Resting Radionuclide Myocardial Perfusion Imaging in a Chest Pain Center Including an Overnight Delayed Image Acquisition Protocol

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Emergency department (ED) patients with chest pain (CP) and a nondiagnostic electrocardiogram (ECG) present difficult management decisions. The purpose of this study was to investigate the utility of resting radionuclide SPECT myocardial perfusion imaging (SPECT MPI)—including an overnight delayed image acquisition protocol—in identifying patients presenting to the ED with CP at risk for cardiac events. **Methods:** Patients presenting to the ED with CP and a nondiagnostic ECG were prospectively enrolled and underwent chest pain center evaluation. All patients also underwent resting gated SPECT MPI using ^{99m}Tc-tetrofosmin tracer. Patients presenting on weeknights between 12 AM and 6 AM had tracer injection in the ED with image acquisition delayed until later in the morning. Patients were monitored for a 30-d occurrence of cardiac events. **Results:** Over a 16-mo period, 479 patients were enrolled and completed follow-up. For the prediction of 30-d cardiac events, resting SPECT MPI demonstrated a sensitivity and a specificity of 76.9% and 92.4%, respectively. Positive and negative predictive values were 22.2% and 99.3%, respectively. Among the 3 patients with a normal perfusion scan who suffered cardiac events, all had tracer injection several hours after resolution of CP. The overnight delayed image acquisition protocol provided a negative predictive value of 100% for the 44 patients whose image acquisition was delayed until the following morning. **Conclusion:** A normal resting SPECT MPI in ED patients presenting with CP predicts a very low occurrence of 30-d cardiac events. A delayed image acquisition protocol did not decrease the accuracy of SPECT MPI. Such a protocol may be useful in increasing the availability of this imaging modality.

Patients often present to the emergency department (ED) with a complaint of chest pain (CP) and a nondiagnostic 12-lead electrocardiogram (ECG). Management decisions with these patients are difficult. Patients with noncardiac CP or low-risk angina can be safely discharged from the ED with appropriate follow-up (*1*). Rarely, patients with true unstable angina (UA) or myocardial infarction (MI) are discharged from the ED with potentially dire consequences (*2*). Standard initial diagnostic evaluation lacks sufficient sensitivity for UA (*2*); therefore, many low-risk patients are admitted, resulting in significant cost to the health care system. Resting myocardial perfusion imaging (MPI) using ^{99m}Tc with gated SPECT has been shown to provide information for risk-stratification of this population beyond the standard evaluation (*3–6*). In this setting, radionuclide MPI has demonstrated favorable test characteristics, including a high negative predictive value for cardiac events (*3,7,8*). Furthermore, MPI in the ED has been shown to be useful for clinical decision making (*7–10*) and to provide further information beyond that provided by serum biomarkers, including troponin (*11*). Rest MPI results also have short and intermediate prognostic implications in this setting (*12,13*). The ability to offer this testing around the clock requires significant human resources with highly trained nuclear technologists and test interpreters. Many previous studies have excluded patients who arrived to the ED at night or on weekends because of the nonavailability of nuclear cardiology services (*9,10*). The purpose of this study was to investigate the utility of resting gated SPECT MPI in identifying patients presenting to the ED with CP who are at risk for cardiac events. Our protocol, however, included radionuclide tracer injection by radiology personnel overnight with image acquisition in the morning. In addition to providing this imaging service around the clock, this protocol has the potential for substantial cost savings through decreased on-call requirements and a decreased admission rate for low-risk patients.

MATERIALS AND METHODS

Patients

Over a 16-mo period, patients presenting to the ED with CP and a nondiagnostic ECG were eligible for enrollment in the study.

