The clinical value of single photon emission computed tomography myocardial perfusion imaging in cardiac risk stratification of very elderly patients (≥80 years) with suspected coronary artery disease

Sanjeev U. Nair, MBBS, MD,[a] Alan W. Ahlberg, MA,[a] Shishir Mathur, MD,[a] Deborah M. Katten, RN,[a] Donna M. Polk, MD, MPH,[a,b] and Gary V. Heller, MD, PhD[a,b]

Background. **The role of single photon emission computed tomography myocardial perfusion imaging (SPECT MPI) in cardiac evaluation of the very elderly patients is unclear. We investigated the clinical value of SPECT MPI in very elderly patients (≥80 years) with suspected coronary artery disease (CAD) as well as in comparison to younger patients.**

Methods and Results. **A retrospective analysis of prospectively collected data from 8,864 patients [1,093 patients ≥80 years (very elderly), 3,369 patients 65-79 years (elderly), and 4,402 patients 50-64 years (middle-aged)] with suspected CAD who underwent exercise and/or pharmacologic stress testing with SPECT MPI between 1996 and 2005 was performed. Clinical and SPECT MPI characteristics, cardiac event rates, early (≤60 days) cardiac catheterization and revascularization rates of very elderly patients were compared to that of younger patients. Mean follow-up for cardiac events (cardiac death or non-fatal myocardial infarction) was 1.9 ± 0.9 years. Very elderly patients with moderate to severely abnormal SSS had a significantly higher annualized cardiac event rate than those with mildly abnormal or normal study (9.6% vs 3.4% and 2.5% respectively, $P < .001$). Across all categories of SSS, very elderly patients had a significantly higher cardiac event rate as compared to younger patients ($P < .001$). Early cardiac catheterization and revascularization referrals in very elderly patients increased as a function of severity of ischemia on SPECT MPI ($P < .001$), although these referral rates were significantly lower in very elderly patients with mild to moderate and severe ischemia as compared to younger patients ($P < .05$).**

Conclusions. **In very elderly patients (≥80 years) with suspected CAD, SPECT MPI has prognostic and incremental value in the noninvasive cardiovascular assessment for risk stratification and may influence medical decisions. (J Nucl Cardiol 2012;19:244–55.)**

Key Words: Elderly · prognosis · single-photon emission-computed tomography myocardial perfusion imaging · revascularization

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From the Division of Cardiology, Nuclear Cardiology Laboratory, Henry Low Heart Center,[a] Hartford Hospital, Hartford, CT; and University of Connecticut School of Medicine,[b] Farmington, CT.

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Reprint requests: Sanjeev U. Nair, MBBS, MD, Division of Cardiology, Nuclear Cardiology Laboratory, Henry Low Heart Center, Hartford Hospital, 80 Seymour Street, Hartford, CT 06102; *doc_nsu@rediffmail.com.*

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INTRODUCTION

Coronary artery disease (CAD) remains the leading cause of morbidity and mortality in the elderly.[1,2] As the population of United States grows older,[3] there is a continuing need to identify effective methods of cardiovascular risk stratification in the elderly which may direct management decisions in such patients.[4] Establishing a diagnosis and stratifying cardiac risk in such patients can be challenging because of frequent atypical symptoms[5,6] and a higher prevalence of co-morbidities. Although the prognostic value of Single Photon Emission Computed Tomographic Myocardial Perfusion

Imaging (SPECT MPI) in the general population is well understood,[7,8] the role of this noninvasive technique in the elderly is less defined, particularly in octogenarians.[9] To date, studies investigating the prognostic value of SPECT MPI in patients ≥80 years of age have included both patients with and without previously diagnosed CAD.[10-13] In such patients who have symptoms suggestive of but without established CAD and normal left ventricular function, an important clinical dilemma is to whether pursue noninvasive vs invasive management, particularly in the presence of abnormal myocardial perfusion imaging. Therefore, we conducted this study to (1) examine the clinical and SPECT MPI characteristics of clinically referred very elderly patients (≥80 years) with suspected CAD as compared to younger patients, (2) to evaluate the role of SPECT MPI in risk stratification of very elderly patients (≥80 years) with suspected CAD, and (3) to study the role of SPECT MPI in decision making regarding cardiac interventions in very elderly patients (≥80 years) with suspected CAD.

METHODS

Patient Selection

Consecutive patients aged 50 years and older with suspected CAD, clinically referred for stress technetium-99m sestamibi SPECT MPI from January 2, 1996 through December 31, 2005 were identified from the clinical database of the Hartford Hospital Nuclear Cardiology Laboratory. Excluded were patients with known CAD, history of myocardial infarction, percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG), and left ventricular ejection fraction <0.45. The method of stress (exercise, vasodilator, combined vasodilator-exercise, dobutamine) was determined most often by the referring physician. In patients with multiple studies, only the initial study was considered for analysis. For the purpose of survival analysis, we excluded those patients who underwent an early (≤60 days) revascularization procedure (CABG or PCI) after stress testing as well as patients who were lost to follow-up. Patients were categorized into "very elderly" (≥80 years), "elderly" (65-79 years of age) and "middle-aged" (50-64 years of age) groups. This study was approved by and conducted within guidelines of the Institutional Review Board at Hartford Hospital.

Stress Testing Protocol

Stress testing was performed as per guidelines of the American College of Cardiology/American Heart Association.[14-16] All patients underwent either exercise stress, vasodilator stress (adenosine or dipyridamole) with or without exercise, or dobutamine stress testing; each performed in approximately equal percentage during the study period. Patients were assigned to a 1 or 2-day rest and stress protocol. Exercise stress testing was based on symptom-limited Standard or Modified Bruce protocol with radionuclide injection prior to cessation of exercise. Vasodilator stress testing was performed in combination with treadmill exercise whenever possible. For all vasodilator stress testing, image acquisition was begun 60 minutes after radionuclide injection. For dobutamine stress testing intravenous atropine and/or arm exercise was added if maximal predicted heart rate (MPHR) was not achieved at the peak dose.

