In Comparison to the Myocardial Perfusion Scintigraphy, a Treadmill Stress Test is a Viable, Efficient and Cost Effective Option to Predict Cardiovascular Events in Elderly Patients

Luciano Janussi Vacanti[1], Andrei Carvalho Sposito[2], Luciano Séspedes[3], Maíra Sarpi[3], José Antonio F. Ramires[4], Anna E. Bortnick[5]

Instituto do Coração – InCor-DF[1], Faculdade de Medicina da Universidade de Brasília - UNB[2], Faculdade de Ciências Médicas de Santos, Fundação Lusíada[3], Instituto do Coração do Hospital das Clínicas – FMUSP[4], Brigham and Women's Hospital, Departament of Internal Medicine[5] - Brasília, DF - Santos, SP - São Paulo, SP - Boston, MA, USA

Summary

Objective: To define the prognostic value and cost-effectiveness of the treadmill stress test (TST) in comparison to the dipyridamole myocardial perfusion scintigraphy (DIP), in individuals ≥75 years of age.

Methods: Consecutive and prospective assessment of 66 patients (40% male) aged 81 ± 5 years of which 57% were hypertensive, 38% had dyslipidemia and 28% were diabetics. The Bruce protocol was adapted for a tilt treadmill and the TST prognostic value was obtained using the Duke treadmill score.

Results: The TST duration, recommended maximum heart rate percentage and double product at peak exercise were respectively: 7 ± 3 minutes, 95 ± 9% and 24,946 ± 4,576 (bpm x mmHg). The TST and DIP presented similar positive results for myocardial ischemia (21% *vs* 15%, respectively). The correlation between the tests was 88% (Kappa 0.63, p<0.01). During 685 ± 120 days of follow-up, nine major events occurred: 6 deaths, 2 acute coronary syndromes and 1 myocardial revascularization. The variables associated with the major events were: age (83 ± 6 *vs* 80 ± 4 years; p=0.048), male gender (78% *vs* 33%; p=0.02), ST segment depression (1 ± 1 mm *vs* 0.25 ± 0.6 mm; p= 0.01), high or intermediate risk determined by the Duke treadmill score – combined in one group (44% *vs* 2%; p=0.001) and abnormal DIP (44% *vs* 10%, p= 0.02).

Conclusion: For this elderly population, the TST was an efficient and viable option with a similar diagnostic value in comparison to the DIP. However, the TST was more accurate in the prediction of major events and offers a lower cost.

Key words: Exercise test; efficacy; costo-benefit analysis; cardiovascular diseases; aged, 80 and over; radionuclide imaging.

Introduction

The elderly (≥ 75 years) represent the fastest growing population segment in the world. In these individuals, coronary artery disease (CAD) symptoms are usually silent or atypical, severe and the main cause of morbidity and mortality[1,2]. These idiosyncrasies justify early disease detection. In these circumstances, doctors are usually concerned about the potential risk of musculoskeletal lesions from a treadmill stress test (TST) and consequently tend to investigate CAD using imaging methods and pharmacological induced stress. However, in addition to the detection of CAD, the TST offers other advantages. First, standardizing the TST as the first test to be requested could improve the cost-effectiveness of CAD detection in this segment, owing to the greater probability of CAD before testing in these individuals[3]. Second, in addition to detecting myocardial ischemia, other relevant information can be obtained using this method such as: functional capacity, and assessment of chronotropic behavior and blood pressure response during and after exertion. This information is essential to determine the prognosis[3-6]. Nevertheless, to date there is very little information in medical literature concerning TSTs as a diagnostic and prognostic tool in the elderly population. Therefore, the main objective of the present study is to evaluate whether the TST is a viable and cost efficient option that is equivalent to the dipyridamole myocardial perfusion scintigraphy to stratify cardiovascular risk in elderly patients.

