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Temporal trends of stress myocardial perfusion imaging: Influence of diabetes, gender and coronary artery disease status

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ABSTRACT

Introduction: Temporal trends of myocardial perfusion imaging (MPI) among diabetics and non-diabetics and the influence of gender and prior coronary artery disease (CAD) status has not been previously investigated.
Materials and methods: Consecutive patients who underwent clinically indicated stress-MPI over a 17-year period (1996 through 2012) were studied. Data were collected prospectively as a part of the ongoing clinical databases. Study patients were divided into 4 temporal subgroups (1996 to 2000, 2001 to 2004, 2005 to 2008 and 2009 to 2012) to compare the trends of cardiac risk factors and the frequency of abnormal and ischemic MPI.
Results: Of 78,344 total stress MPI studies, 30.2% were in diabetics. The frequency of abnormal MPI studies, while substantially higher in diabetics, significantly declined over time both in diabetics (53.6% in 1996 to 39.8% in 2012) and non-diabetics (37% in 1996 to 27.4% in 2012), despite an increase in the cardiac risk factor profile. Furthermore, among patients with no known CAD, the temporal prevalence of abnormal MPI was highest in diabetic men (57.5% in 1996 to 31.9% in 2012), lowest in non-diabetic women (18.8% in 1996 to 11% in 2012), and both intermediate and comparable in non-diabetic men and diabetic women (36.4% and 35.7% in 1996 and 20.7% and 17.5% in 2012, respectively).
Conclusions: Despite a temporal reduction in the prevalence of abnormal studies from 1996 through 2012, stress MPI continues to play an important clinical role, particularly in diabetics, men and patients with known-CAD.

1. Introduction

Diabetes mellitus (DM) is one of the strongest risk factors for coronary artery disease (CAD) and has been considered a CAD-equivalent [1,2]. It thus serves as an important clinical variable in predicting the pretest probability of the presence of CAD in patients referred for stress myocardial perfusion imaging (MPI). More than 25 million US adults currently have type-2 DM and this figure is estimated to nearly double by 2050 [3,4]. This increasing diabetic burden may have a significant impact on cardiovascular mortality and morbidity, as cardiac disease remains the leading cause of death in type-2 DM [2,3].

Stress MPI remains the most commonly used noninvasive modality for the assessment of underlying CAD [5]. Two recent studies have shown a temporal decline in the frequency of both abnormal and ischemic MPI studies in patients referred for stress testing over the past two decades [5,6]. Interestingly, the progressive decline in both abnormal and ischemic MPI studies has occurred within all demographic and clinical risk factor sub-groups despite a concomitant increase in the prevalence of many risk factors and an increased pretest probability of CAD. Other epidemiological data has indicated improved control of CAD risk factors resulting in a temporal decline in the incidence and severity of CAD as well as its associated mortality [7,8]. Furthermore, temporal declines in cardiac mortality have been observed both in patients with and without known CAD signifying important therapeutic advancements in primary and secondary prevention strategies [5].

To the best of our knowledge, an analysis of the temporal trends of MPI results in diabetic patients has not been previously evaluated which may have important clinical implications with regard to stress MPI utilization and the care of diabetic patients. We therefore conducted this study to examine the temporal trends in the prevalence of abnormal and ischemic stress MPI studies among clinically-referred diabetic and non-diabetic patients, as well as the influence of gender and CAD status, at two large academic medical centers.

2. Methods

2.1. Study design

Consecutive clinically-indicated stress single-photon emission computerized tomography (SPECT) and positron emission tomography (PET) MPI studies over a 17-year period at Hartford Hospital (a 900 bed urban teaching hospital) and Mount Sinai Hospital (a 1200 bed inner city teaching hospital) between January 1996 and December 2012 were reviewed. These studies were a part of the ongoing prospective nuclear cardiology databases at both the institutions. The prospectively collected MPI database at Hartford Hospital began in 1996 while the Mount Sinai Hospital database started in 2004. These patients

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reported in this study comprised a subset of a previously published larger study [5]. Tl-201 studies which were performed for the sole purpose of cardiac viability assessment were excluded. The study group of stress MPI studies was divided based on a history of DM and then subdivided into 4 temporal subgroups: 1996 to 2000, 2001 to 2004, 2005 to 2008 and 2009 to 2012. This study was approved by and conducted within guidelines of the Institutional Review Boards at Hartford Hospital and Mount Sinai Hospital.

