Original Research

Evaluation of Heart Rate Variability Indices Using a Real-Time Handheld Remote ECG Monitor

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ABSTRACT

Studies on retrospective electrocardiogram (ECG) recordings of patients during cardiac arrest have shown significant changes in heart rate variability (HRV) indices prior to the onset of cardiac arrhythmia. The early detection of these changes in HRV indices increases the chances for a successful medical intervention by increasing the response time window. A portable, handheld remote ECG monitor designed in this research detects the QRS complex and calculates short-term HRV indices in real-time. The QRS detection of the ECG recordings of subjects from the MIT-Arrhythmia database yielded a mean sensitivity of 99.34% and a specificity of 99.31%. ECG recordings from normal subjects and subjects with congestive heart failure were used to identify the differences in HRV indices. An increase in heart rate, high-frequency spectral power (HFP), total spectral power, the ratio of HFP to low-frequency spectral power (LFP), and a decrease in root mean square sum of RR differences were observed. No difference was found on comparison of the standard deviation of normal to normal interval between adjacent R-waves, LFP, and very-low-frequency spectral power. Based on these, additional analytical calculations could be made to provide early warnings of impending cardiac conditions.

INTRODUCTION AND BACKGROUND

The heart rate variability (HRV) is a marker of the significant relationship between the autonomic nervous system and cardiovascular mortality.1 The parasympathetic influence on heart rate (HR) is mediated via the release of acetylcholine by the vagus nerve. When the parasympathetic nerve is activated, slow diastolic depolarization is initiated. The sympathetic influence on HR is mediated by the release of epinephrine and norepinephrine. Under resting conditions, the variation in the HR is largely dependent on vagal modulation.2 Their respective changes are generally reflected in the low-frequency spectral power (LFP) and high-frequency spectral power (HFP) of the HRV spectrum. Thus, at any instant, the ratio of LFP and HFP (LFP/HFP) may serve as an indicator of sympathovagal balance.3

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Clinically, HRV has emerged as a strong and independent predictor of mortality after an acute myocardial infarction (AMI). Lowered HRV precedes the episodes of atrial fibrillation (AF) in patients after coronary artery bypass graft operation with no structural heart disease. A time-variant algorithm applied to an HRV signal from subjects suffering from transient ischemic attacks suggests an early activation of the LF component in the HRV power spectrum, preceding 1.5-2 min the tachycardia and the ST displacement, generally indicative of the onset of an ischemic episode. Correlation dimensional analysis on RR interval predicted the exact time of occurrence of ventricular fibrillation in a retrospective study. LFP component of HRV is used in the prediction of in-hospital complications after AMI and in the mortality of patients with chronic heart failure.

Ventricular tachyarrhythmias (VTAs) have a circadian rhythm with increasing frequency during early morning and evening. A diurnal variation is also found in HRV. Higher LFP and HFP occur during daytime and night, respectively. An inverse circadian rhythm is observed in patients with a morning VTA peak. Significant changes in HRV in the period immediately preceding a VTA have also been reported. Huijker et al. found significant reduction in HR, very low frequency spectral power (VLFP), LFP, and HFP in post-MI patients who developed cardiac arrest 1 hour prior to the onset of VTA. Shusterman et al. noted an increase in HR and a fall in LFP and LFP/HFP prior to the onset of VT. Pruvot et al. observed an increase in HR and a significant reduction in HRV prior to the onset of VTA in post-MI patients. Other studies have shown a rise in VLFP and decline in HFP with a rise in LFP/HFP. These results suggest an alteration in the interaction between the sympathetic and parasympathetic nervous system prior to the onset of VTAs; this highlights the relevance of HRV in the remote monitoring of patients with potentially advanced cardiac disorders.

Remote monitoring using real-time electrocardiogram (ECG) from a prehospital setting results in reduced response time and improved patient outcome that was achieved by incorporating the Public Switch Telephone Network (PSTN), the Global System for Mobile Communication (GSM), and the Code Division Multiple Access (CDMA) technologies. However, these do not provide real-time ECG analysis or feedback to the patient about his/her medical condition. A handheld real-time ECG monitor incorporating HRV analysis could provide real-time HRV analysis and feedback to the user. This forms the objective of this work, which may prove to be beneficial in early detection of cardiac conditions in order to initiate immediate remedial action.

MATERIALS AND METHODS

A handheld, remote cardiac arrhythmia monitor was designed and implemented. The ECG records from normal subjects and subjects with congestive heart failure (CHF) were reviewed to identify the HRV indices that were best suited for monitoring using a remote cardiac arrhythmia monitor in order to aid the early detection of the onset of cardiac abnormalities. HR, standard deviation of NN intervals (SDNN), and root mean squared sum of successive NN interval differences (RMSSD) were computed among time-domain HRV indices; VLFP, LFP, HFP, total spectral power (TP), and LFP/HFP were computed among the frequency domain HRV indices.