An abnormal rest ECG was defined as the presence of intraventricular conduction defect, left bundle branch block, q waves, ST-T abnormalities or a paced rhythm. An abnormal stress ECG was defined as horizontal or downsloping ST segment depression ≥1 mm or upsloping ≥1.5 mm at 80 ms after J point or if there was a change of >1 mm in a segment with <0.5 mm deviation from the isoelectric line at baseline. Functional capacity was estimated from exercise workload achieved and was expressed in metabolic equivalents (METs), whereby 1 MET equals oxygen consumption at rest (approximately 3.5 ml/kg/minute).[17]

SPECT MPI

Radiopharmaceutical dosing, SPECT acquisition, and image processing were performed within guidelines established by American Society of Nuclear Cardiology.[18,19] SPECT images were interpreted during daily clinical reading sessions by a consensus of 2 or more experienced readers, without knowledge of stress test results. Using the ASNC standardized 17-segment model, regional perfusion was scored with a 5-point scale.[20] A summed stress score (SSS) and a summed rest score (SRS) were calculated. Based on the presence, extent, and severity of perfusion defects using SSS, the study patients in each age category were classified into normal (SSS < 4), mildly abnormal (SSS 4-8), and moderately to severely abnormal (SSS > 8) categories.[21] Summed difference score (SDS) was calculated by subtracting the SRS from the SSS (SSS-SRS). SDS was categorized as no ischemia (SDS < 2), mild-moderate ischemia (SDS 2-7), and severe ischemia (SDS > 7).[22] Left ventricular (LV) cavity size at stress and rest was obtained automatically using QPS software and confirmed visually as follows: If LV cavity size was dilated at stress, it was further classified as fixed (score at stress equal to the score at rest) or transient ischemic dilation (TID).[23,24] Left ventricular ejection fraction was obtained automatically using QGS software and confirmed visually.[25]

Follow-up

Patient follow-up was obtained by scripted telephone interviews and mailed questionnaires. An investigator unaware of clinical, stress, and SPECT data confirmed events by reviewing hospital charts, physician records, appropriate laboratory test results, the public Social Security database, and death certificates. The endpoints for this study were cardiac

death (CD) or non-fatal myocardial infarction (NFMI). Cardiac death was defined as death from lethal arrhythmias, pump failure, myocardial infarction, or sudden death. The follow-up data was censored at 3 years or at the first cardiac event. SPECT MPI results were made available to referring clinicians and were taken into account while making management decisions. Early (≤60 days after SPECT MPI results) cardiac catheterization and revascularization referral data was captured for downstream utilization.

Statistical Analysis

Clinical and stress SPECT MPI characteristics were expressed as mean ± standard deviation or as proportions. Continuous variables are shown as mean ± standard deviation and were compared using the ANOVA test. Categorical variables were analyzed using the chi-square or Fisher's exact test. Annual cardiac event rates were calculated as number of events divided by the sum of each individual follow-up period in years. Cumulative cardiac event-free survival curves were obtained using the Kaplan-Meier procedure and compared by means of the log-rank test.

Significant parameters affecting cardiac events on univariable analysis as well as clinically significant variables regardless of their strength of univariate correlation were entered into Cox proportional hazards regression modeling. Tests for collinearity among covariates were performed as appropriate. A forward stepwise selection procedure, based on the Wald statistic probability, was performed, with a threshold of $P \leq .05$ and $P \geq .1$ for variable entry and removal, respectively. Hazard ratios (HR) and 95% confidence intervals (CI) were calculated from the model. To examine the incremental value of SPECT MPI in predicting cardiac events in very elderly patients, Cox proportional hazards modeling was performed as follows: (1) with clinical and historical data, (2) with addition of stress data (excluding perfusion data), (3) with addition of SRS, and (4) with addition of SSS. A statistically significant increase in the total Wald χ^2 scores between models after addition of perfusion variables defined incremental prognostic value.

Referral rates for early cardiac catheterization and revascularization were calculated as percentages and compared within subcategories of SDS (SDS <2, 2-7, and >7).

In all statistical analyses, a $P < .05$ was considered significant. All statistical analyses were two-tailed and were performed using SPSS version 17.0 software.

RESULTS

We identified 8,864 patients [1,093 (12%) very elderly patients (≥80 years), 3,369 (38%) elderly patients (65-79 years), and 4,402 (50%) middle-aged patients (50-64 years)] who met the inclusion criteria. Follow-up was available in 8,503 patients (96%) and formed the study group. The characteristics of patients lost to follow-up in each of the very elderly (2.4%), elderly (2.5%), and middle-aged (5.7%) groups were not significantly different than those in the study group. There were 692 (7.8%) and 354 (4%) patients who underwent early cardiac catheterization and revascularization, respectively. After excluding patients who underwent early cardiac revascularization, there were 193 (2.2%) cardiac events (125 CDs and 68 NFMIs) over a mean follow-up time of 1.9 ± 0.9 years.

Clinical Characteristics

The clinical characteristics in very elderly patients in comparison to younger patients are summarized in Table 1. Very elderly patients were less likely to have diabetes mellitus, hyperlipidemia, history of smoking and obesity (BMI > 30) than elderly and middle-aged patients ($P < .001$).

Table 1. Clinical characteristics/cardiac risk factors in study patients with suspected CAD

	50–64 years (M) (n = 4,402)	65–79 years (E) (n = 3,369)	≥80 years (VE) (n = 1,093)	*P* value for trend
Male	1839 (42%)	1354 (40%)	353 (32%)	<.001
Hx of CHF	49 (1%)	92 (3%)	71 (7%)	<.001
Diabetes mellitus	1079 (25%)	801 (24%)	184 (17%)	<.001
Hypertension	2362 (54%)	2153 (64%)	749 (69%)	<.001
Hyperlipidemia	1907 (43%)	1416 (42%)	359 (33%)	<.001
Hx of smoking	1440 (33%)	955(28%)	217 (20%)	<.001
BMI ≥ 30	1877 (44%)	1064 (32%)	210 (20%)	<.001
Abnormal resting ECG	1233 (28%)	1209 (37%)	438 (44%)	<.001

BMI, Body mass index; *CAD*, coronary artery disease; *CHF*, congestive heart failure; *E*, elderly; *ECG*, electrocardiogram; *Hx*, history; *M*, middle-aged; *VE*, very elderly.

