

# Surgery as early revascularization after acute myocardial infarction

*Akut miyokard infarktüsü sonrası erken revaskülarizasyonda cerrahi*

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## ABSTRACT

Acute myocardial infarction (AMI) is the leading cause of morbidity and mortality in most industrialized nations throughout the world. Options for myocardial revascularization include thrombolysis or percutaneous coronary intervention (PCI) in the early period after AMI, or coronary artery bypass grafting (CABG) for suitable patients. It has commonly been suggested that surgery in the early period after AMI can be associated with increased morbidity and mortality. However, advances in technology, surgical methods and myocardial protection techniques currently provide a chance for cardiovascular surgeon to achieve CABG in the setting of AMI. In patients with AMI, interest in early surgical revascularization has decreased with widespread use of thrombolytics or PCI. However, early surgical revascularization is beneficial in patients who have mechanical complications, ongoing ischemia, and cardiogenic shock complicating AMI. Failure of thrombolytic agents, unsuccessful PCI or left main coronary artery disease also requires surgery. Theoretically, early surgical revascularization may be useful by minimizing infarct size improving left ventricular function, and increasing patient survival. The optimal timing of surgery after AMI remains undecided as a controversial subject. It ranges from immediate surgical intervention to surgery 30 days after myocardial infarction. Therefore, such a wide variation in the therapeutic strategy of the surgical groups has made way a selection bias in these patients. This review presented highlights optimal timing of surgical revascularization after AMI, surgical methods and controlled reperfusion, risk factors for poor outcomes after surgery for AMI, and the role of surgery in patients with AMI complicated by cardiogenic shock. (*Anadolu Kardiyol Derg 2008; 8 Suppl 2; 84-92*)

**Key words:** Acute myocardial infarction, cardiogenic shock, coronary artery bypass grafting, surgical timing, risk factors

## ÖZET

Akut miyokard infarktüsü (AMI) çoğu endüstri toplumlarında, morbidite ve mortalitenin önde gelen sebebidir. Miyokard revaskülarizasyonu için seçenekler olarak AMI'nün erken döneminde tromboliz, perkütan koroner girişim (PKG) veya uygun hastalarda koroner arter baypas greftlemeyi (KABG) sayabiliriz. Genellikle, AMI'nün erken döneminde yapılan cerrahi girişimin artmış morbidite ve mortalite ile birlikte olabileceği ileri sürülmektedir. Bununla birlikte, günümüzde teknoloji, cerrahi yöntemler ve miyokard koruma tekniklerindeki ilerlemeler, AMI'nde KABG cerrahisinin başarılmasında kardiyovasküler cerraha bir şans vermiştir. Akut miyokard infarktüsülü hastalarda trombolitikler veya PKG'in yaygın kullanımı ile erken cerrahi revaskülarizasyona ilgi azalmıştır. Yine de, erken cerrahi revaskülarizasyon mekanik komplikasyonlar, medikal tedaviye rağmen devam eden iskemi ve AMI'nü komplike eden kardiyojenik şoklu hastalarda yararlıdır. Trombolitik ajanlarla başarısızlık, başarılı olmayan PKG veya sol ana koroner arter hastalığı yine de cerrahiye gerektirir. Teorik olarak, erken cerrahi revaskülarizasyon infarkt boyutunu azaltarak, sol ventrikül fonksiyonunu düzelterek ve hastanın yaşam süresini artırarak faydalı olabilir. Akut miyokard infarktüsünden sonra optimal cerrahi zamanlama tartışmalı bir konu olarak karşımızda durmaktadır. Bu süre AMI'nden hemen sonra cerrahi girişimden 30 gün sonrasında cerrahi girişimine kadar değişmektedir. Bu yüzden, cerrahi grupların tedavi stratejisindeki böyle geniş bir değişim, bu hastalarda hasta seçimi eğilimini yaratmıştır. Sunulmakta olan bu derlemeyle AMI'nden sonra cerrahi revaskülarizasyonun optimal zamanlamasına, cerrahi yöntemler ve kontrollü reperfüzyona, AMI'nde cerrahiden sonra kötü sonuçlara neden olan risk faktörlerine ve kardiyojenik şokla komplike olan AMI'li hastalarda cerrahinin rolüne dikkat çekilmiştir. (*Anadolu Kardiyol Derg 2008; 8 Özel Sayı 2; 84-92*)

**Anahtar kelimeler:** Akut miyokard infarktüsü, kardiyojenik şok, koroner arter baypas greftleme, cerrahi zamanlama, risk faktörleri

## Introduction

Acute myocardial infarction (AMI) continues to be major cause of death in middle aged and elderly population. It is defined as the sudden blockage of one or more coronary arteries leading to myocardial cell death as a result of coronary atherosclerosis, thrombus, and embolus. In the Western world, AMI is associated with significant morbidity and mortality, not only in the short term, but also years following an index AMI. According to the World Health Organization it will be the major cause of death in the world as a whole by the year 2020 (1). In the United States, approximately 800,000 people annually are affected and in spite of a better awareness of presenting symptoms, about 225,000 of whom die before reaching to the hospital (2). In recent decades, improvements in treatment strategies have led to significant increase in survival rate for patients hospitalized with AMI.

