Characteristics and Outcome of Octogenarian Population Referred for Myocardial Perfusion Imaging: Comparison with Non-Octogenarian Population with Reference to Gender

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Summary

Background: Octogenarian patients referred for stress myocardial perfusion imaging (MPI) differ from younger (non-octogenarian) patients in that they have lower prevalence of risk factors for CAD, but more frequent ischemic events and higher cardiac mortality.

Hypothesis: The purpose of this study was to investigate the efficacy of MPI in octogenarian men and women compared with that in the younger population, and to compare the prognostic value of stress MPI in both populations.

Methods: We studied 162 consecutive patients aged ≥ 80 years who were referred for stress MPI, and compared them with 253 consecutive patients aged < 80 years. Patients completed a questionnaire encompassing information about the existence of coronary risk factors, cardiac symptoms, coronary artery disease (CAD), myocardial infarction, coronary artery bypass graft, percutaneous transluminal coronary angioplasty, and results of stress MPI. The patients were followed up for cardiac mortality for a mean of 45 ± 12 months.

Results: There were 61 women and 101 men (17% of all referrals) with a mean age of 83 ± 3 (range 80–90). Parameters of octogenarian patients demonstrated a significantly lower prevalence of non-insulin-dependent diabetes mellitus

($p < 0.02$), hypercholesterolemia ($p < 0.001$), and smoking ($p = 0.001$) compared with non-octogenarian patients. The prevalence of known CAD was similar, but the prevalence of abnormal resting electrocardiogram, left ventricular (LV) dilatation, and stress-induced ischemia was significantly higher in octogenarians ($p < 0.002$). Cardiac mortality rate per year was 4.3% in octogenarians versus 1.3% in the younger population ($p < 0.0001$). The independent predictors according to MPI of cardiac death were LV dilatation and presence of ischemia in octogenarians, and severity of ischemia in non-octogenarians.

Conclusions: The octogenarian population referred for stress single-photon emission computed tomography differed from the non-octogenarian group in that it had a lower prevalence of risk factors for CAD, but more frequent ischemic events and higher cardiac mortality; however, MPI variables predict adverse outcome in both populations.

Key words: octogenarians, non-octogenarians, coronary artery disease, myocardial perfusion imaging, myocardial ischemia, cardiac mortality

Introduction

Until the last decade, the population aged > 65 years was considered to be elderly. Today, with an increase in life expectancy, the size of the octogenarian population is growing, and cardiovascular diseases become the prominent cause of morbidity and mortality in this population.^{1,2} Consequently, more patients are referred for diagnostic tests, including myocardial perfusion imaging (MPI). It was shown that in elderly men aged ≥ 65 years, exercise testing provided prognostic information in addition to clinical data and that the achieved workload (in METs) was the major exercise-testing variable associated with all-cause mortality.^{3–8} Its prognostic importance was the same in elderly as in younger men. Guidelines for stress testing, risk stratification, and cost effectiveness of MPI, as well as reference to gender, are well validated in most subgroups of the population, but only few data are reported

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regarding referrals of octogenarians.^{9–14} We recently reported on the prognostic value of stress MPI in risk stratification of octogenarian patients;¹⁵ however, data comparing this specific population with younger patients is insufficient. We hypothesized that octogenarian patients may have different clinical features and predictors of cardiac death from those in younger patients.

The purpose of this study was to compare the characteristics of the octogenarian population with regard to coronary artery disease (CAD) risk factors and CAD variables at rest and during stress MPI, as well as cardiac mortality and its predictors, with those of the rest of the population.

Methods

During 2000 we prospectively studied 162 consecutive patients (101 men, 61 women) aged ≥ 80 years, referred for stress single-photon emission computed tomography (SPECT) MPI, and compared them with 253 consecutive patients aged < 80 years. All patients completed a questionnaire encompassing information on gender, reason for test, existence of coronary risk factors, cardiac symptoms, CAD, myocardial infarction (MI), coronary artery bypass graft (CABG), percutaneous coronary intervention (PCI), and results of stress MPI. Data for the two groups were compared.

Follow-Up

A clinician blinded to the scan results obtained follow-up data. Patients or family members were contacted by phone, and the outpatient clinic physician or hospital records confirmed the information. Causes of death were categorized as cardiac or noncardiac, and only cardiac deaths were included in the analysis. The average follow-up was 45 ± 12 months.

Stress Myocardial Perfusion Imaging

Each patient was studied under fasting conditions; antianginal medications were discontinued for 24 h, and beta-blocker agents for 48 h. An intravenous line was inserted and each patient underwent stress testing either by exercise on a treadmill (Bruce protocol) or dipyridamole protocol. Heart rate, blood pressure, and electrocardiographic (ECG) tracings were recorded prior to and at each stage of exercise, at peak of symptoms, or at maximal predicted heart rate. Thallium-201 (3–4 mCi) was injected and exercise was continued for 30–60 s. In the case of dipyridamole protocol, thallium was injected 4 min after dipyridamole infusion. Imaging by SPECT was performed about 10 min after thallium injection and 3–4 h later at rest. Additional thallium reinjection imaging was performed in patients with fixed defects.

