Myocardial Perfusion Imaging for Preoperative Risk Stratification

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Learning Objectives: On successful completion of this activity, participants should be able to (1) describe the role of myocardial perfusion imaging in preoperative risk assessment and (2) integrate current guidelines into the application of preoperative myocardial perfusion imaging.

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This review considers the changing nature of surgical risk assessment and the definition of risk; discusses the pathophysiology of perioperative myocardial infarction in relation to tests of coronary flow reserve; surveys the extensive literature on preoperative myocardial perfusion imaging (MPI) and outlines key trends; presents practical points on image interpretation; addresses the needs of special populations; compares MPI with other modalities; and integrates recommendations from practice guidelines on the effective use of MPI in the preoperative patient.

Key Words: myocardial perfusion imaging; preoperative risk stratification; infarct; ischemia

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Weighing treatment risk and benefit is at the crux of medical decision making. Nowhere is the need to assess risk more compelling than in the perioperative patient, for whom the medical or cardiology consultant and surgical team must formulate a treatment plan and mitigate surgical risk. The patients and their close contacts, on their part, must balance their surgical risk carefully against the alternatives.

In tertiary centers providing comprehensive cancer care to patients facing high-risk and complex surgical procedures, careful preoperative risk assessment is a sine qua non of good care.

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THE NATURE OF SURGICAL RISK ASSESSMENT

Although the fundamental nature of preoperative risk assessment seems intuitive, the concept of risk has been explored and refined in the literature.

Historically, perioperative risk has been defined through hard clinical endpoints such as cardiac and all-cause mortality, perioperative myocardial infarction (MI), and perioperative ischemia (*1*). However, as newer endpoints have been developed, the meaning of risk may also be changing. The sensitive troponin assays currently available have introduced a new and relatively frequent clinical marker of morbidity and have complicated the definition of perioperative MI (*2*). For example, it is common for vascular patients to exhibit a mild elevation in troponin (cardiac troponin I > 0.6) even if assessed preoperatively with mild or no inducible ischemia by myocardial perfusion imaging (MPI) or if previously revascularized for coronary artery disease (CAD) (26% and 23%, respectively) (*3*). The presence of moderate-to-severe ischemia by preoperative MPI in these patients confers a risk of virtually one half of developing this troponin-based endpoint. By comparison, with a more historical marker of creatine phosphokinase–MB index of greater than 5%, positive endpoints were observed in just 6.5% for mild or no inducible ischemia, 6.4% for prior revascularization, and 12.5% for moderate-to-severe inducible ischemia.

This increased detection of cardiac biomarker release of roughly 3–4 times that of prior detection norms is typical of our experience as well and has altered how we define risk, how we present potential outcomes to patients and family members, and how we formulate treatment plans with primary teams.

In an era of medical cost containment, risk may also be defined by surrogate measures related to cost, such as length of stay—an integrated outcome of initial recovery time and late postoperative morbidity. Length of stay must be anticipated and minimized. Thus, the prediction of length of stay represents a new target endpoint for preoperative evaluation. Based on our experience in patients undergoing surgery for thoracic cancer, this endpoint is, to a degree, predictable by preoperative stress testing (*4*).

The role of the consultant in preoperative risk assessment would seem intuitively obvious and even vital. Yet studies have questioned the utility of preoperative evaluation. In a multiple-choice survey of surgeons, cardiologists, and anesthesiologists in the New York metropolitan area, (*5*) Katz found "considerable disagreement among anesthesiologists, cardiologists and surgeons as to the purpose and utility of cardiology consultation." Moreover, a review of 55 consecutive preoperative evaluations found these consultations to have little practical utility (*5*). A more recent review of nearly 400 patients—138 of whom received preoperative medical consultations (*6*)—concluded that nearly half the consultations gave no recommendations and that the outcomes of these patients were no different from the group without medical consultation. Thus, there remains a need to provide cogent, practical, and timely guidance to surgeons, anesthesiologists, and patients alike. Risk assessment is a required first step in this process.

DEFINITION OF RISK

The perceived utility of preoperative tests to determine perioperative risk depends on the definition of risk, the purpose of risk stratification, and, significantly, the vantage point from which the information is received. In a review on the definition of risk in high-risk surgical patients (*7*), Boyd and Jackson explored this issue in depth. Societal understanding of risk is poor, as are the terms used to describe risk. Moreover, risk assessment protocols (*8*) and interventions intended to reduce perioperative risk have often proved ineffective (*9*). Differences in perspective among patients, family, a multidisciplinary care team, and hospital administrators lead to misapprehension of risk and differing priorities (*7*). Moreover, risk-guiding tests (e.g., MPI) or other indicators can perform poorly on an individual-patient basis, with poor positive or negative predictive power (*10*).