In the setting of AMI, clinical spectrum may alter from ST elevation myocardial infarction (STEMI) to non-ST elevation myocardial infarction (NSTEMI) (subendocardial), or cardiogenic shock (3). Surgery plays an important role in treatment of all these clinical scenarios by means of advances in myocardial preservation and mechanical support. Coronary artery bypass grafting (CABG) for complete revascularization frequently may be put into practice as an therapeutic option in patients with NSTEMI.

Treatment of patients with AMI has improved over time and the duration of hospital stay has considerably decreased. In spite of this improvement, electrical and mechanical complications such as arrhythmias, papillary muscle dysfunction with mitral regurgitation, ruptured free wall with tamponade, ruptured ventricular septum, and cardiogenic shock challenge the medical community caring for patients presenting with AMI on a daily practice (4). Cardiac arrhythmias and cardiac pump failure are responsible for hospital deaths from AMI (3). Preservation of viable myocardium is the primary goal of revascularization strategies. In patients with AMI, reperfusion modalities include thrombolytic therapy, percutaneous coronary intervention (PCI), and CABG. If coronary flow is reestablished early, infarcted area of the myocardium is limited (5). Revascularization strategies in the early phase of treatment of AMI rapidly help maintaining myocardial tissue perfusion and providing myocardial salvage, thus increasing chance of survival rate. However, timing and methods of revascularization continue to be a controversial issue (4).

## Aims of early reperfusion

While the principal aim is to prevent death, early reperfusion helps to minimize the patient's discomfort and distress, and to limit the extent of myocardial damage in patients with AMI (6). Understanding the changes associated with progressive ischemia and the mechanisms of reperfusion injury are the keys for the understanding of the role of revascularization strategies (7). The pathogenesis of AMI nearly always involves acute thrombosis superimposed on a disrupted atherosclerotic plaque (8). The onset of ischemia is accompanied by rapid changes in myocardial metabolism because of its extreme dependence on aerobic respiration. Myocardial ischemia leads to increased intracellular calcium, diminished amino acid precursors, and

decreased ATP production. Reperfusion reverses these deleterious changes (3). Reperfusion limits infarct size, protects threatened myocardium and rescues hypoperfused border areas that can become arrhythmogenic foci, and thus resulting in mortality reduction. The open-artery hypothesis suggests that the sooner normal flow can be restored in an occluded coronary artery, the better will be the short, medium and longer-term outcome for the patient with AMI.

The relation between normal coronary artery blood flow and mortality after AMI is well documented. A meta-analysis of angiographic infarct trials showing normal flow was associated with a mortality of 3.7% compared with 6.6% in patients with impaired flow and 9.2% in patients with occluded or nearly occluded infarct related arteries (9). Thus, early reperfusion clearly reduces infarct size in the major areas at risk, augments myocardial salvage, preserves left ventricular (LV) function, and, ultimately, increases survival rate in acutely ill patients.

Theoretically, late reperfusion leads to increased peri-infarct hemorrhage, edema, contraction band necrosis, and ultimately myocardial stiffening. Although benefits of late reperfusion beyond 36 hours, particularly in asymptomatic patients, have yet to be reported in large clinical studies, advocates for aggressive management believe that reperfusion is made sure to preserve the border areas that may be underperfused during the early days after AMI (4, 10).

The group of Buckberg (11) has persuasively reported that controlled reperfusion with specially designed perfusate and a decompressed, energy-conserving ventricle resting on cardiopulmonary bypass (CPB) is the best strategy to preserve myocardial function. Appropriate and aggressive invasive therapies such as PCI, CABG, controlled reperfusion, intra-aortic balloon pump (IABP) use, and left ventricular assist device (LVAD) insertion in patients with ongoing ischemia may reduce myocardial injury and rescue borderline areas, even if the interventions occur several hours or days after AMI (4).

## Surgical revascularization

It has commonly been suggested that surgical revascularization in the early period after AMI can be associated with increased morbidity and mortality (3). However, recent advances in myocardial protection techniques, controlled reperfusion, and mechanical support have provided a chance for cardiovascular surgeon to achieve CABG in the setting of AMI.

Emergent or urgent surgical revascularization is indicated in the failed PCI, in patients with hemodynamic instability and coronary anatomy amenable to surgery, or persistent ischemia (2). Surgical revascularization is also indicated in the setting of mechanical complications of AMI such as free-wall rupture, acute ischemic mitral insufficiency, and ventricular septal defect. The efficacy of surgery has been demonstrated in patients with cardiogenic shock complicating AMI, although the reported mortality rate is never less than 20% (4, 11, 12). Early surgical revascularization may be beneficial by limiting infarct size, reducing LV dysfunction, and increasing patient survival. Nevertheless, delay in surgery may potentially lead to the infarct extension and worse long-term prognosis.

In patients with AMI, current indications for emergency CABG, briefly, are limited to those presenting with evolving myocardial ischemia refractory to optimal medical therapy, presence of left main stenosis and/or 3-vessel disease, ongoing ischemia despite successful or failed PCI, complicated PCI, or cardiogenic shock accompanied by complex coronary anatomy (2, 13).

Early studies have reported that CABG within 30 days of infarct onset was associated with increased mortality and morbidity (14). Hemorrhage into the infarct causing expansion of the infarct region may be responsible for poor results. During this era, conservative therapy was believed to be more reasonable treatment (4). On the other hand, the only absolute indications for emergent surgery after AMI were ventricular septal rupture, LV free-wall rupture, and papillary muscle rupture.

