# A Short-Term Assessment of Cardiac Output by Using Instantaneous Pulse Rate Variability

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***Abstract*—A hemodynamically unstable patient has the risk of going into general shock. As fluid therapy is the primary treatment for shock, the fluid responsiveness (FR) of the patient should be evaluated before volume expansion. However, conventional methods predict FR by analyzing the variation of blood pressure signal in time domain which is a nonstationary problem and makes it difficult to provide a stable index for FR. Instantaneous pulse rate variability (iPRV) is a cardiovascular assessment in frequency domain. Furthermore, iPRV uses ensemble empirical mode decomposition (EEMD), which could solve the nonstationary problem and overcome the frequency limitation in power spectrum of heart rate variability (HRV). iPRV provides a new indication in very high frequency (VHF) range (0.4-0.8Hz) of spectrum for peripheral responses. The aim of this study was to verify the ability of iPRV to indicate VHF for cardiac output assessment. Twenty-six healthy participants participated in this study and the acquired signal was recorded in supine baseline, during head-up tilt (HUT), and passive leg raising (PLR), which induces variation of venous return and helps the quantitative assessment of cardiac output individually. The result showed that the normalized power of VHF in HRV was small and there was no corresponding variation in different postures. In contrast, the normalized power of VHF in iPRV presented relative trend with different venous return changes. Overall, iPRV provides a novel and short-term cardiac output assessment in frequency domain and it has potential to evaluate FR.**

***Keywords- fluid responsiveness (FR); instantaneous pulse rate variability (iPRV); ensemble empirical mode decomposition (EEMD); head-up tilt (HUT); passive leg raising (PLR).***

## I. INTRODUCTION

To study blood flow and circulation in humans, hemodynamics is an important part of Physiology. Hemodynamic monitoring plays a key role in hospitals for hemodynamically unstable patients. When they recover after surgery or after a suffered injury, they usually need intensive care and continuous observation of hemodynamic parameters is needed. Furthermore, a patient with unstable hemodynamics is at risk of general shock.

Fluid therapy is the primary treatment for shock. Moreover, the stroke volume of a patient increases by 12% after fluid loading which means a patient responds to fluid administration. However, only half the patients respond to fluid loading in intensive care unit (ICU). Volume expansion for non-responder patients may only exert adverse effects without having any hemodynamic benefit [1][2]. Thus, the fluid responsiveness (FR) of a patient should be evaluated before volume expansion. After fluid loading, the expectation is that it will increase cardiac output significantly. Nevertheless, stroke volume is intrinsically controlled by cardiac preload, so conventional methods evaluate FR by assessing cardiac preload or output. Several ways to evaluate FR are based on static indices and dynamic indices [3][4]. Previous studies demonstrated that static index of cardiac preload can predict FR by pressure and volume markers, but it is affected by respiratory or systolic function [5]. For this reason, dynamic indices have been developed to assess cardiac output by calculating the short-time variation of arterial pulse pressure waveform in mechanical ventilation patient. But dynamic indices are also affected by spontaneous respiration [6], and both indices are based on time domain which present the nonstationary

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problem in signal and make it difficult to provide a stable index for FR.

