

# HyperQ: High-Frequency QRS (HFQRS) Analysis for the Detection of Myocardial Ischemia and CAD

**Medicare Evidence Development & Coverage Advisory Committee**  
**November 9, 2011**

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# ECG-based stress testing: limitations and their implications

- Exercise induced changes in the ECG have been used as a first line test for coronary artery disease for more than 50 years
- However, the performance of ECG-based stress test is limited by its low sensitivity and specificity, which varies considerably (meta analysis results: sensitivity of  $68\pm16\%$  (range 23–100%); specificity  $77\pm17\%$  (range: 17–100%))<sup>1</sup>.
- Sensitivity and specificity values reported for women are even lower (sensitivity  $61\pm7\%$ ; specificity  $70\pm6\%$ )<sup>2</sup>.
- Main implications of the limited clinical accuracy of stress testing include unnecessary radioactive and invasive follow-on tests, false negative results leading to increased mortality, and excessive costs to the health system.

1 Gianrossi R et al. *Exercise-induced ST depression in the diagnosis of coronary artery disease: a meta analysis.* Circulation 1989;80:87–98.

2 Kwok Y et al. Meta-Analysis of exercise testing to detect coronary artery disease in women. The American Journal of Cardiology 1999;83:660-666

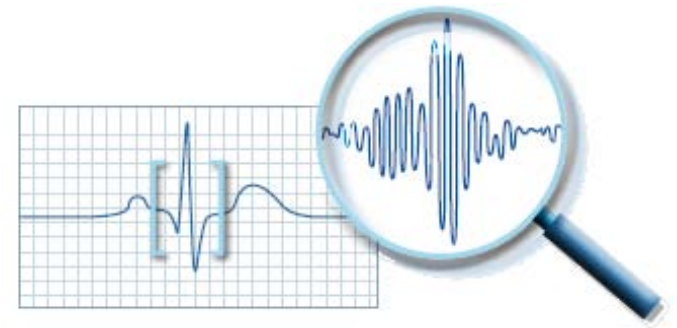
# High Frequency QRS Analysis

## Conventional ECG

- Slowly-varying signal, low frequency band (0.05-100Hz)
- Amplitude measured in millivolts

## High-frequency QRS (HFQRS)

- Fast-varying waveforms within the QRS complex (150-250Hz)
- Low amplitude, measured in micro-volts



**Additional valuable information is hidden in the higher frequency range of the ECG signal<sup>3,4</sup>**

<sup>3</sup> Abboud et al. Detection of transient myocardial ischemia by computer analysis of standard and signal averaged high frequency ECG in patients undergoing percutaneous transluminal coronary angioplasty. *Circulation* 1987;76:585-96

<sup>4</sup> Pettersson J et al. Changes in high-frequency QRS components are more sensitive than ST-segment deviation for detecting acute coronary artery occlusion. *J Am Coll Cardiol* 2000;36:1827-34

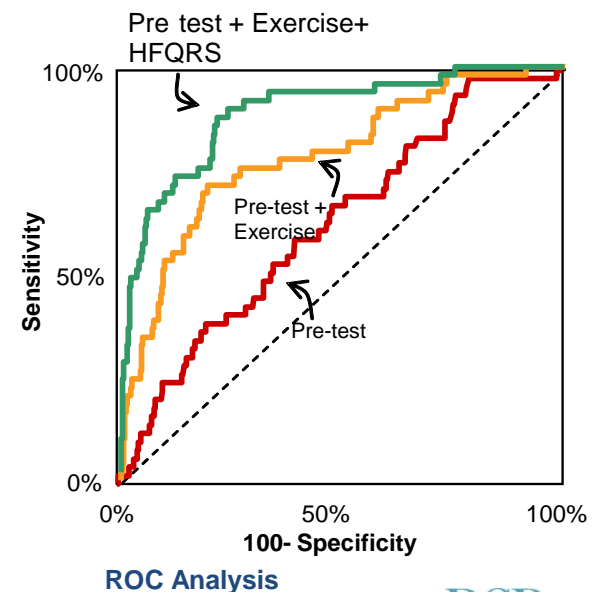
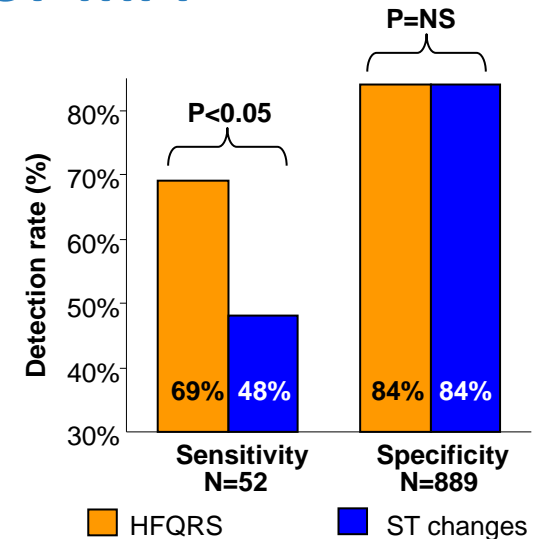
# Clinical application:

## Stress HyperQ for the detection of CAD

- Technology for quantifying ischemic changes in HFQRS during exercise testing, using standard stress protocol
- The underlying algorithms filter and amplify high frequency components in the 150Hz – 250Hz frequency band
- FDA 510(k) cleared (2008, K082564, 21 CFR 870.2300)
- Indications for use (excerpt): “The HyperQ software is intended to be used as an aid to the ECG stress test by means of analysis of high frequency components present within the central portion of the QRS complex.”

