Ischemia Monitoring by Analysis of Depolarization Changes

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Abstract

Myocardial ischemia causes changes in the depolarization phase of the cardiac cycle, which can be quantified by analysis of high-frequency QRS components (HFQRS). We introduce a novel HFQRS analysis technology and evaluate its performance in monitoring transient ischemic episodes in patients hospitalized due to chest pain. Continuous monitoring by high-resolution 12-lead ECG was performed in 43 patients admitted to a chest pain unit, followed by cardiac imaging. Indices of HFQRS based on ischemia-specific morphological changes and conventional ST segment levels were extracted from signal-averaged ECG. HFQRS indices were positive for 5 of 10 patients that were diagnosed with coronary artery disease, while ST analysis was negative for all patients. The severity of the HFQRS indices was directly related to the likelihood of ischemic events. HFQRS is a promising technology for monitoring and early detection of acute coronary syndrome.

1. Introduction

Chest pain is one of the leading reasons for hospital emergency department (ED) visits worldwide. In the US, approximately 6 million people annually undergo evaluation in the ED for acute chest pain. Despite the wealth of knowledge available about acute coronary syndrome (ACS), this condition continues to be among the most difficult to predict or diagnose. Nearly half of patients hospitalized for unstable angina eventually receive a non-cardiac-related diagnosis. Nonetheless, 5% of patients with myocardial infarction (MI) are inappropriately discharged from the ED [1].

Although ECG is a mainstay in the diagnosis of ACS, the initial 12-lead ECG in the ED is often non-diagnostic in ACS patients, especially in non-ST elevation MI and unstable angina [2]. Serial ECG recordings or continuous monitoring of ST-segment changes has been suggested to assist in evaluation of patients with chest pain. In the early hours of acute MI, the ST-segment is often dynamic, exhibiting cyclic patterns of thrombotic occlusion and spontaneous reperfusion. Even tough ST-segment monitoring for 8 to 12 hours of patients with chest pain is recommended by the AHA practical standards [3], studies have shown that its additive value is limited in the diagnostic evaluation of intermediate-risk patients managed in the chest-pain unit [4].

Conventional analysis of ST segment deviations aims at detecting repolarization abnormalities. However, ischemia may also bring about changes in the depolarization phase. These depolarization changes can be detected and quantified using analysis of the high-frequency components of the QRS complex (HFQRS). HFQRS have been previously shown to provide incremental diagnostic value in detecting demand ischemia [5]. HFQRS changes were also used to identify supply ischemia in patients undergoing percutaneous transluminal coronary angioplasty [6].

The aim of this study was to develop an analysis technique, based on HFQRS, for detecting transient ischemia and to evaluate its performance in continuous monitoring of patients hospitalized due to chest pain.

2. Methods

2.1. Patients and protocol

The study was approved by the local ethics committee for medical research. The study included 52 consecutive patients (age 57±11 yo, 39 men) admitted to the chest paint unit (CPU). These patients, classified as having low to medium risk of ACS, were admitted for medical observation, continuous 12-lead ST monitoring, repeated biomarker testing and cardiac imaging tests for diagnosis of ischemic heart disease. Imaging tests included SPECT myocardial perfusion imaging, stress echocardiography or CT-angiography. Patients with positive ACS diagnosis underwent coronary angiography. Patients were continuously monitored by high-resolution 12-lead ECG (HyperQ™ System, BSP, Israel) during CPU stay

(average monitoring time 12.5±3.0 hours). ECG was sampled with bit resolution of 0.15μV at rate of 1000 Hz.

2.2. HFQRS signal processing

Acquired 12-lead ECG was processed in order to extract indices of HFQRS and compute ST segment levels (Figure 1). QRS complexes were detected, and template-based correlation was used to identify valid complexes and exclude noisy or ectopic beats. Accurate beat alignment, followed by beat averaging was used to obtain high signal-to-noise ratio. Signal averaging was done using a 150-second sliding window, moved over the data by time shifts of 10 seconds. The HFQRS signal for each lead was obtained by applying a band-pass filter in the frequency range 150-250 Hz to the QRS region from the averaged ECG beats. HyperQ™ indices of ischemia, based on patterns of intensity and morphology changes of the HFQRS signal, were calculated for each averaged beat, providing a trend line of HyperQ indices during the monitoring period. A visual representation of the monitored HFQRS signals was obtained by the HyperMap™ view, showing the color-coded amplitude envelope at each time point. In addition to HFQRS indices, ST-segment level was measured from each averaged ECG signal, 60ms after the J point.

