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Prevalence and predictors of myocardial ischemia by preoperative myocardial perfusion single photon emission computed tomography in patients undergoing noncardiac surgery

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BACKGROUND: The prevalence and predictors of myocardial ischemia before noncardiac surgery are unknown. In addition the predictive value of myocardial perfusion single-photon emission computed tomography (SPECT) before noncardiac in individual patients is uncertain.

OBJECTIVE: Evaluate the prevalence and predictors of myocardial ischemia before noncardiac surgery, and determine the postoperative cardiac outcome based on results of myocardial perfusion SPECT.

DESIGN: Retrospective.

SETTING: Single tertiary care center.

PATIENTS AND METHODS: We reviewed the records of adult patients diagnosed with myocardial ischemia by myocardial perfusion SPECT who were undergoing noncardiac surgery. Myocardial perfusion SPECT had been performed within 4 weeks prior to noncardiac surgery requiring general anesthesia.

MAIN OUTCOME MEASURES: Prevalence of abnormal myocardial perfusion SPECT results on preoperative evaluation; abnormal myocardial perfusion SPECT results as a predictor for postoperative cardiac events such as cardiac death, nonfatal myocardial infarction, and unstable angina.

RESULTS: Of 131 patients who underwent noncardiac surgery from February 2015 to April 2016, 84 (64%) patients were female and the mean (SD) age was 64.1 (13.6) years. The prevalence of abnormal myocardial perfusion SPECT was 18% (24 of 131). Normal myocardial perfusion SPECT was highly predictive (up to 100%), but a positive myocardial perfusion SPECT had low positive predictive value (4%). Variables associated with an abnormal myocardial perfusion SPECT included ischemic heart disease, congestive heart failure, ASA score of 3 or more, limited exercise capacity (less than 4 METs), male sex, hypercholesterolemia, hypertension, smoking, and abnormal ECG. In a multivariable analysis, history of ischemic heart disease and history of smoking were significant predictors of abnormal myocardial perfusion SPECT (P=.001, and .029, respectively).

CONCLUSIONS: Because of the low positive predictive value of myocardial perfusion SPECT, utilization of the technique in the workup of cardiac patients undergoing noncardiac surgery has been inappropriate. Myocardial perfusion SPECT should be restricted to only clearly defined appropriate use criteria.

LIMITATIONS: Relatively small number of patients and retrospective design.

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The evaluation of preoperative risk in patients undergoing noncardiac surgery has been challenging and difficult. The preoperative evaluation of cardiac risk will continue to be an important issue for many clinicians[1-5] as the prevalence of coronary artery disease (CAD) and noncardiac surgery is predicted to increase over next 30 years.[6] There is a direct link between postoperative ischemia measured by continuous electrocardiographic (ECG) monitoring, with CAD outweighing all other clinical predictors.[7] In two-third of patients, ischemia begins immediately after surgery with increasing heart rate during emergence from anesthesia. Besides assessment of perioperative risk for ischemic cardiac events, myocardial perfusion single photon emission computed tomography (SPECT),[8-11] preoperative stress myocardial perfusion SPECT has long-term prognostic value.[12] Reversible defects are the important prognostic findings in stress myocardial perfusion SPECT with greater extent of reversibility being indicative of higher death, and myocardial infarction (MI).[13] In patients older than 70 years, there is a progressive reduction in hyperemic flow reserve with subsequent reduction in myocardial perfusion.[14] Another common risk factor for myocardial ischemia is diabetes. Patients with diabetes are at a 2-4 fold greater risk of cardiovascular mortality and more likely to have ischemia and less likely to survive a myocardial infarction (MI) than nondiabetic patients.[15] The American Society of Anesthesiology physical status classification (ASA) is now a standard element of the anesthesiologists preoperative assessment of surgical patients worldwide.[16,17] The specific aim of our study was to obtain historical, clinical, diagnostic, and imaging data from patients who underwent noncardiac surgery to determine the association of that data with ischemia seen on myocardial perfusion SPECT before noncardiac surgery.

