Temporal Trends of Single-Photon Emission Computed Tomography Myocardial Perfusion Imaging in Patients With Coronary Artery Disease

A 22-Year Experience From a Tertiary Academic Medical Center

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Background—There has been a gradual decline in the prevalence of abnormal stress single-photon emission computed tomography (SPECT) myocardial perfusion imaging studies among patients without history of coronary artery disease (CAD). The trends of SPECT studies among patients with known CAD have not been evaluated previously.

Methods and Results—We assessed the Mayo Clinic nuclear cardiology database for all stress SPECT tests performed between January 1991 and December 2012 in patients with history of CAD defined as having previous myocardial infarction, percutaneous coronary intervention, and coronary artery bypass grafting. The study cohort was divided into 5 time periods: 1991 to 1995, 1996 to 2000, 2001 to 2005, 2006 to 2010, and 2011 to 2012. There were 19 373 patients with a history of CAD who underwent SPECT between 1991 and 2012 (mean age, 66.2±10.9 years; 75.4% men). Annual utilization of SPECT in these patients increased from an average of 495 tests per year in 1991 to 1995 to 1425 in 2003 and then decreased to 552 tests in 2012 without evidence for substitution with other stress modalities. Asymptomatic patients initially increased until 2006 and then decreased. Patients with typical angina decreased, whereas patients with dyspnea and atypical angina increased. High-risk SPECT tests significantly decreased, and the percentage of low-risk SPECT tests increased despite decreased SPECT utilization between 2003 and 2012. Almost 80% of all tests performed in 2012 had a low-risk summed stress score compared with 29% in 1991 (P<0.001).

Conclusions—In Mayo Clinic, Rochester, annual SPECT utilization in patients with previous CAD increased between 1992 and 2003, but then decreased after 2003. High-risk SPECT tests declined, whereas low-risk tests increased markedly. Our results suggest that among patients with a history of CAD, SPECT was being increasingly utilized in patients with milder CAD. This trend parallels reduced utilization of other stress modalities, coronary angiography, reduced smoking, and greater utilization of optimal medical therapy for prevention and treatment of CAD. **(*Circ Cardiovasc Imaging*. 2017;10:e005628. DOI: 10.1161/CIRCIMAGING.116.005628.)**

Key Words: coronary artery bypass ■ coronary artery disease ■ myocardial infarction ■ tomography, emission-computed, single-photon ■ trends

Cardiovascular imaging utilization including single-photon emission computed tomography (SPECT) grew significantly between 1993 and 2001 in Medicare beneficiaries.[1] This growth raised considerable concern with respect to the cost-effectiveness of cardiovascular imaging and its impact on cost within the US healthcare system.[2] In response to this growth, appropriate use criteria for SPECT were developed in 2005, updated in 2009, and eventually included with other cardiovascular imaging procedures in 2013.[3–5] SPECT utilization has declined since 2006.[6] This decline was noted at multiple medical institutions throughout the United States and could not be explained by test substitution with stress echocardiography or coronary computed tomographic angiography.[7–9]

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Previous studies have reported that despite declining SPECT utilization, fewer patients without known coronary artery disease (CAD) have intermediate- or high-risk SPECT test results (in both symptomatic and asymptomatic patients).[8,9] These findings indicate that SPECT was being increasingly utilized in patients with a lower prevalence of CAD. However, SPECT trends in patients with established CAD have not

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been assessed previously. In this study, we analyze trends of SPECT utilization in patients with documented CAD to determine whether they show similar trends in SPECT results.

Methods

Database

The Mayo Clinic, Rochester, nuclear cardiology laboratory maintains an electronic database of all patients undergoing stress SPECT. Stored data include patient demographics, CAD risk factors, and previous CAD history. CAD history was defined as having documented myocardial infarction (MI), percutaneous coronary intervention (PCI), or coronary artery bypass grafting (CABG) as used previously by the Cedars-Sinai group and in our previous SPECT trends report in patients without CAD.[9,10] Hypertension is defined as being on antihypertensive therapy or systolic blood pressure of ≥140 mm Hg and diastolic blood pressure of ≥90 mm Hg. Diabetes mellitus is defined as fasting blood glucose ≥126 mg/dL on ≥2 occasions, hemoglobin A1c ≥6.5%, or treatment with insulin/oral diabetes mellitus medications. Dyslipidemia is defined as having a total cholesterol of >250 mg/dL or being on lipid-lowering therapy. Recorded symptoms at the time of SPECT include chest pain and dyspnea. Chest pain is further categorized as typical angina, atypical angina, or noncardiac chest pain according to the criteria of Diamond.[11] For patients with both chest pain and dyspnea, chest pain is considered the primary symptom.

All patients who underwent stress SPECT utilizing technetium Tc^{99m} sestamibi between January 1, 1991, and December 31, 2012, were included in this study. This database has been used in previous publications from our laboratory.[9,12,13] The database includes both inpatient and outpatient SPECT tests performed at Mayo Clinic, Rochester. Analyzed data include all variables with a <1% rate of missing data in each of the possible answers. This study was approved by the Mayo Clinic Institutional Review Board. No extramural funding was used to support this study.

Exclusion Criteria

Patients without a history of established CAD (previous myocardial infarction, percutaneous coronary intervention, or coronary artery bypass grafting) before SPECT were excluded. Patients with the following conditions were also excluded: left bundle branch block, paced rhythm, cardiomyopathy, or valvular heart disease. SPECT tests performed with bicycle-exercise/rest-only or with technically inadequate images were excluded. After applying these exclusion criteria, there were 29 886 SPECT tests. For patients with multiple SPECT tests, only the first test was used for analysis, leaving a total of 19 891 unique patients. In accordance with Minnesota state law, patients who did not grant research authorization were excluded (n=518), resulting in a final study cohort of 19 373 patients. There were 9995 repeat SPECT studies of which 255 did not provide research authorization. A total of 9740 repeat SPECT studies were assessed separately.

SPECT Methods

SPECT methodology from our laboratory has been described previously.[9,14,15] In brief, patients underwent either symptom-limited treadmill exercise stress (Bruce, modified Bruce, or Naughton protocol) or pharmacological stress (utilizing adenosine, regadenoson, dipyridamole, or dobutamine). A positive stress ECG for ischemia was defined as ≥1.0 mm horizontal or downsloping ST-segment depression 80 ms after the J point compared with baseline. All SPECT studies were interpreted by consensus of a radiologist and a nuclear cardiologist. Image scoring was performed using a 16-segment short-axis model. Each segment was scored as follows: 4=absent uptake, 3=severely decreased uptake, 2=moderately decreased uptake, 1=mildly decreased uptake, and 0=normal uptake. The summed rest score was calculated by addition of the scores for each of the 16 segments using the resting images. The summed stress score (SSS) was calculated using the post-stress images. The summed difference score (SDS) was calculated by subtracting summed rest score from SSS. SSS results were categorized into 3 groups: 0 to 3 (low risk), 4 to 8 (intermediate risk), and ≥9 (high risk).

