EDITORIAL COMMENTARY

Letter by Garcia A, et al. regarding article: Coronary artery disease risk reclassification by a new acoustic-based score

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Abstract

The best cost-effective non-invasive test for the diagnosis of coronary artery disease (CAD) in patients with intermediate pre-test probability (PTP) is unknown. Nevertheless one of the most common non invasive test used is the exercise treadmill testing (ETT) that is the less expensive non-invasive test but with the lowest sensitivity for the diagnosis of CAD, therefore many patients with intermediate PTP will required another non-invasive test with a higher cost and some of them require exposure to radiation. Despite all these measures, an estimated $108.9 billion is spent annually on CAD treatment. Some studies had showed that diastolic dysfunction is associated to CAD. A novel signal-processed surface ECG (MyoVista hsECG) can detection the abnormal myocardial relaxation and therefore identified CAD. The non-invasive acoustic device CADScore V3 algorithm had lower cost compared with any noninvasive test, with a high negative predictive value but not good enough specificity to diagnose CAD, hence should be the first approach in patients with a low and intermediate probability of CAD, and if to this evaluation will added the Myovista hs ECG to detection of CAD, therefore some patients with intermediate PTP could be reclassified into high risk and a better cost-effective decisions could be taken as referring directly to coronary angiography.

Keywords Coronary artery disease · Non-invasive acoustic device · Diastolic disfunction · Cadscore · Cadence · Non-invasive test · Pre-test probability of coronary artery disease · CAD consortium clinical score · MyoVista hsECG

We congratulate to Schmidt et al. for the non-invasive acoustic device CADScor®System Acarix A/S with the CADScore V3 algorithm to reclassify patients with intermediate pre-test probability (PTP) and clinically suspected stable coronary artery disease (CAD) into a low probability group thereby ruling out significant CAD [1].

Evaluation of individuals without known CAD presenting with stable chest pain syndrome is most cost-effective when exercise treadmill testing (ETT) is performed first, followed by imaging tests for ETT that is equivocal or not able to be performed. In individuals up to high likelihood of significant CAD, stress echocardiography (SE) or coronary computed tomographic angiography (CCTA) represent the most cost-effective strategies [2]. Despite all these measures, an estimated $108.9 billion is spent annually on CAD treatment [3].

The ETT is a less expensive non-invasive test but with the lowest sensitivity for the diagnosis of CAD, therefore many patients with intermediate PTP will require another non-invasive test with a higher cost and some of them require exposure to radiation (see Table 1).

The SCOT-HEART Coronary CTA Cohort study n = 1738, compared 3 risk scores for estimating PTP of CAD, the updated Diamond-Forrester score (UDF), CAD Consortium clinical score (CAD2) and Confirm risk score (CRS). The discrimination of each score was assessed by area under the receiver-operating curve (AUC) and reclassification by net reclassification improvement (NRI) to identify low-risk patients at the 10% probability. The CAD2 provided the best discrimination (CAD2 AUC 0.79, UDF AUC

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Table 1 Non-invasive tests used to diagnose coronary artery disease

Non-invasive test	Sensitivity (%)	Specificity (%)	References
Exercise treadmill testing (ETT)	45–50	85–90	[18]
Stress echocardiography (SE)	82	84	[19]
Coronary computed tomography angiography (CCTA)	85	90	[20]
Single-photon emission computed tomography (SPECT)	83	77	[21]
Vasodilator stress positron emission tomography (PET)	81–97	74–91	[22]
Vasodilator stress magnetic resonance imaging	67–94	61–85	[22]

0.77, CRS AUC 0.75, $p < 0.001$ for both comparisons) and also the best reclassification (CAD2 NRI 0.31, CRS NRI 0.21 vs UDF, $p < 0.001$ for all comparisons) [4].

