Profile of Autonomic Cardiac Control in Patients who are Not Considered Ready for Weaning from Mechanical Ventilation

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Abstract

This study tracks the global tendency of the heart rate variability (HRV) profile over five ventilation modes, aiming to find evidences on the hypothesis that patients who failed during the weaning process manifest important differences in the autonomic nervous system activity. This preliminary study enrols 17 patients (7 successful (S), 10 failure (F)) who underwent weaning with AVEA ventilator. Time- and frequency- domain HRV analysis is applied over 5-min ECG episodes recorded at the beginning of 5 ventilation modes: (1) controlled mechanical ventilation (CMV) on a sedated patient; (2) CMV on a sedated and paralyzed patient; (3) Pressure support ventilation with zero back-up pressure PSV(0); (4) PSV at 12-25 cmH_2O; (5) Spontaneous breathing trial (SBT) at 8 cmH_2O. Our results support the finding of other authors that during SBT, the patients who succeed in weaning show a prevalently sympathetic modulation, while relatively increased vagal activity is typical for the F-group. PSV(0) is however an outstanding test for which F-patients manifest about 3 to 20 fold increased sympathetic and vagal activity compared to the S-group.

1. Introduction

The weaning from controlled mechanical ventilation (CMV) requires an expert decision based on a complex knowledge of a large number of clinical and respiratory parameters, and analysis of their evolution over time [1,2]. CMV discontinuation is a cardiovascular stress so that patients who failed at weaning manifest cardio-vascular insufficiency during the weaning attempt [3]. Analysis of cardiac autonomic control during weaning has been shown to derive valuable information about the presence or absence of pathologic autonomic balance. The associated changes in the autonomic nervous system activity are investigated in a number of studies which use time-frequency heart rate variability (HRV) analysis [4] to unmask any existing abnormalities in one or several control mechanisms of the autonomic regulation response at different phases of the weaning [5-9].

Despite the introduction of several new ventilation modes, assist-control volume-cycled ventilation continues to be the most commonly applicable. However, regional differences are reported in the utilization of ventilation modes [10]. This preliminary investigation applies time and frequency domain HRV analysis during a weaning study with five different modes of mechanical ventilation, aiming to provide a global overview of the profile of the cardiac autonomic control and thus to observe the most outstanding changes which could predict whether the patient is ready or not to maintain spontaneous breathing trial (SBT).

2. Materials and methods

2.1. Study population

This study enrols patients undergoing weaning with AVEA ventilator system (Cardinal Health, USA) in the Central Intensive Care Unit of the University Emergency Hospital ‘N. Pirogov’, Sofia, Bulgaria from August 2011 to July 2012. The study population consists of 13 men and 4 women, mean age of 62.4±14.7 years, Simplified Acute Physiology Score (SAPS II) of 30.4±8. According to inclusion criteria, the enrolled patients do not have cardiac arrhythmias, neurological diseases, do not take pre-medication with cardiovascular drugs, and receive CMV for at least 72 hours prior the study. The decision to start weaning and weaning outcome has been made by the primary care physician following general weaning and extubation criteria [11]. All patients are divided into successful (S, n=7) and failure (F, n=10) group according to the weaning outcome at the 2nd hour of SBT, which is the final phase of the study protocol (as defined below).

Basic respiratory and hemodynamic parameters are measured by AVEA during the whole study, among which are blood pressure (SYS, DIA), respiratory rate (*f*).

2.2. Study protocol

The study follows a predefined protocol, approved by the local ethics committee, including 5 ventilation modes:

(1) *CMV(S)* – CMV on a patient who is sedated with short-acting hypnotic medication. CMV is maintained for at least 10 min, with settings of f = 12 breaths/min, tidal volume V_T = 10 ml/kg, positive end-expiratory pressure (PEEP about 5 cmH_2O) and fraction of inspired oxygen (FIO_2 about 40-45 %) at the same level as were immediately before the study entry.

(2) *CMV(SP)* – CMV is maintained with settings as in phase (1). The sedated patient is additionally paralyzed with a short-acting or intermediate neuro-muscular blocker in order to provide passive respiratory system for at least 10 min.

(3*) PSV(0 Backup)* – After waning of the sedative effect and neuromuscular recovery, the ventilatory mode is switched to pressure support ventilation (PSV) at zero back-up pressure and zero end expiratory pressure (ZEEP) for a closely monitored period of 5 min, with the intent to provoke a brief intense challenge to the patient.