There were few changes in our nuclear cardiology laboratory personnel or technology used over the study period. Camera equipment and analysis software were the same until early 2010 when the laboratory installed D-SPECT cameras (Spectrum Dynamics).

Test Substitution

To assess for test substitution, we evaluated all stress echocardiograms performed at Mayo Clinic, Rochester, between 2000 and 2012, using an established echocardiography database.[16] We also assessed stress ECG studies performed between 2006 and 2012. The same exclusion criteria used for SPECT were applied to the stress echocardiogram and stress ECG tests, yielding a total of 12 783 stress echocardiograms performed in 2000 to 2012 and 3751 stress ECG tests performed between 2006 and 2012. Given overall small numbers of positron emission tomography (PET) stress tests, we did not apply any of the exclusion criteria but assessed utilization in all of the 2834 PET stress tests performed between 2006 and 2012.

Statistical Analysis

Continuous data are summarized as mean±SD. Categorical data are summarized as frequency and group percentage. The study cohort was divided into 5 time periods: 1991 to 1995, 1996 to 2000, 2001 to 2005, 2006 to 2010, and 2011 to 2012. For comparison of categorical data across the 5 study groups, we used the Pearson χ^2 test. When 2 time periods were compared, we used Wilcoxon rank-sum test for skewed continuous data and 2-tailed *t* test for normally distributed data. For comparison of categorical variables between 2 study groups, Fisher exact test was utilized to assess for differences in 2-level categorical variables and Pearson χ^2 tests for ≥3-level categorical variables. We did not perform any statistical testing aimed at specifically testing for trends. Presented data were not adjusted for age, sex, or history of myocardial infarction, percutaneous coronary intervention, or coronary artery bypass grafting. Statistical analyses were performed using computer software (JMP v10.0; SAS Institute Inc, Cary, NC).

Results

A total of 19 373 patients with established history of CAD were assessed. Mean age was 66.2±10.9 years and 75.4% were men. Baseline characteristics of the study groups are shown in Table 1. There was a marked increase in the utilization of SPECT in patients with CAD between 1991 and 2000 where annual utilization increased from an average of 495 tests per year in the 1991 to 1995 period up to 1400 studies performed in 2000 (Figure 1). There was a plateau in SPECT utilization between 2001 and 2003 followed by marked and progressive decrease in utilization that continued through 2012. In 2012, 552 SPECT studies were performed which was 60.6% lower than the utilization in 2000 (n=1400) and was similar to utilization between 1991 and 1995 (average of 495 tests per year).

Using the same inclusion and exclusion criteria used for SPECT tests, utilization of stress echocardiography and stress ECG declined over time. Annual stress echocardiograms averaged 1128 tests per year in 2001 to 2005 and decreased to 675 tests per year in 2011 to 2012. The characteristics of stress echocardiography patients were similar to those of SPECT patients (Table I in the Data Supplement). Annual stress ECG utilization was 611 tests in 2006 and decreased to 500 tests in 2012. Use of PET stress testing started in 2005 at our institution and has been consistently limited in numbers. Without applying any exclusion criteria, average annual PET stress tests including patients with and without history of CAD were

Table 1. Patient Characteristics

	1991–1995 (n=2475)	1996–2000 (n=5168)	2001–2005 (n=6444)	2006–2010 (n=4140)	2011–2012 (n=1146)
Age, y	63.7±10.4	65.9±10.6	66.9±10.9	66.9±11.3	66.6±11.6
Male sex	1808 (73.1)	3942 (76.3)	4890 (75.9)	3113 (75.2)	862 (75.2)
BMI, kg/m^2	30.8±5.5	30±5.8	29.9±5.9	29.9±5.7	30.6±5.9
Hypertension	1404 (56.7)	3229 (62.6)	4786 (74.5)	3301 (79.8)	945 (82.5)
Dyslipidemia	1573 (63.6)	3905 (75.7)	5574 (86.7)	3739 (90.3)	1047 (91.4)
Diabetes mellitus	659 (26.6)	1393 (27)	1864 (29)	1225 (29.6)	352 (30.7)
Past/current smoker	1581 (63.9)	3198 (62.2)	3934 (61.2)	2474 (59.7)	661 (57.7)
Family history of CAD	1056 (42.7)	1904 (37)	2077 (32.5)	1389 (33.6)	320 (28)
Normal baseline ECG	576 (23.3)	1128 (22)	1779 (27.7)	1252 (30.3)	350 (30.5)
Patient symptoms					
Asymptomatic	818 (33.1)	1947 (37.7)	2637 (41)	1772 (42.8)	375 (32.7)
Typical angina	670 (27.1)	1270 (24.6)	1179 (18.3)	552 (13.3)	203 (17.7)
Atypical angina	636 (25.7)	1123 (21.7)	1410 (21.9)	1026 (24.8)	341 (29.8)
Noncardiac chest pain	27 (1.1)	128 (2.5)	93 (1.4)	100 (2.4)	24 (2.1)
Dyspnea	323 (13.1)	684 (13.2)	1051 (16.3)	638 (15.4)	191 (16.7)

Data are presented as number (%) or mean±SD. BMI indicates body mass index; and CAD, coronary artery disease.

433 tests per year between 2006 and 2010 and decreased to 335 tests per year in 2011 to 2012. The declining utilization of these alternative stress modalities argues against test substitution as a possible cause for reduced SPECT utilization.

Overall, patients' age, sex, and body mass index remained unchanged between 1991 and 2012. Hypertension, dyslipidemia, diabetes mellitus, and smoking changed significantly over the 5 time periods (χ^2, P<0.001 for each). There was a gradual and marked increase in patients with hypertension (56.7% in the 1991–1995 group versus 82.5% in the 2011–2012 group; P<0.001 by Fisher exact test). Similarly, dyslipidemia increased dramatically (63.6% in 1991–1995 versus 91.4% in 2011–2012; P<0.001 by Fisher exact test). Patients with diabetes mellitus modestly increased over time (26.6% in 1991–1995 versus 30.7% in 2011–2012; P<0.001 by Fisher exact test). Patients with a history of current or past smoking

