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**Book:**

**Nuclear Cardiology: Basic and Advanced Concepts in Clinical Practice**

**Chapter: Cardiovascular risk stratification prior to non-cardiac surgery.**

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## **List of abbreviations**

AMI: Acute Myocardial Infarction

AUC: Appropriate Use Criteria

BMI: Body Mass Index

CAD: Coronary Artery Disease

CI: Confidence Interval

CTA: Computed Tomography Angiography

CTCA: Computed Tomography Coronary Angiography

DIP: Dipyridamole

EKG: Electrocardiogram

ETT: Exercise Treadmill Test

HF: Heart Failure

LAD: Left Anterior Descending Artery

LVEF: Left Ventricular Ejection Fraction

METS: Metabolic Equivalent of Task

MI: Myocardial Infarction

MPI: Myocardial Perfusion Imaging

NT proBNP: N Terminal Pro B-Type Natriuretic Peptide

RCRI: Revised Cardiac Risk Index

SPECT: Single Photon Emission Computed Tomography

SSS: Stress Summed Score

SDS: Stress Difference Score

TID: Transient Ischemic Dilation

- **Abstract**

Cardiovascular perioperative risk assessment in non-cardiac patients is an important subject in clinical practice, with great impact in global health costs worldwide. It has been defined as the risk of a cardiac event occurring in non-cardiac surgeries. There are national and international society guidelines with relatively similar recommendations; however, some controversies and different approaches exist depending on the available health systems, resources and/or local experience.

Several surgical procedures imply a significant cardiovascular risk to patients with coronary artery disease (CAD), in some of them unknown or with silent presentation, common in diabetics. Patients with peripheral arterial vascular disease are more prone to present CAD and present higher perioperative risks, most prominent in major non-cardiac surgical procedures. There is a strong need to be aware of these conditions in all patients prior to surgical interventions obtaining adequate and standardized risk stratification. The risks are inherent to the required anesthesia procedures and interventional times, fluid requirements and other issues. Then, clinical and surgical risks should always be considered in every case.

In general, it is necessary to know the urgency of the procedure, its inherited cardiovascular risk (low, intermediate or high) and the individual clinical and surgical risks, including different variables such as age, general condition, comorbidities, cardiopulmonary symptoms, kidney function, medications and electrocardiogram (EKG) abnormalities.

In this chapter, we will review the current use of non-invasive techniques to assess cardiovascular risk, mainly with radionuclide myocardial perfusion imaging (MPI), prior to non-cardiac surgery. The high negative predictive value of MPI is well established. Cardiac imaging is preferred in cases with intermediate to high clinical risk.

A concise comparison with other available methods to evaluate this type of risk will be also addressed. Non-invasive stress testing indications are clearly depicted in most latter perioperative risk assessment guidelines. We will give special emphasis to appropriate indications of radionuclide stress testing and safety including vulnerable populations, such as diabetics, chronic failure patients, organ transplant candidates and elderly population.

- **Key words:**

Coronary Artery Disease, Myocardial Infarction, Myocardial Perfusion, SPECT, Perioperative Risk Assessment,

- **General Issues:**

As the world develops, the number of surgeries rises accordingly. A study funded by the WHO estimated over 4000 surgeries per 100.000 inhabitants per year globally, ranging from 148 to 23.369 strongly correlating with the annual per-head expenditure on health. Poor expenditure countries (less than 100 USD per head) that constitute over a third of the world population, have just under 300 surgical procedures per 100.000 inhabitants per year, whereas high expenditure countries (over 1000 USD per head) accounting 15% of the world population, have an estimated rate of over 11.000 procedures. [1] The estimation of adverse events is extremely complicated due to the different realities and the wide range of procedures. Few studies have tried to estimate the overall incidence of surgical adverse events in developed countries, with rates ranging from 14% to 22%. [2, 3] In developing countries, these rates probably are much higher, with as much as half of these events identified as preventable.

The risk of a fatal or non-fatal cardiovascular event defined as cardiac death or myocardial infarction in the perioperative period in major non-cardiac surgery is relatively high. In order to minimize its occurrence, several guidelines and risk – assessment approaches have been described. *Mangano et. al.* [4] made a thorough review in 1995 of perioperative major cardiac events in patients submitted to non-cardiac surgery; those adverse events were dependant of the baseline risk as shown:

- In unselected patients  $\geq 40$  y.o., the pooled average perioperative MI was 1.4% and cardiac death 1.0%
- In consecutive patients with some selection criteria, the pooled average values were 3.2% and 1.7%, respectively
- In patients referred to 201-Thallium MPI, values were obviously higher due to the selection of high cardiovascular risk patients, 6.9% and 3.2% respectively, performed in 6 large studies.