Methods

Population - Between January and September 2002, 79 individuals, ≥75 years of age were consecutively assessed in the outpatient clinic at the Guilherme Álvaro State Hospital in Santos, SP. From these, 13 patients (16%) who presented abnormalities during the electrocardiography at rest (n=7) or significant physical exercise limitations (n=6) were excluded from the study. Therefore, the study sample consisted of 66 individuals (26 males) with an average age of 81 ± 5 years. All medications were suspended for a timeframe equivalent to five half-lives of the respective drugs before the test date. The study was approved by the Institution's Ethics Committee and

Mailing address: Luciano Janussi Vacanti •
Avenida Coronel Joaquim Montenegro, 81/22 – Santos, SP - Brazil
E-mail: lvacanti@cardiol.br
Manuscript received September 11, 2006; revised manuscript received October 26, 2006; accepted November 24, 2006.

all patients signed a free and informed consent form.

Treadmill stress test - The Bruce treadmill test protocol was used, preceded by a 1 minute warm-up at a speed of 1.0 mph, with no slope, and adapted for a tilt treadmill with gradual and moderate increases of speed and slope[7]. The patients were continually monitored with a 12 lead ECG that was also equipped with a CM5 bipolar lead using the software Ergo PC 13 for Windows. Blood pressure measurements were taken at rest, after every three minutes of exercise, at peak exertion and every minute during recovery. The test was stopped due to exhaustion; elevated diastolic blood pressure (DBP), >120mm/Hg for normotensive patients and >140mm/Hg for hypertensive patients; elevated systolic blood pressure (SBP), >260mm/Hg; a sustained SBP drop; clinical manifestation of intense chest pain; depression of the ST segment ≥ 3mm; elevation of the ST segment ≥ 2mm on leads without a Q wave; complex ventricular arrhythmia; onset of sustained supraventricular tachycardia, atrial tachycardia, atrial fibrillation, 2nd or 3rd degree atrioventricular block; signs of left ventricular failure; or failure in the monitoring and/or recording systems. The test was considered positive when one of the following was observed: typical symptoms, a straight or concave ST segment depression ≥1.0 mm or a convex ST segment depression ≥1.5 mm, at 0.08 seconds from the J point, or even a ST segment elevation ≥1.0 mm. The test was considered efficient if the individual attained at least 85% of the maximum heart rate (HR) recommended for the patient's age (220 – age). Exertion induced hypertension was defined as SBP values >220 mmHg and/or elevation of DBP by 15mmHg or more. Indirect measurements of maximum oxygen consumption (VO_2max) in METs was calculated automatically by the software. The double product was obtained by multiplying the maximum heart rate obtained by the systolic blood pressure at peak exertion[3].

Calculation of the Framingham risk score for future coronary events was conducted in accordance with international guidelines. Briefly, the patients were evaluated according to gender and the following variables: age, total cholesterol, HDL cholesterol, blood pressure and whether or not they were smokers. The estimated risk for events within the next ten years was obtained from the total number of points. The participants were stratified in 3 categories, according to the predicted ten year risk: low risk (≤10%), intermediate risk (>10% but ≤20%) and high risk (>20%)[8]. The Duke treadmill score (DTS) and Veterans score (VS) were calculated based on clinical characteristics and information obtained during the TST, as described in literature[9,10]. Briefly, the DTS and VS were calculated as shown below:

VS = Δ Double product (10^{-3}) - 10 (ST segment depression at rest + prior infarction + prior myocardial revascularization) - 4 (ST segment depression during the TST);

DTS = exercise time - (5 x ST segment depression) - (4 x angina scale). The angina scale was classified as: 0 – no angina, 1 – presence of angina and 2 – limiting angina (reason to stop the TST). Patients with a DTS ≥5 were classified as low risk; <5 to (-10) as intermediate risk and when <(-10) as high risk[9].

Myocardial perfusion scintigraphy - All patients were submitted to myocardial perfusion scintigraphy with technetium-99m-sestamibi within at maximum one week of the treadmill stress test. The protocol consisted of two stages, conducted on two different days: at rest and after administration of a vasodilator (0.56 mg/kg of intravenous dipyridamole for 4 minutes). The patients were monitored continuously with a 12 lead ECG and blood pressure measurements were taken at rest, after every three minutes of pharmacological stress, at peak stress and every minute during recovery. Image acquisition and reconstruction were conducted in accordance with the guidelines of the American Society of Nuclear Cardiology[11].

