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**Review Article, Cardiology**

# Cost-Effectiveness of MPI SPECT for Cardiac Evaluation in Patients Undergoing Non-cardiac Surgeries

**Taalab, Kh.**

*Consultant of Nuclear Medicine, Military Medical Academy, Egypt.*

## **ABSTRACT:**

The increasing number of patients with coronary artery disease (CAD) undergoing major non-cardiac surgery justifies the guidelines concerning preoperative cardiac evaluation. This is compounded by increasing chances for a volatile perioperative period if the underlying cardiac problems are left uncorrected prior to major non-cardiac surgeries. Preoperative cardiac evaluation requires the clinician to assess the patient's probability to have CAD, severity and stability of CAD, placing these in perspective regarding the likelihood of a perioperative cardiac complication based

on the planned surgical procedure. Coronary events like new onset ischemia, infarction, or revascularization, induce a high-risk period of 6 weeks, and an intermediate-risk period of 3 months before performing non-cardiac surgery. This delay is unwarranted in cases where surgery is the mainstay of treatment. The objective of this review is to offer a comprehensive algorithm in the preoperative assessment of patients undergoing pre-operative evaluation and highlight the importance of myocardial perfusion imaging in risk stratifying these patients.

**Keywords:** Cardiac risk stratification, coronary artery disease, heart, non-cardiac surgeries, myocardial perfusion imaging, single photon emission tomography.

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**Corresponding Author:** Taalab, Kh.

**E-mail:** ktaalab@gmail.com

## INTRODUCTION:

Of the patients who undergo surgeries in Egypt every year, approximately 30% has risk factor coronary artery disease (CAD).<sup>(1)</sup> Patients with a prior myocardial infarction (MI) have a high-risk of peri-operative re-infarction compared with the normal population (5-8% vs. 0.1-0.7%). There is a 6% risk for re-infarction from surgery in patients with less than 3 months history of MI<sup>(2)</sup>.

In patients undergoing general surgery procedures, the risk for perioperative MI is 0.8% in men over than 50 years<sup>(3)</sup> and varies with the cardiovascular status, comorbidities, and the extent of the procedure, reaching more than 20% among patients undergoing vascular surgery<sup>(4)</sup>.

As patients become older, tend to have more comorbidities, minor surgical procedures even can get complicated with stormy postoperative period with the risk of cardiac death is estimated to be 0.4%,<sup>(5)</sup>.

To ensure a smooth recovery postoperatively, physicians must investigate the cardiac status of patients scheduled for major non-cardiac surgeries. Although guidelines are in place for preoperative cardiac evaluations, however there are differences in the prevalence of

CAD and its morbidity. Risk of surgery is also dependent on surgical skills, anesthetic care, and nursing quality. Each institution should therefore establish its own audit in order to take appropriate decisions when choices have to be made between different treatment modalities.

In this article, we shall strive to emphasize on gated stress myocardial perfusion imaging single photon emission tomography (MPI/SPECT), the commonly used physiological imaging modality for cardiac risk stratification in preoperative setting. It is a non-invasive, cost-effective, and sensitive investigation for detecting ischemic heart disease and also to assess physiological significance of known CAD.

### **Need for Preoperative Coronary Artery Disease Evaluation:**

Preoperative cardiac evaluation aims to lower the perioperative morbidity and mortality. It also helps in limiting the financial implications on the patient and to identify those high-risk patients with underlying CAD who will derive long-term benefit from a change in the perioperative management. However, nowadays advantages in anesthesia, use of beta blockers, statins, postoperative analgesia, and surgical techniques have contributed to a reduced rate of major

cardiac complications. Low risk patients on the other hand need not undergo a preoperative cardiac assessment as it adds to their cost and also can lead to an undue delay in performing the relevant surgery. Thus, one need to understand an easy, cost-effective and robust methodology to risk stratify patients prior to non-cardiac major surgeries.

### **Cardiac Risk Indices and Recommended Approach:**

Numerous risk factors have been set forth by various researchers and organizations to risk stratify patients planned for non-cardiac surgeries. To estimate the cardiac risk, patients are risk stratified by the following factors: clinical predictors, functional capacity predictors, surgical risk predictors, and disease specific predictors.