PATIENTS AND METHODS

This retrospective chart review study was conducted to evaluate the prevalence and predictors of myocardial ischemia diagnosed by myocardial perfusion SPECT in adult patients undergoing noncardiac surgery. Risk stratification in patients with suspected CAD was determined using myocardial perfusion SPECT. The results were correlated with clinical data, including coronary artery disease risk factors, electrocardiography (ECG), chest x-ray, echocardiography, poor functional capacity, history of congestive heart failure , history of ischemic heart disease, and ASA functional status. The ASA functional status is: 1) normal healthy patient, 2) patient with mild systemic disease, 3) patient with severe systemic disease, 4) patient with severe systemic disease

that is a constant threat to life, 5) moribund patient not expected to survive without surgery.[18] Surgery was categorized as high-risk (aortic and major vascular surgery), intermediate–risk (intraperitoneal), and low-risk (superficial surgery).[19] The inclusion criteria included myocardial perfusion SPECT performed within 4 weeks prior to noncardiac surgery requiring general anesthesia. Data on demographics, pre-operative assessment by the anesthesiologist in terms of symptoms, comorbid conditions, and results of myocardial perfusion SPECT were collected from the patient charts and electronic medical records (EMR) on a specially designed case report form (CRF). The design of this observational study was approved by our institutional review board.

Stress and rest SPECT imaging were performed with technetium-99m tetrofosmin according to standard American Society of Nuclear Cardiology guidelines.[20] Most subjects underwent pharmacological stress test with dipyridamole using standard infusion protocols. Medications such as nitrates and beta-blockers were stopped at least 12 hours before testing. The SPECT images were visually interpreted in all three standard projections, along with the gated SPECT and raw image data to assess for perfusion. All images were reoriented in short, vertical, and horizontal views utilizing Auto SPECT (Cedars-Sinai Medical Center, Los Angeles, California) for visual interpretation by an experienced nuclear medicine physician. The reader was not biased by clinical information. Stress and rest perfusion images were scored using 17 tomographic segments, which included 6 segments each for the basal and midventricular slices, and 4 segments for the apical short-axis slices. The final segment is located in the most apical part of the left ventricle. Finally, gated short-axis images were processed with quantitative SPECT software, to measure the ejection fraction. In the visual analysis the 17 segments were scored for perfusion defects on a 4-point system (0=normal; 1=mild; 2=moderate; and 3=severe) for both the stress and rest images. A gated SPECT result was considered normal if as follows: no visual perfusion defect, summed stress score <3, a left ventricular ejection fraction (LVEF) at rest >50%.

Relationships between the categorical variables was tested using the chi-square test the Fisher Exact test with two-sided significance and a P value less than 5% was considered statistically significant. Group means for continuous data were compared using the two independent samples t test. Multivariate logistic regression was used to detect the effect of multiple risk factors on the events of interest. The data was then entered into IBM SPSS Statistics Version 20 for analysis after cleaning.

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RESULTS

In the 15-month period from February 2015 to April 2016, 131 myocardial perfusion SPECT were referred for preoperative evaluation before noncardiac surgery. There were 84 (64%) females and the mean (SD) age of the whole study population was 64.1 (13.6) years (**Table 1**). The mean age for normal myocardial perfusion SPECT patients was 63.6 (13.9), and for abnormal myocardial perfusion SPECT patients it was 66.5 (11.7) (**Table 2**). During preoperative assessment, 49 (37%) of the patients showed a recent decreased exercise capacity (4 or fewer metabolic equivalents [METS]), 38 (29%) had known coronary artery disease, 35 (27%) a history of congestive heart failure. CAD risk factors included: 108 (82%) had hypertension, 83 (63%) diabetes, 40 (30%) hypercholesterolemia, and 33 (25%) of patients were smokers. Underling malignancy was noted in 64 (49%) patients.

Positive findings for myocardial perfusion SPECT were observed in 24 (18%) patients. A statistically significant association was found between abnormal myocardial perfusion SPECT and male gender, ASA status of three or higher, decreased exercise capacity, history of heart failure, history coronary artery disease, hypercholesterolemia, smoking, and abnormal ECG (**Tables 2, 3 and 4**). Seventy-three (56%) patients underwent surgical procedures categorized as high-risk surgery, 40 (35%) patients underwent intermediate risk surgery and the remainder (n=12, 9%) underwent minor risk surgery . A post-surgical cardiac event was observed in one patient with abnormal myocardial perfusion SPECT as a post-surgical myocardial infarction in 75-year- old male patient who underwent high risk surgery. In the multivariate logistic regression, history of CAD and history of smoking were significant predictors of abnormal myocardial perfusion SPECT (*P* value=.001, and .029) respectively (-2 log likelihood=93.53; Hosmer and Lemeshow test, chi-square=5.773, df=8, *P*=.673).

DISCUSSION

The main finding in this study is an estimation of the prevalence of myocardial ischemia with the preoperative myocardial perfusion SPECT in patients who undergo noncardiac surgery. There was an association between several clinical variables and the presence of myocardial ischemia, but there was no association with age, body mass index , chest x-ray or ECG. The preoperative myocardial perfusion SPECT has high negative predictive value (nearly 100%) for perioperative cardiac events but a poor positive predictive value (4%).