Imaging by SPECT was performed with a large-field digital gamma camera (SP-6, Elscint Ltd., Haifa, Israel), over 180° , starting at the 45° right anterior oblique and positioning at 6° intervals for 30 s per image. Redistribution images were repeated 3 to 4 h after exercise using the same parameters.

After the images were reconstructed, two-dimensional polar plot maps were generated for assessment of the extent of perfusion abnormality in each of the three coronary artery territories, and the total extent of myocardial ischemia was expressed as a percentage of global perfusion of the left ventricle. Perfusion defects were analyzed visually and semiquantitatively. Filling defects were diagnosed as ischemia when the two contiguous slices showed reversibility or when bull's-eye mapping showed a decrease in the intensity of perfusion defects of more than 10% in the redistribution phase.^{16,17}

Statistical Analysis

Results are given as means $\pm$ standard deviation. To compare mean continuous parameters between groups, the Student's *t*-test or Duncan multiple comparison option was used. To analyze statistically significant relationships in the distribution of categorical variables, the chi-square test or Fisher's exact test were used, as appropriate.

Pearson correlation coefficient (*r*) and its significance (*p*) were calculated between variables. Probability values ≤ 0.05 were considered statistically significant.

To predict cardiac death, a series of multivariate stepwise logistic regression models was fitted to the data. Odds ratio (OR) and 95% confidence interval (CI) were calculated from the model.

Results

Mean age of the octogenarians (61 women, 101 men) was 83 ± 3 (range 80–90) and that of the non-octogenarian group (103 women, 150 men) was 65 ± 10 (range 48–79). Table I demonstrates the clinical parameters and CAD risk factors in both groups. There was a significantly lower prevalence of non-insulin-dependent diabetes mellitus (NIDDM) ($p < 0.02$) (IDDM was not found in the octogenarian population), hypercholesterolemia ($p < 0.001$), and smoking ($p = 0.001$) in octogenarians than in non-octogenarians. Table II summarizes the CAD characteristics of the two groups, showing a higher prevalence of typical angina in the octogenarians than in the non-octogenarians (32 vs. 21%, $p < 0.01$), but similar prevalence of

TABLE I Comparison of CAD risk factors in octogenarian and non-octogenarian patients

	Age > 80 , n = 162		Age < 80 , n = 253		p Value
Female	61	37%	103	41%	NS
Male	101	63%	150	59%	NS
Hypertension	66	41%	113	45%	NS
DM	19	12%	54	21%	0.02
High cholesterol	44	27%	125	49%	< 0.001
Smoking	12	7%	49	19%	< 0.001

Abbreviations: CAD = coronary artery disease, DM = diabetes mellitus, NS = not significant.

TABLE II Comparison of CAD characteristics in octogenarian and non-octogenarian patients

	Age > 80, n = 162		Age < 80, n = 253		p Value
AP	52	32%	53	21%	0.01
MI	53	33%	70	28%	NS
CAD	73	45%	108	43%	NS
CABG	40	25%	46	18%	NS
PTCA	17	11%	46	18%	0.04

Abbreviations: AP = angina pectoris, MI = myocardial infarction, CABG = coronary artery bypass graft, PTCA = percutaneous transluminal coronary angioplasty. Other abbreviations as in Table I.

MI, known CAD, and CABG; however, more non-octogenarians underwent PCI (18 vs. 11%, $p < 0.04$). Dipyridamole stress testing was performed in 115 (71%) octogenarian patients, whereas only 100 (39.5%) of the younger group needed the dipyridamole test ($p < 0.001$). Treadmill test was used in 47 (29%) of the octogenarian patients. Stress SPECT results of the octogenarian population (Table III) showed more abnormal resting ECGs ($p < 0.001$), as well as left ventricular (LV) dilatation, either fixed or transient. Myocardial ischemia by SPECT was demonstrated in 45 versus 31%, respectively: mild ischemia was similar in both groups but the prevalence of moderate to severe ischemia was significantly higher in the octogenarians (21 vs. 11%, $p < 0.05$).

Comparison between octogenarian and younger women showed a similar prevalence of all clinical, CAD risk factor, and MPI variables, except that hypercholesterolemia was higher in the younger women (38 vs. 58%, $p < 0.01$).

Comparison of men in the two groups showed lower prevalence of the following risk factors in the octogenarians: DM (14 vs. 23%, $p < 0.05$), smoking (8 vs. 25%, $p < 0.001$), and hypercholesterolemia (21 vs. 43%). Among the clinical characteristics, the prevalence of angina and CABG were higher in the octogenarian men ($p < 0.06$). Among the MPI variables, abnormal resting ECG, LV dilatation, prevalence of and moderate to severe ischemia were significantly higher in the octogenarian men ($p < 0.001$).

