

NOVEL EFFORTLESS SCREENING FOR ISCHEMIA: RESULTS FROM CLINICAL TRIALS AND REAL-WORLD DATA

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BACKGROUND

- The noninvasive detection of myocardial ischemia requires complex imaging modalities associated with:
 - Relatively low sensitivity and specificity (EST)
 - Possible radiation exposure (MPI, CT-angiography)
 - Increased costs (stress echo, MPI, CT-angiography)



HEART RATE VARIABILITY

- Heart rate variability (HRV):
 - Noninvasive
 - Relatively inexpensive test
 - Does not expose to ionizing radiation
 - Has been shown to correlate with all-cause mortality, cardiovascular and sudden cardiac death
 - Attenuated in CAD, and may possibly be used for the early detection of myocardial ischemia



HeartTrends

- A novel HRV algorithm developed by Lev El for the purpose of noninvasive detection of myocardial ischemia using simple 1-hour Holter testing

Easy to use Software

HeartTrends™ Client Application <Admin>

Logged User: Admin
Logout

HeartTrends™ Client Application

LevEL
Diagnostics of Heart Diseases

New Patient / Start Test | Download Data / Finish Test | Generate Report | Settings | About

New Patient / Start Test

Patient ID:

Patient Name:

Patient Birth Date: יום שני 10 מרץ 2014

Patient Age:

Gender: Male Female

Holter Device:

Store Clear

Extra Info

- Diabetes
- Established Ischemic Heart Disease
- Atrial Fibrillation or Flutter
- Acute Coronary Syndrome
- Cardiac Pacemaker
- Preliminary Clinical Diagnosis of Heart Failure
- Active Myocarditis
- Drugs
- Alcohol
- Beta Blocker
- Family Heart Diseases History
- Renal Failure
- Hypertension
- Smoking
- Dyslipidemia

LDL: HDL: TG:



Insert card reader to PC



PROOF OF CONCEPT

- We hypothesized that the HeartTrends algorithm is superior to conventional exercise stress testing (EST) for the detection of myocardial ischemia
- We report data from prospective multicenter clinical trials and real world experience on the diagnostic performance of the HeartTrends algorithm for the detection of myocardial ischemia in patients without previously diagnosed coronary artery disease



METHODS



STUDY POPULATION

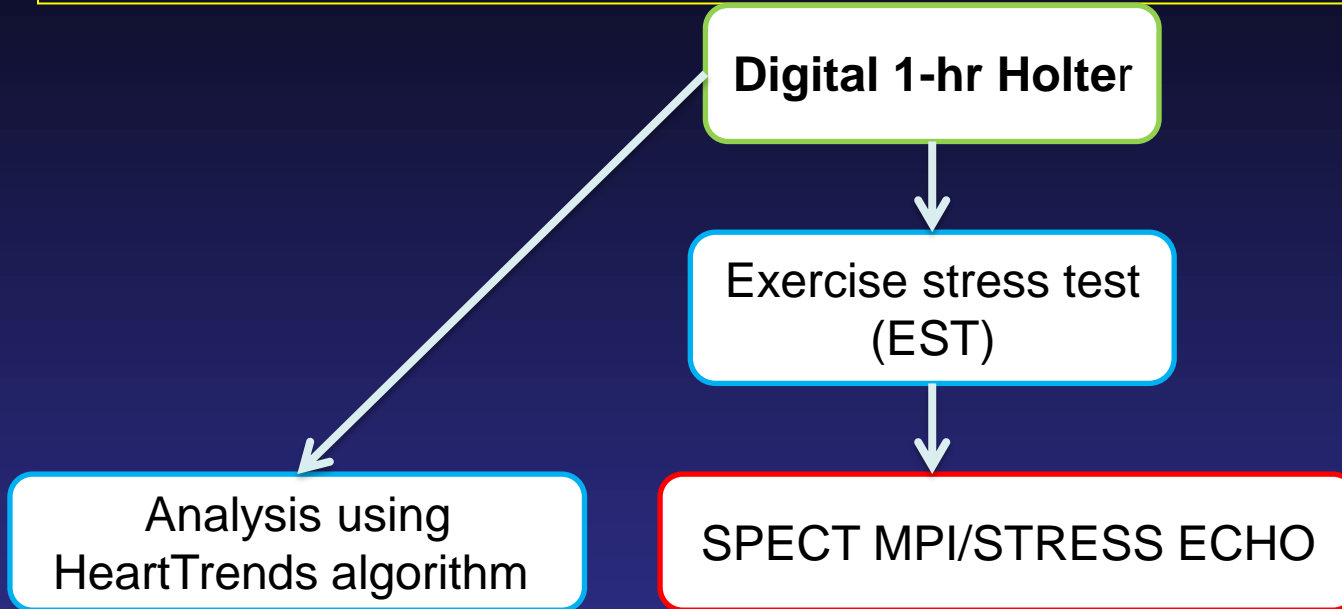
- Pooled analyses from:
 - Completed prospective multicenter clinical trial with MPI as endpoint (Sheba Medical Center and Rabin Medical Center, Shaarai Tzedek Israel)
N = 450
 - Ongoing prospective clinical multicenter trial with stress echo as endpoint (Mayo Clinic, Rochester, MN and Scottsdale, AZ, Sheba Medical Center and Rabin Medical Center)
N = 383
 - Clinical experience at SMC
N = 152
- **Total: N = 985**



