

Is an Exercise Tolerance Test Indicated Before Beginning Regular Exercise? A Decision Analysis

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BACKGROUND AND OBJECTIVE: The present study, using a decision analysis, evaluates whether an exercise tolerance test (ETT) is indicated before initiating regular physical activity to reduce the risk of sudden death during exercise training.

DESIGN: The study encompasses a decision tree, Monte Carlo simulation, and utility analysis for adults at low to high risk for coronary disease, with a time horizon of five years, with or without routine ETT screening before initiating physical activity.

MEASURES: Mortality in Monte Carlo simulation; expected values in utility analysis.

RESULTS: Routine screening decreases mortality in intermediate to high-risk populations but not in low-risk persons. At all risk levels, the number of exercise-induced deaths prevented is less than the added number of deaths from angiography. Utility analysis indicates inferiority of routine screening, regardless of risk. Personal preferences (perceived stigma from having coronary disease and perceived benefit of regular exercise on quality of life) have a strong influence on the optimal choice.

CONCLUSION: Routine screening before initiating regular exercise is not recommended for the purpose of reducing the risk of sudden death during exercise training.

KEY WORDS: exercise; screening; coronary disease; decision analysis; utility; Monte Carlo simulation.

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INTRODUCTION

Regular exercise is beneficial to health, in part by reducing morbidity from coronary artery disease (CAD), and professional organizations strongly recommend regular exercise for nearly

everyone.^{1,2} However, physical activity may transiently increase the risk for myocardial infarction (MI) and sudden death, especially in CAD patients³ (although emotional stress may be a more substantial cause for cardiac arrest⁴). Proactive identification of people with CAD and referral to a cardiac rehabilitation program might be safer than issuing blanket recommendations for exercise. Exercise tolerance test (ETT) with ECG treadmill testing would be a non-invasive, low-cost, and convenient tool for identifying people with a high probability of CAD and at risk of sudden cardiac death as suggested in some studies.⁵⁻⁷ However, because of its limited sensitivity and specificity, ETT might be a poor universal screening tool for people with low probability of CAD and could generate many false positives.⁸ The American College of Cardiology recommends that an ETT be considered for diabetics, men older than 45 years, and women older than 55 years who plan to start vigorous exercise, especially if they have been sedentary.⁹ However, this recommendation does not address non-vigorous exercise, is classified as IIb (not well supported by evidence), and is controversial.² Indeed, no randomized study has ever addressed this question, and because exercise-induced cardiac events are rare, a clinical trial might require a prohibitively large number of participants and a prohibitively long follow up. In the U.S.A., many fitness clubs require an ETT prior to enrollment. In Israel, by law, registration to a gym requires authorization by a physician, who often will refer people to ETT before clearing them to exercise. In this paper, we used formal decision analysis to examine this issue.

MATERIAL AND METHODS

The Decision Model

We used the software package DATA 4.0 (TreeAge Software, Williamstown, MA) to construct the decision tree shown in Fig. 1. The main branches represent the two strategies tested: (I) ETT or (II) no ETT before initiating regular physical activity. Sub-branches represent possible clinical consequences, chance events presented as dichotomous nodes with probability for occurrence and for non-occurrence. The time horizon was set at five years to allow stabilization of the beneficial effects from exercise or medical therapy.^{10,11} Main outcomes used for comparison between strategies were death, MI, and complications from coronary angiography.