Preoperative myocardial perfusion SPECT and prediction of perioperative cardiac events

Our data indicated a prevalence of ischemia in the preoperative setting in noncardiac surgery of up to 18% (24/131) and only one postoperative nonfatal MI in patients who underwent high-risk surgery with positive ischemia on myocardial perfusion SPECT. This finding is consistent with multiple prior studies. An absence of thallium redistribution (equivalent to myocardial ischemia) is strongly associated with a low perioperative cardiac event rate (high negative predictive value), but the positive predictive value is low.[21] A normal perioperative myocardial perfusion SPECT incurs both a low perioperative risk and a low long-term risk (up to 2 years), even in groups with high clinical risk. Since positive results are less predictive, the benefit of preoperative myocardial perfusion SPECT is less if the result is positive. Therefore, preoperative myocardial perfusion SPECT has greatest utility in the management of intermediate to high-risk patients with limited exercise

Table 1. Patient characteristics (N=131).

Factors	n (%)
Gender	
Female	84 (64)
Male	47 (36)
Age, years	64.1 (13.5)
Body mass index (BMI)	32.3 (7.9)
ASA status	
I	2 (1.5)
II	64 (49)
III	62 (47)
IV	2 (1.5)
V	1 (0.8)
CAD risk factors	
Hypertension	108 (82)
Diabetes mellitus	83 (63)
Hypercholesterolemia	40 (30)
Smoking	31(25)
Type of surgery	
High risk	73 (56)
Intermediate risk	46 (35)
Low risk	12 (9)

Data are mean (standard deviation) or number (percentage).

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Table 2. Patient characteristics as predictors of myocardial perfusion SPECT results.

	MPI negative) (n=107, 82%)	MPI (positive) (n=24, 18%)	Total (n=131)	P value
Gender				
Female	75	9	84	**.003**
Male	32	15	47	
Age/years	63.6 (13.9)	66.5 (11.7)		.350
Body mass index	32.8 (8.2)	29.8 (5.8)		**.038**
ASA status at MPI				
I	2	0	2	
II	56	8	64	
III	49	13	62	**.016**
IV	0	2	2	
V	0	1	1	

SPECT: single-photon emission computed tomography, MPI: myocardial perfusion imaging. Statistically significant P values are bolded.

tolerance whose signs or symptoms suggest but do not prove ischemic heart disease. The benefit of preoperative myocardial perfusion SPECT is unproven in low-risk patients. Our study indicates there is overinvestigation of cardiac risk with preoperative myocardial perfusion SPECT in some patients. This may be an unnecessary cost to the health care system.

Ischemic heart disease

Our study showed a strong association between a history of ischemic heart disease and the presence of myocardial ischemia with preoperative myocardial perfusion SPECT (P=.001). A history of ischemic heart disease is known to be one clinical specific factor on the revised cardiac risk index module to estimate the perioperative cardiac events.[22] Several studies have shown that the incidence of perioperative myocardial ischemia is highest in patients who have CAD. Patients with verified CAD account for approximately one-third of all patients undergoing noncardiac surgery.[23] In a prospective study by Mangano et al, 474 patients with CAD (n=243) or at high risk for CAD (n=231) who underwent noncardiac surgery, 83 (18%) patients had postoperative events, ischemic events (cardiac death, myocardial infarction, or unstable angina) . Postoperative myocardial ischemia was associated with 12.8-fold increase in the odds of an ischemic event.[2]

Congestive heart failure

Our data suggest an association between the presence of heart failure with an abnormal myocardial perfusion SPECT in the preoperative evaluation, although ischemic heart disease is known to be the most independent risk factor for postoperative cardiac events. Several studies indicated that symptomatic heart failure is equally important.[24,25] The prevalence of symptomatic heart failure is estimated to be around 2-3% and increases with age.[26] The term heart failure describes a clinical syndrome. Asymptomatic left ventricular dysfunction is considered a precursor of symptomatic heart failure and is associated with high mortality.[26] During surgery, high catecholamine production is responsible for vasoconstriction and hemodynamic stress and preoperative fluid administration increases ventilation and pre- and afterload.[27]

Conventional CAD risk factors as predictors of abnormal myocardial perfusion SPECT

