

## Heart Rate Variability During Weaning Mechanical Ventilation

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### ABSTRACT

**INTRODUCTION:** Heart rate variability (HRV) is a noninvasive method that analyzes fluctuations of intervals between heartbeats and it is related to the influences of the autonomic nervous system during weaning.

**AIM:** To describe the behavior of cardiac autonomic modulation during the weaning process.

**METHOD:** A search was conducted in PubMed. Initially 206 articles were found. After restriction search we identified 28 potentially eligible publications.

**RESULTS:** Nine studies were included, among which eight were performed in adults and concluded that HRV during weaning becomes important because it can provide information on pathophysiological imbalances reflected in the success or failure of weaning. Only one article conducted the study in children and stated that the value of HRV as a predictor of extubation still requires further evaluation.

**CONCLUSION:** Behavior of the cardiac autonomic modulation during the weaning process is characterized by reduced HRV and vagal withdrawal in patients with failure weaning needing to be reconnected to the mechanical ventilation support.

**Key words:** Autonomic nervous system; Cardiovascular physiology; Weaning ventilator

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### INTRODUCTION

Mechanical ventilation (MV) totally or partially replaces spontaneous ventilation and is indicated for acute respiratory failure (ARF) or acute exacerbations of chronic respiratory failure<sup>[1]</sup>. The number of patients requiring prolonged time of MV has noticeably increased, encouraging work in the intensive care unit (ICU) resulting in greater survival of patients with incapacity of the respiratory system to perform its functions. Researchers discussed that weaning starts as soon as the patient is placed on mechanical ventilation<sup>[2]</sup>.

Both delayed and premature extubation increase the rates of complications, need for tracheotomy, duration of ICU stay and mortality<sup>[3]</sup>. One review summarized the predictors of extubation failure in the general ICU as follows: demographic predictors,

predictors assessing respiratory mechanics, parameters assessing airway protection, parameters assessing airway patency, and parameters assessing hemodynamics and tissue perfusion<sup>[4]</sup>.

On the other hand, in a systematic review and meta-analysis with neurocritical patients, some traditional weaning parameters were shown to poorly predict extubation failure in neurocritical patients<sup>[3]</sup>.

After cardiac surgery, for example, early weaning of patients from mechanical ventilation enhances the cardiopulmonary function and early ambulation, reduces the length of ICU and/or hospital stay, and causes an improvement in the intrapulmonary shunt fraction after extubation<sup>[5]</sup>.

Indeed, MV and subsequent removal changes normal ventilatory mechanics and produces alterations in cardiac preload and afterload that influence global hemodynamic state and delivery of oxygen and nutrients. Adverse cardiovascular responses to mechanical ventilation and weaning from ventilation include hemodynamic alterations and instability, myocardial ischemia, autonomic dysfunction, and cardiac dysrhythmias<sup>[6]</sup>.

Heart rate variability (HRV) is the physiological phenomenon of variation in the time interval between heartbeats due to the joint action of the sympathetic and parasympathetic divisions of the autonomic nervous system (ANS) and is measured by the change in the beat-to-beat interval. Its analysis can be performed in function of two parameters: time domain and frequency domain<sup>[7,8]</sup>.

The time domain parameter is called because the results expressed in units of time (milliseconds), are measured in each normal RR intervals (sinus beats) over a given time interval based on statistical or geometric methods (mean, standard deviation and histogram-derived indexes or the Cartesian coordinates map of the RR intervals), it is calculated the translator indexes of fluctuations during the cardiac cycles<sup>[7,8]</sup>.

The frequency domain parameter is the power spectral density which is more widely used, when it comes to studies with subjects in rest conditions. This analysis decomposes HRV in fundamental oscillatory components, and the main ones are: High Frequency component (HF), ranging from 0.15 to 0.4 Hz, which corresponds to the respiratory modulation and is an indicator of the vagus nerve action upon the heart; Low frequency component (LF), ranging between 0.04 and 0.15 Hz, which is due to the joint action of the vagal component and friendly on the heart, with a predominance of sympathetic; Very Low Frequency components (VLF) and Ultra Low Frequency (ULF) -Indexes less used whose physiological explanation is not well established and seems to be related to the renin-angiotensin-

aldosterone system, thermoregulation and the peripheral vasomotor tone. The LF/HF ratio reflects the absolute and relative changes between the sympathetic and parasympathetic components of the ANS, by characterizing the sympathetic-vagal balance on the heart<sup>[7,8]</sup>.