Stress Test and MPI Characteristics

The stress MPI results are summarized in Table 2. The very elderly patients underwent significantly more vasodilator stress testing than elderly and middle-aged patients (63% vs 35% and 20%, respectively, $P < .001$). The Summed Stress Scores and Summed Rest Scores were significantly higher in the very elderly patients as compared to younger patients ($P < .001$). The Summed Difference Scores were significantly higher in the very elderly and elderly patients as compared to middle-aged patients indicating a higher degree of ischemia in these patients ($P = .001$).

Cardiac Catheterization and Early Revascularization (Figure 1)

The referral for early cardiac catheterization was reduced in the very elderly group with SDS 2-7 on SPECT MPI as compared to the elderly and middle-aged patients (14% vs 23% and 25%, respectively, $P < .001$). A lower referral for early cardiac catheterization was also seen in the very elderly high risk group with SDS > 7 in comparison to elderly and middle-aged patients (41% vs 57% and 59%, respectively, $P < .001$).

Referral rate for early cardiac revascularization in very elderly patients with SDS 2-7 on SPECT MPI was significantly lower than elderly and middle-aged patients (7% vs 11% and 11%, respectively, $P < .001$). Similarly, a lower referral rate for early cardiac revascularization was seen in very elderly patients with SDS > 7 on SPECT MPI as compared to elderly and middle-aged patients (26% vs 45% and 40%, respectively, $P < .001$).

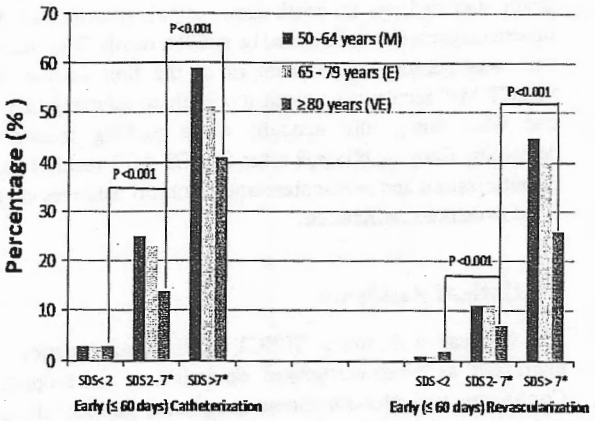

Figure 1. Very elderly patients (≥80 years) show significant increase in early catheterization and revascularization referral as a function of the severity of ischemia on SPECT MPI. *$P < .05$ between VE group and the other two groups (E and M). *E*, elderly; *M*, middle-aged; *SDS*, summed difference score; *VE*, very elderly.

Table 2. Stress test characteristics and MPI data in study patients with suspected CAD

	50–64 years (M) (n = 4,402)	65–79 years (E) (n = 3,369)	≥80 years (VE) (n = 1,093)	*P* value for trend
Indication for stress testing				
Chest pain	3150 (72%)	2291 (68%)	754 (69%)	.147
Dyspnea	94 (2%)	146 (4%)	52 (5%)	<.001
Exercise stress test	2452 (56%)	1145 (34%)	104 (10%)	<.001
Vasodilator-exercise stress test	741 (17%)	650 (19%)	179 (16%)	.009
Vasodilator stress test	858 (20%)	1170 (35%)	689 (63%)	<.001
Dobutamine stress test	355 (8%)	406 (12%)	121 (11%)	<.001
Abnormal stress ECG	1215 (28%)	1437 (43%)	593 (55%)	<.001
TID	47 (1%)	57 (2%)	17 (2%)	.06
SSS (mean ± SD)	1.47 ± 3.19	2.02 ± 3.89	2.24 ± 3.99	<.001
SRS (mean ± SD)	0.61 ± 1.76	0.96 ± 2.38	1.23 ± 2.98	<.001
SDS (mean ± SD)	0.86 ± 2.43	1.06 ± 2.735	1.02 ± 2.43	.001
SSS < 4	3790 (86%)	2667 (79%)	840 (77%)	<.05
SSS 4–8	430 (10%)	466 (14%)	166 (15%)	<.05
SSS > 8	182 (4%)	236 (7%)	87 (8%)	<.05

CAD, Coronary artery disease; *E*, elderly; *ECG*, electrocardiogram; *M*, middle-aged; *MPI*, myocardial perfusion imaging; *NS*, not significant; *SRS*, summed rest score; *SSS*, summed stress score; *SDS*, summed difference score; *SD*, standard deviation; *TID*, transient ischemic dilatation; *VE*, very elderly.

Across all age categories, a low rate of early cardiac catheterization and revascularization was observed in patients with SDS < 2 on SPECT MPI.

Predictors of Cardiac Events in the Very Elderly Patients (≥80 years)

Table 3 presents the univariate predictors of cardiac events in very elderly patients. Using these variables, a multivariable analysis using Cox regression was performed in these patients. The multivariable predictors of cardiac events in very elderly patients were age (hazard ratio = 1.087, 95% confidence interval 1.026-1.166, $P = .006$), SSS (hazard ratio = 1.090, 95% confidence interval 1.047-1.135, $P < .001$) and presence of DM (hazard ratio = 2.962, 95% confidence interval 1.726-5.083, $P < .001$).

