

CHEST[®]

Official publication of the American College of Chest Physicians



Management of Perioperative Myocardial Infarction in Noncardiac Surgical Patients *

Adebola O. Adesanya, James A. de Lemos, Nancy B. Greilich and Charles W. Whitten

Chest 2006;130:584-596
DOI 10.1378/chest.130.2.584

The online version of this article, along with updated information and services can be found online on the World Wide Web at:
<http://chestjournal.chestpubs.org/content/130/2/584.full.html>

Chest is the official journal of the American College of Chest Physicians. It has been published monthly since 1935. Copyright 2006 by the American College of Chest Physicians, 3300 Dundee Road, Northbrook, IL 60062. All rights reserved. No part of this article or PDF may be reproduced or distributed without the prior written permission of the copyright holder.
(<http://chestjournal.chestpubs.org/site/misc/reprints.xhtml>)
ISSN:0012-3692

A M E R I C A N C O L L E G E O F
 C H E S T
P H Y S I C I A N S[®]



Management of Perioperative Myocardial Infarction in Noncardiac Surgical Patients*

Adebola O. Adesanya, MBBS, FCCP; James A. de Lemos, MD; Nancy B. Greilich, MD; and Charles W. Whitten, MD

Perioperative myocardial infarction (PMI) is a major cause of morbidity and mortality in patients undergoing noncardiac surgery. The incidence of PMI varies depending on the method used for diagnosis and is likely to increase as the population ages. Studies have examined different methods for prevention of myocardial infarction (MI), including the use of perioperative β -blockers, α_2 -agonists, and statin therapy. However, few studies have focused on the treatment of PMI. Current therapy for acute MI generally involves anticoagulation and antiplatelet therapy, raising the potential for surgical site hemorrhage in this population. This article reviews the possible mechanisms, diagnosis, and treatment options for MI in the surgical setting. We also suggest algorithms for treatment. (CHEST 2006; 130:584–596)

Key words: anticoagulation; myocardial ischemia; noncardiac surgery; percutaneous coronary intervention; perioperative myocardial infarction; platelet inhibitors

Abbreviations: ACC = American College of Cardiology; ACE = angiotensin-converting enzyme; AHA = American Heart Association; CABG = coronary artery bypass grafting; CAD = coronary artery disease; CHF = congestive heart failure; CK-MB = creatinine kinase-MB; HMG-CoA = hydroxy-3-methylglutaryl coenzyme A; IABP = intra-aortic balloon pump; LMWH = low-molecular-weight heparin; MI = myocardial infarction; NSTEMI = non-ST-segment elevation myocardial infarction; PCI = percutaneous coronary intervention; PMI = perioperative myocardial infarction; STEMI = ST-segment elevation myocardial infarction; UFH = unfractionated heparin

Learning Objectives: 1. Understand what risk factors are useful in assessing risk for perioperative myocardial infarction. 2. Understand the diagnostic criteria for myocardial infarction and how those criteria may be altered in the perioperative setting. 3. Understand therapeutic options for perioperative myocardial infarction.

THE CLINICAL PROBLEM

Approximately 30 million surgeries are performed annually in the United States. One million of these patients have known coronary artery disease (CAD), and an additional 2 to 3 million are at risk for CAD. The patients with CAD and those at risk for CAD have higher rates of perioperative myocardial

infarction (PMI), cardiac death, and other morbidity related to ischemic heart disease. Mortality from myocardial infarction (MI) after noncardiac surgery is believed to be 10 to 15%,¹ similar to that in nonsurgical patients. This is in contrast to older studies^{2,3} that indicate higher mortality in postsurgical patients.

Many recent studies, reviews, and guidelines have focused on the prevention of myocardial ischemia and MI in the perioperative period, but available

*From the Department of Anesthesiology and Pain Management (Drs. Adesanya, Greilich, and Whitten), and Department of Medicine, Division of Cardiology (Dr. de Lemos), University of Texas Southwestern Medical Center at Dallas, Dallas, TX. Manuscript received June 16, 2005; revision accepted December 20, 2005.

The following authors have indicated to the ACCP that no significant relationships exist with any company/organization whose products or services may be discussed in this article submission: Adebola O. Adesanya, MBBS, FCCP; James A. DeLemos, MD; Nancy B. Greilich, MD; Charles W. Whitten, MD.

Reproduction of this article is prohibited without written permission from the American College of Chest Physicians (www.chestjournal.org/misc/reprints.shtml).

Correspondence to: Adebola O. Adesanya, MD, FCCP, Department of Anesthesiology and Pain Management, University of Texas Southwestern Medical Center, 5323 Harry Hines Blvd, Dallas, TX 75390; e-mail: adebola.adesanya@utsouthwestern.edu
DOI: 10.1378/chest.130.2.584

literature on the management of postoperative MI once it has occurred is limited. No randomized controlled trials addressing the management of MI in the postoperative period exist, hence the need to extrapolate management strategies from existing studies.

INCIDENCE

The incidence of PMI is expected to increase as the population ages and more complex operations are performed on high-risk patients. In a prospective cohort study of men undergoing noncardiac surgery, Ashton et al⁴ found that patients with coronary disease (high-risk stratum) had a 4.1% incidence of MI, patients with peripheral vascular disease but no evidence of coronary disease (intermediate-risk stratum) had a 0.8% incidence, and patients with high atherogenic risk factor profiles but no clinical atherosclerosis (low-risk stratum) had a 0% incidence. Factors independently associated with MI included age > 75 years, signs of heart failure on the preoperative examination, evidence of CAD, and a planned vascular operation.

Eagle et al⁵ reviewed patients enrolled in the Coronary Artery Surgery Study registry who then underwent noncardiac surgery. Patients with medi-

For instructions on attaining CME credit, see page A-85

cally treated CAD undergoing major surgery (abdominal, thoracic, and head and neck) had a PMI rate of 2.7% and an overall death rate of 3.3%. This compared to rates of 0.8% and 1%, respectively, in patients undergoing similar surgery who did not have CAD. Cardiac complications and PMI occurred more commonly in patients undergoing major vascular surgery. However, since major vascular surgery makes up only a small percentage of all surgeries, most patients who present with PMI are likely to be undergoing another type of surgery.

Based on the available literature,³⁻⁸ the incidence of PMI in low-risk patients without a history of CAD undergoing noncardiac surgery is 1 to 3% but up to 38% in some studies⁶⁻¹⁰ of high-risk patients with a history of CAD. The reported incidence is dependent on the sensitivity and specificity of the method of diagnosis, which varies widely in published studies. In addition, since most PMIs are silent,^{3,4,9,10} the true incidence of PMI may be underestimated.

RISK FACTORS

Major abdominal, thoracic, and head and neck surgeries are associated with a high risk of cardiovas-

cular complications.⁵ In particular, patients undergoing vascular surgical procedures are at especially high risk for PMI.^{4,11} The risk factors for CAD and vascular disease overlap, and these patients also have a higher prevalence of asymptomatic coronary disease.¹¹

Sprung et al¹² identified 107 patients from the Cleveland Clinic Vascular Surgery Registry in whom PMI developed during hospitalization for a vascular surgery procedure. The variables found to be associated with an increased risk of cardiac death in multivariate analysis were recent congestive heart failure (CHF) and increased intraoperative use of blood. Landesberg et al⁹ found the presence of postoperative "long-duration" ST-segment depression (single duration > 20 to 30 min or cumulative duration > 1 to 2 h) to be associated with adverse cardiac outcome. Short-duration ST-segment depression (< 10 min) was not associated with cardiovascular complications. Diehl et al¹³ also found that increased perioperative blood loss and transfusion during vascular surgery cases were associated with a higher incidence of postoperative complications and death. In the case of low-risk patients, Barone et al¹⁴ found intraoperative hypotension as the only significant factor associated with an elevated risk of PMI and death. In summary, the combined data suggest that the risks for postoperative MI are as follows: (1) poor preoperative cardiac status (CAD, history of CHF); (2) postoperative hypotension; (3) new (long-duration) intraoperative ST-T changes; and (4) increased intraoperative blood loss and transfusion.

Patients scheduled to undergo noncardiac surgery should undergo a comprehensive risk assessment to stratify them into low-risk and high-risk groups. The American College of Cardiology (ACC) and American Heart Association (AHA) have published practice guidelines¹⁵ that recommend assessment of comorbidities and exercise tolerance, as well as the type of surgery to be performed, to determine the overall risk of perioperative cardiac complications. Patients who have undergone a revascularization procedure within the previous 5 years and are asymptomatic, as well as those who have undergone adequate noninvasive testing with favorable results within the preceding 2 years, are deemed at low risk and may proceed to surgery.