In frequency domain, one of the important cardiovascular assessment is heart rate variability (HRV). However, HRV studies are restricted by the feasibility and the reproducibility with an inconvenient measurement [7]. In addition, the maximum frequency of power spectrum is restricted at 0.5 Hz by tachogram [8]. Pulse rate variability (PRV) was proposed as a substitute measurement of HRV. PRV uses pulse wave, which collected from photoplethysmography (PPG), to replace ECG recording in HRV and has been examined as a surrogate of HRV during nonstationary conditions in a previous study [9]. Besides, the arterial pulse wave is regulated by complex physiological controls which make PRV provide much more peripheral information than HRV [9]. However, the frequency band indication in power spectrum of PRV is still a limitation that needs to be overcome. Instantaneous pulse rate variability (iPRV) is a novel method to extend frequency limitation [10]. It adopted the frequency range extension method and IF projecting technique help for PRV spectral analysis. Furthermore, iPRV used ensemble empirical mode decomposition (EEMD), which could solve the nonstationary problem. Also, iPRV provides a new indication, named very high frequency (VHF) band (0.4-0.8 Hz), in the power spectrum for more information. The literature has proposed that VHF of HRV is a novel index of left ventricular function evaluation [11]. VHF has the ability to indicate cardiac function, venous return, and FR. However, the variation and interpretation of VHF in iPRV have to be further explored and examined. The aim of this study was to verify the ability of iPRV to indicate VHF for cardiac output assessment. It thought of an experiment of change in venous return such as passive leg raising (PLR) and head-up tilt (HUT). PLR as a volume challenge induces a translocation of venous blood, and HUT induces blood pooling in the legs which can decrease venous return and cardiac output. These two positions can offer variation of venous return to verify cardiac output assessment as iPRV. The remainder of the paper is structured as follows. The next section presents the experiment design, data collection, introduction of iPRV analysis and comparison methods. Section III illustrates the similarity between iPRV and RRI and also explains the results of power spectrum in iPRV and HRV during different postures. Section IV provides the discussion about mechanism of different frequency band indication in iPRV. Moreover, it presents iPRV is a potential short-term FR evaluation. Conclusion and future work are given in the last section.

## II. MATERIAL AND METHOD

### A. *Experiment design and subjects*

The procedure of this study contained five steps. First, participants were resting in supine position with 10-minute recording as a baseline. Second, participants were tilting up passively (HUT) on the automatic tilting table and kept in tilt-up position for 10 minutes. Then, participants were back to the supine position with 5 minutes for recovering to baseline. Finally, participants were raising leg passively (PLR) for 10 minutes. After PLR, participants were resting with 5 minutes for recovering to steady state.

The signal acquisition was as follows: (i) electrical activity of ECG signal was recorded by BEST-C-04056 (BioSenseTek Corp., Taiwan); (ii) peripheral information of PPG signal was recorded by Nonin 8500 (Nonin Medical Inc., Plymouth, MN). The signal acquisition with sampling frequency is 200Hz.

Thirty healthy participants (male: 15; age: 24±1.8 years old) participated in this study. Twenty-six participants had no history of cardiovascular disease and no uncontrollable distortion in acquired data. Four exclusive participants contained distortion in certain data, such as motion artifacts from PPG signal and ECG abnormality. All measurements were performed in a quiet temperature-controlled room and the experiment was approved by the institutional review board (IRB) of Tungs' Taichung Metro Harbor Hospital.

### B. *Instantaneous pulse rate variability*

The process of iPRV includes two parts (Figure 1). The first part is decomposition, the pulse wave component was searched from PPG by sifting process in EEMD. Sifting process is an iteratively detrending operation which is used to compute finite set of components, named intrinsic mode functions (IMFs), from source nonstationary data. Moreover, before the sifting process, EEMD provides noise-assisted method into original data for eliminating multiple characteristic problem in IMFs. After mixtures of added noise and source data, the detrending operation contains several steps. First, local extrema of data $x(t)$ are identified by peak-valley detection. The upper envelope $U(t)$ and lower envelope $L(t)$ are generated by cubic spline interpolation according to the local maxima and local minima. The trend in current timescale is computed by calculating the mean of $U(t)$ and $L(t)$, as $M(t)$.

$$M(t) = \frac{U(t)+L(t)}{2} \quad (1)$$

The new timescale $H(t)$ is the representation after detrending operation by data $x(t)$ subtracting the trend.

$$H_k(t) = H_{k-1}(t) - M_k(t), k \geq 1 \quad (2)$$

where $H_0(t) = x(t)$.. After k times detrending operation, if the trend of $H_k(t)$ satisfies the criterion as the steady constant trend, then the components $H_k(t)$ were extracted from $x(t)$ as IMF. After $n$ sifting process, $x(t)$ was decomposed into $n$ IMFs, $IMF_1(t) \sim IMF_n(t)$ , and one residue $r(t)$.

$$x(t) = \sum_{i=1}^{n} IMF_i(t) + r(t) \quad (3)$$

Since IMFs were decomposed from different mixtures, the ensemble IMFs are computed by averaging each corresponding IMF.