Although the predictors of delayed extubation cannot be defined easily, the ability to identify high-risk patients and pre- and perioperative risk factors may help to develop surgical and medical modifications which will allow earlier extubation<sup>[5]</sup>.

Weaning from mechanical ventilation to spontaneous breathing is associated with changes in the hemodynamic and autonomic nervous systems that are reflected by heart rate variability. Although cardiac dysrhythmias are an important manifestation of hemodynamic alterations, the impact of heart rate variability during weaning has not been specifically studied<sup>[9]</sup>.

This research on HRV for weaning patients becomes important because its assessment during this process can provide information on pathophysiological imbalances reflected in the success or failure of weaning thus avoiding the re-intubation of patients. In this sense, we aimed to describe the behavior of the cardiac autonomic modulation during the weaning process.

## METHODS

### Search Strategies

The search for scientific articles was conducted by independent researchers in PUBMED, held from February to October 2014. In the searches, the following terms, in English, were considered "mechanical ventilation" (weaning OR extubation) and "heart rate variability" or "autonomic nervous system". The initial electronic search yielded 206 articles. By checking this breadth of topics related to heart rate variability, the search process followed with the following descriptor: "Heart Rate Variability" and "weaning ventilator". Through this search procedure, were initially identified 28 potentially eligible papers for inclusion in this review. The review process of the studies involved reading titles, abstracts and full texts (evaluating the inclusion criteria already mentioned the top), totaling 9 articles for inclusion in this study (Figure 1).

### Inclusion Criteria

This review included observational studies in patients undergoing mechanical ventilation for more than 24 hours. Inclusion criteria: publications maximum period of 13 years (2003 to 2015), in which the samples should include only human beings, satisfaction studies

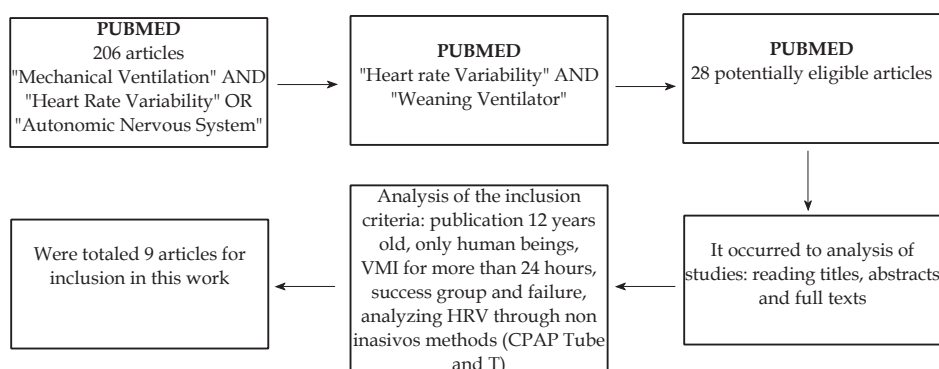


Figure 1 Search chart ao articles.

with success and failure groups, analyzing heart rate variability through non-invasive methods (CPAP Tube and T). Studies should be only in English and analyze heart rate variability during the weaning.

**Exclusion Criteria**

Samples containing intervention by health professionals with techniques used in the ICU; studies containing drug intervention.

**RESULTS**

We included in this review a total of 9 articles on the subject, and

8 were performed in adults, accounting for 89%, and found that HRV analysis for weaning patients becomes important, since this assessment can provide information on the pathophysiological imbalances reflected in the success or failure of weaning, taking into consideration that a low HRV is associated with an abnormal and insufficient adaptation of the ANS and high HRV is a sign of good adaptation, featuring a healthy individual and ready to breathe spontaneously. Only 1 item, accounting for 11%, carried out the study in children; despite it did not find the same result compared with adults for low and high HRV, the authors stated that the value of HRV as a predictor of extubation still requires further evaluation.

