

# Prognostic Value of the Duke Treadmill Score in the Elderly

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<b>OBJECTIVES</b>	The purpose of this study was to test the hypothesis that the Duke treadmill score works less well for risk stratification in patients age 75 years or above.
<b>BACKGROUND</b>	Although the Duke treadmill score is generally effective for risk stratification, its prognostic value in the elderly may be limited because they have a higher prevalence of coronary artery disease (CAD), more severe CAD and a lower exercise tolerance.
<b>METHODS</b>	The study population consisted of 247 patients age 75 years or above, and the control population consisted of 2,304 patients below 75 years of age. All patients were symptomatic, had undergone exercise thallium testing between 1989 and 1991 and were followed for a median of >6.5 years. The Cox regression model was used to test the association of the Duke score (utilized both as a continuous variable and using previously published risk group cutoffs) with outcomes (cardiac death, nonfatal myocardial infarction [MI], late revascularization).
<b>RESULTS</b>	Using the Duke score to risk-stratify the elderly, 26% were in the low risk group, 68% were in the intermediate risk group and 6% were in the high risk groups; seven-year cardiac survival was 86%, 85% and 69%, respectively ( $p = 0.45$ ). There was also no significant association between these Duke score risk groups and all other outcome end points in the elderly. The Duke score as a continuous variable did not predict cardiac death ( $p = 0.43$ ) or cardiac death or MI ( $p = 0.42$ ), but did predict total cardiac events (which included late revascularization) ( $p = 0.0027$ ). For the control population, more patients (55%) were in the low risk group, and the Duke score (as a continuous variable or in risk groups) was highly predictive of all end points ( $p = 0.0001$ ).
<b>CONCLUSIONS</b>	The Duke score predicted cardiac survival in younger patients but not in patients age 75 years or above. The majority of the elderly were classified as intermediate risk by the Duke score. Only a minority of the elderly were classified as low risk, but this group still had an annual cardiac mortality of 2%/year. (J Am Coll Cardiol 2002;39:1475-81) © 2002 by the American College of Cardiology Foundation

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Aging of the population is evident at the turn of the millennium; there are more elderly patients undergoing exercise testing for the diagnosis of coronary artery disease (CAD) and risk stratification. The diagnostic and prognostic value of exercise testing has been studied extensively (1-12). The Duke treadmill score has been recommended by the American College of Cardiology/American Heart Association (ACC/AHA) exercise testing guideline for risk stratification (13). However, the score was derived from patients with a median age of 49 years, and only a small number of elderly patients were included (1). Elderly patients have a higher prevalence of CAD and severe CAD, as well as a lower exercise tolerance than younger patients; it may not be accurate to interpret exercise test results of the elderly in the same manner as that of the younger population. The aim of this study was to test the hypothesis that the Duke treadmill score works less well for risk stratifica-

tion in patients age 75 years or above in comparison with patients below the age of 75 years.

## METHODS

**Patient populations.** Patients were identified retrospectively from the Mayo Clinic Nuclear Cardiology Laboratory database. Patients were eligible for the study if they: 1) were age 75 years or above at the time of exercise thallium testing between January 1, 1989 and December 31, 1991; 2) performed a treadmill test according to the Bruce or Naughton protocol; 3) were symptomatic with chest pain but had no valvular, congenital or cardiomyopathic disease or previous cardiac surgery or coronary angioplasty. A total of 334 patients met the inclusion criteria. Patients were excluded for the following reasons: 1) myocardial infarction (MI) within three months preceding the exercise test (10 patients); 2) digoxin therapy (51 patients); 3) presence of complete left bundle branch block or pre-excitation syndrome on resting electrocardiogram (ECG) (5 patients); 4) presence of a permanent pacemaker (1 patient); or 5) technically unsatisfactory studies or missing exercise data (20 patients). Consequently, 247 patients made up the study population. The control population consisted of 2,304

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#### Abbreviations and Acronyms

ACC/AHA	= American College of Cardiology/ American Heart Association
CAD	= coronary artery disease
CABG	= coronary artery bypass grafting
ECG	= electrocardiogram/electrocardiographic
MI	= myocardial infarction
PTCA	= percutaneous transluminal coronary angioplasty

patients below the age of 75 years who otherwise met the same inclusion and exclusion criteria. The clinical characteristics of the study and the control populations were recorded prospectively at the time of testing.