(4) *PSV* – PSV is set with pressure support level in the range 12-25 cmH_2O, initially providing $V_T \geq$ 8ml/kg. The PEEP level is kept the same as in CMV mode. This phase is maintained for at least 30 min.

(5) *SBT* – PSV is set at 8 cmH_2O (ZEEP) as an equivalent of spontaneous breathing trial. The patient is monitored for at least 2h or in case of failed SBT accordingly classified in the failure group.

2.3. HRV analysis

The related electrocardiogram (ECG) processing is performed offline in Matlab 7.5 (MathWorks Inc.), using a continuously recorded single-lead ECG, sampled at 500 Hz during the whole weaning process.

First, the QRS complexes are automatically detected and classified as normal sinus or pathological beats by scanning deviations of the moment interbeat RR-interval and QRS waveform relative to the features of the mean QRS pattern of the sustained rhythm [12].

Second, time series of normal-to-normal RR-intervals (NN-intervals), deduced from the adjacent normal sinus beats in stable artifact-free 5-min episodes under stationary conditions are extracted after the beginning of each weaning phase. Time - and frequency- domain HRV analysis is applied to calculate the standard measures, recommended by the ESC/NASPE Task Force [13].

• Time-domain features – SDNN (standard deviation of all NN-intervals), RMSSD (square root of the mean squared differences of successive NN intervals); pNN50 (proportion of NN intervals differing by >50 ms from the preceding NN interval).

• Frequency-domain features – Fast Fourier Transform (FFT) of the NN interval time series resampled at 4Hz is used to derive the power spectrum density components: total power (TP = 0.003–0.4 Hz, representing the overall activity of the autonomic nervous system (ANS); very low frequency range (VLF = 0.003–0.04 Hz, reflecting sympathetic activity); low-frequency range (LF = 0.04–0.15 Hz, reflecting mixed sympathetic and vagal activity, considering that LF is widely suggested as an index of predominantly sympathetic activity); high frequency range (HF = 0.15–0.4 Hz, reflecting vagal activity); ratio LF/HF (reflecting sympathetic-vagal balance).

3. Results

Table 1 summarizes the measurements of the defined hemodynamic and HRV indexes over 5 ventilation phases. T-test is applied to compare the distribution of means comparing failure vs. successful group (F vs. S). Figure 1 additionally illustrates the HRV profile of failure

Table 1. Mean ± standard error of hemodynamic, time- and frequency- domain HRV indices for the failure group (F, 10 patients) and successful group (S, 7 patients) during 5 ventilation phases. *: p<0.05 comparing F vs. S groups by T-test.

	CMV(S)		CMV(SP)		PSV(0)		PSV		SBT	
	F	S	F	S	F	S	F	S	F	S
HR (bpm)	94±7	110±5	92±6	102±6	92±5	107±6	95±7	106±6	97±6	106±5
SYS (mmHg)	129±7	141±9	112±6	117±11	127±9	117±7	140±10	128±10	154±13	140±11
DIA (mmHg)	73±5	68±5	57±4	55±5	69±5	66±4	78±6	64±4	83±9	77±4
f (br/min)	12±0	12±0	12±0	12±0	37±4	29±2	25±2	20±3	33±3	27±3
SDNN (ms)	16±3	21±4	13±3	15±3	45±3*	19±4	14±3	17±6	16±2	15±5
RMSSD (ms)	12±4	11±4	10±3	9.3±3	29±7	10±3	13±3	7.8±2	14±3	8.8±2
pNN50(min^{-1})	1.3±0.8	1.1±.9	0.8±0.5	0.7±0.4	5.3±2	0.5±0.2	1.7±1	0.3±0.2	1.4±0.6	0.5±0.3
TP (ms^2)	200±69	317±168	121±46	76±32	1668±558*	205±64	168±76	361±243	114±31	290±192
VLF(ms^2)	84±26	236±134	56±17	60±29	1369±694	173±56	58±21	293±197	55±20	238±166
LF (ms^2)	68±35	70±49	38±21	4.4±2	426±248	19±9	63±40	49±37	22±10	37±22
HF (ms^2)	49±30	13±4	28±14	11±5	322±116*	15±6	48±19	19±11	37±16	16±8
LF/HF	2.4±1	3.2±2	1.3±0.4	0.7±0.1	3.5±1.5	1.4±0.3	1.7±0.5	3.3±0.9	2.1±0.8	3.2±2