There is growing evidence indicating that patients who have recently undergone coronary revascularization with PCI and stent implantation may be at increased risk of perioperative in-stent thrombosis and MI.^{16,17} The ACC/AHA guidelines¹⁵ recommend a delay of at least 2 weeks and ideally 4 to 6 weeks between implantation of a bare metal stent and noncardiac surgery to reduce the risk of PMI. This allows for 4 full weeks of dual-antiplatelet

therapy during stent re-endothelialization and 2 weeks for the antiplatelet effect to dissipate. The risk period for in-stent thrombosis may be further extended in patients implanted with a drug-eluting stent, since the drug that prevents neointimal proliferation delays in-stent endothelialization. We recommend delaying elective surgery for 3 months following a sirolimus-eluting stent and 6 months following a paclitaxol-eluting stent to allow administration of the full recommended treatment courses of aspirin and clopidogrel to prevent stent thrombosis. In some circumstances, it may be preferable to place a bare metal stent, or perform balloon angioplasty without stenting, when surgery is anticipated in the near future.

MECHANISMS

The risk of perioperative MI peaks within the first 3 postoperative days,¹⁻³ a period of time when patients begin to mobilize fluids administered in the operating room, and a time when the thrombotic risk may be most pronounced. Surgery is accompanied by a catecholamine surge that is exacerbated by postoperative pain.¹⁸ Subsequent increases in heart rate and BP can lead to a diffuse myocardial oxygen supply/demand mismatch in the postoperative patient.^{19,20}

More recently, Badner et al¹ found that PMI occurred earlier than previously thought, with most events occurring on the day of surgery or the day after surgery. They also confirmed previous findings that PMI is most often silent^{4,9,10} and of the non-ST-segment elevation type.^{6,9}

Compared to nonoperative MI, the pathophysiology and mechanisms underlying PMI are less well understood. Nonoperative MIs are thought to occur from the rupture of a "vulnerable" atherosclerotic plaque due to shear forces from within the lumen of the vessel or from inflammatory processes within the plaque itself. A vulnerable plaque is one with a large inner lipid core consisting of thrombogenic lipids and macrophages covered by a thin fibrous cap, which often shows signs of inflammation at the shoulder region. Disruption of the fibrous cap leads to local platelet aggregation and thrombosis, which can lead to interruption of coronary blood flow and myocardial ischemia. Prolonged and severe ischemia may then progress to myocardial necrosis and clinically evident infarction. The pathophysiologic events described above are thought to cause the entire spectrum of acute coronary syndromes (unstable angina, non-ST-segment elevation MI [NSTEMI], and ST-segment elevation MI [STEMI]); the individual presentation (which includes asymptomatic

plaque rupture) is determined by the severity of blood flow limitation due to thrombus and the presence of adequate collateral circulation to the affected myocardium. STEMI results when complete thrombotic occlusion of an epicardial coronary artery occurs and there is poor collateral flow to the affected myocardial territory. The severity of stenosis diagnosed at coronary angiography does not predict which coronary vessel will develop plaque rupture and thus be the "culprit" vessel during MI.^{21,22} In fact, less severe occlusions and less mature coronary plaques are the ones most likely to rupture and cause acute MI.²³ This is probably because of the inability of angiography to identify and distinguish unstable plaques from critical but stable coronary stenosis.

With regard to PMI, the mechanism of ischemia and infarction is not as well understood but is thought to be similar to nonoperative MI. Increases in sympathetic discharge^{19,20} with accompanying elevation of heart rate and BP as well as the procoagulant postoperative environment²⁴ may promote plaque rupture and coronary thrombosis.

Ischemia begins in most patients at the end of surgery and during emergence from anesthesia. It usually manifests as ST-segment depression on continuous ECG monitoring.^{6,9} The ST-segment depression is preceded by an increase in heart rate, which may not exceed 90 to 100 beats/min and may resolve even if untreated.⁶ Patients with prolonged ST-segment depression often have biochemical evidence of PMI in the form of increased cardiac troponin levels.⁶ The majority of PMIs are silent, showing no signs or symptoms, and can be completely overlooked if serum troponin levels are not measured and continuous ECG with trend analysis is not performed. The events described above may lead one to believe that PMI is most likely due to prolonged stress-related ischemia (manifesting as ST-segment depression on ECG) rather than plaque rupture. However, it is not known whether stress induced ischemia alone or in combination with plaque rupture is responsible for PMI.

In the case of fatal PMI, Dawood et al²⁵ found evidence of plaque disruption in 55% and plaque hemorrhage in 45% of 42 heart specimens at autopsy. The degree of coronary artery stenosis did not predict infarct territory in more than half of the patients. Cohen and Aretz²⁶ also found that plaque rupture was associated with 46% of fatal PMI at autopsy. Intracoronary thrombus was observed in 35% of patients, and 31% had the thrombus at the site of plaque rupture. From existing autopsy studies,^{25,26} approximately one half of the patients who die after PMI do not have evidence of plaque rupture or thrombosis in their coronary arteries even when they have extensive CAD. Cardiac death oc-

curred in these patients in the early postoperative period (days 1 to 3)²⁶ when postoperative ischemia peaks.⁹ In the other half in whom plaque rupture or coronary thrombosis was detected, cardiac death had no correlation to the end of surgery.²⁶

In summary, coronary plaque rupture with thrombosis is an important etiologic mechanism of postoperative MI. It is very likely that PMI also results from prolonged ischemia (manifested as ST-segment depression on the ECG) in the presence of severe but stable CAD. This would explain the outcome benefits of perioperative β -blockade.^{27–29} Prolonged ischemia and coronary plaque rupture are not likely mutually exclusive in any given patient.

DIAGNOSIS

The World Health Organization criteria for MI in nonsurgical patients require that at least two of the following three conditions be met: history of ischemic-type chest pain, serial ECG changes, and elevated serum cardiac markers. A joint task force³⁰ of the ACC and European Society of Cardiology recommended that the definition of MI be broadened to include all patients who have elevation in cardiac biomarkers above the decision limit in the context of a clinical presentation consistent with acute ischemic heart disease. The diagnosis of PMI is more difficult because of the low incidence of chest pain.^{1–4} Pain, if present, is often masked by analgesia and residual anesthetics. The initial ECG findings in nonsurgical patients after MI are diagnostic in 50% of cases, abnormal but not diagnostic in 40%, and normal in 10%.³¹

Martinez et al³² also found that routine ICU monitoring with a five-electrode/two-lead ECG with ST-segment trending detected ischemia in only 3% of high-risk postoperative patients when compared to the 12-lead ECG. The majority of ischemic events occurred in leads V₂, V₃, and V₄, and not in the more commonly monitored leads II and V₅. Preexisting abnormalities such as left bundle-branch block, left ventricular hypertrophy with strain, paced rhythm, and digitalis effect can make the ECG difficult to interpret. Nonspecific ST-segment changes due to a variety of clinical conditions such as pericarditis or chest trauma can also complicate ECG interpretation. Postoperative MI is therefore often diagnosed using biomarkers. Creatinine kinase-MB (CK-MB) has traditionally been the marker of choice. It has a sensitivity of 77 to 92% in nonsurgical patients and 60 to 75% in surgical patients, and a specificity of 100% in nonsurgical and 80 to 95% in surgical patients.^{30,33}

Troponin T and troponin I are newer cardiac

biological markers that are rapidly released into the circulation after myocyte injury. They have nearly absolute myocardial tissue specificity, as well as high sensitivity,^{34–36} and are now the biomarkers of choice to detect myocardial injury. An increased value for cardiac troponin is defined as a measurement exceeding the 99 percentile of a reference control group and is determined by each laboratory. Troponin values, however, have a low sensitivity in the early phase of MI, raising the possibility of underdiagnosis in early MI. Simultaneous measurement of biomarkers with higher sensitivity in early MI (CK-MB, myoglobin) can help clarify the diagnosis. To date, there are no definitive criteria or guidelines for the diagnosis of MI in the surgical setting. Figure 1 shows the timing of release of various biomarkers following acute, ischemic MI.

Cardiac troponin values may remain elevated for 10 to 14 days after myocardial necrosis. When the duration of troponin elevation is unclear, measurement of early release biomarkers (increased in blood within 6 h after onset of myocardial ischemia) such as CK-MB or myoglobin can indicate if troponin elevation is due to new-onset ischemia.^{36,37} While troponin elevation is indicative of myocardial necrosis, it does not imply an ischemic etiology of myocardial injury. Indeed, other causes of cardiac injury including CHF,³⁸ pulmonary embolism,³⁹ and sepsis⁴⁰ are commonly associated with troponin elevation. These situations may present similarly to PMI, and thus additional testing may be required with echocardiography and/or CT angiography. Table 1 illustrates different techniques that can be used to diagnose MI in the postoperative patient.