**Exercise testing.** Resting heart rate, blood pressure and 12-lead ECG were recorded before exercise. Treadmill exercise testing was performed in all subjects to the end points of severe fatigue, moderate (limiting) angina, serious arrhythmia or  $\geq 2$  mm ST-segment depression. During exercise, three ECG leads were continuously monitored. A 12-lead ECG was recorded every minute at peak exercise and every 3 min and 6 min of recovery. ST-segment deviation (depression or elevation) was interpreted visually by the physician or nurse supervising the exercise test. Maximum ST depression (in mm) was defined as the greatest exercise-induced ST depression 80 ms after the J point, which was horizontal or downsloping in leads with or without baseline ST depression; it was calculated by subtracting the maximum ST-segment depression during exercise or postexercise from the resting ST-segment level in the corresponding lead. Maximum ST segment depression was categorized into the following groups:  $< 1.0$  mm, 1.0 mm, 1.5 mm, 2.0 mm or  $\geq 2.5$  mm. ST-segment elevation of  $\geq 1$  mm (in ECG leads without pathologic Q-waves, and without ST depression of  $\geq 1$  mm in any leads) was regarded as 1 mm ST-segment deviation. Exercise time (in min) was defined as the duration of exercise for patients performing the Bruce protocol; for those performing the Naughton protocol, a conversion factor was applied to equate the exercise duration with the Bruce protocol (14). Treadmill angina index was coded as 0 if no angina, 1 if typical angina occurred during exercise and 2 if angina was the reason to stop exercise (1). The Duke treadmill score (1,2) was calculated as: exercise time - (5  $\times$  maximum ST deviation) - (4  $\times$  angina index).

**Follow-up.** Mailed questionnaires, telephone interviews and reviews of patients' medical records or physician contacts were used to acquire information regarding subsequent events. Events of interest were cardiac death, nonfatal MI and revascularization by percutaneous transluminal coronary angioplasty (PTCA) or coronary artery bypass grafting (CABG). Death was confirmed by reviewing the hospital chart, a death certificate or a clinician's report. The cause of death of each patient was coded as cardiac or noncardiac by a reviewer blinded to the baseline information and the

exercise results. Myocardial infarction was defined on the basis of chest pain, ECG changes and elevated serum creatine kinase isoenzyme levels. Revascularization procedures were defined as early ( $< 3$  months of exercise test) or late ( $\geq 3$  months after exercise test). Early revascularization was not counted as an end point, but was used to censor follow-up. Median duration of follow-up was 6.4 years (95% complete) for the study population and 7.1 years (94% complete) for the control population.

**Statistical analysis.** Clinical and exercise variables of the study population and the control population were compared using the chi-square test for categorical variables and the Wilcoxon rank-sum test for continuous variables.

Patients were stratified into risk groups by the treadmill score according to the Duke classification (2). Patients with a treadmill score of  $\geq 5$  were classified as low risk, those with a score of  $< 5$  to  $-10$  were designated as intermediate risk and those with a treadmill score of  $< -10$  were classified as high risk. The Kaplan-Meier method was used to generate survival curves for four end points: 1) cardiac survival (censoring of patients with noncardiac death or PTCA/CABG at any time after the exercise test); 2) survival free of cardiac death and nonfatal MI (censoring of patients with noncardiac death or PTCA/CABG at any time after the exercise test); 3) survival free of cardiac death, nonfatal MI and late PTCA/CABG (censoring of patients with noncardiac death or early PTCA/CABG). The relationships of the Duke treadmill score as a continuous variable to the three end points were evaluated using the Cox proportional hazards model for both the study and the control populations. Differences among risk groups and comparisons within the same risk group between the study and the control populations for the three end points were investigated with the log-rank test. Statistical significance was defined as  $p < 0.05$ .