Cardiac Events

In follow-up, very elderly patients had 65 (6.3%) cardiac events as compared to 82 (2.6%) and 46 (1.1%) in elderly and middle-aged patients, respectively ($P < .001$) after exclusion of patients who had early cardiac revascularization (n = 354). As demonstrated in Table 4, the incidence of cardiac events was significantly associated with age category. Across all three categories of SPECT MPI, there were significantly more cardiac events in very elderly patients as compared to the elderly and middle-aged patients ($P < .05$) (Figure 2). Very elderly patients with moderately to severely abnormal SPECT MPI had a significantly higher event rate than those with mildly abnormal or normal SPECT MPI ($P < .05$) (Figure 2). Risk adjustment for clinical and historical data (age, gender, DM, history of CHF, hypertension, hyperlipidemia, history of smoking, BMI ≥ 30, and abnormal rest ECG) as well as stress data (type of stress test and abnormal stress ECG) was performed for the three SSS categories in each age group. After risk adjustment, a similar pattern of significantly higher risk of cardiac events in very elderly patients as compared to younger patients was observed (Figure 3).

The relationship of cardiac events in the very elderly group was further examined using Kaplan-Meier procedure and this showed significant difference in cardiac-event free survival among SSS categories (Figure 4). Patients in the very elderly group with moderate to severely abnormal SPECT MPI had a significantly lower cardiac event-free survival than those with mildly abnormal or normal SPECT MPI ($P < .05$).

A low cardiac death rate (0.7%/year) was observed in the very elderly patients who underwent exercise SPECT MPI and had a normal perfusion score (SSS < 4).

Table 3. Univariable predictors of cardiac events in very elderly patients (≥80 years)

	Patients with no cardiac events (n = 963)	Patients with cardiac events (n = 65)	*P* value
Age	83.74 ± 3.40	84.65 ± 3.82	.048
Male	304 (93%)	22 (7%)	.34
Hx of CHF	59 (6%)	7 (11%)	.08
Diabetes mellitus	152 (16%)	21 (36%)	<.001
Hypertension	658 (68%)	42 (65%)	.60
Hyperlipidemia	324 (33%)	18 (28%)	.64
Hx of smoking	201 (21%)	6 (9%)	.05
Abnormal resting ECG	455 (44%)	30 (46%)	.72
Exercise stress test	89 (9%)	4 (6%)	.53
Vasodilator-exercise stress test	164 (17%)	6 (9%)	.18
Vasodilator stress test	606 (62%)	42 (65%)	.18
Dobutamine stress test	110 (11%)	7 (11%)	.90
Abnormal stress ECG	522 (54%)	31 (53%)	.93
TID	11 (1%)	1 (2%)	.70
SSS (mean ± SD)	1.97 ± 3.69	3.80 ± 5.037	<.001
SRS (mean ± SD)	1.12 ± 2.91	2.24 ± 3.49	<.001
SDS (mean ± SD)	0.85 ± 2.15	1.56 ± 2.88	<.001

CHF, congestive heart failure; *ECG*, electrocardiogram; *SRS*, summed rest score; *SSS*, summed stress score; *SDS*, summed difference score; *SD*, standard deviation; *TID*, transient ischemic dilation; *VE*, very elderly.

Table 4. Cumulative cardiac event rates in study patients with suspected CAD

	50–64 years (M)	65–79 years (E)	≥80 years (VE)	*P* value for trend
Cardiac death	29 (0.7%)	55 (1.7%)	41 (4%)	<.001
NFMI	17 (0.4%)	27 (0.9%)	24 (2.3%)	<.001

CAD, Coronary artery disease; *E*, elderly; *M*, middle-aged; *NFMI*, non-fatal myocardial infarction; *VE*, very elderly.

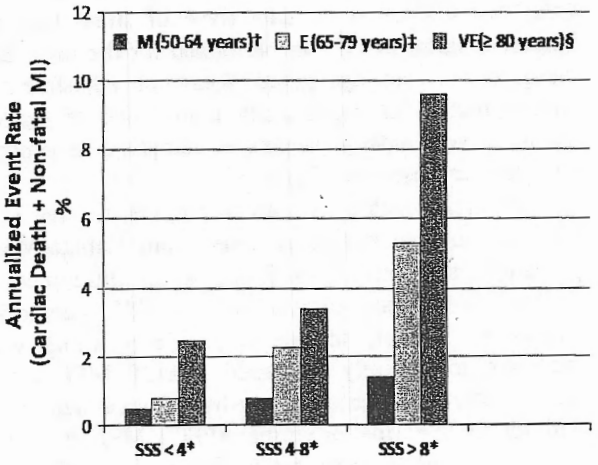

Figure 2. Very elderly patients (≥80 years) have significantly more cardiac events than younger groups of patients in each category of SSS. Within the very elderly group, patients with moderate-severely abnormal SSS have significantly more cardiac events than those with mildly abnormal or normal SSS. *$P < .05$ across M, E, and VE groups. †$P < .05$ for SSS < 4 or SSS 4-8 vs SSS > 8. ‡$P < .05$ across SSS categories. §$P < .001$ for SSS < 4 or SSS 4-8 vs SSS > 8. *E*, elderly; *M*, middle-aged; *MI*, myocardial infarction; *SSS*, summed stress score; *VE*, very elderly.

Incremental Value of SPECT MPI in the Very Elderly Patients (≥80 years)

COX proportional-hazards modeling was performed to evaluate the incremental value of SPECT MPI in predicting cardiac events in very elderly patients. The addition of SRS or SSS to the models with clinical and historical data (age, gender, DM, history of CHF, hypertension, hyperlipidemia, history of smoking, and abnormal rest ECG) ± stress data (type of stress test and abnormal stress ECG) leads to a significant increase in Wald χ^2 suggesting the incremental prognostic value of using SPECT MPI perfusion data in very elderly patients (Figure 5).

Gender and SPECT MPI in the Very Elderly Patients (≥80 years)

Among very elderly patients, men were more likely to be younger, have diabetes, have a history of smoking, undergo exercise stress, and have an abnormal MPI ($P < .05$) than women. In contrast, women were more likely than men to have a history of hypertension, hyperlipidemia, an abnormal resting ECG and undergo vasodilator stress testing ($P < .05$). In very elderly patients with an abnormal MPI, there was no significant gender difference in annualized cardiac event rates (women vs men, 4.7% vs 6.1%, respectively, $P = .506$).