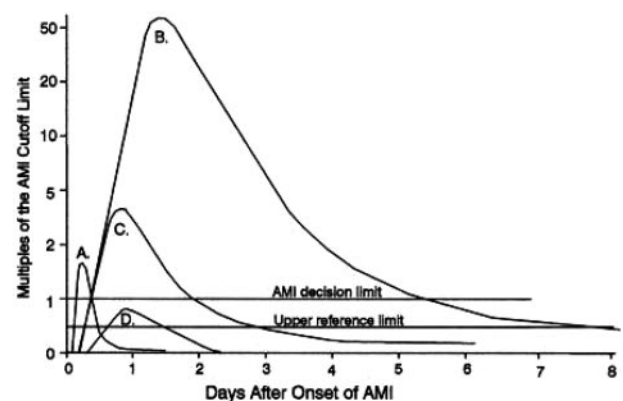


FIGURE 1. Timing of release of various biomarkers following acute, ischemic MI (AMI). Peak A indicates early release of myoglobin or CK-MB isoforms after acute MI. Peak B indicates cardiac troponin after acute MI. Peak C indicates CK-MB after acute MI. Peak D indicates cardiac troponin after unstable angina. Data are plotted on a relative scale, where 1.0 is set at the acute MI cutoff concentration. Reproduced with permission from Wu et al.³⁴

Table 1—Diagnosis of MI by Different Techniques*

Variables	Factors
Pathology	Myocardial cell death
Biochemistry	Markers of myocardial cell death recovered from blood samples (CK-MB, myoglobin, troponin T, or troponin I)
ECG	Evidence of myocardial ischemia; ≥ 1 mm of ST-segment elevation in more than two contiguous leads; ST-segment depression; T-wave inversion; evidence of new Q waves
Imaging (two-dimensional echocardiogram)	Cardiac wall motion abnormalities

*Modified from Alpert et al.⁴¹

For patients suspected of having myocardial ischemia or MI, blood should be obtained for measurement of biomarkers immediately and serially through 6 to 9 h.^{37,42} Along with other clinical factors such as left ventricular function, the degree of biomarker elevation is related to clinical risk.^{6,43} Biomarkers have also been shown to be independent predictors of outcome after noncardiac surgery even when the diagnostic criteria for MI are not met.^{29,42,43} In patients with known or suspected CAD who are undergoing high-risk procedures, ACC/European Society of Cardiology joint guidelines recommend obtaining ECGs at baseline, immediately after surgery, and on the first 2 days following surgery. Cardiac biomarkers are used for high-risk patients and those with clinical, ECG, or hemodynamic evidence of cardiovascular dysfunction.⁴⁴

THERAPEUTIC STRATEGIES

For the purpose of treatment, PMI can be categorized into NSTEMI and STEMI as is done in the nonsurgical setting. Most patients with PMI have NSTEMI manifesting as ST-segment depression on the ECG.^{4,6,9,19}

Generally, the initial treatment of NSTEMI in the nonoperative setting includes medical stabilization and risk stratification, whereas STEMI requires acute reperfusion therapy with fibrinolytic agents or percutaneous coronary intervention (PCI). Fibrinolytic therapy is not currently recommended in NSTEMI and in fact may be detrimental.⁴⁴ The treatment options for PMI are limited by the risk of surgical site bleeding in the early postoperative period.

Risk Stratification in ACS

Risk stratification plays a critical role in identifying patients at risk for PMI. The discussion of preoperative risk assessment is beyond the scope of this review but is covered in the updated ACC/AHA guidelines¹⁵ for preoperative cardiovascular evalua-

tion for noncardiac surgery. Risk stratification also plays a key role in selecting the intensity and type of therapy for patients with NSTEMI. In the nonoperative setting, simple tools such as cardiac troponin, ECG changes, and clinical scoring systems incorporating clinical variables with ECG findings and cardiac biomarker results are used to categorize patients into those at high risk vs low risk of death and recurrent ischemic complications.^{45,46} This information is used to select candidates for aggressive antiplatelet and antithrombotic therapies, as well as for coronary angiography and revascularization. Table 2 shows characteristics of patients with NSTEMI who should be considered to be at high risk.

A clear benefit of early angiography and PCI, when needed, has been reported in high-risk groups. In contrast, little benefit has been observed for routine coronary angiography and revascularization in low-risk groups.^{48,49}

Other markers of severe underlying disease such as history of known CAD, previous MI, prior PCI or coronary artery bypass grafting (CABG), CHF, pulmonary edema, new mitral regurgitation murmur, elevated inflammatory markers (*ie*, C-reactive protein, fibrinogen, interleukin-6), B-type natriuretic protein, or N-terminal prohormone of B-type natriuretic hormone in upper quartiles, and renal insufficiency might also be helpful for risk assessment in NSTEMI.^{50,51}

Table 2—Characteristics of Patients With Nonoperative NSTEMI at Acute High Risk for Rapid Progression to MI or Death Who Should Undergo Coronary Angiography Within 48 h*

Recurrent resting pain
Dynamic ST-segment changes: ST-segment depression ≥ 0.1 mV or transient (< 30 min) ST-segment elevation ≥ 0.1 mV
Elevated troponin-I, troponin-T, or CK-MB levels
Hemodynamic instability within the observation period
Major arrhythmias (ventricular tachycardia, ventricular fibrillation)
Early postinfarction unstable angina

*Adapted from Silber et al.⁴⁷

The application of these risk stratification tools to patient management in the perioperative setting is challenging because limited data are available in perioperative patients and the bleeding risk associated with aggressive antiplatelet and antithrombotic therapies (which are required with PCI) is increased. Thus, in the perioperative setting, a more conservative approach is recommended, with urgent angiography and PCI reserved for patients with STEMI or those with NSTEMI who are at very high risk or hemodynamically unstable. Figures 2, 3 illustrate the suggested algorithm for management of perioperative NSTEMI and STEMI.

Medical Therapy

Medical therapy in the postoperative patient with MI consists of aggressive pain control, β -blockade, antiplatelet therapy, and anticoagulants (if not contraindicated) [Table 3].

Antiplatelet Therapy

Antiplatelet therapy is achieved principally by means of aspirin, which should be administered (325 mg, chewed) as soon as MI is suspected. Aspirin inhibits platelet aggregation and has been shown to improve outcomes when administered early.⁵²⁻⁵⁶ As-