**Table 1** Articles included and their participants.

Author/Year	Participants (Total Included in Study)	Total number of participants the group success	Total number of participants the group failure	Inclusion criterion for the failure group	Test Used
Chun-Ta/2014[1]	101	64	37	Reintubated within 72 hours	Spontaneous Breathing (T Tube) for 1 hour
Caminal/2010[2]	133	94	39	Reintubated within 30 minutes	Spontaneous Breathing (T Tube) for 30 minutes
Hsiu -Nien/2003[3]	24	12	12	Reintubated within 48 hours	Spontaneous Breathing (T Tube) for 2 hours
Michele Orini/2008[4]	130	91	39	Reintubated within 30 minutes	Spontaneous Breathing (T Tube) for 30 minutes
Kaczmarek/2013[5]	47	36	11	Reintubated within 72 hours	Nasal or VNI CPAP
Arcentales/2011[6]	131	92	39	Reintubated within 30 minutes	Spontaneous Breathing (T Tube) for 30 minutes
Frazier SK/2008[7]	43	28	15	Reintubated within 24 hours	CPAP during 24 hours
Vallverdú/2006[8]	78	50	28	Reintubated within 30 minutes	Spontaneous Breathing (T Tube) for 30 minutes
Seely/2014[9]	391	344	47	Reintubated within 48 hours	-

Legend: T Tube (spontaneous breathing test used to wean).

**Table 2** Main Outcomes.

Article	Objective	HR analysis of time	Main Outcomes
1	To evaluate the association between change in HRV and weaning results in critically ill patients..	During test for weaning	A reduced HRV is associated with SBT failure and the inability to increase the heart rate variability after extubation is correlated with extubation failure in patients who have SBT.
2	To show that joint symbolic dynamic analysis provides enhanced information about different interactions between HR and BR, when comparing patients with successful trials and patients that failed to maintain spontaneous breathing in the weaning procedure.	During test for weaning	A reduced HRV in the failure group compared to the Success group for the time domain analysis, but not for the frequency domain.
3	To investigate the change in the activity of the autonomic nervous system for weaning patients by analysis of HRV.	FC variables (HF and LF) were measured in 3 phases: Helping mandatory ventilation; PSV and SBT.	Moving from PSV to SBT, HRV components significantly reduces the failure group, but not in the success group.
4	Assess whether there are differences in autonomic regulations among patients who are considered ready for spontaneous breathing and those who are not.	During test for weaning	The respiratory rate, heart rate and the frequency of the LF and HF components of the two groups showed significant differences throughout trial of weaning.
5	Compare differences in HRV between children successfully extubated and those who do not, and to assess the accuracy of HRV as maturity predictor of extubation.	60 minutes before extubation	All HRV analysis of the components decreased significantly in babies who failed to wean.
6	Propose a non linear analysis of the complexity of HRV.	During the test to weaning	The average values of HRV analysis are higher in the success group than in the group fails.
7	To assess autonomic tone for 24 hours and mechanical ventilation for a 24 hours period which includes the initial spontaneous breathing trial with CPAP.	One hour prior to the trial CPAP	The use of mechanical ventilation may influence the heart rate because of significant changes in alveoli and intrathoracic pressure and subsequent changes in cardiac output and mean arterial pressure
8	Analyze nonlinear statistical dependencies between HRV and the variability of respiratory pattern.	During test for weaning	The group of 28 patients failed to maintain spontaneous breathing and were reconnected; Group B of 50 patients with successful test.
9	(1) to compare variability in patients who passed and failed extubation using a wide array of HRV and RRV measures, and (2) to investigate the added value of HRV and RRV in the prediction of extubation outcomes, both individually and in combination, as compared to commonly used clinical variables, namely heart rate (HR), respiratory rate (RR), tidal volume (TV), and RSBI.	From 30 minutes prior to the SBT until 30 minutes following its conclusion.	Altered HRV and RRV (during the SBT prior to extubation) are significantly associated with extubation failure. A predictive model using RRV during the last SBT provided optimal accuracy of prediction in all patients, with improved accuracy when combined with clinical impression or Rapid Shallow Breathing Index.

HRV: Heart Rate Variability; SBT: spontaneous breathing trial; HF: High Frequency; LF: Low Frequency; PSV: Pressure Support ventilatory; CPAP: Positive Pressure Continuous Airway.