It is easier to define high risk relative to large groups perceived to be at lower or baseline risk. In the United Kingdom, the National Confidential Enquiry into Perioperative Deaths estimated a 30-d mortality of 0.7%–1.7% for 2.8–3.3 million operations (1991–1992 survey). Notably, such surveys indicate that surgeons misperceive risk in nearly half of their individual patients. One practical scheme has defined high risk as a mortality risk of greater than 5% and extremely high risk as a mortality risk of greater than 20% (*7*). Clinical scoring systems have been widely used to assess risk, including the American Society of Anesthesiologists grading scale (*11*), a basic yet predictive risk estimator, and others derived and validated institutionally (*7*). This classification (factoring only the presence and severity of systemic disease) remains predictive after nearly 70 y of use.

Anaerobic threshold by cardiopulmonary testing has been found to be a powerful predictor of perioperative mortality (*12*), with a threshold of less than 11 mL/min/kg defining a morbidity risk of 18% versus 0.8%. Significantly, an ischemic electrocardiography (EKG) component on such testing raised the mortality risk to 42% in the patients with a low anaerobic threshold, compared with 4% in the high-threshold group. However, these methods are arduous and not routinely available.

Although the ultimate goal of risk stratification is to reduce risk, efforts to translate perioperative risk data into risk reduction have been complicated by the low positive predictive accuracy of abnormal test results and clinical risk markers (*10*). For pharmacologic MPI, the positive predictive value for death or MI ranges from 5% to a high of 20%, the negative predictive value is 96%–100%, and the likelihood ratio is 1.5–3. Dobutamine stress echocardiography and the Revised Cardiac Risk Index likewise have poor positive predictive value for events. This low positive predictive value has prompted discussion of a shift in paradigm from risk prediction to risk reduction through interventions on groups at risk (*10,13*), a process that itself has met with only limited success (*9*).

PATHOPHYSIOLOGY OF PERIOPERATIVE MI: DETECTION OF PATHOLOGIC SUBSTRATE BY MPI

Myocardial ischemia plays a central role in postoperative morbidity and mortality. Understanding the physiology of perioperative ischemia and infarction is fundamental to the prediction and treatment of perioperative coronary complications (*14*). Mangano et al. showed a direct link between postoperative events and early postoperative ischemia by continuous EKG monitoring in patients with CAD (*15*), outweighing all other clinical predictors tested. In autopsy specimens from patients with fatal perioperative MIs, 93% had obstructive CAD and nearly half had left main or 3-vessel disease. Unstable plaque and plaque hemorrhage were found in 44%. The site of infarction could not be predicted from the degree of underlying stenosis. In all respects, these findings were indistinguishable from a smaller group of nonoperative control infarcts (*16*). In a separate autopsy study of fatal postoperative MIs, plaque rupture was found in nearly half, and intracoronary thrombus in a third. Significantly, MI from plaque rupture was fatal at 7.8 d after surgery, versus only 4.4 d without plaque rupture (*17*), suggesting that infarction occurs later in the perioperative course with plaque rupture than without.

When monitored after vascular surgery with continuous EKG recording (*18*), one fifth of patients had ischemic ST depression. Twelve of 185 patients had a perioperative troponin I level greater than 3.1, with all troponin elevation occurring during or immediately after prolonged ST depression (average time of ST depression with acute MI, 226 min, vs. 38 min in ST depression without infarction). Peak troponin correlated strongly with the duration of ST depression, and all ischemic events resulting in a significant troponin release were preceded by relative tachycardia (32-bpm increase from baseline). Two thirds of these episodes occurred at the end of surgery and early in the recovery. This was the first study to show the strong temporal association between prolonged ischemia defined by ST depression and postoperative MI.

From the foregoing and other studies, Landesberg has formulated a useful model for understanding perioperative ischemia and infarction (*19*): The basic substrate resembles nonsurgical MI—underlying CAD; plaque rupture and thrombosis; tachycardia; and changes in blood pressure, coronary tone, platelet aggregability, and fibrinolysis. In two thirds of patients, ischemia begins immediately after surgery and during emergence from anesthesia, coinciding with increased heart rate, blood pressure, sympathetic tone, and procoagulation. This ischemia is usually silent and identified by ST depression. The change in heart rate may be subtle and the ST depression undetectable without continuous monitoring, even though a third of ischemic patients have ST depression lasting greater than 100 min. Ischemia may progress to myocardial troponin release, but only half these patients with release of troponin develop symptoms or other signs of acute MI. The remaining infarcts would be undetectable in the absence of continuous EKG monitoring or troponin screening. Troponin usually rises by 8–24 h after surgery, consistent with the early postoperative ischemia that induced the infarct. In half the patients with fatal postoperative MI, no plaque rupture or thrombus is found at autopsy, even with severe CAD. Death occurs within 3 d after surgery, consistent with the early onset of ST depression in these patients. Timing in the other half of patients with fatal postoperative MIs whose infarcts are induced by plaque rupture or thrombosis is evenly distributed over the earlier and later periods after surgery.

In a more recent review, Landesberg et al. (*20*) have further characterized these substrates as type I (rupture of unstable plaque) and type II (myocardial O_2 supply–demand imbalance).