SPECT MPI with regards to gender in very elderly patients was compared after risk-adjustment for the above variables. This demonstrated similar risk stratification of very elderly patients as per SSS in both men and women (Figure 6). The overall rate of referral for early cardiac catheterization and revascularization was significantly higher in men as compared to women, however, the referral rates for these procedures with respect to SDS categories were similar.

Diabetes in the Very Elderly Patients (≥80 years)

In the very elderly group, only 184 patients (17%) had diabetes mellitus as compared to 801 patients (24%) in the elderly group and 1,079 patients (25%) in the middle-aged group ($P < .001$). In the very elderly group, diabetics as compared to non-diabetics were more likely to be male, obese, have a history of hypertension or congestive heart failure and undergo vasodilator stress testing (72% vs 61%, respectively, $P < .05$). After risk-adjustment for the above variables in the very elderly group, the diabetics had a significantly lower cardiac event-free survival as compared to non-diabetic patients, across all SSS categories ($P < .05$) (Figure 7).

Cardiac Death Rate with Normal SPECT MPI

To examine the impact of age on outcomes in patients with normal SPECT MPI, the cardiac death index due to ischemic heart disease in the general US population was compared with the annualized CD rate of study patients (Figure 8).[26] In all age groups, the CD rate in patients with a normal SPECT MPI was similar to the age-adjusted CD rate due to ischemic heart disease in the general US population.

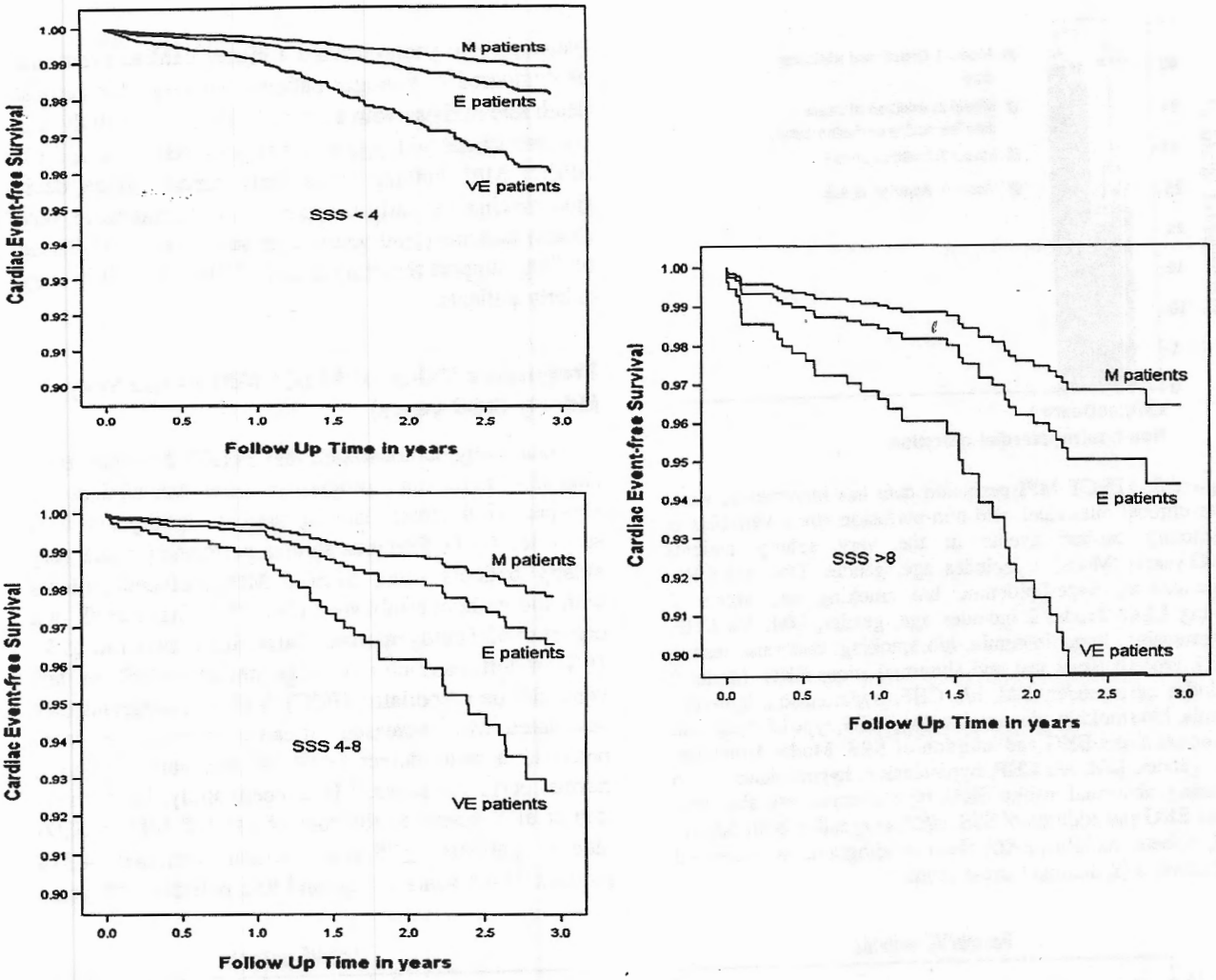

Figure 3. Risk-adjusted survival curves show a significant difference in cardiac event-free survival between middle-aged, elderly, and very elderly patients within each SSS category ($P < .05$). *E*, elderly; *M*, middle-aged; *SSS*, summed stress score; *VE*, very elderly.