Some studies had shown that diastolic dysfunction is associated with CAD [5]. Hoffmann et al. showed that patients with significant CAD compared with those without significant CAD had more abnormal echocardiographic diastolic parameters. After multivariable analysis tissue Doppler echocardiography (TDE) parameters of early diastolic velocity (e′) and systolic velocity (s′) remained independent predictors of CAD, e′ odds ratio (OR) 1.5 (1.1–1.9, $p < 0.01$) per cm/s decrease and s′ OR 1.7 (1.1–2.5, $p < 0.05$) per cm/s decrease. AUC for ETT in combination with TDE was significantly higher than AUC for ETT alone (0.84 vs 0.79, $p < 0.01$) [6]. Hwang et al. demonstrated in patients with heart failure with preserved ejection fraction (HFpEF) the 68% had angiographically-proven CAD [7]. HFpEF is defined by left ventricular ejection fraction (LVEF) $\geq$ 50 percent and the dominant abnormality resides in diastole [8]. Therefore early recognition of left ventricular diastolic performance alteration may signal the presence of CAD.

Recently some electrocardiographic (ECG) novel signs for detection of diastolic dysfunction has come out. The QT interval is measured from the beginning of the QRS complex to the end of the T wave and approximates the time it takes the ventricles to repolarize. Long QT syndrome (LQTS) is the prolongation of the QT interval. LQTS may be either congenital or acquired [9]. The National Health and Nutrition Examination Survey III (n = 8561) showed that risk factors for acquired prolonged QTc interval were the age, female sex, hypocalcemia, hypokalemia, history of thyroid disease, history of myocardial infarction and taking QT-prolonging medications [10]. LQTS has traditionally been considered to be purely electrical, but mechanical alterations in patients with LQTS were reported. Leren et al. Showed in patients with genotyped LQTS compared with healthy controls had a lower systolic function by global longitudinal strain (GLS), longer contraction duration and reduced diastolic function [11]. Disturbed diastolic function occurs with impaired sarcoplasmic reticulum calcium handling as occurs in myocardial ischemia, hypertension or diabetes [12]. Thus, the delayed uptake of calcium is pathophysiologically

associated with prolongation of QT interval [13]. Wilcox et al. Showed that QTc was inversely associated with TDE e′ with a correlation coefficient (R) = − 0.54 ($p < 0.0001$), using a cut-off value of QTc $\geq$ 435 ms had a sensitivity 73% and specificity 74% for detection of diastolic dysfunction, when restricted to patients with known or suspected heart failure (HF) had a sensitivity 80% and specificity 90% [14].

Another diastolic dysfunction ECG sign is the T-peak to T-end interval (TpTe). Sauer et al. demonstrated that increased TpTe was inversely associated with reduced TDE e′ (R = − 0.66, $p < 0.0001$) and used a cut-off value of TpTe $\geq$ 75 ms for detection of abnormal diastolic stress test (Peak exercise E/e′ > 13) [15]. Moreover, Namdar et al. showed that T-peak to P wave (Tend-P) interval using cut-off value of $\leq$ 311 ms had a sensitivity 79% and specificity 72% for detection of diastolic dysfunction, but using a novel index calculated as Tend-P interval/PQ interval × age using cut-off value of $\geq$ 0.0333 had a AUC 0.91, sensitivity 82% and specificity 93% for detection of diastolic dysfunction [16]. Many physicians are unaware of those ECG signs, and most of these signs require exact manual measurements that can take time. Sengupta et al. used a novel signal-processed surface ECG algorithm to extract electrophysiological signal patterns uniquely associated with abnormal myocardial relaxation (MyoVista hsECG Informatics, HeartSciences, Southlake, Texas), showing an AUC 0.91, sensitivity 80% and specificity 84% for prediction of low e′ velocity (septal e′ < 7 cm/s and/or lateral < 10 cm/s), low e′ velocity also correctly identified concomitant significant CAD in the 82% [17].

CADScore® System and CADenceTM Ironman are the non-invasive acoustic device approved by the CE (Conformité Européenne), CADenceTM Ironman also is approved by the FDA (Food and Drug Administration). These non-invasive acoustic devices are feasible, easy to perform at the office visit or bedside, lower cost compared with any non-invasive test, with a high negative predictive value but not good enough specificity to diagnose CAD. The pre-test probability of CAD should be calculated using the CAD2 clinical score. Definitely the non-invasive acoustic devices should be the first approach in patients with a low and intermediate probability of CAD and patients with low risk for UA. If to this evaluation will add the signal-processed surface ECG

algorithm (MyoVista hsECG) to the detection of abnormal myocardial relaxation and therefore identified CAD, hence some patients with intermediate PTP can be reclassified into high risk, and a better cost-effective decision could be taken as referring directly to coronary angiography.

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