Most of the centers worldwide follow the guidelines of American Heart Association and American College of Cardiology (AHA/ACC) to assess perioperative risk<sup>(6)</sup>.

### **Clinical predictors or risk factors include:**

**Patient related factors:** High-risk factors include symptomatic CAD, advanced congestive cardiac failure (CCF), major valvular abnormalities, and arrhythmias<sup>(7,8)</sup>.

**Cardiac related factors:** Preoperative electrocardiogram (ECG) is recommended in all patients with history and physical findings suggesting heart disease. Men in the age group of 40–45 years, women over 55 years, patients with systemic conditions that may be associated with unrecognized cardiac abnormality, patients on cardio-toxic drugs and patients at risk for major electrolyte abnormalities are in need for further cardiac investigation.

Based on the presence or absence of cardiac diseases, patients can be divided into major, intermediate and minor predictors as described by Goldman<sup>(9)</sup>. This multifactorial index (used for cardiac risk assessment is known as Goldman index or “cardiac risk index.” It predicts the life-threatening cardiac complications or perioperative cardiac death based on the presence of preoperative risk factors. In this, probability of complications is shown on a logarithmic scale. The risks of major complications, defined as pulmonary edema, arrhythmic cardiac arrest, myocardial infarction, and death from cardiac causes were calculated by multiplying the prior odds of complications by the likelihood ratio for each class. The classes are defined as follows: Class I, 0-5 points on the index; Class II, 6-12 points; Class III, 13-25 points; and Class IV, 26 or more points.

**A. Major risk factors include:** Recent MI (less than 6 weeks), Unstable angina (UA) (Class III-IV),

Ischemia post MI, Ischemia and CCF, and Malignant arrhythmias.

In patients with one or more of these major risk factors, the perioperative risk increases five-fold due to sympathetic stimulation and hypercoagulability.<sup>(3)</sup> These patients require an extensive preoperative cardiac evaluation with stress testing, echocardiography, nuclear myocardial perfusion to determine the severity and extent of CAD. Of these investigations, MPI SPECT indicates a high negative predictive value for perioperative cardiac events when it is reported normal.

**B. Intermediate predictors include:**

Previous MI, stable angina (Class I-II), renal insufficiency and diabetes mellitus, low left ventricular ejection fraction (less than 35%), and compensated heart failure.

A few factors which are still considered to be controversial are age more than 70 years, hypertension and left ventricular hypertrophy (LVH). They either fall in intermediate or minor risk category.

However, all patients in intermediate-risk category also need further evaluation by stress MPI or stress echocardiography before proceeding for surgery.

**C. Minor risk factors include:** Family history of coronary artery disease CAD, Uncontrolled hypertension, hypercholesterolemia, smoking, baseline ECG abnormalities (LVH, LBBB, arrhythmia), Post MI more than 3 months, asymptomatic without treatment, post coronary artery bypass grafting (CABG)/percutaneous coronary angioplasty more than 3 months and less than 6 years, asymptomatic without treatment.

In patients with minor predictors or low risk, further preoperative cardiac testing is not recommended as it may not alter the management of patients post major non-cardiac surgeries.

**Functional capacity predictors:**

Functional capacity of a patient can be estimated from treadmill exercise or from the ability to perform daily activities<sup>(11)</sup>. This measure is shown to be reliable for perioperative and long term prediction of cardiac events. Patients with a low functional capacity of less than 4 metabolic equivalents (METS), marked stress-induced ST-segment changes or angina at low workloads, is markers for high risk and need further investigations to evaluate cardiac risk.

**Surgical risk predictors:** The surgical risk factors are dependent on certain factors, like the type of surgery, timing of surgery and the degree of hemodynamic

stress that can happen during the procedure. The reported rate of cardiac death or nonfatal myocardial infarction (MI) is more than 5 percent in high-risk procedures, between 1 and 5 percent in intermediate-risk procedures, and less than 1 percent in low-risk procedures. Institutional and/or individual surgeon experience with the procedure may increase or lower the risk. Emergency surgery is associated with particularly high risk, as cardiac complications are two to five times more likely than with elective procedures<sup>(12)</sup>.