Perioperative major adverse cardio and cerebro-vascular events occur in 1 of every 33 hospitalizations for non-cardiac surgery in USA. Despite reductions in death rate and acute myocardial infarction (AMI), ischemic stroke has increased over time. The events occurred most frequently in patients undergoing vascular (7.7%), thoracic (6.5%), and transplant surgery (6.3%). The same group published in an observational, cohort study, that perioperative AMI occurred in 0.9% of patients undergoing non-cardiac surgery, being the condition strongly associated with in-hospital mortality. [5, 6]

The decision to undergo diagnostic testing according to Fleisher and Beckman, [7] are discussed in the American and European Societies of Cardiology guidelines, with algorithms proposed for CAD evaluation, based on the available evidence incorporating class of recommendations in different steps. They consider Bayesian strategy using clinical markers, previous coronary evaluation and directed therapy,

functional capacity, and surgery-specific risk and type, as well as the diagnostic test influence on perioperative management.

- **Assessing the surgery timing:**

The initial assessment will always be to determine if an emergency surgery is required or if the procedure is elective and there is time to complete further evaluation. In cases with a life-threatening situation or a relative short period available to stabilize the patient, there is no option to proceed with a non-invasive type of risk assessment. The anesthesiologists will use their prevention strategies to diminish the risk of early and delayed adverse perioperative events.

- **Assessing the surgery risk:**

The surgery risk is based on the complexity of the procedure, the organs and pathologies involved and the type of anesthesia required. Several Risk Indexes are available; one of the most used for cardiac assessment prior to non-cardiac surgery [8, 9] employs a scoring system that correlates to complications. The best situation (0 - 5 points) is Class I with 7% of complications, and the worst (26 - 100 points) is Class IV with 100% of complications. Risk factors include prior MI, angina, pulmonary edema, cardiac valve disease, arrhythmias, medical status, age over 70 y.o. and emergency operation.

Different Medical Societies have published information regarding this issue and several classifications are available. By instance, the UCLA categorizes risks (<https://www.uclahealth.org/anes/risk-stratification#top>) according to the type of surgical procedure:

-conditions with very low risk such as procedures requiring only minimal or moderate sedation and with few physiologic effects, such as: eye surgery, gastrointestinal endoscopy without stents or dental

-other conditions with very high risk, with hemodynamic impact, fluid shifts or eventual major blood loss, such as: aortic or cardiac surgery, intra-thoracic with lung resection or major transplant organ surgery.

The European Society of Cardiology (ESC) has published guidelines for perioperative assessment of different interventions according to their risk, referred to 30 days of cardiovascular death and MI post-procedure [10, 11]

-Low-Risk (<1%): breast, dental, eye, carotid symptomatic, reconstructive, minor gynecologic, minor orthopedic (meniscectomy), minor urologic (transurethral prostate resection).

-Intermediate-Risk (1-5%): intraperitoneal, hiatal hernia, splenectomy, cholecystectomy carotid symptomatic, peripheral arterial angioplasty, endovascular aneurysm repair, head and neck surgery, neurological / major orthopedic (hip and spine surgery), renal transplant, intrathoracic non-major procedures.

-High-Risk (>5%): aortic and major vascular surgery, open lower limb revascularization / amputation / thrombectomy, duodenal-pancreatic surgery, esophagectomy, adrenal resection, bowel, total cystectomy, pneumonectomy, pulmonary or liver transplant.

In cardiovascular asymptomatic patients referred to elective surgery corresponding to low risk procedures, there is no need to perform non-invasive stress testing. Symptomatic cardiac patients requiring high-risk surgery (not emergency) should be studied with a more aggressive methodology such as coronary angiography.

Those asymptomatic patients requiring an intermediate to high cardiovascular risk surgery need to be stratified in order to determine their real risk of perioperative cardiovascular events.

A validated algorithm named *MysurgeryRisk* has been applied preoperatively to predict major postoperative complications. This software was compared to clinical judgement in a quarterly level academic institution, resulting in a significant higher prediction of global postoperative complications, but did not significantly improve cardiovascular adverse events prediction. [12]

- **Assessing the clinical cardiovascular risk:**

In intermediate or high-risk elective surgeries, the correct assessment of the patient's cardiovascular risk is critical. History of prior MI or angor are strongly related to ischemic heart disease, as well as HF symptoms, stroke or transient ischemic attack, renal dysfunction and insulin requiring diabetes mellitus.[11]

Diverse models are available to estimate the preoperative cardiovascular risk considering individual variables; the best known is the revised cardiac risk index (RCRI) scores. This index is able to discriminate between patients at low versus high risk for cardiac events after non-cardiac surgeries, but did not perform well at predicting events post vascular non-cardiac surgery or predicting death.[13] There are controversies regarding the real value of this index-based approach in the clinical practice; however, most guidelines are including it. The risk factors include age, gender, functional status and muscular capacity, body mass index (BMI), smoking, prior cardiovascular diseases, symptoms of heart or respiratory failure, EKG abnormalities, other co-morbidities (systemic or chronic conditions), steroid use and current medications, allergies, prior anesthetics problems, a family history for cardiovascular disease, etc. [14]