STUDY POPULATION

- **Inclusion criteria:**
 - **Age \geq 21 years**
 - **Referral for exercise MPI/stress echo by treating physician**
 - **Willing and able to provide written informed consent**

STUDY DESIGN



Comparison between:

- EST
- HeartTrends HRV

Gold standard:

MPI/STRESS ECHO
positivity

DEFINITIONS: EST

- **Positive EST:**
 - ≥ 1 mm of horizontal or down-sloping ST-segment depression ≥ 80 milliseconds after the J-point (as compared to the level of the PQ interval)
 - ST segment elevation ≥ 1 mm in a non-Q wave lead other than V1 or AVR
 - Evidence of ischemia (clinical or electrocardiographic) and >10 mmHg BP drop during effort



DEFINITIONS: HeartTrends

- **Positive HeartTrends result:**
 - HeartTrends analyzes the R-R wave intervals data based on a proprietary algorithm
 - The output translated into a score called the Dy/Dx indicator value
 - A Dy/Dx indicator value which is < 2.0 is considered to be positive

STATISTICAL ANALYSIS

- Parameters assessed:
 - Sensitivity
 - Specificity
 - Positive predictive value
 - Negative predictive value
- Comparative analysis for the end point of a positive MPI/stress echo

RESULTS



CLINICAL CHARACTERISTICS

Age	61 ± 11 years
Age ≥ 65 years	42 %
Women	41 %
Hypertension	49 %
Dyslipidemia	56 %
DM	20 %
Familial Hx	48 %
Prior TIA/CVA	2 %
<i>Smoking condition</i>	
Past	21 %
Present	18 %
BMI	28 ± 5
Positive MPI/stress echo	8%



DIAGNOSTIC YIELD

	HeartTrends	EST
Sensitivity	75%	36%
Specificity	71%	89%
PPV	16%	15%
NPV	96%	94%



MULTIVARIATE ANALYSIS

Test	Odds Ratio for Ischemia*	95% Confidence Interval
HeartTrends (positive)	7.8	2.9 – 23.3
EST (positive)	2.3	0.9 – 8.5

- For the gold standard of MPI
- Adjusted for age, gender, Htn, dyslipidemia, DM, BMI

Relative incremental value X 4.2



CONCLUSIONS

- Our data indicate that the novel HeartTrends HRV algorithm shows a high sensitivity and negative predictive value for the detection of myocardial ischemia in patients without known CAD
- Sensitivity and relative incremental value is significantly higher than conventional EST



CLINICAL IMPLICATIONS

- **These findings suggest that the HeartTrends algorithm can be used as a simple screening modality for the early detection of coronary artery disease**

THANK YOU



Sheba Medical Center
Tel Hashomer

