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Achieving an Exercise Workload of ≥10 Metabolic Equivalents Predicts a Very Low Risk of Inducible Ischemia

Does Myocardial Perfusion Imaging Have a Role?

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Objectives We sought to identify prospectively the prevalence of significant ischemia (≥10% of the left ventricle [LV]) on exercise single-photon emission computed tomography (SPECT) imaging relative to workload achieved in consecutive patients referred for myocardial perfusion imaging (MPI).

Background High exercise capacity is a strong predictor of a good prognosis, and the role of MPI in patients achieving high workloads is questionable.

Methods Prospective analysis was performed on 1,056 consecutive patients who underwent quantitative exercise gated ^{99m}Tc-SPECT MPI, of whom 974 attained ≥85% of their maximum age-predicted heart rate. These patients were further divided on the basis of attained exercise workload (<7, 7 to 9, or ≥10 metabolic equivalents [METs]) and were compared for exercise test and imaging outcomes, particularly the prevalence of ≥10% LV ischemia. Individuals reaching ≥10 METs but <85% maximum age-predicted heart rate were also assessed.

Results Of these 974 subjects, 473 (48.6%) achieved ≥10 METs. This subgroup had a very low prevalence of significant ischemia (2 of 473, 0.4%). Those attaining <7 METs had an 18-fold higher prevalence (7.1%, $p < 0.001$). Of the 430 patients reaching ≥10 METs without exercise ST-segment depression, none had ≥10% LV ischemia. In contrast, the prevalence of ≥10% LV ischemia was highest in the patients achieving <10 METs with ST-segment depression (14 of 70, 19.4%).

Conclusions In this referral cohort of patients with an intermediate-to-high clinical risk of coronary artery disease, achieving ≥10 METs with no ischemic ST-segment depression was associated with a 0% prevalence of significant ischemia. Elimination of MPI in such patients, who represented 31% (430 of 1,396) of all patients undergoing exercise SPECT in this laboratory, could provide substantial cost-savings. (J Am Coll Cardiol 2009;54:538–45)

The sequelae of coronary artery disease (CAD) continue to cause significant morbidity and impose high economic costs. Identifying those at the highest risk of major adverse cardiac events is imperative for guiding therapy and maximizing the benefits of revascularization. Noninvasive diagnostic imaging assists with this process and consequently has grown more than any other physician service under Medicare reimbursement (1). In 2005 alone, 9.3 million nuclear myocardial perfusion studies were performed at significant cost to the health care system (2). Improved pre-test risk stratification is essential to use this expensive imaging modality in a cost-effective manner. The incremental value of stress myocardial perfusion imaging (MPI) is small for patients with a low-risk stress test, a low-risk Duke Treadmill Score, or a high rate-pressure product without ST-segment depression (3–5).

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Exercise capacity measured in metabolic equivalents (METs) alone is a powerful predictor of cardiovascular events (6). Higher workloads achieved during exercise stress predict improved survival rates, irrespective of age and sex (6–8). A cutpoint of 10 METs achieved predicts low mortality, even in the setting of significant CAD (9,10). Its

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association with the prevalence of significant ischemia by quantitative single-photon emission computed tomography (SPECT), as compared with the Duke Treadmill Score, would be of interest (11,12).

Accordingly, the primary objective of this study was to determine prospectively the relationship of cardiac workload attained to the prevalence and extent of myocardial abnormalities by gated SPECT in patients with known or an intermediate-to-high probability of CAD who achieved ≥85% of their maximum age-predicted heart rate (MAPHR). The hypothesis tested was that individuals reaching diagnostic heart rates (≥85% of their MAPHR) and ≥10 METs have a low prevalence of significant ischemia (≥10% of the left ventricle [LV]). A second hypothesis tested was that individuals achieving ≥85% of their MAPHR with lower workloads have a greater prevalence of ischemia. The third hypothesis was that patients reaching <85% of their MAPHR but ≥10 METs would still have a low prevalence of significant ischemia but greater than that seen in those attaining their target heart rate.

Methods

Prospectively collected data from the University of Virginia Nuclear Databank were analyzed in a cohort of consecutive patients undergoing exercise testing and SPECT imaging at the University of Virginia Medical Center.

