy. Consequently, there are no large multicenter randomized clinical trials focused on primary CABG in evolving AMI. Nonetheless, CABG is considered a primary revascularization option in select ACS patients, such as those with unsuccessful PCI, incomplete revascularization, mechanical complications of AMI, or cardiogenic shock.

# ACC / AHA / SCAI guidelines - 2021<sup>20</sup>

## REVASCULARISATION OF INFARCT & NON INFARCT ARTERIES IN PATIENTS WITH STEMI

Class of		Levels of
Recommendation	Recommendation	
	STEMI + Cardiogenic shock or Hemodynamic instability: PCI / CABG	
	(when PCI is not feasible) is indicated to improve survival irrespective of	
	time delay from MI onset.	В
	In patients with STEMI who have mechanical complications—free wall	
	rupture, VSR, MR due to papillary muscle infarct/rupture—CABG is	
	recommended at the time of surgery to improve survival.	В
	- Patients with STEMI in whom PCI is not feasible/successful,	
	emergency/urgent CABG can be effective as a reperfusion modality to	
2(a)	improve clinical outcomes.	С
	- Patients with residual complex multi-vessel disease after PCI: elective	
	CABG is reasonable to reduce the risk of cardiac events.	С
	Patients with STEMI: Emergency CABG should not be performed after	
	failed PCI in the absence of ischemia/large area myocardium at risk, poor	
III (Harm)	distal targets, or no-reflow phenomenon.	С

# Guidelines - ESC 2023<sup>21</sup>

# RECOMMENDATIONS FOR REVASCULARIZATION OF INFARCT AND NON-INFARCT RELATED ARTERIES IN PATIENTS WITH ACS

Class of		Level of
Recommendation	Recommendation	Evidence
	Emergency CABG is recommended for ACS-related cardiogenic shock if PCI of IRA is not feasible/unsuccessful.	В
	It is recommended to base revascularization strategy (PCI/CABG) on patient's clinical status, comorbidities, and disease complexity according to principles of myocardial revascularization.	
I	DAPT after CABG should be continued for at least 12 months.	В
II(a)	CABG should be considered in patients with occluded IRA when PPCI is not feasible/unsuccessful and a large area of myocardium is in jeopardy.	С

# Conclusion

Surgical revascularization in ACS is a therapeutic options but to limited extent. Its role is primarily in patients with ACS complicated by structural abnormalities severe MR, VSR and free wall rupture and is the only strategy in failed incomplete PCI, though at higher risk of adverse CV events.

## Conflict of Interest:

The authors declare that they have no competing interest or relevant relationship with industries pertaining to this subject.

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## Contributions:

Both authors have contributed to review of scientific literature of subject and writing up article.

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