During the 1980s, reports showed that mortality rates were less than 5% in patients undergoing CABG after AMI, and surgery was preferred to conservative treatment. Critics argued that these studies were not randomized and subject to selection bias, that enzyme levels were not included. Thus, the reason for the excellent surgical outcomes was inherent bias that favored surgery in low-risk patients (4, 15, 16). No randomized controlled trials have exactly characterized the benefits of surgery versus other therapeutic strategies in AMI.

Berg et al. (17) reported that 430 patients were operated upon on an emergency basis. In their study, mortality rate was 5.2%. These patients had a much lower mortality rate than that of medically treated patients. They expressed that lower surgical mortality coupled with the early and late clinical results proves that emergency surgery is superior therapy in selected patients with AMI.

The overall mortality in a study from our institution (18) with 65 consecutive patients underwent emergency CABG within first 6 hours of AMI was 6.1%, identical to that observed by the early study groups. Nonetheless, in low risk patients with no preoperative medical complications, mortality rate was 2.3%, while 13% in high-risk patients with cardiogenic shock and acute pulmonary edema and cardiac arrest before the angiography or on the way to the operating room. Therefore, we believe that emergent CABG during very early period of AMI is a life-saving procedure with an acceptable mortality in the high-risk patients.

Emergent or urgent surgery as first-line treatment after AMI may be necessary approximately in 5% of patients. Another 5% receive surgery before hospital discharge for failed PCI or for definitive management of multivessel coronary disease or for repair of the mechanical complications of AMI (3).

The place of surgery in the treatment strategy of AMI has been reported in a detailed study of the primary angioplasty in myocardial infarction-2 (PAMI-2). In this prospective, controlled trial, cardiac catheterization was performed in 1,100 patients within 12 hours of onset of AMI at 34 centers, followed by primary PTCA when appropriate. Surgery was performed before hospital discharge in 120 (10.9%) patients (19). Coronary artery bypass surgery was performed in 6.1% of the 982 patients who had primary PCI, and in 44.9% of 118 patients not undergoing primary PCI. Only 4 (0.4%) cases required surgery emergently for failed PCI. In analysis of this population, patients who underwent surgery were older and more frequently diabetic and more frequently had 3-vessel disease. In-hospital mortality was 6.4% in patients undergoing urgent/emergent surgery, 2.0% after

elective surgery, and 2.6% in patients not undergoing surgery. After multivariate correction for baseline risk factors, early and late reinfarction rates were equivalent in patients undergoing and not undergoing surgery. Thus, surgery is an integral component of the first-line PCI treatment within early hours of AMI, and frequently used to optimize the prognosis of a high-risk AMI cohort with unfavorable baseline features (19).

Up to now there have been no large randomized clinical trials comparing CABG with PCI and thrombolytic therapy after AMI (4). Many trials have been conducted comparing CABG to PCI in patients with stable angina and elective revascularization for ischemic heart disease. In these studies, current trends favor surgery in patients with multivessel disease. The Stent or Surgery (SoS) Trial is a recent randomized, controlled trial comparing PCI with CABG for patients with multivessel disease (20). Initial results at a median follow-up of 2 years showed a survival advantage for patients randomized to CABG. At a median follow-up of 6 years, a continuing survival advantage was observed for patients managed with CABG, which is not consistent with results from other stent-versus-CABG studies.

The advantages of CABG compared with PCI for AMI include (3,4): (i) surgery is a definitive revascularization treatment with long-term patency of revascularized stenotic and occluded arteries demonstrated in elective cases (90% internal mammary artery patency at 10 years); (ii) complete revascularization strategy with more vessels potentially treated and this concept becomes especially important in patients with multivessel disease or patients in cardiogenic shock, in whom remote myocardium may continue to be comprised with only culprit vessel revascularization and inadequate restoration of collateral flow; (iii) difficult distal obstructions can be bypassed; (iv) reperfusion can be controlled to minimize ischemic injury and reperfusion injury, and (v) as with other forms of reperfusion, surgery halts the progression of ischemia and necrosis and minimizes infarct size.

### Surgical timing

The optimal timing of surgery after AMI remains undecided as a controversial topic. It ranges from immediate surgical intervention to repair 30 days after the onset of AMI (21). This controversy particularly continues in patients with uncomplicated AMI, but retrospective studies indicate that when surgery is performed as early as 3 to 7 days after AMI, operative mortality is equivalent to CABG performed in patients with non-myocardial infarction.

Although no exact recommendation exists related to the optimal timing of surgery after AMI, the opinion that these patients are exposed to a greater risk for short-term mortality is gaining consensus (21-24). This is not surprising given that the majority of patients who undergo early surgical revascularization present with a higher degree of clinical acuity, which, in turn, translates to higher mortality rates (25).