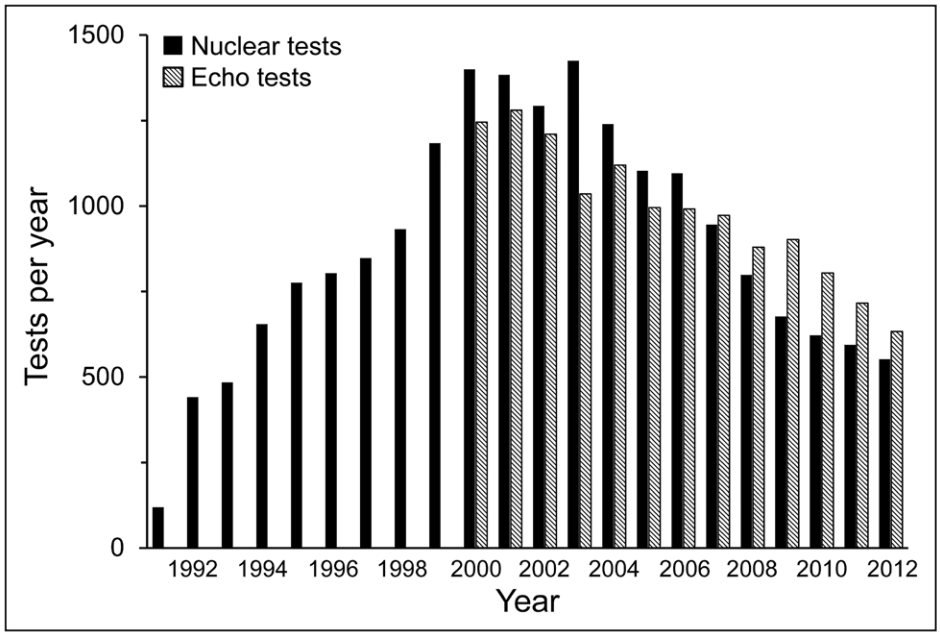

Figure 1. Single-photon emission computed tomography (SPECT) and stress echocardiography utilization in patients with an established history of coronary artery disease (CAD). The diagram illustrates the annual utilization of SPECT in patients with a history of CAD between 1991 and 2012. SPECT utilization increased significantly between 1991 and 2000 parallel to national trends. There was a plateau between 2000 and 2003 followed by decreased utilization of SPECT starting in 2004 ahead of publication of SPECT appropriate use criteria in late 2005. Stress echocardiogram tests performed between 2000 and 2012 are also illustrated in the figure above demonstrating no evidence for test substitution to account for the decreased utilization in SPECT.

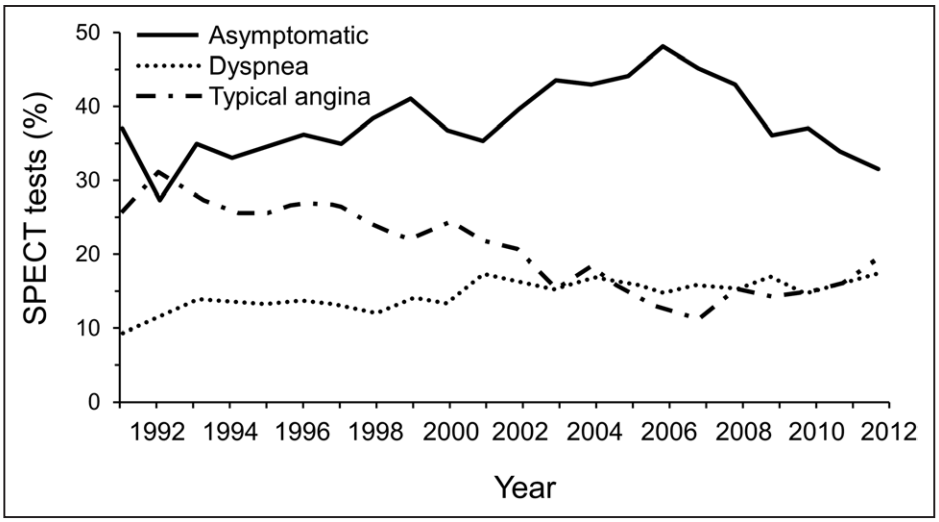

Figure 2. Trends of single-photon emission computed tomography (SPECT) by frequency of presenting symptoms. Testing of asymptomatic patients increased between 1991 and 2006 but later decreased. The frequency of asymptomatic patients compared with all tested patients in 2012 is similar to the first study period (1991–1995). The percentage of patients presenting with typical angina decreased, whereas patients with dyspnea increased. The frequency of patients with atypical angina also increased over time (not depicted in the graph).

decreased (63.9% in 1991–1995 versus 57.7% in 2011–2012; $P<0.001$ by Fisher exact test).

SPECT testing in asymptomatic patients increased from 33.1% in 1991–1995 to 42% in 2006–2010 ($P<0.001$ by Fisher exact test). However, a gradual decline in the percentage of asymptomatic patients started in 2006 and persisted through 2012 (Figure 2). In 2011–2012, 32.7% were asymptomatic, nearly identical to the percentage of asymptomatic patients in 1991–1995. Patients presenting with typical angina decreased (27.1% in 1991–1995 versus 17.7% in 2011–2012; $P<0.001$ by Fisher exact test). On the contrary, patients presenting with atypical angina and dyspnea (without chest pain) both increased over time (25.7% and 13.1% in 1991–1995 versus 29.8% and 16.7% in 2011–2012, respectively; $P<0.001$ by Fisher exact test).

SPECT test results are summarized in Table 2. Exercise SPECT decreased over time from 64.3% in 1991–1995 to 48.2% in 2011–2012; $P<0.001$ by Fisher exact test. More importantly, there was a significant and progressive decline in SSS over the study period, from an average of 10.3±9.1 in 1991–1995 to 3.2±5.8 in 2011–2012 ($P<0.001$ by Wilcoxon rank-sum test). Similarly, SDS decreased over time (6.8±8.1 in 1991–1995 to 2.7±5.6 in 2011–2012; $P<0.001$ by Wilcoxon rank-sum test). When SSS is stratified as low risk (SSS: 0–3), intermediate risk (SSS: 4–8), and high risk (SSS ≥9), there was a significant change in SSS categories over the 5 time periods (χ^2, $P<0.001$). Low-risk SPECT tests increased with a corresponding decrease of intermediate- and high-risk SPECT tests. In 1991–1995, 27.8% of all tests were low risk compared with 77.1% in 2011–2012; $P<0.001$ by Fisher exact test. High-risk stress tests decreased markedly from 47.8% in 1991–1995 to 8.1% in 2011–2012; $P<0.001$ by Fisher exact test. The trends of low-, intermediate-, and high-risk SPECT studies are illustrated in Figure 3. The frequency of positive stress electrocardiograms also decreased. Left ventricular ejection fraction was assessed in patients in sinus rhythm because irregular rhythms such as atrial fibrillation or frequent ectopic beats make ECG gating and ejection fraction estimation unreliable. Overall, left ventricular ejection fraction showed little change over time (57.2±12.3% in 1991–1995 [n=846 tests] versus 56±11.3% in 2011–2012 [n=1050]).

