Changes of Heart Rate Complexity during Weaning from Mechanical Ventilation

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Abstract

The aim of this study was to investigate heart rate (HR) variability in patients with weaning failure or success, using both linear and nonlinear techniques.

Thirty-two surgical patients were enrolled in the study. Signals were analyzed for 10 minutes during two phases: 1. pressure support (PS) ventilation (15-20 cm H_2O) and 2. weaning trials with PS: 5 cm H_2O. Low and high frequency (LF, HF) components of HR signals, HR multiscale entropy (MSE) and α1 exponent derived from detrended fluctuation analysis (DFA) were computed in all patients and during the two phases of PS.

Weaning failure patients exhibited significantly decreased LF, HF and α1 exponent, whereas MSE increased both between and within groups.

1. Introduction

Discontinuation of mechanical ventilation in critically ill patients is a challenging task and involves a careful weighting of the benefits of early extubation and the risks of premature spontaneous breathing trial (SBT). Most of the investigators examining their discriminating power for weaning readiness assessment have focused on the observation of trend evolution over time by means of statistical tests (i.e., mean and standard deviation). Nevertheless, the majority of these variables do not take into account the impact of a number of factors on weaning outcome, such as days of mechanical ventilation before weaning, differences between patient populations and aetiology of respiratory failure [1].

Recognition that physiologic time series contain hidden information related to an extraordinary complexity that characterizes physiologic systems, has led to the investigation of new techniques from statistical physics for the study of living organisms. Through those techniques different 'physiomarkers' can be estimated, which include variability and complexity indices of both heart and respiratory rate. Only a few studies have explored indices derived from breathing pattern variability analysis for the estimation of weaning readiness [2]. However, different weaning protocols were implemented in heterogeneous groups of patients, whereas heart rate (HR) dynamics was not studied.

In the present study, we tried to investigate heart rate dynamics using a 'toolkit' of both linear and nonlinear methods, in a homogeneous group of surgical critically ill patients during weaning from mechanical ventilation. We wanted to test the hypothesis that reduced HR complexity might discriminate weaning failure or success groups. In addition, we examined whether these domains of measurements and their change during weaning trials can predict weaning outcome and therefore identify a unique value of such analysis.

2. Methods

This study was performed in a mixed 12-bed Intensive Care Unit (ICU) in the University hospital of Alexandroupolis, Greece, after approval by local Scientific and Ethics Committee and after obtaining informed consent from patient's next of kin. A total of 32 consecutive patients admitted to the ICU from June to December 2009 who underwent major abdominal surgery with a mean Acute Physiology and Chronic Health Evaluation (APACHE) II score upon admission 16.5 (4.2), were enrolled. There were 23 men and 9 women, with a mean age of 60.4 (3.7) years. The whole studying population was divided into successful (S, n=22) and unsuccessful (U, n=10) groups according to the weaning outcome. All patients enrolled in the study received mechanical ventilation (model Evita 2 *Dura,* Dräger, Germany) for at least 48 hours and when they met the recommended weaning criteria [1,2], they underwent their first SBT using low pressure support ventilation (PSV). Those with cardiac arrhythmias, neurological diseases or pre-medication with cardiovascular drugs were excluded from the study.

2.1. Weaning protocol

Patients were ventilated with pressure support (PS) mode for 30 minutes, whereas the pressure level setting was between 15 and 20 cm H_2O to maintain a tidal

volume (V_T) of approximately 8-10 ml/Kg (stage 1, high support-H). Positive end-expiratory pressure (PEEP) was 5 cm H_2O, fraction of inspired oxygen concentration was 40% and pressure triggering sensitivity was set on -2 cm H_2O. Sedatives were discontinued in all patients, 24 hours prior to the study. At the end of this stage, minute ventilation (MV), respiratory rate (RR), V_T, HR and blood gases were measured in all patients and since they met the weaning criteria, the ventilator mode was switched to 5 cm H_2O PS plus 5 cm H_2O PEEP and the other settings remained the same (stage 2, low support-L) for other 30 minutes. When patients completed the 30-min SBT with low PS they were either extubated and considered as weaning success group (S), meaning free from invasive or non-invasive ventilation for over 48 hours, or were put back to high PS and considered as weaning failure group (U) [1]. All subjects were kept in semisitting position and left undisturbed throughout the study.

