

## PERIOPERATIVE MYOCARDIAL INFARCTION IN NEUROSURGICAL PATIENTS: MANAGEMENT ISSUES

Dr. Praveen Kumar Neema<sup>1</sup> Dr. Manikandan Sethuraman<sup>2</sup>  
Dr. Subrat Singha<sup>3</sup> Dr. Ramesh Chandra Rathod<sup>4</sup>

### SUMMARY

The incidence of perioperative myocardial infarction (PMI) following neurosurgery is not known. The perioperative cardiac events commonly occur in patients having significant coronary artery disease or its risk factors, in patients having prolonged postoperative myocardial ischemia, and in patients undergoing high-risk surgery.<sup>1</sup> Neurosurgical patients may be prone for adverse cardiac events as these patients often suffer from hemodynamic stress (hypertension), particularly, during brain manipulation, administration of epinephrine containing local anesthetic, head-pin application, periosteal dissection, and emergence.<sup>2</sup> The management of patients sustaining MI in the perioperative period includes antiplatelet therapy, thrombolytic therapy, coronary angioplasty and stenting, and intraaortic balloon counterpulsation (IABP). However, anticoagulation in postoperative neurosurgical patients is of special concern because of the fear of intracranial bleeding. This review addresses etiology, pathophysiology and management of PMI. The issue of possibility of intracranial bleeding secondary to the use of anticoagulants employed to treat MI is also discussed.

**Keywords :** Perioperative myocardial infarction; Neurosurgery;

### Perioperative myocardial ischemia in neurosurgical patients:

The association of ECG abnormalities with subarachnoid hemorrhage (SAH) was described as early as 1947.<sup>3</sup> Transient cardiac abnormalities are a well-recognized phenomenon that occurs in a large percentage of patients with acute aneurysmal SAH,<sup>4</sup> it has been estimated that 50-72% of these patients have ECG abnormalities.<sup>5</sup> The common ECG changes include depression or elevation of ST segment, prolongation of Q-T interval, U-waves, and T-wave inversion.<sup>3</sup> The changes are often associated with elevation of CK-MB<sup>6</sup> and troponin levels,<sup>7</sup> wall motion abnormalities on echocardiography, and cardiac failure.<sup>8</sup> These findings indicate ongoing myocardial ischemia, yet there may not be evidence of coronary artery disease, coronary vasospasm, or cardiac hypoperfusion.<sup>9</sup> Resolution of ECG changes occurs after clinical recovery from SAH.<sup>10</sup> Neurogenic stunned myocardium with ECG and echocardiography changes and resolution of the changes after phenytoin and steroid therapy has been reported in a patient with multiple brain metastasis at bilateral parietal and frontal lobes.<sup>11</sup>

### Pathophysiology of perioperative myocardial ischemia and infarction:

Myocardial ischemia is characterized by an imbalance between myocardial oxygen demand and supply. Increase in myocardial oxygen demand occurs with tachycardia, emotional stress, or exercise and is mostly responsible for ischemic episodes in chronic stable angina in the presence of fixed coronary artery stenosis.<sup>12</sup> The most common ECG finding during episodes of symptomatic or silent myocardial ischemia in patients with chronic stable angina is ST segment depression. When ischemia is confined predominantly to the subendocardium, the overlying ECG leads show ST segment depression.<sup>13</sup> This subendocardial pattern is typical of spontaneous ischemic episodes of angina pectoris induced by exercise or by a stress test. The mechanisms of myocardial infarction in **nonsurgical** patients include plaque disruption and thrombosis. The initiating event or trigger that may lead to the disruption of the plaque is often an external activity associated with increased sympathetic stimulation, such as physical or emotional stress or vasoconstriction.<sup>14</sup> The rupture of the vulnerable plaque exposes the blood stream to the thrombogenic contents of the plaque or the denuded endothelial surface, leading to thrombus formation and, consequently, acute myocardial infarction. An associated transient increase in coagulability, inflammation, viscosity, or vasoconstriction may further predispose to the formation of a thrombus.<sup>14</sup>

However, the mechanism of PMI is the subject of debate.<sup>15</sup> Existing data are inconclusive and do not allow definitive decision whether long duration subendocardial

1. M.D., Asso. Prof., Anaesthesiology
2. M.D., Asso. Prof., Anaesthesiology
3. M.D., Asst. Prof., Anaesthesiology
4. M.D.,D.A.,Prof. and Head, Anaesthesiology  
Dept. of Anaesthesiology  
Sree Chitra Tirunal Institute for Medical Sciences and  
Technology, Trivandrum - 695011, Kerala, India