The timing of surgery also plays a role and affects the patient's risk of perioperative cardiac complications. There can be significant hemodynamic abnormalities like variations in heart rate, blood pressure, vascular volume, pain, bleeding etc., intra-operatively. Thus, one need to take into account the type of procedure that is planned, the total time including the amount of blood loss that may occur during the surgery. **High-risk procedures** include major emergency surgery particularly in elderly patients, major and peripheral vascular surgery, and other prolonged procedures. **Intermediate-risk** procedures include carotid end-arterectomy, head and neck procedures, intra-peritoneal and intra-thoracic, orthopedic, and prostate surgeries.

**Low-risk procedures** include endoscopic, superficial procedures, cataract, and breast surgery.

**Disease specific predictors:** Associated cardiovascular diseases like CAD, hypertension, arrhythmias, CCF, peripheral vascular disease, valvular heart diseases like aortic stenosis will need thorough evaluation and it is included in the Cardiac Risk Index.

#### **Assessment of Coronary Artery Disease**

Many algorithms have been proposed combining clinical risk indices, exercise treadmill testing, ECG, nuclear techniques such as radionuclide ventriculography, MPI, and coronary angiography. Myocardial perfusion abnormalities as function imaging have high negative prediction value to exclude CAD.

#### **Stress SPECT / PET MPI in Cardiac**

**Assessment:** Cardiac nuclear medicine has evolved in the last 4 decades from <sup>201</sup>Thallium (<sup>201</sup>Tl) chloride perfusion imaging to <sup>99m</sup>Technetium (<sup>99m</sup>Tc) SestaMIBI/Tetrofosmin single photon emission computed tomography,<sup>(13)</sup> and positron emission tomography (PET) cardiac perfusion imaging using tracers such as <sup>82</sup>Rubidium (<sup>82</sup>Rb), <sup>13</sup>Ammonia adding sensitivity and image resolution; yet both radionuclides are not available in Egypt.

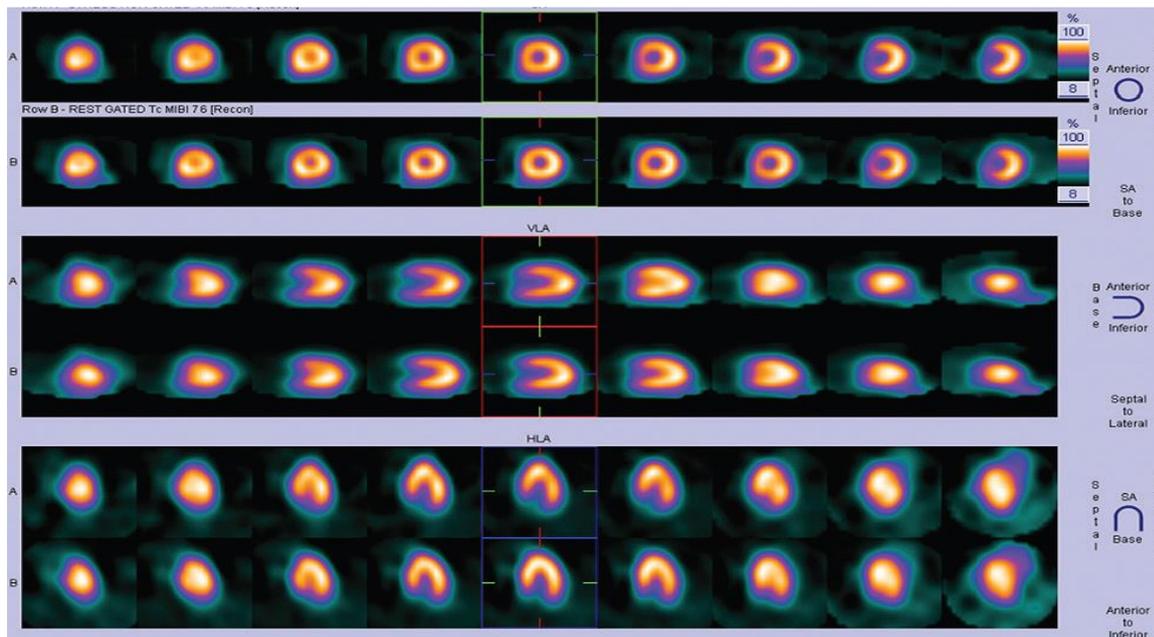
Physical exercise on a treadmill or Pharmacological stress with either

vasodilators (adenosine, dipyridamole) or with dobutamine a beta agonist, as a method of stress during MPI is adopted.