In an interesting prospective single-center study on non-cardiac surgery patients  $\geq$  50 y.o. employing retrospectively a perioperative calculator for cardiac risk assessment, myocardial infarction (MI) was a common complication associated with a 90-day mortality of 30%. They studied 385 patients with systematic ischemia screening, 7.0% of them had perioperative MI. The incidence was highest in vascular procedures (11.0%). The 90-day mortality was 29.6% in patients with perioperative MI and 5.6% in non-perioperative ones ( $p < 0.001$ ). The perioperative risk calculator predicted it with an AUC of 0.73 (95% CI: 0.64-0.81). The authors

concluded that the ability of the calculator to predict perioperative MI as helpful. The mentioned risk index was described as better than the well-known RCRI.[15, 16]

The clinical risk may be depicted as major, intermediate or minor according to the type of problem including:

- Major: unstable coronary syndromes, non-compensated HF, significant arrhythmias and severe valve disease
- Intermediate: mild angina pectoris, prior MI, compensated or prior HF; diabetes mellitus or renal insufficiency
- Minor: advanced age, abnormal EKG; rhythm other than sinus, low functional capacity, stroke history and arterial hypertension

Functional capacity is a very important parameter; patients unable to reach 4 metabolic equivalents of task (METs) should be studied with non-invasive methods, including stress MPI.[17-19] Reaching 4 - 6 METs during exercise treadmill test (ETT) may predict favorable outcomes, contrary to those unable to exercise at this level. However, there is a significant group unable to exercise, in whom the functional capacity is unknown. These patients may be subject to pharmacological stress testing, with a worse prognosis than those able to perform adequately an ETT, as demonstrated in a meta-analysis.[20] On the other hand, patients able to reach 10 METs or more have good cardiovascular prognosis.[21] A practical estimation of the functional capacity is the ability of climbing two flights of stairs, which may correspond to 4 METs; high intensity sports represent 10 METs or more.[11]

See:[https://www.escardio.org/static\\_file/Escardio/Guidelines/publications/PERIOP2014\\_ESC\\_ESA\\_SLIDES-NON-CARDIAC\\_SURGERY\\_pptx.ppt](https://www.escardio.org/static_file/Escardio/Guidelines/publications/PERIOP2014_ESC_ESA_SLIDES-NON-CARDIAC_SURGERY_pptx.ppt)

- **General methods (non-stress imaging) for non-invasive perioperative cardiovascular risk assessment:**

Information from the medical exam should be taken in account: symptoms and signs of CAD, HF and data regarding eventual lung pathologies and renal failure.

The first method to assess the cardiac risk is the EKG. It is clear that rest EKG is not adequate unless it shows a clear arrhythmia or myocardial injury or necrosis. The stress EKG employing treadmill or bicycle is not sensitive enough to rule-out CAD. A positive test is helpful; it has been reported that 0.1 mV or more of ST depression in exercise electric test is an independent predictor of perioperative cardiac complications in non-cardiac surgery patients.[22] However, is not always possible to obtain an adequate test in non-cardiac preoperative patients with the required maximal effort and /or interpretable recording.

Two peripheral blood markers such as N-terminal pro-B-type natriuretic peptide (NT proBNP) and the cardiac subtype of troponin-T, found post-myocardial injury



have been mentioned regarding perioperative cardiovascular assessment; some authors and guidelines support their use instead of imaging.[23] Higher preoperative NT proBNP level lead to increased risk of perioperative major cardiac events in non-cardiac surgery. *Binh* et al. state that the combination of NT proBNP with the RCRI and other factors does not improve the accuracy in predicting cardiac events.[24] Troponin T appears as more helpful to predict postoperative cardiovascular events; among patients undergoing non-cardiac surgery, peak post-operative measurement during the first 3 days after surgery was significantly associated with 30-day mortality. Postoperative monitoring improves the risk stratification and may help identify patients requiring further therapeutic interventions.[25, 26]

- **Radionuclide stress testing, SPECT MPI to assess perioperative cardiovascular risk and some technical issues:**

MPI diagnostic and prognostic value. -

In general, the diagnostic value of SPECT MPI is high. The gold standard is the coronary angiography but lately, the fractional flow reserve (FFR) has been promoted as a better gold standard. In a meta-analysis comparing the performance of MPI and other techniques to detect obstructive CAD using the traditional gold standard employing 50% coronary stenosis or more, as abnormal; SPECT had a pooled sensitivity of 88% [95% confidence interval (CI): 88% to 89%], and a specificity of 61% [95% CI: 59% to 62%], being SPECT widely available and most extensively validated.[27] Other meta-analysis using FFR as gold standard, SPECT presented sensitivity of 0.70 and specificity of 0.78 on patient based analysis.[28] A latter similar meta-analysis found a pooled sensitivity of 0.69 [95% CI: 0.56-0.79] and specificity of 0.69 [95% CI: 0.56-0.79] for SPECT.[29]

