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Use of observation followed by outpatient stress testing in chest pain patients with prior coronary artery disease history: An evaluation of prognostic utility

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ABSTRACT

Objective: To determine the outcomes of patients with chest pain (CP) and prior history of coronary artery disease (CAD) managed with observation followed by outpatient stress myocardial perfusion imaging (MPI).
Methods: Retrospective analysis of patients with CP managed with observation followed by outpatient stress MPI, comparing cardiovascular (CV) event rates stratified by CAD history.
Results: 375 patients were included: 111 with and 264 without a CAD history. All patients underwent outpatient stress MPI within 72 h of observation. MPI identified patients at risk for CV events. However, while patients with negative MPI and without a CAD history had very low rates of short- and long-term CAD events (0.8%, 0.8%, and 1.3% at 30 days, 1 year, and 3 years, respectively), event rates of those with a negative test but a CAD history were significantly higher (2.6%, 5.3%, and 6.6% at 30 days, 1 year and 3 years, respectively; $p = 0.044$ and $p = 0.034$ compared to CAD− patients at 1 year and 3 years, respectively). In a multivariable logistic regression model, a positive MPI proved to be an independent predictor of long-term CV events in patients with CP and prior CAD.
Conclusion: Observation followed by stress MPI can effectively risk stratify CP patients with prior CAD for CV risk. These patients are at increased risk of CV events even after a low-risk stress MPI study. Patients presenting with CP and managed with a strategy of observation followed by a negative stress MPI warrant close short- and long-term monitoring for recurrent events.

1. Introduction

Chest pain (CP) accounts for greater than 8 million emergency department visits and 2 million hospital admissions per year in the United States [1,2]. As a result, the economic burden of CP management is enormous and methods to reduce the cost of managing chest pain are the subject of a large body of literature. An increasingly popular strategy for the management of CP patients over that past decade has been the use of the emergency department (ED)-based observation unit [3,4]. This strategy typically involves a defined period of observation of less than 24 h, during which time high risk CP features associated with an acute coronary syndrome (ACS) such as changes in the electrocardiogram (ECG) or elevated biomarkers are excluded. Patients are then discharged from the observation unit following arrangement of clinical follow-up. An integral part of this approach is stress testing with or without cardiac imaging to further risk stratify patients, with testing typically performed either immediately or several days after ACS has been ruled out [1].

A growing body of literature has demonstrated the cost-effectiveness and safety of an observation unit strategy in identifying CP patients who can be safely discharged either following stress testing or with plans for early follow-up stress testing [5,6]. Studies have shown that patients managed in a CP unit followed by a non-ischemic outpatient stress test have very low short- and long-term rates of cardiovascular (CV) events. Of note, the vast majority of these studies have been generated using patient cohorts without known CAD. There have been limited studies that have attempted to address the appropriate criteria for CP observation admission [7], and even fewer studies have examined outcomes of patients with known CAD who present with CP and are managed using an observation strategy [8,9].

In the present study we evaluated the use of stress myocardial perfusion imaging in the management of patients with prior documented CAD who present with CP and are triaged to a CP observation unit. Our goal was to determine these patients' short- and long-term outcomes as well as the prognostic value of stress myocardial perfusion imaging (MPI) in predicting adverse CV events.

Abbreviations: CP, chest pain; CAD, coronary artery disease; MPI, myocardial perfusion imaging; CV, cardiovascular; ACS, acute coronary syndrome; ECG, electrocardiogram; TnI, troponin I.

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2. Methods

The study was a retrospective evaluation of a strategy of observation followed by outpatient stress MPI. Patients who met entry criteria and who were entered into the observation program during calendar years 2005–2007 were included in the analysis. The study was approved by the Institutional Review Board of Lehigh Valley Health Network.

The Lehigh Valley Health Network chest pain observation program utilizes continuous cardiac telemetry beds on a dedicated unit of the hospital. To be admitted to the unit, patients are required to have 3 specific criteria on presentation to the ED: resolution of their CP during initial ED evaluation and treatment, a normal initial cardiac troponin I (TnI), and an initial ECG that is normal or unchanged versus a prior ECG. For the present study patient demographics and history were collected from documentation of the admission assessment. Patients were considered to have a "history of CAD" if they had prior MI or coronary revascularization. Patients whom the ED staff suspected to have alternative diagnoses (such as pulmonary embolism or aortic dissection) were considered for admission to the unit if these alternative diagnoses were definitively ruled out by appropriate imaging studies. Patients were excluded from the unit if they had abnormal levels of TnI and are presenting ECG which was different from prior tracings or recurrent chest pain following admission. Patients were kept on continuous telemetry until at least 2 negative TnI results were obtained on presentation and at least 12 h after admission to the unit. If any of the TnI were abnormal or the patient developed recurrent pain with new ECG changes or arrhythmias they were withdrawn from the observation protocol and treated accordingly. Following the negative observation workup patients were scheduled for an outpatient stress test with myocardial perfusion imaging within 72 hours after discharge. They were given instructions on preparation for the test and a contact number to call if they were unable to comply with the instructions.

