Higher Frequencies in QRS Complex for the Detection of Myocardial Ischemia

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Abstract

Several studies investigating the high frequency QRS (HF-QRS) behavior have reported the superiority of the HF-QRS method compared to the standard ST-segment changes in acute coronary syndrome and ischemic heart disease (IHD).

The potential diagnostic contribution of five selected parameters was tested in three frequency ranges - HFQRS (150-250Hz), VHFQRS (250-500Hz) and UHFQRS (500-1000Hz) in healthy subjects and IHD patients.

Significant differences were found between healthy and IHD subjects in all tested parameters and analyzed passbands. All parameters have comparable diagnostic contribution with minimal or no effect of the different frequency ranges. Despite significant differences between the groups, the parameters evince very large inter-individual variation that limits the clinical usefulness of the parameters to discriminate between healthy subjects and IHD patients. The implementation of a heart rhythm excitation would allow analyzing the changes of the parameters during increased oxygen demand of myocardium.

1. Introduction

ST-segment deviations in ECG signal represent the fundamental diagnostic technique for assessing myocardial ischemia. ST-segment changes can occur nonspecifically, and not only during myocardial ischemia, but also due to other reasons [1]. Many new methods using ECG signal aim at improving the diagnostic accuracy of myocardial ischemia detection.

Myocardial ischemia emerges also in QRS complex. In 1960, Langner et al. [2] presented "notching" and other high frequency deformities in QRS complex as a consequence of myocardial ischemia. In 1981, Goldberger et al. [3] presented the effect of myocardial infarction on low-voltage high frequency (HF) potentials located in QRS complex in frequency range 80-300Hz. He introduced the Root-Mean-Square (RMS) value as a direct index of a HF voltage describing the properties of an HF-QRS signal (HF-QRS RMS). The HF-QRS RMS values were found higher in healthy subjects then in patients after myocardial infarction [3], as well as in patients suffering from ischemic heart disease (IHD) [4]. Pettersson et al. [5] showed that for the frequency range 150-250 Hz the changes in HF-QRS RMS values are more sensitive in comparison to conventional ST-segment deviations in patients suffering from acute coronary syndrome (ACS) during percutaneous transluminal coronary angioplasty. But the large inter-individual variation of the HF-QRS RMS parameter limits its clinical use for discriminating IHD patients [4, 6].

Abboud et al. [7] introduced the Reduced Amplitude Zone (RAZ) parameter that is based on evaluation of pattern of notches in HF-QRS amplitude envelope. Empirically determined criteria of RAZ were later refined by Schlegel et al. showing the correlation with risk factors of coronary artery disease in asymptomatic patients [8].

Kurtosis as a statistical parameter estimating the peakedness of a data distribution set was introduced by the same group for assessing the HF-QRS morphology properties [8].

There is currently no available data in literature regarding the influence of myocardial ischemia on QRS diagnostic information behind mostly used frequency passband 150-250Hz. Our aim was to test the diagnostic contribution and behavior of the parameters, proposed for HF-QRS analysis of myocardial ischemia, in healthy subjects and IHD patients in frequencies ranging between 150-1000Hz.

2. Methods

The Mason-Likar 12-lead ECG configuration was acquired using high dynamic range recording system (sampling frequency 5 kHz, amplitude resolution 26 bits and low pass cutoff frequency 2 kHz) (SciSDA14, M&I s r.o., Prague, Czech Republic) for 5 minutes during supine resting position in 103 healthy subjects with no history or

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signs of heart problems and 80 Ischemic Heart Disease (IHD) patients confirmed by coronary angiography and with no conduction system abnormalities.

The ECG data were analyzed offline. Because the power of QRS components rapidly decreases with increasing frequency, signal averaging technique was used to improve the signal-to-noise ratio. The precise R-wave detection and exact categorization of the different QRS morphologies was performed prior QRS averaging. The QRS complexes were detected and sorted using a robust multichannel correlation algorithm [9, 10]. Only regular beats were included into further analysis. The QRS amplitude envelopes, calculated from at least 300 averaged QRS complexes for each lead, were computed by the Hilbert transform in the following frequency ranges: HFQRS (150-250Hz), VHFQRS (250-500Hz) and UHFQRS (500-1000Hz).

