# Recurrence Quantification Analysis of Heart Rate Variability and Respiratory Flow Series in Patients on Weaning Trials

Andrés Arcentales, Beatriz F. Giraldo, Member, IEEE, Pere Caminal, Salvador Benito, Andreas Voss

Abstract—Autonomic nervous system regulates the behavior of cardiac and respiratory systems. Its assessment during the ventilator weaning can provide information about physiopathological imbalances. This work proposes a non linear analysis of the complexity of the heart rate variability (HRV) and breathing duration  $(T_{Tot})$  applying recurrence plot (RP) and their interaction joint recurrence plot (JRP). A total of 131 patients on weaning trials from mechanical ventilation were analyzed: 92 patients with successful weaning (group S) and 39 patients that failed to maintain spontaneous breathing (group F). The results show that parameters as determinism (DET), average diagonal line length (L), and entropy (ENTR), are statistically significant with RP for T<sub>Tot</sub> series, but not with HRV. When comparing the groups with JRP, all parameters have been relevant. In all cases, mean values of recurrence quantification analysis are higher in the group S than in the group F. The main differences between groups were found on the diagonal and vertical structures of the joint recurrence plot.

#### I. INTRODUCTION

Mechanical ventilation allows patients to recover from acute respiratory failure and major surgical procedures [1]. Withdrawal of mechanical ventilation should be performed as soon as autonomous respiration can be sustained. Various studies have been carried out to detect which physiological variables are related to weaning trial [2]-[4]. The assessment of autonomic control provides information about heart physiology imbalances within the cardiorespiratory system. Weaning process represents a period of transition from mechanical ventilation to spontaneous breathing and is associated with a change in autonomic activity; change of heart rate variability during weaning is to be expected [5].

The recurrence plot (RP) is a qualitative tool for visualizing non-linear dynamics in time series data, while

Manuscript received April 15, 2011. This work was supported in part by Ministerio de Ciencia e Innovación from Spanish Government under grants TEC2007-68076-C02-01 and TEC2010-21703-C03-01.

A. Arcentales and P. Caminal are with Dept. ESAII, Universitat Politècnica de Catalunya (UPC) and CIBER de Bioingeniería, Biomateriales y Nanomedicina (CIBER-BBN). (e-mail: <u>Andres.Arcentales</u> <u>@upc.edu Pere.Caminal @upc.edu</u>).

A. Voss is with Department of Medical Engineering and Biotechnology, University of Applied Sciences Jena, Germany (e-mail: <u>Voss@fh-jena.de</u>). recurrence quantification analysis (RQA) is used to quantify structure in the recurrence plots [6]. RP shows when a point in the phase space is near (at a distance lower than a certain threshold) to another point [7], [8]. Meanwhile, this technique has received a broad interest in various disciplines and has been successfully applied for the detection of dynamical transitions and synchronization, to study protein structures, cardiac and bone health conditions, ecological regimes, economical dynamics, or chemical reactions, to monitor mechanical behavior and damages in engineering, to mention only a few prospective applications [9]-[12].

Recurrence is a fundamental property of dynamical systems, which can be exploited to characterize the system's behavior in phase space. The parameter space of nonlinear dynamical systems often exhibits a rich variety of qualitatively different types of behavior, such as periodic and chaotic regimes [10]. A possibility to compare different systems is to consider the recurrences of their trajectories in their respective phase spaces separately, and look for the times when both of them recur simultaneously, i.e. when a joint recurrence occurs (JRP). By means of this approach, the individual phase spaces of both systems are preserved [7].

Traditional time-domain techniques of data analysis are often not sufficient to characterize the complex dynamics of the cardiorespiratory interdependencies during the weaning trials. In this paper, we explore RP and JRP for studying the breathing duration ( $T_{Tot}$ ), heart rate variability (HRV) and their interactions in patients on weaning trials from mechanical ventilation, to identify patients with successful spontaneous breathing trials and patients with unsuccessful trials.