Stress testing was carried out using a standard treadmill exercise Bruce protocol. Tc99-Sestamibi was utilized as the resting and post-exercise MPI agent per standard protocol. For patients that were unable to exercise, pharmacologic stressor utilizing either adenosine or dobutamine was performed. Exercise and pharmacologic ECG tests were interpreted as "positive" for ischemia if the ECG demonstrated ≥1 mm flat or slow upsloping ST depression in 2 or more contiguous leads. Exercise ECG responses were termed "indeterminate" if the patient failed to achieve a peak heart rate of 85% maximum predicted heart rate or baseline ECG abnormalities precluded the ability to interpret stress-related changes. Tc99-Sestamibi MPI scans were defined as "positive for ischemia" if the post-exercise or post-adenosine perfusion scan demonstrated reduced tracer uptake in ≥1 myocardial perfusion segment that was not present on the resting scan. Quantitative degrees of ischemia (i.e., ischemic segment models) were not reported, as these are not routinely used in the nuclear reports at our center. Scans were interpreted as "negative for ischemia" if no such areas were detected. The management of patients with positive stress MPI was left to the discretion of the cardiologist who followed up with each patient following the completion of the test.

Patients were assessed for survival status based on review of the national death database. Cardiac events were extracted from the hospital electronic medical record. Adverse cardiac events that were included as endpoints were death, myocardial infarction or the requirement for urgent percutaneous or surgical coronary revascularization. Patients who underwent elective catheterization either with or without percutaneous coronary intervention for positive MPI were not counted as a CV endpoint unless they presented with evidence of an unstable coronary syndrome before or at the time of the procedure.

Continuous data were analyzed using Student's t-test and categorical data were interpreted using a chi-squared test. All data analyses were performed using SigmaStat software (Systat, Chicago IL). For all statistical analyses a p value < 0.05 was considered significant.

3. Results

A total of 375 patients completed the observation protocol and outpatient stress testing, and had complete 3 year follow-up data available. It should be noted that these patients were identified after completion of the CP unit protocol: thus, data on the number of patient who "failed" the CP unit protocol and were converted to inpatient status is not available. Of these patients, 111 (29.6%) had a history of CAD. Demographics and clinical characteristics of patients with and without CAD history are summarized in Table 1. Compared to patients without CAD history, patients with a CAD history were older and more likely to be male and have diabetes mellitus, hypercholesterolemia, and hypertension. Not surprisingly, patients with a CAD history were significantly more likely to be taking ASA, clopidogrel (both alone and in combination with ASA), and statins, which would represent appropriate secondary prevention measures for these patients.

Of the patients with a CAD history, 72/111 (64.9%) underwent exercise stress testing and 39 underwent pharmacologic testing. Of the patients without a CAD history, 224/264 (84.8%) underwent exercise stress testing and 40 underwent pharmacologic testing. There were no CV complications during stress testing in our patient population as a whole. Stress testing, MPI results, and early (within 1 week following stress testing) cardiac catheterization data are summarized in Table 2. While there was no significant difference between rates of positive stress ECG between patients with and without a CAD history, significantly more patients with a CAD history had MPI scans interpreted as ischemic (31.5% vs. 10.6%, $p < 0.001$) and had reduced left ventricular ejection fraction (<50%) in gated SPECT assessment (17.9% vs. 5.7%, $p < 0.001$). Based on the results of post-discharge stress myocardial perfusion imaging, significantly more patients with a CAD history were referred for cardiac catheterization and coronary angiography vs. patients without a CAD history (13.5% vs. 5.3%, $p = 0.012$). A total of 15 patients underwent revascularization (12 PCIs, 3 CABG). Twelve of the 15 patients who underwent revascularization had ischemic MPI; the remaining 3 had positive stress ECG. In patients with history of CAD, 5 PCIs and 1 CABG were performed. While in patients without CAD history, there were 7 PCIs and 2 CABG.

Cumulative cardiovascular event rates at 30 days, 1 year, and 3 years following ED observation and outpatient stress testing were compared between patients with and without a CAD history (Table 3A). Not surprisingly, patients with documented prior CAD history had higher CV event rates throughout the follow-up period, with a nearly 4-fold increase in CV events by 3 years of follow-up in patients with known CAD. There were 2 deaths in the cohort during the follow-up period — a 72 year old male with prior CAD expired 2 years after a positive stress MPI from a gastrointestinal bleed, and a 50 year old female without prior CAD expired 1 year after an ischemic MPI from sudden cardiac death following non-cardiac surgery. No patients who underwent index revascularization had a CV event during the 3 year follow-up period. Three patients who underwent cardiac cath but no PCI had CV events during the f/u period (1 at 30 days, 2 at 3 years).

Table 1
Patient demographics, comparing patients with vs. without prior CAD history.

	+CAD history (n = 111)	−CAD history (n = 264)	p
Age, years (range)	65.3 (51–89)	52.4 (19–86)	<0.001
Male, %	69.4	52.3	0.003
Hypertension, %	90.1	37.9	<0.001
Diabetes mellitus, %	33.3	9.5	<0.001
Current/prior smoker, %	6.3	12.5	0.111
Hypercholesterolemia, %	95.5	33.0	<0.001
Family history CAD, %	5.4	10.6	0.160
ASA use, %	81.1	16.7	<0.001
Clopidogrel use, %	45.0	1.1	<0.001
ASA + clopidogrel use, %	39.6	0.4	<0.001
Statin use, %	80.2	25.0	<0.001