#### Correspond to :

Dr Praveen Kumar Neema,  
E-mail : neema@sctimst.ac.in, praveenneema@yahoo.co.in

myocardial ischemia or acute coronary occlusion due to plaque disruption or thrombosis is the primary mechanism of PMI in an individual patient.<sup>12</sup> Myocardial ischemia of sufficient severity or prolonged duration may result in reversible (myocardial stunning) or irreversible myocardial damage (infarction), ventricular arrhythmias, or cardiogenic shock.<sup>16</sup> Deleterious increases in myocardial contractility and oxygen demand may occur during the perioperative period because of  $\alpha$ 1- adrenoceptor stimulation by endogenous catecholamines.<sup>16</sup> Left ventricular preload and afterload increases affects myocardial oxygen demand by altering end-diastolic and end-systolic wall tension.<sup>16</sup> Several studies using perioperative ECG monitoring have shown that postoperative ischemia duration, and not only the ischemia per se, is associated with cardiac complications after major noncardiac surgery.<sup>17,18,19</sup> By using continuous 12 lead ECG and ST trend monitoring and troponin-1 (cTn-1) measurements in the first 3 postoperative days in 185 patients undergoing major vascular surgery, it was shown that the rise in cTn-1 occurred during or shortly after prolonged (> 100 min), silent, postoperative ischemia and the duration of ischemia was strongly associated with the peak cTn-1 level.<sup>20</sup> Moreover, ischemia was preceded in all cases by an increase in heart rate (heart rate at the onset of ischemia  $104 \pm 19$  and at peak ischemia  $114 \pm 19$  compared with  $86 \pm 14$  in the preceding 30 min before the onset of ischemia) and the majority of ischemic events, including those culminating in PMI, started within 2 hours from the end of surgery and emergence from anesthesia,<sup>20</sup> a time characterized by increase in heart rate, blood pressure, sympathetic discharge, and procoagulant activity.<sup>21</sup> Hypertension after craniotomy is common, and in one study, more than 90% of the patients developed hypertension.<sup>22</sup> It is well recognized that an increase in heart rate in the presence of stable coronary artery stenosis causes impairment of subendocardial/epicardial blood flow distribution because of the shortening of the diastolic time interval, and may cause subendocardial ischemia and myocardial dysfunction.<sup>23</sup> Often, myocardial ischemia is silent and not associated with hemodynamic disturbances that are known to increase myocardial O<sub>2</sub> demand.<sup>24</sup> Consequently, it is believed that such episodes of ischemia are because of microcirculatory disturbances that regulate O<sub>2</sub> supply.<sup>25</sup> The decreased supply may be the result of hypotension, anemia, hypoxia, vasospasm or plaque rupture with thrombosis.<sup>1</sup> The PMI may result from plaque rupture and thrombosis at the site of a hemodynamically insignificant atherosclerotic plaque.<sup>26</sup> The location of perioperative myocardial infarction (PMI) is not always related to the location of culprit coronary lesion.<sup>27</sup>

### Diagnosis of perioperative myocardial ischemia and infarction:

The majority of perioperative ischemic episodes are silent.<sup>18,28</sup> The incidence of silent ischemia is higher in diabetics than in nondiabetics. The two important clinical implications of silent ischemia are – the presence and/or frequency of angina may not be indicative of ongoing myocardial ischemia; second, since majority episodes of perioperative myocardial ischemia are silent, angina is a very poor monitor of myocardial ischemia.<sup>29</sup> The ECG is the best overall monitor for detection of perioperative ischemia. Diagnostic criteria for ECG ischemia are horizontal or down sloping ST depression (>0.1 mV) or ST elevation (>0.2mV) occurring 60-80 msec after the J point and of slow onset and slow offset.<sup>29</sup> London et al showed that almost all ECG episodes of ischemia are associated with ST depression, that lead V is the most sensitive (75%) and that with combined leads the sensitivity can approach 100%.<sup>30</sup> Monitoring the correct lead is very important since less than 10% of ischemic episodes were detected in leads I, aVR and aVL. Preexisting ECG abnormalities may limit the usefulness of ECG detection of myocardial ischemia in patients with cardiac pacemaker, left bundle branch block, left ventricular hypertrophy, or digitalis induced ST changes. In patients without coronary artery disease, hyperventilation, and changes in posture, glucose, and potassium plasma concentration have been shown to affect ST changes. The monitors should be properly calibrated and appropriately filtered (diagnostic mode) so that any ST depression is neither magnified nor artifactual. The pulmonary artery catheters are not considered useful since PCWP may change for the reasons other than myocardial ischemia such as fluid shift or valvular dysfunction.<sup>31</sup> One of the earliest manifestations of myocardial ischemia is decreased contraction of myocardial fibers resulting in regional systolic dysfunction that may be detected by echocardiography (Transthoracic or transesophageal), cardiokymography or angiography.<sup>29</sup> Wall motion abnormalities appear to be the most sensitive monitor for intraoperative myocardial ischemia.