## RESULTS

**Baseline characteristics and exercise test results.** The clinical and exercise test results of the study and the control populations are shown in Table 1. The elderly had a higher prevalence of hypertension, previous MI and typical angina. A higher proportion of the elderly was tested using the Naughton treadmill protocol rather than the Bruce protocol. As expected, the elderly had a shorter exercise duration, a lower exercise heart rate and rate-pressure product and a lower Duke treadmill score. As a result, only 26% of the elderly were classified as low risk, compared with 55% of the younger population ( $p < 0.0001$ ) (Tables 2 and 3). A much greater percentage of the elderly patients were classified as intermediate risk (68%, compared with 43% of the control population;  $p < 0.0001$ ) and high risk (6% vs. 2%,  $p = 0.0031$ ).

**The relationship of the Duke score to subsequent events.** During follow-up in the study population, there were 33 cardiac deaths, 17 nonfatal MIs and 40 late PTCA/CABG

**Table 1.** Clinical Characteristics and Exercise Parameters of the Study and the Control Populations

	Study Population (n = 247)	Control Population (n = 2,304)	p Value
Age (yrs)	77 (76,78)	60 (52,67)	< 0.0001
Gender			
Male	139 (56%)	1,341 (58%)	NS
Female	108 (44%)	963 (42%)	
Risk factors			
Current cigarette smoking	7 (3%)	293 (13%)	< 0.0001
Diabetes			
On insulin	11 (4%)	78 (3%)	NS
Not on insulin	18 (7%)	155 (7%)	
Hypertension	132 (53%)	1,021 (44%)	0.006
Hypercholesterolemia	94 (38%)	1,117 (48%)	0.002
Previous MI	42 (17%)	260 (11%)	0.008
ECG anterior Q-wave	13 (5%)	63 (3%)	0.026
Chest pain			
Typical angina	125 (51%)	746 (32%)	] <0.0001
Atypical angina	119 (48%)	1,444 (63%)	
Noncardiac pain	3 (1%)	114 (5%)	
Antianginal medications			
Beta-blockers	71 (29%)	544 (24%)	NS
Long-acting nitrates	76 (31%)	370 (16%)	< 0.0001
Calcium channel blockers	109 (44%)	743 (32%)	0.0002
Resting ST-T ECG abnormalities	96 (39%)	737 (32%)	0.028
Exercise protocol			
Bruce	199 (81%)	2,226 (97%)	] < 0.0001
Naughton	48 (19%)	78 (3%)	
Peak heart rate (beats/min)	120 (108, 136)	142 (125, 158)	< 0.0001
Peak blood pressure (mm Hg)	172 (154, 190)	180 (160, 196)	< 0.0001
Peak rate-pressure product	20,700 (16,650, 24,480)	25,500 (21,090, 29,410)	< 0.0001
Exercise duration (min)	5.1 (3.7, 6.8)	7.8 (6.0, 9.5)	< 0.0001
Exercise angina	75 (30%)	559 (24%)	NS
Angina index = 1	46 (18%)	361 (16%)	
Angina index = 2	29 (12%)	198 (9%)	
Magnitude of ST deviation (mm)	0 (0, 1.0)	0 (0, 1.0)	NS
Duke treadmill score	2.3 (-3.2, 5.0)	5.5 (0.5, 8.4)	< 0.0001

Data other than numbers of patients are presented as median value with 25th, 75th percentile in parentheses.  
 ECG = electrocardiogram; MI = myocardial infarction.

(25 CABG and 15 PTCA). For the control population, there were 60 cardiac deaths, 121 nonfatal MIs and 337 late PTCA/CABG (180 CABG and 157 PTCA). The events in each population by risk group are shown in Tables 2 and 3.