System description

Raw ECG data was displayed on the handheld monitor (client) at a remote location (home/clinic) and transmitted using a wireless interface over a high-speed broadband connection to the central server. The central server (at a large clinic/hospital) analyzes raw ECG in real-time and stored the data and results for offline analysis (when required). The results of the analysis of various HRV indices were sent back to the client to provide feedback in real-time. An early-warning alarm was used on the handheld and the server in the case of potentially dangerous cardiac arrhythmia. The server was also designed to accept connections from remote healthcare providers/medical experts.

The communication modules were developed in Visual Basic 6.0 (Microsoft Corp, Redmond, WA) and analytical modules (QRS detection, computation of HRV indices) in Matlab.
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(The Mathworks Inc., Natik, MA). Further details of the design and implementation of client and remote server are given elsewhere.25

QRS detection

A QRS detector based on a biorthogonal wavelet, which enables the detection of the QRS complex as an extreme and further detects the premature ventricular contraction beats, was implemented. The sensitivity and specificity of the QRS detection scheme are given by

\[
\text{Sensitivity} = \frac{\text{Beats Detected} - \text{False Negative}}{\text{Beats Detected}} \times 100
\]

\[
\text{Specificity} = \frac{\text{Beats Detected} - \text{False Positive}}{\text{Beats Detected}} \times 100
\]

Heart rate variability

The variations in the RR intervals measured were used to determine the HRV indices. A short-term HRV duration (5 min) was chosen for the following measurements. Time-domain measurements

(i) SDNN26

\[
\text{SDNN} = \sqrt{\frac{1}{N-2} \sum_{n=2}^{N} (\delta(n) - \overline{\delta})^2}
\]

where \(\overline{\delta}\) is the average NN signal from N beats, given by

\[
\overline{\delta} = \frac{1}{N-1} \sum_{n=2}^{N} \delta(n)
\]

The scaling factor is N-2 because there are N-1 intervals in the record and 1 degree of freedom is used to estimate the mean NN interval. SDNN reflects all the cyclic components responsible for the variability in the period of recording.

\[
\text{RMSSD} = \sqrt{\frac{1}{N-2} \sum_{n=3}^{N} (\delta(n) - \delta(n-1))^2}
\]

Frequency domain measurements

Power spectral density analysis provides basic information about power (i.e., variance) distribution as a function of frequency. The frequency indices calculated from short-term recordings are:

(i) TP—refers to power in the frequency range 0.001–1.5 Hz
(ii) VLF—Power within 0.001–0.04 Hz
(iii) LF—Power within 0.04–0.15 Hz
(iv) HF—Power within 0.15–0.4 Hz
(v) LF/HF—Low- to high-frequency power ratio averaged every 5 min

Measurements of VLF, LF, and HF were carried out in absolute units (ms²).

The NN data sequence was obtained after the removal of ectopic or missing beats that can corrupt the frequency domain characteristics.27 In the continuous ECG record, QRS complexes (RR intervals) were detected using a wavelet-based QRS detector.28 The ECG data segments containing more than 10% premature ventricular contractions (PVCs) were discarded. The missing and ectopic beats associated with variations of more than 12.5% were removed. The resulting gaps were filled with an average value computed in the local neighborhood of the missing beat. By this procedure, temporary changes in the RR interval sequence representing missing or ectopic beats were removed and more stationary data were obtained. Prior to power spectral density (PSD) estimation, a linear detrend was applied to the resulting NN interval data and regularly sampled at 4 Hz by a moving window curve-fitting algorithm. The PSD was estimated using 512-sample Fast Fourier Transform (FFT) by Welch’s periodogram method. Each data segment was divided into 8 subsegments that overlapped on each other for 50% of their lengths. For each subsegment, the data were weighted with a Hanning window, and the periodogram was estimated. The PSD, calculated from the average of the periodograms and then rescaled taking into account the power loss due to windowing, was obtained. The spectral power present in the VLF, LF, and HF bands was finally estimated.
**RESULTS**

The mean sensitivity and specificity of the QRS detection to the ECG recordings of subjects in the absence of arrhythmia were 100% and 99.62%.

HRV indices were computed in 5-min intervals. A comparison of the averaged HRV indices is summarized in Table 1. In time-domain, an increase in HR ($p < 0.001$, t-test at 95% CI) and a decrease in RMSSD ($p < 0.01$) were observed in the ECG recordings of subjects with CHF as compared to those in normal subjects. No statistical difference was observed in SDNN measurements ($p = 0.245$). Among the frequency domain measurements, HFP ($p < 0.001$) and TP ($p < 0.01$) were significantly higher in the normal subjects as compared to subjects with CHF. No statistical difference was found on comparison of VLFP ($p = 0.813$) and LFP ($p = 0.606$). The LFP/HFP was higher in subjects with CHF ($p < 0.001$).