Subjective and semi-quantitative image interpretation was performed by a qualified independent observer. Questionable cases were reevaluated by another observer. Tests that showed a uniform distribution of the radioactive tracer in the left ventricle at rest and under stress were considered negative. Stationary defects shown on both images were defined as fibrosis, and transient defects as ischemia.

Clinical evolution and follow-up - Clinical follow-up, after the tests were completed, was conducted by telephone and by consulting the medical charts of the patients enrolled in the study. Major events were classified as: death (any cause), acute coronary syndromes (ACS) [myocardial infarction and unstable angina], and myocardial revascularization (percutaneous or surgical). The diagnosis for ACS was obtained from: a) medical history of ischemic chest pain; b) alterations in electrocardiogram serial readings (depression or elevation of the ST segment) and c) rise and fall of cardiac enzymes (in the case of myocardial infarction).

Statistical analysis - Data were expressed as averages and standard deviations and the null hypothesis rejection level was established as 0.05 or 5% ($\gamma \leq 0.05$) for all tests. The Kolmogorov-Smirnov test was used to analyze quantitative variables. The categorical variable frequencies were compared using the Fisher test. Univariate analysis was conducted using the Student's t-test for parametric data and the Mann-Whitney test for non-parametric data. The individuals were compared according to event predictive variables using the Kaplan-Meier method and log-rank test. The Cox model was used to obtain the odds ratio with a confidence interval of 95% (CI). Statistical calculations were conducted with the computer program SPSS version 10.0 for Windows.

Cost-effectiveness - The respective costs of the TST and DIP were estimated at seventy-seven Reals and fifty cents R$ 77,50 and four hundred and eighty-six Reals R$ 486,00 based on the 1999 Brazilian Medical Association table, which was in force at the beginning of the study. For international comparison purposes, the respective costs based on previous studies were one hundred and seventy-five US dollars US$175 and eight hundred and forty US dollars US$840[12]. The cost-effectiveness ratio was defined as the cost per event detected on the abnormal DIP and on an intermediate or high risk DTS according to the TST[13].

Results

Sixty-six individuals (39% males) with an average age of 81 ± 5 years (75 to 94 years) were able to perform the TST.

Among them, 41 (62%) presented hypertension, 27 (41%) dyslipidemia, 16 (24%) diabetes, 5 (8%) were overweight, 1 (1.5%) was a smoker and 31 (48%) had comorbidities: osteoarthritis (n=22), affective disorders (n=3), vertigo (n=3) and sequelae due to strokes (n=3). Confirmed prior CAD was observed in 12 (18%) patients. Atypical chest pain was observed in 18 (28%) and typical chest pain in 8 (12%) of the patients. The remaining 40 individuals (60%) were asymptomatic before the tests.

No complications were observed during or after the test and 92% of the tests were efficacious. The tests were stopped, on average, at 95 ± 9% of the heart rate predicted for the patient's age. Average test duration was 7.2 ± 2.5 minutes, attaining a double product of 24,109 ± 4,541 (bpm x mmHg) and 7 ± 2 METs.

Consonance between the TST and DIP - Myocardial ischemia was observed in 10 individuals (15%) during the DIP and in 14 (21%) during the TST, of which 3 (4.5%) presented angina during the TST. Fifty-eight individuals (88%) presented corresponding TST and DIP tests. All individuals that had positive DIP tests also had positive TST tests for myocardial ischemia. The negative TST tests were not confirmed by DIP in 2 cases (4%), and in 6 cases (43%) the negative DIP tests were not confirmed by the TST. The overall consensus between the two tests was 0.63 (p<0.01, Kappa).

Clinical evolution - All individuals included in the study received clinical follow-up. During the 685 days ± 118 days (300 to 836 days) of follow-up after the tests had been conducted there were six deaths, one myocardial revascularization surgery and two episodes of acute coronary syndromes (unstable angina) (Table 1). Two individuals died after acute coronary events, two suffered from sudden death and two died during treatment of a respiratory tract infection.