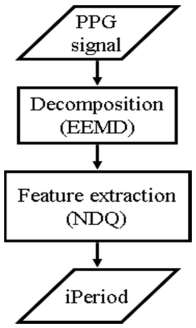


Figure 1. The flow illustration of the process of iPRV.

The second part is feature extraction. The continuous-time heartbeat rhythm can be extracted by EEMD. To resent the frequency of oscillation in IMF at a specific time instant, iPRV proposed normalized direct quadrature (NDQ) to calculate IF of relative IMF. The algorithm of NDQ is shown in Figure 2. First, the amplitude modulation of the main component $IMF_{main}$ was eliminated by iteratively normalization for conquering Bedrosian' s theorem [12]. Then, the empirical frequency modulation signal $F(t)$ of $IMF_{main}$ is assumed to be cosine function, and its quadrature $sin\emptyset(t)$ can be computed directly.

$$sin\emptyset(t) = \sqrt{1 - F^2(t)} \quad (4)$$

The instantaneous phase $\emptyset(t)$ is calculated by taking arctangent of $F(t)$ and its quadrature, then the IF is obtained from divided derivative of $\emptyset(t)$ by 2π.

$$\emptyset(t) = tan^{-1}\left(\frac{\sqrt{1-F^2(t)}}{F(t)}\right) \quad (5)$$

The instantaneous period (iPeriod) was estimated by the inversion of IF of $IMF_{main}$ in order to indicate time series of heartbeat rhythm as RR intervals (RRI) in HRV.

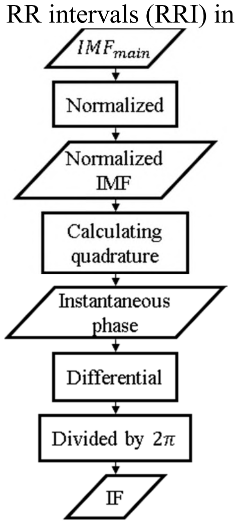


Figure 2. The flow illustration of the algorithm of NDQ.

*C. Comparison method*

iPeriod was calculated by feature extraction, and the analysis of iPeriod included frequency domain analysis and time domain analysis. Frequency domain analysis adopted power spectrum to compare power variation in different frequency band with RRI. The procedure of frequency domain analysis includes two steps. Firstly, fast Fourier transform (FFT) was performed as the spectrum analysis in each frequency band of iPeriod and RRI. The partition of power spectrum in HRV and iPRV is shown in Figure 3. The frequency band of HRV is divided into low frequency (LF) band (0.04-0.15 Hz), high frequency (HF) band (0.15-0.4 Hz) and very high frequency (VHF) band (0.4-0.5 Hz). Frequency band of iPRV is divided into LF (0.04-0.15 Hz) and HF (0.15-0.4 Hz), and VHF (0.4-0.8 Hz). Then, the power of each frequency band is calculated by integration for comparison of variation during different positions.

The purpose of time domain analysis is to examine the reliability of iPeriod. Before time domain analysis, there is a preprocessing for filtering high frequency band of iPeriod by EEMD in order to be compared with RRI. The procedure of preprocessing is shown in Figure 4. At first, iPeriod was filtered by EEMD into IMFs with high frequency and residue. Then, residue was extracted as low pass of iPeriod ($iPeriod_{LP}$, $f(t)$ ).Time domain analysis adopted cross correlation coefficient to ensure similarity between iPRV and HRV. Cross correlation coefficient also offered time lag information to discuss changes in different position. RRI series $g(t)$ is an interpolation of RRI by using cubic spline. The calculation of cross correlation coefficient shows in (6).

$$r(d) = \frac{\sum_{t=0}^{N}[(f(t)-\bar{f}(t))*(g(t)-\bar{g}(t))]}{\sqrt{\sum_{t=0}^{N}(f(t)-\bar{f}(t))^2}*\sqrt{\sum_{t=0}^{N}(g(t)-\bar{g}(t))^2}} \quad (6)$$

where $d$ is the time lag. $\bar{f}(t)$ and $\bar{g}(t)$ are the mean of the corresponding series.