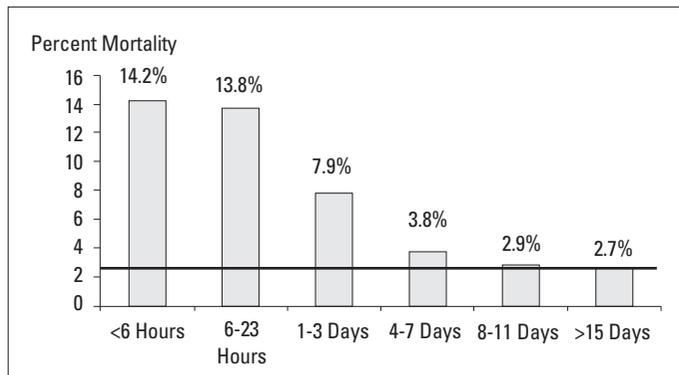
Historically, higher mortality, ranging from 5% to 30%, for emergent CABG after AMI has been documented since the early 1970s, with especially poor prognosis in patients who had transmural AMI (14, 16). In the early 1980s, studies reported by DeWood et al. (15, 26, 27), focusing on surgical timing showed a benefit to performing early CABG. The mortality rate of surgery within 6 hours after the onset of AMI was improved over that of

medically treated nonrevascularized patients. Their conclusions were derived from a retrospective study of 440 patients with transmural AMI. The authors suggested that surgery within 6 hours of AMI decreased short-term and long-term mortality and improved late event-free survival. Mortality for CABG after 6 hours was 8.5% versus 3.8% for CABG within 6 hours. In-hospital mortality for non-transmural AMI was 3.1% and 5.2% for transmural AMI. However, while these early studies were criticized for selection bias and were not controlled, their study did demonstrate that surgical revascularization may be performed with an acceptable mortality in the presence of AMI with improved anesthesia, myocardial protection, and surgical techniques (4).

More recently, retrospective analyses have shown that surgery should be deferred for 3 or more days after AMI, when possible (21-23, 25, 28, 29).

A study of the New York State Cardiac Surgery Registry (21) has investigated valuable information concerning the optimal surgical timing in patients with AMI as part of a strategy to improve outcome after AMI. This study was a retrospective multicenter analysis of 32,099 patients who underwent CABG as the sole procedure after transmural AMI between 1991 and 1996 by 179 surgeons at 33 hospitals in New York State (21). Overall hospital mortality for all patients who underwent surgery with a history of TM AMI was 3.3%. Hospital mortality decreased with increasing time interval between surgery and transmural AMI (Fig. 1) (21). Day 3 was a point of inflection between the steep rise of mortality after early surgical revascularization and the lower mortality later. After 3 days, mortality rapidly approached baseline.

Columbia group (21, 22) evaluating the state of New York databases showed that the risk of early surgical revascularization is substantially higher before hospital day 3, with a doubling of mortality risk compared with patients who underwent later surgery. The conclusion was that a 3-day waiting period should be considered to allow this high-risk period to subside in the absence of absolute indications for emergent surgery. On the other hand, they also showed that waiting for surgical intervention, especially in patients with TM AMI results in better outcomes.



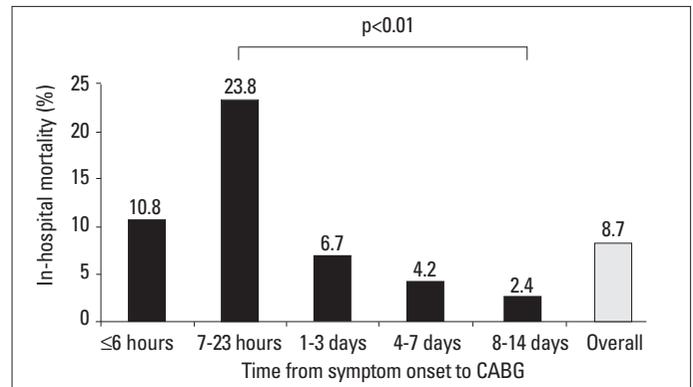
**Figure 1. Hospital mortality versus timing of CABG. The horizontal bar represents the baseline mortality rate (2.7%) from the entire patient population**

CABG-coronary artery bypass grafting  
(Reproduced from Lee DC, Oz MC, Weinberg AD, Ting W. Appropriate timing of surgical intervention after transmural acute myocardial infarction. *J Thorac Cardiovasc Surg* 2003;125(1):115-20, Copyright © 2003 with permission of Elsevier)

In addition, Lee and colleagues (22) have shown that patients undergoing CABG after transmural AMI and non-transmural AMI have distinctively different patterns of mortality with respect to surgical timing. If surgery was performed within 6 hours of AMI onset, mortality for patients with non-transmural AMI reached a peak level, then decreased steeply. On the other hand, mortality for patients with transmural AMI remained high during the first 3 days before returning to baseline. Thus, multivariate analyses verified that surgical revascularization within 6 hours of non-transmural AMI or 3 days of TM AMI were associated with increased in-hospital mortality.

A recent retrospective study performed by the Johns Hopkins group using California Discharge Data has attempted to objectify the optimal timing of surgery after AMI. Weiss et al. (25) reviewed this data to identify 40,159 patients who were hospitalized for AMI (day 0) and underwent subsequent CABG. Patients were stratified by the timing of surgical revascularization to early (days 0-2) and late groups (day 3 or later). A peak mortality rate among patients undergoing CABG on day 0 was 8.2% versus 3.0% among patients undergoing CABG on day 3. The authors concluded that CABG may best be deferred for 3 or more days after admission for AMI in non-urgent cases.

Thielmann et al. (28) reported a study of 138 consecutive patients with STEMI undergoing surgical revascularization. In this study, overall in-hospital mortality was 8.7%, but mortality varied depending on time interval from symptom onset to operation. As shown in Figure 2, a one-sided Cochran-Armitage trend test has revealed a significant difference between those STEMI patients who underwent CABG therapy between 7 and 24 hours from symptom onset to revascularization and those who were postponed with conservative maximal nonsurgical therapy to 3 to 7 days or even 8 to 14 days after symptom onset (19). Thus, the authors concluded that surgical revascularization should be postponed at least for 3 days after symptom onset.