Comparison of the patients who presented cardiovascular events with those who presented an uneventful evolution revealed statistically significant differences in relation to age, gender, presence of ST segment depression, DTS, presence of ischemia during DIP and maximum heart rate during the test (Tables 2 and 3). The remaining study variables did not present statistically significant differences between the groups (Tables 2 and 3). Even after excluding two patients who were being treated for pulmonary infection, the differences remain significant in relation to gender (p=0.01), ST segment depression (p=0.04), DTS (p<0.001) and the presence of ischemia during DIP (p=0.009). During the second analysis, the Framingham high risk score (p=0.04) and the presence of typical chest pain (p=0.04) were significantly associated with cardiovascular events. The other variables remained unrelated to events.

Owing to the univariate analysis findings, an actuarial curve was generated to separate the patients according to abnormal DTS and DIP. Analysis of the Kaplan-Meier curve demonstrated that patients with a positive DIP presented a greater possibility to have events during follow-up than those with negative results (Log Rank p=0.02) (Figure 1A). Similarly, the patients with a DTS of high or intermediate risk presented a greater possibility of events than those with a DTS of low risk (Log Rank p=0.0006) (Figure 1B). The Cox regression model was adjusted to obtain the odds ratio for events. The co-variables included in this model were: age, indicative symptoms of myocardial ischemia, Framingham score, DTS, VS, positive DIP, functional capacity during the TST, hypertension, smoking, diabetes, excess weight, dyslipidemia, prior CAD and use of ASA, beta blockers or statins. After adjustment of these variables, only two were identified as independent and predictive variables for events: age (OR 1.2, CI 95%, 1.0 - 1.4, p=0.03) and an intermediate or high risk DTS (OR 8.5, CI 95%, 2 - 35.6, p=0.003).

Cost-effectiveness - The cost-effectiveness ratio to perform a DIP or TST to predict an event was three thousand five hundred and sixty-four Reals (R$ 3.564,00) and five hundred and sixty-eight Reals and twenty cents (R$ 568,20), respectively. When the Framingham risk score was taken into consideration, the cost-effectiveness ratio to perform a DIP to predict an event was eight thousand seven hundred and forty-eight Reals (R$ 8.748,00) for low risk individuals, four thousand three hundred and seventy-four Reals (R$ 4.374,00) for intermediate risk individuals and one thousand four hundred and fifty-eight Reals (R$ 1.458,00) for high risk individuals. The cost-effectiveness ratios to perform a TST to predict an event were R$ 1.395,00,

Table 1 - Characteristics of the patients who presented cardiovascular events

Case	Age	Sex	Event	Prior CAD	TST	DIP
1	84	M	Sudden death	No	negative	negative
2	78	M	Sudden death	No	negative	negative
3	92	F	Pneumonia	No	negative	negative
4	94	F	Sudden death	No	negative	negative
5	78	M	Sudden death	No	positive	Positive
6	79	M	Pneumonia	No	negative	negative
7	80	M	Unstable angina	Yes	positive	positive
8	81	M	Unstable angina	Yes	positive	positive
9	84	M	MR	No	positive	positive

MR - myocardial revascularization; CAD - coronary artery disease; TST - treadmill stress test, DIP - dipryidamole myocardial perfusion scintigraphy; M - male; F - female.

Table 2 - Clinical Characteristics: differences between the patients with and without events

Variable	With events	Without events	p
n (number)	9	57	
Age	83±6	80±4	0.048
Male gender	7 (78%)	19 (33%)	0.02
Hypertension	5 (55%)	36 (63%)	1
Dyslipidemia	2 (22%)	25 (43%)	0.4
Diabetes	2 (22%)	14 (25%)	0.7
Overweight	0	5 (9%)	1
Smoker	0	1 (1.7%)	1
Coronary artery disease	2 (22%)	10 (17%)	1
Framingham annual risk	2.5±1	1.8±1	0.4
Framingham risk score	10.1±2	10.7±3	0.5
Comorbidities	5 (55%)	26 (46%)	1
Use of beta-blockers	3 (33%)	9 (16%)	0.3
Use of acetylsalicylic acid	2 (22%)	13 (23%)	1
Use of statins	1 (11%)	4 (7%)	0.5
Typical chest pain	3 (33.3%)	5 (8.8%)	0.2
Atypical chest pain	2 (22.2%)	15 (26.3%)	0.2