It is important to realize that the ischemic ECG changes are often transient and reverts to baseline in majority of the patients including those who develop PMI.<sup>20</sup> Consequently, presence of baseline ECG does not rule out developing myocardial infarction. Rapp et al<sup>32</sup> who correlated postoperative Holter monitoring results with cardiac troponin-T measurements in 20 patients undergoing vascular surgery have obtained similar results. Persistent ECG

abnormalities, ST depression or elevation, malignant arrhythmias and hemodynamic instability, indicates ongoing myocardial injury. PMI is preceded almost exclusively by ST depression type of ischemia. ST elevation type of ischemia leading to myocardial infarction in surgical patients is relatively uncommon after noncardiac surgery.<sup>23</sup> Various biochemical markers are used in the diagnosis of myocardial infarction, however, the use of these markers in the diagnosis of PMI is problematic because of the release of these markers from damaged muscle as well as from the myocardium during cardiac surgery. Consequently cardiac enzymes (LDH, AST, HBD, and CK) myoglobin and CK-MB are of little value.<sup>33,34</sup> The national academy of clinical biochemistry recommends the use of cTnI or cTnT for the detection of PMI in noncardiac surgery patients, and suggests that the same decision limit should be used as for acute MI.<sup>35</sup> cTnT has also been reported to be an independent predictor of early postoperative cardiovascular complications following noncardiac surgery.<sup>36</sup> The potential of H-FABP (Heart type fatty acid binding protein) for the identification of PMI is yet to be explored. This relatively small molecule is cytoplasmic in origin, released early after myocardial injury.<sup>37</sup> The definition of PMI include an increase in cTnI > 3.1 ng/ml accompanied by at least one of the following: typical ischemic symptoms, ECG changes indicative of myocardial ischemia (ST segment elevation or depression), or new pathological Q waves.<sup>20</sup>

Subarchnoid hemorrhage is often associated with clinical cardiac dysfunction, abnormal ECG, wall motion abnormalities and reduced ejection fraction on echocardiography (EF <40%), and elevated cTnI and cTnT levels. Myocardial injury is believed to be mediated by catecholamine surge.<sup>38</sup> The myocardial catecholamine concentrations rise and fall rapidly after an intracranial catastrophe. ECG changes and left ventricular dysfunctions resolve after clinical recovery from SAH. The raised cTn levels raises two anesthetic management issues – first the optimum timing for anesthesia and surgery, second, the risk of perioperative cardiovascular deterioration. A recent MI has been consistently identified as a risk factor for perioperative cardiac events.<sup>39</sup> Therefore, it is important to differentiate myocardial infarction from neurogenic left ventricular dysfunction. Bulsara et al,<sup>40</sup> in the setting of aneurysmal subarchnoid hemorrhage, found that a cTn values less than 2.8ng/ml with EF less than 40% indicates neurogenic left ventricular dysfunction (myocardial stunning).

### Management of myocardial infarction

The treatment objectives are immediate relief of ischemia and prevention of adverse outcomes (death, MI/reinfarction). The objectives are achieved by improvement in myocardial oxygen demand-supply relationship (antiischemic therapy) by – oxygen therapy, nitrates,  $\beta$ -blockade, and morphine; prevention of further propagation of thrombosis by antiplatelet and/or anticoagulant therapy; and establishment of reperfusion by thrombolysis, fibrinolysis, and by PCI (coronary angioplasty and stenting), or surgical revascularization and support of circulation by IABP.<sup>41</sup>