**Figure 2. In-hospital mortality rates with respect to the time interval from symptom onset to coronary artery bypass grafting (CABG; black columns) and overall in-hospital mortality (gray column). A value of  $p < 0.01$  (calculated by Cochran-Armitage trend test) is overall significance between a time interval of 7 to 24 hours and 8 to 14 days after symptom onset to CABG**

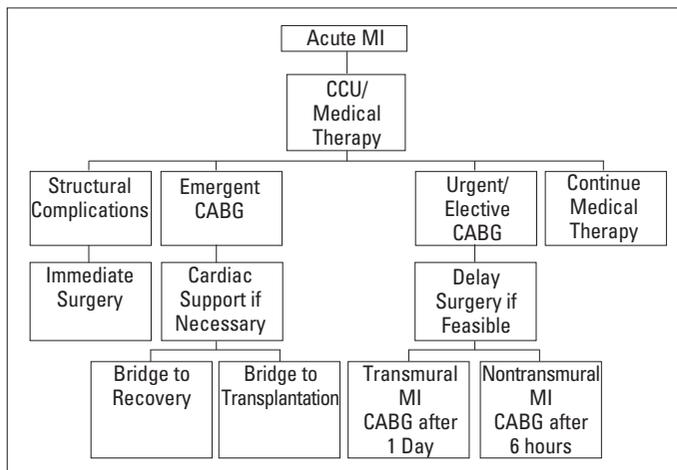
CABG-coronary artery bypass grafting  
(Reproduced from Thielmann M, Neuhäuser M, Marr A, Herold U, Kamler M, Massoudy P, et al. Predictors and outcomes of coronary artery bypass grafting in ST elevation myocardial infarction. *Ann Thorac Surg* 2007;84(1):17-24, Copyright © 2007 with permission of Elsevier)

Another study by Voisine et al. (23) reported only 77 of 7219 patients who underwent surgery within 24 hours of admission from a single center. They concluded that CABG is best deferred for a period of 7 days after AMI.

In a study reported by Applebaum et al. (29), 406 patients were operated on within 30 days of AMI. Hospital mortality was 2.4%. In the subgroup of patients with history of recent AMI mortality rate was 6.7%, compared with 1.1% in the subgroup with no history of previous AMI.

Advantages of early surgery include limitation of both infarct size expansion and adverse ventricular remodeling, thus preservation of ventricular function (30). However, the risk of reperfusion injury is well known, which may lead to hemorrhagic infarction resulting in extension of infarct size, poor infarct healing, and scar development (31), suggesting caution against early revascularization, particularly among patients within the first 3 days after transmural AMI (28). Theoretically, there would be some advantage in waiting for the AMI to heal (4 to 6 weeks), allowing complete recovery of the stunned myocardium and preventing risk of myocardial damage after reperfusion, which may even lead to hemorrhagic infarction (32). However, the risks associated with this waiting period must be weighed, such as recurrent ischemia, with possible reinfarction due to the lesions; infarct extension with ventricular remodeling, which can generate aneurysm; and significantly higher costs from prolonged hospital stay (21, 22, 32).

A proposed scheme of patient management for those with AMI is summarized in Figure 3 (22). This algorithm is based on the summary of results from the New York State Cardiac Surgery Registry (22). Surgery certainly should not be delayed in emergent cases, but non-emergent cases may obtain an advantage from delay of surgery, particularly in patients with transmural AMI. Because early surgical revascularization after transmural AMI has a significantly higher risk, aggressive cardiac support including LVAD should be available in this patient group. Awaiting strategy may be useful to optimize surgical outcome in some cases. This requires careful patient selection, optimal surgical timing, and preoperative support, possibly with IABP (3, 4, 21, 22).



**Figure 3. Proposed management algorithm for patients with acute myocardial infarction (MI)**

CCU - coronary care unit, CABG coronary artery bypass grafting  
(Reproduced from Lee DC, Oz MC, Weinberg AD, Lin SX, Ting W. Optimal timing of revascularization: transmural versus nontransmural acute myocardial infarction. *Ann Thorac Surg* 2001;71(4):1198-204, Copyright © 2001 with permission of Elsevier)

### Risk factors for surgery

Many studies have been made to identify which group of patients are at higher surgery risk after AMI (21-23, 28, 29, 32, 33). The mortality risk associated with CABG after AMI remains a controversial subject. Although elective CABG is quite safe, the effects of recent myocardial infarction, gender, and other clinical factors on perioperative mortality rates are not completely understood (33).

In a detailed study by Lee et al. (21), multivariate analysis of 43 risks factors showed that surgery within 3 days of transmural AMI was an independent predictor of mortality. Risk factors for poor outcomes after surgery for AMI are shown in Table 1 (3). These include surgical timing, urgent surgery, cardiogenic shock, transmural AMI, previous myocardial infarction, female gender, increased age, renal failure, hypo/hypertension, left main disease, multivessel disease, poor LV wall motion score, depressed LV function, need of IABP use, previous CABG surgery, and the need for cardiopulmonary resuscitation (3, 4, 21, 22, 33).

Using the National Registry of Myocardial Infarction 2 database, Zaroff et al. (33) evaluated 71,774 (21,270 women) patients with AMI who underwent CABG. The results of logistic regression modeling showed that age >75, previous CABG, heart failure on presentation, and female gender were the independent predictors for mortality.