The foregoing concepts of perioperative MI reveal both the compelling suitability of MPI for preoperative risk assessment and its limitations. As an almost unparalleled noninvasive marker of coronary flow reserve and for PET, absolute blood-flow, perfusion imaging provides critical physiologic information about coronary circulation and exposes the pathologic substrate of type II perioperative MI (severe CAD with supply–demand imbalance). The strong correlation between moderate-to-severe inducible ischemia on preoperative MPI and low-level troponin release (troponin I > 0.6) in half the patients after vascular surgery (*3*) supports both the view of supply–demand mismatch as a major substrate for perioperative MIs and the rationale for the role of preoperative MPI in predicting such events.

However, in the approximately half of patients whose MI is related to plaque rupture, the link to abnormal coronary flow reserve (and hence abnormal MPI) is more tenuous. Though clearly predictive of cardiac events in groups, the predictive value of MPI in individual patients is problematic (*10*), in keeping with the idiosyncratic nature of plaque rupture. Moreover, in most of these patients, even those with known CAD or multiple cardiac risk factors, both perioperative and long-term deaths were due to noncardiac causes (*21*).

PERFORMANCE OF MPI FOR PERIOPERATIVE RISK STRATIFICATION THROUGH THE DECADES

Even as our understanding of perioperative MI was still evolving, the potent prognosticating power of MPI was extended into the preoperative arena.

In 1985, Boucher et al. (*22*) performed preoperative dipyridamole MPI on 54 stable patients before vascular surgery and reported postoperative cardiac events in 8 of 16 patients with thallium redistribution, compared with no events in 32 patients with either fixed or no defects; clinical indicators were not predictive of events.

Leppo et al. (*23*) then compared dipyridamole scintigraphy with exercise testing in 100 patients undergoing vascular surgery and again found thallium redistribution to be the most predictive tested variable for events, with an odds ratio of 23 versus no redistribution.

Subsequently, through multiple studies, single-photon perfusion imaging has proven durable and reproducible as a predictor of risk, with a scope far exceeding its roots in vascular patients. Preoperative MPI has risk-stratified patient groups from a conventional case-mix to special populations and has provided additional valuable prognostic information beyond the perioperative period (*24*).

Perfusion tracers and imaging technology have evolved from thallium planar imaging to thallium SPECT, ^{99m}Tc-sestamibi and tetrofosmin SPECT, and, more recently, dual-tracer protocols with thallium and ^{99m}Tc agents and ^{82}Rb PET, maintaining prognostic power with each imaging refinement. At Memorial Sloan-Kettering Cancer Center, protocols in current use include exercise, dipyridamole, adenosine, regadenoson, and (rarely, of late) dobutamine stress; and ^{99m}Tc-tetrofosmin, dual-tracer thallium-tetrofosmin SPECT and ^{82}Rb PET imaging.

A representative sample of studies on preoperative MPI is provided in Table 1, annotated with salient results.

From such studies, trends for both the utility and the limitations of preoperative MPI have emerged:

- The predominant population studied is patients with vascular disease, in keeping with the perceived high inherent risk of both the surgery and this patient group.
- Consistent with these patient groups, exercise stress is seriously underrepresented in the literature in favor of pharmacologic stress.
- Spanning over 20 y, the bulk of these studies originated in the early era of MPI and used planar imaging. These studies predated current coronary intervention methods.

TABLE 1
Representative Sample of Studies on Preoperative MPI

Study	Year	Group	Method	Findings	Comments
Kayano (*61*)	2009	211, aortic surgery	Dipyridamole gated SPECT	Multiple predictive scan and gated markers	Only end-systolic volume on gated was multivariate predictor
Stratmann (*62*)	1996	285, nonvascular	Dipyridamole sestamibi SPECT	Abnormal scan, Goldman class, only predictors for major surgery 1% event rate if normal scan Low events in minor surgery regardless of scan	No value in low-clinical-risk group having minor surgery
Van Damme (*63*)	1997	156, vascular	Dobutamine sestamibi SPECT	Abnormal scan; relative risk, 7.4; negative predictive value, 0.97	Nonpredictive if no clinical CAD markers
Brown (*1*)	1993	231, vascular and nonvascular	Dipyridamole thallium planar	Reversible defects, diabetes, multivariate predictors	Extent of redistribution was important
Younis (*64*)	1994	161, major noncardiac, intermediate/high CAD likelihood	Dipyridamole thallium planar	Multiple defects only independent predictor of death or MI; abnormal scan 27% vs. 6% events	Intervention or change in treatment reduced risk
Kresowik (*65*)	1993	190, vascular	Dipyridamole thallium planar	Redistribution in 45% and 46% whether CAD clinically apparent or not	Left main coronary artery/3-vessel disease by catheterization in 13%
Fleisher (*66*)	1999	6,895, vascular, Medicare	MPI or dobutamine stress echocardiography	7% mortality, aortic surgery 16% 1-y mortality, infrainguinal surgery	Stress testing with revascularization strategy reduced mortality at 30 d and 1 y
Koutelou (*29*)	1995	106, vascular	Adenosine thallium SPECT	No events if no ischemia vs. 11% if ischemia	54% had abnormal scans; 82% had reversible defects Low positive predictive value
Baron (*67*)	1994	457, abdominal aortic aneurysm	Dipyridamole thallium SPECT	MPI not predictive of events	Only age and definite CAD were predictive
Lette (*68*)	1992	360 total, 194 surgical (vascular or major general) with normal scans or fixed defects	Dipyridamole thallium planar	1% risk of preoperative cardiac events 1.4% cardiac morbidity at 6 mo 15× noncardiac vs. cardiac risk	Argued against angiography/ revascularization in such patients
Mangano (*69*)	1991	60, vascular	Dipyridamole thallium planar	Redistribution not correlated with perioperative events	Included continuous monitoring
Marshall (*28*)	1995	122, vascular	Adenosine thallium planar in 108 patients Adenosine sestamibi planar in 18 patients	Number of reversible defects only multivariate predictor of events	Only prior heart failure predicted perioperative heart failure
Lette (*30*)	1992	360, noncardiac vascular or major general	Dipyridamole thallium planar	1% perioperative events 3.5% 15 mo if normal scan or fixed defects 17% perioperative, 23% late events if redistribution	Clinical variables were not predictive; risk proportional to extent and severity of ischemia