Five parameters were chosen to describe the properties of QRS signal in selected frequency bands – (1) Amax – maximal amplitude of an envelope, (2) RMS±80ms - RMS value of an envelope in area ± 80 ms around the R wave, (3) RMS0.1Am - RMS value of an envelope in the area with amplitude over 10% of maximal amplitude, (3) Kurtosis – statistical evaluation of an envelope signal in the area ± 100 ms around the R wave and (4) RAZ – reduced amplitude zone – the following criteria were used: the distance between two peaks at least 10 ms, the amplitude of lower/second peak at least 0.3 of amplitude of first peak and the valley between peaks deeper than 0.3 of amplitude of lower peak.

The results from all leads were averaged according to each subject. The statistical comparison between IHD patients and healthy subjects was evaluated using non-paired t-test.

The dependence among the chosen parameters was tested by a correlation analysis.

3. Results

Mean values of parameters over healthy and IHD patients, together with statistical significance of differences are presented in Table 1-3.

Table 1. The differences of selected parameters between healthy subjects and IHD patients in HF passband. The values are represented as a mean value ± SD over the subjects.

HF (150-250Hz)	**Healthy**	**IHD**	**p**
Amax [µV]	14.7±6.6	8.7±3.3	<0.0001
RMS±80ms [µV]	4.7±1.9	3.1±1.1	<0.0001
RMS0.1Am [µV]	7.6±3.4	4.3±1.7	<0.0001
Kurtosis [-]	7.1±1.2	5.4±1.5	<0.0001
RAZ [-]	0.4±0.2	0.6±0.3	<0.0001

Table 2. The differences of selected parameters between healthy subjects and IHD patients in VHF passband. The values are represented as a mean value ± SD over the subjects.

VHF (250-500Hz)	**Healthy**	**IHD**	**p**
Amax [µV]	7.0±3.0	4.0±1.6	<0.0001
RMS±80ms [µV]	2.2±0.9	1.4±0.6	<0.0001
RMS0.1Am [µV]	3.6±1.5	2.0±0.9	<0.0001
Kurtosis [-]	7.2±1.5	5.2±1.7	<0.0001
RAZ [-]	0.3±0.2	0.6±0.3	<0.0001

Table 3. The differences of selected parameters between healthy subjects and IHD patients in UHF passband. The values are represented as a mean value ± SD over the subjects.

UHF (500-1000Hz)	**Healthy**	**IHD**	**p**
Amax [µV]	1.8±0.8	1.2±0.5	<0.0001
RMS±80ms [µV]	0.6±0.3	0.4±0.2	<0.0001
RMS0.1Am [µV]	1.0±0.5	0.6±0.3	<0.0001
Kurtosis [-]	6.6±1.1	4.7±1.5	<0.0001
RAZ [-]	0.2±0.2	0.3±0.2	<0.001

95% percentile confidence ellipsoids of independent parameters for healthy subjects and IHD patients are displayed in Figure 1. Parameters have very large variation and ellipsoids are overlapped for healthy and IHD patients.

4. Discussion

Significant differences exist between healthy and IHD subjects in all tested parameters and analyzed passbands. Healthy subjects have significantly higher mean value of Amax, RMS parameters, Kurtosis and significantly lower RAZ parameter compared to IHD patients.

Despite significant differences between healthy subjects and IHD patients, the selected parameters evince very large inter-individual variation that limits the clinical usefulness of the parameters to discriminate between normal subjects and IHD patients as showed by overlapping of 95% percentile confidence ellipsoids of the independent parameters displayed in Figure 1.

The Table 1-3 and Figure 1 show minimal or no effect of different passbands on diagnostic contribution of selected parameters. The level of P coefficient values over all passbands is below $P < 1e^{-5}$ except for RAZ parameter in UHF passband. The P coefficient values overall exhibit lower values in UHF passband compared to HF and VHF passbands. Lower signal-to-noise ratio in UHF passband may be the reason because the power of QRS components rapidly decreases with increasing frequency.

While the RMS parameters assess the amount of amplitude components in a QRS signal in given passband, the RAZ represents a morphologic indicator of pathology in a QRS amplitude envelope.

Significant correlation (R > 0.98 in healthy; R > 0.96 in

IHD) exists among the amplitude parameters (Amax, RMS±80ms and RMS0.1Am). These parameters are dependent and only one of them should be used. Minimal correlation (|R| < 0.48 in healthy; |R| < 0.24 in IHD) exists among the amplitude parameters, Kurtosis and RAZ.

