Real-time monitoring of heart rate variability in critically ill patients

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Abstract
Purpose: Heart rate variability (HRV) is widely used to evaluate autonomic nervous function; however, real-time monitoring of HRV has rarely been attempted in the intensive care unit (ICU). We report our experience in performing real-time monitoring of HRV in our ICU.

Methods: We investigated 10 critically ill patients on total ventilatory support. Heart rate variability analysis was performed using the MemCalc system, which is a noninvasive, real-time analysis system. The low-frequency (LF) component of HRV reflects sympathetic and parasympathetic modulation, whereas the high-frequency (HF) component mainly reflects parasympathetic modulation. The LF/HF ratio represents a measure of sympathetic/parasympathetic balance.

Results: The HRV parameters for patients breathing spontaneously after extubation were significantly higher than those for patients on total ventilatory support. These findings suggest that mechanical ventilation under sedation may reduce autonomic nervous function in critically ill patients. In a representative case with septic shock, systolic blood pressure and LF/HF ratio showed a significant increase after intravenous infusion of epinephrine and then the HF component showed a significant increase due to vagal reflex.

Conclusions: The MemCalc system is practicable for real-time monitoring of HRV in the ICU. Heart rate variability parameters may offer useful information in the management of critically ill patients.

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1. Introduction

Various means of monitoring living-body information (eg, blood pressure, heart rate, and body temperature) are indispensable for treating critically ill patients in the intensive care unit (ICU); however, these parameters are not always reliable predictors of physiologic status. Heart rate variability (HRV) analysis, a technique that examines beat-to-beat variations in heart rate, has been used in a variety of disciplines to predict morbidity and mortality (eg, acute myocardial infarction and diabetic neuropathy) and to detect autonomic nervous dysfunction [1]. Winchell and Hoyt [2] speculated that monitoring of HRV parameters has the potential to detect physiologic deterioration or response to therapy in the ICU. The fast Fourier transform (FFT) has been used for spectral analysis of HRV [1]. However, the FFT is an offline analysis method and is not suitable for real-time monitoring. Recently, a new system for HRV analysis—the MemCalc system—has been developed and is starting to

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be used in several clinical situations [3–7]. The MemCalc system enables estimation of HRV based on a series of R-R intervals for 30 seconds, thereby enabling the real-time monitoring of HRV parameters in the ICU. Such monitoring could provide useful information in the treatment of critically ill patients; however, it has rarely been attempted. We report our experience in using the MemCalc system for real-time monitoring in our ICU.

2. Methods

2.1. Subjects

This study was approved by the Institutional Review Board of Yamaguchi University Hospital. We investigated 10 critically ill patients diagnosed with systemic inflammatory response syndrome in our ICU at Yamaguchi University Hospital. All patients were mechanically ventilated due to respiratory failure. The diagnosis of systemic inflammatory response syndrome was based on the criteria of the American College of Chest Physicians and the Society of Critical Care Medicine Consensus Conference [8]. Patients with permanent arrhythmia or cardiac pacing were not included. We also described a case for which we performed real-time monitoring of HRV parameters in septic shock.

2.2. Measurements

Electrocardiograms were obtained using a bedside monitor (BSS-9800; Nihon Kohden, Tokyo, Japan) and transferred to a personal computer on which the MemCalc system (MemCalc/Tarawa; Suwa Trust, Tokyo, Japan) had been installed. An online analysis of HRV was performed using the MemCalc system, which is a noninvasive, real-time analysis system that uses the maximum entropy method for spectral analysis [3,4]. The MemCalc system is used to transform the R-R fluctuations into frequencies. The spectral bands used were 0.15 to 0.40 Hz (high frequency, or HF) and 0.04 to 0.15 Hz (low frequency, or LF). The spectral measures were computed as amplitudes (ie, areas under the power spectrum) and are presented in square milliseconds. Further details of the MemCalc system are described elsewhere [7]. The LF component of HRV reflects sympathetic and parasympathetic modulation, whereas the HF component mainly reflects parasympathetic modulation. The LF/HF ratio represents a measure of sympathetic/parasympathetic balance [1]. It has been reported that the reference values for LF component, HF component, and LF/HF ratio are 1170 ± 416 ms², 975 ± 203 ms², and 1.5:2.0, respectively [1]. In the present study, we started continuous measurements of HRV parameters after intubation and finished measurements before discharge from our ICU. We calculated the mean values for 5 minutes on total ventilatory support under sedation and on spontaneous breathing within 5 days after extubation. We selected 5-minute periods in which the patients were hemodynamically stable.