For the elderly, the seven-year cardiac survival in the low risk, intermediate risk and high risk groups was 86%, 85% and 69%, respectively (p = 0.45) (Fig. 1A). Although there was a trend toward different event rates among risk groups for the other end points (nonfatal MI or late revascularization), none of these was statistically significant (Figs. 1B and

1C). When the Duke score as a continuous variable (with-out regard to risk groups) was tested for its association with the three end points in the elderly population, it was significantly associated with the combined end points of cardiac death, nonfatal MI or late PTCA/CABG (p = 0.0027), but not with cardiac death (p = 0.43) or cardiac death or nonfatal MI (p = 0.42).

The results in the control population were strikingly different. The low risk and intermediate risk groups of the control population had significantly better outcomes than

**Table 2.** Events by Risk Group in the Study Population During Follow-Up

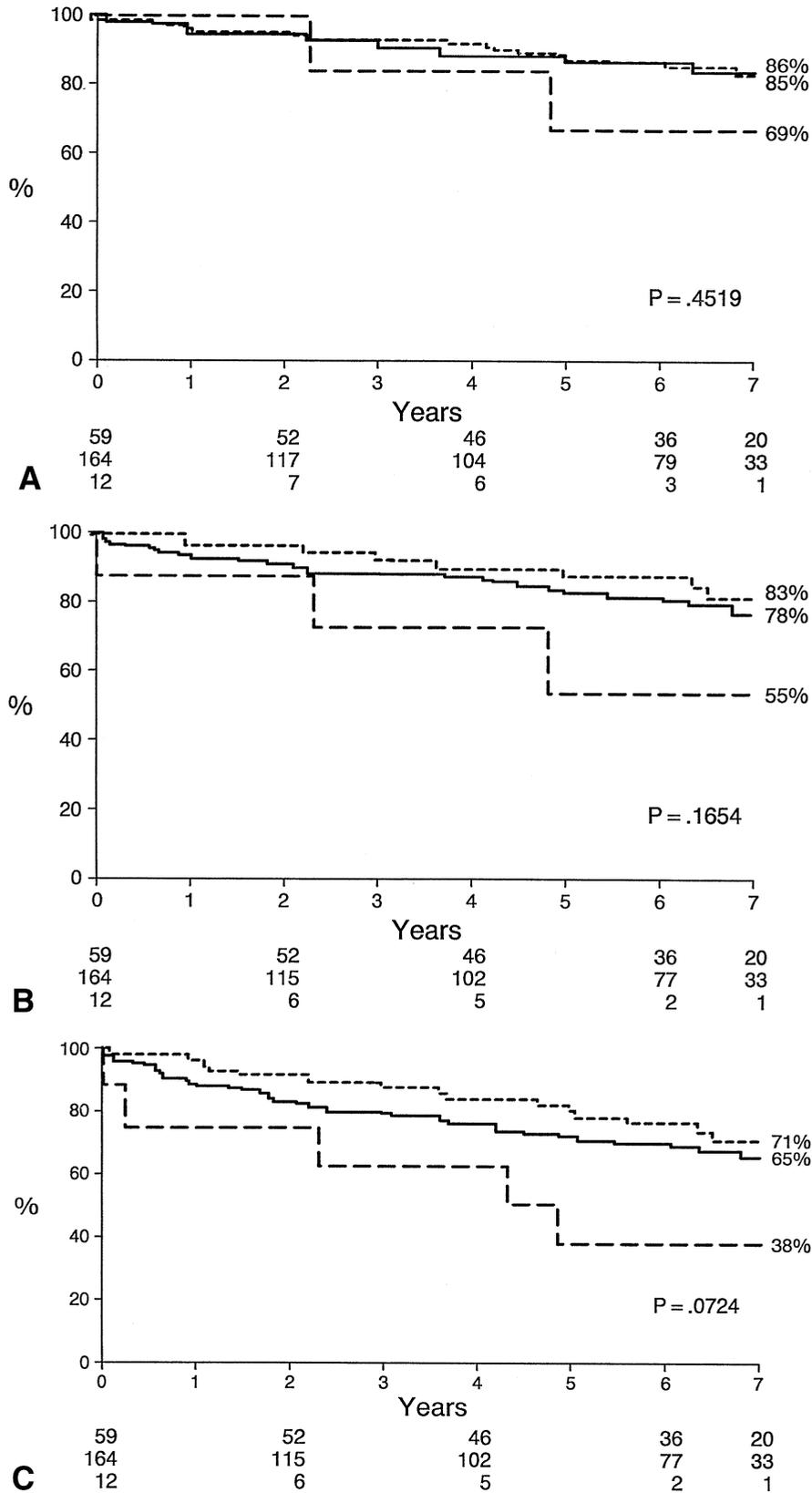
Risk Group	Patient No.	Cardiac Death	MI	Late Revas	Early Revas
Low	65 (26%)	8	3	7	1
Intermediate	168 (68%)	23	13	31	20
High	14 (6%)	2	1	2	4
Total	247	33	17	40	25