These downward trends in SSS occurred in asymptomatic patients (10.9±9.6 in 1991–1995 to 3±5.6 in 2011–2012; $P<0.001$ by Wilcoxon rank-sum test) and symptomatic patients

Table 2. SPECT Characteristics

	1991–1995 (n=2475)	1996–2000 (n=5168)	2001–2005 (n=6444)	2006–2010 (n=4140)	2011–2012 (n=1146)
Exercise SPECT-MPI	1591 (64.3)	3128 (60.5)	3503 (54.4)	2046 (49.4)	522 (48.2)
SSS	10.3±9.1	8.8±8.6	6.2±7.6	5.1±7.4	3.2±5.8
SDS	6.7±8.1	5.2±7	3.7±6.1	3.2±6.3	2.7±5.6
Low risk (SSS: 0–3)	688 (27.8)	1890 (36.6)	3325 (51.6)	2569 (62.1)	883 (77.1)
Intermediate risk (SSS: 4–8)	603 (24.4)	1187 (23)	1374 (21.3)	610 (14.7)	93 (8.1)
High risk (SSS ≥9)	1181 (47.8)	2090 (40.4)	1739 (27)	961 (23.2)	170 (14.8)
Positive stress ECG	474 (19.2)	906 (17.5)	833 (13)	383 (9.3)	115 (10)

Data are given as number (%) or mean±SD. SDS indicates summed difference score; SPECT-MPI, single-photon emission computed tomography-myocardial perfusion imaging; and SSS, summed stress score.

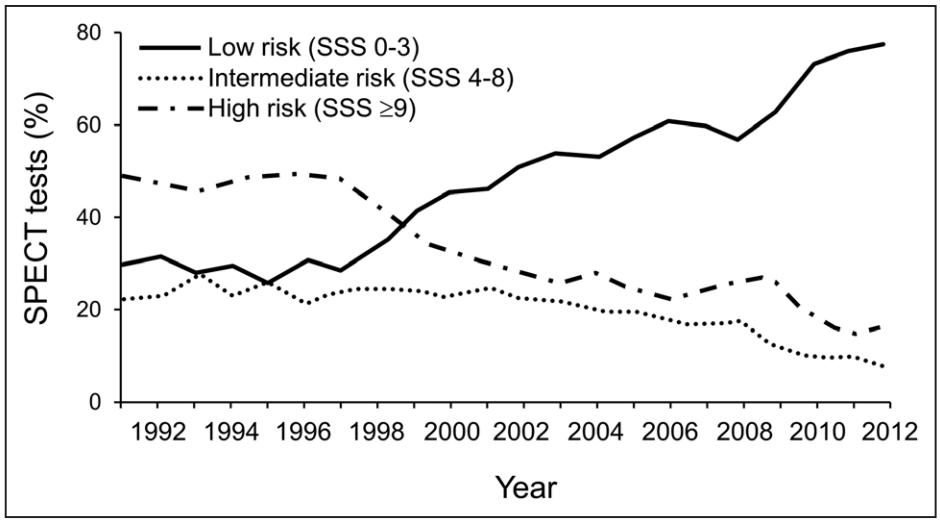

Figure 3. Summed stress score (SSS) trends. The figure represents percentages of patients among SSS risk categories over the span of 22 y. The frequency of low-risk tests (SSS, 0–3) increased significantly over time and accounted for 77.7% of all tests in 2012 compared with 29.4% in 1991, $P<0.001$ by Fishers exact test. Despite decreased single-photon emission computed tomography (SPECT) utilization starting in 2004 and less asymptomatic patients, low-risk SPECT tests continued to increase over time.

(10±8.9 in 1991–1995 to 3.3±5.9 in 2011–2012; $P<0.001$ by Wilcoxon rank-sum test; Figure 4). In asymptomatic patients, low-risk tests comprised 25.6% in 1991 versus 78.1% in 2012 ($P<0.001$ by Fisher exact test). Similarly, low-risk tests increased significantly over time in symptomatic patients from 30% in 1991 to 76.5% in 2012 ($P<0.001$ by Fisher exact test). These observed trends were also evident regardless of stress modality (pharmacological versus exercise, Figure 5).

We also assessed SPECT trends from a CAD diagnosis standpoint in 3 subgroups: (1) MI alone without revascularization, (2) MI with PCI or CABG, and (3) PCI or CABG without history of MI (Table 3). The percentage of patients with CAD who had MI without revascularization decreased over time (28.2% in 1991–1995 versus 10.3% in 2011–2012; $P<0.001$ by Fisher exact test). The percentage of patients with CAD who had MI and revascularization showed little change. The percentage of patients with CAD who had revascularization without MI increased over time. The percentage of patients with MI and no revascularization that were asymptomatic decreased from 45.1% in 1991–1995 to 41.5% in 2011–2012. Patients with history of revascularization (with or without MI) who were asymptomatic showed a larger decrease between 2006–2010 and 2011–2012, from 43.2% to 31.6% in those with MI and from 42.2% to 31.8% in those without MI. More importantly, SSS decreased and low-risk SPECT tests increased in all 3 subgroups even in the subgroup with history of MI without revascularization where-low risk tests increased from 20.5% in 1991–1995 to 63.6% in 2011–2012;