In a recent study (32), the authors determined that, among the factors analyzed, the presence of preoperative cardiogenic shock and history of angiography were associated with poorer prognosis in AMI patients.

Recently, Thielman et al. (28) reported that female sex, preoperative cardiac troponin I level, preoperative cardiogenic shock, the preoperative Killip class, and time to operation seem to be major variables of mortality or major adverse cardiac events that should be necessarily considered.

### Controlled reperfusion

Surgery, currently, is the only means of applying controlled reperfusion in the setting of AMI (12). Clinical data have confirmed the experimental data showing the superiority of controlled reperfusion methods, especially in high-risk patients (11).

**Table 1. Risk factors for poor outcomes after surgery for acute myocardial infarction**

Early CABG	CHF
Urgent/emergent	Decreased LV function, low EF
Age	Preoperative CPR
Renal insufficiency	Left main disease
Number of previous MI	Female
Hypotension	Poor LV wall motion scor
Reoperation	IABP preoperatively
Cardiogenic shock	TM AMI

CABG-coronary artery bypass grafting, CHF-congestive heart failure, CPR- cardiopulmonary resuscitation, EF- ejection fraction, IABP- intra-aortic balloon pump, LV-left ventricular, MI- myocardial infarction, TM AMI- transmural acute myocardial infarction  
(Data from Comas GM, Esrig BC, Oz MC. Surgery for myocardial salvage in acute myocardial infarction and acute coronary syndromes. *Heart Fail Clin* 2007;3(2):181-210, Copyright © 2007 with permission of Elsevier)

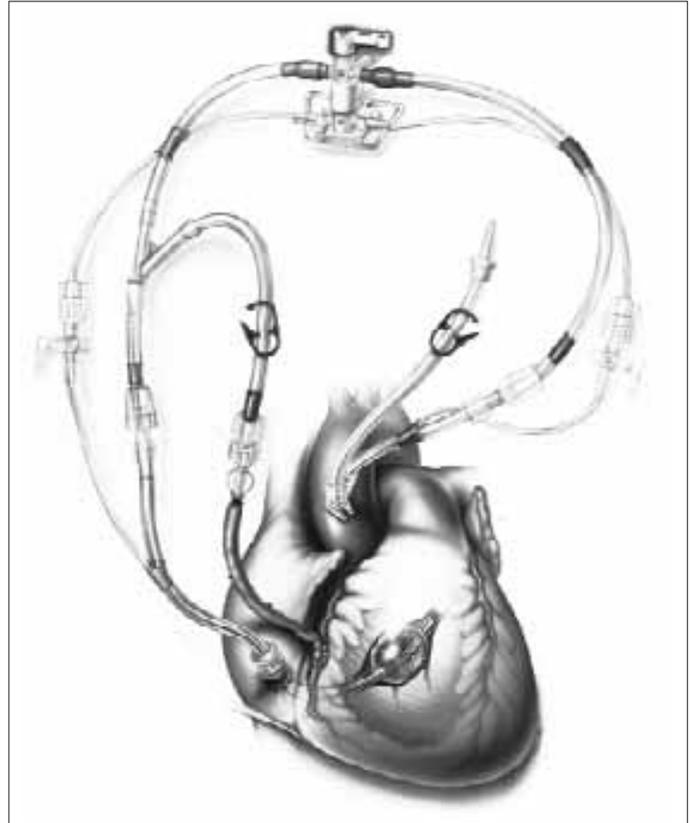
Controlled reperfusion is a strategy of salvaging myocardium in the surgical revascularization of AMI. This method may reduce reperfusion injury, limit infarct size, and maximize myocardial protection (3, 4).

Treatment of the ischemic myocardium able to restore pre-ischemic conditions or limit reperfusion injury includes cardiac work reduction and LV decompression by means of CPB, myocardial protection achieved by means of blood cardioplegia, controlled reperfusion using a substrate-enriched blood cardioplegic solution, and protection of ischemic territories surrounding or distant from the infarcted area (12).

Surgery puts forward the advantage of controlled reperfusion and complete revascularization in the setting of myocardial ischemia. Buckberg et al. (11, 34, 35) emphasized that controlling the conditions of reperfusion through composite of the perfusate may minimize reperfusion injury and maximize benefits if heart tissue is ischemic but not yet infarcted. Surgery allows myocardium rested on bypass to be recovered with gradual controlled reperfusion using balanced chemically optimized perfusate. The Buckberg solution, administered during cardioplegia, is an erythrocyte-containing, basic hyperosmolar solution stocked with aspartate, glutamate, and calcium chelators (Table 2) (3). The composition of the reperfusate was designed to provide oxygen, reduce calcium influx, reverse acidosis, mobilize edema, and replenish substrates (4). To accomplish this, the cardioplegic solution was hyperosmolar and basic and contained blood, a chelating agent, aspartate, and glutamate (35). The duration of reperfusion, 20 minutes, as well as the dose, were critical (36). In addition, myocardial oxygen consumption can be minimized by using warm induction and warm reperfusion. The heart can be arrested with cardioplegia thus minimizing demand but maintained normothermic so that enzymatic activities can replete ATP stores (3).

Simultaneous aortic root and coronary sinus perfusion is a viable myocardial protection strategy that takes advantage of the benefits of both antegrade and retrograde delivery. Strategies for myocardial protection include warm versus cold blood cardioplegia, antegrade versus retrograde delivery, and intermittent versus continuous perfusion. Administration of the Buckberg solution is part of the overall strategy of controlled reperfusion, referred to as the integrated technique (3). An integrated myocardial preservation technique coordinates the myocardial protective strategies with the continuity of the operation so that the surgical procedure is never interrupted (37).

