A Novel Heart Rate Variability Algorithm for the Detection of Myocardial Ischemia: Pilot Data from a Prospective Clinical Trial

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Background

- Detecting asymptomatic IHD is complex as current modalities have either, low sensitivity and specificity, or involve exposure to radiation and have a significant cost.

- HRV - non-invasive, relatively inexpensive, does not involve radiation.

- Heart rate variability (HRV) analysis has been shown to be a predictor of all cause and CV mortality.
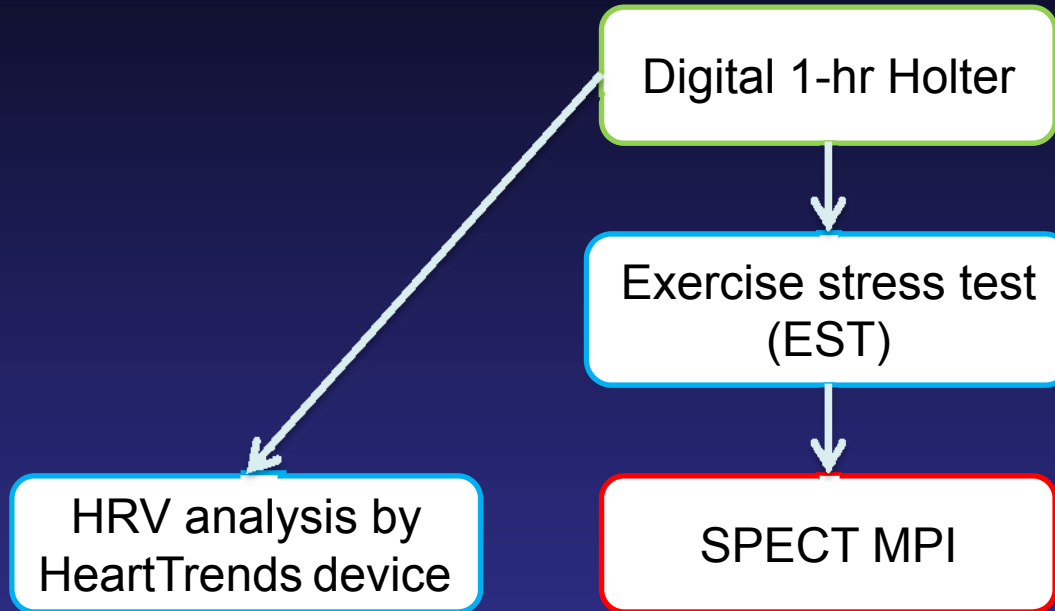
Objective

- We hypothesized that new HRV analysis algorithms, as used by the HeartTrends device, may be superior to conventional exercise stress testing (EST) for the detection of myocardial ischemia in patients without known CAD.

- To validate the diagnostic performance of the HeartTrends device for the detection of myocardial ischemia in patients without previously diagnosed coronary artery disease who are referred for myocardial perfusion imaging (MPI).

Study Design

- Prospective single-center clinical trial

- Inclusion criteria:

  - Age ≥ 21

  - Referral for exercise MPI by treating physician

  - Willing and able to provide written informed consent

Study Design

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                    │  Digital 1-hr Holter │
                    └─────────────────────┘
                       /              │
                      /               ▼
                     /        ┌─────────────────────┐
                    /         │ Exercise stress test │
                   /          │        (EST)         │
                  /           └─────────────────────┘
                 ▼                      │
    ┌─────────────────────┐            ▼
    │   HRV analysis by   │   ┌─────────────────────┐
    │ HeartTrends device  │   │     SPECT MPI       │
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Comparison between:	Gold standard:
– EST	MPI positivity
– HeartTrends HRV	

Study Population

- Sample size: 325 patients to show 70% sensitivity of HRV algorithm

- <u>Current report</u>: pilot data of first 100 patients enrolled

Definitions: EST

- Positive EST:

  - ≥1mm 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 ≥ 1mm in a non-Q wave lead other than V1 or AVR