At the time of testing, pertinent demographic information, past cardiac history and CAD risk factors, and stress test results were recorded. Risk factors for CAD including hypertension, diabetes (DM), and hyperlipidemia were defined on the basis of patient report or medical records. A family history of premature CAD was defined as a CAD diagnosis present in a first degree relative ≤55 years of age. Smoking history was considered positive if smoking was prior or current. A patient was considered to have prior known-CAD based on previously diagnosed atherosclerotic heart disease with a positive stress test or a positive diagnostic cardiac catheterization result for CAD in the medical record, history of myocardial infarction, history of percutaneous coronary intervention (PCI), or history of coronary artery bypass grafting (CABG). Congestive heart failure (CHF) was considered to be present based upon the patient's history of systolic or diastolic CHF in the medical record. An abnormal ECG was defined as any abnormal findings more serious than atrial or ventricular premature beats and first-degree AV block. This included nonspecific or abnormal T waves or ST segments, pathologic Q waves, bundle branch blocks, paced rhythms, atrial fibrillation, atrial flutter, and second or higher degree AV block.

2.2. Stress and imaging protocols

Standard imaging and radionuclide dosing protocols for SPECT and PET as endorsed by the American Society of Nuclear Cardiology (ASNC) were used in all patients [9]. For ambulatory patients with known or perceived functional limitations at the time of testing, a combined stress protocol of vasodilator stress with adjunctive exercise was also utilized. In such cases, exercise stress began after completion of dipyridamole infusion, at the start of adenosine infusion, and if a patient was unable to reach a standard exercise testing endpoint, regadenoson was used as needed.

2.3. Image interpretation

Semi-quantitative perfusion scoring of the stress and rest images was performed by board certified nuclear cardiologists. Using a 17-segment model and visual semi-quantitative scoring system, each segment was scored at the time of the clinical performance of the test with access to the patient's clinical and stress test data. With the introduction and routine utilization of attenuation correction (both Gd-153 line source and prone imaging), all images were visually interpreted and scored in sequence, non-attenuation-corrected data first followed by attenuation-corrected data using the same 17-segment model and semi-quantitative scoring system. In visual assessment of myocardial perfusion, each segment was scored on a scale of 0 to 4 (0 = normal, 1 = mild, 2 = moderate, 3 = severe and 4 = absent photon activity). Summed stress scores (SSSs), summed rest scores (SRS), and summed difference score (SDS) were calculated. In classification of the presence and severity of defects, a stress and difference total perfusion defect (TPD) % was calculated by dividing the SSS and SDS respectively, by the maximum score possible using the 17-segment model and scoring system. An ischemic MPI was defined as a defect on stress imaging that demonstrated any reversibility with rest imaging (SDS ≥1) and an abnormal study was defined as a clinically interpreted abnormal study with a SSS >3 for non-attenuation corrected images, or a SSS >1 for attenuation-corrected images. Substantial left ventricular ischemia was considered if the difference TPD was ≥10%. Left ventricular ejection fraction (LVEF) was calculated with an automated quantitative method using electrocardiographic gating whenever available and was confirmed visually.

2.4. Statistical analysis

Clinical and baseline characteristics were expressed as mean ± standard deviation or as percentages. Inter-group comparisons were performed using one-way ANOVA for continuous variables and Chi square for a trend for categorical variables. Binary logistic regression was performed to calculate odds ratios with 95% confidence intervals. A p-value < 0.05 was considered statistically significant. Statistical analyses were performed with SPSS software version 19 (IBM/SPSS, Armonk, NY USA 2012).