TABLE 1 (Continued)

Study	Year	Group	Method	Findings	Comments
Fleisher (*24*)	1995	180, noncardiac	Dipyridamole thallium planar	Strongly positive defect by quantitation only result with worse long-term survival Low positive predictive value for perioperative events	Performed ambulatory EKG as well—similar prediction
Lette (*27*)	1992	355, vascular and major general	Dipyridamole thallium planar	Three-step method, 3 segments only Normal→1.3% event rate Left main or multivessel (extensive ischemia) →52% events; then, age > 70 y, diabetes, 1 vs. 2 segments→5%–36% risk	Added clinical markers only if intermediate scan results
Coley (*70*)	1992	100, nonvascular	Dipyridamole thallium planar	For age > 70 y or history of heart failure, 3% vs. 33% had events based on redistribution For age ≤ 70 y, no heart failure→no events	Nearly half of patients were low risk by clinical variables
Hashimoto (*71*)	2007	1,220, intermediate, low risk, noncardiac	Dipyridamole thallium SPECT	SPECT predictive in intermediate risk only, not predictive in low-risk surgery	Functional data were of incremental value in intermediate clinical and surgical risk
Bai (*72*)	2008	284, diabetes without chest pain, noncardiac surgery	Dipyridamole SPECT	Low events in normal scans; abnormal scan increases risk proportional to extent of surgery	No clinical predictors except duration of diastolic murmur
Cutler (*73*)	1992	327, vascular	Dipyridamole thallium planar	Death or MI, 14% if redistribution 1% if normal scan 15% late events (mean, 31 mo) Fixed defects best predictor of late events	Different predictor for late vs. early events
Cutler (*74*)	1987	116, aortic	Dipyridamole thallium planar	MI: 0/65 normal scan MI: 8/31 abnormal scan	Early study was more predictive than all symptoms
Eagle (*75*)	1989	200, vascular	Dipyridamole thallium planar	Thallium redistribution stratified intermediate-risk group into 3% vs. 30% event rate	Was less useful in high- or low-clinical-risk group
Younis (*76*)	1990	111, vascular	Dipyridamole thallium planar	7% vs. 0%, death/MI perioperative for abnormal vs. normal scan At mean 18 mo, 17% vs. 5.6%	Redistribution was predictive only of late events
McFalls (*26*)	1993	116, nonvascular	Exercise thallium SPECT	Angina, CAD signs, abnormal thallium, low ejection fraction correlated with postoperative MI	Angina, fixed defects, were independent predictors
Hashimoto (*25*)	2003	481, noncardiac high or intermediate risk	Dipyridamole tetrofosmin and sestamibi SPECT	Perfusion and function results both independent predictors among clinical variables Quantitation of perfusion and function predictive	Gated helped stratify only patients with normal perfusion

- The absence of thallium redistribution is strongly associated with a low perioperative cardiac event rate (high negative predictive value), but positive predictive value is low.
- A normal preoperative myocardial perfusion scan (MPS) incurs both a low perioperative risk and a low long-term risk (~2 y), even in groups with high clinical risk; positive results are less predictive.
- The benefit of preoperative MPI is unproven (and likely minimal) in low-risk patients.

IMAGE INTERPRETATION: SCAN INDICATORS OF PERIOPERATIVE RISK

Gating of SPECT Images

Hashimoto et al. (*25*) assessed the incremental value of quantitative gated SPECT over nongated perfusion imaging. Functional data were independently correlated with events and added risk stratification to patients with normal scan findings.

