



Exercise tolerance test for predicting coronary heart disease in asymptomatic individuals: A review

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ABSTRACT

In symptom-free subjects, exercise tolerance testing (ETT) has a doubtful utility for detecting latent coronary heart disease (CHD) because of frequent false positives, but it may be valuable for predicting future CHD. To clarify the latter question, we calculated CHD incidence associated with presence or absence of ETT-induced abnormalities of ST-segment depression, exercise capacity, and heart rate using published prospective ETT studies in primary prevention populations.

Based on 5–23 years of follow-up, yearly incidence of fatal and non-fatal CHD ranged from 0.9 to 5.8% in the presence of ST-segment depression and from 1.2 to 1.7% in the presence of impaired maximal heart rate, and pooling of all data provided a linear positive relationship between pre- and post-test CHD incidence. Yearly incidence of CHD death was 0.8% in the presence of ST-segment depression, 0.2–0.3% in the presence of impaired heart rate recovery, and 0.5% in the presence of low exercise capacity. Absence of ST-segment depression was associated with <1.5% yearly incidence of fatal and non-fatal CHD events, except for one study and <0.2% yearly incidence of CHD or CVD death in all populations analyzed.

Lastly ETT-induced ST-segment depression conveys a CHD risk superior to that associated with ETT-induced heart rate and exercise capacity abnormalities. This may be due to difference in pretest CHD incidences in ETT studies.

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1. Introduction

In symptom-free subjects without known history of cardiovascular disease (CVD), exercise tolerance testing (ETT) is not recommended for detecting underlying coronary heart disease (CHD) because of many false positives of ST-segment depression related to low pretest CHD probability [1]. However, it has been suggested that ETT abnormalities, in particular those unrelated to ST-segment but linked with exercise capacity and heart rate, may be of prognostic utility for predicting a future CHD event in subjects with moderate cardiovascular risk [2–4]. Despite its prognostic potential, ETT remains controversial and is not used much for assessing cardiovascular risk, comparison with non-invasive subclinical atherosclerosis testing such as coronary artery calcium scanning, ankle brachial index measurement and carotid artery ultrasound [5,6]. To try to clarify this debate we have undertaken a review of the main prospective ETT studies in primary prevention with the objective of describing association of ETT-induced

abnormalities of ST-segment, heart rate and exercise capacity with absolute risk of CHD event.

2. Methods

2.1. Subjects

Our analysis was restricted to studies whose published data allowed the calculation of the incidence of CHD events by the presence or absence of ETT abnormality at the onset of the follow-up. All subjects at inclusion were free from cardiovascular symptoms or history of clinical cardiovascular disease. Their sex, age and main risk characteristics are shown in Tables 1 and 2.

2.2. ETT abnormalities

Alterations of ST-segment, exercise capacity and heart rate induced by maximal graded exercise treadmill testing, were analyzed [2,7–11]. ST-segment depression was defined as a J point depression with flat or downsloping ST-segment ≥ 1 mm [8–16] or 2 mm [17] in men, or ≥ 1.5 or 2 mm in women [9]; In addition, ST-segment depression should occur in most complexes in any lead [8–12] or in 3 or more consecutive beats during exercise or post-exercise recovery [9,18]. Another definition was ST integral

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Table 1
Incidence of coronary events according to ETT-induced abnormalities of ST-segment, and heart rate in asymptomatic people. CHD, coronary heart disease; MI, myocardial infarction; RV, revascularization; FRS, Framingham risk score; BLSA: Baltimore Longitudinal Study of aging; JHSS: John Hopkins Sibling Study; SHWS: Seattle Heart Watch Study; KIHD: Kupio Ischemic Heart Disease; LRC: Lipid Research Clinics; MRFIT: Multiple Risk Factor Intervention Trial; FHS: Framingham Heart Study; NR, non-relevant; HC, hypercholesterolemia; max HR, maximum heart rate.

Study	Sex distribution age, y characteristics	Type of event	Exercise ECG result	No. of subjects	Prevalence of abnormal/normal ST, %	Follow-up duration, y	No. of events	Yearly incidence of event, %
ETT-induced abnormalities of ST-segment BLSA [8]	100% men	Angor/MI/coronary death	ST-segment depression ≥ 1 mm	137	22	6.9	23	2.4
	>40 Healthy volunteers		Normal ST-segment	360	59	10.5	14	0.4
BLSA [8]	100% women	Angor/MI/coronary death	ST-segment depression ≥ 1 mm	76	16	8.0	8	1.3
	>40 Healthy volunteers		Normal ST-segment	251	53	8.4	7	0.3
JHSS [9]	69% men	Cardiac death/MI/RV	Abnormal ST-segment ^a	26	10	4.6	7	5.8
	37–59 Siblings of premature CHD		Normal ST-segment	232	90	6.2	12	0.8
Giagnoni [12]	73% men	Angor/MI/sudden death	ST-segment depression ≥ 1 mm	135	NR	6	21	2.6
	35–55 Case-control Workers cohort		Normal ST-segment	379	NR	6.4	13	0.5
Allen [14]	65% men	Angor/MI/coronary death	ST-segment depression ≥ 1 mm	104	12	5	15	2.8
	44 on average Hospital cohort		Normal ST-segment	735	83	5	30	0.8
SHWS [16]	100% men	Angor/MI/sudden cardiac death	ST-segment depression ≥ 1 mm	264	11	5.6	14	0.9
	44 on average Industrial/clinical cohort		ST-segment depression < 1 mm	2101	89	5.6	33	0.2
KIHD [18]	100% men	Acute MI	ST-segment depression ≥ 1 mm	145	8	10	29	2.0
	42–60 Population-based cohort		Normal ST-segment	1580	92	10	145	0.9
LRC [17]	100% men	MI/coronary death	ST-segment depression ≥ 2 mm or ST integral depression $20 \mu\text{Vs}$	50	3	7.4	11	3.0
	35–59 Untreated HC		Intermediate ST depression	104	6	7.4	16	2.1
			Normal ST-segment	173	91	7.4	167	1.3
MRFIT [15]	100% men	Angor/MI/coronary death	ST integral depression $\geq 16 \mu\text{Vs}$	734	12	7	201	3.9
	35–57 10–15% upper FRS		Normal ST-segment	5416	88	7	888	2.3
ETT-induced abnormalities of heart rate FHS [10]	100% men	Angor/MI/coronary death	$< 85\%$ age-predicted max HR	327	24	7.7	44	1.75
	43 on average Healthy volunteers		$\geq 85\%$ age-predicted max HR	1248	76	7.7	51	0.53
SHWS [16]	100% men	Angor/MI/sudden cardiac death	$< 90\%$ age-predicted max HR	132	6	5.6	9	1.21
	44 on average Industrial/clinical cohort		$\geq 90\%$ age-predicted max HR	2233	94	5.6	38	0.30

^a ST-segment depression > 1 mm in men, > 1.5 or 2 mm in women depending of ECG leads.

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