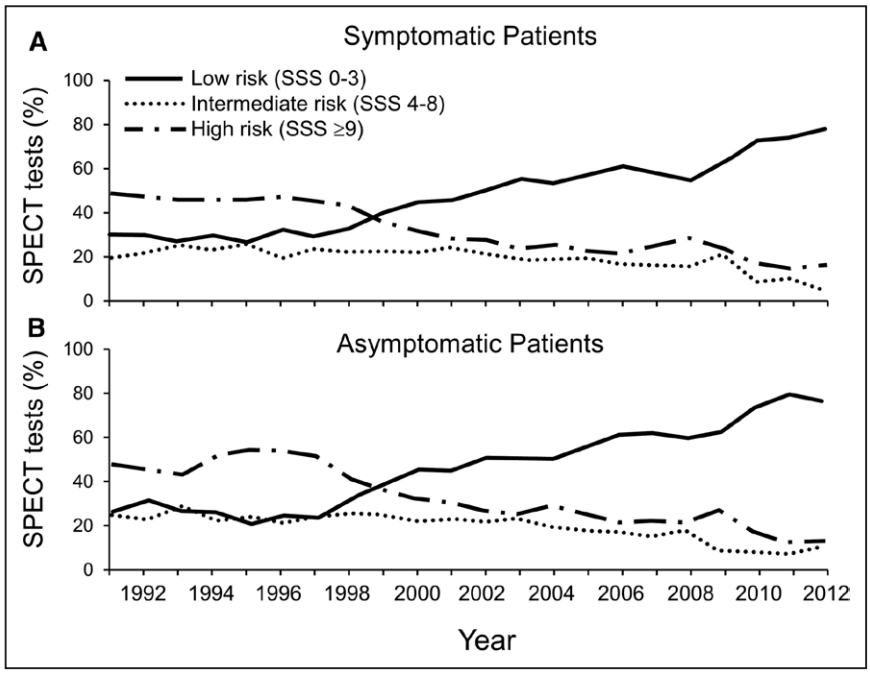

Figure 4. Trends of summed stress score (SSS) risk groups by symptomatic status. The frequency of each of the SSS risk categories is depicted above in symptomatic vs. asymptomatic patients. Despite having a documented history of coronary artery disease and regardless of presenting symptomatic status, low-risk single-photon emission computed tomography (SPECT) tests increased in frequency over time in both symptomatic (**A**) and asymptomatic patients (**B**).

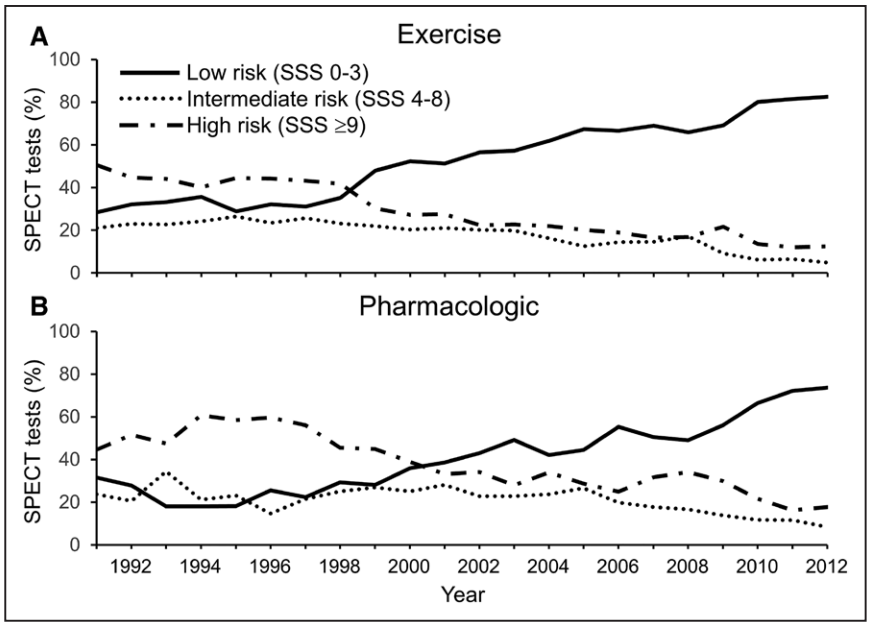

Figure 5. Trends of summed stress score (SSS) risk groups by stress modality. Percentages of patient among the three SSS risk categories were assessed by exercise vs pharmacological stress testing. Regardless of single-photon emission computed tomography (SPECT) stress modality, exercise (**A**) vs pharmacological (**B**), low-risk stress tests continued to increase in frequency over time.

P<0.001 by Fisher exact test. The time difference between MI, PCI, or CABG and SPECT testing was also found to increase modestly over the study period from a median of 2.62 years (25%–75% interquartile range, 0.55–6.56) in 1991–1995 to 3 years (0.99–8) in 2011–2012; *P*<0.001 by Wilcoxon rank-sum test (Table II in the Data Supplement).

Table 4 demonstrates trends of SPECT risk categories over time stratified by modality of stress and stress ECG results. Among patients with exercise SPECT and negative stress ECG, high-risk results decreased significantly parallel to the overall observed trends in our study from 32.6% of these patients in 1991–1995 down to 9.5% in 2011–2012; *P*<0.001 by Fisher exact test. The same overall trend was evident in exercise SPECT patients with positive stress ECG; high-risk tests decreased from 48.9% in 1991–1995 to 23% in 2011–2012; *P*<0.001 by Fisher exact test. Exercise patients with a positive stress ECG and low-risk results increased over time from 27.5% of these patients in 1991–1995 to 70.9% in 2011 to 2012; *P*<0.001 by Fisher exact test. Similarly, the proportion of high-risk tests in patients who underwent pharmacological stress testing and had a positive stress ECG decreased from 65% in 1991–1995 to 20.7% in 2011–2012; *P*<0.001 by Fisher exact test.

Among repeated SPECT studies (n=9,740), similar trends of SSS, low-risk tests, time difference to SPECT, and percentage of patients with history of revascularization without MI were observed compared with the main study cohort (Table III in the Data Supplement). Overall, there were fewer

Table 3. Patient and Single-Photon Emission Computed Tomography Characteristics From a Diagnosis Standpoint

	1991–1995 (n=2475)	1996–2000 (n=5168)	2001–2005 (n=6444)	2006–2010 (n=4140)	2011–2012 (n=1146)
MI alone without revascularization*	699 (28.2)	1003 (19.4)	870 (13.5)	415 (10)	118 (10.3)
Asymptomatic†	315 (45.1)	477 (47.6)	403 (46.3)	185 (44.6)	49 (41.5)
SSS	13±10.1	11.6±9.5	8.1±9	6.9±8.6	5.2±7.3
Low risk (SSS: 0–3)	143 (20.5)	249 (24.8)	380 (43.7)	215 (51.8)	75 (63.6)
MI with PCI or CABG	800 (32.3)	1860 (36)	2266 (35.2)	1596 (38.6)	389 (33.9)
Asymptomatic	242 (30.3)	710 (38.2)	966 (42.6)	689 (43.2)	123 (31.6)
SSS	12±9.4	10.9±9.1	8.6±8.7	7.3±8.5	5.5±7.3
Low risk (SSS: 0–3)	150 (18.8)	483 (26)	882 (38.9)	773 (48.4)	237 (60.9)
PCI or CABG without MI	976 (39.4)	2305 (44.6)	3308 (51.3)	2129 (51.4)	639 (55.8)
Asymptomatic	261 (26.7)	760 (33)	1268 (38.3)	898 (42.2)	203 (31.8)
SSS	6.9±6.8	5.8±6.7	4.1±5.6	3.1±5.4	1.4±3.4
Low risk (SSS: 0–3)	395 (40.5)	1158 (50.2)	2063 (62.4)	1581 (74.3)	571 (89.4)

Data are given as number (%) or mean±SD. CABG indicates coronary artery bypass grafting; MI, myocardial infarction; PCI, percutaneous coronary intervention; and SSS, summed stress score.