Exclusion criteria included ST-segment elevation, ST-segment depression > 1 mm in 2 electrically contiguous leads, history of coronary artery disease (CAD), clinical syndrome consistent with UA, or hemodynamic instability. The CP center protocol consisted of ST-segment trend monitoring and serial cardiac markers (cardiac troponin T and creatine kinase MB) at 0, 3, and 6 h. Resting gated SPECT MPI was performed on all study patients while in the ED. In all cases, the tracer used was ^{99m}Tc-tetrofosmin, with a typical dose range of 740–1,110 MBq (20–30 mCi). The protocol recommended that the radiotracer not be injected if CP had resolved for >2 h, although discretion was left to the physician. Perfusion images were obtained with an ECG-gated, dual-head SPECT camera using a low-energy, high-resolution, parallel-hole collimator. A Butterworth filter was used for reconstruction without attenuation correction, and a 20% symmetric energy window was centered on 140 keV. Interpretation of perfusion scans was performed by an attending nuclear medicine physician or cardiologist experienced in the interpretation of cardiac perfusion scans. After normal working hours, scans were interpreted remotely on a personal computer using commercially available software (Images-on-Call; Images on Call Teleradiology Networks). For the purposes of study analysis, perfusion scan results were classified as normal or abnormal. An abnormal scan was defined by an area of decreased myocardial tracer uptake or a regional area of decreased myocardial thickening. Equivocal scans were regarded as abnormal. A normal perfusion scan was defined by uniform myocardial uptake and normal regional wall thickening. Scans showing global left ventricular dysfunction or increased chamber volume in the absence of a regional perfusion defect were classified as normal with regard to ischemic findings. In addition to the usual daytime schedule for nuclear medicine technologists, an on-call technologist was available from 1:30 PM to 12 AM on weekdays. An on-call technologist provided imaging services during the daytime on weekends. Between the hours of 12 AM and 6 AM on weekdays, radionuclide injections took place in the CP center by radiology personnel trained in handling radioactive imaging material. In this subset of patients, gated SPECT image acquisition was delayed until shortly after 6 AM when nuclear medicine technologists arrived at the hospital.

Patients were prospectively enrolled and followed for 30 d after the ED visit. Primary endpoints included MI, abnormal coronary angiogram (defined by at least one coronary stenosis > 50% severity), percutaneous coronary intervention (PCI), coronary artery bypass grafting (CABG), ventricular tachycardia/ventricular fibrillation (VT/VF) arrest, heart failure admission, or cardiac-related death. Follow-up consisted of medical records review, phone contact, mail contact, and review of state and national death registries. The research protocol was approved by the institutional review board.

Statistical Analysis

Test characteristics were determined using a 2×2 matrix of the categoric variables of a normal or abnormal perfusion scan and the presence or absence of 30-d cardiac events as described. The Fisher exact test was applied to determine nonrandom association between the variables. The statistical significance level was set at $P < 0.05$.

RESULTS

Four-hundred eighty-four patients were enrolled. Five were lost to follow-up, resulting in 479 patients in the final analysis. The study population demographics are shown in Table 1. The age ranged from 20 to 80 y with a mean age of approximately 45 y. The ratio of males to females was approximately equal. African–Americans made up the largest racial demographic, followed by Whites. Cardiovascular risk factor prevalence was typical for a low-risk population with the exception of smoking and cocaine abuse, both of which were high. Cardiovascular medication use was low in the study population. No individual class of medication was used in >10% of the study population.

Subjects underwent a protocol-driven evaluation in the CP center and received gated SPECT MPI. Four-hundred thirty-four patients had normal resting MPI and 45 had abnormal MPI consistent with ischemia. In the normal MPI group, 3 (0.7%) patients had cardiac events. In the abnormal MPI group, 10 (22.2%) patients had cardiac events (Table 2). The difference in cardiac events between the 2 groups was highly significant statistically ($P < 0.001$). The test characteristics of gated SPECT MPI in predicting 30-d events were as follows: sensitivity, 76.9%; specificity, 92.4%; positive predictive value, 22.2%; and negative predictive value, 99.3%.