Fixed Defects

McFalls et al. (*26*) found the presence of fixed thallium defects (at 3–4 h) and angina to be the only 2 independent risk markers in vascular patients assessed by exercise MPI.

Evidence of Severe CAD

In vascular patients with either transient ischemic dilatation, reversible defects in all 3 segments assessed by planar imaging, or at least one severe reversible defect, half had a perioperative infarction or cardiac death (*27*). Marshall et al. (*28*) found the number of reversible thallium defects to be the only multivariate predictor of perioperative events in vascular patients. A severe defect found by quantitative dipyridamole thallium imaging was the only predictor of long-term mortality in vascular patients (*24*). Again, in vascular patients, only patients with thallium SPECT redistribution had events, but positive predictive value was low. Large defect size and ischemic fraction (23% and 20% of the myocardium, respectively, in patients with events) increased the predictive power of the test (*29*). Quantitation and transient ischemic dilatation predicted both perioperative and long-term events in vascular patients (*30*). The extent of myocardium at risk (number of segments with thallium redistribution) was the best indicator of preoperative risk in high-risk procedures (*1*).

Etchells et al. (*31*) performed a meta-analysis of 9 studies involving 1,179 patients with semiquantitative MPI before vascular surgery. They found that an extent threshold of reversibility of 20% of myocardial segments (found in only 23% of scans) defined an increased risk of cardiac death and nonfatal MI. Reversible defects below this threshold incurred a more than 2-fold risk of events (8.8% vs. 3.1% for normal scans), although this difference did not meet statistical significance. The authors of this meta-analysis cited publication bias and methodologic problems in the primary studies but believed that such bias would have overestimated the inherent risk of highly abnormal scans (because of enhanced surveillance and unblinded assessment of patients perceived to be at higher risk). The severity and location of reversible defects, transient ischemic dilatation, and EKG changes with dipyridamole were deemed important but not fully evaluated in this meta-analysis.

PROGNOSTIC IMAGING CONSIDERATIONS FROM NONSURGICAL POPULATIONS WITH POTENTIAL APPLICATION TO PREOPERATIVE RISK STRATIFICATION

Peri-Infarct Ischemia

Peri-infarct ischemia is not typically interpreted as a high-risk preoperative finding. But in a study of 345 patients with prior MI and reversible sestamibi scans, annual cardiac death rates were higher for peri-infarct ischemia than for ischemia remote from the infarct zone (2.8% vs. 1.2%) (*32*).

Transient Ischemic Dilatation in an Otherwise Normal Scan

Transient ischemic dilatation in an otherwise normal scan is a discordant finding that has uncertain implications preoperatively, but in 1,560 general patients with transient ischemic dilatation, normal tracer distribution and normal left ventricular (LV) size at rest, the highest transient ischemic dilatation quartile had more total events than the others (*33*).

Contemporaneous Coronary Calcium Screening

Contemporaneous coronary calcium screening by CT is of uncertain independent or incremental value preoperatively but was recently evaluated for prognosis in nonsurgical groups. Rogandi et al. (*34*) found no increase in cardiac events at a mean of 32 mo in 1,089 nonischemic patients with high cardiac calcium scores (>1,000). However, in a study of more than 1,000 patients followed for nearly 7 y (*35*), cardiac events increased with high cardiac calcium score (>400) in patients with both normal and abnormal SPECT results, with separation of survival curves at 3 y for cardiac events and 5 y for death or MI. Total and regional calcium scoring is reported on our ^{82}Rb PET perfusion studies at Memorial Sloan-Kettering Cancer Center.

Differences in Imaging Modalities and Protocols

We know of no direct comparison of tracers, imaging methods, or stress protocols in preoperative patients. In nonsurgical patients, no difference was found between ^{99m}Tc-tetrofosmin SPECT and ^{99m}Tc-sestamibi SPECT ($n > 900$ in each group) in predicting events at 1.5 y with a mix of stress protocols (*36*).

Temporal Validity of Preoperative MPI

The clinically germane issue of how long the predictive power of a given perfusion scan remains in effect has not been established in the preoperative setting. For general patient referrals, Hachamovitch et al. (*37*) attempted to determine the "warranty period" of a normal scan in more than 7,000 patients. In patients without previous CAD, risk (events per unit time) from the time of imaging was uniform for a mean of 2 y; with known CAD, risk increased over time. The temporal properties of a normal scan were affected by multiple clinical factors (with diabetic women, notably, incurring an annual event rate of >3 times that of nondiabetic women and an accelerated risk over time). This effect may produce a warranty period for a normal preoperative MPS as well, but this period is unknown.

PREOPERATIVE RISK STRATIFICATION IN SPECIAL POPULATIONS

As we have outlined, studies on preoperative risk stratification with MPI have been heavily weighted toward vascular surgery (patients expected to have more extensive and severe CAD undergoing intensive procedures, who are often poor candidates for standard exercise testing) and major nonvascular surgery. Some studies on preoperative MPI have included special populations and merit particular attention.