*The first line within each subgroup represents the overall number of patients within that subgroup and the percentage compared with the overall number of patients in the corresponding time period.

†The other lines within the subgroups represent number and percentage compared with the overall number within the same subgroup.

Table 4. Trends of Single-Photon Emission Computed Tomography Risk Categories Stratified by Exercise and Stress ECG Results

	1991–1995	1996–2000	2001–2005	2006–2010	2011–2012
Exercise stress with negative stress ECG	709	1799	2405	1658	410
Low risk (SSS: 0–3)	289 (40.8)	887 (49.3)	1527 (63.5)	1222 (73.7)	348 (84.9)
Intermediate risk (SSS: 4–8)	189 (26.7)	412 (22.9)	409 (17)	193 (11.6)	23 (5.6)
High risk (SSS: ≥9)	231 (32.6)	500 (27.8)	469 (19.5)	243 (14.7)	39 (9.5)
Exercise stress with positive stress ECG	393	733	658	279	86
Low risk (SSS: 0–3)	108 (27.5)	238 (32.5)	331 (50.3)	143 (51.3)	61 (70.9)
Intermediate risk (SSS: 4–8)	93 (23.7)	178 (24.3)	154 (23.4)	55 (19.7)	5 (5.8)
High risk (SSS: ≥9)	192 (48.9)	317 (43.2)	173 (26.3)	81 (29)	20 (23.3)
Pharmacological stress with negative stress ECG	504	1378	2291	1803	527
Low risk (SSS: 0–3)	111 (22)	440 (31.7)	1079 (47.1)	1034 (57.3)	412 (78.2)
Intermediate risk (SSS: 4–8)	145 (28.8)	335 (24.2)	575 (25.1)	292 (16.2)	47 (8.9)
High risk (SSS: ≥9)	248 (49.2)	612 (44.1)	637 (27.8)	477 (26.5)	68 (12.9)
Pharmacological stress with positive stress ECG	80	173	174	104	29
Low risk (SSS: 0–3)	11 (13.8)	50 (28.9)	52 (29.9)	45 (43.3)	21 (72.4)
Intermediate risk (SSS: 4–8)	17 (21.3)	46 (26.6)	53 (30.5)	22 (21.1)	2 (6.9)
High risk (SSS: ≥9)	52 (65)	77 (44.5)	69 (39.7)	37 (35.6)	6 (20.7)

Data are given as number (%) of the total number within the corresponding subgroup. SSS indicates summed stress score.

patients with history of MI without revascularization compared with the main study cohort (4.1% versus 10.3% in the 2011–2012 time period; $P<0.001$ by Fisher exact test) and more patients with history of MI and revascularization although the difference does not reach statistical significance (40.1% versus 33.9% in the 2011–2012 time period; $P=0.06$ by Fisher exact test). The percentages of patients with history of revascularization without MI were similar. Over time, asymptomatic status in repeat SPECT studies followed the same pattern observed in the original study cohort, but the decrease in the 2011–2012 time period was less marked in the repeat SPECT group.

Discussion

SPECT utilization in patients with CAD at our institution increased significantly in the 1990s in a similar fashion to US trends.[17] However, SPECT growth plateaued between 2000 and 2003 followed by a strong trend toward reduced utilization. In 2012, SPECT utilization in patients with CAD was similar to that in the first study period of 1991–1995. The prevalence of CAD risk factors such as hypertension, dyslipidemia, and diabetes mellitus increased while smoking decreased. The increased prevalence of hypertension and dyslipidemia over time likely reflects increased recognition and treatment of these conditions. Testing in asymptomatic patients increased until 2006, but then decreased significantly and was similar in 2011–2012 compared with 1991–1995. Atypical angina and dyspnea increased over time, whereas typical angina decreased.

More importantly, despite having a documented history of CAD, SSS and SDS both decreased significantly over time. Low-risk stress tests increased over time and accounted for 77.1% in 2011–2012 compared with only 27.8% in 1991–1995. Intermediate- and high-risk tests decreased significantly. Interestingly, these trends persisted despite reduced utilization in the 2011 to 2012 period. Regardless of SPECT stress modality (exercise versus pharmacological) or patients' symptomatic status, these trends were evident. When the study group was divided into 3 subgroups on the basis of CAD diagnosis (MI without revascularization, MI with revascularization, and revascularization without MI), the percentage of patients who had MI without revascularization decreased. The percentage of patients who had coronary revascularization without MI increased. The decline in asymptomatic patients after 2006 was seen in all 3 subgroups, but was most dramatic in patients with revascularization (with or without MI). SSS decreased and low-risk stress tests increased in all 3 subgroups. To the best of our knowledge, our study is the first to demonstrate a reduced prevalence of abnormal SPECT studies in patients with an established history CAD similar to what was reported previously in patients without a history of CAD.[8,9]

We have also assessed repeat SPECT studies separately and demonstrated similar overall trends to the main study cohort. After 2001, the majority of repeated tests were performed >2 years after MI, PCI, or CABG, which would probably make them of uncertain appropriateness or appropriate. SPECT testing has the most robust risk stratification and prognostication data among cardiac stress testing modalities. Repeat SPECT testing probably reflects the ordering physicians' desire for better risk stratification for their patients with CAD although repeat testing may not necessarily be appropriate.

In our study, SPECT utilization increased between 1991 and 2000, similar to national trends.[6] SPECT utilization started decreasing nationally in 2006.[6,7] It is reasonable to

attribute this national trend to the first publication of appropriate use criteria for SPECT in late 2005.[3] Changes in Medicare reimbursement, radiology benefits management programs, and radiation exposure concerns probably also contributed to the observed decline in national utilization.[18,19] Decreased utilization at our institution seems to have started in 2004, 2 years before national trends and publication of appropriate use criteria. Although the exact causes of this earlier decrease are unclear, they likely reflect continuous quality improvement and efforts by the nuclear cardiology laboratory at our institution to promote the use of treadmill ECG stress testing.[20,21] The timing of decreased utilization in patients with CAD appears similar to what we have reported previously in patients without a previous history of CAD.[9]

Test substitution was also examined in our current study as a possible cause for decreased SPECT utilization. We have demonstrated previously that in patients without a history of CAD, utilization of stress echocardiography and treadmill stress testing has declined over time, arguing against test substitution.[9] In this study, we demonstrated similar findings showing declining utilization of stress echocardiography, stress PET, and stress ECG testing. Our findings suggest that test substitution is unlikely to be a major factor in decreasing SPECT utilization. Similarly, McNulty et al[7] have demonstrated decreased utilization of SPECT at Kaiser Permanente in Northern California without any evidence for test substitution with stress echocardiography or coronary computed tomography.