The severity of the patients was evaluated using the Sequential Organ Failure Assessment (SOFA) score, which was calculated at the beginning of HRV monitoring.

2.3. Statistical analysis

Values are expressed as mean ± SD. Data were analyzed using standard software (JMP, version 5; SAS Institute Inc, Cary, NC). A Wilcoxon test was used to compare the 2 groups. A P value less than .05 was considered statistically significant.

3. Results

The mean (SD) age of the patients was 53 (15) years, and 7 of the 10 patients were male. The causes of admission to our ICU were infection in 5 patients, trauma in 4 patients, and lymphoma in 1 patient. The mean (SD) SOFA score was 7 (3), and the mean (SD) mechanical ventilation time was 562 (349) hours.

Table 1 lists the clinical characteristics and HRV parameters of the patients. The LF components, HF components, and LF/HF ratios for patients breathing spontaneously after extubation were significantly higher than those for patients on total ventilatory support (92.6 ± 151.0 ms² vs 5.1 ± 6.2 ms², P = .012; 71.0 ± 176.2 ms² vs 3.2 ± 5.7 ms², P = .028; 7.2 ± 5.6 vs 2.5 ± 2.3, P = .017, respectively).

Fig. 1 shows the HF components plotted during 5-minute HRV monitoring when the patients were under mechanical ventilation (Fig. 1A) and on spontaneous breathing (Fig. 1B). The values were logarithmically transformed due to the 1000-fold range of values and were plotted every 10 seconds. We experienced an interesting case of HRV monitoring using the MemCalc system (Fig. 2). The patient was a 54-year-old woman with septic shock caused by acute peritonitis. Systolic blood pressure deteriorated to 50 mm Hg because of septic shock. After an intravenous infusion of epinephrine 0.02 mg, systolic blood pressure increased to 150 mm Hg and LF/HF ratio showed a significant increase (Fig. 2A). After the sudden increase in systolic blood pressure, the HF component showed a significant increase, and the heart rate decreased from 114 to 75 beats/min (Fig. 2B). The time course of HRV parameters suggests that the sudden decrease in heart rate was caused by vagal reflex.

4. Discussion

The main finding of our study is that the MemCalc system is practicable for real-time monitoring in the ICU and that the parameters measured using this system may be useful in estimating autonomic nervous function in critically ill
patients. The monitoring of vital signs is indispensable in the management of critically ill patients in the ICU. Heart rate is useful in this regard; however, HRV parameters could provide additional useful information [9].

The FFT is commonly used for spectral analysis of the beat-to-beat interval [1,2]. In mathematics, the FFT is an operation that transforms one complex-valued function of a real variable into another. This analysis requires a 4-minute (256 beats) block of R-R interval data for an LF measurement and an HF measurement. In addition, the FFT is an offline analysis method in the ICU, meaning that measurements subjected to FFT cannot be used in making an immediate decision regarding the management of critically ill patients. Winchell and Hoyt [2] presented a figure of serial HRV measurements using the FFT. However, the measurements were plotted every 6 hours. In contrast, the MemCalc system requires only a 30-second block of R-R interval data for measurement, and measurements are renewed every 4 seconds, online [6,7]. As demonstrated in our study (Figs. 1 and 2), the MemCalc system may prove to be superior over conventional methods using the FFT in terms of real-time monitoring of HRV parameters. Recently, it was reported that the MemCalc system was useful for the HRV analysis during anesthesia and during exercise stress testing [5-7]. However, there is no report on real-time monitoring of HRV using the