MI = myocardial infarction; Revas = revascularization.

**Table 3.** Events by Risk Group in the Control Population During Follow-Up

Risk Group	Patient No.	Cardiac Death	MI	Late Revas	Early Revas
Low	1259 (55%)	15	52	129	26
Intermediate	989 (43%)	42	66	191	116
High	56 (2%)	3	3	17	25
Total	2,304	60	121	337	167

Abbreviations as in Table 2.



**Figure 1.** Kaplan-Meier survival curves of the elderly population based on risk groups classified by the Duke treadmill score. **(A)** Cardiac survival; **(B)** Survival free of cardiac death or nonfatal myocardial infarction (MI); **(C)** Survival free of cardiac death or nonfatal MI or late revascularization. Numbers below abscissa = numbers of patients available for analysis at each time point (see text for details). The number of high risk patients is small, which makes the estimates for this subgroup less reliable. **Short-dashed lines** = low risk; **solid lines** = intermediate risk; **long-dashed lines** = high risk.

**Table 4.** Survival Rates by Risk Group in Study and Control Populations

Risk Group	No of Patients (%)	7 Yr Cardiac Survival	7 Yr Survival Free of CD/MI	7 Yr Survival Free of CD/MI/Revas
Low (s)	65 (26%)	86%	83%	71%
Low (c)	1,259 (55%)	99%	95%	87%
p Value	< 0.0001	< 0.0001	< 0.0001	0.0001
Intermediate (s)	168 (68%)	85%	78%	65%
Intermediate (c)	989 (43%)	96%	91%	75%
p Value	< 0.0001	< 0.0001	0.0001	0.0148
High (s)	14 (6%)	69%	55%	38%
High (c)	56 (2%)	89%	85%	48%
p Value	0.0031	0.2331	0.0687	0.5902
Total (s)	247	84%	78%	66%
Total (c)	2,304	98%	93%	81%
p Value		< 0.0001	< 0.0001	< 0.0001

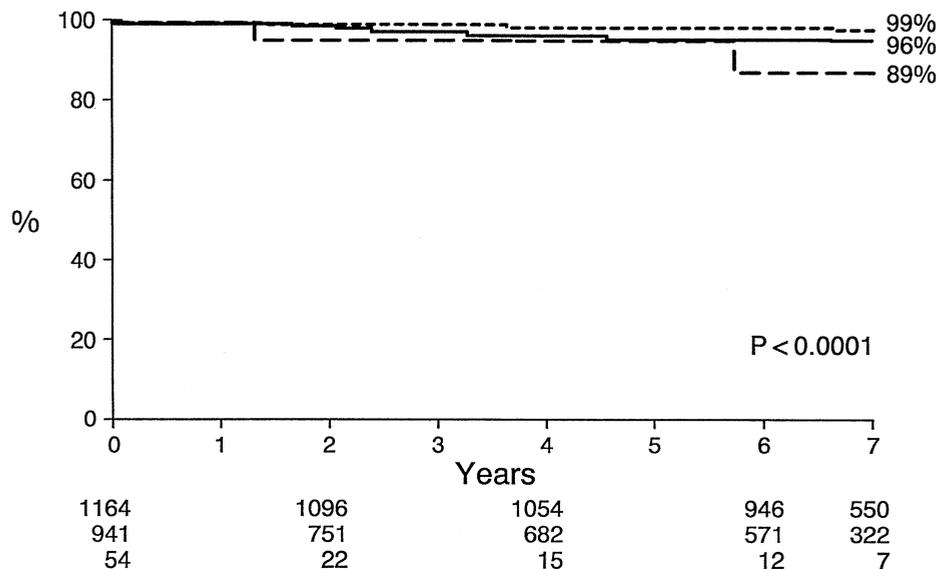
c = control population; CD = cardiac death; p value = comparison between study and control subgroups; s = study population. Other abbreviations are the same as that of Table 3.