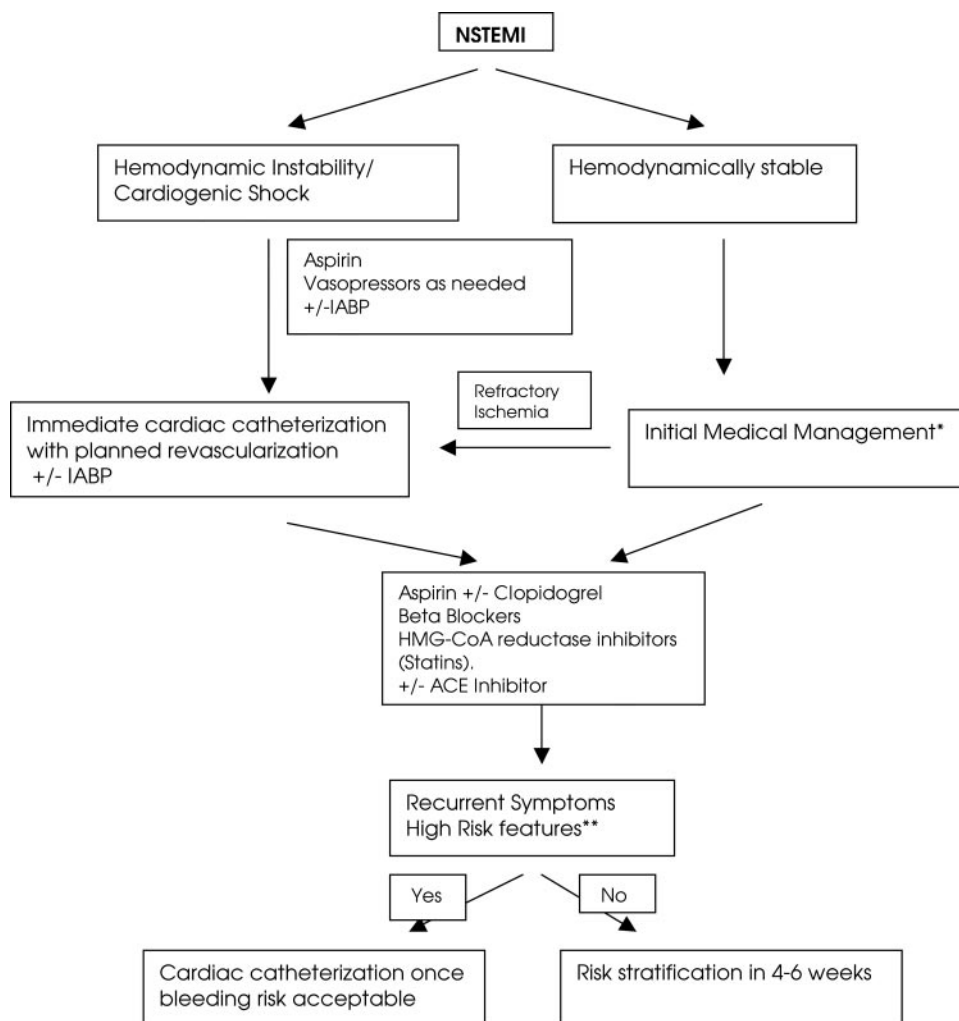


FIGURE 2. Suggested algorithm for management of perioperative NSTEMI. *Initial medical management includes morphine sulfate, oxygen, nitroglycerin, aspirin with or without UFH if bleeding risk is acceptable. **High-risk features include major arrhythmias (ventricular tachycardia, ventricular fibrillation), dynamic ST-segment depression in multiple leads, an ECG pattern that precludes assessment of ST-segment changes, evidence of severe CHF, or left ventricular dysfunction. Refractory ischemia is ischemia unresponsive to medical management.

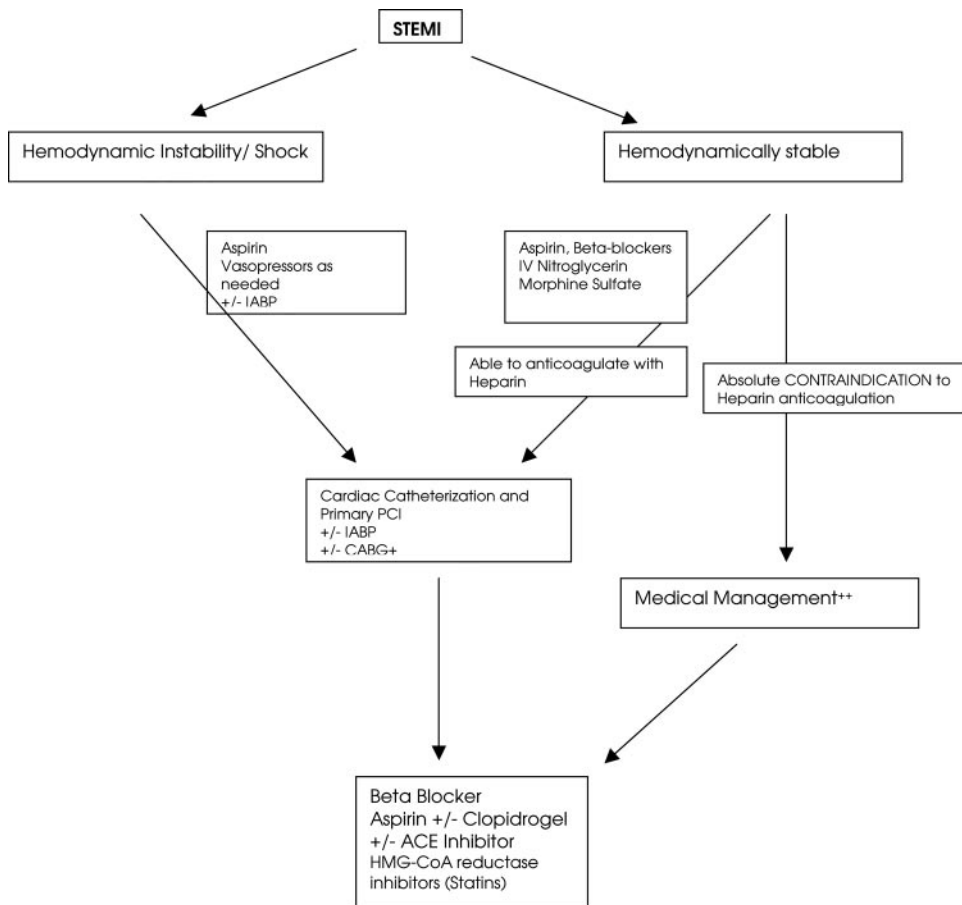


FIGURE 3. Suggested algorithm for management of perioperative STEMI. + Clopidogrel should not be administered if CABG is planned within 5 days. ++ Medical management includes morphine sulfate, oxygen, nitroglycerin, and aspirin.

pirin, however, is a weak antiplatelet agent because it inhibits only one of the pathways (thromboxane A₂) leading to platelet aggregation.

Other platelet inhibitors include the thienopyridines

ticlopidine and clopidogrel, agents that block adenosine diphosphate-mediated platelet aggregation. Because of its preferable side effect and safety profile, clopidogrel has completely replaced ticlopidine for all clinical indi-

Table 3—Medical Therapy for AMI

Medications	Dosage	Goals of Treatment
Aspirin	325 mg po	Inhibition of platelet aggregation and activation
Morphine sulfate	2 to 5 mg IV; repeat as needed	Pain control
Nitroglycerin infusion	50 µg/min IV; titrate upwards as mean arterial pressure tolerates	Pain elimination, ST-segment normalization
β-Adrenergic blockade		Heart rate < 70 beats/min while maintaining mean arterial pressure > 75 mm Hg; pain resolution; ST-segment normalization
Metoprolol	1 to 5 mg IV; incrementally repeat as needed up to 15 mg total dose	
Esmolol	10 to 50 mg IV bolus; infusion up to 200 µg/kg/min	
ACE inhibitors		Improve long-term and short-term outcomes
Captopril	6.25 to 12.5 mg po q8h; increase cautiously to avoid hypotension	
Ramipril	2.5 to 5 mg po bid	

cations. Clinical trials^{57,58} have demonstrated a small reduction in stroke, MI, or vascular death with clopidogrel when compared to aspirin. Clopidogrel can be used as an alternative to aspirin in patients with aspirin allergy or intolerance but is primarily used in combination with aspirin in patients with acute coronary syndrome and those who have recently had an intracoronary stent placed. When administered in combination with aspirin, clopidogrel increases the relative risk for major perioperative bleeding by approximately 50%^{44,57,58} and should be discontinued at least 5 days before elective surgical procedures. However, the absolute risk for hemorrhage remains low, and urgent or emergent surgery should not be delayed because a patient is receiving clopidogrel and aspirin. Glycoprotein IIb/IIIa platelet receptor antagonists interfere with the glycoprotein IIb/IIIa platelet receptor that is involved in the final common pathway in platelet aggregation. These agents include the chimeric monoclonal antibody abciximab and the nonantibody agents tirofiban and eptifibatid. IV use of these agents produces a high degree of inhibition of platelet aggregation, which is most beneficial in the setting of PCI. The increased risk of major bleeding with these agents precludes their use in the perioperative setting except in rare circumstances.

Anticoagulants

Acute MI is known to be associated with increased thrombin activity.^{44,59,60} Plaque instability and rupture result in tissue factor expression leading to thrombin generation.^{59,60} Thus, fibrinolytic and antiplatelet therapy could be combined with anticoagulant or antithrombin therapy. Unfractionated heparin (UFH) is an indirect thrombin inhibitor and works only after binding to antithrombin III. It is frequently used to treat patients with MI. Low-molecular-weight heparins (LMWHs) also activate antithrombin III but have greater activity against Factor Xa. They have predictable kinetics, can be administered by twice-daily subcutaneous injections, and do not require monitoring of the partial thromboplastin time at subsequent dosage adjustment. These pharmacologic properties offer advantages for their use in clinical practice, but the long half-life is a disadvantage in the early perioperative setting when bleeding risks are highest.

In a meta-analysis,⁶¹ the use of enoxaparin (LMWH) resulted in a 20% reduction in the combined end point of death and MI when compared to UFH. The reduction in the combined end points achieved statistical significance at day 8 and persisted through days 14 and 43 after treatment. Minor hemorrhage was clearly increased in patients treated with enoxaparin.

In the nonoperative setting, either IV UFH or subcutaneous LMWH are routinely administered in combination with aspirin.^{62,63} In the operative setting, IV UFH is indicated if the suspicion of plaque rupture is high and the bleeding risks are acceptable based on the type of operation. For example, even small amounts of bleeding may be unacceptable in neurosurgical procedures. In contrast, with surgery involving the limbs, bleeding may be easily identified and controlled so that the tolerance for anticoagulation may be higher. Extremity fascial compartment pressures may need to be monitored to avoid compartment syndromes. Following major body cavity procedures, there are usually concerns about occult bleeding that may be difficult to diagnose.