The prognostic value of SPECT MPI is well recognized, and a negative study assures a very low probability (<1%) of major cardiac adverse events as MI or cardiac death in 2 years. In groups with higher clinical risk such as diabetics or with renal insufficiency, this period is shortened and the probability increases to 2-3%. Patients with abnormal MPI may have even 12 times more events than those with a normal study (7,4% annual); this was observed in a large review with more than 12.000 cases, where patients with stable precordial pain syndrome and normal SPECT had a very low risk of major cardiac events.[30] Thus, the negative predictive value of MPI is very good. The post-stress drop in left ventricular ejection fraction (LVEF) or any left ventricular motion abnormality (mainly obtained in early post-stress imaging), the right ventricle visualization or blood retention in the lungs in the stress phase, as well as transient left ventricular ischemic dilation (TID) may imply a balanced three vessel disease even without segmental perfusion defects or reversible defects only in one territory.[31, 32] See Figure 1.

As previously discussed, there is a good prognosis in patients able to reach 10 METs in the ETT, independent of their other risk factors or the presence of known CAD, however still there is a significant group with ischemia shown in MPI studies. [21, 33, 34]

Specifically, in relation to studies performed in preoperative population, there is evidence, in a group of 1220 patients, that preoperative MPI provides a prognostic value in intermediate but not in low cardiovascular risk patients being evaluated for non cardiac surgery.[35] Univariate analysis indicated that age ( $p < 0.001$ ), diabetes mellitus ( $p < 0.01$ ), HF history ( $p < 0.05$ ) or MPI and QGS software analysis ( $p < 0.0001$ , both) were able to obtain significant risk stratification; data from a study including 481 patients submitted to preoperative non-cardiac surgery evaluation.[36] In diabetic patients without chest pain submitted to preoperative assessment, a normal MPI ensured a low likelihood of perioperative cardiac events. [37] On the other hand, the same group of authors published an incremental prognostic value of SPECT results over information regarding clinical and surgical risk, using a mathematical model in a large group of patients.[38]

#### Technical issues. -

Single photon tracers such as  $^{201}\text{Tl}$ -Thallium initially, and  $^{99\text{m}}\text{Tc}$ -Technetium agents (sestamibi and teboroxime) currently the most employed agents for MPI due to their better imaging characteristics and lower radiation exposure, have been employed for prognosis assessment in CAD population.  $^{99\text{m}}\text{Tc}$  agents require two phases; one to demonstrate segmental or global myocardial ischemia, and another at rest to compare especially if the stress phase is abnormal. It is recognized that the ideal stress for ischemia assessment is ETT; it allows obtaining data from the stress EKG and from perfusion and function in the gated MPI; however, as mentioned earlier, it is not possible to perform in cases with preoperative conditions in order to assess their cardiovascular risk. Even more, patients under beta-blockers, with poor physical condition or left bundle branch block should not be submitted to an ETT due to false negatives or false positives in the latter case.

If a gated stress MPI phase is absolutely normal (including all perfusion and function parameters and good quality images) the rest phase could be skipped without diminishing the accuracy of the test.[39] For that, it is necessary to perform the stress phase first, independent of the stressor and a responsible specialist should be available to supervise and interpret the scan adequately. It is required also to assure that the quality control and quality assurance parameters are met in all cases. It should be remembered that motion during acquisition could cause a false positive mimicking ischemia; processed images miss-alignment may cause false positives in visual and quantitative interpretation.[40-42]

Pharmacological stress using vasodilators is the preferred option for perioperative cardiovascular assessment. The most employed in many places is dipyridamole (DIP) due to its lower cost compared to adenosine or regadenoson, a more specific coronary dilator. Aminophylline should be always ready to revert major or minor cardiovascular or splanchnic adverse effects of DIP. In cases with chronic bronchial obstructive disease under specific bronchodilator therapy is advisable to avoid vasodilators and prefer i.v. dobutamine, which requires more infrastructures. These tests should always be supervised by a trained cardiologist with cardiac arrest support available near-by.[41]

Caffeine abstinence by at least 12-24 hours prior to the use of vasodilators; is an important, although controversial indication; it corresponds to a non-selective antagonist at the adenosine receptor and the ingestion could decrease MPI sensitivity.[43, 44] The restriction should be more strictly performed, as established by a recent interesting publication; false negatives were observed in myocardial blood flow measured with 82-Rubidium PET even with low plasma caffeine levels; those authors recommend avoiding caffeine at least by 36 hours.[45-47]