2.2. Data analysis

Analog multichannel electrocardiographic (ECG) signals (at 250 Hz sampling frequency) were obtained from monitors (Marquette 8000, GE Milwaukee, Wis, USA). Data were collected and downloaded using the software BedMaster Version 1.3 (Excel Medical Electronics Inc, Florida, USA) and analyzed in an HP Pavilion 6181, 2GHz PC. Heart rate intervals (R-R intervals) were extracted from 250 Hz ECG signals using the KubiosHRV^{TM} software, developed from the Department of Physics of the University of Kuopio, Finland (http://kubios.uku.fi/) [3]. Within each 30-min interval and after 10 minutes in each stage (H & L), a stable 10 min time series that was artefact free was chosen for off-line analysis. Moreover, episodes of tracheal suctioning, sights or cough were event-marked by the principal investigator and subsequently removed from the HR time series, before analysis. Both linear and nonlinear properties of HR signals were estimated by someone blind to weaning trials outcome, according to open-source software from the website www.physionet.org, and the software Kubios HRV^{TM}, using a computer package (MATLAB 5.3, the Mathworks, USA).

Prior to spectral analysis, a smoothed instantaneous HR time series was constructed from R-R intervals, with a frequency of 4 Hz by use of Berger tachometer method [4]. The different frequency components of HR signals were estimated through a Fast Fourier Transformation (FFT) of the R-R interval time series. In this study, we measured normalised low frequency (LFnu) and high frequency (HFnu) components, which were calculated as the ratio of absolute powers of LF and HF to total power (TP) and multiplied by 100.

Detrended fluctuation analysis (DFA) quantifies intrinsic fractal-like correlation properties of dynamic systems, whose basic features is scale invariance, meaning that the same features repeat themselves on different measurement scales. The R-R interval data time series after integration are divided into windows of the same size n and subsequently, analysed in relation to a local trend in each window. The variability is depicted on a log-log scale as a function of different sizes of windows in a form of linear slope and characterises the fractal-like correlation properties of the signal. We measured the short-term scaling exponent $\alpha 1$ (over periods of 11 or 16 beats) that is believed to be affected by respiration.

Multiscale entropy (MSE) was recently introduced for quantifying heart rate complexity [5]. Briefly, for a given R-R time series, multiple 'coarse-graining' time series are constructed by averaging the data points within non-overlapping windows of increasing length τ, where τ represents the scale factor. Subsequently, sample entropy (SampE) that represents the negative natural logarithm of the conditional probability that two sequences similar for m points remain similar at the next point with a tolerance r, is calculated for each time series and then plotted against the scale factor, giving rise to the MSE curve. The sum of SampE over all scaling factors represents the MSE of a signal. For our MSE analysis, the parameter r was set at 15% of standard deviation (SD) of the time series, after normalization (SD=1) and the parameter m (embedding dimension), that is the length of sequences to be compared was set at 2 (data length ranging from 100 to 5000 data points) [5]. Furthermore, we extracted two more features from MSE curves after log transformation of SampE and scale factor, the fast slopes for small time scales, i.e., those defined by SampE values between scale 1 and 5 and the long slopes for higher scale values.

The HR frequency components were logarithmically transformed for satisfying the requirements of normal data distribution. Differences of continuous variables between groups S and U were evaluated with independent t-test or Wilcoxon rank test, whereas their values over the 2 phases of PSV were compared with a repeated analysis of variance and a *post hoc* paired t-test or Wilcoxon paired test. Furthermore, we constructed receiver operating characteristic curves (ROC) for assessing the predictive performance of all measured parameters through estimation of areas under the curve (AUC). Data are presented as mean (standard deviation). All tests were performed with SPSS Software Version 13.0 (SPSS Inc, Chicago III) whereas values of $p<0.05$ were considered to be significant.

3. Results

The respiratory parameters, blood gases and demographic data did not differ between the 2 groups before the performance of the weaning trials, although group U showed increased RR, HR, MV and decreased V_T at the end of the high PSV phase (phase H). In

addition, mean APACHE II score upon admission and duration of ventilation before the start of SBTs were significantly higher compared with group S. Heart and respiratory rate at the end of SBT (phase L) in group U was significantly increased compared with group S [106.2 (13.5) vs 88.3 (5.4) and 31.3 (7.5) vs 23.6 (6.6), p<0.001, respectively]. In both groups, HR and RR between the two phases showed significant increase (data not shown).