Trends of SPECT results in patients with an established history of CAD have not been described previously. Two previous studies assessed trends in patients without a previous history of CAD, and both demonstrated a progressive decline of SSS over time with fewer intermediate- or high-risk tests and significantly more low-risk tests.[8,9] In these 2 studies, the observed trends of decreased SSS and more frequent low-risk tests were consistent despite some differences between the 2 studies such as geographic location, patients' characteristics, and presenting symptomatic status. In another study by McNulty et al,[7] SPECT utilization in patients with and without previous CAD was assessed but they did not report SPECT results or SSS risk categories. However, they demonstrated a significant decline in incident myocardial infarction and coronary artery revascularization after SPECT between 2000 and 2011, which may reflect a decline in high-risk SSS, similar to what we reported previously in patients without a history of CAD[9] and what we are reporting in this study in patients with CAD.

The gradually increasing prevalence of low-risk SPECT stress tests over time indicates milder CAD (assessed by SSS) and less inducible ischemia (assessed by SDS). The causes of this observation are likely multifactorial. Physicians at our institution may have referred less sick patients for SPECT testing although the trends in hypertension, diabetes mellitus, and dyslipidemia increased over time. The increased proportion of patients with history of CABG or PCI without MI would support the notion of less sick patients. Treatment of hypertension and dyslipidemia has improved dramatically over the past 20 years, both nationally and within Minnesota.[22,23] Although the prevalence of hypertension and dyslipidemia increased in our study over time, this likely corresponds to increased treatment and compliance with guideline-directed medical therapy over the past 10 years.[24] Smoking rates have also decreased over time.[25] Declining national CAD mortality between 1980 and 2000 has been attributed to favorable risk factors at the population level, improved primary prevention (in patients without CAD), and better secondary prevention in patients with established CAD.[26]

It has also been shown from the nuclear arm in the COURAGE trial (Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation) that optimal medical therapy results in improved myocardial perfusion; SSS decreased in the optimal medical therapy arm from 14.7±11 at baseline to 11.4±10 ($P<0.01$) after 6 to 18 months.[27] Similarly, statins have been shown to reduce SSS by SPECT[28] and also improve myocardial blood flow by PET.[29] Management of patients presenting with a myocardial infarction has also improved over the past 20 years with increasing adherence to guideline-directed medical therapy.[30,31] Another possible contributor to increased low-risk tests is increasing frequency of complete revascularization with multi-vessel PCI and CABG.

Study Limitations

Our study was based on SPECT studies performed at a tertiary academic medical center, which makes it subject to referral bias. Additional community-based studies are needed to confirm these findings in patients with a history of CAD. Our definition of CAD on the basis of a history of myocardial infarction or coronary revascularization excluded patients without such history but with moderate coronary atherosclerosis found on coronary angiography (such as in the work-up of pre-transplantation patients) if these patients later underwent SPECT stress testing. Major limitations of our study include inability to assess appropriateness of SPECT tests, downstream coronary angiography/revascularization, medical therapy, or cardiovascular outcomes, which warrant further research in the future. Medication data were incomplete in the database to permit reliable analysis. The specialty of the ordering physician was not available for analysis, and patient-specific preferences could not be examined. Finally, assessment of coronary angiography trends as a possible cause for reduced SPECT utilization was not feasible. However, national trends in Medicare beneficiaries suggest declining rates of coronary angiography and PCI since 2006.[32]

Conclusion

SPECT utilization in patients with a documented history of CAD increased between 1991 and 2000 but later decreased. Utilization in 2012 was similar to utilization between 1991 and 1995. More SPECT tests were low risk regardless of presenting symptoms, stress modality, or the diagnostic subgroup of CAD. SSS, SDS, and positive stress ECG all decreased despite reduced SPECT utilization. Our results suggest that among patients with a history of CAD, SPECT was being increasingly utilized in patients with milder CAD. This trend parallels reduced utilization of stress ECG, stress echocardiography, and coronary angiography, reduced smoking, and greater utilization of medical therapy including statins for

prevention and treatment of coronary heart disease, as well as reductions of CAD events nationally.

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Disclosures

Dr Gibbons is a consultant for Lantheus Medical Imaging, Astellas Pharmaceuticals, and Stealth Pharmas. The other authors report no conflicts.

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CLINICAL PERSPECTIVE

This study describes long-term trends over >20 years in stress single-photon emission computed tomography myocardial perfusion imaging (SPECT) studies in patients with a documented history of coronary artery disease (CAD) at an academic medical center. CAD was defined as previous myocardial infarction, percutaneous intervention, and coronary artery bypass grafting. Annual SPECT utilization in patients with previous CAD increased between 1992 and 2003 but then decreased after 2003. Fewer patients had typical angina, whereas patients with atypical angina and dyspnea increased over time. High-risk SPECT tests declined, whereas low-risk SPECT tests increased markedly. These results, which are similar to those reported previously for patients without CAD, suggest that SPECT was being increasingly utilized in patients with milder CAD. This trend parallels reduced utilization of coronary angiography and greater utilization of optimal medical therapy for prevention and treatment of CAD.

Temporal Trends of Single-Photon Emission Computed Tomography Myocardial Perfusion Imaging in Patients With Coronary Artery Disease: A 22-Year Experience From a Tertiary Academic Medical Center

Hayan Jouni, J. Wells Askew, Daniel J. Crusan, Todd D. Miller and Raymond J. Gibbons

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Temporal Trends of SPECT Myocardial Perfusion Imaging in Patients with Coronary Artery Disease: A 22-Year Experience from a Tertiary Academic Medical Center

Supplementary Material

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Table 1. Stress SPECT and Stress Echocardiography Patient Characteristics

