The Complex Interpretation of Heart Rate Variability Components in Mechanically Ventilated Patients

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Abstract

Mechanical ventilation (MV) is a critical therapeutic intervention to support patients with respiratory failure. Using a dataset of 54 adult ICU patients under MV, this study analyzes respiratory signals and ECG-derived HRV data to identify the appearance of additional frequency components, particularly at harmonic frequencies, beyond the traditional low-frequency (LF) and high-frequency (HF) bands of HRV. It is observed that, in controlled and support ventilation modes, these additional harmonics appear as a result of ventilator-induced respiratory signal modulations. This phenomenon occurs up to 93.39% of the time in the controlled ventilation mode. Specifically, when the second harmonic frequency exceeds half the heart rate, aliasing occurs, manifesting as components at $F_{\text{HR}} - 2F_{\text{R}}$. These findings underscore the importance of considering these additional frequency components for a more comprehensive understanding of HRV and its role in assessing the success of weaning from mechanical ventilation.

1. Introduction

Mechanical Ventilation (MV) is a therapeutic strategy that involves assisting or replacing the respiratory function of an individual through a mechanical device, when this function is absent or insufficient for life. Its primary objective is to improve oxygenation and contribute to pulmonary mechanics.

Ventilation modes include controlled, support, and continuous positive airway pressure (CPAP) [1]. Controlled ventilation fully drives respiration, requiring no effort from the patient. Support modes assist efforts by delivering partial ventilation in response to pressure or flow changes. CPAP maintains constant positive airway pressure during expiration, but relies entirely on the patient's spontaneous breathing.

Invasive MV is required in approximately 40% of ICU patients [2, 3], often due to critical pulmonary, neurological, or cardiac conditions [4]. Although lifesaving, prolonged MV increases the risk of complications —e.g., ventilator-associated pneumonia, vocal cord injury, and tracheomalacia— which exacerbate morbidity, mortality, and hospital stays [5]. Timely recovery of spontaneous breathing is therefore a key clinical goal. However, premature weaning can cause cardiopulmonary instability and diaphragmatic dysfunction. The weaning process, which involves the gradual withdrawal of ventilatory support and extubation, remains a major challenge [3]. Despite the existence of established protocols for that, such as the spontaneous breathing trial (SBT), still 20% of extubated patients require reintubation due to respiratory failure, leading to worse outcomes [6].

Furthermore, there is a high incidence of autonomic nervous system (ANS) dysfunction in ICU patients. Accordingly, ANS markers, such as heart rate variability (HRV) and other cardiopulmonary coupling (CPC) indices, have been studied to improve weaning outcomes [7]. However, the relationship between heart rate (HR) and respiration in mechanically ventilated patients is complex, as evidenced by the presence in HRV of additional components beyond those typically observed in the low-frequency (LF) and respiratory-related high-frequency (HF) ranges. The aim of this study is to characterize the complex relationship between heart rate and respiration in these patients, exploring the potential origin and implications of these additional components.

2. Materials and Methods

2.1. Data set

Lead II of the ECG and respiratory airflow signals of 54 adult intubated ICU patients (median age 69 [IQR: 61–78], 61.8% male), undergoing invasive mechanical ventilation in controlled (50.36%), support (44.76%) or CPAP (4.88%) modes, were continuously recorded during the 24 hours preceding the SBT. Successful weaning was achieved in 65.5% of the cases.

Recordings were acquired using the Better Care® connectivity platform (Barcelona, Spain, U.S. Patent No. 12/538,940). This system is designed to acquire, standardize, synchronize, analyze, and store digital signals from bedside monitors and mechanical ventilators, with a sampling frequency of 200 Hz.

The study protocol and database were approved by the Institutional Review Boards of the Comitè d'Ètica d'Investigació amb Medicaments of the Corporació Sanitària Parc Taulí and the Clinical Research Ethics Committee of the Fundació Unió Catalana d'Hospitals [8].

2.2. Respiratory Signal Analysis

In this study, respiration is characterized through the analysis of the tidal volume (TV) signal. It is obtained by integrating the instantaneous airflow signal followed by baseline subtraction [7]. Afterwards, signals were resampled to 4 Hz.