It is important to gate both phases of the MPI study, the information obtained from left ventricular function is additive to perfusion parameters; it is especially valuable if perfusion appears normal and there are indirect signs of ischemia such as transient dilation or post-stress LVEF drop. In more than 450 patients requiring non-cardiac surgery studied preoperatively, gated sestamibi-DIP SPECT presented an incremental prognostic value over non-gated stress perfusion imaging in predicting perioperative cardiac events.[36]

Even though PET 82-Rb is an excellent method to evaluate CAD with better diagnostic and prognostic value than SPECT MPI, mainly in balanced three-vessel disease and obese population, it is not used for perioperative purposes, due to its higher cost, lower availability and technical complexity [27-29] ; there are no specific publications regarding this application to date.[48-53]

- **Safety of radionuclide non-invasive stress testing:**

Over 15000 patients studied by Lette et al.[54], were submitted to intravenous DIP infusion with 0.56 mg/kg during 4 min as the standard protocol. They demonstrated that the procedure was as safe as an ETT, with a rate of MI or cardiac deaths of 1/10000. A normal 201-Tl DIP MPI predicted a good cardiovascular outcome for at least 2-years following the test.[55] Even higher DIP doses (0.84 mg/kg) such as those usually employed by the echocardiogram specialists are safe.[56, 57] In our experience, from 985 patients with a DIP stress SPECT, 22% were due to non-cardiac pre-operative assessment including oncologic cases; with minor secondary effects that were always reverted with i.v. aminophylline. As expected, we observed larger mortality in follow up (median: 65 months; inter-quartile range 54-86 months) in those cases with abnormal SPECT results, including reduced LVEF, LV dilation, reversible or fixed perfusion defect and those with ischemia compared with those without it.[58] Reanalyzing the perioperative cases subgroup there was no mortality in the 30 days period, we could not obtain data from the clinical management of the positive cases. It is interesting to know that a publication comparing the reason to select pharmacological stress instead of ETT was similar between MPI and echocardiography, despite a higher level of disease acuity in the former group; the main reason was musculoskeletal conditions.[59]

- **Radionuclide stress testing in special or vulnerable population**

Diabetics are patients with higher risk for CAD, mainly due to their accelerated atherosclerosis course and decreased symptoms appreciation, with frequent silent myocardial ischemia. As mentioned, a Japanese study in diabetic patients without chest pain demonstrated that perfusion and/or functional abnormalities in myocardial SPECT were associated with adverse outcome especially in high-risk surgery. Normal findings ensured a low likelihood of perioperative cardiac events.[37]

Vascular surgery patients are a special group due to their higher risk of CAD than other patients; multiple studies have evaluated them for preoperative non-cardiac purposes including clinical risk models factors, serum, and noninvasive cardiac stress tests.[60-62] Cutler et al.[63] showed that logistic regression analysis selected DIP 201-Thallium planar scintigraphy redistribution as the best predictor of perioperative events in patients with indication of diverse vascular surgeries; fixed defects were not predictive. In the same work, using a life-table analysis, a cluster of perioperative events occurred primarily in patients with ischemic MPI, being most of the late cardiac morbidity and deaths observed in patients with fixed defects; if the scan was normal the cumulative survival was 97.2% at 48 months of follow-up. Another important work, from *Hendel and Leppo* [64] in 360 patients submitted to vascular surgery, preoperative clinical indexes were predictive of both perioperative and late cardiac events in patients; however, DIP MPI presented better and supplementary prognostic value.

Oncologic patients are also a more difficult group. In over 780 cases from a tertiary cancer center that were referred to MPI employing dual isotope (mostly pharmacological stress, either dobutamine or adenosine), the test could predict 3-year cardiac outcomes; increasing age, atrial fibrillation, and smoking were associated with worse outcomes, whereas LVEF as well as aspirin use were protective. The group included 71% of preoperative evaluations prior different cancer therapies or surgeries, and the rest for evaluation of suspected CAD. The authors recognized that their work may have had a bias due to its retrospective nature. The effect of surgery on overall survival, cardiac specific survival, and total cardiac-event-free survival was evaluated; surgery status was modeled as a time-dependent covariate in a univariate Cox proportional hazard model for each of the survival endpoints, no significant association was detected between surgery status and any endpoint.[65]

In patients undergoing elective aortic artery aneurysm repair, preoperative pharmacologic stress MPI is not only safe, but is also a useful method to predict long-term cardiovascular mortality; studies with stress summed score (SSS)  $\geq 9$  as well as the presence of diabetes or chronic renal disease are at higher risk after elective repair.[66]

The safety of dipyridamole MPI has also been proved in patients undergoing lung volume reduction surgery.[67] On the other hand, in a cohort study of

octogenarians, MPI provided effective long-term risk stratification, regardless of the stress type used or underlying cardiac function.[68]