# II. ANALYZED DATA

Electrocardiography (ECG) and respiratory flow (FLW) signals were measured in 131 patients on weaning trials from mechanical ventilation (WEANDB data base). These patients were recorded in the Departments of Intensive Care Medicine at Santa Creu i Sant Pau Hospital in Barcelona, Spain, and Getafe Hospital, Getafe, Spain, according to the protocols approved by the local ethic committees.

The patients were classified using the clinical criteria based on the T-tube test, which decide to begin the spontaneous breathing test. Patients were disconnected from the ventilator, maintaining spontaneous breathing through an endotraqueal tube during 30 min. According to the test

B.F. Giraldo is with Dept. ESAII, Escola Universitaria Enginyeria Tècnica Industrial de Barcelona (EUETIB), Universitat Politècnica de Catalunya (UPC), Institut de Bioingenyeria de Catalunya (IBEC) and CIBER de Bioingeniería, Biomateriales y Nanomedicina (CIBER-BBN). c/. Pau Gargallo, 5, 08028, Barcelona, Spain (e-mail: <u>Beatriz.Giraldo</u> <u>@upc.edu</u>).

S. Benito is with Dept. Intensive Care Medicine, Hospital de la Santa Creu i Sant Pau, Barcelona, Spain.

result, 92 patients exceeded the weaning trials successfully (group S: 60 male, 32 female, aged  $65\pm17$  years), and 39 patients failed to maintain spontaneous breathing and were reconnected to the mechanical ventilator (group F: 24 male, 15 female, aged  $67\pm15$  years).

The ECG signal was recorded using a SpaceLab Medical monitor. The FLW signal was acquired using a neumotachograph (Datex-Ohmeda monitor with variable reluctance transducer). Both signals were recorded at 250 Hz sampling rate for 30 min. Cardiac interbeat duration (RR series) was obtained by processing the ECG signal using an algorithm based on wavelet analysis [13]. Time series of the breathing durations ( $T_{Tot}$  series) were extracted automatically using an algorithm based on the zero-crossing of the respiratory flow signal.

# III. METHODOLOGY

#### A. Signal Preprocessing

According to our previous studies [14], [15], we used records of 20 min., rejecting first and last 5 min. Outliers were removed, considering a threshold five standard deviation, for the series. The heart rate variability (HRV) was obtained by calculating the standard deviation of the RR series in a moving window [16]. HRV and  $T_{Tot}$  series were re-sampled at 1 Hz using a cubic spline function. Finally, both time series were synchronized and normalized.

# B. Recurrence plot and joint recurrence plot

Recurrence plot (RP) is a technique based on the study of the recurrence in the phase space trajectory of the non-linear data. Let's consider a time discrete measurement defined by  $u_i = u(i\Delta t)$ , where i = 1, ..., N, and  $\Delta t$  is the sampling period. The phase space has to be reconstructed using the time delay method defined as

$$\vec{x}_i = \sum_{j=1}^m u_{(i+(j-1)\tau)} \, \vec{e}_j \tag{1}$$

where *m* is the embedding dimension,  $\tau$  is the time delay. The vectors  $\vec{e}_j$  are unit vectors and span an orthogonal coordinate system [17].

The tool for measure recurrence in the phase space is the recurrence matrix (RM) defined as

$$RM_{i,j} = \begin{cases} 1: \vec{x}_i \approx \vec{x}_j \\ 0: \vec{x}_i \not\approx \vec{x}_j \end{cases} \quad i,j = 1, \dots, N_R \qquad (2)$$

where  $N_R = (N - \tau (m - 1))$  is the number of considered states, and the criteria to define  $\vec{x}_i \approx \vec{x}_j$  is the threshold distance (RAD) [17], [18]. Therefore, the recurrence matrix is defined by the Heaviside function  $\Theta(\cdot)$  and the norm  $\|\cdot\|$ , as

$$RM_{i,j} = \Theta \left( RAD - \left\| \vec{x}_i - \vec{x}_j \right\| \right) \quad i, j = 1, \dots, N_R \quad (3)$$