the elderly population for all three end points (Table 4). Although the high risk group of the elderly had higher event rates for all three end points than the control population, this group was small (n = 14) and the differences were not statistically significant. The seven-year cardiac survival in the low risk, intermediate risk and high risk groups of the control population was 99%, 96% and 89%, respectively (p = 0.0001) (Fig. 2). The risk groups defined by the treadmill score also predicted the outcomes of cardiac death or nonfatal MI (p < 0.0001); and cardiac death, nonfatal MI or late PTCA/CABG (p < 0.0001). The Duke score as a continuous variable was strongly (p < 0.0001) associated with outcome for all three end points in the control population.

**DISCUSSION**

The clinical value of any noninvasive prognostic test is primarily to risk-stratify the population by identifying low risk patients who can be safely treated medically and high risk patients who generally require angiography to determine if they will benefit from revascularization. Ideally, there should be a limited number of patients who fall between the two groups and, therefore, constitute the intermediate risk subgroup, as the clinical management of these patients is less clear.

These results demonstrate that the Duke treadmill score performs less well for risk stratification in patients age 75 years or above. There was no statistically significant differ-



**Figure 2.** Kaplan-Meier curve for cardiac survival of the control population based on risk groups classified by the Duke treadmill score. Numbers below abscissa = numbers of patients available for analysis at each time point (see text for details). **Short-dashed lines** = low risk; **solid lines** = intermediate risk; **long-dashed lines** = high risk.

ence in outcomes among the risk groups defined by the Duke score, and there was no association between the score (as a continuous variable) and either cardiac death (33 events) or cardiac death or MI (50 events). Only a minority (25%) of elderly patients were classified as low risk; these patients still had substantial cardiac event rates with an annual cardiac mortality of 2%/year, which was higher than that of the low risk group of the control population in this study (0.14%) ( $p < 0.0001$ ), or the low risk group reported by Mark et al. (2) (0.25% annual mortality). Almost two-thirds of the elderly patients were classified as intermediate risk, the category that provides the least guidance for clinical management.

**Exercise testing in the elderly.** The elderly are a distinct group of patients with respect to exercise testing. Patients age 75 years or above generally achieve a lower exercise workload than younger patients. Exercise capacity in the elderly may decline because of deconditioning, muscle weakness, orthopedic problems, neurologic problems or peripheral vascular disease. Many are not able to exercise long enough (5 min on a Bruce protocol) to achieve a low-risk Duke score. On the other hand, the exercise workload that they do achieve may be inadequate to induce ischemia; thus, exercise-induced ST depression or angina may not be evident despite the presence of prognostically important CAD, which is more prevalent in the elderly. ST depression and angina are both required for a high risk classification by the Duke score. As a result, the majority of the elderly are in the intermediate risk group by the Duke classification.