# Clinical Value: HFQRS improves the accuracy of exercise ECG in patients referred to SPECT-MPI

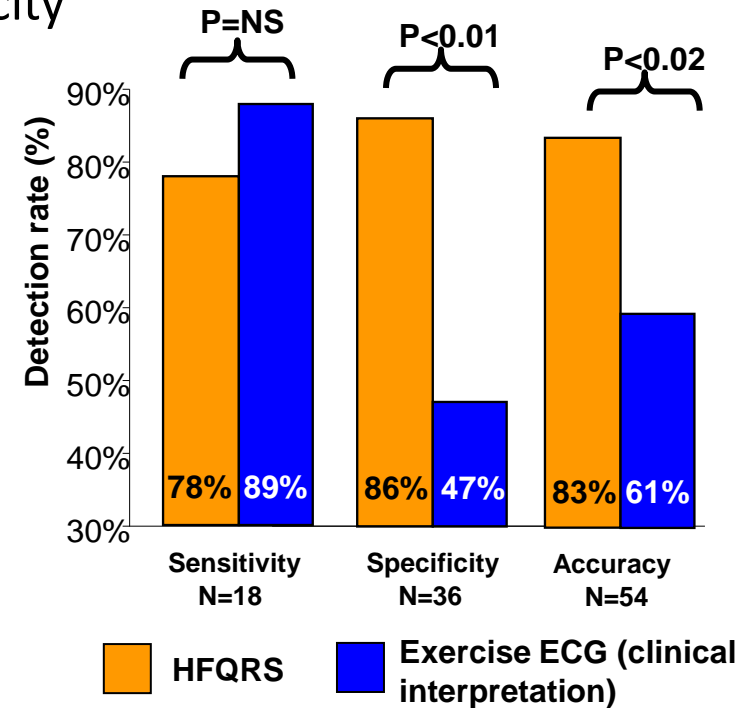
- Objectives: Assess the diagnostic value of HFQRS for detecting stress-induced ischemia; Determine the incremental value of HFQRS over ECG-based stress test for the diagnosis of CAD.
- Population: 941 consecutive patients (630 men), referred for evaluation of CAD at two medical centers. SPECT MPI served as the reference standard
- Results: HyperQ (HF QRS) index was more sensitive than ST segment analysis (69% vs 48%,  $p=0.03$ ) with similar specificity (84%).
- Conclusions: HyperQ index offered significant incremental diagnostic value over clinical and exercise test data and correlated to ischemia severity ( $R^2=0.8$ ,  $p<0.001$ ).



Sharir T et al. Detection of Stress-Induced Myocardial ischemia Using Analysis of Depolarization Abnormalities. *J Am Coll Cardiol* 2009; 53(10):A297 (abstract, presented at the ACC meeting 2009)

# Clinical Value: HFQRS has higher accuracy than ST segment analysis in women

- Objectives: Evaluate the diagnostic accuracy of HFQRS in detecting exercise-induced ischemia in women
- Population: 54 women referred for non-urgent angiography. Angiography served as the reference standard.
- Results: HFQRS analysis provided higher specificity (86% vs 47%) and higher total accuracy (83% vs 61%) than exercise ECG, with comparable sensitivity
- Conclusions: HFQRS analysis improved the specificity and the overall accuracy of the stress test. Incorporation of HFQRS analysis into the diagnostic routine in women may reduce the number of unnecessary angiography procedures.



Rosenmann D et al. Novel technology enhances specificity of exercise testing in Women referred for angiography. *Eur Heart J* 2010; 31:980 (abstract, presented at the ESC Congress 2010)

# Summary of Stress HyperQ (HFQRS) Studies

Study	No. of Patients	Reference standard	Sensitivity		Specificity	
			HyperQ	ECG	HyperQ	ECG
Assuta-Sheba (Israel)	996 pts	SPECT	69%*	39%	86%*	82%
Duke-CAMC (US)	101 pts	SPECT	79%*	41%	71%*	57%
Shaare- Zedek (Israel)	107 women pts	Angiography	70%	72%	78%*	58%
Rabin MC (Israel)	98 pts	SPECT	76%*	59%	85%*	57%
Samsung MC (S. Korea)	175 pts	Angiography / CTA	71%*	44%	76%	73%

\* Statistically significant difference vs. ECG (P<0.05)

## Inclusion of stress test combined with HFQRS analysis in the clinical work-up of suspected CAD: Main Benefits

- Improved sensitivity decreases false-negative rate and lowers mortality and morbidity
- Improved specificity may prevent unnecessary nuclear tests and decreases unwarranted exposure to radiation
- Improved accuracy in women population allows better clinical evaluation of women for possible CAD \*
- Combined analysis of ST-segment and HFQRS in stress testing reduces the rate of non-diagnostic and inconclusive cases and enables effective stress testing for broader populations

\* "The accuracy of the exercise ECG for diagnosis of coronary disease in women is problematic." (ACC/AHA Guidelines for Exercise Testing: Executive Summary. Circulation 1997;96:345-354)



# Summary and Recommendations

- Improvement to first line diagnostic tests for CAD has significant impact on health outcomes
- HFQRS analysis during stress testing has demonstrated significantly improved clinical accuracy for the detection and diagnosis of CAD
- Devices that incorporate HFQRS analysis in stress ECG testing and that are cleared by FDA should be incorporated in coverage policies.