LMWH is preferred^{61,63} in conservatively managed patients with nonoperative MI, provided renal insufficiency is not present. In the postoperative patient with MI, however, UFH is the anticoagulant of choice for both conservative management and PCI due to its easy reversibility with protamine if needed.

Pain Relief

Pain, if present, should be treated with opioid analgesics. IV morphine is preferred due to its preload-reducing properties. The ultimate goal of therapy is to eliminate ischemia. In addition to making patients more comfortable, pain relief may reduce the outpouring of catecholamines characteristic of the early stages of acute MI and thereby reduce myocardial oxygen consumption.

Nitroglycerin can also be added for pain relief. Nitrates cause nonendothelium-dependent coronary vasodilatation, reduced cardiac preload (venodilatation), and enhanced perfusion of ischemic myocardial zones. Two large studies^{64,65} found no survival benefit for nitrates, either early or at 1-year follow-up. Thus, the use of nitrates is probably optional in patients without evidence of ongoing ischemia. For patients with symptomatic ischemia, however, IV nitroglycerin may be very effective.

β-Adrenergic Blockade

IV β-blockers are indicated in the acute phase of MI unless there are major contraindications such as significant bradycardia (heart rate < 50 beats/min), decompensated CHF (rales over one half of lung fields), or severe COPD. Beneficial mechanisms may include reduced myocardial oxygen consumption, antagonism of arrhythmogenic and toxic biochemical effects of catecholamines, and direct reduction of ventricular fibrillation threshold.

Pooled data from 28 trials of β-adrenergic receptor blockers revealed that the average mortality rate

decrease was 28% at 1 week, and that the most benefit was obtained in the first 48 h; reinfarction was reduced an average of 18%, and cardiac arrest was reduced 15%.⁶⁶ Early IV β -blockers followed by oral administration should be given to the majority of patients with MI who do not have overt CHF or shock at hospital admission.^{66,67} When left ventricular dysfunction is present, a short-acting β -adrenergic receptor blocker such as esmolol can be tried and then discontinued if hypotension or increased pulmonary congestion occurs.

Calcium-channel blockers should not be substituted for β -blockers. Most studies of calcium-channel entry blockers have failed to demonstrate any definite survival benefit, and some have shown an increased risk of death.^{68,69} The lack of benefit is probably related to the negative inotropic action of the calcium-channel blockers, with an adverse effect in patients with left ventricular failure.

Angiotensin-Converting Enzyme Inhibitors

Angiotensin-converting enzyme (ACE) inhibitors are an important adjunctive therapy in acute infarction. The mechanism by which these agents act to reduce mortality remains unclear. Several trials^{70–75} have demonstrated a clinically and statistically significant reduction in mortality.

It is reasonable to initiate therapy with ACE inhibitors within the first 48 h in the absence of contraindications and then discontinue the therapy in patients who do not have high-risk characteristics such as left ventricular ejection fraction < 45% with clinical evidence of heart failure, significant mitral regurgitation, or hypertension. Treatment should be initiated orally with low doses of any ACE inhibitor. Captopril has the shortest half-life; overdosing and inadvertent hypotension may be most easily correctable if it is used initially. If hypotension results from the early administration of ACE inhibitors, short-term mortality may be increased.⁷⁶ In the Heart Outcomes Prevention Evaluation trial,⁷⁶ the magnitude of benefit of ramipril was comparable to that observed with other secondary prevention measures, such as β -blockers, aspirin, and lipid-lowering agents.

Lipid-Lowering Agents

Survivors of acute coronary syndromes who were discharged receiving statin (hydroxy-3-methylglutaryl coenzyme A [HMG-CoA] reductase inhibitors) treatment had a reduced mortality at 6 months and 1 year.^{77,78} In the Myocardial Ischemia Reduction With Aggressive Cholesterol Lowering study,⁷⁷ statin therapy was associated with a significant reduction in the composite end point of death, nonfatal myocar-

dial reinfarction, and cardiac arrest with resuscitation or recurrent symptomatic myocardial ischemia. If statins are withdrawn after admission for an acute coronary syndrome, mortality rates and nonfatal reinfarction increase compared with patients who continue to receive them, and tend to be higher when compared with patients who never received statins at all.⁷⁸

Other Therapies

Combining medical therapy with an intra-aortic balloon pump (IABP) is an option that can be considered in patients refractory to medical therapy and in the setting of ischemic cardiogenic shock. Intra-aortic balloon counterpulsation increases coronary blood flow by raising diastolic BP. In addition, it reduces left ventricular stroke work by decreasing systemic afterload.

In nonsurgical patients, treatment with an IABP has been shown to increase early and late coronary artery patency rates when treatment with thrombolytic therapy has not recanalized the infarct-related artery.^{79,80} Other data also suggest that IABP therapy results in early recovery of left ventricular function^{81,82} and improved survival in patients presenting with ischemic cardiogenic shock treated with thrombolytic therapy.⁸³

The ACC/AHA guidelines for the management of patients with STEMI⁵⁶ recommend that intra-aortic balloon counterpulsation be used in the following: (1) patients with refractory hypotension (systolic BP < 90 mm Hg or 30 mm Hg below baseline mean arterial pressure); (2) patients with low cardiac output state; and (3) patients with recurrent ischemic-type chest discomfort and a potentially large area of myocardium at risk already receiving medical therapy. Patients with refractory polymorphic ventricular tachycardia or refractory pulmonary congestion may also benefit from intra-aortic balloon counterpulsation.

Urgent cardiac catheterization is recommended for patients with NSTEMI in whom ischemic signs and symptoms cannot be controlled with medical therapy, or those in whom ischemia leads to hemodynamic compromise. In addition, patients with heart failure or ventricular arrhythmias following an ischemic episode are at particularly high risk and should be considered for cardiac catheterization prior to discharge.

Acute Reperfusion Therapy

In the case of STEMI, although fibrinolytic therapy is normally indicated for patients with a diagnosis within 12 h of presentation in the nonoperative setting,^{52–55} it is a poor reperfusion choice after

noncardiac surgery due to the risk for severe bleeding. Other reperfusion treatment involves coronary angiography and direct PCI. Primary PCI is known to reduce mortality from MI and compares favorably with fibrinolytic therapy in MI unrelated to surgery.⁵⁹ In the setting of perioperative STEMI, primary PCI would be the reperfusion modality of choice, due to its lower risk for major hemorrhage. Berger et al⁶⁰ identified 48 patients at the Mayo Clinic between 1990 and 1998 who underwent coronary angiography for acute MI within 7 days after noncardiac surgery; 33 of the patients had STEMI (75%) and 15 had NSTEMI (25%) with ongoing chest pain or hemodynamic instability. Of 48 patients, 41 underwent angioplasty, 3 were referred for bypass surgery, and 1 was treated with intracoronary fibrinolytic therapy after unsuccessful angioplasty. The survival rate was 65% in this series (31 of 48 patients). The survival of 11 of 21 patients with cardiogenic shock and 9 of 12 patients with cardiac arrest was superior when compared to the outcome of patients not receiving reperfusion therapy. None of the patients had surgical site bleeding in the catheterization laboratory. Based on their study, the patients with PMI most likely to benefit from a strategy of immediate PCI or bypass surgery were those with acute thrombotic coronary occlusion reflected by a sudden onset of symptoms and significant ST-segment elevation on the ECG.

There are no prospective randomized studies directed at postoperative patients with MI. In fact, patients who have recently undergone surgical procedures have generally been excluded from all the major trials of fibrinolytic therapy because of the high risk of bleeding at the surgical site. The most important finding of the study by Berger et al⁶⁰ is that immediate coronary angiography and direct angioplasty, if appropriate anatomy is present, is feasible and appears to be safe in selected patients with MI early after noncardiac surgery. Cardiogenic shock and severe coronary disease are common in such patients. PCI involves balloon dilatation (angioplasty) of the culprit coronary vessel with or without stent placement. Postmortem observations and angiography suggest that balloon angioplasty very often leads to rupture of the obstructing plaque and vessel wall dissection followed by mural thrombus formation. This can lead to abrupt vessel closure during or shortly after balloon angioplasty in 2 to 5% of patients.^{84,85} Abrupt closure may result in MI (10 to 35%) and death (2 to 5%) despite urgent reintervention. Stents are placed in the majority of PCI procedures, partly because they are very effective in avoiding vessel closure.^{86,87} However, stenting is associated with a unique and devastating complication, namely (sub)acute thrombosis, which occurs in 1 to 4% of procedures.^{87,88} Unfortunately, the majority of patients who have this complication suffer

from MI and/or die,^{79,80} hence the need for dual-antiplatelet therapy with aspirin and clopidogrel to prevent thrombotic complications after PCI.