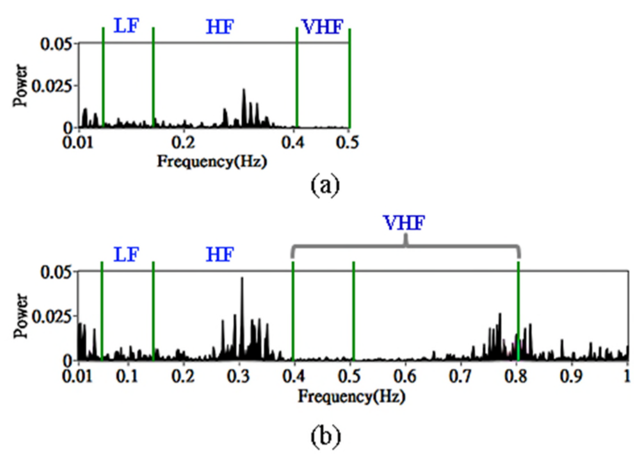


Figure 3. (a) is power spectrum in HRV with LF, HF and VHF, and (b) is power spectrum in iPRV with LF, HF, NHF and FHF.

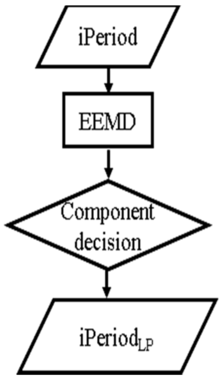


Figure 4. The procedure of preprocessing in time domain analysis.

### D. Normalized power in frequency band

For summarizing spectral analysis with whole database during different condition, this study adopted two normalized power calculations as follows: (i) for comparing with HRV, the following normalization formula was used:

$$Power_{total}\,(\mathrm{TP}) = Power_{LF} + Power_{HF}$$

$$\rightarrow \frac{\mathrm{TP}}{\mathrm{TP}} = \frac{Power_{LF}}{\mathrm{TP}} + \frac{Power_{HF}}{\mathrm{TP}} = \mathrm{nLF} + \mathrm{nHF} = 1 \quad (7)$$

Where nLF is normalized power of LF and nHF is normalized power of HF; (ii) for exploring power of VHF information, the following normalization formula was used:

$$Power_{total}\,(\mathrm{TP}) = Power_{LF} + Power_{HF} + Power_{VHF}$$

$$\rightarrow \frac{\mathrm{TP}}{\mathrm{TP}} = \frac{Power_{LF}}{\mathrm{TP}} + \frac{Power_{HF}}{\mathrm{TP}} + \frac{Power_{VHF}}{\mathrm{TP}}$$

$$= \mathrm{nLF} + \mathrm{nHF} + \mathrm{nVHF} = 1 \quad (8)$$

Where nLF is normalized power of LF, nHF is normalized power of HF and nVHF is normalized power of VHF.

## III. RESULT

### A. Comparison result in frequency domain

Table I shows the comparison result with HRV. The normalized power of HRV and iPRV had the same trend between supine and other postures. The sympathetic activities increased (nLF increasing) when the venous return decreased (HUT). The parasympathetic activities increased (nHF increasing) when the venous return increased (PLR). Different venous return activated the autonomic nervous system (ANS), normalized power of iPRV responded relatively as HRV.

TABLE I. COMPARISON VARIATION WITH HRV IN LF AND HF DURING DIFFERENT POSTURES.

| | | **nLF (0.04-0.15 Hz)** | **nHF (0.15-0.4 Hz)** |
|---|---|---|---|
| **HRV** | Supine | 0.51±0.19 | 0.49±0.19 |
| | HUT | 0.54±0.20 | 0.46±0.20 |
| | PLR | 0.49±0.17 | 0.51±0.17 |
| **iPRV** | Supine | 0.41±0.17 | 0.59±0.17 |
| | HUT | 0.44±0.18 | 0.56±0.18 |
| | PLR | 0.40±0.16 | 0.60±0.16 |

The form is (mean ± standard deviation). Color in red means increasing of normalized power. Color in green means decreasing of normalized power.