### Myocardial infarction following neurosurgery - The Management issues:

The treatment of MI includes antiplatelets, anticoagulants, and thrombolytic therapy. Insufficient information exists regarding safety, dosing, and monitoring of these drugs in neurosurgical practice. The association between anticoagulation therapy and intracranial hemorrhage is well known.<sup>42</sup> In an analysis of 1564 patients receiving fractionated heparin (for deep vein thrombosis prophylaxis) within 24 hours after intracranial surgery, the authors found CT confirmed hemorrhage in 31 patients.<sup>43</sup> All hemorrhages occurred in patients undergoing major intracranial procedures. Recently, Dickinson et al have shown that enoxaparine administered before the induction of anesthesia increased the incidence of postoperative intracranial hemorrhage in patients with brain tumors.<sup>44</sup> The doses of unfractionated heparin and enoxaparine were 5000 units 8<sup>th</sup> hourly and 40 mg daily until discharge, respectively. These doses are much less as compared to the doses of antiplatelets, anticoagulants, and thrombolytics generally used during the management of myocardial infarction. It is intuitive that the use of these drugs immediately following intracranial surgery would be accompanied by increased tendency to intracranial hemorrhage. Moreover, little knowledge exists in the management of patients sustaining MI in the perioperative period following intracranial surgery. The issues are safety concerns and monitoring during antiplatelet, anticoagulation and thrombolytic therapy. In addition, how to manage a patient in an unfortunate event of intracranial hemorrhage is not known. Kawamata et al,<sup>45</sup> reported their experience of management of intracranial hemorrhage in 27 patients receiving warfarin alone, or in combination with ticlopidine or aspirin for cardiac disorders including valve prosthesis, atrial fibrillation, acute myocardial infarction and aorto-coronary bypass. Anticoagulants were stopped as soon as the diagnosis of intracranial hemorrhage was established.

The patients received vitamin K immediately. Of 27 patients, 17 underwent surgical intervention; in patients with chronic subdural hematoma (SDH), intraoperative hemostasis was brought under control despite low thrombotest values (13-68%; INR 1.9-1.1) at the time of surgery. In two of three patients of acute SDH, effective intraoperative hemostasis could not be obtained and all the three had fatal outcome. Anticoagulant therapy was restarted within 3 days in 9 of the 17 patients because of sufficient perioperative hemostatic control and the presence of mechanical prosthesis. They conclude that patients may undergo surgery with thrombotest values of 20-60% and anticoagulants can be restarted after an interval of 3 days. It must be realized that the majority of the patients who had good outcome had chronic SDH. The outcome was poor in patients with acute SDH. Only one case report addresses management of postoperative adverse cardiac event following neurosurgery. Kitagawa<sup>46</sup> reported their patient with triple vessel disease, the patient, while waiting for coronary artery bypass grafting (CABG) surgery, developed pituitary apoplexy and following intracranial surgery developed ventricular fibrillation that was managed with IABP. Later the patient was taken for CABG surgery after 20 hours when the bleeding from subcutaneous tissue stopped. In our experience, one patient developed acute PMI after emergency transcranial decompression of the orbit for a painful pyocoele. The patient underwent emergency coronary angioplasty and stenting, and IABP for stabilization of hemodynamics. Heparin, 10000-units, was administered intravenously at the start of angioplasty and stenting, thereafter an infusion of 600-units per hour was continued for 48 hours, in addition, the patient received antiplatelet drugs – ticlopidine 250 mg and clopidogrel 100 mg through Ryle's tube. During angioplasty and stenting and for the following 48 hours, activated clotting time (ACT) was maintained between 200-250 seconds. Patients' hemodynamics improved steadily and the IABP was weaned over next 24 hours. During angioplasty and stenting and thereafter the patient was kept well sedated with continuous infusion of midazolam, and the level of consciousness, pupillary size and its reaction, and muscle power in all the four limbs was monitored to assess neurological status. A repeat CT scan after removal of IABP did not show any intracranial hematoma. Over the next 24 hours the patient was weaned off ventilator, the antiplatelet drugs were continued. The patient was discharged from the hospital on 10<sup>th</sup> day without any neurologic deficit. Keith et al,<sup>47</sup> studied risk of anticoagulation in experimental craniotomies and found that risk of intracranial bleeding is greatest within 7 days

and safe period for starting anticoagulation is after 10 days. In another experimental study, Laohaprasit et al,<sup>48</sup> found that judicious heparin therapy might be safely initiated at 48 hours after craniotomy in rats, whereas supratherapeutic anticoagulation is associated with intracranial hemorrhage at intervals of up to 5 days. In view of significant hazards of therapy of MI, it is most important to prevent PMI in these patients.