	2001-2005	2000-2005	2006-2010		2011-2012	
	SPECT N= 6444	**Stress Echo N= 6885**	**SPECT N= 4140**	**Stress Echo N = 4549**	**SPECT N= 1146**	**Stress Echo N = 1349**
*Age, y	66.9 ± 10.9	68.3 ± 11	66.9 ± 11.3	68 ± 11.1	66.6 ± 11.6	67.8 ± 11.2
Male gender	4890 (75.9%)	4912 (71.3%)	3113 (75.2%)	3313 (72.8%)	862 (75.2%)	971 (72%)
BMI, kg/m^2	29.9 ± 5.9	28.7 ± 5.5	29.9 ± 5.7	29.6 ± 5.5	30.6 ± 5.9	29.8 ± 5.5
Hypertension	4786 (74.5%)	5047 (73.3%)	3301 (79.8%)	3655 (80.3%)	945 (82.5%)	1115 (82.7%)
Dyslipidemia	5574 (86.7%)	5637 (81.9%)	3739 (90.3%)	3979 (87.5%)	1047 (91.4%)	1218 (90.3%)
Diabetes mellitus	1864 (29%)	1842 (26.8%)	1225 (29.6%)	1351 (29.7%)	352 (30.7%)	409 (30.3%)
Ever smoker	3934 (61.2%)	4359 (63.3%)	2474 (59.7%)	2846 (62.6%)	661 (57.7%)	814 (60.3%)
Typical angina	1179 (18.3%)	1182 (17.2%)	552 (13.3%)	492 (10.8%)	203 (17.7%)	181 (13.4%)
Atypical angina	1410 (21.9%)	1307 (19%)	1026 (24.8%)	977 (21.5%)	341 (29.8%)	293 (21.8%)
Non-cardiac chest pain	93 (1.4%)	242 (3.5%)	100 (2.4%)	41 (0.9%)	24 (2.1%)	15 (1.1%)
MI alone without revascularization	870 (13.5%)	1247 (18.1%)	415 (10%)	625 (13.7%)	118 (10.3%)	169 (12.5%)
MI with PCI or CABG	2266 (35.2%)	2686 (39%)	1596 (38.6%)	1739 (38.2%)	389 (33.9%)	526 (39%)
PCI or CABG without MI	3308 (51.3%)	2952 (42.9%)	2129 (51.4%)	2185 (48%)	639 (55.8%)	654 (48.5%)

*Data are presented as number (percentage) or mean ± SD.

BMI: body mass index; CABG: coronary artery bypass grafting; MI: myocardial infarction; PCI: percutaneous coronary intervention

Table 2. Time Difference between MI Diagnosis, PCI, or CABG and SPECT Testing

	1991-1995 N= 2475	1996-2000 N= 5168	2001-2005 N= 6444	2006-2010 N= 4140	2011-2012 N= 1146
MI*	N = 1429 3.02 (0.32-9.04) 5.61 ± 6.81	N = 2691 3.32 (0.5-9.13) 5.9 ± 6.91	N = 3006 3.64 (0.76-9.76) 6.39 ± 7.51	N = 1985 4.18 (0.99-10.18) 6.85 ± 7.73	N = 507 4 (0.99-9.99) 6.65 ± 7.32
PCI	N = 1003 1.5 (0.38-3.97) 2.52 ± 2.7	N = 2569 1.79 (0.46-4.9) 3.2 ± 3.68	N = 3716 2.07 (0.67-5.26) 3.68 ± 4.16	N = 2693 2.2 (0.74-6) 4.14 ± 4.75	N = 739 2.99 (0.99-6.99) 4.48 ± 4.77
CABG	N = 1029 5.48 (2.24-9.25) 6.32 ± 4.83	N = 2208 5.44 (2.21-9.98) 6.65 ± 5.37	N = 2612 5.79 (2.53-10.36) 7.18 ± 5.76	N = 1434 6.83 (2.45 - 12) 8.05 ± 6.57	N = 339 7 (2.99-12.99) 8.99 ± 7.17
All	N= 2428 2.62 (0.55-6.56) 4.45 ± 5.26	N = 5048 2.5 (0.6-6.79) 4.54 ± 5.35	N = 6324 2.83 (0.84- 6.78) 4.77 ± 5.48	N = 4018 2.89 (0.88-7.41) 5.05 ± 5.83	N = 1071 3 (0.99-8) 5.22 ± 5.68

*The first line within each subgroup represents the corresponding number of patients with the CAD qualifying history with available dates of MI, PCI, or CABG. The second line represents the median (25%-75% interquartile range) time difference in years. The third line represents the mean ± standard deviation of time difference in years. There is overlap between the subgroups. For the "All" group, the listed time difference is between the most recent MI, PCI, or CABG and time of SPECT testing.

CABG: coronary artery bypass grafting; MI: myocardial infarction; PCI: percutaneous coronary intervention.

Table 3. Repeat SPECT Patient Characteristics from a Diagnosis Standpoint

	1991-1995 N=299	1996-2000 N= 1742	2001-2005 N= 3792	2006-2010 N= 3062	2011-2012 N= 845
***MI alone without revascularization**	55 (18.4%)	202 (11.6%)	291 (7.7%)	174 (5.7%)	35 (4.1%)
†Asymptomatic	23 (41.8%)	90 (44.6%)	150 (51.5%)	105 (36.1%)	16 (45.7%)
SSS	13.7 ± 9.9	11.8 ± 9	10.6 ± 9.8	8.6 ± 9.7	8.5 ± 10.6
Low risk (SSS: 0-3)	10 (18.2%)	44 (21.8%)	84 (28.9%)	73 (42%)	19 (54.3%)
MI with PCI or CABG	124 (41.5%)	703 (40.4%)	1479 (39%)	1228 (40.1%)	339 (40.1%)
Asymptomatic	34 (27.4%)	295 (42%)	643 (43.5%)	551 (44.9%)	132 (38.9%)
SSS	11.3 ± 8.7	11.1 ± 8.7	8.9 ± 8.6	7.5 ± 8.6	5.9 ± 7.4
Low risk (SSS: 0-3)	29 (23.4%)	167 (23.8%)	525 (35.5%)	583 (47.5%)	199 (58.7%)
PCI or CABG without MI	120 (40.1%)	837 (48%)	2022 (53.3%)	1660 (54.2%)	471 (55.7%)
Asymptomatic	35 (29.2%)	329 (39.3%)	924 (45.7%)	762 (45.9%)	192 (40.8%)
SSS	6.9 ± 6.7	5.8 ± 6.2	4 ± 5.3	3.1 ± 5.3	1.9 ± 4
Low risk (SSS: 0-3)	46 (38.3%)	388 (46.5%)	1266 (62.7%)	1226 (73.9%)	405 (86%)
‡Time difference to SPECT Testing	N = 297 2.42 (0.78-5.97) 4.0 ± 4.48	N = 1731 3.75 (1.59-7.85) 5.31 ± 5.01	N = 3764 4.78 (2.19-8.57) 6.15 ± 5.25	N = 3022 5.6 (2.57-10) 7 ± 5.8	N = 808 6.49 (3-11.66) 7.84 ± 6.06

*The first line within each subgroup represents the overall number of patients within that subgroup and the percentage compared to the overall number of patients in the corresponding time-period.
† The other lines within the subgroups represent number and percentage compared to the overall number within the same subgroup.
‡ N represents number of patients with available MI, CABG, or PCI dates; the second line represents the median (25%-75% interquartile range) time difference between SPECT and the most recent MI, PCI, or CABG in years. The third line represents the mean ± standard deviation of time difference in years. CABG: coronary artery bypass grafting; MI: myocardial infarction; PCI: percutaneous coronary intervention; SSS: summed stress score.