Table II shows the spectral analysis with venous return changes. nVHF of iPRV decreased when the venous return decreased (HUT), and nVHF of iPRV increased when the venous return increased (PLR). nVHF of iPRV is effective to indicate venous return changes during different postures. nVHF of HRV was not only small but also can't indicate venous return decreasing. However, nHF of iPRV shows different trend with HRV in Table II.

TABLE II. COMPARISON VARIATION WITH HRV IN LF, HF AND VHF DURING DIFFERENT POSTURES.

| | | **nLF (0.04-0.15 Hz)** | **nHF (0.15-0.4 Hz)** | **nVHF (0.4-0.8 Hz)** |
|---|---|---|---|---|
| **HRV** | Supine | 0.49±0.19 | 0.46±0.18 | 0.05±0.05 |
| | HUT | 0.52±0.19 | 0.44±0.18 | 0.05±0.03 |
| | PLR | 0.46±0.18 | 0.47±0.16 | 0.08±0.10 |
| **iPRV** | Supine | 0.28±0.17 | 0.37±0.13 | 0.35±0.17 |
| | HUT | 0.31±0.17 | 0.38±0.13 | 0.31±0.11 |
| | PLR | 0.25±0.14 | 0.36±0.12 | 0.39±0.15 |

The form is (mean ± standard deviation). Color in red means increasing of normalized power. Color in green means decreasing of normalized power.

### B. Comparison result in time domain

The results in the time domain analysis with the whole database are summarized in Table III. Before preprocessing for filtering high frequency band of iPeriod, all participants' *r* value between iPeriod and RRI series showed low correlation. In contrast, after filtering high frequency band of iPeriod, *r* value between $\mathrm{iPeriod}_{LP}$ and RRI series there was middle positive correlation (0.667±0.109 in baseline; 0.672±0.096 in HUT; 0.675±0.105 in PLR). Moreover, *r* value of $\mathrm{iPeriod}_{LP}$ and RRI series at all postures was significant difference with value of iPeriod and RRI series ($p<0.01$ at all postures). Time lag at all postures was not significant difference ($p = 0.14$ in baseline; $p = 0.23$ in HUT;

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$p$ = 0.33 in PLR) which means increasing of $r$ value was only influenced by high frequency band.

## IV. DISCUSSION

nVHF in iPRV showed the ability of evaluating cardiac output from PPG signal. This study adopted NDQ, which eliminated amplitude modulation, as an IF estimation to calculate periodic changes of pulse waveform for presenting cardiac output information. However, NDQ as a suitable IF estimation for pulse waveform has to be further explored. Previous studies proposed that component for NDQ needs to be a single-term expansion which absorb some of the properties [13]. The composition of PPG signal includes pulse waveform and reflected waveform, and pulse waveform is a sinusoid-like function which satisfy condition of single-term expansion. Furthermore, the pulse waveform extracted by EEMD with frequency band around 1 Hz.

TABLE III. THE RESULT OF CROSS CORRELATION COEFFICIENT IN THE TIME DOMAIN ANALYSIS

| | Supine | HUT | PLR |
|---|---|---|---|
| RRI series vs. iPeriod | | | |
| ***r*** | 0.240±0.096 | 0.255±0.102 | 0.275±0.096 |
| **Time lag** | 2.09±1.39 | 2.07±1.76 | 2.27±1.76 |
| RRI series vs. $iPeriod_{LP}$ | | | |
| ***r*** | 0.667±0.109* | 0.672±0.096* | 0.675±0.105* |
| **Time lag** | 1.93±1.46 | 2.37±1.70 | 2.42±1.61 |

The form is (mean ± standard deviation). * defines as $p$<0.01 relative to r between RRI and iPeriod

TABLE IV. COMPARISON VARIATION WITH HRV IN LF, HF, NHF AND FHF DURING DIFFERENT POSTURES.

