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High-frequency electrocardiogram analysis in the ability to predict reversible perfusion defects during adenosine myocardial perfusion imaging

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Abstract

Background: A previous study has shown that analysis of high-frequency QRS components (HF-QRS) is highly sensitive and reasonably specific for detecting reversible perfusion defects on adenosine myocardial perfusion imaging (MPI) scans. The purpose of the present study was to try to reproduce those findings.

Methods: Twelve-lead high-resolution electrocardiogram recordings were obtained from 100 patients before (baseline) and during adenosine ^{99m}Tc-tetrofosmin MPI tests. The HF-QRS were analyzed regarding morphology and changes in root mean square voltages from before the adenosine infusion to peak infusion.

Results: The best area under the curve (AUC) was found in supine patients (AUC = 0.736) in a combination of morphology and root mean square changes. None of the measurements, however, were statistically better than tossing a coin (AUC = 0.5).

Conclusion: Analysis of HF-QRS was not significantly better than tossing a coin for determining reversible perfusion defects on MPI scans.

Keywords: HF-QRS; MPI; Adenosine; Myocardial ischemia

Introduction

Analysis of the electrocardiographic (ECG) signal has shown that particularly the QRS complex contains frequencies higher than the 0.05 to 150 Hz range used in the standard ECG.[1] These high-frequency QRS components (HF-QRS) have been studied mainly in the 150 to 250 Hz range. Analysis of HF-QRS has been shown to provide promising clinical information, particularly in patients with ischemic heart disease. A previous study has documented reduced HF-QRS in patients with ischemic heart disease compared with healthy individuals, but the interindividual variation in HF-QRS was large.[2] Analysis of HF-QRS has been shown to have a higher sensitivity than that of ST-segment elevation for detecting coronary artery occlusion.[3,4] Standard ECG, however, seems to be a better method for identifying the location of the ischemic area compared to HF-QRS.[4]

Rahman et al[5] investigated the ability of HF-QRS to estimate perfusion defects during adenosine myocardial perfusion imaging (MPI). They found that analysis of HF-QRS is highly sensitive (94%) and reasonably specific (83%) for detecting perfusion defects on MPI and is significantly more sensitive than analysis of conventional ST segments (18%). This study used a new, advanced, real-time ECG software application developed by the National Aeronautics and Space Administration (NASA) based on HF-QRS root mean square (RMS) voltage values and reduced amplitude zones (RAZ) measurements.[6,7] Beker et al[8] found that analysis of HF-QRS was 72% sensitive and 73% specific for identifying coronary artery disease in 62 subjects during treadmill exercise tests. Thus, these studies indicate that analysis of HF-QRS could provide an adjunctive tool in the diagnosis of coronary artery disease.

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The use of adenosine MPI has been firmly established in numerous clinical studies and has become an essential component of clinical practice.[9]

The purpose of the present study was to try to reproduce the findings of Rahman et al[5] in another study population, thus investigate the ability of HF-QRS to predict perfusion defects at adenosine MPI.

Methods

Study population

The study population consisted of 100 patients admitted for MPI at the Department of Clinical Physiology, Lund University Hospital, Lund, Sweden. Patients with pacemaker were excluded from the study. Of the 100 patients, 29 were excluded because of high noise levels in the ECG recording (RMS value within the QRS complex less than 3 times the RMS isoelectric noise level) and 2 because of atrial fibrillation. After exclusions, 69 patients were therefore included in the study.

The study protocol was approved by the local research ethics committee and complied with the Declaration of Helsinki. Informed consent was obtained from each subject before enrolment.

Myocardial perfusion imaging acquisition and analysis

During pharmacologic stress, patients were injected intravenously with a body weight–adjusted dose (450-820 MBq) of ^{99m}Tc-tetrofosmin. Stress was performed with adenosine, infused at a rate of 140 μg/(kg·min) for 3 minutes before tracer injection, and continued for 2 minutes after injection. Low-load exercise on bicycle was performed when possible to avoid adverse effects of adenosine. The ^{99m}Tc-tetrofosmin rest study was performed within 4 days (450-820 MBq).