The dilemma in treating postoperative MI lies in the fact that virtually all treatment strategies require some form of anticoagulation, which may lead to excessive surgical site bleeding and hematoma formation. As discussed above, medical therapy with or without fibrinolytic therapy usually requires the administration of IV heparin in addition to analgesics, aspirin, β -blockers, and nitrates. In NSTEMI, the addition of clopidogrel (adenosine diphosphate receptor antagonist) is also recommended unless there is a need for urgent CABG, or if there is a high bleeding risk.⁴² The administration of a platelet glycoprotein IIb/IIIa inhibitor may be warranted in cases of ongoing ischemia with elevated cardiac troponin levels.⁴⁴ Coronary angiography and angioplasty with or without stent placement also requires infusion of heparin and often platelet glycoprotein IIb/IIIa receptor inhibitors followed by clopidogrel. The decision to administer anticoagulant and antiplatelet medications should be made in conjunction with the operating surgeon and cardiologist. The management of surgical patients who acquire PMI but require absolute hemostasis such as neurosurgical patients depends on whether the benefits of reperfusion outweigh bleeding risks.

FOLLOW-UP CARE OF PATIENTS AFTER PMI

Care of patients after PMI is more conservative than in the nonoperative setting, where cardiac catheterization and coronary revascularization are increasingly used in clinical practice. It is not uncommon to detect cardiac enzyme elevation after noncardiac surgery in patients with a low suspicion of cardiac ischemia. In such patients, it is reasonable to treat medically (non-invasively) and to defer definitive evaluation⁸⁹ in stable patients until 4 to 6 weeks after surgery. Typically, noninvasive stress testing is used for risk stratification in most patients, but cardiac catheterization is recommended for high-risk patients. At the time of discharge, most patients with PMI should be treated with aspirin,⁹⁰ a β -blocker,⁹¹ a statin agent (HMG-CoA reductase inhibitor),^{92,93} and commonly an ACE inhibitor,⁷⁰⁻⁷⁶ as these agents have all been shown to prevent recurrent ischemic events and cardiac death.

SUMMARY

The best strategy for management of PMI is one that emphasizes prevention. Preventive strategies should be based on preoperative utilization and optimization of β -blockers⁹⁴⁻⁹⁷, α_2 -agonists if

β -blockers cannot be used,^{98,99} and HMG-CoA reductase inhibitors (statins).^{100–101} If MI does occur, a multidisciplinary approach involving the operating surgeon, cardiologist, and intensivist should be followed. The decision to pursue interventional or medical treatment should be individualized based on the category and severity of infarction (STEMI vs NSTEMI), type of surgery, and the need for hemostasis. Anticoagulant use is often needed. Particular vigilance will be required regarding the recognition and treatment of occult and overt bleeding and related complications.

REFERENCES

- 1 Badner NH, Knill RL, Brown JE, et al. Myocardial infarction after noncardiac surgery. *Anesthesiology* 1998; 88:572–578
- 2 Tarhan S, Moffitt EA, Taylor WF, et al. Myocardial infarction after general anesthesia. *JAMA* 1972; 220:1451–1454
- 3 Becker RC, Underwood DA. Myocardial infarction in patients undergoing noncardiac surgery. *Cleve Clin J Med* 1987; 54:25–28
- 4 Ashton MC, Petersen JN, Wray PN, et al. The incidence of perioperative myocardial infarction in men undergoing noncardiac surgery. *Ann Intern Med* 1993; 118:504–510
- 5 Eagle KA, Rihal CS, Mickel MC, et al. Cardiac risk of noncardiac surgery: influence of coronary disease and type of surgery in 3368 operations. *Circulation* 1997; 96:1882–1887
- 6 Landesberg G, Mosseri M, Zahger D, et al. Myocardial infarction following vascular surgery: the role of prolonged, stress-induced, ST-depression-type ischemia. *J Am Coll Cardiol* 2001; 37:1839–1845
- 7 Landesberg G, Shatz V, Akopnik I, et al. Association of cardiac troponin, CK-MB, and postoperative myocardial ischemia with long-term survival after major vascular surgery. *J Am Coll Cardiol* 2003; 42:1547–1554
- 8 Landesberg G, Mosseri M, Shatz V, et al. Cardiac troponin after major vascular surgery: the role of perioperative ischemia, preoperative thallium scanning, and coronary revascularization. *J Am Coll Cardiol* 2004; 44:569–575
- 9 Landesberg G, Luria MH, Cotev S, et al. Importance of long-duration postoperative ST-segment depression in cardiac morbidity after vascular surgery. *Lancet* 1993; 341:715–719
- 10 Mangano DT, Hollenberg M, Fegert G, et al. Perioperative myocardial ischemia in patients undergoing noncardiac surgery: I. Incidence and severity during the 4-day perioperative period. *J Am Coll Cardiol* 1991; 17:843–850
- 11 Hertzner NR, Beven EG, Young JR, et al. Coronary artery disease in peripheral vascular patients: a classification of 1000 coronary arteriograms and results of surgical management. *Ann Surg* 1984; 199:223–233
- 12 Sprung J, Abdelmalak B, Gottlieb A, et al. Analysis of risk factors for myocardial infarction and cardiac mortality after major vascular surgery. *Anesthesiology* 2000; 93:129–140
- 13 Diehl JT, Cali RF, Hertzner NR, et al. Complications of abdominal aortic reconstruction: an analysis of perioperative risk factors in 557 patients. *Ann Surg* 1983; 197:49–56
- 14 Barone EJ, Bull J, Cussatti EH, et al. Perioperative myocardial infarction in low-risk patients undergoing noncardiac surgery is associated with intraoperative hypotension. *J Intensive Care Med* 2002; 17:250–255
- 15 Eagle KA, Berger PB, Calkins H, et al. ACC/AHA guideline update for perioperative cardiovascular evaluation for Noncardiac surgery—executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Update the 1996 Guidelines on Perioperative Cardiovascular Evaluation for Noncardiac Surgery). *J Am Coll Cardiol* 2002; 39:542–553
- 16 Kaluza GL, Joseph J, Lee JR, et al. Catastrophic outcomes of noncardiac surgery soon after coronary stenting. *J Am Coll Cardiol* 2000; 35:1288–1294
- 17 Wilson SH, Fasseas P, Orford JL, et al. Clinical outcome of patients undergoing non-cardiac surgery in the two months following coronary stenting. *J Am Coll Cardiol* 2003; 42:234–240
- 18 Breslow MJ, Parker SD, Frank SM, et al. Determinants of catecholamine and cortisol responses to lower extremity revascularization. The PIRAT Study Group. *Anesthesiology* 1993; 79:1202–1209
- 19 Sametz W, Metzler H, Gries M, et al. Perioperative catecholamine changes in cardiac risk patients. *Eur J Clin Invest* 1999; 29:582–587
- 20 Indolfi C, Ross J Jr. The role of heart rate in myocardial ischemia and infarction: implications of myocardial perfusion-contraction matching. *Prog Cardiovasc Dis* 1993; 36:61–74
- 21 Ambrose JA, Tannenbaum MA, Alexopoulos D. Angiographic progression of coronary artery disease and the development of myocardial infarction. *J Am Coll Cardiol* 1988; 12:56–62
- 22 Brown G, Albers JJ, Fisher LD, et al. Regression of coronary artery disease as a result of intensive lipid-lowering therapy in men with high levels of apolipoprotein B. *N Engl J Med* 1990; 323:1289–1298
- 23 Ellis SG, Hertzner NR, Young JR, et al. Angiographic correlates of cardiac death and myocardial infarction complicating major nonthoracic vascular surgery. *Am J Cardiol* 1996; 77:1126–1128
- 24 Sautter RD, Myers WO, Ray JF 3rd, et al. Relationship of fibrinolytic system to postoperative thrombotic phenomena. *Arch Surg* 1973; 107:292–296
- 25 Dawood M, Gutpa DK, Southern J, et al. Pathology of fatal perioperative myocardial infarction: implications regarding pathophysiology and prevention. *Int J Cardiol* 1996; 57:37–44
- 26 Cohen MC, Aretz TH. Histological analysis of coronary artery lesions in fatal postoperative myocardial infarction. *Cardiovasc Pathol* 1999; 8:133–139
- 27 Lee TH. Reducing cardiac risk in noncardiac surgery. *N Engl J Med* 1999; 341:1838–1840
- 28 Poldermans D, Boersma E, Bax JJ, et al. The effect of bisoprolol on perioperative mortality and myocardial infarction in high-risk patients undergoing vascular surgery. Dutch Echocardiographic Cardiac Risk Evaluation Applying Stress Echocardiography Study Group. *N Engl J Med* 1999; 341:1789–1794
- 29 Mangano DT, Layug EL, Wallace A, et al. Effect of atenolol on mortality and cardiovascular morbidity after noncardiac surgery. *N Engl J Med* 1996; 335:1713–1720
- 30 Zimmerman J, Fromm R, Meyer D, et al. Diagnostic marker cooperative study for the diagnosis of myocardial infarction. *Circulation* 1999; 99:1671–1677
- 31 Zimetbaum PJ, Josephson ME. Use of the electrocardiogram in acute myocardial infarction. *N Engl J Med* 2003; 348:933–940
- 32 Martinez EA, Kim LJ, Faraday N, et al. Sensitivity of routine intensive care unit surveillance for detecting myocardial