The Elderly

The aging U.S. population translates to an increasingly elderly surgical population. In a study of more than 4,000 major abdominal procedures in patients older than 50 y, major cardiac and noncardiac complications occurred in 5.7% of those 60–69 y old, 9.6% of those 70–79 y old, and 12.5% of those more than 80 y old. Specifically, the risk of cardiogenic pulmonary edema, MI, ventricular tachycardia, pneumonia, and respiratory failure increased with age. Patients older than 80 y had a higher hospital mortality (2.6% vs. 0.7%; cause of death not specified) and a longer stay than younger patients in this study (*38*). Hachamovitch et al. (*39*) assessed the predictive value of dual-tracer MPI to risk-stratify 5,200 nonsurgical patients older than 75 y. Both ischemic and fixed defects added incrementally to clinical data for both adenosine and exercise studies, with further stratification by gated SPECT. A normal MPS incurred a lower risk than an age-matched cohort. Modeling of a subgroup with an extended follow-up of 6 y showed an increasing survival benefit of early revascularization with increasing ischemia and a survival benefit of medical treatment with little or no ischemia. These findings may be useful in formulating perioperative plans, because weighing the long-term effects of revascularization is critical in deciding on the benefit of preoperative revascularization.

Though not specifically addressing MPI, Older et al. (*12*) evaluated the use of exercise cardiopulmonary testing in 548 patients older than 60 y before major abdominal surgery. All cardiopulmonary deaths occurred in patients with either EKG evidence of ischemia on the treadmill or an anaerobic threshold of less than 11 mL/min/kg (positive predictive value, 4.6%). This group used preoperative cardiopulmonary testing to assign postoperative care to either a ward, a high-dependency unit, or an intensive care unit. In a retrospective study of more than 1,300 patients, Bai et al. (*40*) grouped perioperative patients by an age of less than 75 y or an age of 75 y or more and by dipyridamole SPECT results. Age was found to be an independent predictor of postoperative events in patients with abnormal SPECT studies, but in patients with normal scans, perioperative risk was independent of age.

Women

Although the literature on preoperative MPI has been weighted toward men, some studies included a nearly equal proportion of women (*41*). The poorer sensitivity and specificity of stress EKG alone in women (*42*) and referrals for noninvasive testing in women unable to exercise will generate the need for both more preoperative stress imaging and more research in this area.

Cancer Surgery

Cancer patients present unique challenges in perioperative care (*43*) because of the complexity of the surgery, perceived hypercoagulation in cancer, and high comorbidity rate. In addition to surgery, risk assessment is needed for bone marrow transplants and cardiotoxic and thrombogenic chemotherapy regimens in patients of increasingly advanced age. There is little in the literature pertaining to such patients. A recent study from M.D. Anderson Cancer Center (*44*) used gated MPI to assess risk in nearly 400 cancer patients. Death, MI, and heart failure, up to 1 mo postoperatively, occurred in 4.7% of patients with abnormal scans versus none with normal scans. The low event rate in their population likely reflects a relatively low-risk case mix in this study.

Thoracic Surgery

The literature on preoperative risk stratification of thoracic patients is robust; most of these studies focused on clinical markers and physiologic exercise or cardiopulmonary stress testing. In elderly patients undergoing lobectomy, performance on symptom-limited stair climbing was the most potent multivariate predictor of postoperative complications (*45*). From the strictly pulmonary standpoint, Datta and Lahiri (*46*) advocate a stepped approach that tests forced expiratory volume in 1 s and diffusing capacity, estimates postoperative forced expiratory volume in 1 s and diffusing capacity by lung scanning in selected patients, and then performs cardiopulmonary exercise testing in still fewer patients. In our institution, we found preoperative treadmill performance to be a strong predictor of length of stay after thoracic surgery (*4*). Thus, it would appear that assessment of exercise performance is an important ingredient in predicting outcomes in thoracic surgery patients.

In one retrospective study, detailed preoperative testing in 184 thoracic patients (including dobutamine stress echocardiography, exercise or dipyridamole MPI, exercise treadmill testing, or coronary angiography) yielded a rate of perioperative MI similar to that in 110 patients without such testing. Predictably, positive results from cardiac testing were much more frequent in patients with than without known CAD (*47*).

Patients Who Have Undergone Bypass Surgery

The prognostic power of MPI to risk-stratify at 11 ± 7 mo after bypass surgery was assessed in 411 patients by exercise thallium SPECT (*48*). Exercise duration, number of thallium defects, and treadmill-induced angina were independent predictors of events at a mean of 5.8 y. A subsequent study of postbypass patients (*49*) found summed stress scores to predict annual cardiac death rates, with the greatest benefit in symptomatic patients within 5 y and in all patients after 5 y. Thus, MPI provides long-term prognostic value after bypass surgery and may be beneficial independent of its value in preoperative risk stratification.

IMPORTANCE OF DYSPNEA AND EXERCISE TOLERANCE

Although, as we have seen, pharmacologic stress has dominated the preoperative MPI literature, the limited available data on exercise tolerance and dyspnea both before surgery and beyond appear compelling.