MPI has a recognized clinical value as a screening tool in liver transplant candidates. Patients with mild to moderate reversible perfusion defects may have inferior survival characteristics in comparison with patients with normal results.[69]

There is a good correlation between clinical outcomes and appropriateness grading for referral to MPI preoperative evaluation of non-cardiac surgery, supporting the appropriate use criteria (AUC) recommendations for risk stratification selective role of testing, considering the type of surgery and functional class.[70]

- **Other images available for non-invasive assessment of cardiovascular risk:**

Stress trans-thoracic echocardiography is another available option for perioperative risk assessment before non-cardiac surgery. The pharmacological technique is easy to perform, reproducible, and cost-effective.[71] Pharmacological stress could be dipyridamole, adenosine or dobutamine; specifically, dobutamine has been proved as a good tool in elderly population.[72] A meta-analysis of 15 studies of DIP 201-Thallium SPECT and dobutamine echo prior to vascular surgery demonstrated that the prognostic value of stress abnormalities for predicting perioperative ischemic events was comparable between the available techniques but the accuracy varies with CAD prevalence.[73] However, stress echo has to be performed by experienced operators and in patients with good echocardiographic windows to allow a good quality test, not always possible in the presence of chronic airway obstruction, frequent in smokers, issue not relevant for MPI. A systematic review approach in a USA center, observed heterogeneous, but similar reasons for pharmacologic stress between MPI and echo stress, despite a much higher level of disease acuity in the MPI group. On the other hand, the preferences for selecting a noninvasive imaging study after an inconclusive exercise test are dependent mostly on the local experience as well the goals of the testing, patient factors (pretest likelihood of disease) and contraindications.[59, 74]

Computed tomography coronary angiography (CTCA) is another option to assess perioperative cardiac risk as an addition to RCRI scores as published by *Ahn et al.*; they studied over 200 patients with intermediate-risk non-cardiac surgeries; however as an editorial to that work depict, there is no evidence of an eventual reduction in the perioperative risk or mortality yet. [75, 76]

Stress cardiac magnetic resonance has demonstrated high negative predictive value for CAD risk stratification and its advantage correspond to the fact it is not an ionizing radiation technique, making it as a very interesting option.[77, 78] However, there is not enough evidence yet for preoperative risk assessment. *Engbers et al.* consider that CAC and SPECT are independent predictors of major cardiac adverse events in patients with suspected CAD and are helpful to stratify

risk during follow-up.[79] The same group published that the risk for cardiac events is similar for both genders when stratified by CAC score, and also that a high score implies a higher event risk, even in the presence of a normal MPI.[80]

As mentioned earlier, PET blood flow assessment is the best method to measure absolute blood flow with 82-Rb or NH<sub>3</sub>; however, is not a current election in perioperative cardiac assessment setting due to its high cost and low availability. [50, 52, 53]

- **Role of images in Guidelines for cardiovascular perioperative risk assessment:**

ESC and AHA perioperative guidelines mentioned earlier include MPI in their algorithms as an important tool to stratify risk in perioperative assessment of non-cardiac surgery. [10, 11, 18, 19]

In an individual case, the cardiac stress test should position the patient as having extensive left ventricular ischemia or in the opposite absence or just moderate stress-induced ischemia. In the first situation, the patient requires an individualized perioperative management, considering the benefits of the surgical procedure contrasted with the predicted outcome and the effect of medical therapy and / or coronary revascularization. In the second situation, the patients could continue with the surgical procedure.[11]

*Hashimoto* et al. reviewed the current 2015 American College of Cardiology/American Heart Association (ACC/AHA) Task Force perioperative guidelines for non-cardiac surgery; they consider the strategy, operative performance and management relying on the urgency of the procedure, the patient's risk factors, cardiac testing results and specific surgical considerations. Non-invasive cardiac testing including MPI is recommended to be used mainly in patients with poor functional capacity, when the results will affect treatment and outcomes.[17]

*Padma* and *Sundaram* [81] made also a review of the available guidelines for non-cardiac surgeries, intending to offer a comprehensive algorithm in the setting and highlighting the importance of MPI in risk stratification. The authors conclude that the presence of perfusion defects is a powerful long-term predictor of major ischemic events with special value for the extent of reversibility. A normal preoperative scan presents a low perioperative risk and a low long-term risk (2-years) even in high clinical risk groups.