Acquisition was performed approximately 45 to 60 minutes after tracer injection for both stress and rest images using a dual-head gamma camera (Vertex, ADAC Corporation, Milpitas, CA) equipped with high-resolution, parallel-hole collimators. Data were collected at 32 projections over a 180° orbit, 40 seconds per projection, and 64 × 64 matrix zoomed to a pixel size of 5 mm. The starting angle was 315°. Attenuation correction was not used. Single-photon emission computed tomography images were reconstructed and postfiltered (Butterworth order, 5.0; cutoff frequency, 0.6 for supine images and 0.66 for prone images). The single-photon emission computed tomography reconstruction and reorientation were automatic (Autospect plus, ADAC Corporation), but an experienced operator checked reorientation into 3 orthogonal views and made correction if needed. The images were evaluated by an experienced nuclear cardiologist completely blinded to the HF-QRS results. The MPIs were considered to represent reversible perfusion defects if there was a larger perfusion defect in the adenosine study compared with the resting study. Similar perfusion defects at rest and during adenosine infusion may represent infarction, hibernation, or attenuation artifacts and were reported as "fixed defects" in the current study.

Electrocardiogram acquisition and signal averaging

Electrocardiograms were recorded for 5 minutes before adenosine infusion, while the patient was resting in the supine position, and during the entire adenosine infusion. Electrodes were placed at standard locations for chest leads and at the proximal part of the arms and the left iliac crest for limb leads.[10]

Data collection of the ECG was performed on a Windows XP–based laptop with software supplied by CardioSoft (Houston, TX). A frequency response range of 0.5 to 300 Hz and a sampling rate of 1000 Hz were used to acquire the ECGs. A signal-averaging algorithm was applied in each lead to identify and average the QRS complexes in order to reduce the noise level. Premature complexes and noisy beats were automatically eliminated via a cross-correlation function that rejects beats with a cross-correlation coefficient of less than 0.90. The first 100 accepted beats during rest were used for baseline. During the infusion, a 100-beat sliding template was established, going forward in time (ie, most recent beat in, oldest beat out), and the values at peak infusion were used for analysis. The signal was bandpass-filtered by the software using a Butterworth filter[11] in the time domain to include only frequencies between 150 and 250 Hz. The QRS duration was delineated from the standard ECG.

Analysis of HF-QRS

The presence or absence of 3 types of RAZs of the HF-QRS was noted. The 3 types include the Abboud (RAZ A), Abboud Percent (RAZ AP), and NASA (RAZ N) RAZs.[5,9] A RAZ score, ranging from 0 to 108, was calculated.[5,7] This score was calculated from 2 subscores: the "general RAZ burden" (0-36) and the "RAZ contiguity" subscore (0-72). The general RAZ burden derives from the severest RAZ type that is present is any given lead, with 3 points for a RAZ N, 2 points for a RAZ AP, and 1 point for a RAZ A. The contiguity score was calculated as follows: if a RAZ N was present, 3 points were given, and then 3 additional points were also given for every nth RAZ N present that was spatially contiguous to another RAZ N. Similarly, 2 points were given for RAZ AP and 1 point for RAZ A. For contiguity, the orderly (Cabrera) sequence was used for limb leads. The RAZ scores at baseline (RSAB) were calculated for all patients, both for V leads and CR leads. The CR leads are precordial leads referenced to the right arm electrode and maximizes the QRS voltages.[12,13]

The RMS values of each HF-QRS were determined by (1) squaring the amplitude of each sample, (2) determining the mean of these squares, and (3) determining the square root of this mean. Changes in RMS values from the rest recording to the end of the adenosine infusion were expressed as percentage (%ΔRMS). The 3 contiguous leads that had the greatest change in %ΔRMS (positive and negative) were determined, and their individual %ΔRMS was summed to create a %ΔRMS-3 score, both in V leads and CR leads. The same procedure was repeated for 4 contiguous leads to produce a %ΔRMS-4 score.[5]