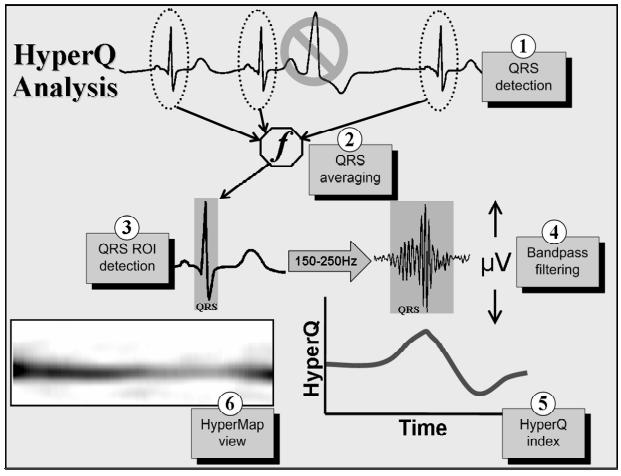

Figure 1: HFQRS analysis by the HyperQ algorithm. See text for details.

2.3 Data analysis

Nine patients were excluded from the analysis due to complete or incomplete bundle branch block (5 pts), lack of imaging results (3 pts) or inadequate signal quality (1 pt). The remaining 43 patients (56±10 yo, 31 men) were stratified by the likelihood of experiencing ischemic events, based on imaging results and the risk of ACS by the ACC/AHA guidelines [6] (Table 1): high (positive imaging test or angiography), medium (negative imaging with high risk of ACS) and low (negative imaging with low or intermediate risk of ACS). Receiver operating characteristics (ROC) technique was used to determine cut-off values for HFQRS indices per lead, and for the number of leads indicating a positive result. The relation between the severity of the HFQRS indices and the likelihood of ischemic events was examined. The diagnostic performance of ST-segment changes was evaluated by the ACC/AHA guidelines for management of unstable angina and non-ST elevation MI [7].

3. Results

HFQRS indices were positive in 5 of 10 patients (50%) with high likelihood of ischemia. HFQRS indices were negative in 7 of 9 patients (78%) with medium and 22 of 24 patients (92%) with low likelihood of ischemia (Figure 2a). Of all patients with negative imaging results, 88% had negative HFQRS indices during monitoring period. The area under the ROC curve was 0.75. The average number of positive HFQRS leads was directly related to the likelihood of ischemic events, increasing from 1.5±0.8 for the low-likelihood group to 2.6±1.3 for the high-likelihood group ($p<0.005$, Figure 2b). ST analysis was negative for ischemic events in all 43 patients.

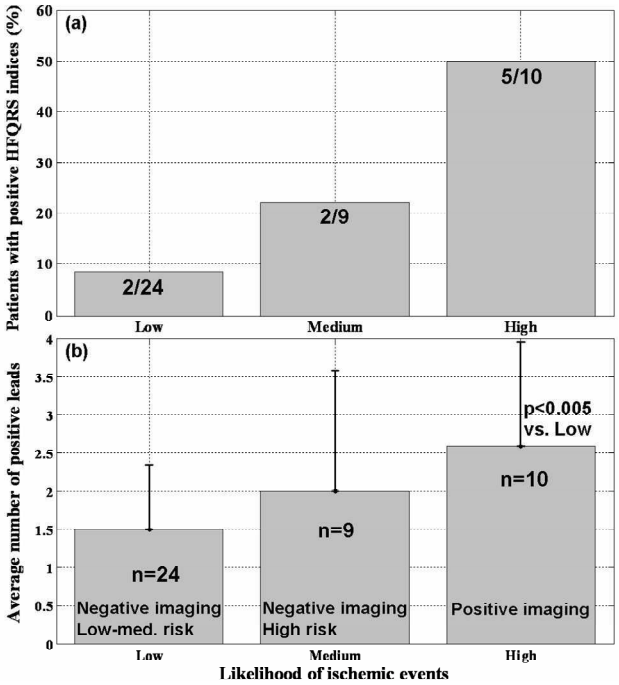

Figure 2: Percentage of patients with positive HFQRS indices (a) and average number of positive HFQRA leads (b) against the likelihood of ischemic events.