Weaning failure patients exhibited significantly decreased LF nu [5.89 (0.31) vs 6.62 (0.10)], HF n.u [4.65(0.30) vs 5.06 (0.26), p<0.001 for both comparisons] and DFA α1 exponent [0.75 (0.11) vs 1.27 (0.16), p<0.05] compared with weaning success subjects. HR MSE demonstrated inverse changes [1.09 (0.29) vs 0.76 (0.32), p<0.05] between groups. In the weaning success group, fast MSE slope and DFA α1 exponent increased significantly from high to low PSV [0.005 (0.028) vs 0.007 (0.029) and 1.01 (0.24) vs 1.2 (0.21) respectively, p<0.005 for both comparisons], whereas opposite changes were found in the weaning failure group [0.12 (0.062) vs 0.02 (0.061) and 1.27 (0.16) vs 0.75 (0.11) respectively, p<0.001 for all comparisons]. Heart rate MSE increased between the two phases in both groups [0.68 (0.28) vs 0.76 (0.32) in group S, p=0.351, and 0.69 (0.25) vs 1.09 (0.29) in group U, p<0.001] but only in group U reached statistical significance. The analysis of ROC curves identified DFA α1 exponent and MSE of HR signals after SBT as significant predictors of weaning outcome, with area under the curve values: 0.791 (0.054) and 0.724 (0.082) respectively, (p<0.005 for both predictors).

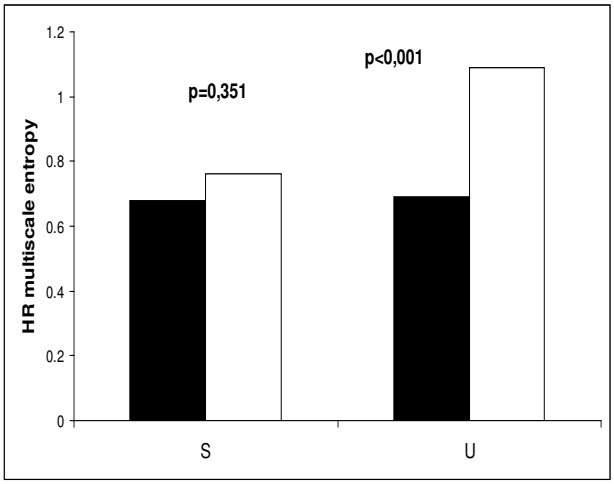

Figure 1. Bar chart of HR MSE of weaning success (S) and weaning failure (U) patients between the two different phases of PSV (High support for black and Low support for white bars). In group S, intrapatient changes are not significant, whereas in both groups, MSE increases between the two phases.

In the present study, different profiles of MSE curves on small time scales between the two groups and according to fast slopes may be due to the impact of respiratory rhythm on heart rate dynamics (respiratory sinus arrhythmia-RSA). In general, the lower the amplitude of respiratory modulation, the higher the entropy values tend to be [5]. Thus, in both groups but especially in weaning failure patients, sum MSE was significantly increased between different PS levels, whereas reduced fast slopes could reflect different time constants of respiratory effect upon heart rate control mechanisms. A possible limitation of this analysis could be the association between decreased variability of heart rate time series in group U and low signal-to-noise ratio, as it has been shown in heart failure patients [5]. Moreover, lack of guidelines in the literature for optimizing the values of m and r parameters, could limit diagnostic accuracy of the method.

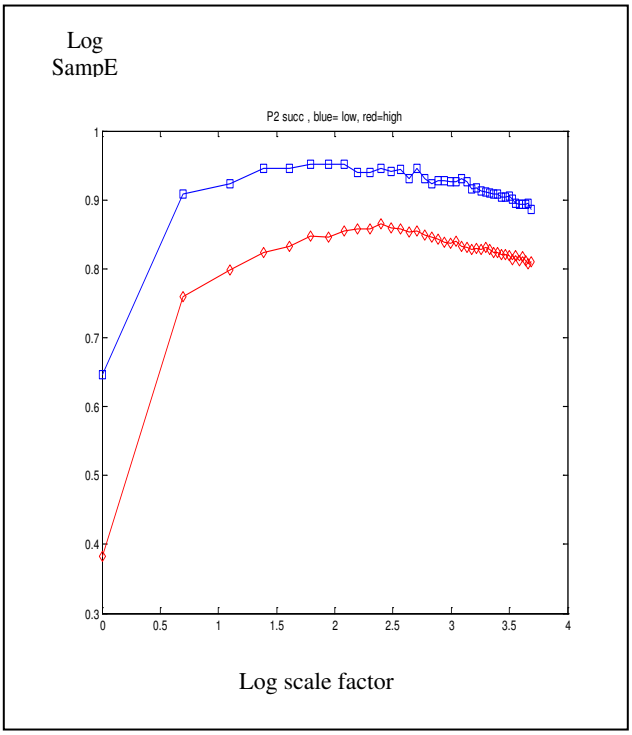

Figure 2. Log-log plot of heart rate multiscale entropy (log SampE) curves versus log scale factor, between phase H (high PSV-red downward line) and spontaneous breathing trial (SBT) or phase L (low PSV-blue upward line) in a weaning success patient (P2 suc). The MSE curve during the SBT has increased SampEn values; moreover, the slope during small scales (fast slope) looks similar with the slope during the high PSV phase.