The Power Spectral Density (PSD) of the TV signal, $\hat{S}_R(f)$, was estimated in 5-minute segments using Welch's periodogram with a 40-second Hamming window and a 35-second overlap.

Another relevant parameter is the respiratory rate (F_{R}), which was estimated as the frequency of the maximum peak in $\hat{S}_R(f)$ in the range (0.15, $\frac{F_{\mathrm{HR}}}{2}$) Hz, which covers the entire spectrum of the respiratory signal in mechanically ventilated patients.

2.3. ECG and HRV Analysis

QRS complexes in the ECG signal were detected using a wavelet-based method [9]. The instantaneous HR signal was derived from the detected beat occurrence times using the integral pulse frequency modulation model (IPFM) [10], which takes into account the potential presence of ectopic beats, and was resampled at 4 Hz, yielding $d_{\mathrm{HR}}(n)$. Then, the ANS modulating signal was obtained as $m(n) = \frac{d_{\mathrm{HR}}(n)-d_{\mathrm{HRm}}(n)}{d_{\mathrm{HRm}}(n)}$, where $d_{\mathrm{HRm}}(n)$ was estimated by low-pass filtering $d_{\mathrm{HR}}(n)$ at 0.04 Hz to capture the HRV signal. This approach enables the analysis of the frequency components of HRV and provides insights into the autonomic regulation of heart rate.

The PSD of the modulating signal, $\hat{S}_{HRV}(f)$, was calculated in 5-minute segments in the same way as $\hat{S}_R(f)$. To ensure high-quality signals and a robust methodology, 5-minute windows were discarded when more than 10% of their duration was affected by signal loss or poor quality. These issues may arise from the presence of ectopic beats, arrhythmia episodes, or other anomalies in the ECG signal that compromise accurate heart rate detection and HRV computation, as previously described in the literature [11].

2.4. Aliasing in HRV Signals

The additional components observed in the HRV signal could be explained by considering that the intrinsic sampling rate of HRV is determined by the heart rate (HR) itself. This implies that the maximum physiologically relevant frequency that can be analyzed is limited to half the mean HR within the analyzed interval. However, if the modulating signal carrying information from the ANS activity includes frequency components that exceed this limit, aliasing will occur at the natural heart-driven sampling rate, resulting in the appearance of low-frequency components below half the mean HR [12]. In mechanically ventilated patients, $\hat{S}_R(f)$ might exhibit components not only at the main respiratory rate, F_{R}, but also at its harmonics. Thus, the component at $2F_{\mathrm{R}}$ might generate an alias in the HRV signal at $F_{\mathrm{HR}} - 2F_{\mathrm{R}}$, whenever $2F_{\mathrm{R}} > \frac{F_{\mathrm{HR}}}{2}$, and similar effects will occur at higher harmonics, with a progressively reduced effect, as each successive harmonic has less power. This results in the appearance of new frequency components in $\hat{S}_{HRV}(f)$. In windows where $2F_{\mathrm{R}} < \frac{F_{\mathrm{HR}}}{2}$, no aliasing occurs, and a new component appears in the HRV spectrum at $2F_{\mathrm{R}}$. However, when $2F_{\mathrm{R}} \geq \frac{F_{\mathrm{HR}}}{2}$, aliasing occurs, and the component manifests at $F_{\mathrm{HR}} - 2F_{\mathrm{R}}$. In the case of $F_{\mathrm{HR}} - 3F_{\mathrm{R}}$, there is not a clear interpretation, as it is part of the LF band, $\Omega_{LF} = [0.04, 0.15]$. An example of this aliasing effect can be seen in Fig. 1.