Table 3 - TST Results: differences between the patients with and without events

Variable	With events	Without events	p
n (number)	9	57	
ST segment depression (mm)	1.1 ± 1.3	0.25 ± 0.6	0.01
Duke treadmill score	-8.9 ± 7.9	4.9 ± 4.2	0.005
DIP positive	4 (44%)	6 (10%)	0.02
SBP (at rest) (mmHg)	130 ± 18	132 ± 13	0.6
Maximum HR (bpm)	128 ± 20	132 ± 14	0.1
DP (bpm x mmHg x 103)	22 ± 5	24 ± 4	0.2
Duration (minutes)	6.6 ± 2	7.3 ± 2	0.4
METs	6.5 ± 2	6.9 ± 2	0.5
Chronotropic response	2 (22%)	7 (12.3%)	0.2
Veterans score	26.7	34.6	0.2

SBP - systolic blood pressure; DP - double product; METs - metabolic equivalents; HR - heart rate.

R$ 697,50 and R$ 232,50, respectively.

The cost-effectiveness ratios (in American reimbursement rates for comparison with international literature) for the DIP and TST to predict an event were six thousand one hundred and sixty US dollars (US$ 6,160) and one thousand two hundred and eighty-three US dollars (U$ 1,283) respectively.

When the Framingham risk score was taken into consideration, the cost – effectiveness ratios to perform a DIP to predict an event were fifteen thousand one hundred and twenty US dollars (US$15,120) for low risk individuals, seven thousand five hundred and sixty US dollars (US$7,560) for intermediate risk individuals and two thousand five hundred and twenty US dollars (US$2,520) for high risk individuals. The cost – effectiveness ratios to perform a TST to predict an event were US$ 3,150, US$ 1,575 and US$ 525, respectively.

Discussion

This is the first study to prospectively compare the DIP to a tilt TST in order to estimate cardiovascular risk in an elderly

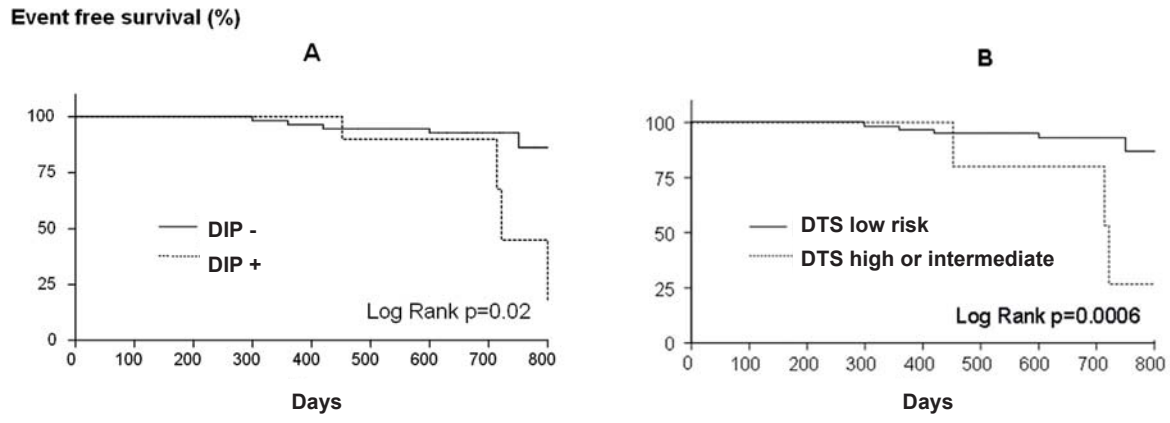

Fig. 1 - *Kaplan-Meier event free survival curve, stratified by DIP (A) and DTS (B).*

population. Our results demonstrate that: (i) a tilt TST is a safe and viable option for elderly individuals; (ii) both tests are equally reliable to detect myocardial ischemia, and (iii) stratification of individuals with high or intermediate risk according to the DTS was superior to the positive myocardial perfusion scintigraphy to predict cardiovascular events.

