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EDITORIAL COMMENTARY

Letter by Garcia A, et al. regarding article "The clinical evaluation of the CADence device in the acoustic detection of coronary artery disease"

Artemio García-Escobar[1] · Juan Manuel Grande[1] · Fernando Cabestrero[1]

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We congratulate Joseph L Thomas et al., Marie Johnson and Aum Cardiovascular work team that created CADence a novel device for acoustic detection of coronary artery disease (CAD) with CE (Conformité Européenne) marking and Food and Drug Administration (FDA) approval 08 of August 2017.

According to Brown et al., in their study performed with data from the National Hospital Ambulatory Medical Care Survey (NHAMCS) from 2002 to 2003 in 428 emergency departments (EDs) a total of 40,253 patients visit due to acute chest pain [1]. The Department of General Practice and Primary Care in UK reports that chest pain is a frequent cause of consultation to the family physician with almost the 2% of the population [2]. Clinical assessment like the Diamond-Forrester score [3] and the physician's judgment were used to estimate the pretest likelihood of CAD since the guidelines say that patients with chest pain of intermediate probability for CAD need a non invasive test as the first approach as well patients with stable ischemic heart disease (SIHD) or low risk for unstable angina (UA) [4, 5]. The non-invasive test probably less expensive is the exercise electrocardiography (ECG) although with a low sensitivity for the diagnosis of CAD, nevertheless there are noninvasive tests with higher sensitivity (Table 1), with higher cost too and some of them require exposure to radiation. A cost-effectiveness analysis showed that initial evaluation of patients without known CAD presenting with stable angina, the most cost-effective test is to perform first the exercise ECG test and add stress echocardiography if another assessment is required and with this approach had the best cost-effective ratio individual of $10,995; patients with more pre-test likelihood (intermediate or high) of CAD the most cost-effective test is initial stress echocardiography with $11,356 or initial Coronary Computed Tomography Angiography (CCTA) $12,274 [6]. One study showed that CCTA had a cost-effectiveness ratio ranged from $26,200/QALY (quality-adjusted life year) in men and to $35,000/QALY in women, with reducing the nonfatal myocardial infarction (MI) and stroke events compared with using the least cost-effectiveness tests, taking into account that health outcomes were marginally less favorable in women when radiation risks were considered [7]. Despite all these measures, an estimated $108.9 billion is spent annually on CAD treatment [8].

Recently a new biomarkers to diagnose CAD has come out, Ibrahim et al. The CASABLANCA study, 109 biomarkers were tested and four biomarkers (midkine, adiponectin, apo C-1 and kidney injury molecule-1) predicted CAD with high positive predictive value of 90% [14]. There are some studies showed that high-sensitivity cardiac troponin (hs-cTn) is not only used for diagnosis of MI, McCarthy et al. In their study, showed that patients without MI that had Hs-cTnI concentration ≥ 6 ng/L had a specificity of 72% for obstructive CAD [15]. The hs-cTnI it can also be a marker for guiding lipid-lowering therapy, in the WOSCOPS study, patients at office visit with Hs-cTnI > 5.2 ng/L was at the highest risk for nonfatal MI or death from coronary heart disease (CHD) and patients taking statins had a greater reduction in troponins concentration [16]. There is novel ECG sign the fragmented QRS, Das et al. Defined fragmented QRS as QRS duration < 120 ms with additional r′ or notching in the nadir of the S wave in two contiguous leads corresponding to a major coronary artery territory had more sensitivity than Q wave for myocardial scar detected by SPECT [17]. Also, fragmented QRS with QRS duration ≥ 120 ms defined as

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✉ Artemio García-Escobar
dr_garciaescobar@hotmail.com

[1] Cardiology Service, Hospital Universitario Severo Ochoa, Leganés, Madrid, Spain

Table 1 Tests commonly used to diagnose coronary artery disease

Noninvasive test	Sensitivity (%)	Specificity (%)	References
Exercise electrocardiography (ECG)	45–50	85–90	[9]
Exercise stress echocardiography (ESE)	82.7	84	[10]
Coronary computed tomography angiography (CCTA)	85	90	[11]
Single-photon emission computed tomography (SPECT)	83	77	[12]
Magnetic resonance imaging (MRI)	91	80	[12]
Vasodilator stress positron emission tomography (PET)	81–97	74–91	[13]
Vasodilator stress magnetic resonance imaging	67–94	61–85	[13]