In 600 patients assessed preoperatively for noncardiac surgery, self-reported exercise tolerance of less than 4 blocks or 2 flights incurred a 2-fold excess of perioperative complications (20% vs. 10%, including ischemic and neurologic events) (*50*).

As mentioned earlier regarding surrogate endpoints, objective exercise tolerance was predictive of length of stay after thoracic cancer surgery in 191 patients (*4*). At the extremes, a prolonged stay (≥10 d) occurred in 9 of 31 patients achieving no more than 4 metabolic equivalents (METs), versus none of 23 patients exceeding 10 METs.

In nearly 18,000 patients free of cardiomyopathy and valve disease, undergoing SPECT MPI, and followed for 2.7 ± 1.7 y, self-reported dyspnea incurred a much higher rate of cardiac and all-cause mortality (all-cause mortality, 6.2% vs. 2.5% of patients without CAD and 11.7% vs. 4.1% with known CAD) and further stratified each clinical subgroup (*51*). Preoperative cardiac or medical evaluation represents an opportunity to perform a comprehensive evaluation and to assess global risk (*52*). Thus, although generated from a general referral base, these results should be weighed carefully when assessing perioperative risk as well.

COMPARISON OF MPI TO OTHER MODALITIES

A comprehensive review of all preoperative stress testing modalities is beyond the scope of this review.

In a meta-analysis of published studies of ambulatory EKG, exercise EKG, radionuclide ventriculography, MPI, dobutamine stress echocardiography, and dipyridamole stress echocardiography from 1995 to 2001, dobutamine stress echocardiography had the highest weighted sensitivity of 85% and a specificity of 70% for predicting perioperative deaths and MI, slightly superior to the other modalities (*53*). Ambulatory EKG showed both poor sensitivity and poor specificity, and resting EKG changes often precluded its use. Radionuclide ventriculography was specific but insensitive. These tests were not recommended in this setting. Exercise EKG, though favored by the American College of Cardiology/American Heart Association (ACC/AHA) guidelines (*52*), is not feasible in many vascular or other higher-risk patients with limited exercise capability or resting EKG changes.

Beattie et al. (*54*) compiled data from 68 studies and more than 10,000 patients undergoing either thallium imaging (^{99m}Tc-sestamibi was included in the search criteria but was poorly represented in the data) or stress echocardiography before (predominantly vascular) surgery. There was no difference in cumulative receiver operating characteristic curves between the 2 modalities (20 studies). However, the likelihood ratio was higher for a positive stress echocardiogram (4.09 vs. 1.83 for thallium) and lower for a negative stress echocardiogram (0.23 vs. 0.44 for thallium). This apparent disparity in diagnostic power in favor of stress echocardiography should be considered in the context of the more than 2-fold use of screening for MI in the stress echocardiography studies versus the thallium studies; the higher tendency for thallium studies than for stress echocardiography to direct treatment; the current predominant use of ^{99m}Tc agents and attenuation correction, not well represented in this study (at Memorial Sloan-Kettering Cancer Center, the use of ^{99m}Tc-tetrofosmin with attenuation correction results in a high rate of reinterpretation of initial defects as breast or diaphragmatic attenuation); and the difference in referral patterns of the 2 tests as used clinically.

The relative value of stress echocardiography and stress MPI should be appreciated in the context of their referred patient base. A recent comparison of referral patterns of more than 5,000 patients at a single institution revealed that, versus stress echocardiography, patients referred for MPI were older and more heavily weighted to diabetes, prior MI (39% vs. 15%), prior revascularization (38% vs. 12%), and LV dysfunction (23% vs. 7%). The authors surmised that similar referral patterns likely exist in other centers and advised caution in interpreting comparisons between these modalities (*55*).

The clinical utility of rest echocardiography to predict perioperative risk was assessed in 339 consecutive men with known or suspected CAD before noncardiac surgery, targeting LV ejection fraction, wall motion, and the presence of LV hypertrophy. In multivariate analysis, an LV ejection fraction of less than 40 was a mild predictor of all cardiac outcomes but not heart failure. The addition of transthoracic echocardiography to known clinical risk markers did not significantly alter their predictive power; its routine preoperative use was not recommended by the authors of that study (*56*).

A contemporaneous study of 87 patients assessed the relative predictive power of dipyridamole thallium imaging and rest echocardiography before noncardiac surgery (>50% vascular). Half of patients had reversible perfusion defects, and nearly a third had LV dysfunction shown by echocardiography. All the postoperative events occurred in patients with both redistribution and LV dysfunction, and the positive predictive value of dipyridamole thallium imaging was markedly improved by the presence of LV dysfunction. The authors advocated the combined use of MPI and echocardiography in identifying high risk in such patients (*57*). However, because echocardiography was performed solely to assess LV function in this study, these results may now be reinterpreted in the current era of gated SPECT to support combined perfusion and functional assessment preoperatively. On the basis of the above studies and others, current ACC/AHA guidelines recommend against the routine perioperative use of rest echocardiography (*52*).