Despite the general concern regarding the risk of musculoskeletal lesions during the TST, our findings reveal that the TST is a safe and viable option for the elderly. This was proved by the fact that more than 88% of the patients achieved the sub-maximum heart rate proposed for their age. It should be emphasized that 48% of the participants in the sample had comorbidities such as: osteoarticular diseases, prior strokes, depression and vertigo that were not limiting factors for the TST. The high prevalence of comorbidities in our population is also described in American and European populations[14-16]. In the elderly, similar to young adults[17], there is great deal of agreement between the TST and DIP. Similar to younger individuals, the disagreement between the two tests was higher for the patients with an abnormal TST than those with a normal TST (43% *vs* 4%). This observation reinforces the indication of the TST as the first test to be requested for CAD detection. Additionally, value-added risk stratification is obtained with the Duke treadmill score. This is probably due to the fact that the score incorporates two prognostic markers obtained from the TST. Maximum exercise capacity (duration), is one of the most consistent prognostic markers along with exercise induced ischemia.

Contrary to our findings, Kwok et al[18] did not obtain an adequate predictive value from the DTS to predict events in individuals ≥ 75 years. One possible explanation for this inconsistency between these two studies could reside in the protocol used. The Bruce protocol used in the Kwok et al[18] study, presents large and unequal load increments resulting in a nonlinear relation between the work and myocardial oxygen consumption, reducing the accuracy of the indirect determination of maximum oxygen consumption (VO_2 max) and contributes to early TST interruption in the elderly population[19,20]. Consequently, a large percentage of patients were not able to walk long enough (≥5 minutes) to be stratified as low risk on the DTS. Actually, in the Kwok et al[18] study, the average TST duration was 5 minutes and only 26% of the patients were classified as low risk. In contrast, our patients had and average duration of 7 minutes and 92% of the patients were classified as low risk.

Data from the American Public Healthcare System (Medicare) in 1998 demonstrate that DIP indications were three times higher than for TSTs[3]. In other words, approximately US$820 million was spent on DIPs to detect myocardial ischemia versus US$56 million for TSTs. This discrepancy would probably be even higher if only the tests conducted on the elderly population were considered. It is expected that the American population ≥ 80 years will double over the next twenty years[21]. Therefore, a progressive strategy to establish the TST as first method to be used would probably reduce current and future geriatric health care costs.

Limitations - The greatest limitation of the present study was that it did not have sufficient statistical power to evaluate the classic CAD risk factors as indicators for cardiovascular events in this elderly population. Further studies are required to evaluate this issue. Nevertheless, within the scope of our main objective, the study had sufficient power to demonstrate that the DTS score obtained from the tilt TST is superior to the presence of transient defects on the myocardial perfusion scintigraphy. A less significant limitation should be noted in relation to the Framingham risk score and the patient's age, as no distinction is made for patients over 74 years. Or in other words, the scores for 75 year old individuals and 85 year old individuals are the same. Nevertheless, all other available scores also have this limitation.

Conclusions

Our findings demonstrate that the TST is a safe, viable and cost-effective option that is superior to the myocardial perfusion scintigraphy to predict cardiovascular risk in the elderly. These findings can contribute to cost reductions in the detection of myocardial ischemia and stratification of the elderly.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