Conventional risk factors associated with abnormal myocardial perfusion SPECT include diabetes, hypocholesteremia, hypertension, and smoking. Cigarette smoking increases the risk of obstructive CAD. Coronary endothelial dysfunction might precede epicardial obstructive atherosclerosis in long-term smokers and in other individuals at risk for CAD.[28] Patients with hypercholesterolemia have impaired coronary and peripheral endothelial dysfunction. This improvement is due to functional restoration of the coronary endothelium before anatomic progression of coronary stenosis, which can occur following long term-treatment.[13] In addition, the association between diabetes and an abnormal myocardial perfusion SPECT is consistent with diabetic patients having a high incidence of occult CAD, ranging from 20% to 60% depending on the patient population.[29] However, the prevalence of occult CAD depends largely on the severity of diabetes. Diabetic patients with normal myocardial perfusion SPECT still present a greater cardiovascular risk than nondiabetic patients. This indicates the need for a more refined selection for those patients with diabetes who are likely to benefit from preoperative myocardial perfusion SPECT.[30]

Preoperative decreased exercise capacity

Our data showed that decreased exercise tolerance (METS class 4 or less) is a predictor of ischemia on preoperative myocardial perfusion SPECT. Patients with poor exercise tolerance on formal testing have more perioperative complications and cardiac events. A previous study among patients undergoing vascular surgery, those with good performance on treadmill

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testing or arm ergometry, had fewer postoperative cardiovascular complications.[31] Poor exercise tolerance by self-reported exercise tolerance has shown that poor exercise tolerance predicts risk for all serious complication independent of all other patients characteristic, including age, cardiovascular illness, smoking history.[32] All patients reporting poor exercise tolerance were at increased risk, regardless of the cause of their limitation, although the risk is particularly high in those limited by cardiac symptoms.[33] Patients with poor exercise tolerance may have more significant medical problems such as diabetes, congestive heart failure, hypertension and higher ASA scores.

American Society of Anesthesiologist classification as a predictor of myocardial ischemia

The American College of Surgeons National Surgical Quality Improvement Program database was used to determine risk factors associated with intraoperative, postoperative myocardial infarction, or cardiac arrest (MICA). On multivariate logistic regression analysis, five factors were identified as predictors of MICA: type of surgery, dependent functional status, abnormal creatinine, increased age, and ASA class.[33] The ASA physical status system is meant to stratify systemic illness. Operative procedures are not a part of the ASA classification system. Many studies have shown a correlation between mortality and ASA status, but tonly in a surgery-specific analysis. An ASA score of 3 or more has been reported as a significant predictor for postoperative morbidity and mortality, and an independent risk factor for postoperative complications.[34,35]

Myocardial perfusion SPECT before cancer surgery

About 50% of our study population were cancer patients (64/131). In the presence of cancer there was no statistically significant difference between patients with and without cancer in predicting myocardial ischemia. Patients with cancer frequently undergo major surgical procedures for resection or for reconstruction surgery. These patients often have several comorbidities, including anemia, hypercoagulability, or pain related to underlying malignancy. These factors add stress to the heart during major operative procedures. In addition, patients with tumors near the heart who receive radiation before surgery may already have subclinical radiation induced CAD.[36] In a preoperative risk stratification using gated myocardial perfusion SPECT in consecutive cancer patients with normal myocardial perfusion SPECT (n=201) and abnormal myocardial perfusion SPECT (n=193), normal perfusion patients had a high negative predictive value for perioperative cardiac

Table 3. Clinical data and CAD risk factors as predictors of myocardial perfusion SPECT results (N=131).

	MPI (negative) (n=107, 80%)	MPI (positive) (n=24, 20%)	Total (n=131)	*P* value
Decreased exercise capacity				**.018**
Negative	72	10	82	
Positive	35	14	49	
Known history of congestive heart failure				**.006**
Negative	84	12	96	
Positive	23	12	35	
Known history of ischemic heart disease				**.001**
Negative	83	8	83	
Positive	24	16	38	
Diabetes mellitus				**.019**
Negative	44	4	42	
Positive	63	20	79	
Hypercholesterolemia				**.023**
Negative	79	12	84	
Positive	28	12	37	
Hypertension				**.043**
Negative	22	1	20	
Positive	85	23	101	
Smoking				**.003**
Negative	86	12	90	
Positive	21	12	31	
Cancer surgery				
Negative	58	9	67	.105
Positive	49	15	64	

SPECT: single-photon emission computed tomography, MPI: myocardial perfusion imaging. Statistically significant *P* values are bolded.

Table 4. Chest x-ray, ECG, and echocardiography as predictors of results of myocardial perfusion SPECT.