The Canadian Cardiovascular Society Guidelines do not include any non-invasive imaging in this setting; they strongly recommend measuring NT pro BNP before surgery to enhance perioperative cardiac risk estimation in  $\geq 65$  y.o., in the 45-64 y.o. patients with significant cardiovascular disease or with a RCR Index score  $\geq 1$ . The group is against performing preoperative resting echocardiography, CTCA, ETT, pharmacological stress echocardiography or radionuclide imaging to enhance

perioperative cardiac risk estimation.[23] Some controversy has been published regarding frail population with this approach. However, any center should consider, in a multidisciplinary overview, the most accepted guidelines and apply the available options in their media, in order to minimize the risk of perioperative major cardiovascular events.[82]

The American Society of Nuclear Cardiology (ASNC) published a simple guide to clarify the use of exercise stress test (ETT), CTA or SPECT MPI in preoperative assessment. Ref. Wisely Resource, link: [asn.org/referwisely](http://asn.org/referwisely). See Figure 2. As the flowchart shows, they recommend assessing first the exercise capacity, then surgical risk factors, optimize medical therapy and last, perform testing -which are rarely indicated- based on the number of METs achieved, cardiovascular risk factors and symptoms and surgery's risk. The only appropriate indication is MPI in case of unknown METs with presence of risk factors, and a high-risk surgery. In the same scenario, ETT may be appropriate. For unknown METs with risk factors and an intermediate risk surgery, both ETT and MPI may be appropriate. On the other hand, CTA assessment is rarely recommended in any scenario in these patients.

- **Conclusions**

SPECT MPI is a helpful method for assessing perioperative cardiovascular risk, in very selected cases following the international guidelines and individual situation analysis (type of surgery, physical condition and clinical cardiovascular risks) and, according to the appropriate use criteria for non-invasive cardiovascular testing. [83, 84]

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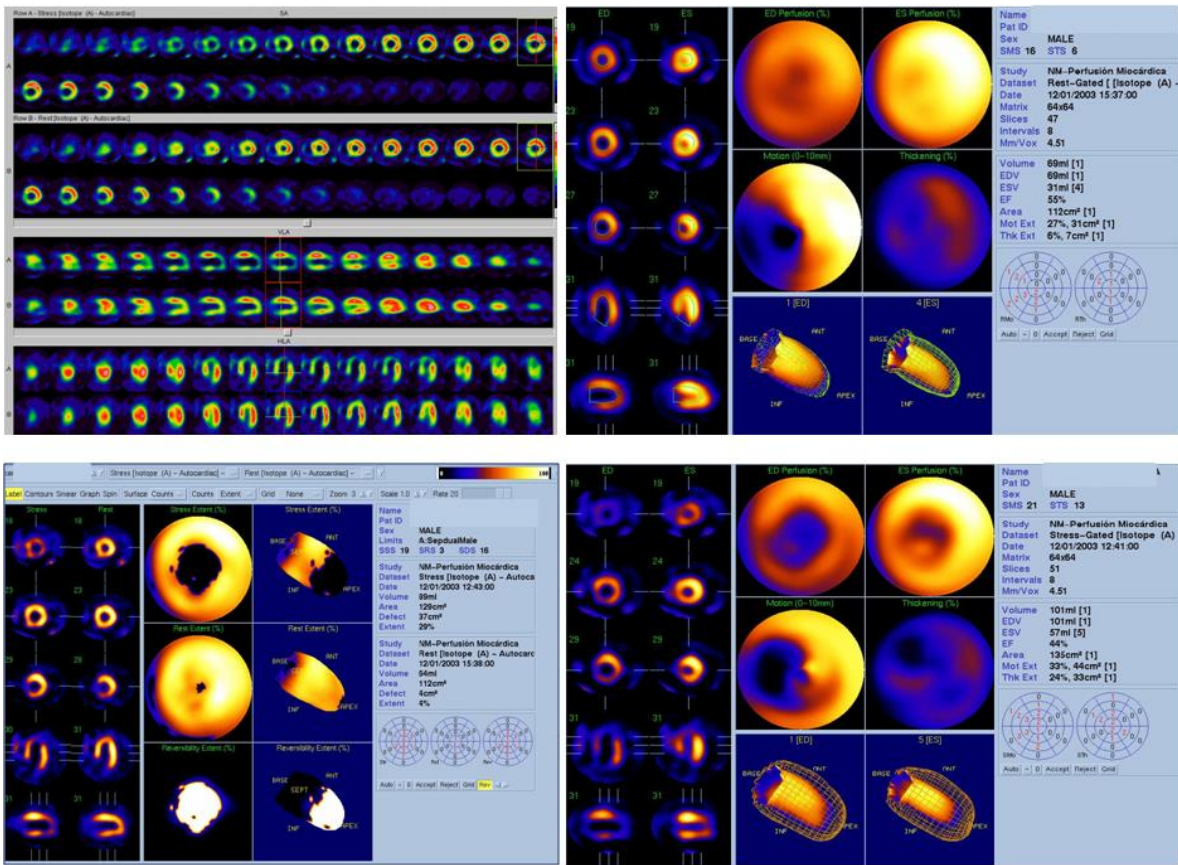
## Legend to Figure 1

### Preoperative assessment of cardiac risk in a vascular surgery case.-

A 73 y.o. male patient with peripheral occlusive artery disease in the lower extremities and cardiac asymptomatic was studied with DIP gated MPI using sestamibi (2 days SPECT protocol). His BMI was  $23.5\text{m/kg}^2$ , presented arterial hypertension and no diabetes mellitus or smoking.