#### **Perioperative prevention of cardiac morbidity:**

It is very important to identify patients at high risk of perioperative cardiac morbidity. A number of risk indices have been developed over the past two decades, such as the Goldman cardiac risk index, the Detsky modified multifactorial risk index and Eagles risk score.<sup>49, 50, 51</sup> Recently, Lee et al,<sup>52</sup> reviewed the predictive value of several clinical risk factors in patients scheduled for noncardiac surgery. Six risk factors – high-risk surgery, stroke, diabetes mellitus, renal failure, congestive heart failure and ischemic heart disease, were identified in a study population of 2893 patients and later validated in a population of 1422 patients. The rate of major perioperative complications in the presence of 0, 1, 2, or 3 3-risk factor was 0.4%, 0.9%, 7% and 11%, respectively. The American College of Cardiology (ACC) and American heart Association (AHA) guidelines for perioperative cardiovascular evaluation for noncardiac surgery provide an outline for considering risk of noncardiac surgery in a variety of patients.<sup>53</sup> Risk stratification of patients with known or at risk of CAD is usually based on three elements.<sup>54</sup> 1) the patient risk factors<sup>53, 55</sup>, 2) the functional capacity of the patient, and 3) the risk factors of surgery.<sup>55</sup> Exercise tolerance (functional capacity) is a major determinant of perioperative risk.<sup>53, 55</sup> It is usually evaluated by the estimated energy requirement for various activities, and graded in metabolic equivalents (MET) on a scale defined by Duke Activity Status Index.<sup>56</sup> The inability to climb two flights of stairs is associated with a positive predictive value of 89% for cardiopulmonary complications.<sup>57</sup> Patients with good functional capacity and no symptoms can be considered free of any severe CAD.<sup>58</sup> The surgical procedures are stratified into three categories according to the level of perioperative physiological stress.<sup>53, 55</sup> Neurosurgical procedures are categorized as intermediate risk surgical procedure. Based on the risk stratification, stress tests are performed. Stress tests (exercise ECG, Dipyridamole thallium scintigraphy, or Dobutamine stress echocardiography) are dynamic investigations that demonstrate the ischemic threshold, the maximal tolerated heart rate, the localization and the amount of the threatened myocardium. The hallmark of myocardial ischemia during stress echocardiography is

the occurrence of reduced systolic wall thickening when myocardial O<sub>2</sub> demand exceeds myocardial blood supply; this change precedes the occurrence of chest pain and ST-T changes.<sup>59</sup> An interruption of the test before reaching the maximal theoretical heart rate identifies an increased risk of perioperative ischemic events.<sup>60</sup> The positive predictive value of all stress tests is modest (20-30%), whereas their negative predictive value is excellent (95-100%).<sup>61</sup> Coronary arteriography may be safely avoided in all patients if stress echocardiography is normal. The prognostic value of pharmacological stress echocardiography relative to coronary arteriography was addressed in a subgroup of 4037 patients who underwent coronary arteriography without an intervention. Coronary arteriographic data did not add any significant predictive power. The value of stress echocardiography during low doses of Dobutamine accurately discriminates between stunned and necrotic myocardium after acute myocardial infarction. The most powerful marker of mortality is the absence of Dobutamine response of the infarct related region, irrespective of whether patients subsequently underwent revascularization or medical treatment.<sup>62</sup> In a metaanalysis of six noninvasive tests, DSE showed higher overall sensitivity and specificity.<sup>63</sup> DSE seems particularly informative because it investigates the segmental coronary blood supply and allows simultaneous quantification of ventricular function. However, it must be appreciated that the predictions are only probabilities of events, a negative preoperative test in particular patient, although reassuring, does not mean that cardiac complications are excluded. The value of the stress echocardiography lies in the fact that it provides a close replication of an equivalent increase in myocardial O<sub>2</sub> consumption and may define the limits of physiological stress for the perioperative hemodynamic management. Nevertheless, it must be appreciated that no test adequately mimics the physiological stress response to surgery, with prolonged sympathetic stimulation and tachycardia, increased coronary vasomotor tone, hypercoagulability, potential atheromatous plaque rupture leading to thrombus formation, hypothermia and blood loss.<sup>64,65,66</sup> Therefore, it is difficult to define the real impact of stress tests on outcome in relation to various surgical procedures.