Table 2 Handy markers of coronary artery disease

Midkine, adiponectin, apo C-1 and kidney injury molecule-1	649 Patients undergoing scheduled coronary angiography	Sensitivity 77%, specificity 84%, positive predictive value (PPV) 90% and negative predictive value (NPV) 67% to diagnose CAD	Ibrahim et al. [14]
Hs-cTnI ≥ 6 ng/L	Of 991 patients undergoing coronary angiography in patient without acute myocardial infarction	Sensitivity of 44%, specificity of 72%, the positive predictive value of 72%, and negative predictive value of 43% to diagnose CAD	McCarthy et al. [15]
ECG sign the fragmented QRS with QRS duration < 120 ms	479 Patients undergoing SPECT	Sensitivity 85.6% and specificity 89% and NPV 92.7% to diagnose myocardial scar	Das et al. [17]
ECG sign the fragmented QRS with QRS duration ≥ 120 ms	879 Patients undergoing SPECT or catheterization with ventriculography	Sensitivity 86.8%, specificity 92.5% and NPV 87.5% to diagnose myocardial scar	Das et al. [18]
MPV ≥ 10.35 fl	282 Patients who arrived at an emergency department with acute chest pain	Sensitivity 78.3% and specificity 74.6% to diagnose ACS	Chu et al. [20]
MPV 10.4 ± 1.03 fl	981 Patients undergoing to coronary angiography	Patients control group without CAD had MPV 8.2 ± 0.95 fl. Patients with UA that required immediate PTCA had MPV 10.4 ± 1.03 fl	Pizzulli et al. [21]
MPV ≥ 10.3	398 Patients with ACS treated with PTCA	Sensitivity of 61.9% and specificity of 74.3% to predict angiographic no-reflow	Huczek et al. [22]
MPV ≥ 9 fl	213 Patients undergoing to coronary angiography indicated due to ACS	Predict more significant CAD (55% vs. 35%, p = 0.005). Multivariate analysis showed that high MPV and high troponin demonstrated a 4.8 fold increased risk for significant CAD compared to those with normal MPV and high troponin (odds ratio 4.8, 95% confidence interval 1.31–17.6, p = 0.001)	Taskesen et al. [23]

> 2 notches (r′ or nadir s) had nearly same sensibility as fragmented QRS with QRS < 120 ms and was an independent predictor of mortality [18]. The mean platelet volume (MPV) is a parameter included in the routine blood test, it represents the variability in size of circulating platelets and could predict their reactivity [19]. There are some studies reported that high MPV can predict CAD and ACS. One of them showed that MPV ≥ 10.35 fl had sensitivity 78.3% to predict acute coronary syndrome (ACS) in patients with chest pain who arrived at an emergency department (ER) [20]. Another study showed that patients with CAD and stable angina had MPV 8.7 ± 1.13 fl and patients with UA that required immediate percutaneous transluminal coronary angioplasty (PTCA) had MPV 10.4 ± 1.03 fl. [21]. Huczek et al. Showed in their study patients with ACS treated with PTCA those with MPV ≥ 10.3 fl had a sensitivity of 61.9% and specificity of 74.3% to predict angiographic no-reflow [22]. Taskesen et al. in patients undergoing coronary angiography indicated due to ACS, those with MPV ≥ 9 fl had more significant CAD and in

the multivariate analysis showed that high MPV and high troponin demonstrated a 4.8 fold increased risk for significant CAD compared to those with normal MPV and high troponin [23].

CADence™ Ironman designed by Aum Cardiovascular is a novel device in the acoustic detection of CAD, as well the CADscore® System (Acarix A/S) and Cardiac Sonospectrographic Analyzer SonoMedica model 3.0. These acoustic detection devices can rule out CAD with a high NPV but not good enough specificity. Taking into account that are feasible, quick and easy to perform at the office visit or in the urgency room and low cost compared with any noninvasive test to diagnose CAD. Definitely 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 added the four biomarkers of CASABLANCA study, hs-cTnI, MPV and ECG looking for fragmented QRS (Table 2), could get higher specificity to diagnose CAD, so some noninvasive tests can be avoided, as well as better cost-effective decisions regarding referring a patient directly to coronary angiography could be taken.

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