Study cohort. This prospective study cohort comprised 2,794 consecutive patients who underwent ^{99m}Tc SPECT MPI between February 2006 and January 2007. After excluding those who underwent pharmacologic stress or achieved <10 METs and <85% of their MAPHR, our final study cohort included 1,056 subjects (Fig. 1). Patients reaching <10 METs and <85% of their MAPHR were not studied, because it is well-recognized that such patients are at high risk for CAD and future cardiac events due to deconditioning and other factors. Imaging provides added diagnostic and prognostic information in this patient population (13).

Patients achieving ≥85% of their MAPHR (n = 974) were subdivided into 3 groups (<7 METs [n = 267], 7 to 9 METs [n = 234], and ≥10 METs [n = 473]). To test the third hypothesis, a second group of 82 individuals who attained ≥10 METs but <85% of their MAPHR was also examined.

Clinical information collection and management. Clinical information was collected from patients at the time of their exercise test and entered into the University of Virginia Nuclear Databank, including demographic data, comorbidities, physical examination, and baseline electrocardiogram (ECG) findings. Exercise test parameters and SPECT results (volumes, perfusion, and function) were also recorded (14,15). Protocol approval and waiver of informed consent were obtained from the University of Virginia Institutional Review Board.

Exercise testing. All subjects underwent exercise treadmill stress with electrocardiographic monitoring with standard exercise protocols; 1,033 of 1,056 (99%) exercised according to a Bruce or modified Bruce protocol. The decision of whether to stop anti-ischemic medication before testing was left up to the discretion of the referring physician. Testing was symptom-limited unless prematurely terminated for reasons recommended in the exercise testing guidelines (16). Exercise workload was defined as the total METs achieved (17). Ischemic ST-segment depression was defined as ≥1 mm horizontal or down-sloping depression of the ST-segment ≥80 ms after the J-point for 3 consecutive beats.

Abbreviations and Acronyms

CAD = coronary artery disease
ECG = electrocardiogram
LV = left ventricle/ventricular
LVEF = left ventricular ejection fraction
MAPHR = maximum age-predicted heart rate
MET = metabolic equivalent
MI = myocardial infarction
MPI = myocardial perfusion imaging
SPECT = single-photon emission computed tomography

Radionuclide SPECT imaging. Subjects underwent ^{99m}Tc sestamibi rest-stress gated-SPECT MPI with either a 1- or 2-day protocol (for a body mass index ≥36 kg/m^2). With the 1-day protocol, patients received first 10 mCi of ^{99m}Tc sestamibi at rest, and images were acquired after a 60-min delay. They subsequently received 30 mCi of ^{99m}Tc sestamibi at peak stress with gated-SPECT imaging performed after a 30-min delay. The 2-day protocol differed in that subjects received 30 mCi of ^{99m}Tc sestamibi (45 mCi in

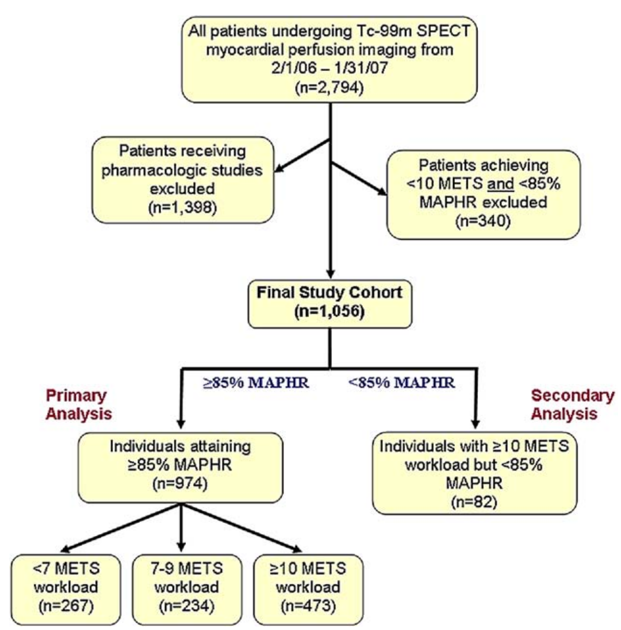

Figure 1 **Study Cohort Derivation Flowchart**

MAPHR = maximum age-predicted heart rate; MET = metabolic equivalent; SPECT = single-photon emission computed tomography.