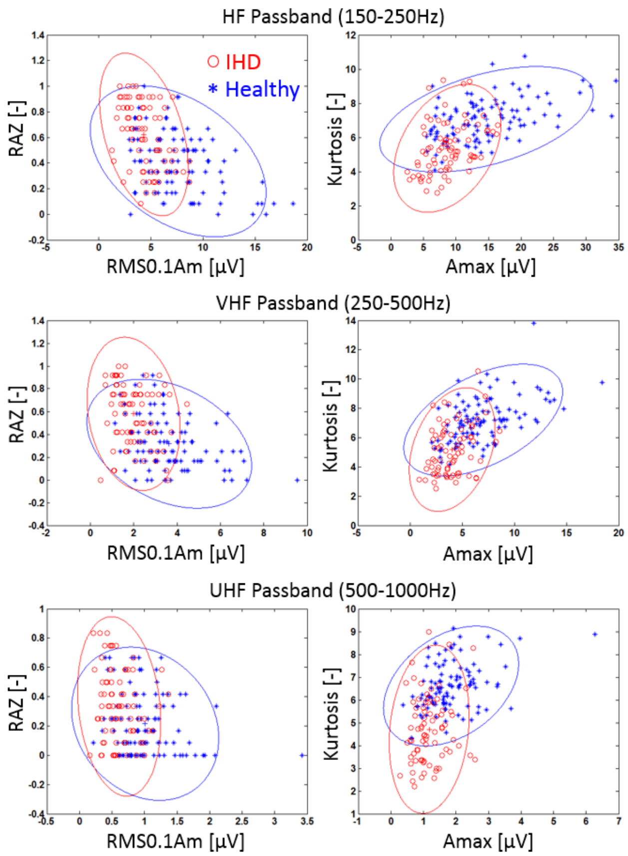

Figure 1. 95% percentile confidence ellipsoids of the independent parameters for healthy subjects (blue color) and IHD patients (red color) in three passbands.

All chosen parameters are clearly defined except for RAZ. The RAZ parameter is characteristic by binary (Yes/No) classification that depends on the exact definition of a shape of RAZ. Occurrence of RAZ in resting HF-QRS was previously suggested to be a marker of acute myocardial ischemia and IHD [7, 8]. But the RAZ (including the classical shape - two peaks with nearly the same amplitude and valley below 60% of peaks level) can also be found in healthy subjects (Tables 1-3). Binary classification strongly depends on the definition and thus limits the application of this parameter. The level of P coefficient of the RAZ parameter between healthy controls and IHD patients was similar or worse in comparison with other presented parameters.

Kurtosis, as the fourth standardized moment, describes the probability distribution of an envelope amplitudes. The statistical significance of the differences between healthy subjects and IHD patients is higher compared to other parameters. Kurtosis, as an independent parameter, is possible to use together with other parameters.

The mean level of the parameters over all leads was analyzed. We also analyzed the mean level over V leads only with very similar results.

Diagnostics of IHD based on ECG measurement only under resting conditions has low specificity and sensitivity. The ROC area based on all presented parameters is 0.732. The diagnostic strength of the parameters could be improved by a heart rhythm excitation. IHD is most frequently clinically diagnosed by exercise stress tests (EST), such as with ECG. The benefit of HF-QRS RMS analysis during EST has been evaluated during several clinical studies that overall favor the HF-QRS RMS analysis against standard ST-segment deviation analysis [11]. The criterion for positive detection of ischemia was defined as a decrease of at least 50% in HF-QRS RMS amplitude during exercise in three or more leads.

Our presented analysis worked with the mean level of parameters over all ECG leads. Involvement of EST (rest and heart rhythm excitation) would enable analyzing changes of selected parameters in separate ECG leads which could better describe the diagnostic contribution of the parameters.

5. Conclusion

Higher frequencies components in QRS complex significantly differ between healthy subjects and IHD patients. The differences are similar between HF and VHF in frequency area from 150 to 500 Hz. In the UHF passband (500-1000Hz), the decreased signal-to-noise ratio slightly limits the differences in selected parameters between healthy subjects and IHD patients.

Healthy subjects have significantly higher Amax, RMS parameters, Kurtosis and significantly lower RAZ than IHD patients.

All parameters have comparable diagnostic contribution, and also high inter-subject variability. Diagnosis based on measurement only in rest, has a low sensitivity and specificity, and thus cannot serve as a reliable standalone diagnostic tool for stratifying IHD patients. The implementation of a heart rhythm excitation would allow analyzing the changes of the parameters during increased oxygen demand of myocardium.

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