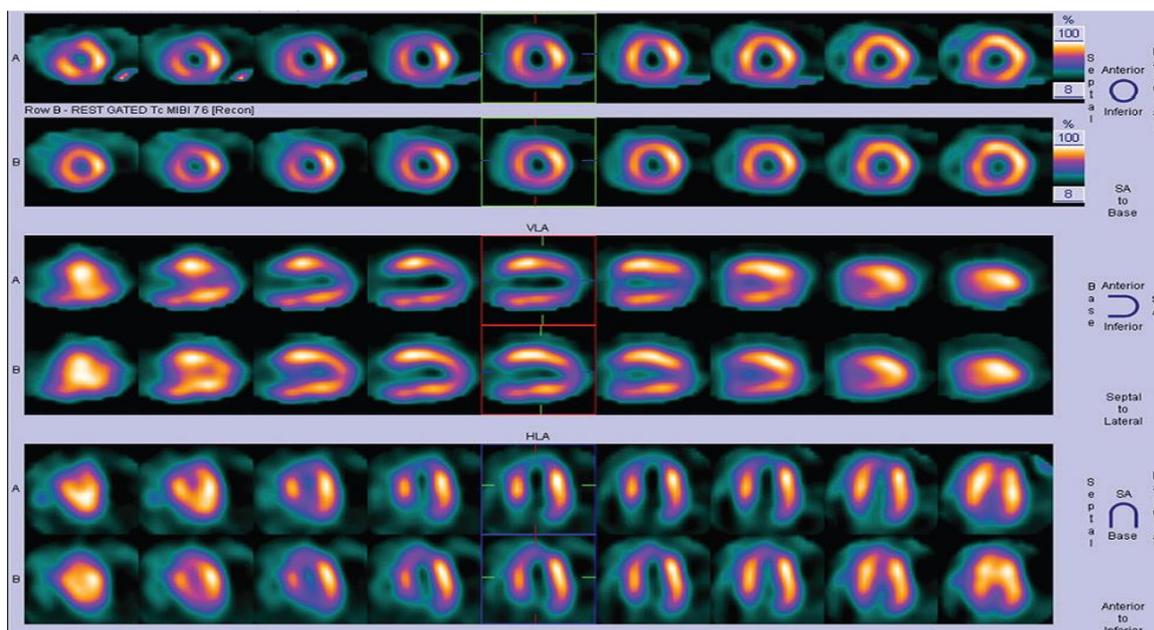
**Risk assessment by stress myocardial perfusion imaging single photon emission computed tomography (MPI SPECT):** 99mTc Sesta-MIBI imaging has been studied most often. A negative scan predicts very low risk of CAD (likelihood ratio, 0.12; post-test probability, 1%), and a positive scan indicates increased risk (likelihood ratio, 3.02; post-test probability, 23%). There is strong evidence that this imaging technique has a good predictive value for determining a low or high operative risk when applied to a selected population of **clinical intermediate risk**, vascular patients. However, it has no real screening value, when applied to a large unselected vascular or nonvascular population, or among patients already classified clinically as low or high risk candidates for surgery<sup>(14 - 21)</sup>.