Among the 3 patients in the normal MPI group with cardiac events, 2 had abnormal coronary angiographic studies and PCI and the third had a MI on the same day as the scan. This last patient was later found to have a history of CAD and presented with CP in the setting of

TABLE 1
Demographics, Cardiovascular Risk Factors, and Medications ($n = 479$)

Parameter	Value
Age (y)	
Mean ± SD	44.8 ± 11.6
Range	20–83
Sex	
Male	243 (50.7)
Female	236 (49.3)
Race	
African–American	290 (60.0)
White	181 (37.7)
Asian/Pacific	2 (0.4)
Other	6 (1.3)
Cardiovascular risk factors	
Dyslipidemia (known history)	55 (11.4)
Hypertension	187 (39.1)
Diabetes	61 (12.8)
Smoking	283 (59.2)
Family history of CAD	196 (41.0)
Recent cocaine abuse	85 (17.9)
Medication	
β-Blockers	11 (2.2)
Calcium antagonist	33 (6.8)
Nitrate	12 (2.6)
Lipid-lowering agent	35 (7.3)
Aspirin	17 (3.5)

Values in parentheses are percentages.

TABLE 2
Cardiac Events

Cardiac event	Normal MPI (n = 434)	Abnormal MPI (n = 45)
MI	1 (0.3)	5 (11.1)
PCI	2 (0.6)	9* (20.0)
CABG	0	0
Abnormal angiogram	0†	0
Heart failure admission	0	0
VT/VF arrest	0	0
Cardiac death	0	0
Total cardiac events	3 (0.7)	10 (22)

*Includes MI undergoing PCI.
†Excludes those undergoing PCI.
Values in parentheses are percentages.

TABLE 4
Delayed Image Acquisition

Parameter	Value
Resting perfusion scan results	
Normal	41
Abnormal	3
Cardiac events	0
Time intervals	
CP to injection	
Mean	51 min
Injected during pain*	64%
Maximum	4 h 20 min
Injection to image acquisition	
Mean	3 h 20 min
Minimum	45 min
Maximum	5 h 15 min

*Time interval = 0.

significant anemia and several comorbidities. Cardiac biomarkers were mildly elevated, and the patient was treated conservatively. The details of these 3 "false-negative" scans are shown in Table 3. CP had resolved for >2 h before tracer injection in each of the 3 patients. Patients with cardiac events in the abnormal MPI group included 4 cases of MI undergoing PCI and 1 case of MI managed conservatively. The remaining 5 patients had significant coronary stenosis at catheterization and underwent PCI.

Forty-four (9.1%) patients presented in the early morning hours and, therefore, underwent a delayed-image acquisition protocol. Details of this patient group are shown in Table 4. Most patients received tracer injection during or shortly after the cessation of CP. The average time from injection to image acquisition was 3 h 20 min, with the longest delay remaining under 6 h. Forty-one of these patients had normal scans and were free of cardiac events. Three had abnormal perfusion scans without cardiac events. All 3 had normal coronary angiography or normal follow-up stress MPI. None of the patients undergoing delayed image acquisition had a normal perfusion scan and later suffered a cardiac event.

DISCUSSION

Gated SPECT MPI has been shown to add significant diagnostic information to the standard ED CP evaluation in previous studies (3,5,6). One of the impediments to implementation of gated-SPECT MPI in EDs has been the logistic challenge of providing prompt image acquisition and interpretation 24 h per day, 7 d per week. The present study illustrates that—through the use of prompt tracer injection combined with flexible nuclear medicine technologist scheduling and image interpretation by local teleradiology—accurate results can be obtained. Previous reports of resting MPI in the ED excluded patients presenting in the late evening, in the early morning, or on weekends when nuclear cardiology staff are unavailable (9,10). A portion of our study population underwent a delayed imaging protocol. This protocol involved radionuclide injection by trained personnel in the early morning hours with image acquisition after 6 AM when nuclear medicine technologists arrived at the hospital. ^{99m}Tc perfusion imaging reflects relative myocardial blood flow at the time of tracer injection. There is no significant redistribution; therefore, imaging can occur some time after injection. There is a risk of image degradation with a prolonged injection-imaging interval as the agent decays. The half-life of ^{99m}Tc is approximately 6 h. Most of the imaging in our study, including the overnight delayed acquisition, occurred within one half-life. Of the 44 patients undergoing delayed image acquisition, 3 had abnormal scans and none of these patients