- ischemia. *Crit Care Med* 2003; 31:2302–2308
- 33 Hossein-Nia M, Kallis P, Brown PA, et al. Creatine kinase MB isoforms: sensitive markers of ischemic myocardial damage. *Clin Chem* 1994; 40:1265–1271
 - 34 Wu AH, Apple FS, Gibler WB, et al. National Academy of Clinical Biochemistry Standards of Laboratory Practice: recommendations for the use of cardiac markers in coronary artery diseases. *Clin Chem* 1999; 45:1104–1121
 - 35 Lee TH, Thomas EJ, Ludwig LE, et al. Troponin T as a marker for myocardial ischemia in patients undergoing major noncardiac surgery. *Am J Cardiol* 1996; 77:1031–1036
 - 36 Adams JE 3rd, Sicard GA, Allen BT, et al. Diagnosis of perioperative myocardial infarction with measurement of cardiac troponin I. *N Engl J Med* 1994; 330:670–674
 - 37 Schreiber WE. Laboratory assessment of myocardial damage. *Am J Clin Path* 1997; 107:383–384
 - 38 Horwich TB, Patel J, MacLellan WR, et al. Cardiac troponin I is associated with impaired hemodynamics, progressive left ventricular dysfunction, and increased mortality rates in advanced heart failure. *Circulation* 2003; 108:833–838
 - 39 Giannitsis E, Muller-Bardorff M, Kurowski V, et al. Independent prognostic value of cardiac troponin T in patients with confirmed pulmonary embolism. *Circulation* 2000; 102:211–217
 - 40 Ver Elst KM, Spapen HD, Nguyen DN, et al. Cardiac troponins T and I are biological markers of left ventricular dysfunction in septic shock. *Clin Chem* 2000; 46:650–657
 - 41 Alpert JS, Thygesen K, Antman E, et al. Myocardial infarction redefined: a consensus document of The Joint European Society of Cardiology/American College of Cardiology committee for the redefinition of myocardial infarction. *J Am Coll Cardiol* 2000; 36:959–969
 - 42 Lopez-Jimenez F, Goldman L, Sacks DB, et al. Prognostic value of cardiac troponin T after noncardiac surgery: 6-month follow-up data. *J Am Coll Cardiol* 1997; 29:1241–1245
 - 43 Kim LJ, Martinez EA, Faraday N, et al. Cardiac troponin I predicts short-term mortality in vascular surgery patients. *Circulation* 2002; 106:2366–2371
 - 44 Bertrand ME, Simoons ML, Fox KA. Management of acute coronary syndromes: acute coronary syndromes without persistent ST segment elevation: recommendations of the Task Force of the European Society of Cardiology. *Eur Heart J* 2000; 21:1406–1432
 - 45 Antman EM, Cohen M, Bernink PJ, et al. The TIMI risk score for unstable angina/non-ST elevation MI: a method for prognostication and therapeutic decision making. *JAMA* 2000; 284:835–842
 - 46 Morrow DA, Cannon CP, Rifai N, et al. TACTICS-TIMI 18 Investigators. Ability of minor elevations of troponins I and T to predict benefit from an early invasive strategy in patients with unstable angina and non-ST elevation myocardial infarction: results from a randomized trial. *JAMA* 2001; 286:2405–2412
 - 47 Silber J, Albertsson P, Aviles FF, et al. Guidelines for percutaneous coronary interventions. The Task Force for Percutaneous Coronary Interventions of the European Society of Cardiology. *Eur Heart J* 1995; 26:804–847
 - 48 Boersma E, Pieper KS, Steyerberg EW, et al. Predictors of outcome in patients with acute coronary syndromes without persistent ST-segment elevation: results from an international trial of 9461 patients. The PURSUIT Investigators. *Circulation* 2000; 101:2557–2567
 - 49 Cannon CP. Evidence-based risk stratification to target therapies in acute coronary syndromes. *Circulation* 2002; 106:1588–1591
 - 50 de Lemos JA, Morrow DA, Bentley JH, et al. The prognostic value of B-type natriuretic peptide in patients with acute coronary syndromes. *N Engl J Med* 2001; 345:1014–1021
 - 51 Sabatine MS, Morrow DA, de Lemos JA, et al. Multimarker approach to risk stratification in non-ST elevation acute coronary syndromes: simultaneous assessment of troponin I, C-reactive protein, and B-type natriuretic peptide. *Circulation* 2002; 105:1760–1763
 - 52 Gruppo Italiano per lo Studio della Streptochinasi nell'Infarto Miocardico (GISSI). Effectiveness of intravenous thrombolytic treatment in acute myocardial infarction. *Lancet* 1986; 327:397–402
 - 53 The GUSTO Investigators. An international randomized trial comparing four thrombolytic strategies for acute myocardial infarction. *N Engl J Med* 1993; 329:673–682
 - 54 The Global Use of Strategies to Open Occluded Coronary Arteries (GUSTO III) Investigators. A comparison of reteplase with alteplase for acute myocardial infarction. *N Engl J Med* 1997; 337:1118–1123
 - 55 Franzosi MG, Santoro E, De Vita C, et al. Ten-year follow-up of the first megatrial testing thrombolytic therapy in patients with acute myocardial infarction: results of the Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto-I study. *Circulation* 1998; 98:2659–2665
 - 56 Antman EM, Anbe DT, Armstrong PW, et al. ACC/AHA guidelines for the management of patients with ST-elevation myocardial infarction: executive summary: a report of the ACC/AHA Task Force on Practice Guidelines (Committee to Revise the 1999 Guidelines on the Management of Patients With Acute Myocardial Infarction). *J Am Coll Cardiol* 2004; 44:671–719
 - 57 CAPRIE Steering Committee. A randomised, blinded, trial of clopidogrel versus aspirin in patients at risk of ischaemic events (CAPRIE). *Lancet* 1996; 348:1329–1339
 - 58 Harker LA, Boissel JP, Pilgrim AJ, et al. Comparative safety and tolerability of clopidogrel and aspirin: results from CAPRIE. *Drug Saf* 1999; 21:325–335
 - 59 Grines CL, Browne KF, Marco J, et al. A comparison of immediate angioplasty with thrombolytic therapy for acute myocardial infarction. *N Engl J Med* 1993; 328:673–679
 - 60 Berger BP, Bellot V, Bell MR, et al. An immediate invasive strategy for the treatment of acute myocardial infarction early after noncardiac surgery. *Am J Cardiol* 2001; 87:1100–1102
 - 61 Antman EM, Cohen M, Radley D, et al. Assessment of the treatment effect of enoxaparin for unstable angina/non-Q-wave myocardial infarction: TIMI 11B-ESSENCE meta-analysis. *Circulation* 1999; 100:1602–1608
 - 62 The International Study Group. In-hospital mortality and clinical course of 20,891 patients with suspected acute myocardial infarction randomised between alteplase and streptokinase with or without heparin. *Lancet* 1990; 336:71–75
 - 63 The Assessment of the Safety and Efficacy of a New Thrombolytic Regimen (ASSENT)-3 Investigators. Efficacy and safety of tenecteplase in combination with enoxaparin, abciximab, or unfractionated heparin: the ASSENT-3 randomised trial in acute myocardial infarction. *Lancet* 2001; 358:605–613
 - 64 Gruppo Italiano per lo Studio della Sopravvivenza nell'infarto Miocardico. GISSI-3: effects of lisinopril and transdermal glyceryl trinitrate singly and together on 6-week mortality and ventricular function after acute myocardial infarction. *Lancet* 1994; 343:1115–1122
 - 65 ISIS-4 (Fourth International Study of Infarct Survival) Collaborative Group. ISIS-4: a randomised factorial trial assessing early oral captopril, oral mononitrate, and intravenous magnesium sulphate in 58,050 patients with suspected