INTEGRATING MPI INTO PATIENT MANAGEMENT: RECOMMENDATIONS FROM PRACTICE GUIDELINES

Both the American College of Physicians (*58*) and the ACC/AHA have published guidelines on preoperative cardiac evaluation and risk assessment (*52,59*). Guidelines from these practice groups have differed historically, with their recommendations for preoperative testing often being discordant (*58*). Overutilization of preoperative stress testing in relation to either set of guidelines has been reported (*58*). The American College of Physicians Clinical Efficacy Assessment Subcommittee (the body developing and updating guidelines) considers guidelines older than 5 y to be no longer active—their recommendations potentially outdated. Hence, we turn to the 2007 ACC/AHA recommendations for guidance (*52*).

Patients with poor or uncertain exercise tolerance (<4 metabolic equivalents—e.g., climbing hills) and 3 or more clinical risk factors (ischemic heart disease, compensated heart failure, diabetes, renal insufficiency, and cerebrovascular disease) are considered reasonable candidates for noninvasive testing before vascular surgery (class IIa recommendation) if the results will change the management. Stress testing "may be considered" (class IIb recommendation) in patients with poor or uncertain exercise tolerance and 3 or more risk factors undergoing intermediate risk surgery or 1–2 risk factors before either vascular or intermediate risk surgery. Note that there are no class I ("should be performed") recommendations for preoperative noninvasive stress testing. Moreover, stress testing is not recommended in patients before urgent surgery, before low-risk procedures regardless of functional capacity, or with good exercise tolerance regardless of intrinsic surgical risk. Patients with unstable coronary syndromes, decompensated heart failure, major arrhythmias, and severe valvular disease are evaluated and treated for their conditions before surgery can be considered. The ACC/AHA guidelines call for simple exercise treadmill testing in ambulatory patients with an interpretable baseline EKG, exercise imaging for nondiagnostic EKGs, and pharmacologic stress imaging for patients unable to exercise adequately.

These guidelines stress the overriding themes that interventions are rarely necessary to lower the surgical risk in itself unless also indicated for the long-term benefit of the patient, that the purpose of the preoperative evaluation is not to provide "clearance" but to perform a comprehensive cardiac evaluation for intermediate perioperative and long-term benefit, and that tests should be performed only if results will influence treatment.

With these guiding principles, our experience at Memorial Sloan-Kettering Cancer Center is that MPI (along with other stress imaging modalities) can be invaluable to the perioperative care of select cancer patients whose surgical procedures are often extensive and prolonged (respective median and maximum operating room times: genitourinary, 278 and 873 min; thoracic, 128 and 780 min; hepatobiliary, 220 and 608 min; orthopedic, 178 and 1,330 min; head or neck, 163 and 1,346 min; neurosurgery, 231 and 840 min; and gynecology, 198 and 974 min). Because of these patients' underlying cancer, active or recent chemotherapy and radiation treatment, and intercurrent illness, their exercise capacity is often either poor or uncertain, making them potential candidates for stress testing by ACC/AHA guidelines. We reserve stress testing for those with suggestive symptoms, multiple risk factors, and an abnormal baseline EKG that requires interrogation as part of the comprehensive cardiac evaluation. The value of exercise treadmill EKG testing without imaging has been highly limited in this setting. The prognostic information from MPI has provided a critical element in the preoperative evaluation that often influenced the choice of cancer therapy, extent of surgery, and intensity and venue of postoperative care even when coronary interventions were not pursued.

However, experience in our specialized population has confirmed the limited use of preoperative stress imaging when not indicated by ACC/AHA guidelines. When existing ACC/AHA guidelines were retrospectively applied to 776 consecutive cancer patients referred for stress echocardiography before intermediate-risk surgery, fully 84% of tests were not indicated by the guidelines. This group incurred a low perioperative event rate, and cardiac events were not predicted by stress results. Stress results risk-stratified only when testing was indicated by the guidelines (*60*).

KEY POINTS AND CONCLUSION

Perioperative myocardial ischemia and infarction result from coronary plaque rupture or from supply–demand imbalance, giving rise both to the strong suitability of MPI for perioperative risk assessment and to its limitations. Preoperative MPI has a high negative predictive value; a normal preoperative MPS result incurs both a low perioperative risk and a low long-term risk. The benefit of MPI is unproven in low-risk patients and is probably not cost-effective. Preserved exercise tolerance is associated with a low perioperative risk, and as stated in current guidelines, MPI is unlikely to help with perioperative decision making in such patients. In our experience, preoperative MPI has the greatest utility in the management of intermediate- to high-risk patients with limited exercise tolerance whose signs or symptoms suggest but do not prove the presence of potentially severe or unstable coronary disease. For patients in whom the diagnosis of unstable or severe disease is clearer (including those with limited exercise tolerance), proceeding directly to cardiac catheterization in consideration of coronary revascularization is likely the better strategy.

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