Independent scintigraphic predictors to be considered during interpretation of a positive study include; (a) number of reversible perfusion defects which act as a measure of ischemic extent, (b) magnitude of reversible perfusion defects which serves as a measure of ischemic severity, (c) heart rate achieved during stress (d) regional wall motion abnormalities. Evidence of residual ischemia after an MI

is found to be a strong predictor of both fatal and nonfatal cardiac events. Patients with no scintigraphic evidence of ischemia have a very low cardiac events (less than 5%) while approximately 40-50% of patients with inducible ischemia develop subsequent cardiac events. MPI also adds incremental value to LV ejection fraction, LVEF. There is also a significant correlation of ischemic events with the magnitude of ischemia in perioperative period [22]. Certain scintigraphic variables that indicate underlying LV dysfunction include increased lung uptake of Thallium/ SestaMIBI or Tetrofosmin, transient ischemic LV dilatation (TID) and marked ST segment changes associated with angina. Magnitude of jeopardized myocardium (as shown by reversible perfusion defects and TID) has an exponential relationship to the likelihood of cardiac events. Patients with no stress perfusion defects are rated as low risk [Figure 1] while patients with or without infarcts with reversible ischemia [Figures2] are categorized as intermediate to high risk depending on the extent and size of perfusion defects. Quantification of their delayed redistribution of 201Tl chloride at 4-24 h is more predictive of cardiac death or MI than simple dichotomous interpretation in positive/negative results.



**Figure 1:** Low risk for cardiac events normal stress myocardial perfusion scan in a 48-year-old lady planned for total hip replacement surgery.



**Figure 2:** Intermediate risk patient in a 56-year-old male with peripheral vascular disease showing a small infarct involving apex with peri-infarct reversible ischemia.

Apart from the cardiac risk stratification, assessment of myocardial viability with  $^{99m}\text{Tc}$  labeled SestaMIBI radiopharmaceutical is particularly important in patients with impaired LV function consequent to CAD, and the potential of revascularization preoperatively can be estimated. Studies have shown excellent correlation of  $^{99m}\text{Tc}$  labeled SestaMIBI MPI with Post-operative cardiac events, both peri-operatively, within 30 days and at long term follow up <sup>(5, 22)</sup>.

Only 1.2% of normal MPI scan patients suffered coronary events post-surgery compared with 15.6% patients with reversible ischemia. While, only 5% of surgical cases got cancelled due to highly abnormal MPI with fixed defects and increased to 15% in patients showing reversible defects in MPI <sup>(14,21)</sup>.

#### **Strategy for dealing with non-cardiac surgery:**

1. Patients scheduled for a low risk procedure can proceed to surgery without testing (Class I, Level B).
2. Patients undergoing intermediate risk or vascular surgery who have unknown functional capacity but no clinical risk factors may proceed to surgery without testing (Class I, Level B).
3. Patients requiring urgent non-cardiac surgery should proceed to the operating room with perioperative surveillance (Class I, Level C).
4. Patients scheduled for intermediate risk surgery or vascular surgery is to be assessed by functional capacity and clinical risk factors. Proceeding with planned surgery is appropriate in patients with good functional capacity (Class IIa, Level B). In patients with poor or unknown functional capacity undergoing vascular surgery who have three or more clinical risk factors, testing should be considered if the results would change management (Class IIa, Level B).
5. Patients with one or more clinical risk factors undergoing intermediate risk surgery and those with fewer than three clinical risk factors undergoing vascular surgery may proceed to planned surgery with control of heart rate to diminish the stress response per-operatively (Class IIa, Level B), or they may undergo noninvasive testing, but only if the results would change management (Class IIb, Level B).
6. Patients with active cardiac conditions who are undergoing non urgent surgery should be evaluated and treated per ACC/AHA guidelines before proceeding for surgery (Class I, Level B).

## CONCLUSIONS:

Myocardial perfusion imaging has emerged as a key guide for major medical decisions involving patient with suspected and known CAD in preoperative situations.

Presence of perfusion defects is a powerful long term predictor of major ischemic events that enhances the prediction provided by clinical, exercise testing and coronary angiographic data. In

view of its prognostic significance, extent of reversible perfusion defects might provide original information about improving prognosis by coronary revascularization.

A normal preoperative MPI had low perioperative risk with a low long term risk (2 years) even in groups with high clinical risk. Coronary revascularization prior to non-cardiac surgery is generally indicated only in unstable patients with high risk of CAD.

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