| | | nLF (0.04-0.15 Hz) | nHF (0.15-0.4 Hz) | nNHF (0.4-0.5 Hz) | nFHF (0.5-0.8 Hz) |
|---|---|---|---|---|---|
| **HRV** | Supine | 0.49±0.19 | 0.46±0.18 | 0.05±0.05 | |
| | HUT | 0.52±0.19 | 0.44±0.18 | 0.05±0.03 | |
| | PLR | 0.46±0.18 | 0.47±0.16 | 0.08±0.10 | |
| **iPRV** | Supine | 0.37±0.17 | 0.53±0.15 | 0.10±0.09 | |
| | HUT | 0.41±0.18 | 0.52±0.17 | 0.08±0.04 | |
| | PLR | 0.36±0.15 | 0.54±0.15 | 0.10±0.06 | |
| **iPRV** | Supine | 0.28±0.17 | 0.37±0.13 | 0.06±0.04 | 0.29±0.15 |
| | HUT | 0.31±0.17 | 0.38±0.13 | 0.05±0.02 | 0.25±0.11 |
| | PLR | 0.25±0.14 | 0.36±0.12 | 0.06±0.03 | 0.32±0.14 |

The form is (mean ± standard deviation). Color in red means increasing of normalized power. Color in green means decreasing of normalized power.

Overall, pulse waveform is suitable component to NDQ for calculating IF.

After obtained iPeriod by using NDQ, FFT transformed iPeriod into power spectrum for comparing with HRV in frequency domain. Nevertheless, the normalized power of iPRV showed different trend with HRV in HF. Previous study claimed that fluctuations in the PPG signal in a normal person, which synchronous with ventilation, with a frequency in the 0.2-0.45 Hz [14]. Therefore, HF in iPRV is a complex frequency band with respiration and parasympathetic activities. In addition, VHF contains much more information than HRV, and it also affects the nHF in iPRV to present parasympathetic activities. To find out more detail, VHF was separated into near high frequency (NHF) band (0.4-0.5 Hz) and far high frequency (FHF) band (0.5-0.8 Hz). Table IV revealed that iPRV and HRV had the same trend in each frequency band when calculation in normalized power without FHF. However, there is different result if we calculate normalized power with FHF. The nHF expressed different trend with HRV, as seen in the result in Table II. As a result, cardiac output information could be narrowed down into FHF. Moreover, the power of FHF had higher proportion in total power which affected normalized power calculation.

This study showed that the iPRV spectrum can be assessed by simple PPG measurement. Moreover, it has potential to be a short-term evaluation. Conventionally, HRV needs long-term (greater than 5 min) data to evaluate autonomic nervous

TABLE V. THE NVHF OF IPRV IN SUPINE AND PLR WITH DIFFERENT DATA LENGTH.

| | Data length | Supine | PLR |
|---|---|---|---|
| nVHF | 10 minutes | 0.35±0.17 | 0.39±0.15 |
| | 130 seconds | 0.34±0.17 | 0.41±0.19 |

The form is (mean ± standard deviation).

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activities and left ventricular information in VHF. Furthermore, conventional evaluations also adopt 5 min data to assess cardiac output. Then, iPRV has the potential to be a short term evaluation by using IF estimation method. On the other hand, iPeriod has the ability to indicate enough information with short data length in PPG signal. This study used fragment data of PPG signal in supine and PLR. Table V showed that PPG signal with 130 seconds was no significant difference ($p = 0.28$ in supine; $p = 0.19$ in PLR) with whole data length, and it also had relative trend between supine and PLR. This result demonstrated that iPRV has potential as a short-term cardiac output evaluation.

## V. CONCLUSION

nVHF in iPRV had relative variation to venous return change in different postures, and it showed that iPRV is a potential evaluation for assessing cardiac output. Furthermore, result in time domain comparison illustrated that iPeriod contained high frequency information, and $\text{iPeriod}_{LP}$ had positive correlation with RRI series. In conclusion, iPRV is not only able to present ANS activity but also reliable to evaluate cardiac output. iPRV has potential to predict FR as short-term assessment and to be a reliable system for ICU in order to avoid delaying definitive therapy or produce additional damage patients. In the future, iPRV in FR assessment has to be further explored and examined with clinical patient.

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