2.5. Features and Statistical Analysis

Firstly, in order to identify when harmonics appear in the respiratory signal, a search was performed for those 5-minute segments where the power associated with the second harmonic of the respiratory signal is, at least, 5%

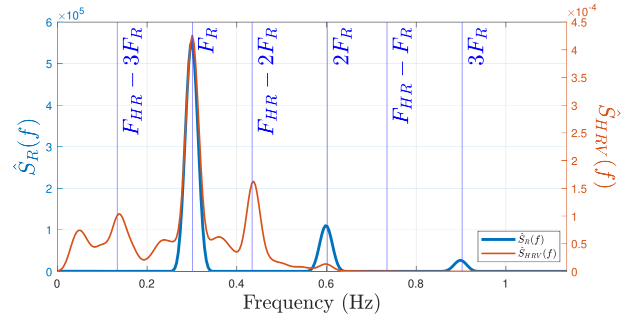

Figure 1. PSD of the respiratory signal (in blue) and HRV (in orange) reveals the appearance of components in the HRV spectrum at a $F_{\text{HR}} - 2F_{\text{R}}$ frequency, due to aliasing.

of the power at the fundamental respiratory peak, i.e., $P^{\text{R}}_{2F_{\text{R}}} > 0.05P^{\text{R}}_{F_{\text{R}}}$. The proportion of time within the 24-hour recording where this condition is met was calculated, along with the median in the selected time windows of the following indices, which measure the relative power associated with the second harmonic of respiration with respect to the fundamental respiratory rate, both in $\hat{S}_R(f)$ ($\frac{P^{\text{R}}_{2F_{\text{R}}}}{P^{\text{R}}_{F_{\text{R}}}}$) and in $\hat{S}_{HRV}(f)$, differentiating in this last case whether aliasing is present ($\frac{P^{\text{HRV}}_{F_{\text{HR}}-2F_{\text{R}}}}{P^{\text{HRV}}_{F_{\text{R}}}}$) or not ($\frac{P^{\text{HRV}}_{2F_{\text{R}}}}{P^{\text{HRV}}_{F_{\text{R}}}}$).

Lastly, the following indices were computed to assess the relative contribution of respiratory components to HRV power, as an indicator of the system's output (HRV) relative to its input (respiration) in the cardiopulmonary coupling (CPC) mechanism:

- $\alpha^2(F_{\text{R}}) = \frac{P^{\text{HRV}}_{F_{\text{R}}}}{P^{\text{R}}_{F_{\text{R}}}}$
- $\alpha^2(2F_{\text{R}}) = \frac{P^{\text{HRV}}_{2F_{\text{R}}}}{P^{\text{R}}_{2F_{\text{R}}}}$, computed only in windows that do not present aliasing (i.e., $2F_{\text{R}} < \frac{F_{\text{HR}}}{2}$)
- $\alpha^2(F_{\text{HR}} - 2F_{\text{R}}) = \frac{P^{\text{HRV}}_{F_{\text{HR}}-2F_{\text{R}}}}{P^{\text{R}}_{2F_{\text{R}}}}$, computed only in windows where aliasing occurs (i.e., $2F_{\text{R}} \geq \frac{F_{\text{HR}}}{2}$)

To evaluate the amplification of harmonic components with respect to the fundamental frequency, the following ratios were calculated using the previous indices: $\frac{\alpha^2(2F_{\text{R}})}{\alpha^2(F_{\text{R}})}$ and $\frac{\alpha^2(F_{\text{HR}}-2F_{\text{R}})}{\alpha^2(F_{\text{R}})}$.

To assess statistically significant differences between ventilation modes, the Mann-Whitney U test has been performed, and the significance level set to p-value < 0.05.

3. Results and Discussion

Cardiopulmonary coupling operates as a dynamic system, where variations in the input (respiration) result in corresponding changes in the output (HRV).

It is observed that, most of the time, frequency components appear at $\hat{S}_R(2F_{\text{R}})$. In the case of controlled ventilation, the median percentage of time is 93.39% [IQR: 72.34-99.9%]. In support ventilation, it is 83.51% [58.55-100%]. In CPAP, it is 83.33% [25.35-100%].

Fig. 2 shows the effect of a second harmonic at $\hat{S}_R(2F_{\text{R}})$ in power indices. A different behavior is observed between respiratory and HRV signals: the HRV signal exhibits higher median values in the evaluated indices, especially in controlled and support modes. This suggests that CPC works as the described system, where the respiratory signal acts as the input (boxplot on the left) and the HRV signal as the output (central and right boxplots, in the absence and presence of aliasing, respectively).