#### **Implications of preoperative myocardial infarction and coronary revascularization:**

Earlier it was a rule to wait for six months after myocardial infarction before accepting a patient for noncardiac surgery.<sup>67,68</sup> It appears now that the risk after a previous infarction is related to the functional status of the ventricles and to the amount of the myocardium at risk from further ischemia.<sup>53,69</sup> A small infarction without residual angina and a good functional status allows noncardiac

surgery as soon as 6 weeks after the ischemic episode.<sup>54</sup> On the contrary, a patient with a large infarct, residual symptoms and ejection fraction below < 0.35 has a further probability of cardiac event, even after 6 months after myocardial infarction. In general, the period from 6 weeks to 3 months is of intermediate risk; this period is extended beyond 3 months in cases with complications such as arrhythmias, ventricular dysfunction, or continued medical therapy.<sup>70</sup> In uncomplicated cases no benefit can be demonstrated for delaying surgery more than 3 months after an ischemic accident.<sup>54</sup>

Asymptomatic, functionally active patients with previous successful coronary revascularization within the last 6 years are in a low risk category and need not be investigated further for a noncardiac operation. This cutoff point is based on a slight but non-significant increase in postoperative infarction rate among patients 6 years after CABG.<sup>71</sup> Patients having a negative stress test or satisfactory angiography in the last 2 years can be cleared for noncardiac surgery without further testing if the symptomatology and treatment have not changed since the examination.<sup>53,55</sup> Myocardial revascularization following PTCA and stenting presents a different sets of problems. Any surgery performed within 6 weeks of PTCA presents an excessive risk of stent thrombosis and infarction if the antiplatelet medication is stopped or of major bleeding if the treatment is maintained throughout the operation. Documented stent thrombosis is associated with a mortality rate of 7%.<sup>72</sup> The optimal timing for surgery is a delay of 3 months after PTCA and stenting. This scenario might be different in view of increasing use of drug eluting stents. The current medical therapy following myocardial infarction, CABG and stenting includes life-long therapy with aspirin with or without anticoagulants and antiplatelets. In general surgical setting, in high-risk patients these drugs are usually replaced with heparin or low molecular weight heparin while in others they are discontinued. In neurosurgical setting aspirin, anticoagulants, and antiplatelets must be stopped as their continued use can result in intracerebral hemorrhage. However stopping these drugs in high-risk patients may result in life threatening thrombotic events. How to resolve these conflicting requirements are yet to be defined.

#### **Pharmacological interventions:**

Since the pathophysiology of PMI is poorly understood, effective interventions to prevent adverse cardiac events are assumed. In general, the perioperative drug therapy aims at reducing the myocardial O<sub>2</sub> demand associated with tachycardia and hypertension, and by enhancing the O<sub>2</sub> supply by coronary vasodilators. The pharmacological interventions aim at inhibition of central

sympathetic flow, b-adrenergic blockade and coronary vasodilatation. The drugs commonly used are nitroglycerine, b-blockers,  $\alpha$ -2 agonists, and Ca<sup>+</sup> channel blockers. Among all the drugs used, only  $\beta$ -blockers have substantial evidence to support its use during perioperative period.<sup>73,74,75</sup> The treatment is started a few days before surgery and continued during the first postoperative week. The dose is titrated to achieve a resting heart rate of about 50-60 beats per minute. If preoperative administration is not possible, intravenous  $\beta$ -blockade at the start of anesthesia followed by continuous postoperative treatment is also effective.<sup>76</sup> There might be non-responders, as recent investigations have disclosed less effect of  $\beta$ -blockade in American black individuals than in the white population.<sup>77</sup>

### Conclusion:

Insufficient data exists regarding management of patients developing PMI following intracranial surgical procedure. Interventions, CABG or angioplasty and stenting, carried out to improve myocardial oxygenation and treat CAD impose dilemma of discontinuing anticoagulants and antiplatelet therapy. Discontinuation in presence of stent carries risk of stent thrombosis while continuation of anticoagulants poses risk of excessive bleeding during and after surgery. Therefore, in patients with CAD, in order to balance the risk, it might be necessary to limit the extent of the planned procedure or to stage the operations, in addition, the risk reduction strategies such as maintaining normothermia, avoiding extreme anemia, controlling postoperative pain, and prescribing perioperative  $\alpha$ -blockade must be applied. Perioperative monitoring should focus on detection of myocardial ischemia. Prolonged ischemia as diagnosed by persistent ST segment depression of > 30 min should be followed by serial estimation of biological markers of myocardial injury, CK-MB and cTn-I, or cTn-T. In an unfortunate event of PMI, hemodynamic determinants of myocardial O<sub>2</sub> consumption should be optimized. If the patient needs angioplasty and stenting or hemodynamic support with IABP, the optimal management guidelines are yet to evolve. The management of PMI discussed in this review, is based on anecdotal case reports and yet to be critically analyzed.

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