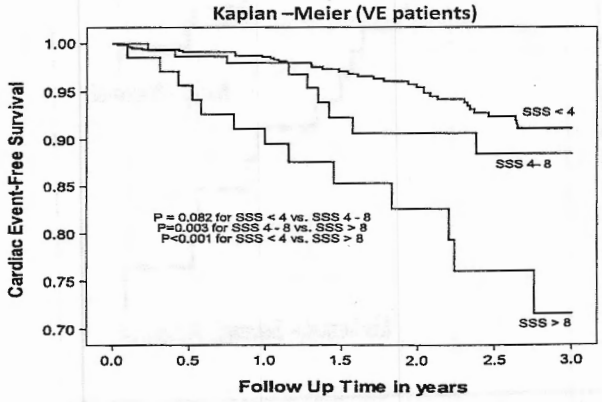

Figure 4. Kaplan-Meier analysis of very elderly patients (≥80 years) reveals a significantly lower cardiac event-free survival in patients with SSS > 8 as compared to those with SSS 4-8 and SSS < 4 ($P < .05$). *SSS*, summed stress score; *VE*, very elderly.

DISCUSSION

The evaluation process for the presence of CAD and subsequent risk stratification in the very elderly (≥80 years) patients is becoming commonplace due to an aging population, and a high prevalence of CAD in this group,[27] although few data are available for guidance. In such patients who present with symptoms suggestive of CAD but with no previous history, further management decisions pose a conundrum in the presence of abnormal perfusion abnormalities on stress testing. We examined the role of SPECT MPI for risk stratification and clinical decision making in very elderly patients as well as in comparison to younger patients. The most important findings in our study were (1) SPECT MPI adds incremental prognostic value in very elderly patients (≥80 years) with suspected CAD, (2) across all SPECT MPI risk categories, very elderly

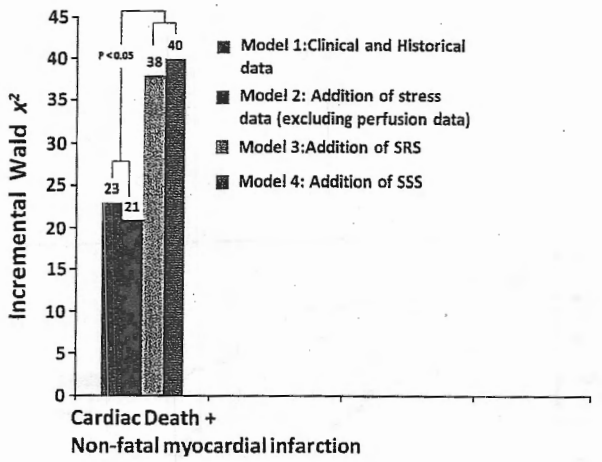

Figure 5. SPECT MPI perfusion data has incremental value over clinical, historical, and non-perfusion stress variables in predicting cardiac events in the very elderly patients (≥80 years). Model 1 includes age, gender, DM, h/o CHF, hypertension, hyperlipidemia, h/o smoking and abnormal resting EKG. Model 2 includes age, gender, DM, h/o CHF, hypertension, hyperlipidemia, h/o smoking, abnormal resting EKG, type of stress test and abnormal stress EKG. Model 3 includes age, gender, DM, h/o CHF, hypertension, hyperlipidemia, h/o smoking, abnormal resting EKG, type of stress test, abnormal stress EKG and addition of SRS. Model 4 includes age, gender, DM, h/o CHF, hypertension, hyperlipidemia, h/o smoking, abnormal resting EKG, type of stress test, abnormal stress EKG and addition of SSS. *CHF*, congestive heart failure; *DM*, diabetes mellitus; *EKG*, electrocardiogram; *SRS*, summed rest score; *SSS*, summed stress score.

patients (≥80 years) carried a higher cardiac event rate as compared to younger patients, although the cardiac death rate in those with a normal SPECT MPI study was commensurate with age-matched vital statistics, and (3) SPECT MPI findings significantly impact clinical decision making for early cardiac revascularization in very elderly patients (≥80 years) with suspected CAD. These findings support the clinical use of SPECT MPI in very elderly patients.

Prognostic Value of SPECT MPI in the Very Elderly (≥80 years)

Our study demonstrated that SPECT MPI perfusion data adds incremental prognostic value over clinical and non-perfusion stress data in patients ≥80 years with suspected CAD. Previous studies performed in the very elderly patients using SPECT MPI included patients with and without established CAD.[10-13] Curtis et al, in a cohort of 439 octogenarians, found that a moderate (5%-10% of left ventricle) or large defect (>10% of left ventricle) on vasodilator SPECT MPI was independently associated with increased all-cause mortality as compared to a mild defect (<5% of left ventricle) or a normal perfusion score.[10] In a recent study, Hachamovitch et al[11] examined the role of SPECT MPI in 5200 elderly patients ≥75 years which included 4,318 patients 75-84 years of age and 882 patients ≥85 years