In both the controlled and support modes, with a strong ventilator influence, additional components at $2F_{\text{R}}$ and $F_{\text{HR}} - 2F_{\text{R}}$ appear in $\hat{S}_{HRV}(f)$, which would not be found in natural breathing. In the case of CPAP, which is a spontaneous mode, this effect is not visible.

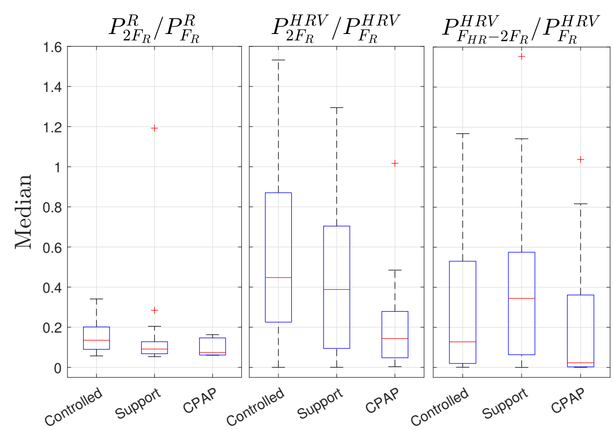

Figure 2. Distribution of power indices, obtained in 5-minute segments where $P^{\text{R}}_{2F_{\text{R}}} > 0.05P^{\text{R}}_{F_{\text{R}}}$.

Fig. 3 illustrates power ratios in both non-aliasing and aliasing scenarios. They represent the gain of the CPC system, that is, how variations in the respiratory signal lead to the presence of additional frequency components in the HRV signal. It is observed that, in all ventilation modes, especially in controlled and support modes, the occurrence of harmonics in the respiratory signal results in the manifestation of harmonics in the HRV signal, which will be visible at different frequencies depending on the absence or presence of aliasing.

It is worth noting the effect of amplification of higher frequencies —a sort of high-pass behavior— which is not characteristic of the ANS or CPC under normal conditions. In addition to the aliasing effects explored, it is also plausible that nonlinear interactions contribute to the appearance of additional components in the HRV spectrum. This highlights the need for further simulation studies that incorporate nonlinear relationships, in order to investigate and better understand the physiological mechanisms underlying this phenomenon.

Although some trends are observed between ventilation modes, differences do not reach statistical significance.

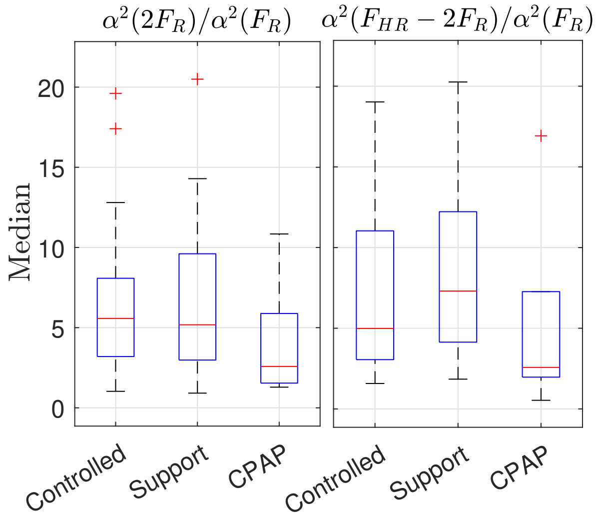

Figure 3. Distribution of the obtained ratios, in the absence of aliasing (left) and when aliasing occurs (right).

4. Conclusion

Mechanical ventilation generates a series of harmonics in the respiratory signal, with the second harmonic being the most prominent, which translates into the appearance of new frequency components in the HRV signal beyond the classical LF and HF bands. Since these components, in some scenarios, exceed the $\frac{F_{\text{HR}}}{2}$ threshold, they do not always manifest at a frequency of $2F_{\text{R}}$, but may instead appear as aliases at the frequency $F_{\text{HR}} - 2F_{\text{R}}$. These observations highlight the need for a new interpretation of the HRV signal in machine-ventilated scenarios.

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