**Comparison to younger patients.** As expected, the elderly had higher overall event rates than the control population for all three end points. Thus, although the study population was modest in size compared with the control population, there were sufficient events to provide adequate statistical power, except in the very small high risk subgroup. Elderly patients had a more adverse prognosis even if classified into the same risk group by the Duke score (Table 4). For example, the overall seven-year cardiac survival was only 84% in the elderly, compared with 98% in the controls ( $p < 0.0001$ ). The higher prevalence of both CAD and severe CAD in the elderly is one reason why a favorable Duke score does not imply a good prognosis. Although the cardiac mortality of the high-risk group of the elderly (4.4%/year) was higher than that of the control population (1.6%), the difference was not statistically significant ( $p = 0.23$ ), likely because of the small numbers of patients classified into the high risk groups.

When the Duke score was applied to risk-stratify the elderly, although there was a trend toward different cardiac event rates among the risk groups, it was not statistically significant for any of the three end points. The Duke score as a continuous variable only predicted the endpoint of total cardiac events, but not other end points; therefore, it is unlikely that other cutoffs for risk groupings would help stratify the elderly more effectively. In addition, using the

Cox regression model, we found that the individual components of the Duke score (exercise duration, magnitude of ST depression and exercise angina) were not univariately associated with cardiac death in the elderly. Thus, even if the weights of the variables were adjusted, the treadmill score would not predict cardiac death in the elderly. Because previous studies have shown that the magnitude of ST-segment depression, exercise duration and exercise angina are the most important predictors of prognosis in exercise testing (1,2,4,8,12), other exercise parameters are unlikely to predict cardiac outcome in the elderly. Because exercise capacity in the elderly can be limited by their general physical condition instead of their cardiac function, exercise variables that are prognostically useful in younger patients may not predict cardiac outcomes in the elderly.

**Comparison to previous studies.** The Duke treadmill score was derived from a retrospective cohort of inpatients and then validated prospectively in an outpatient cohort (1,2). The score incorporates all the independent prognostic information available from the treadmill test in a simple quantitative equation, and adds independent prognostic information to clinical and cardiac catheterization data. Although the Duke score has been well validated to predict cardiac mortality in younger patients and, therefore, has been recommended by the ACC/AHA guidelines for exercise testing for risk assessment (13), the impact of age on the utility of the score has not been studied.

There are no large-scale studies examining the utility of treadmill exercise testing in the elderly, especially for prognosis. The limited available data are based on patients over the age of 65 years using a variety of stress modalities. Glover et al. (15) demonstrated that  $\geq 1$  mm ST-segment depression was associated with an increased risk of cardiac death in 104 patients over 65 years of age (mean age 68 years) who underwent treadmill testing, bicycle ergometer testing or supervised walk. Gaul et al. (16) reported that using  $\geq 2$  mm ST-segment depression as a diagnostic criterion, ergometer exercise testing had equivalent value for the diagnosis of CAD in patients over the age of 65 years compared with younger patients. Martinez-Caro et al. (17) demonstrated exercise-induced ST depression, exercise heart rate, blood pressure response and functional capacity could aid the diagnosis of CAD in patients age 65 years or more undergoing an ergometer stress test. Samek et al. (18) showed that the magnitude of exercise-induced ST depression was associated with three-vessel CAD. These findings were based primarily on the "young old" (age 65 to 75 years); however, our study sought to test the prognostic value of the Duke score in the "old old" (over age 75 years) for whom there are no data supporting the prognostic value of exercise testing.

**Study limitations.** There are two inherent limitations in this study. First, our study population was referred for treadmill thallium imaging and not standard treadmill testing. Many factors affect this referral process. It is possible that exercise capacity of patients referred for dif-

ferent stress modalities could be different. Second, there were only a small number of patients in the elderly high risk subgroup, limiting the ability of this study to demonstrate significant differences between the high risk subgroups or to accurately determine outcome in this subset of the elderly. However, there were a sufficient number of events in both the low risk and intermediate risk subgroups. Third, 19% of our elderly patients were not able to exercise on the Bruce protocol, reflecting the limited exercise capacity of the elderly. Despite these limitations, this study demonstrates that the Duke score predicts outcomes in patients younger than 75 years, but has limited prognostic power in patients age 75 years or above. Therefore, it would appear to have little role in the management of elderly patients.

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