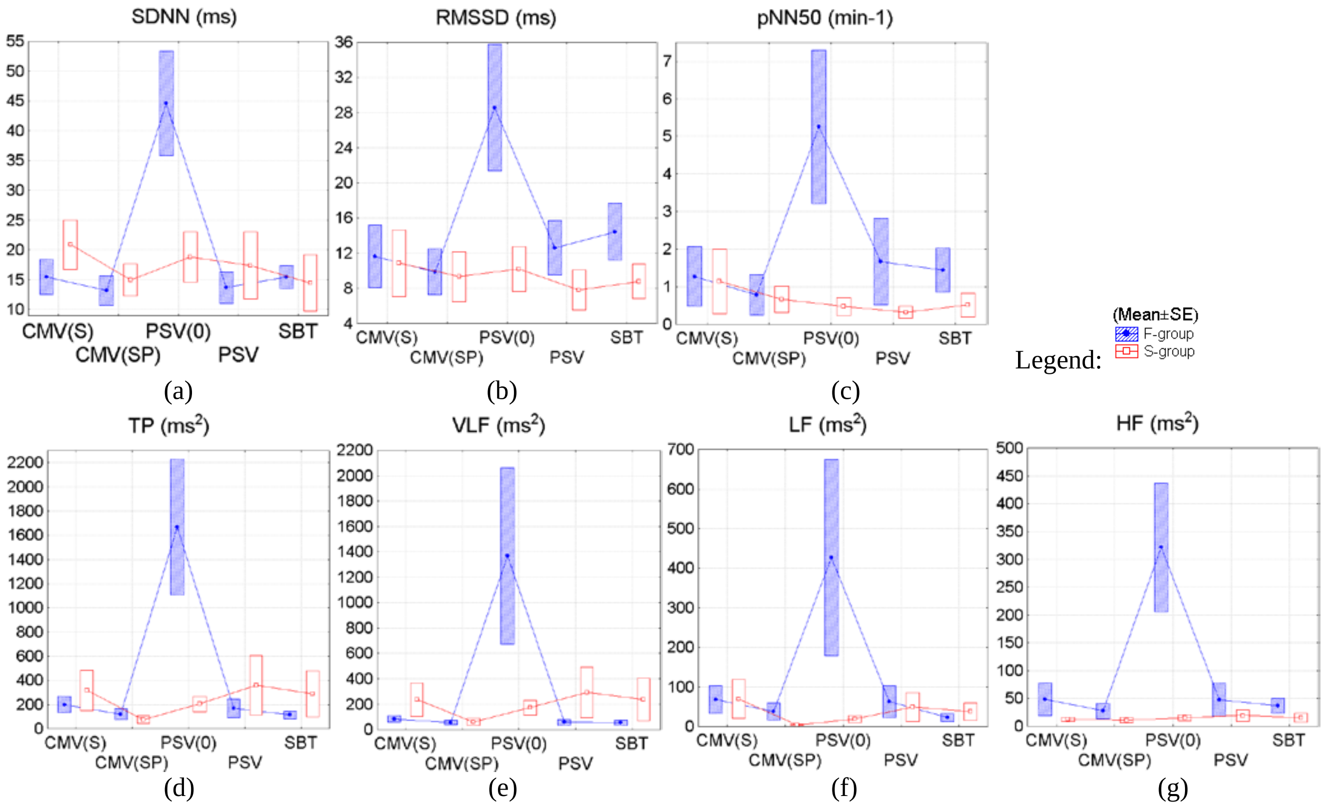

Figure 1. HRV profile over 5 ventilation phases, represented by box-plot distributions (Mean ± standard error) of 7 HRV indices: time-domain (a-c); frequency-domain (d-g), all estimated for F-group (blue solid) vs. S-group (red transparent).

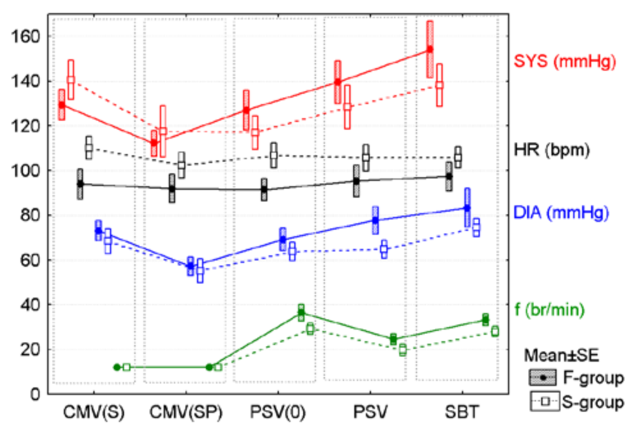

Figure 2. Profile of hemodynamic indices (HR, SYS, DIA) and breathing rate (f) over 5 ventilation phases, represented by mean ± standard error for F group (solid boxes) and S-group (transparent boxes). p>0.05 for all.

and successful patients because the observed trends are the basis for deriving conclusions about the most relevant differences. The hemodynamic profile in Figure 2 is also illustrative about the insignificant differences among F and S groups, as well as it shows the gradual trend of SYS, DIA, HR, f when switching the 5 ventilation modes.