	MPI (-ve)	MPI (+ve)	Total	*P* value
Chest x-ray				
Abnormal	22	7	29	.415
Normal	36	5	41	
Electrocardiography				
Abnormal	84	23	107	.05
Normal	21	0	21	
Echocardiography				
Abnormal	38	10	48	.768
Normal	50	11	61	

SPECT: single-photon emission computed tomography, MPI: myocardial perfusion imaging.

events. However, patients with abnormal results and ischemia or scarring had a rate of cardiac events (death, MI, congestive heart failure) of 4.7%. Therefore, an abnormal myocardial perfusion SPECT should prompt perioperative management and more cardiac work up. The low event rate in this study population most likely reflects a relatively low risk mix in this study.[37] The finding in that study is comparable to our study. In our study, there was only a 4% postoperative myocardial infarction rate and our patients were of low- to-moderate risk of cardiac events.

Preoperative chest X-ray, electrocardiography, and echocardiography as predictors of an abnormal myocardial perfusion SPECT
In our study, chest x-ray performed on 70 patients was positive in 29 (41%) patients and was found to have no association with abnormal myocardial perfusion SPECT (*P*=.415). This finding is consistent with many previous studies. Kovacevic et al. showed that preoperative chest x-ray did not statistically influence postoperative management and did not predict postoperative cardiovascular complications.[38] However, preoperative chest x-ray may be indicated in certain patients, including males, patients with a history of cardiovascular disease, the elderly, and patients with an ASA score of 3 or more.[39] There was association between ECG and an abnormal preoperative myocardial perfusion SPECT (*P*=.008). The prevalence of ECG abnormalities in an older population varies depending on the type of population. One study showed that a prevalence of left ventricular hypertrophy of up to 6.9%.[40] Common ECG abnormalities in the preoperative setting include left

ventricular hypertrophy, atrial fibrillation, left bundle branch block, T wave changes, and a high percentage of Q/QS pattern. Another study showed that the presence of ECG abnormalities does not provide incremental information in predicting the occurrence of postoperative cardiac complications. The low specificity of the preoperative ECG in predicting postoperative cardiac complication also suggests that a normal ECG does not exclude occult cardiac disease; nevertheless, obtaining preoperative ECG as a baseline test may be of value in a subset of patients who are at high risk or who are undergoing procedures with an increased cardiac risk.[41] There was no association between resting preoperative echocardiography and the presence of ischemia on myocardial perfusion SPECT (*P*=.761). The clinical evidence for preoperative utilization of echocardiography is scanty. Resting echocardiography has a relatively weak association in predicting postoperative outcomes even in patients with active cardiac conditions and poor functional status.[42] Cardiologists, cardiac anesthesiologists and anesthesiologists need to formulate a new strategy for using echocardiography in the assessment of peri-operative risk stratification of patients afflicted with cardiac pathology.[43]

Appropriate use criteria and myocardial perfusion SPECT for preoperative evaluation before noncardiac surgery
The goal of various professional societies in creating appropriate use criteria is to promote rational and effective use of health care resources while providing high quality care.[44] The rapid growth of myocardial perfusion SPECT utilization causes a significant strain on healthcare resources. Appropriate use criteria in cardiac radionuclide imaging was developed to guide clinicians on optimal utilization of myocardial perfusion SPECT in various clinical conditions, including preoperative evaluation before non-cardiac surgery. Appropriate use criteria included further imaging in patients undergoing vascular or major surgery with less than 4 METS and at least 3 or more CAD risk factors. If imaging might change patient management, there was no indication for imaging in patients undergoing emergent surgery, minor surgery, or patients with more than 4 METS. Using appropriate use criteria, it was reported that the most common source of inappropriate referral to myocardial perfusion SPECT was preoperative risk stratification.[45] Koh et al studied the relationship between appropriate grading by appropriate use criteria and postsurgical outcomes and found that myocardial perfusion SPECT results predict outcome in appropriately tested patients, but not in patients whose test

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were classified as inappropriate.[46] In our study, it was obvious that there were many patients who were inappropriately referred for myocardial perfusion SPECT. Subsequently, the test was not helpful in predicting the postsurgical outcome. Inappropriate use of such an expensive test may cause a severe burden and strain on healthcare resources.

Study limitations and conclusions

The study was retrospective with relatively few subjects. The myocardial perfusion SPECT was categorized as normal or abnormal without further subcategorization into high or low risk. The study was not randomized so there was possible confounding or bias that may have impacted the results. Monitoring of postoperative cardiac events was observed only during hospital admission. Some cardiac events may occur over a prolonged time course, although most perioperative cardiac events occur in the first 3 days postoperatively

Because of the low positive predictive value, the wide use of myocardial perfusion SPECT may have been a waste of resources. Physicians should be educated to use myocardial perfusion SPECT based only on clearly defined appropriate use criteria.

Acknowledgments

Conflict of interest

None.

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