Joint recurrence plot (JRP) is an extension of RP and it allows studying the relationship between two different signals. JRP considers the recurrence of the trajectory of each signal on their own phase space looking for when a joint recurrence occurs [17], and is defined as

$$JRM_{i,j}^{x_{i},y_{j}} = \Theta(RAD^{\vec{x}} - \|\vec{x}_{i} - \vec{x}_{j}\|) \Theta(RAD^{\vec{y}} - \|\vec{y}_{i} - \vec{y}_{j}\|)$$
  
$$i, j = 1, ..., N_{R}$$
(4)

For each system a different threshold value is considered according to each time series.

## C. Threshold distance and Embedding dimension

Threshold distance (RAD) is a very important parameter, and it requires special attention, because its value modifies the recurrence analysis of time series. RM calculated with small RAD values contains almost no recurrence points; on the other hand, with too large values include points in the neighborhood, which are simple consecutive points on the phase space [11].

A strategy to select the optimum RAD is to calculate the density of recurrence points (%REC) in the RM for different percentages of the maximum RAD. For the selection, the values are represented in logarithmic scale. The radius must fall with the linear region of the plot [19], and may not exceed 10% of maximum phase space diameter. Additionally, %REC must be kept under 2% [20]. Figure 1 illustrates the relationship between RAD and %REC when applied to RP and JRP of HRV and  $T_{Tot}$  series for the two groups of patients (S and F).

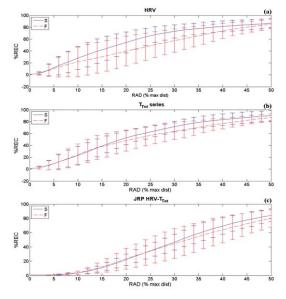


Fig. 1. RAD versus %REC plot for (a) RP of HRV, (b) RP of T<sub>Tot</sub> series, and (c) JRP between HRV-T<sub>Tot</sub>.

Figure 2 illustrates the performance of %REC when m is increasing, applied to RP and JRP of HRV and T<sub>Tot</sub> series for the two groups of patients (S and F). This parameter has to be chosen sufficiently large in order to contain the relevant dynamics of the system, taking care the effect of noise.

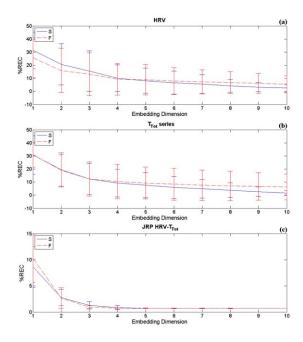


Fig. 2. Embedding dimension versus %REC plot for (a) RP of HRV, (b) RP of T<sub>Tot</sub> series, and (c) JRP between HRV-T<sub>Tot</sub>.

## D. Recurrence quantification analysis

Recurrence and joint recurrence matrix are characterized by the quantification of their diagonal and vertical line structure, and the recurrence point density. The parameters extracted from the RM are the following [17]:

- Determinism (DET) is the ratio of recurrence points that form a diagonal structure, where P(l) is the histogram of the length of diagonal lines

$$DET = \frac{\sum_{l=l_{min}}^{N_R} l P(l)}{\sum_{l=1}^{N_R} l P(l)} .$$
 (5)

- Average diagonal line length (L)

$$L = \frac{\sum_{l=l_{min}}^{N_R} l P(l)}{\sum_{l=l_{min}}^{N_R} P(l)} .$$
 6)

- Entropy (ENTR) refers to the Shannon entropy of the probability  $p(l) = P(l)/N_l$  to find a diagonal line of length l (  $N_l = \sum_{l \ge l_{min}} P(l)$  )

$$ENTR = -\sum_{l=l_{min}}^{N_R} p(l) \ln(p(l)) . \qquad (7)$$

- The maximal diagonal line of the matrix  $(L_{max})$ .
- Laminarity is analogous to DET, applied to vertical lines

$$LAM = \frac{\sum_{v=v_{min}}^{N_R} v P(v)}{\sum_{v=1}^{N_R} v P(v)} .$$
 (8)

Average vertical line length (TT).

$$TT = \frac{\sum_{v=v_{min}}^{N_R} v P(v)}{\sum_{v=v_{min}}^{N_R} P(v)} .$$
(9)

- The maximal vertical line of the matrix  $(V_{max})$ .

