# Usefulness of the Integrated Scoring Model of Treadmill Tests to Predict Myocardial Ischemia and Silent Myocardial Ischemia in Community-Dwelling Adults (from the Rancho Bernardo Study)

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**To investigate the association between analyses of submaximal treadmill exercise test (TMT) and long-term myocardial ischemia (Mis) and silent Mis in community-dwelling older adults, 898 Rancho Bernardo Study participants (mean age 55 years) without coronary heart disease underwent TMT and were followed up to 27 years. The main outcome measures are incidence of Mis and silent Mis. During follow-up, 97 Mis and 103 silent Mis events occurred. We measured ST change, inability to achieve target heart rate, abnormal heart rate recovery (HRR), and chronotropic incompetence (ChI). Each parameter was a significant predictor for Mis and silent Mis. An integrated scoring model was based on these 4 parameters and defined as sum of numbers of abnormal parameters. After multiple adjustments, an integrated scoring model independently predicted Mis and silent Mis. The incidence rates of abnormalities of parameters are 36.5% for 1 abnormality, 9.1% for 2 abnormalities, and 2.0% for 3 or 4 abnormalities. Compared with those with normal results, participants with 1 or 2 abnormalities had significantly increased risk for Mis (hazard ratio [HR] 1.79 or 2.34, respectively) and silent Mis (HR 1.80 or 2.64, respectively). Participants with 3 or more positive findings showed an even greater risk for Mis (HR 7.96 [3.02 to 21.00]) and silent Mis (HR 3.22 [0.76 to 13.60]). In conclusion, ST change, ChI, abnormal HRR, inability to achieve target heart rate, and integrated scoring model of TMT were independent predictors of long-term Mis and silent Mis in an asymptomatic middle-aged population. Management of ChI or abnormal HRR in an asymptomatic population may prevent future ischemic heart disease and thus improve the quality of life.**  **(Am J Cardiol 2015;115:1049–1055)**

It is well known that chronotropic incompetence (ChI) and abnormal heart rate recovery (HRR) are independent predictors of major adverse cardiovascular events and overall mortality.[1–4] However, the independent value of the treadmill exercise test (TMT) used as a screening tool in asymptomatic adults to predict future coronary artery disease, and especially to predict silent ischemia, is not yet known.[5,6] The present study was designed to assess ST change, ChI, inability to achieve target heart rate (iTHR), abnormal HRR, and integrated analysis of these parameters as predictors of myocardial ischemia (Mis) and silent Mis in community-dwelling asymptomatic older adults followed up to 27 years.

## Methods

The Rancho Bernardo Study is a prospective population-based study of older adults residing in a suburban southern California community. The cohort of residents enrolled was quite homogeneous—they were almost entirely Caucasian and most were white-collar workers. From 1972 to 1974, a total of 1,789 community-dwelling adults participated in a heart disease risk factor survey, which served as the baseline visit for the present study. Participants with a history of coronary heart disease (CHD: myocardial infarction, angina, or coronary artery bypass surgery) were excluded from the TMT. The data of 898 participants who underwent TMT at baseline are used for this analysis (Figure 1). The study protocol was approved by the Human Research Protection Program at the University of California, San Diego; all participants gave written informed consent before participation. Participants were followed by annual mailed questionnaires, and they returned for research clinic visits approximately every 4 years through 1999, up to 27 years.

A submaximal TMT was administered to participants[7,8]; exclusions included aortic stenosis, congestive heart failure, severe hypertension, R-on-T–type premature ventricular contractions, ventricular tachycardia, parasystolic focus, atrial flutter, congenital heart disease, and second reschedule required. The exercise test was terminated for any of the

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See page 1054 for disclosure information.

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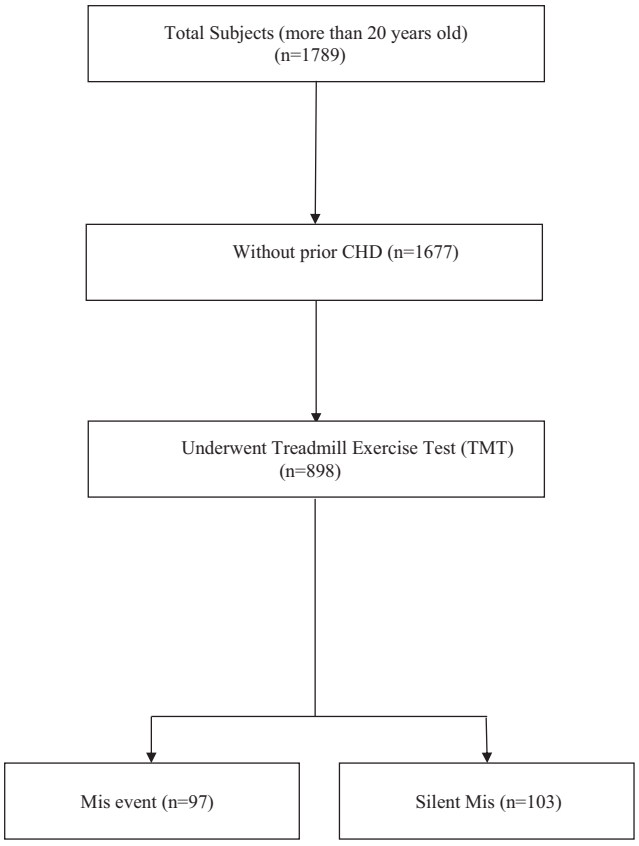


Figure 1. Summary of study population.

following reasons: (1) subjective response: the subject was unwilling or unable to continue exercise; (2) development of potential hazards to the subject; and (3) attainment of near-maximal exercise—exercise was stopped if the subject attained age-predicted target heart rate (THR) and maintained it for 1 minute, if the subject maintained THR until the end of the ongoing exercise stage, or if subject's heart rate exceeded target heart rate by 8 beats/min, whichever occurred first.[8,9] A test result was considered to be positive if (1) ST depression or elevation of $\geq$1 mm was recorded by the visual coders, (2) the ST integral decreased by at least 10 diV-seconds from its resting value to a value of 10 gV-seconds or less, or (3) the ST integral rose by at least 10 gV-sec from its resting value.