TABLE III Stress SPECT results in octogenarian and non-octogenarian patients

	Age > 80, n = 162		Age < 80, n = 253		p Value
Abn rest ECG	100	62%	114	45%	0.001
Increased LU	34	21%	46	18%	NS
LV dilatation	54	34%	60	24%	0.03
Ischemia (TI)	72	45%	81	32%	0.01
Mild ischemia	34	21%	51	20%	NS
Mod-sev ischemia	38	21%	28	11%	0.05

Abbreviations: SPECT = single-photon emission computed tomography, ECG = electrocardiogram, LU = lung uptake, LV = left ventricular, TI = transient ischemic, Mod = moderate, Sev = severe.

Cardiac mortality occurred in 26 octogenarians (16 %) versus 12 (4.7%) in the younger population ($p < 0.0001$) during follow-up of 45 ± 12 months. Mean event rate was 4.3% per year in the octogenarians versus 1.3% in the younger group. There were five (8.2%) cardiac deaths in octogenarian women compared with 2 (0.2%) in non-octogenarian women ($p = NS$), and 21 (21%) in octogenarian men compared with 10 (0.6%) in non-octogenarian men ($p < 0.0001$).

On univariate analysis including all the variables presented in Tables I–III, the predictors for cardiac death in octogenarians were LV dilatation (fixed or transient) and presence of ischemia by scan; in non-octogenarians, predictors were previous MI, LV dilatation by scan, abnormal scan, and high degree of ischemia (Table IV).

The independent predictors of cardiac death in octogenarians were LV dilatation (OR = 6.9, 95% CI 2.7–17.4, $p < 0.0001$) and presence of ischemia (OR = 2.75, 95% CI 1.09–6.96, $p < 0.03$); in non-octogenarians, the only independent predictor of death was severity of ischemia (OR 9.39, CI 2.79–31.5, $p < 0.0001$).

Discussion

Our results showed that although the octogenarian population referred for MPI has a lower prevalence of CAD risk factors, this group has more incidences of stress-induced ischemia of marked severity. Furthermore, cardiac mortality rate was higher in the octogenarian population and was predicted by MPI variables.

Previous published literature on this issue addressed the elderly aged ≥ 65 years and selected only those who were able to exercise. The patients in those studies were risk stratified according to exercise Duke score^{9–11} and its relationship with MPI results.^{5, 6, 11–14} Several studies have examined the prognostic value of exercise testing in the elderly compared with a younger population and have shown that the achieved workload was the major exercise-testing variable

TABLE IV Univariate predictors of cardiac mortality

Predictors	r	p Value
Octogenarian population		
Known CAD	0.15	0.055
Lung uptake	0.25	0.0016
LV dilatation	0.42	<0.0001
Abnormal scan	0.34	<0.001
Presence of ischemia	0.29	0.0002
Extent of ischemia	0.24	0.0028
Non-octogenarian population		
Previous MI	0.152	0.01
LV dilatation	0.18	0.004
Abnormal scan	0.20	0.001
High-degree ischemia	0.28	<0.0001

Abbreviations as in Tables I, II, and III.

associated with all-cause mortality, and that its prognostic importance was the same in elderly and younger men. Steingart *et al.*¹² found that in elderly patients, male gender, age, extent of ischemia, and exercise tolerance were all independent predictors of subsequent death or nonfatal MI and concluded that treadmill exercise remains a valuable tool. Recently, Valeti *et al.*¹⁸ examined patients aged ≥ 75 years who were able to perform exercise according to the Bruce protocol and showed that exercise SPECT provides effective risk stratification in these patients.

Our study is different from previous ones as it included older patients unselected for referral for MPI. It seems that in "real life" the majority of octogenarian patients are unable to perform interpretable exercise testing and need to be stratified by pharmacologic stress test combined with MPI. As shown in our study, the majority of the octogenarian population differ from the younger population, not only in their inability to exercise, but also by having a more frequent incidence of abnormal resting ECGs and of stress-induced ischemia of greater severity. Moreover, we have shown in a previous study¹⁵ that LV dilatation and myocardial ischemia detected by stress MPI were the only independent predictors for cardiac death or nonfatal MI in the octogenarian population after a mean of 45 months of follow-up. This differs from the younger population in whom the severity of ischemia by MPI was the independent predictor of cardiac death.

It is noteworthy that the differences between the two groups are related to male gender, in contrast to the similarity between octogenarian and non-octogenarian women.

Limitations

Our study was limited by the relatively small numbers of the studied populations, especially the number of women in both groups. Left ventricular function and volumes were not included, as gating ECG was not performed routinely in these patients. Not reporting on comorbid diseases of the octogenarian patients may increase the sample rate of dipyridamole tests and, hence, the outcome in these patients.¹⁹ Other major adverse events such as MI were not included, nor was the number of patients who underwent revascularization. However, the data succeeded in showing the difference between the very elderly and the younger populations.

Conclusions

Octogenarian populations referred for stress SPECT differ from the non-octogenarian patients in that they have a lower prevalence of risk factors for CAD but more ischemic events

and higher cardiac mortality. As MPI variables are the best predictors for cardiac mortality, it seems that the octogenarian population, with and without known CAD, may benefit from risk stratification by pharmacologic stress testing, as the majority are unable to exercise.

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