### Table 1  Clinical characteristics and HRV measurements of the patients

<table>
<thead>
<tr>
<th>Case</th>
<th>Sex</th>
<th>Age (y)</th>
<th>Diagnosis</th>
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<th>MV time (h)</th>
<th>LF (ms²)</th>
<th>HF (ms²)</th>
<th>LF/HF</th>
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<tr>
<td></td>
<td></td>
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<td></td>
<td></td>
<td>VS</td>
<td>SB</td>
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<td>Sepsis</td>
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<td>583</td>
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<td>9.3</td>
<td>1.1 15.8</td>
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<td>12.9</td>
<td>14.4</td>
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<td>363</td>
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<tr>
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<td>0.2 3.3</td>
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<tr>
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</table>

MV indicates mechanical ventilation; VS, ventilatory support; SB, spontaneous breathing; NA, not available due to death.

### Fig. 1  High-frequency components plotted during 5-minute HRV monitoring when the patients were under mechanical ventilation (A) and on spontaneous breathing (B). The values were logarithmically transformed due to the 1000-fold range of values and were plotted every 10 seconds.

### Fig. 2  A representative case of HRV monitoring using the MemCalc system. The bold line indicates the HF component, and the solid line indicates LF/HF. After intravenous infusion of epinephrine, systolic blood pressure increased to 150 mm Hg, and the LF/HF value showed a significant increase (A). After the sudden increase in systolic blood pressure, the HF component showed a significant increase and heart rate decreased from 114 to 75 beats/min (B).
epinephrine (Fig. 2A), thereby indicating that epinephrine showed a significant increase after an intravenous infusion of tissue might cause depressed HRV values in ICU patients. In both extrinsic mechanisms and intrinsic factors in cardiac siveness. In a recent review, Schmidt et al[14] reported that features of sepsis could down-regulate myocardial respon-
function in critically ill patients. It has been reported that HRV parameters in septic patients show a significant decrease with increasing severity of illness [11-13]. The mechanism of HRV decrease has yet to be elucidated; however, Garrard et al [11] suggested that several mediators known to contribute to the clinical and pathophysiologic features of sepsis could down-regulate myocardial respons-
siveness. In a recent review, Schmidt et al [14] reported that both extrinsic mechanisms and intrinsic factors in cardiac tissue might cause depressed HRV values in ICU patients. In our representative case with septic shock, the LF/HF ratio showed a significant increase after an intravenous infusion of epinephrine (Fig. 2A), thereby indicating that epinephrine could improve myocardial responsiveness from the autonomic nervous system. We consider that the real-time monitoring of HRV parameters might prove useful in immediately assessing the clinical conditions of critically ill patients. In addition, the examined case showed a sudden decrease in heart rate due to vagal reflex. The monitoring of HRV may be useful in investigating the cause of bradycardia and in making an immediate decision regarding treatment. In recent studies, HRV parameters were used to predict the occurrence of septic shock, development of multiple organ dysfunction syndrome, and favorable outcome after ther-
apeutic hypothermia for cardiac arrest [15-18]. Further studies are required to assess the usefulness of HRV monitoring in critically ill patients.

Our study is limited by the relatively small number of patients and a heterogeneous patient population. Heart rate variability in critically ill patients may be affected by various factors (eg, sedation and ventilatory pattern). To assess the usefulness of HRV monitoring using the MemCalc system, further studies are needed involving a large number of critically ill patients.

In conclusion, the MemCalc system is practicable for real-time monitoring of HRV parameters in the ICU. Heart rate variability parameters may offer additional useful informa-
tion in the management of critically ill patients.

References