**DISCUSSION**

The noninvasive, minimally intrusive, handheld cardiac monitor was developed to transmit raw single-lead ECG data to a distant site for real-time HRV analysis. The handheld monitor incorporated wireless networking capability to further provide mobility and convenience to the user. The widespread use of high-speed broadband to access the Internet has provided a reliable means to establish and maintain a connection over the Internet from a remote site to a medical facility.

Handheld remote monitors provided (1) a reliable means to monitor HRV in real-time, (2) storage of raw and processed analyzed results, (3) feedback to the user and alarms (when required), and (4) ease of use (minimal user training). Modifications to the software can be made without user intervention.

Modern long-term (24-48 h) ECG recorders such as IQmark Advanced Holter (Midmark Diagnostic Group, Torrance, CA) and CardioMera (PMS Instruments, Ltd., Berkshire, UK) incorporate offline HRV analysis. These

<table>
<thead>
<tr>
<th>HRV parameter</th>
<th>Normal subjects (mean ± SE)</th>
<th>Subjects with CHF (mean ± SE)</th>
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</thead>
<tbody>
<tr>
<td>Time domain</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heart rate (bpm)</td>
<td>73.50 ± 1.10*</td>
<td>90.90 ± 2.90</td>
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<tr>
<td>SDNN (ms)</td>
<td>164.90 ± 7.66**</td>
<td>145.40 ± 14.90</td>
</tr>
<tr>
<td>RMSSD (ms)</td>
<td>239.70 ± 11.78***</td>
<td>181.40 ± 14.80</td>
</tr>
<tr>
<td>Frequency domain</td>
<td></td>
<td></td>
</tr>
<tr>
<td>VLFP (ms*ms)</td>
<td>1443.90 ± 190.00*</td>
<td>1553.70 ± 420.70</td>
</tr>
<tr>
<td>LFP (ms*ms)</td>
<td>2653.90 ± 357.80***</td>
<td>2269.30 ± 648.60</td>
</tr>
<tr>
<td>HFP (ms*ms)</td>
<td>6401.50 ± 724.70*</td>
<td>2225.4 ± 500.20</td>
</tr>
<tr>
<td>Total spectral power (ms*ms)</td>
<td>10,499.30 ± 1121.60**</td>
<td>6048.3 ± 1538.20</td>
</tr>
<tr>
<td>LFP/HFP</td>
<td>0.46 ± 0.04**</td>
<td>0.74 ± 0.08</td>
</tr>
</tbody>
</table>

SDNN, standard deviation of normal to normal; RMSSD, root mean square sum of RR differences; VLFP, very low frequency spectral power; LFP, low-frequency spectral power; HFP, high-frequency spectral power.

$p$-values are represented by *$p < 0.001$, **$p < 0.01$, ***$p < 0.05$.
monitors are expensive and required a PC for downloading ECG data for offline analysis. In our system, the HRV indices are computed in 5-min intervals in real-time. By overlapping consecutive time segments, HRV monitoring could be made pseudo real-time along with cardiac arrhythmic monitoring. Variations in the identified HRV indices could aid in the prediction of the onset of cardiac abnormalities.

Although the sample size used in this study is small, these patients have shown the emergence of a pattern that could identify cardiac malfunction through changes in the HRV. This technique could be applied not only to the elderly but also to pediatric subjects with cardiac malfunction. The present handheld device provides distinct features where HRV changes could be seen by patients and aids decision making by clinicians.

Instantaneous feedback is ideally suited for monitoring cardiac parameters during day-to-day activities such as heart rate after exercise or medication. Critical patients can also be monitored at remote locations by an experienced staff member and advised for an unexpected condition. The handheld monitor using HRV indices was tested in real-time to detect the onset of cardiac arrhythmias. An early detection of changes in time and frequency domain indices could prove invaluable for early intervention.

Among the HRV indices to monitor, RMSSD was strongly recommended by a consensus committee because it determines the HRV from differences between successive beats and is indicative of high-frequency power. The differences in HRV indices in the ECG of normal and CHF subjects were in agreement as reported by others. The frequency indices, TP, HFP, and LFP/HFP were found to separate the ECG recordings from the normal and CHF subjects. The TP reflects the changes in the variance of HR, whereas the LFP/HFP reflects the sympathovagal balance. Higher values of LFP/HFP, associated with higher HR, could indicate higher sympathetic activation in subjects with CHF. VLFP accounts for long-term regulation mechanisms (probably thermoregulation, rennin-angiotensin system, and other factors). These mechanisms could not be satisfactorily resolved by short-term analysis. The variation in the spectral components of the subject was found to be very subjective and dependent on patient age and prior cardiac history.

CONCLUSION

Based on the present work, it has been observed that the knowledge of the resting value of indices improves the interpretation of changes in HRV measures. The availability of data on prior cardiac history is also helpful in determining the risk posed by arrhythmia. Larger, statistically adequate studies using this methodology would be required to assess clinical value in predicting the risks of significant cardiac dysrhythmias. Further applications of this procedure under varied ECG recording conditions using a large number of subjects could help in establishing this as a routine procedure.

REFERENCES


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