Recent studies show that the combined benefits of antegrade and retrograde perfusion can be achieved by simultaneous antegrade and retrograde delivery via the coronary sinus and aorta or vein grafts, and a manifold has been developed to facilitate intraoperative delivery (Fig. 4) (37). Experimental and clinical studies have documented the safety of simultaneous arterial and coronary sinus perfusion to reduce myocardial edema during this combined perfusion method (38).



**Figure 4. Clinical method of simultaneously delivering antegrade/retrograde cardioplegia to ensure protection of jeopardized myocardium. Please note that this system allows for antegrade or retrograde delivery separately or simultaneous coronary graft and retrograde delivery. In addition, pressure monitoring is easily accomplished**  
(Reproduced from Buckberg GD. Surgical myocardial protection: update on current techniques of myocardial protection. Ann Thorac Surg 1995;60(3):805-14, Copyright © 1995 with permission of Elsevier)

**Table 2. Components of Buckberg solution**

Component	Concentration	Purpose
Blood	20 -30% Hct	O2 delivery
THAM - trishydroxylmethylaminomethane	pH 7.5 -7.6	Buffer acidosis
Osmolarity	350 -400 mOsm	Decrease edema
Aspartate, glutamate	13 mmol/L each	Replenish substrates
CPD - citrate phosphate dextrose	0.15 -0.25 mmol/L-Ca	Limit calcium
Glucose	>400 mg/dL	Hyperglycemia
KCl	8 -10 mEq/L	Cardioplegia

(Data from Comas GM, Esrig BC, Oz MC. Surgery for myocardial salvage in acute myocardial infarction and acute coronary syndromes. Heart Fail Clin 2007;3(2):181-210, Copyright © 2007 with permission of Elsevier)

The surgical strategy of controlled reperfusion includes several stages (3, 4, 11, 12). First, CPB is employed with LV decompression as required. Initially, antegrade cardioplegia with warm Buckberg solution is begun to re-supply ATP stores. Cold high  $K^+$  cardioplegia is given for rapid diastolic arrest. The Buckberg solution also delivers glutamate and aspartate, substrates of the Krebs cycle, which allows ATP generation to continue. Retrograde cardioplegia is given to promote sufficient cooling and arrest in ischemic areas. Uniform temperature is assessed. Following each distal anastomosis, cold cardioplegia is infused into each graft and the aorta at 200 mL/min over 1 minute and retrograde infusion through the coronary sinus for 1 minute. After completing distal anastomoses, warm blood cardioplegia enriched with metabolic substrates and the protective components is infused at 150 mL/min for 2 min into the aortic root and all grafts. This is followed by unclamping of the aorta and further infusion of the warm blood cardioplegia into the appropriate vein grafts at 50 mL/min for 18 minutes while proximal anastomoses are performed. This controlled rate of reperfusion minimizes cellular edema and myocyte damage. Revascularization occurs in an order that addresses ischemic areas first. The heart is allowed to recover in an empty, beating state on bypass for 30 min or more, as aerobic metabolism gradually supports return of regional contractile function.

The use of the Buckberg solution and technique has been shown to preserve myocardium and improve outcomes. In a multicenter trial (11), the results of surgical revascularization with controlled reperfusion using the Buckberg solution were evaluated in 156 consecutive patients with acute coronary occlusion and compared to 1203 patients who underwent PTCA as the primary therapy. In this series of patients with ischemic times averaging 6 hours, overall mortality was 3.9% despite the high prevalence of multivessel disease and cardiogenic shock. This integrated technique particularly is practicable to patients in cardiogenic shock, thus average mortality has been decreased to 9.1% in this patients (3, 4, 11, 36).

### Other surgical approaches

The other approaches for surgical revascularization in the setting of AMI include off-pump CABG (OPCAB), beating on-pump CABG (ONCAB), and right heart-assisted CABG (39). The intent of OPCAB procedure on a beating heart is to avoid the adverse side effects typically associated with CPB (40). OPCAB has lower morbidity and mortality, shorter hospital length of stay, lower troponin and other inflammatory markers levels, less time on mechanical ventilation, less blood transfusions, and cost containment.

In a large retrospective study utilizing prospectively collected data from the Society of Thoracic Surgery database, Magee et al. (41) have sought to analyze the contemporary use of OPCAB in patients undergoing multivessel CABG, to determine the benefits in terms of mortality and morbidity associated with beating heart techniques and avoidance of CPB, and to examine subsets of patients most likely to benefit from OPCAB. They concluded that OPCAB provides some survival benefit to most patient subgroups. Higher risk patients such as reoperative CABG, diabetics, and the elderly may gain the most benefit. The OPCAB can be performed with a reasonably low morbidity and

lower early and late mortality in high-risk patients with AMI. It has also become an applicable approach, even in patients with multi-vessel disease.

The OPCAB on a beating heart causes significant hemodynamic compromise during displacement of the heart. Right heart -assisted CABG is a good alternative to avoid this adverse effects mainly caused by right-heart compression (42). There is no an oxygenator in CPB circuit in this technique.

