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Editorial

Coronary artery disease diagnosis by analysis of ECG depolarization

For both men and women, coronary artery disease (CAD) is the leading cause of death in industrialized countries. CAD often shows atypical patterns in women, which makes its diagnosis particularly challenging, and in many instances misleading. Accurate CAD diagnosis is essential to provide appropriate treatment and increase the chances of positive outcome. Traditional non-invasive techniques for CAD diagnosis are based on exercise electrocardiogram (ECG) tests, from which ST-deviation is measured. Exercise ECG testing is limited in terms of sensitivity and specificity, and this is even more accentuated in women. Imaging techniques and other invasive procedures have emerged as an alternative to the ECG. However, most of those alternative methodologies are costly and some of them expose the patients to ionizing radiation. Analysis of high-frequency QRS components (HFQRS), measured on high-resolution ECG, has been suggested as an adjunct tool to conventional stress testing to improve the accuracy of a non-invasive low cost technique, such as the ECG, for CAD diagnosis.

The clinical value of HFQRS analysis has been reported in a number of studies in the literature, following its introduction by Abboud et al. in the 1980s.[1] Studies have been published where a reduction in HFQRS has been correlated to abnormal local conduction[2] and has been used to detect acute coronary occlusion.[3] Despite HFQRS showing good short-term and long-term reproducibility,[4] the large inter-individual variation exhibited by HFQRS initially suggested that this index might not be qualified for separation of subjects with and without CAD. However, recent studies have reported that reduction in HFQRS intensity during an exercise test presents a good diagnostic capacity to detect stress-induced ischemia as assessed by Myocardial Perfusion Imaging (MPI).[5]

Mechanisms underlying the reduction in HFQRS have been related to delayed ventricular activation time (AT), as proved in experimental studies where AT delay was increased by administration of sodium channel blockers[2] and in simulation studies where it was increased by regional reduction in conduction velocity.[6] HFQRS attenuation has been considered as a marker to identify CAD, as ischemia delays ventricular activation time, causing a decrease in the fragmentation of the activation wavefront. This leads to a more synchronous activation of ventricular myocardium, which thus shifts high-frequency activation to frequency components lower than those strictly contained in the 150–250 Hz band.[6]

In the present issue of the *Journal of Electrocardiology*, Rosenmann et al.[7] examine the value of HFQRS analysis for CAD diagnosis in a female population referred for angiography. Their main findings are that stress-induced attenuation of HFQRS outperforms the performance of conventional exercise ECG test, reaching sensitivity and specificity values of 70% and 80%, respectively, in the detection of angiographically significant coronary obstruction. Additionally, the number of ECG leads with positively attenuated HFQRS correlates well with the severity of CAD.

The study by Rosenmann et al. is the first one reporting results of HFQRS analysis for diagnosing CAD using angiography as the gold standard. The reported findings are consistent with those provided in previous studies, in male and female subjects, that used MPI as the gold standard. The study by Rosenmann et al. focuses on women and confirms the high specificity of HFQRS already observed in prior studies in small female subpopulations,[5] where HFQRS specificity in women was shown to be as high as that in men. Additionally, there is consistency between the results reported by Rosenmann et al. and previously published findings in terms of HFQRS performance in subpopulations of subjects with inconclusive exercise ECG and also regarding the correlation between leads with positive HFQRS and the severity of CAD.[5,8]

It is worth noting that, despite the encouraging results shown by HFQRS analysis for CAD diagnosis in the study by Rosenmann et al. as well as in other studies, the methodology used for its computation is limited by the large number of patients with non-interpretable HFQRS due to high noise levels in their ECGs. Although that number is similar to that of patients with inconclusive exercise tests and of patients with non-specific ST-T changes in their resting ECGs reported in the literature, it would be advisable to examine ways to overcome such an important limitation. In particular, alternative methodologies for quantification of depolarization changes could be explored. Evaluation of QRS slopes has been proposed to quantify changes in depolarization and has shown improved performance over HFQRS for detection of ischemia-induced alterations due to

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prolonged percutaneous coronary intervention (PCI).[9–11] QRS slopes can be measured on the raw ECG signal rather on an averaged version of it and do not require signal filtering for their measurement, avoiding any restriction on the noise level and problems such as filter ringing that can mask the nature of the measured high-frequency components, thus overcoming the major limitation associated with HFQRS. Other methodologies proposed to characterize depolarization changes, which also avoid problems associated with HFQRS measurement, include QRS duration, QRS angles, QRS fragmentation and R wave amplitude. Regarding fragmentation of the QRS complex, low-amplitude (1–50 μV) notches and slurs in the QRS complex have been defined as abnormal intra-QRS potentials (AIQPs) and have been measured using parametric modeling of the high-resolution ECG.[12] In both myocardial ischemia and infarction, localized changes in ventricular activation, due to alterations in conduction velocity around a region of functional block, have been postulated to produce AIQPs. In PCI recordings, AIQPs have been shown to significantly increase in amplitude during balloon inflation as compared to pre-inflation, which would apparently contribute to augment high-frequency QRS components. However, measurement of HFQRS in the same recordings has proved that HFQRS significantly decreases during balloon inflation, therefore confirming that the global effect of delayed ventricular activation represented by decreased HFQRS overtakes the localized low-amplitude alterations represented by increased AIQPs. Regarding R wave amplitude, augmented R-waves have been found during exercise ECG testing,[13] substantiating the diversity of alterations occurring in ventricular depolarization as a result of myocardial ischemia. Rosenmann et al. mention some of those alternative depolarization methodologies in their study, but do not establish a comparison between the performances of HFQRS and other QRS indices on their analyzed database. Furthermore, the study by Rosenmann et al. quantifies HFQRS for a specific frequency band (150–250 Hz) and considering the whole QRS complex, while other bands and temporal regions of the QRS could be explored. In relation to this, some studies in the literature have shown that frequency bands other than the traditional 150–250 Hz contain as much, or even more, information for detection of ischemia- or infarction-induced alterations in the QRS.[9,14] It would be interesting to recognize whether stress-induced changes in the above described depolarization indices, in particular the QRS slopes, outperform HFQRS analysis for CAD diagnosis, thus improving the ECG diagnostic value while retaining the property of being measurable in the whole study population.

The main conclusion of the study by Rosenmann et al. postulates that HFQRS analysis could be used as an adjunct tool to conventional exercise stress testing for detection of angiographically significant CAD. More studies are needed to investigate the degree of complementariness between HFQRS analysis and ECG exercise testing. Future studies should additionally prove whether alternative depolarization indices, with less stringent criteria on ECG noise levels, could provide diagnostic information that is even more independent from exercise testing. This would further emphasize the possibility of using the ECG to improve detection of stress-induced ischemia while reducing costs to the healthcare system.

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