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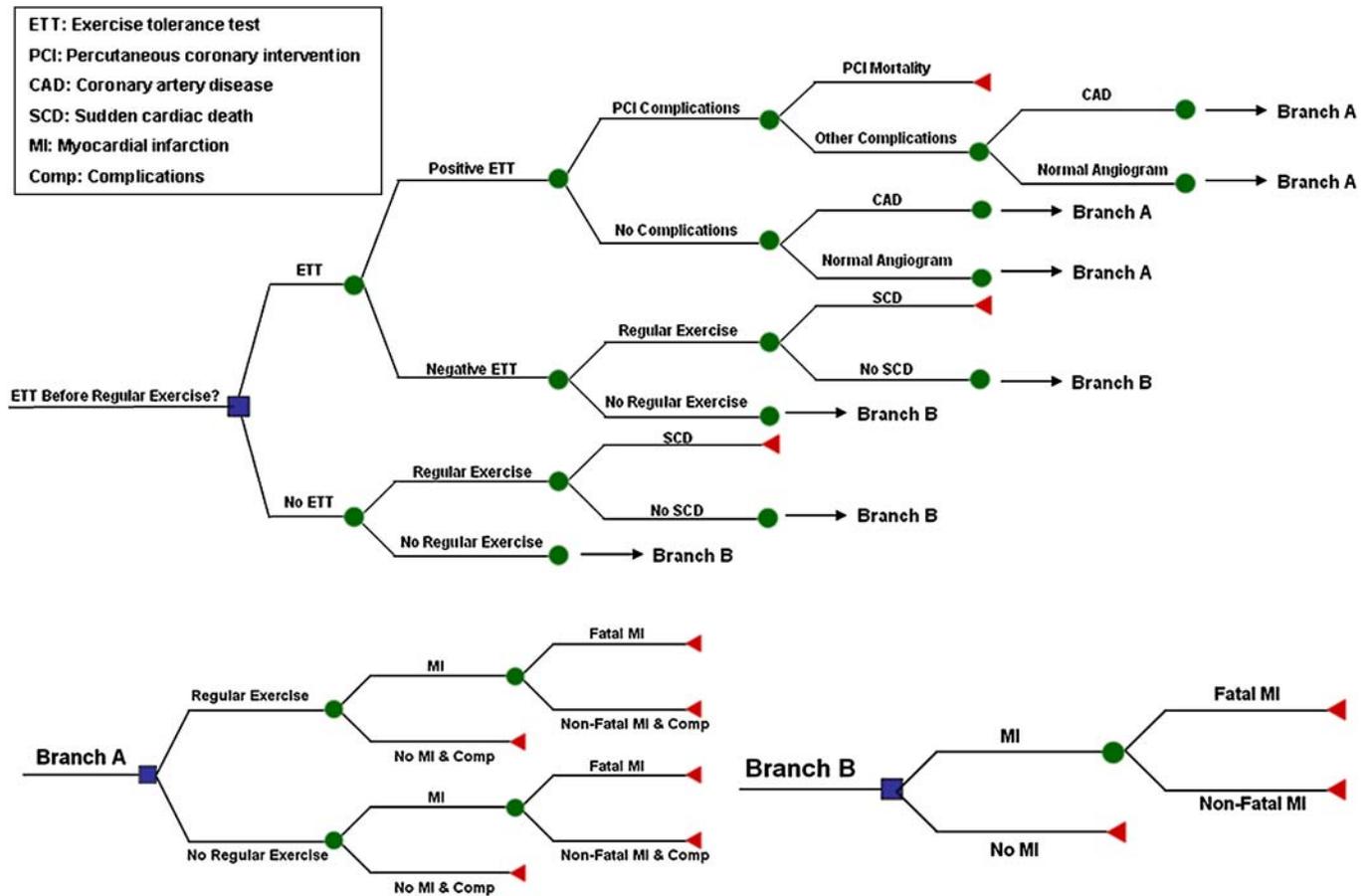


Figure 1. The decision tree. Truncated subtrees continue as branches A and B shown in the lower panel. See inset for abbreviations.

Quantitative Assumptions

The probabilities for variables in the tree, obtained from the literature (using MEDLINE search) or estimated (if no data were available), are listed in Table 1. We assumed that with a negative ETT, the risk for exercise-induced death would be reduced by 50% and that in the case of a positive ETT, the risk would be eliminated after percutaneous coronary intervention (PCI) and medical management.

We used two different models:

- (1) A Monte Carlo simulation (see below);
- (2) A decision analysis where a utility function represented the estimated quality of life in the different conditions. In this model, we examined the optimal utility under variable assumptions for different variables (see Utility and Sensitivity Analysis, below).

Monte Carlo Simulation

We used Monte Carlo simulations to generate a probabilistic distribution of outcomes for specified ranges of variables.¹² We modeled populations at low, medium, and high risk for CAD (5%, 25%, and 50%), enrolling 200,000 persons per category (100,000 per strategy). The clinical outcomes compared were the number of deaths (including from MI, during exercise, or during angiography), the number of MIs, and complications

from angiography, as well as the number of angiographies and the number of people who exercised, at five years.

Utility and Sensitivity Analyses

In a utility analysis, a value was assigned to each terminal node in the tree to represent the estimated quality of life in the health-state represented. These utility values, ranging from 1 for good health to 0 for death and based on literature whenever possible, are shown in Table 1. We defined disutility and added utility as reduction and increment in utility from a specific condition. A one-way sensitivity analysis was performed, replacing the value of each variable in the decision model with its upper and lower limits shown in Table 1, while holding the other values constant. In the base case scenario, the pretest probability for CAD was 5%, the rate of regular exercise was 75% and the risk of sudden cardiac death during exercise 0.05% (see Table 1). Three-way sensitivity analyses were performed with selected variables found most influential on a Tornado diagram.