3. Results

3.1. Demographics and clinical characteristics

A total of 80,453 consecutive clinically-indicated stress MPI's over the 17-year study period were reviewed. Patients with incomplete data were excluded finally yielding 78,344 stress MPI studies for analysis. Of these studies, 24,297 (30.2%) were in patients with DM. The demographics, clinical characteristics and stress test results over time among diabetics and non-diabetics are shown in Tables 1 and 2 respectively. There was a minimal increase in the mean age over time in both diabetics and non-diabetics. Percentage of males slightly increased over time among diabetics. The prevalence of risk factors for CAD including hypertension, hyperlipidemia, and smoking history showed a rising trend over time in both diabetics and non-diabetics ($p < 0.001$), while the prevalence of a family history of CAD decreased. The prevalence of hypertension and hyperlipidemia was higher in diabetics than non-diabetics over all time periods. Smoking prevalence over time was comparable among diabetics and non-diabetics. The percentage of patients with known CAD decreased over time among both diabetics and non-diabetics. The prevalence of CABG as a revascularization strategy decreased over time in both diabetics and non-diabetics though the percentage remained significantly higher in diabetics compared to non-diabetics across all four time periods. The prevalence of percutaneous coronary interventions (PCIs) showed a rising trend over time in both diabetics and non-diabetics, but more so in diabetics. The prevalence of congestive heart failure (CHF) remained relatively stable across all time periods in diabetics though it showed a slight increasing trend in non-diabetics.

3.2. Stress MPI results

Although the prevalence of pharmacological stress testing was substantially higher than exercise stress in diabetics compared to non-diabetics over all four-time periods, the relative increase in use of pharmacological stress testing was more substantial in non-diabetics over time (70.5% vs. 46.1% and 71.3% vs. 53.4% in the first and last time periods respectively; $p < 0.001$). The abnormal and ischemic MPI prevalence was significantly higher among diabetics as compared to non-diabetics over all four-time periods (Fig. 1), although there was a significant temporal reduction in both groups (abnormal MPI prevalence being 53.6% among diabetics vs. 37% among non-diabetics in the first time period and 40% among diabetics vs. 27.8% among non-diabetics in the last time period, $p < 0.001$).

Among patients with abnormal MPI studies, the mean stress and difference TPD demonstrated a sequential temporal reduction in both diabetics and non-diabetics (Tables 1 and 2). The prevalence of substantial myocardial ischemia (defined as ≥10% difference TPD) was higher among diabetics as compared to non-diabetics for all time-periods with a temporal reduction among both groups (from 11.4% to 8.6% among diabetics and from 7.1% to 5.8% among non-diabetics).

Abnormal and ischemic MPI temporal prevalence was also calculated based on patients' prior CAD status in addition to their diabetes status (Fig. 2). While diabetics with known CAD had the highest prevalence of abnormal MPI and non-diabetics with no-known CAD had the lowest prevalence during each time period, there was a decreasing temporal trend in abnormal MPI prevalence irrespective of the DM or CAD status. Diabetics with no-known CAD demonstrated the greatest temporal reduction in abnormal MPI prevalence while non-diabetics with known CAD demonstrated fluctuations in abnormal MPI prevalence (with least difference among the first and last time periods). Similarly, diabetics with known-CAD had the highest prevalence of ischemic MPI and non-diabetics with no-known CAD had the lowest among all four time periods. There was a significant decreasing temporal trend of ischemic MPI in patients with no-known CAD while patients with known-CAD demonstrated some temporal variability including an initial reduction followed by a subsequent increase with both a plateau in the last time period and prevalence comparable to that in the first time period [Fig. 2b]. Similar trends were observed for substantial myocardial ischemia (≥10% difference TPD) among both diabetics and non-diabetics with known and no-known CAD [Fig. 2c].

Univariate odds ratios for having an abnormal MPI in relation to demographic characteristics and traditional CAD risk factors among diabetic and non-diabetic patients are represented in Tables 3 and 4. The likelihood of having an abnormal MPI in diabetics as well as non-diabetics increased with time in patients with known CAD (including history of PCI and CABG) (odds ratio increased from 5.56 to 6.18 in