The images showed an important and extensive reversible antero-septo-apical perfusion defect (SSS 19 and SDS 16); his rest LVEF was 55% and presented a drop of 11% post pharmacological stress associated to transient ischemic dilation (TID: 1.46) even though end diastolic volumes remain under normal limits. There were segmental wall motion abnormalities in the hypoperfused segments. The MPI report was: severe myocardial ischemia with stunning in the left anterior descendant (LAD) territory of approximately of the 30% of the left ventricle. The surgery was delayed and the coronary angiography demonstrated a 60% right coronary stenosis and a proximal circumflex and LAD occlusion. He was submitted to triple coronary by-pass surgery and amputation without incidents. He survived 8 more years.

Figure 1





## Legend to Figure 2

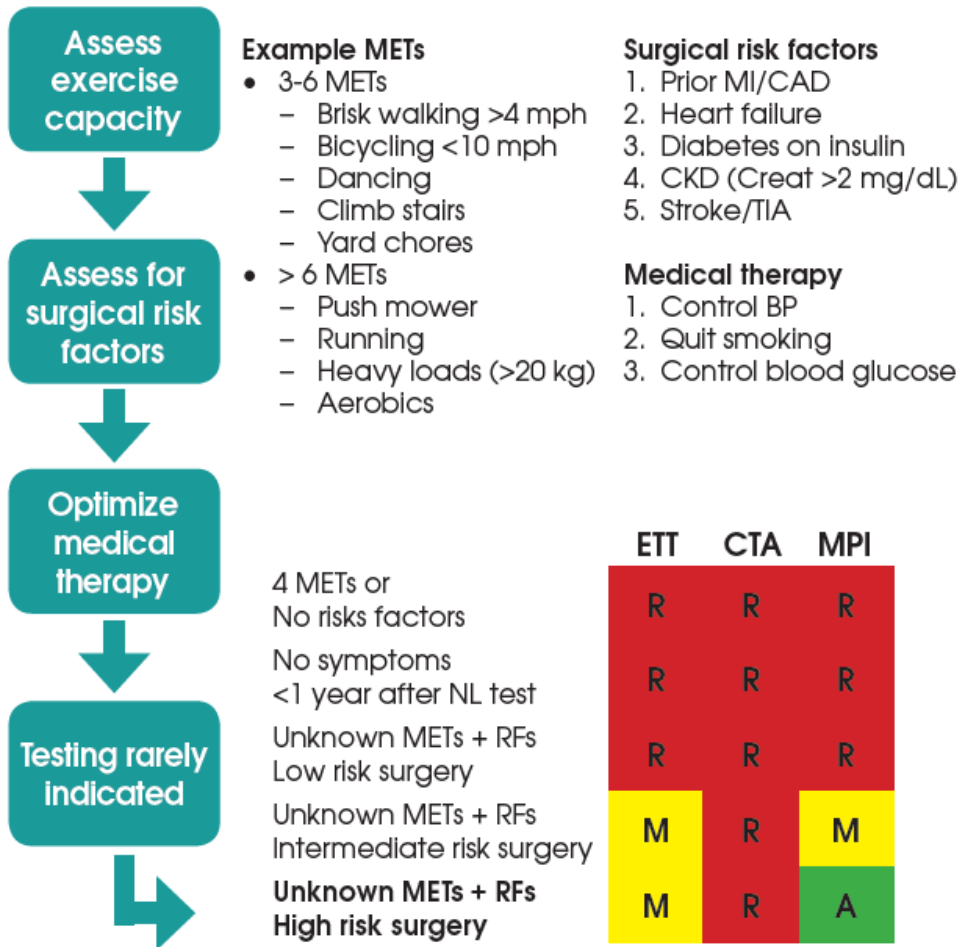
American Society of Nuclear Cardiology (ASNC) Wisely Resource, Choosing Wisely , Perioperative Assessment. [asnc.org/referwisely](http://asnc.org/referwisely).

With permission from ASNC /Choose Wisely.

A = appropriate, M = maybe appropriate, R = rarely appropriate, ETT = exercise treadmill test, CTA = computed tomography angiography, MPI = myocardial perfusion imaging

Figure 2

# Preoperative Assessment



Don't perform cardiac imaging as a pre-operative assessment in patients scheduled to undergo low- or intermediate-risk non-cardiac surgery.

An initiative of the ABIM Foundation