## IV. RESULTS

The selection of parameters is evaluated in terms of the classification between successful and failed groups of patients. RM was calculated using RAD = 6% of the maximum phase space diameter (Fig. 1), and an embedding dimension between  $3 \le m \le 5$  (Fig. 2).

Nonparametric Mann-Whitney U-test was performed to obtain RQA parameters. No one of the parameters extracted from the RM of the HRV presented statistically significant differences.

Table I presents the mean, standard deviation, and *p*-value of the most relevant RQA parameters of RM - T<sub>Tot</sub> series, for the two groups of patients (group S and group F). In all parameters, the mean values are higher in group S than in group F.

TABLE I RQA PARAMETERS OF $T_{Tot}$ SERIES				
т	Group S Mean ± SD	Group F Mean ± SD	<i>p</i> value	
Determini	ism (DET)			
3	$0,53 \pm 0,19$	$0,42 \pm 0,24$	*	
4	$0.54 \pm 0.19$	$0,42 \pm 0,25$	*	
5	$0,56 \pm 0,19$	$0,43 \pm 0,26$	*	
Average d	liagonal line length (L)	)		
3	$9,24 \pm 4,24$	$8,25 \pm 2,99$	n.s.	
4	$9,47 \pm 3,94$	$8,03 \pm 3,65$	*	
5	$9,79 \pm 3,76$	$7,94 \pm 4,14$	*	
Entropy (I	ENTR)			
3	$2,16 \pm 0,46$	$1,85 \pm 0,72$	*	
4	$2,12 \pm 0,52$	$1,75 \pm 0,81$	*	
5	$2,02 \pm 0,62$	$1,63 \pm 0,89$	*	

Table II presents the mean, standard deviation, and pvalue of the most relevant RQA parameters of JRM between RM of HRV and T<sub>Tot</sub> series, for the same groups of patients. All parameters shown in table II are statistically significant. The maximum differences are obtained with DET and L for m = 3.

#### V. DISCUSSION AND CONCLUSION

Values of RAD and m were selected according to the methodology presented before, and trying to minimize the dispersion respect to the mean value of the patients for each group. When RAD decreases, the standard deviation is reduced, and also decreases %REC, especially in JRP. Similarly, with increasing RAD also increases % REC.