  - Evidence of ischemia (clinical or electrocardiographic) **and** >10 mmHg BP drop during effort.
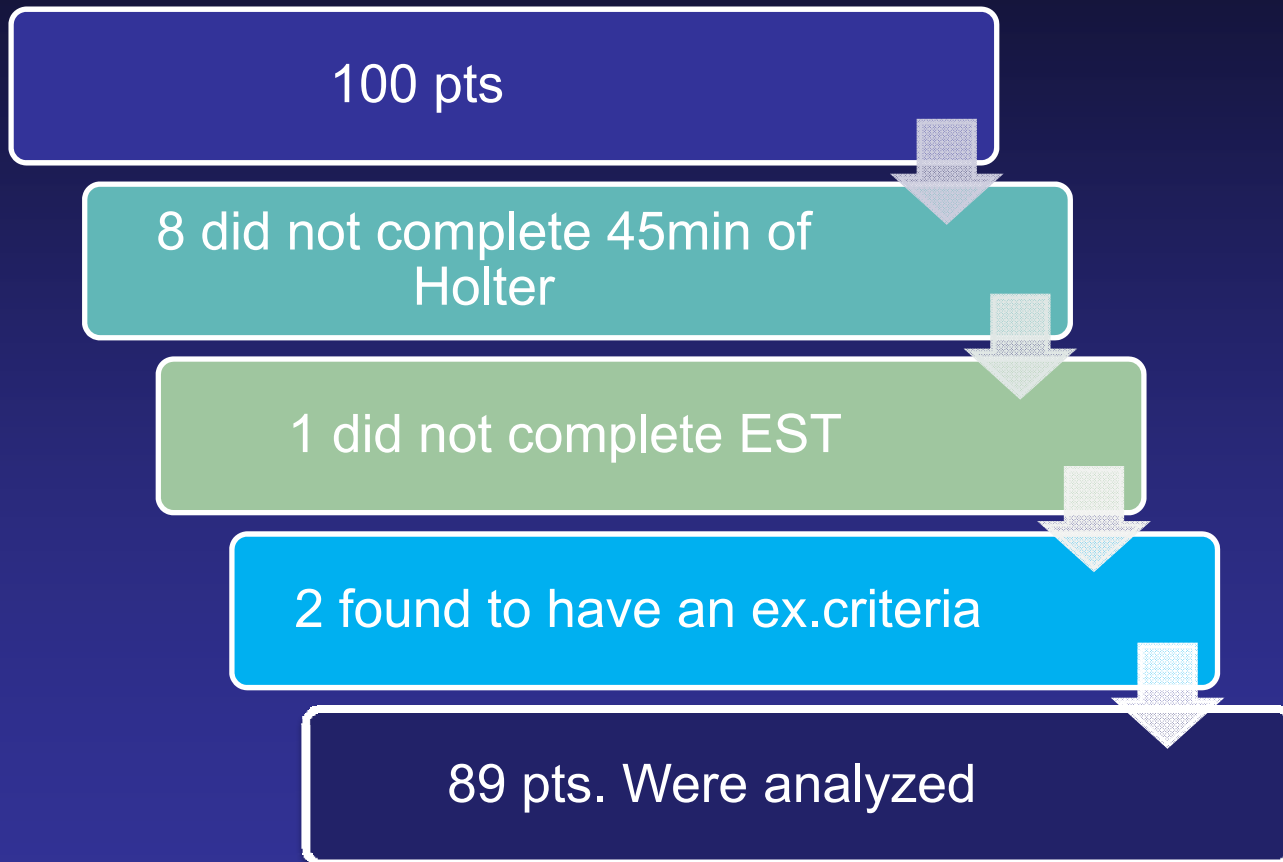
Definitions: HRV

- Positive HRV (HeartTrends):
  - HeartTrends analyzes the R-R wave intervals data based on a proprietary algorithm
  - The output received is 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

Results

100 pts

8 did not complete 45min of Holter

1 did not complete EST

2 found to have an ex.criteria

89 pts. Were analyzed

Clinical Characteristics

Baseline characteristics	
Age	61 ± 10 years
Age ≥ 65	35 %
Male	59 %
Hypertension	52 %
Dysplipidemia	64 %
DM	21 %
Familial Hx	44 %
PVD	0 %
Prior TIA/CVA	2.4 %

Smoking condition
    Past
    Present
	
	20 %
	25 %

BMI	28.7 ± 5.6

Outcome Analysis

Test	Relative Risk for CAD*	95% Confidence Interval
HRV (positive)	16.8	4 – 71.4
EST (positive)	3.48	1.34 – 9.00

* As evident by MPI

Relative incremental value X 4.83

Diagnostic Yield

- In our study cohort 15% of pts were found to have a positive MPI.

	HRV	HRV in ≥65 Years
Sensitivity	**85 %**	**100 %**
Specificity	86 %	89 %
PPV	50 %	57 %
NPV	**97 %**	**100 %**
Accuracy	85 %	

Conclusions

- Our pilot data suggest that the novel HeartTrends HRV algorithm shows improved sensitivity and NPV for the detection of CAD compared with EST.

- The diagnostic yield may be even more pronounced among subjects ≥ 65 years.

- Validation of pilot findings are expected at completion of enrollment.

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