References

1. Statistics NCfH. Data Warehouse on Trends in Health and Aging. [acesso em 2006 may 12]. Available on http://wwwcdcgov/nchs/agingacthtm>.
2. Fleg JL, Gerstenblith G, Zonderman AB, Becker LC, Weisfeldt ML, Costa PT Jr, et al. Prevalence and prognostic significance of exercise-induced silent myocardial ischemia detected by thallium scintigraphy and electrocardiography in asymptomatic volunteers. Circulation. 1990;81:428-36.
3. Gibbons J, Balady GJ, Bricker JT, Chaitman BR, Fletcher GF, Froelicher VF, et al. ACC/AHA 2002 Guideline Update for Exercise Testing: Summary Article. A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Update the 1997 Exercise Testing Guidelines). Circulation. 2002;106:1883.
4. Goraya T. Prognostic value of treadmill exercise testing in the elderly persons. Ann Intern Med. 2000;132:862-70.
5. Wilkoff BL, Miller RE. Exercise testing for chronotropic assessment. Cardiol Clin. 1992;10(4):705-17.
6. Mundal RKS, Sandvik L, Eriksen G, Thaulow E, Erikssen J. Exercise blood pressure predicts mortality from myocardial infarction. Hypertension. 1996;27:324-9.
7. Vacanti LJ, Sespedes LBH, Sarpi MO. O teste ergométrico é útil, seguro e eficaz, mesmo em indivíduos muito idosos, com 75 anos ou mais. Arq Bras Cardiol. 2004;82:147-50.
8. Wilson PW, D'Agostino RB, Levy D, Belanger AM, Silbershatz H, Kannel WB. Prediction of coronary heart disease using risk factor categories. Circulation.

1998;97(18):1837-47.

9. Mark DB, Shaw L, Harrell FE Jr, Hlatky MA, Lee KL, Bengtson JR, et al. Prognostic value of a treadmill exercise score in outpatients with suspected coronary artery disease. N Engl J Med. 1991;325:849-53.

10. Lai S, Kaykha A, Yamazaki T, Goldstein M, Spin JM, Myers J, et al. Treadmill scores in elderly men. J Am Coll Cardiol. 2004;43(4):606-15.

11. Port SC. Imaging Guidelines for Nuclear Cardiology Procedures, Part 2. J Nucl Cardiol. 1999;6:G47-84.

12. Berman DS, Hachamovitch R, Kiat H, Cohen I, Cabico JA, Wang FP, et al. Incremental value of prognostic testing in patients with known or suspected ischemic heart disease: a basis for optimal utilization of exercise technetium-99m sestamibi myocardial perfusion single-photon emission computed tomography. J Am Coll Cardiol. 1995; 26 (3): 639-47.

13. Hachamovitch R, Berman DS, Kiat H, Cohen I, Friedman JD, Shaw LJ. Value of stress myocardial perfusion single photon emission computed tomography in patients with normal resting electrocardiograms: an evaluation of incremental prognostic value and cost-effectiveness. Circulation. 2002;105(7):823-9.

14. Manton KG, Gu X. Changes in the prevalence of chronic disability in the United States black and nonblack population above age 65 from 1982 to 1999. Proc Natl Acad Sci USA. 2001;98(11):6354-9.

15. Freedman VA, Martin LG, Schoeni RF. Recent trends in disability and functioning among older adults in the United States: a systematic review. JAMA. 2002;288(24):3137-46.

16. Ebrahim S, Papacosta O, Wannamethee G, Adamson J. Social inequalities and disability in older men: prospective findings from the British regional heart study. Soc Sci Med. 2004;59(10):2109-20.

17. Mattera JA, Arain SA, Sinusas AJ, Finta L, Wackers FJ. Exercise testing with myocardial perfusion imaging in patients with normal baseline electrocardiograms: cost savings with a stepwise diagnostic strategy. J Nucl Cardiol. 1998;5(5):498-506.

18. Kwok JM, Miller TD, Hodge DO, Gibbons RJ. Prognostic value of the Duke treadmill score in the elderly. J Am Coll Cardiol. 2002;39(9):1475-81.

19. Inoguchi T, Yamashita T, Umeda F, Mihara O. High incidence of silent myocardial ischemia in elderly patients with non insulin-dependent diabetes mellitus. Diabetes Res Clin Pract. 2000;47(1):37-44.

20. Hashimoto A, Palmer E. Complications of excercise and pharmacologic stress tests: differences in younger and elderly patients. J Nucl Cardiol. 1999;6:612-9.

21. U.S. Census Bureau. International database. Table 094. Midyear population, by age and sex. [acesso em 2006 nov 10]. Available: <http://www.census.gov/population/www/projections/natdet-D1A.html>.