## DISCUSSION

Current literature has studies about HRV in various environments and situations, but in hospitals and during the weaning process is not very comprehensive. HRV is a noninvasive tool used in order to predict the success or failure to wean the patient<sup>[10-12]</sup> in order to prevent some episodes of discomfort and risk to patients, for example, re-intubation. Although promising data were found the value of HRV as a predictor of extubation requires more evaluation<sup>[13-16]</sup> and should not be the sole criterion for weaning, the ideal is to be added to other criteria, since each body reacts in a way and can surprise.

This review showed that the cited authors presented two different methods and different HRV moments of analysis using non-invasive tools such as ECG. It has been found positive results (success group) which were increased HRV in all studies of this review, and the reduction in the spontaneous breathing trial/CPAP and inability to increase HRV after extubation are correlated with the group of failure and requires the return to mechanical ventilation.

Another relevant point is that there are few studies evaluating exclusively HRV during the weaning process. From nine studies cited, only five had the most focus on HRV analysis for weaning. The other also included activity of the autonomic nervous system, autonomic regulations, autonomic tone assessment and breathing patterns; six used the spontaneous breathing trial (T tube) and only two used CPAP as a tool.

The analysis criteria for the rejection of HRV during the weaning process in some studies were tracheostomy patients, patients with cardiac arrhythmias (atrial or ventricular), chronic antiarrhythmic drug, patients with congenital abnormalities, congenital heart disease, sedation extubation and those who were not able to follow verbal instructions.

Hsiu-Nien *et al.*<sup>[10]</sup>, in 2003, conducted a prospective observational study of spontaneous breathing trial (T tube) for 2 hours in 24 patients. They observed that changing the PSV for SBT components of HRV (HF and LF) decreased significantly in the failure group, but not in the success group. It was concluded that the reduction of HRV and vagal withdrawal of activity of the autonomic nervous system are the major changes in patients with weaning failure. The authors described that there are reasons for the reduced HF component in the failure group: the withdrawal of parasympathetic nervous system activity could be related with the intense sympathoadrenal stimulation during weaning from mechanical ventilation. Besides that, the increased respiratory rate and decreased tidal volume found in the failure group related with HF component of HRV decreases.

Thus, this study showed that HRV is a reliable method for detecting the activity of the autonomic nervous system in patients during weaning and changes of HRV components can be a potential tool of meeting parameters for weaning<sup>[10]</sup>.

Similarly to Hsiu-Nien *et al.*<sup>[10]</sup>, Caminal *et al.*<sup>[11]</sup>, in 2010, observed in their study of spontaneous breathing trial (T tube) for 30 minutes in 133 patients, that there was a reduced HRV in the failure group compared to the success group for the time domain analysis, but not for the frequency domain.

Lower variability of the breathing rate was found in group successful weaning. Respiratory center responds mainly with tachypnea in front of acute respiratory failure. This fact may justify that the time intervals of respiratory pattern obtained more significant results than the time intervals of cardiac pattern. The presence of alternant patterns in heart period variability has been linked to vagal modulation.

As Hsiu-Nien *et al.*<sup>[10]</sup>, Arcentales *et al.*<sup>[12]</sup> (2011) and Chun-Ta *et*

*al.*<sup>[13]</sup> (2014) also with their observational and prospective studies, performed the spontaneous breathing trial (T tube) for 30 minutes in 131 patients and 1 hour in 101 patients, respectively, and reached the same end result that reduced HRV and its components is associated with failure of spontaneous breathing trial. Chun Ta *et al.*<sup>[13]</sup> found in their study that the reduced HRV was significantly associated with spontaneous breathing trial (SBT) failure among patients with their first SBT, and the inability to increase HRV after extubation correlated with extubation failure in patients who passed SBT. Different of Caminal *et al.*, in this study, in patients undergoing SBT, breathing variability is greater in those successfully weaned from mechanical ventilation. However, as other authors, this study also found significant association between increased HRV and successful extubation in patients who passed SBT. A higher probability of extubation failure is correlated with incapability to increase HRV.

They concluded that the HRV responses differ between patients with different results weaning and for that reason, measure change in HRV during the weaning process may help clinical professionals to predict final results from weaning to improve care and patient outcomes<sup>[13]</sup>.