Table 1: Patient stratification based on the likelihood of ischemic events

Group	Likelihood of ischemia	Description	#Patients	Imaging modality (no. of patients)
Positive 10 pts	High	positive angiography	5	angiography (5)
		positive imaging	5	SPECT (4), echo (1)
Negative 33 pts	Medium	negative imaging & high risk	9	SPECT (7), echo (1), angiography (1)
	Low	negative imaging & intermediate-low risk	24	SPECT (9), echo(2), CT(13)

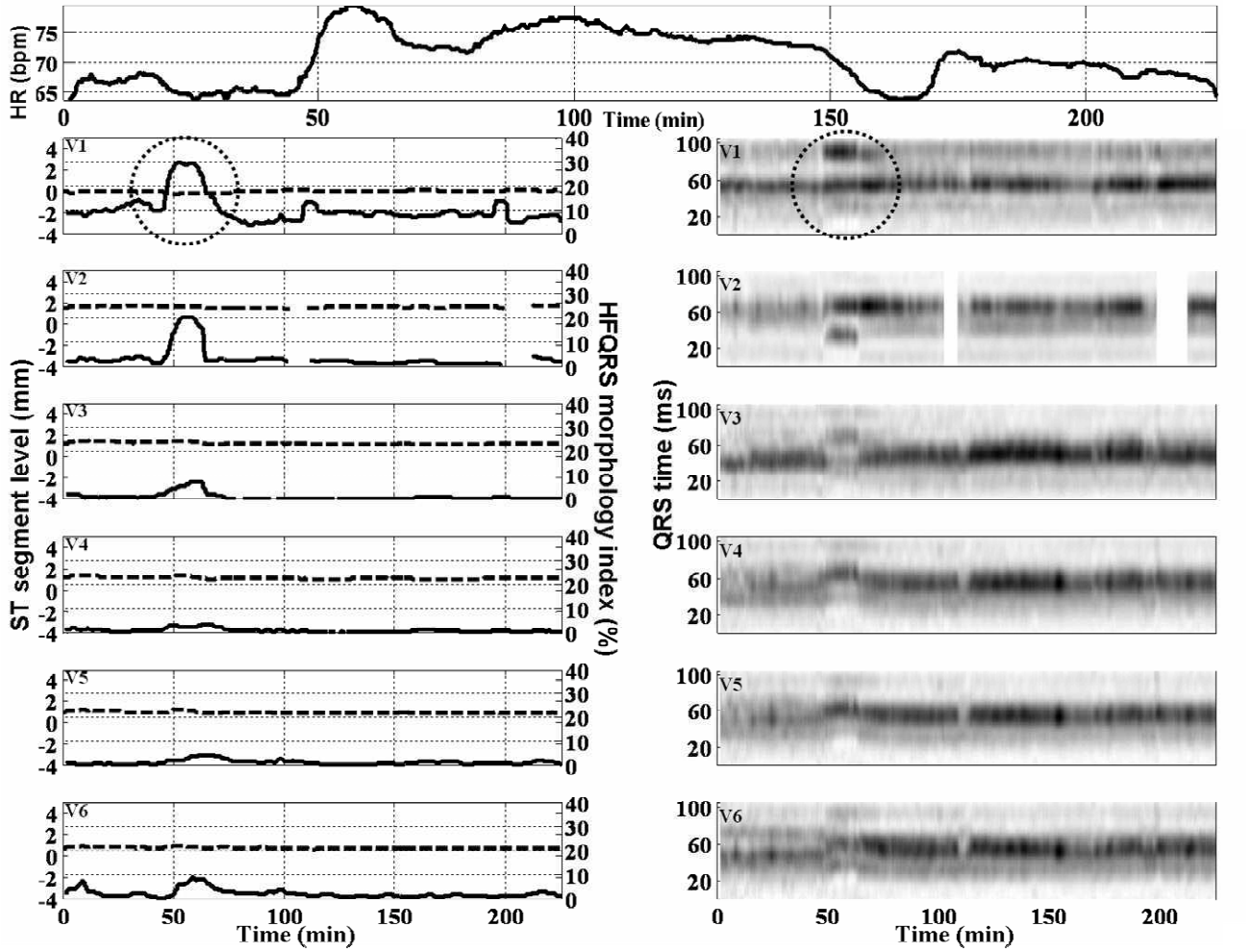

Figure 3: A suspected ischemic episode. Heart rate (top panel), ST-segment levels (left panel, dashed lines), HFQRS index (left panel, solid lines) and HyperMap view (right panel) of leads V1-V6 during 230 minutes of continuous monitoring of a 45 year-old male patient with positive angiography. While there is no change in ST levels, HFQRS indices in all leads exhibit a pattern suspected as an ischemic event.