- acute myocardial infarction. *Lancet* 1995; 345:669–685
- 66 Lau J, Antman EM, Jimenez-Silva J, et al. Cumulative meta-analysis of therapeutic trials for myocardial infarction. *N Engl J Med* 1992; 327:248–254
 - 67 Gottlieb SS, McCarter RJ, Vogel RA. Effect of β -blockade on mortality among high-risk and low-risk patients after myocardial infarction. *N Engl J Med* 1998; 339:489–497
 - 68 Koenig W, Lowel H, Lewis M, et al. Long-term survival after myocardial infarction: relationship with thrombolysis and discharge medication; results of the Augsburg Myocardial Infarction Follow-up Study 1985 to 1993. *Eur Heart J* 1996; 17:1199–1206
 - 69 Leitch JW, McElduff P, Dobson A, et al. Outcome with calcium channel antagonists after myocardial infarction: a community-based study. *J Am Coll Cardiol* 1998; 31:111–117
 - 70 Lonn EM, Yusuf S, Jha P, et al. Emerging role of angiotensin-converting enzyme inhibitors in cardiac and vascular protection. *Circulation* 1994; 90:2056–2069
 - 71 Chinese Cardiac Study Collaborative Group. Oral captopril versus placebo among 13,634 patients with suspected acute myocardial infarction: interim report from the Chinese Cardiac Study (CCS-1). *Lancet* 1995; 345:686–687
 - 72 ACE Inhibitor Myocardial Infarction Collaborative Group. Indications for ACE inhibitors in the early treatment of acute myocardial infarction: systematic overview of individual data from 100,000 patients in randomized trials. *Circulation* 1998; 97:2202–2212
 - 73 Brown NJ, Vaughan DE. Angiotensin-converting enzyme inhibitors. *Circulation* 1998; 97:1411–1420
 - 74 Pfeffer MA. ACE inhibitors in acute myocardial infarction: patient selection and timing. *Circulation* 1998; 97:2192–2194
 - 75 Sigurdsson A, Swedberg K. Left ventricular remodeling, neurohormonal activation and early treatment with enalapril (CONSENSUS II) following myocardial infarction. *Eur Heart J* 1994; 15(suppl B):14–19; discussion 26–30
 - 76 Yusuf S, Sleight P, Pogue J, et al. Effects of an angiotensin-converting-enzyme inhibitor, ramipril, on cardiovascular events in high-risk patients: the Heart Outcomes Prevention Evaluation Study Investigators. *N Engl J Med* 2000; 342:145–153
 - 77 Schwartz GG, Olsson AG, Ezekowitz MD, et al. Effects of atorvastatin on early recurrent ischemic events in acute coronary syndromes: the MIRACL study; a randomized controlled trial. *JAMA* 2001; 285:1711–1718
 - 78 Aronow HD, Topol EJ, Roe MT, et al. Effect of lipid-lowering therapy on early mortality after acute coronary syndromes: an observational study. *Lancet* 2001; 357:1063–1068
 - 79 Gurbel PA, Anderson RD, MacCord CS, et al. Arterial diastolic pressure augmentation by intra-aortic balloon counterpulsation enhances the onset of coronary artery reperfusion by thrombolytic therapy. *Circulation* 1994; 89:361–365
 - 80 Kono T, Morita H, Nishina T, et al. Aortic counterpulsation may improve late patency of the occluded coronary artery in patients with early failure of thrombolytic therapy. *J Am Coll Cardiol* 1996; 28:876–881
 - 81 O'Rourke MF, Norris RM, Campbell TJ, et al. Randomized controlled trial of intraaortic balloon counterpulsation in early myocardial infarction with acute heart failure. *Am J Cardiol* 1981; 47:815–820
 - 82 Ohman EM, Califf RM, George BS, et al. The use of intraaortic balloon pumping as an adjunct to reperfusion therapy in acute myocardial infarction. The Thrombolysis and Angioplasty in Myocardial Infarction (TAMI) Study Group. *Am Heart J* 1991; 121:895–901
 - 83 Kovack PJ, Rasak MA, Bates ER, et al. Thrombolysis plus aortic counterpulsation: improved survival in patients who present to community hospitals with cardiogenic shock. *J Am Coll Cardiol* 1997; 29:1454–1458
 - 84 Kohchi K, Takebayashi S, Block PC, et al. Arterial changes after percutaneous transluminal coronary angioplasty: results at autopsy. *J Am Coll Cardiol* 1987; 10:592–599
 - 85 White CJ, Ramee SR, Collins TJ, et al. Coronary thrombi increase PTCA risk: angiography as a clinical tool. *Circulation* 1996; 93:253–258
 - 86 Haude M, Höpp HW, Rupprecht HJ, et al. Immediate stent implantation versus conventional techniques for the treatment of abrupt vessel closure or symptomatic dissections after coronary balloon angioplasty. *Am Heart J* 2000; 140:820–830
 - 87 Topol EJ. Coronary-artery stents: gauging, gorging, and gouging. *N Engl J Med* 1998; 339:1702–1704
 - 88 Mak KH, Belli G, Ellis SG, et al. Subacute stent thrombosis: evolving issues and current concepts. *J Am Coll Cardiol* 1996; 27:494–503
 - 89 Madsen JK, Grande P, Saunamäki K, et al. Danish multicenter randomized study of invasive versus conservative treatment in patients with inducible ischemia after thrombolysis in acute myocardial infarction (DANAMI). *Circulation* 1997; 96:748–755
 - 90 Antiplatelet Trialists' Collaboration. Secondary prevention of vascular disease by prolonged antiplatelet treatment. *BMJ* 1988; 296:320–331
 - 91 Freemantle N, Urdahl H, Eastaugh J, et al. What is the place of β -blockade in patients who have experienced a myocardial infarction with preserved left ventricular function? Evidence and (mis)interpretation. *Prog Cardiovasc Dis* 2002; 44:243–250
 - 92 Aronow HD, Topol EJ, Roe MT, et al. Effect of lipid-lowering therapy on early mortality after acute coronary syndromes: an observational study. *Lancet* 2001; 357:1063–1068
 - 93 Stenestrand U, Wallentin L. Early statin treatment following acute myocardial infarction and 1-year survival. *JAMA* 2001; 285:430–436
 - 94 Zaugg M, Tagliente T, Lucchinetti E, et al. Beneficial effects from β -adrenergic blockade in elderly patients undergoing noncardiac surgery. *Anesthesiology* 1999; 91:1674–1686
 - 95 Auerbach AD, Goldman L. β -Blockers and reduction of cardiac events in noncardiac surgery: scientific review. *JAMA* 2002; 287:1435–1444
 - 96 Yang H, Raymer K, Butler R, et al. Metoprolol after vascular surgery (MaVS) [abstract]. *Can J Anesth* 2004; 71:A7
 - 97 Urban MK, Markowitz SM, Gordon MA, et al. Postoperative prophylactic administration of β -adrenergic blockers in patients at risk for myocardial ischemia. *Anesth Analg* 2000; 90:1257–1261
 - 98 Wallace AW, Galindez D, Salahieh A, et al. Effect of clonidine on cardiovascular morbidity and mortality after noncardiac surgery. *Anesthesiology* 2004; 101:284–293
 - 99 Stevens RD, Burri H, Tramèr MR. Pharmacologic myocardial protection in patients undergoing noncardiac surgery: a quantitative systematic review. *Anesth Analg* 2003; 97:623–633
 - 100 Poldermans D, Bax JJ, Kertai MD, et al. Statins are associated with a reduced incidence of perioperative mortality in patients undergoing major noncardiac vascular surgery. *Circulation* 2003; 107:1848–1851
 - 101 Durazzo AE, Machado FS, Ikeoka DT, et al. Reduction in cardiovascular events after vascular surgery with atorvastatin: a randomized trial. *J Vasc Surg* 2004; 39:967–975

Management of Perioperative Myocardial Infarction in Noncardiac Surgical Patients

Adebola O. Adesanya, James A. de Lemos, Nancy B. Greilich and Charles W. Whitten

Chest 2006;130; 584-596
DOI 10.1378/chest.130.2.584

This information is current as of July 8, 2011

Updated Information & Services

Updated Information and services can be found at:

<http://chestjournal.chestpubs.org/content/130/2/584.full.html>

References

This article cites 97 articles, 51 of which can be accessed free at:

<http://chestjournal.chestpubs.org/content/130/2/584.full.html#ref-list-1>

Cited By

This article has been cited by 2 HighWire-hosted articles:

<http://chestjournal.chestpubs.org/content/130/2/584.full.html#related-urls>

Permissions & Licensing

Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at:

<http://www.chestpubs.org/site/misc/reprints.xhtml>

Reprints

Information about ordering reprints can be found online:

<http://www.chestpubs.org/site/misc/reprints.xhtml>

Citation Alerts

Receive free e-mail alerts when new articles cite this article. To sign up, select the "Services" link to the right of the online article.

Images in PowerPoint format

Figures that appear in *CHEST* articles can be downloaded for teaching purposes in PowerPoint slide format. See any online figure for directions.

A M E R I C A N C O L L E G E O F



C H E S T

P H Y S I C I A N S[®]