### Cardiogenic shock

Cardiogenic shock is the leading cause of death in patients hospitalized with AMI and is associated with a poor prognosis (4, 43, 44). The incidence of cardiogenic shock complicating AMI ranges from 5% to 15%. Cardiogenic shock is accompanied by 80 to 90% mortality rates; the loss of more than 40% of functioning LV mass and its accompanying systemic inflammatory response are the chief contributors of cardiogenic shock. Other causes include severe right ventricular infarction, ventricular septal rupture, free wall rupture, and papillary muscle rupture with acute severe mitral regurgitation.

Cardiogenic shock complicating AMI is a medical emergency. To improve outcomes, early recognition, prompt supportive measures and definitive management is mandatory. Treatment strategies should focus on prompt reperfusion and hemodynamic support (45). The primary approach includes emergent angiography and revascularization using PCI or CABG, with the assistance of IABP counterpulsation.

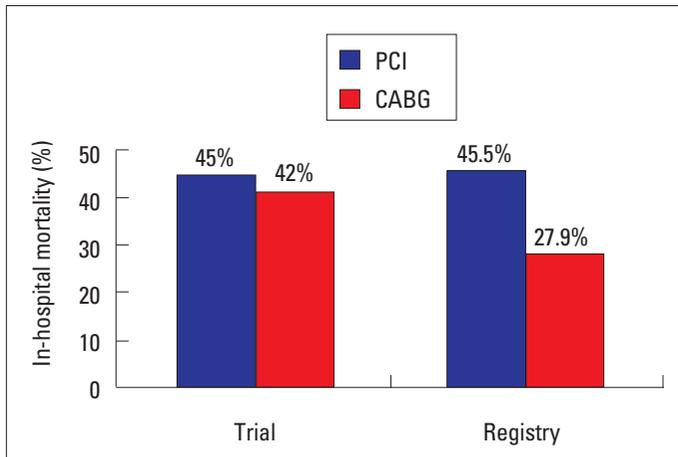
Emergency surgical revascularization in AMI complicated by cardiogenic shock has been shown to improve survival (46-49). Many studies support early surgery as valid alternative in the treatment of cardiogenic shock after AMI (46-51).

Recently, in the SHOCK (Should We Emergently Revascularize Occluded Coronaries for Cardiogenic Shock) trial, Hochman et al. (50) showed that early revascularization (PCI or CABG) within 6 hours of diagnosis of cardiogenic shock confers survival benefits over medical treatment, especially in those patients under 75 years of age.

There are no trials randomizing patients to PCI versus CABG in the setting of cardiogenic shock (51). In the SHOCK trial, surgically revascularized patients were more likely to have left main disease and 3-vessel disease, and higher prevalence of diabetes than those treated with PCI (50). In-hospital mortality for patients undergoing PCI was equivalent to surgical mortality rate (45.3% vs 42.1%) (Fig. 5) (51). The trial was not designed to compare percutaneous and surgical revascularization strategies. Furthermore, the SHOCK trial demonstrated that one third of catheterized patients underwent surgery (49, 50). In the SHOCK Registry, among 136 patients with cardiogenic shock who underwent emergent CABG, in-hospital mortality was 27.9% compared to 45.5% in 268 patients undergoing PCI (Fig. 5).

The SHOCK trial showed that early revascularization not only provided substantial survival benefit in patients with cardiogenic shock, but also resulted in much better long-term quality of life during one-year follow-up (49).

In another randomized trial, Hochman et al. (48) showed that a strategy of early revascularization resulted in a 13.2% absolute and a 67% relative improvement in 6-year survival compared with initial medical stabilization.



**Figure 5. In-hospital mortality with percutaneous coronary intervention (PCI) and coronary artery bypass graft surgery (CABG) in the early revascularization arm of the randomized SHOCK trial compared to the non-randomized larger SHOCK registry**  
(Reproduced from Menon V, Hochman JS. Management of cardiogenic shock complicating acute myocardial infarction. *Heart* 2002;88(5):531-7, Copyright© 2002 with permission of BMJ Publishing Group Ltd)

Lastly, a recent report from the SHOCK Trial and Registry showed a clear survival advantage for CABG over PCI at 30-day follow-up in patients with left main coronary disease (46).

The IABP counterpulsation is beneficial for the initial stabilization of patients with cardiogenic shock, and is favored over the use of vasopressors and inotropes alone. Studies have shown that IABP use results in initially hopeful clinical and hemodynamic responses; however, death was only delayed by this modality in the majority of studies (52). It is particularly helpful as a bridge to PCI or CABG in ventricular septal defect, acute mitral regurgitation, intractable ventricular arrhythmias and refractory angina (47). It is most applicable in the scenario of cardiogenic shock (53).

Many mechanical circulatory supports used in various clinical scenarios of cardiogenic shock include LVAD or biventricular assist devices or extracorporeal membrane oxygenation as a bridge to heart transplantation (43-47, 54).

## Conclusion

Surgery or PCI as early revascularization strategy after AMI currently remains a controversial topic. Each revascularization strategy is a safe and useful therapeutic means in selected patients.

Emergency CABG is an important component of an optimal treatment strategy in patients with AMI. Surgery also may be performed with excellent results when surgical timing and selected subset of patients with AMI are appropriate.

It is important that the optimal treatment strategy in patients with AMI is decided after joint consultation between an invasive cardiologist and a cardiovascular surgeon. Alternatively, hybrid intervention (PCI+CABG) should be put on the agenda.

Lastly, surgery as early revascularization after AMI should be considered after a 3-day waiting period, especially in patients without structural complications and ongoing ischemia.

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