Three nonelectrocardiographic measurements were defined as (1) an abnormal HRR—a decrease of <22 beats/min after 2 minutes of recovery[10]; (2) ChI—the inability to achieve 80% of heart rate reserve, using a standard equation to define the percentage heart rate reserve [(maximal heart rate − resting heart rate)/(174 − 0.54 × age) − (resting heart rate) × 100][11]; (3) THR was considered achieved when 90% of maximal heart rate predicted for subject's age was attained.[2]

The primary outcomes were Mis and silent Mis. Mis, determined using standard epidemiologic methods (such as annual mailed questionnaires and interviews at regular clinic visits), consisted of a history of myocardial infarction, angina pectoris, coronary revascularization, or coronary artery bypass graft history.

Silent Mis was defined as $\geq$1 ischemic resting electrocardiographic (ECG) abnormalities, newly revealed at a follow-up visit with no history of myocardial infarction, angina pectoris, or chest pain not meeting the Rose algorithm.

(1) "ECG coronary probable"—major Q or QS wave [Minnesota Code 1.1, 1.2]; complete left bundle branch block [Minnesota Code 7.1.1].
(2) "ECG coronary possible"—small Q or QS wave [Minnesota Code 1.3]; ST depression [Minnesota Code 4.1 − 4.3]; T wave items [Minnesota Code 5.1 to 5.3].[12]

No Evidence of Cardiovascular Disease was defined as no ECG changes and no history of myocardial infarction, angina pectoris, or chest pain ($\geq$30 minutes).

Data on vital status were collected on all participants. More than 99% of this cohort was followed for vital status by annual mailer through 1999.

Death certificates were obtained for all decedents and coded for cause of death by a certified nosologist using the ninth revision of the "International Classification of Diseases, Adapted." Deaths due to CHD included coronary death, myocardial infarction, coronary insufficiency, and

Table 1
Baseline characteristics of study population

| Variable | Total cohort (n=898) | Myocardial Ischemia | |
|---|---|---|---|
| | | Apparent (n=97) | Silent (n=103) |
| Age (years) | 55.04 ± 14.85 | 65.65 ± 10.46 | 59.5 ± 98.33 |
| BMI (Kg/m$^2$) | 24.96 ± 3.46 | 24.77 ± 3.37 | 24.97 ± 3.54 |
| Total Cholesterol (mg/dL) | 228.54 ± 43.58 | 238.05 ± 40.58 | 230.53 ± 43.14 |
| Triglycerides (mg/dL) | 141.87 ± 101.92 | 127.05 ± 71.18 | 141.00 ± 87.49 |
| HDL (mg/dL) | 58.20 ± 18.76 | 58.71 ± 18.41 | 60.32 ± 18.65 |
| LDL (mg/dL) | 152.51 ± 40.53 | 164.46 ± 37.89 | 153.72 ± 42.66 |
| SBP (mmHg) | 147.57 ± 18.78 | 158.02 ± 20.89 | 151.42 ± 17.08 |
| DBP (mmHg) | 99.23 ± 9.47 | 100.20 ± 10.03 | 100.00 ± 9.31 |
| HR (beats/min) | 84.24 ± 13.14 | 81.53 ± 11.64 | 81.69 ± 13.43 |
| Fasting plasma glucose (mg/dL) | 99.30 ± 18.23 | 103.71 ± 27.62 | 98.58 ± 13.36 |
| Current Smoker | 218(24.3%) | 25(26.3%) | 19(18.4%) |
| Daily Alcohol Drinker | 366(40.8%) | 46(48.4%) | 43(41.7%) |
| Regular Exercise (3+ times per week) | 109(88.6%) | 9(90.0%) | 10(90.9%) |
| Family History of CVD | 147(16.6%) | 18(19.4%) | 25(24.3%) |
| Diabetes mellitus | 38(4.2%) | 8(8.4%) | 3(2.9%) |
| Metabolic Syndrome (Modified WHO) | 180(20.0%) | 20(21.1%) | 22(21.4%) |
| Lipid-modifying agent | 68(7.6%) | 25(26.3%) | 14(13.6%) |
| Anti-Diabetes mellitus agent | 15(1.7%) | 4(4.2%) | 1(1.0%) |
| Anti-Hypertension | 99(11.0%) | 18(18.9%) | 13(12.6%) |
| Diuretics | 44(5.1%) | 6(6.4%) | 7(6.8%) |
| Anti-Arrhythmia | 6(0.7%) | 0 | 1(1.0%) |

Categorical variables are reported as number (percentages) and continuous variables as mean (standard deviation). CVD—cardiovascular disease.