A representative example of a suspected episode of ischemia in a 45 year-old male patient (Figure 3) shows a concurrent transient rise of HFQRS indices in all leads, lasting about 20 minutes, while there are no apparent changes in the ST segment levels. The beginning of this suspected ischemic event is also accompanied by a small rise in heart rate. The HyperMap view reveals a pattern of changes in the intensity and the morphology of the HFQRS signal during the suspected ischemic episode: the amplitude of the signal is attenuated and its amplitude envelope is fragmented into a multiple-peak structure. A closer look at the HFQRS morphology in normal and ischemic segments is provided in Figure 4. The analyzed patient, who had atypical chest pain without ECG

changes, negative biomarkers and no history of cardiac disease, was diagnosed with significant coronary artery disease by angiography. HFQRS monitoring provided an alert within 50 minutes of ECG monitoring.

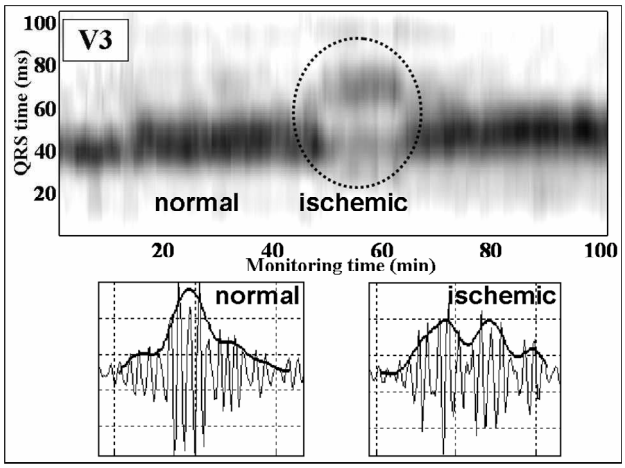

Figure 4: A closer examination of the HFQRS signal from lead V3 during suspected ischemic episode, showing the typical normal and ischemic HFQRS morphology.

4. Discussion and conclusions

Transient ischemia at rest is a difficult condition to diagnose. Most of the ischemic episodes are silent, without accompanying chest pain. ST-segment changes are the only 'gold-standard' currently available for detecting transient ischemia. However, in patients admitted for observation in chest pain units, continuous ST monitoring does not provide a reliable diagnostic tool. Current ST analyzers often have high rate of false-alarms, which require manual override by the physician. The sensitivity of such semi-automatic ST monitor, as well as of automatic ST measurements from signal-averaged ECG, is low. In this study, ST monitoring did not indicate any ischemic episodes, while HFQRS analysis pointed out 5 of the patients which were diagnosed with ischemic heart disease by imaging or angiography. Positive end-point diagnosis does not oblige positive monitoring result, as the identified coronary disease may be stable. Negative end-point diagnosis rules out significant coronary artery disease, but cannot rule out transient ischemia caused by subendocardial micro-infarcts or vasospasm. Consequently, in the absence of a gold-standard, the diagnostic performance of HFQRS analysis could not be quantified as the sensitivity and specificity of detection. Instead, we examined the relation between HFQRS diagnosis and the likelihood that the patient experienced ischemic events. Using this analysis, we have shown that both the percentage of patients with positive HFQRS indices and the average number of positive HFQRS leads are directly related to the likelihood of transient ischemia. Further studies in larger groups of patients with higher prevalence of ACS are required in order to validate the technique for routine clinical use. The current results demonstrate the potential benefit of HFQRS analysis in both early diagnosis and early rule-out of ACS.

In conclusion, HFQRS morphological indices are superior to conventional ST monitoring in detecting ischemic episodes, in patients hospitalized with chest pain. HFQRS analysis is a promising technology, which may aid in monitoring of transient ischemic episodes and management of acute coronary syndrome.

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