TABLE II RQA parameters of JRP between HRV-T  $_{\rm Tot}$ 

$\begin{tabular}{ c c c c c c } \hline Group S & \\ \hline Mean \pm SD & \\ \hline Determinism (DET) & \\ \hline 3 & 0,24 \pm 0,17 & \\ 4 & 0,26 \pm 0,19 & \\ 5 & 0,27 \pm 0,20 & \\ \hline \end{tabular}$	Group F Mean $\pm$ SD $0,17 \pm 0,18$ $0,18 \pm 0,19$ $0,19 \pm 0,21$	p value ** *
Mean $\pm$ SD   Determinism (DET)   3 0,24 $\pm$ 0,17   4 0,26 $\pm$ 0,19	$\begin{array}{c} 0,\!17\pm0,\!18\\ 0,\!18\pm0,\!19 \end{array}$	**
$\begin{matrix} 3 & 0,24 \pm 0,17 \\ 4 & 0,26 \pm 0,19 \end{matrix}$	$0,\!18 \pm 0,\!19$	
4 0,26 ± 0,19	$0,\!18 \pm 0,\!19$	
• • • • • • • • • • • • • • • • • • • •		*
5 $0.27 \pm 0.20$	$0,\!19 \pm 0,\!21$	
0,2, -0,20		*
Average diagonal line length (L)		
3 6,34 ± 2,46	$4,86 \pm 2,85$	**
4 5,81 ± 3,14	$4,25 \pm 3,43$	*
5 $5,58 \pm 3,74$	$4,05 \pm 3,74$	*
Entropy (ENTR)		
3 1,16±0,69	$0,84 \pm 0,72$	*
4 $0,97 \pm 0,71$	$0,71 \pm 0,73$	*
5 $0,83 \pm 0,71$	$0,57 \pm 0,74$	*
Maximal diagonal line length (Lmax)	)	
3 18,77 ± 14,01	$14,41 \pm 13,90$	*
4 $16,96 \pm 14,04$	$12,\!60 \pm 13,\!64$	*
5 15,21 ± 13,72	$10,76 \pm 12,87$	*
Laminarity (LAM)		
3 0,19±0,18	$0,14 \pm 0,19$	*
4 $0,15 \pm 0,17$	$0,11 \pm 0,17$	*
5 $0,12 \pm 0,16$	$0,09 \pm 0,16$	*
Average vertical line length (TT)		
3 5,62 ± 2,83	$4,33 \pm 2,78$	*
4 $4,49 \pm 3,09$	$3,28 \pm 3,02$	*
5 $3,70 \pm 3,30$	$2,56 \pm 3,06$	*
Maximal vertical line length (Vmax)		
3 11,91 ± 8,62	$9,22 \pm 7,33$	*
4 $9,79 \pm 7,91$	$7,15 \pm 6,09$	*
5 8,12 ± 7,30	$5,76 \pm 5,30$	*
<i>p</i> - value < 0.05		

\*\* *p*-value < 0.01

The main statistically significant differences between the two groups were associated to the diagonal structures of the recurrence matrix.  $T_{Tot}$  series of the group S shows more determinism or predictability comparing to group F.

Most of parameters with statistically significant difference were extracted from the study of relationship between HRV and  $T_{Tot}$  series analyzed by the JRP.

These results allow considering the recurrence plot technique and especially the JRP as a promising tool to characterize patients on weaning trials. Further application will be concentrated on the selection of the recurrence quantification parameters and its application to the classification of the patients.

### ACKNOWLEDGMENT

The authors would like to thank the staff of the Intensive Care Departments at Santa Creu i Sant Pau Hospital, Barcelona, and at Universitario de Getafe Hospital, Getafe, Spain, for their collaboration with the signal database.

#### REFERENCES

 M J Tobin, "Advances in mechanical ventilation", New Engl. J. Med. 344 1986–96,2001