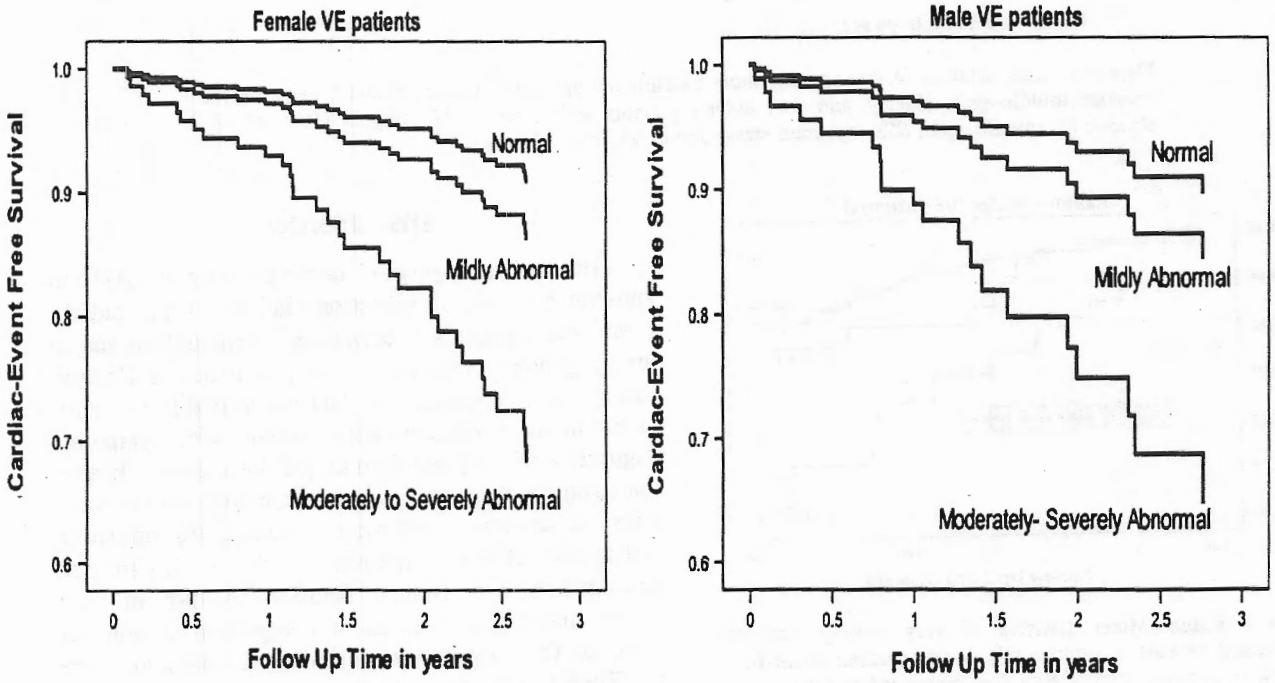

Figure 6. Risk-adjusted survival curves comparing SSS categories as per gender of very elderly patients (≥80 years). $P < .05$ between moderately to severely abnormal SSS and mildly abnormal or normal SSS. *SSS*, summed stress score; *VE*, very elderly.

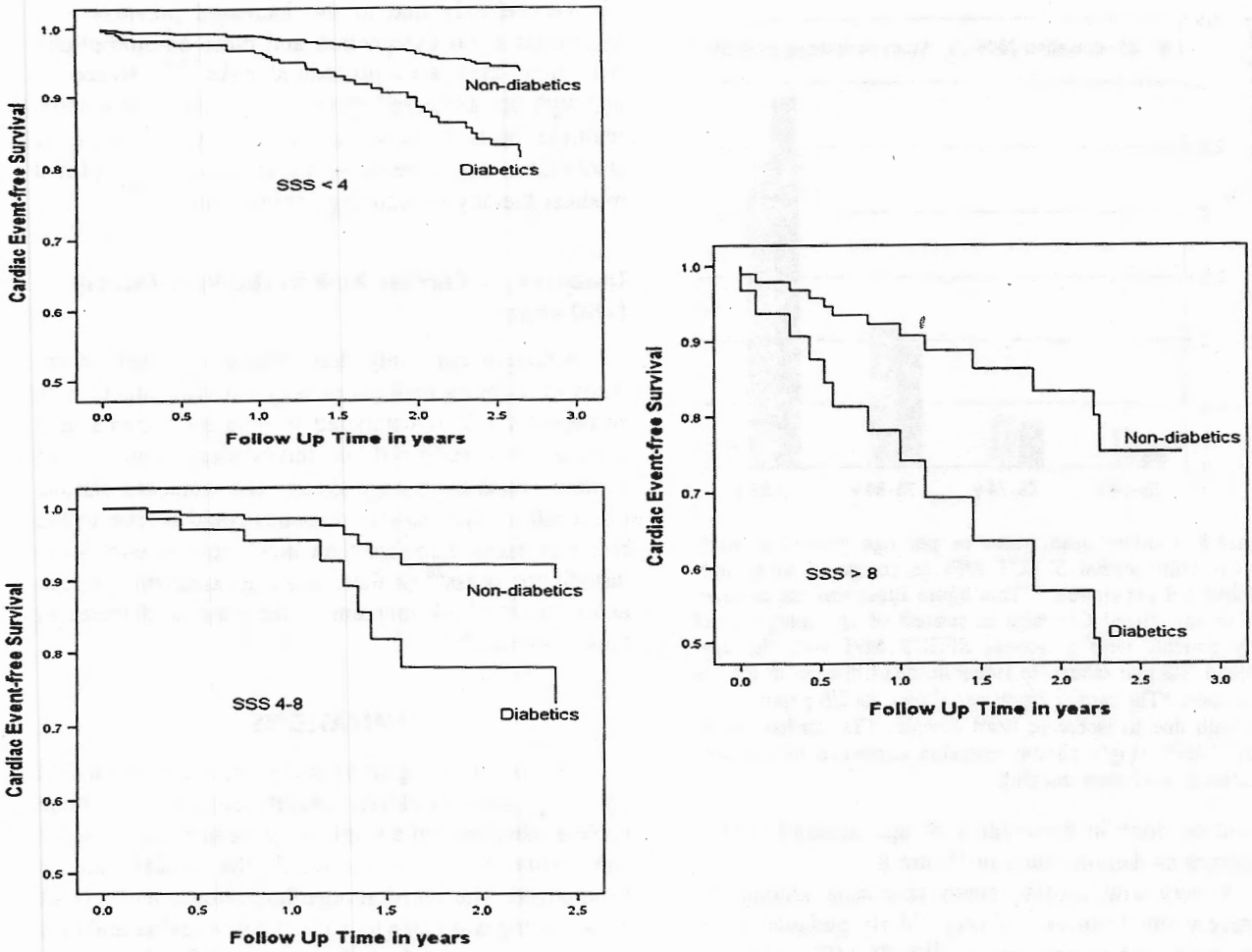

Figure 7. Risk-adjusted survival curves in very elderly patients (≥80 years) show a significantly lower cardiac event-free survival of diabetic as compared to non-diabetic patients ($P < .05$). *VE*, very elderly.