RESULTS

Monte Carlo Simulations

The results of the Monte Carlo simulations are shown in Table 2. In a population with a 5% prevalence of CAD, ETT prior to initiating regular exercise did not reduce cardiac morbidity and mortality when compared to no ETT: although

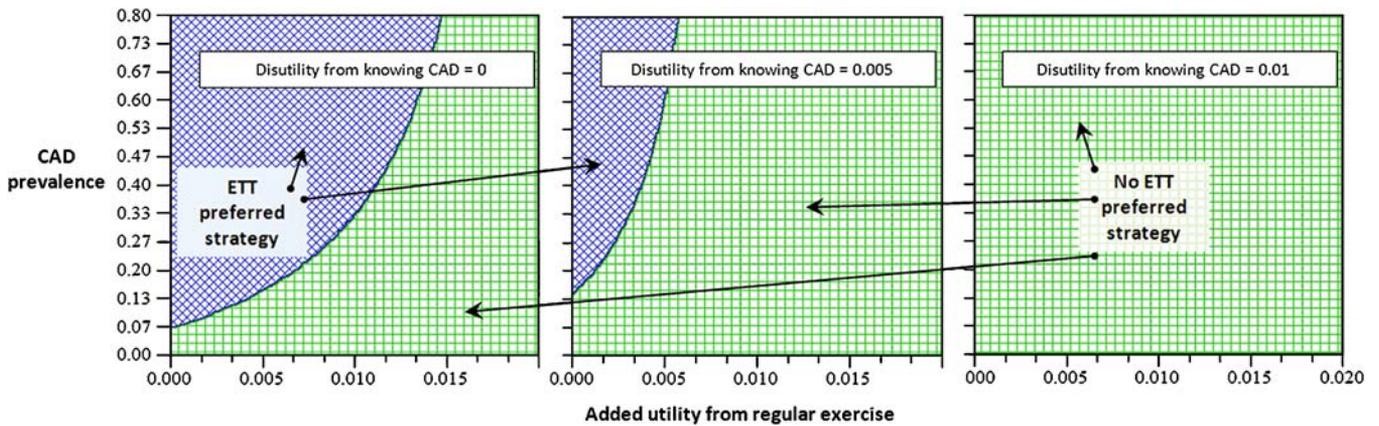


Figure 2. Preferred strategy (ETT or no ETT) at various CAD prevalence rates and for individual preferences: added utility from regular exercise and disutility from knowing CAD. For instance, at a CAD prevalence rate of 20% (0.20), if there is no perceived inconvenience from knowing this diagnosis (Disutility from knowing CAD = 0, left panel), and if there is no perceived quality of life advantage from physical activity (Added utility from regular exercise = 0.000), the preferred strategy falls in the blue area, i.e., ETT is recommended before beginning regular exercise. On the other hand, if there is some perceived inconvenience from knowing CAD (Disutility from knowing CAD = 0.01, right panel), at any CAD prevalence rate and regardless of the perceived quality of life advantage from physical activity, the preferred strategy falls in the green area, i.e., no ETT is recommended before beginning regular exercise.

identifying real CAD patients. Stigmatizing asymptomatic persons as CAD patients carries the risk of reducing the quality of life of healthy people, while patients who actually have CAD benefit from options for preventing morbidity and mortality through medical management. Finding the appropriate balance between these competing effects benefits from formal decision analysis, because intuition is ineffectual for computing multiple probabilities and utilities.

The ETT strategy appeared to decrease mortality in persons at intermediate or high risk for CAD. This reduction was due to the prevention of CAD-related deaths by medical management, not from the prevention of exercise-induced deaths that would have been off-set by the added deaths from PCI (see Table 2). This result speaks directly to the current controversy about whether to screen a healthy population for CAD.⁸ The decision about whether to perform a screening ETT should be separated from the decision about whether to start an exercise program and should not prevent the initiation of regular physical activity.

Our study has several limitations. Little empirical evidence about preventing exercise-induced death via therapy is available. Our assumptions (that exercise-induced death is 50% lower among those with a negative ETT and is eliminated following PCI and medical management) might be overly optimistic; therefore, our conclusion could be biased in favor of the screening ETT. The rate of referral to cardiac rehabilitation after positive ETT and PCI for asymptomatic people could be higher than after MI, but sensitivity analysis showed that our conclusion was not affected over the wide range of referral rate tested. Our model is a simplified theoretical approach that may or may not accurately represent reality, but it does provide a framework for decision-making in the absence of randomized controlled trials. In the future, as ETT is refined by elegant but costly coronary imaging modalities,¹⁴ our conclusions will need to be re-evaluated (once data on sensitivity and specificity become stable) and will benefit from an added economic evaluation. Finally, our study did not address other potential values from ETT prior to initiating physical activity, such as determining baseline fitness level and adapting appropriate individual exercise intensity.

If screening ETT is unsatisfactory for preventing exercise-induced cardiac events, other modalities should be explored, such as promoting public education about the need for gradual initiation of physical activity and about alarming symptoms (including through signs at gyms), while improving the availability of semi-automatic defibrillators and personnel trained in life support at sports facilities.²

In conclusion, our analysis does not support routine ETT before initiating regular exercise for the purpose of reducing the risk of sudden death during exercise training.

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