TABLE 3
Cardiac Events and Gated SPECT MPI Findings in "False-Negative Scans"

False-negative MPI events	Gated SPECT MPI findings	Timing of injection
PCI 3 d after MPI: LCx, 70% midvessel stenosis	Normal perfusion and function	CP resolved for >3 h
PCI 3 d after MPI: LCx, 90% stenosis; LAD, 20% stenosis; RCA, 50% stenosis	Normal perfusion and function	CP resolved for 4 h
NSTEMI on same day as MPI	Normal perfusion and function	CP resolved for 5 h

LCx = left circumflex coronary artery; LAD = left anterior descending artery; RCA = right coronary artery; NSTEMI = non–ST-elevation myocardial infarction.

had events. More importantly, none of the patients with a normal perfusion scan had cardiac events. Our results indicate that prompt tracer injection followed by delayed image acquisition did not diminish the high negative predictive value of gated-SPECT MPI.

The overall results of the current study are consistent with previous reports. Kontos, et al. conducted a study in which low-to-moderate risk patients underwent rest MPI in the ED and were followed for 5 d (*3*). For the combined endpoint of MI or revascularization, the sensitivity and negative predictive value of rest MPI were 81% and 99%, respectively—very similar to our findings. That study had a more stringent definition of positive scan findings, requiring both a perfusion defect and regional wall motion abnormality. Equivocal scans were classified as normal. The primary utility of resting cardiac perfusion imaging in a population of patients presenting to the ED with CP is in identification of patients at low risk for cardiac events. These low-risk patients may be discharged from the ED with appropriate outpatient follow-up. The current study adds to the literature a large, single-center experience showing the utility of gated SPECT MPI in identifying patients at low risk for cardiac events at 30-d follow-up.

The present study also provides details of the 3 patients who had perfusion scans interpreted as normal in the ED and later had cardiac events. Although the number of these patients is small, they are of great concern to practitioners in the ED who make decisions to release patients to home with chest discomfort. Some similarities were noted in this group. All 3 had radionuclide tracer injection after CP had resolved, in some cases several hours later. In 2 patients the cardiac event was abnormal angiography requiring PCI. One patient with a normal perfusion scan had a MI. This patient had tracer injection 5 h after resolution of CP and was admitted despite the normal MPI due to her overall clinical presentation. Furthermore, this patient was found to have a history of CAD, an exclusion criterion for this study. The appropriateness of resting MPI in this individual is questionable. Similar to our current study, previous publications have reported administration of ^{99m}Tc tracer for several hours after the resolution of CP (*2*). The detailed description of the patients with normal scans having cardiac events in our study suggests that the accuracy of resting MPI could be improved further if tracer injection occurred during or shortly after CP.

This study is a single-center, case-control analysis of MPI of patients with a complaint of CP in an urban ED. Our institution handles a high volume of cardiac nuclear imaging from both the ED and the nuclear cardiology laboratory. Generalization of our findings to another practice setting may be difficult. Also, the lack of a control group and nonrandomized patient assignment fails to control for potential patient selection bias.

CONCLUSION

A normal resting gated SPECT radionuclide MPI scan predicts a very low incidence of 30-d cardiac events. Abnormal scans identify patients at higher risk for 30-d events who should receive further diagnostic testing for atherosclerotic CAD. A delayed image acquisition protocol did not diminish the accuracy of resting MPI for prediction of cardiac events in the present study. Lastly, radionuclide injection after resolution of CP may be associated with a higher rate of false-negative MPI results.

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