of age with and without CAD. They reported increased cardiac death rates in those patients with worsening perfusion abnormalities, fixed or reversible and demonstrated the incremental value of SPECT MPI in the elderly. Unlike their study, we chose to primarily examine very elderly patients ≥80 years with suspected CAD and normal left ventricular function on the assumption that this group would be especially challenging to clinicians for appropriate diagnostic and post-test management as compared to younger elderly and middle-aged patients. Our study confirms and extends the previous reports on the incremental value of SPECT MPI in the very elderly and provides important insights into cardiac evaluation in these patients. Our data demonstrates the presence of a higher risk group for both cardiac death and non-fatal myocardial infarction in very elderly patients with moderate to severely abnormal perfusion defect on SPECT MPI. Data from all 3 studies support an initial conservative strategy for very elderly patients with either normal or mildly abnormal SPECT MPI, reserving an interventional approach for more severe findings.

Cardiac Death Risk with Normal SPECT MPI

Among our study patients with a normal SPECT MPI, the very elderly had a higher cardiac death rate than that seen with younger patients (1.8% vs 0.3% and 0.6%, respectively, $P < .001$). This was observed in spite of the very elderly having fewer cardiac risk factors compared to younger patients, notably diabetes. The higher cardiac mortality in the very elderly patients with a normal SPECT MPI in our study and that seen with previous studies[10,11] could be accounted for by their advanced age as well as the fact that few of these patients were able to perform exercise stress.[28] This emphasizes that the interpretation of SPECT MPI data in cardiac risk stratification of the very elderly patients

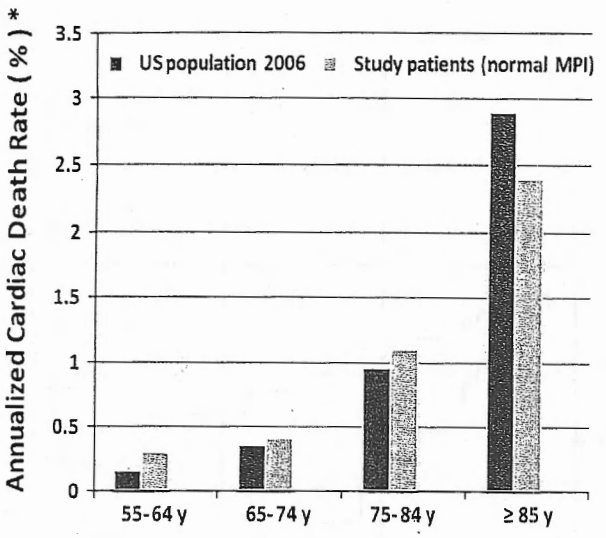

Figure 8. Cardiac death rates as per age groups in study patients with normal SPECT MPI as compared to an age-matched US population.[26] This figure illustrates the comparison of annualized CD rates in subsets of age categories of study patients with a normal SPECT MPI with the age-matched CD rate related to ischemic heart disease in the US population. *The cardiac death rate shown for US population is for death due to ischemic heart disease. *CD*, cardiac death; *SPECT MPI*, single photon emission computed tomography myocardial perfusion imaging.

should be done in the context of age-adjusted cardiac outcomes as demonstrated in Figure 8.

A very low cardiac death rate seen among the relatively small number of very elderly patients in our study who performed exercise SPECT MPI and had a normal perfusion scan demonstrates that perhaps exercise is a significant prognostic indicator even in the very elderly similar to what has been reported in younger patients.[29-31]

Cardiac Revascularization in the Very Elderly (≥80 years)

Even though the referral rate for early (≤60 days) revascularization seen in very elderly patients increased as a function of the severity of ischemia on nuclear scan, this was lower than what was observed in younger patients indicating a conservative approach being adopted by clinicians in the very elderly. Our study results are similar to what has been previously reported by Amanullah et al.[32] In their study of 1,009 octogenarians, the rate of referral for early cardiac revascularization was significantly more with severely abnormal as compared to normal or mildly abnormal SPECT MPI, but the overall referral rate was low (22%) even with severely abnormal scans. The results from both of these studies indicates the fact that perhaps clinicians are reluctant to pursue cardiac interventions in the very elderly due to the increased prevalence of significant renal dysfunction and other co-morbidities, with their associated procedural risks.[33-35] Moreover, although not addressed specifically in the very elderly, multiple trials have shown that revascularization of stable CAD may have no added advantage over optimal medical therapy in reducing cardiac events.[36-38]

Diabetes as Cardiac Risk in the Very Elderly (≥80 years)

Although our study demonstrated a lower prevalence of diabetes mellitus in very elderly patients with suspected CAD as compared to younger patients, this disease state remained an independent predictor of cardiac events in this age group. The increased cardiac event rate in very elderly diabetics could be due to the fact that more diabetics than non-diabetics underwent vasodilator stress[28] or there is an unexplained intrinsic cardiovascular risk inherent to the state of diabetes in these patients.[28,39-41]

LIMITATIONS

This was a retrospective study which was conducted on a large group of elderly patients referred to a cardiac nuclear laboratory of a single large tertiary care hospital and limits the extent to which the results can be generalized. The decision regarding referral and type of stress testing was made by various cardiologists and thus there is a potential for selection and referral bias that affects the results. Concurrent anti-ischemic therapy at the time of stress testing as well as exclusion of patients referred for early revascularization in the outcome analysis could have affected the prognostic impact of SPECT MPI. Since the aim of our study was to evaluate the very elderly patients (≥80 years) with suspected CAD and a normal LV function, we excluded patients with a left ventricular ejection fraction <0.45 from the study.

CONCLUSIONS

Despite the increased cardiovascular risk of very elderly patients relative to younger patients, SPECT MPI has prognostic and incremental value in cardiac risk stratification and may influence clinical decision making in very elderly patients (≥80 years) with suspected CAD.

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Disclosures

None.

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