Entropy quantifies the regularity and 'predictability', being informative about the underlying complexities within a signal. The more regular and predictable are the

time series, the lower the value of entropy. However, except for the information derived from sum MSE that reflects systems' operation across multiple spatial and temporal scales, different curve profiles can been of significant value for further analysis of inherent heart rate dynamics.

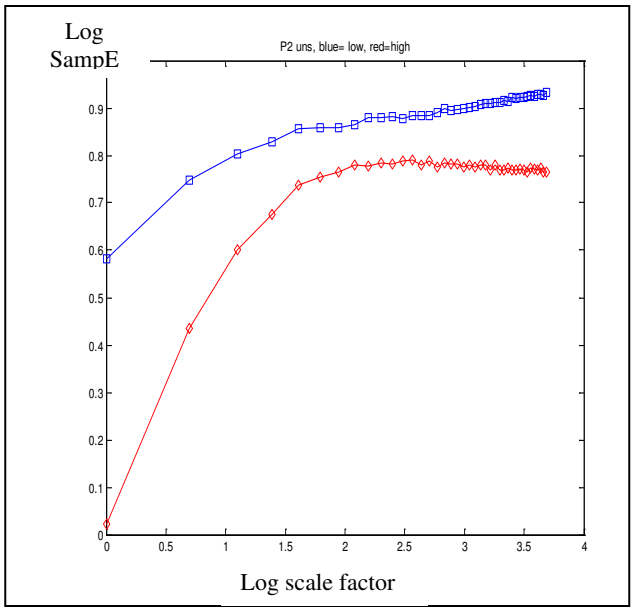

Figure 3. Heart rate multiscale entropy (MSE) curves between phase H and spontaneous breathing trial (SBT) or phase L in a weaning failure patient (P2 uns). SampE and scale factor have been logarithmically transformed. The MSE curve during the SBT has increased SampE values; however, the slope during small scales (fast slope) is decreased compared with the high PSV phase.

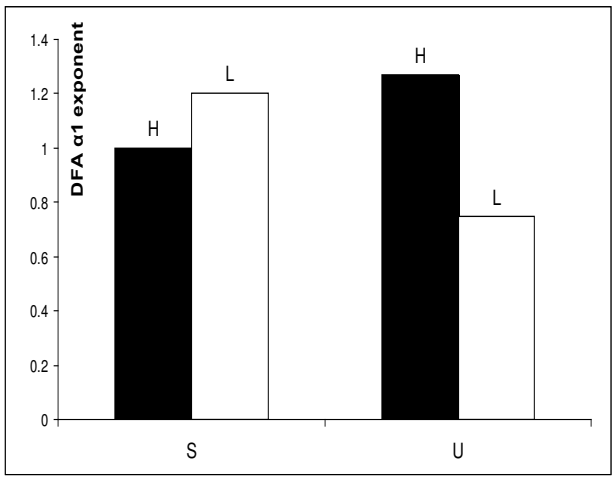

Figure 4. Bar chart of DFA α1 (or fast) exponent of HR signals in weaning success (S) and weaning failure (U) patients between the two different phases of PSV (H and L). In both groups, intrapatient changes are significant however, interpatient changes are opposite between the two phases.

It has been postulated that DFA α1 reflects HF at higher heart rates, whereas recent experimental observations have suggested that increased levels of catecholamines decrease its values [6]. In our case, we suppose that increased sympathoadrenal stimulation in weaning failure patients could be the cause of the reduction in α1 between the two phases.

4. Discussion and conclusions

Complexity analysis must incorporate many methods that capture different properties of cardiorespiratory signals. In this study, we applied a 'toolkit' of measures of HR complexity and concluded that their reduction is associated with weaning failure. Thus, we suggest that novel methods of assessment of cardiac dynamics could be a useful tool in predicting weaning outcome, at least in surgical patients, providing insight into the mechanisms of weaning failure. Nevertheless, these findings cannot yield information about weaning prediction in different groups of patients.

References

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