4. Discussion and conclusions

This preliminary study tracks the global tendency of the HRV profile over 5 ventilation modes. Although the limitation of the small cohort of patients, it provides evidences on the hypothesis that patients who succeed and failed during the weaning process have important differences in the ANS regulation, as have been suggested in recent works [6-9].

In this respect, considering only SBT, Orini et al [6] report that normalized amplitudes of LF and HF components of HRV differ in the last half of a 30 minute SBT, suggesting that patients who succeed in weaning show a prevalently sympathetic modulation. Our data for the SBT trial are in concord to this conclusion – the mean values of VLF and LF in the successful group are 238 and 37 ms^2, with VLF substantially enhanced in comparison to the failure group with values of 55 and 22 ms^2, respectively. Accordingly, we find evidences for increased vagal activity in the failure group which is manifested by elevation of the three outstanding vagal indices (pNN50 = 1.4 vs. 0.5 min^{-1}, RMSSD = 14 vs. 8.8 ms, HF = 37 vs. 16 ms^2, considering F vs. S-groups). The sympathetic-vagal balance ratio LF/HF is also reflecting the same trend with a prevalence of the sympathetic activity in the successful vs. failure group (3.2 vs. 2.1).

Our results are also in concord to the finding of Shen et al [7], who report insignificant changes of spectral HRV components in all patients when shifting from CMV to PSV. In contrast, significant decrease of TP, LF and HF components is observed only for the failure group after switching the ventilator mode from PSV to SBT [7-9]. We also observe such decreasing trend, however, it is insignificant for both groups. A larger number of patients is needed to confirm or disprove the hypothesis for vagal withdraw of the ANS activity after switching of SBT.

We observe that the most outstanding differences between failure vs. successful patients are manifested by all HRV indices during the ventilation mode PSV(0). To our knowledge, this is the first study, which tests the autonomic regulation response during a brief, but challenging the patient PSV trial. The failure patients react by increasing the total activity of the autonomic control system (SDNN and TP) in contrast to the successful group (SDNN = 45 vs. 19 ms, TP = 1668 vs. 205 ms^2, p<0.05). The two parts of the autonomic regulator are about 3 to 20-fold more intensively activated in the failure than the successful group, as measured by both the sympathetic HRV components (VLF = 1369 vs. 173 ms^2, LF = 426 vs. 19 ms^2) and vagal HRV components (pNN50 = 5.3 vs. 0.5 min^{-1}, RMSSD = 29 vs. 10 ms, HF = 322 vs. 15 ms^2). Such increasing trends are incompatible with the HRV profile decrease in switching of PSV and SBT.

We suggest that the ventilation modes with positive pressure – CMV(S), CMV(SP), PSV, SBT do not stimulate all normal mechanisms for breathing adaptation to the extent that PSV(0) triggers by challenging the patient with unsupported spontaneous breathing attempt. PSV(0) indeed activates all mechanisms for recovery of the spontaneous breathing, including also the autonomic control. The transition to a total absence of ventilatory support is a stress when the normal regulation increases sympathetic tone and suppresses the activity of autonomic contour, thus reducing heart rate variability. Our hypothesis is that during PSV(0) the patients are capable to manifest one of two different reactions:

(1) patients in whom the autonomic control is able to respond in a way that closely follows the normal autonomic regulation with elevated sympathetic activity. Such patients are indicative that they are further ready to maintain SBT and thus have a positive weaning outcome at the 2nd hour of SBT;

(2) patients in whom the autonomic contour keeps high tension, the vagal tone is relatively increased, HRV is considerable. Such pathologic autonomic regulation indicates the inability for maintenance of continuous SBT and thus the negative weaning outcome.

In a summary, findings from ICU studies suggested that the ANS profile is a major indice for predicting the outcome for patients who are not considered ready for weaning from mechanical ventilation.

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