Kaczmarek J *et al.*<sup>[14]</sup> (2013) studied a total of 47 children, in whom 36 were successfully extubated and 11 were re-intubated. With these data they reached the same end result of the previously mentioned authors concerning the association of HRV to the success (increased HRV) and failure (decreased HRV) of weaning, but instead of using the spontaneous breathing trial (T tube) they used nasal CPAP or NIPPV (Nasal intermittent positive pressure ventilation) as a tool for 60 minutes. In contrast with Hsiu-Niem *et al.*<sup>[10]</sup>, this study found that despite promising, the value of HRV as a predictor of extubation still requires further evaluation, mainly because there are differences in ANS maturation of children<sup>[14]</sup>.

In 2006, Vallverdú *et al.*<sup>[15]</sup> conducted a prospective observational study in order to analyze the nonlinear statistical dependencies between HRV and the variability of respiratory pattern using the spontaneous breathing trial (T tube). 78 patients were included in this study, in which 28 failed to maintain spontaneous breathing and were restarted the mechanical ventilation within 30 minutes and 50 who were successful in the test. The results show lower complexity with an increase of information flow in successful group than in failure group. Furthermore, a more coupled nonlinear oscillator behavior was observed in the series of failure group than in successful group.

Frazier *et al.*<sup>[16]</sup> (2008) evaluated the autonomic tone of 43 critically ill patients during ventilatory support 24 hours, including the initial spontaneous breathing trial with continuous positive airway pressure. From 43 patients, 15 were not able to sustain spontaneous ventilation, reducing HRV, and 28 remained in spontaneous ventilation increasing HRV. The result was that mechanical ventilation use can influence the HR because of significant changes in alveoli and intrathoracic pressure and subsequent changes in cardiac output and mean arterial pressure. Intravascular and interstitial volumes and a hypervolemic state were increased by reductions in natriuretic peptide secretion, increases in arginine vasopressin and a significant release of renin with subsequent elevations in angiotensin II and aldosterone. These modifications may have contributed to the global reduction in HRV because some of the circadian rhythms of these hormones are reflected in the HRV measures. Thus, patients in failure group had the lowest values of the HRV components compared to successful group<sup>[16]</sup>.

Orini *et al.*<sup>[17]</sup>, in 2008, conducted a study in the same line of reasoning of Hsiu-Nien *et al.*<sup>[10]</sup> 2003 to determine whether there are differences in autonomic adjustments among patients who are considered ready for spontaneous breathing and which are not. We



included 130 patients, among which 91 were successfully extubated while 39 were not considered ready for discontinuation and returned to the mechanical ventilation support. Unlike all other studies that concluded in percentage the classification based on HR, RR intervals and spectral components of HRV has been able to correctly classify over 80% of cases<sup>[17]</sup> At the same time, the data found in this study suggested that there are important differences in autonomic regulation between patients who are considered ready for SBT and patients who are not, as well as in other studies.

Seely *et al*<sup>[18]</sup> (2014) conducted a prospective, blinded observational multicenter cohort study with 391 patients, among which 344 were successfully extubated and 47 failed. They aimed primarily to compare variability in patients who passed and failed extubation using a wide array of HRV and Respiratory Rate Variability (RRV) measures. As seen in the other studies, HRV and RRV decreased (during the SBT prior to extubation) are significantly associated with extubation failure<sup>[18]</sup>. As extubation is associated with an increase in work of breathing, and extubation failure is commonly due to the inability of the cardiorespiratory system to tolerate this increased workload, the authors hypothesized that variability monitoring would improve the ability to detect stress and inability to tolerate the increased workload of breathing associated with an SBT, and subsequently extubation.

Although studies have been published on different dates, using two different methods (tube T and CPAP), analyze HRV during periods and many times, the result of HRV analysis has become homogeneous among the nine studies. Of the 1,078 patients involved in all studies analyzed in this review, 811 were successful in weaning and only 267 had mechanical ventilation return for failing to maintain and/or increase the heart rate variability, thus demonstrating an abnormal and insufficient adaptation of SNA indicating physiological malfunction of individuals.

In conclusion, behavior of the cardiac autonomic modulation during the weaning process is characterized by reduced HRV and vagal withdrawal in patients with failure weaning needing to be reconnected to the mechanical ventilation support.

## CONFLICT OF INTERESTS

There are no conflicts of interest with regard to the present study.

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