- [2] Jubran, A., Grant, B. J. B., Laghi, F., Parthasarathy, S., and Tobin, M. J. (2005). Weaning Prediction: Esophageal Pressure Monitoring Complements Readiness Testing. Am. J. Respir. Crit. Care Med., 171(11):1252–1259.
- [3] Casaseca, J. P., Martin-Fernandez, M., and Alberola-Lopez, C. (2006). Weaning from mechanical ventilation: a multimodal signal analysis. IEEE Transactions on Biomedical Engineering, 53(7):1330–1345.
- [4] Tobin, M. J. (2004). Of principles and protocols and weaning. Am. J. Respir. Crit. Care Med., 169(6):661–662.
- [5] P. Caminal, B.F. Giraldo, M. Vallverdú, S. Benito, R. Schroeder and A. Voss, "Symbolic Dynamic Analysis of Relations Between Cardiac and Breathing Cycles in Patients on Weaning Trials", Annals of Biomedical Engineering, Vol. 38, No. 8, August 2010, pp. 2542– 2552. DOI: 10.1007/s10439-010-0027-1.
- [6] P.I. Terrill, S. Wilson, S. Suresh, D.M. Cooper, "Developing robust recurrence plot analysis techniques for investigating infant respiratory patterns", 29th Annual International Conference of the IEEE-Engineering-in-Medicine-and-Biology-Society, Lyon, France 2007.
- [7] N. Marwan, J.F. Donges, Y. Zou, R.V. Donner, J. Kurths, "Complex Network Approach for Recurrence Analysis of Time Series", Physics Letters, Volume 373, Issue 46, Publisher: Elseiver B.V., Pages 23. DOI: 10.1016/j.physleta.2009.09.042.
- [8] N. Marwan, A Historical Review of Recurrence Plots, European Physical Journal – Special Topics 164 (1) (2008) 3–12, doi: 10.1140/epjst/e2008-00829-1.
- [9] M.A. García-González, M. Fernández-Chimeno, J. Ramos-Castro, "Errors in the Estimation of Approximate Entropy and Other Recurrence-Plot-Derived Indices Due to the Finite Resolution of RR Time Series", IEEE Trans. Biomed. Eng., Vol. 56, N. 2, 2009.
- [10] Y. Zou, RV. Donner, JF. Donges, N. Marwan, J. Kurths, "Identifying complex periodic windows in continuous-time dynamical systems using recurrence-based methods", Chaos 20, 043130, pp. 1-13.
- [11] J.P. Zbilut, N. Thomasson and C. L. Webber, "Recurrence quantification analysis as a tool for nonlinear exploration of nonstationary cardiac signals," Med. Eng. Phys., vol. 24, pp. 53-60, JAN, 2002.
- [12] P.I. Terrill, S.J. Wilson, S.Suresh, D.M. Cooper and C. Dakin, "Attractor Structure Discriminates Sleep States: Recurrence Plot Analysis Applied to Infant Breathing Patterns", IEEE Trans. Biomed. Eng., Vol. 57, N. 5, pp. 1108-1116, 2010.
- [13] J. P. Martinez, R. Almeida, S. Olmos, A. P. Rocha and P. Laguna, "A wavelet-based ECG delineator: Evaluation on standard databases," IEEE Transactions on Biomedical Engineering, vol. 51, pp. 570-581, APR. 2004.
- [14] Orini M., B.F. Giraldo, R. Bailón, M. Vallverdú, L. Mainardi, S. Benito, I. Díaz, P. Caminal, (2008). "Time-Frequency Analysis of Cardiac and Respiratory Parameters for the Prediction of Ventilator Weaning", 30th International Conference of the IEEE Engineering in Medicine and Biology Society, Vancouver, Canada, August 20-24, 2008, pp. 2793-2796.
- [15] B. Giraldo, C. Arizmendi, E. Romero, R. Alquezar, P. Caminal, S. Benito and D. Ballesteros, "Patients on Weaning Trials from Mechanical Ventilation Classified with Neural Networks and Feature", 28th Annual International Conference of the IEEE-Engineering-in-Medicine-and-Biology-Society, New York, August 30 - September 3, 2006, Selection. 2006, pp. 4112.
- [16] TASK FORCE OF ESC AND NASPE, T. Heart rate variability. Standards of measurement, physiological interpretation, and clinical use. Eur. Heart J., vol. 17, 1996, pp. 354–381.
- [17] N. Marwan, M. C. Romano, M. Thiel and J. Kurths, "Recurrence plots for the analysis of complex systems," Physics Reports-Review Section of Physics Letters, vol. 438, pp. 237-329, JAN, 2007.
- [18] J. P. Eckmann, S. O. Kamphorst and D. Ruelle, "Recurrence Plots of Dynamic-Systems," Europhys. Lett., vol. 4, pp. 973-977, 1987.
- [19] Charles L. Webber, Joseph P. Zbilut, "Recurrence Quantification Analysis of Nonlinear Dynamical Systems," Tutorials in contemporary nonlinear methods for the behavioral sciences, pp. 27-94. Retrieved February 1, 2011, from http://www.nsf.gov/be/bcs/pac/ nmbs/nmbs.jsp.
- [20] M. Javorka, Z. Turianikova, I. Tonhajzerova, K. Javorka and M. Baumert, "The effect of orthostasis on recurrence quantification analysis of heart rate and blood pressure dynamics," Physiol. Meas., vol. 30, pp. 29-41, 2009.