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Analysis of the Respiratory Pattern Variability of Patients in Weaning Process using Autoregressive Modeling Techniques

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***Abstract*— One of the most challenging problems in intensive care is the process of discontinuing mechanical ventilation, called weaning process. An unnecessary delay in the discontinuation process and an early weaning trial are undesirable. This paper proposes to analysis the respiratory pattern variability of these patients using autoregressive modeling techniques: autoregressive models (AR), autoregressive moving average models (ARMA), and autoregressive models with exogenous input (ARX). A total of 153 patients on weaning trials from mechanical ventilation were analyzed: 94 patients with successful weaning (group S); 38 patients that failed to maintain spontaneous breathing (group F), and 21 patients who had successful weaning trials, but required reintubation in less than 48 h (group R). The respiratory pattern was characterized by their time series. The results show that significant differences were obtained with parameters as model order and first coefficient of AR model, and final prediction error by ARMA model. An accuracy of 86% (84% sensitivity and 86% specificity) has been obtained when using order model and first coefficient of AR model, and mean of breathing duration.**

I. Introduction

Mechanical ventilators are used to provide life support in patients with respiratory failure. Assessing autonomic control during the ventilator weaning provides information of physiopathological imbalances. Autonomic parameters can be derived and used to predict success in discontinuing from the mechanical support. Some investigations reported that near 40% of the intensive care unit patients need mechanical ventilator for sustaining their lives. Among them, 90% of the patients can be weaned from the ventilator in several days while the other 5% - 15% of the patients need longer ventilator support. However, ventilator support should be withdrawn promptly when no longer necessary so as to reduce the likelihood of known nosocomial complications and costs [1]. The variability of breathing pattern is non-random and may be explained either by a central neural mechanism or by instability in the chemical feedback loops [2]. Several studies have evidenced the nonlinear dynamical behavior of the respiratory system [3]-[6].

The respiratory pattern describes the mechanical function of the pulmonary system, and can be characterized by the following time series: inspiratory time (T_I), expiratory time (T_E), breathing duration (T_{Tot}), tidal volume (V_T), fractional inspiratory time (T_I/T_{Tot}), mean inspiratory flow (V_T/T_I) and rapid shallow breathing (f/V_T), where f is respiratory rate.

In our previous work, we characterized the respiratory pattern of patients in weaning process through variability of the respiratory time series, separated into correlated, oscillatory and random fractions [5]. In this paper, we propose the study of variability in this respiratory pattern, using autoregressive models (AR), autoregressive moving average models (ARMA), and autoregressive models with exogenous input (ARX). The most relevant parameters are used in order to classify these patients. The aim of this study is to provide enhanced information in order to identify patients with successful spontaneous breathing trials and patients with unsuccessful trials.

II. Methodology

A. Subjects

Respiratory flow signals were measured in 153 patients on weaning trials from mechanical ventilation (WEANDB database). These patients were recorded in the Departments of Intensive Care Medicine at Santa Creu i Sant Pau Hospital, Barcelona, Spain, and Getafe Hospital, Getafe, Spain, according to the protocols approved by the local ethic committees.

Using clinical criteria based on the T-tube test, the patients were submitted under spontaneous breathing test, were disconnected from the ventilator, and maintained spontaneous breathing through an endotraqueal tube during 30 min. The records were obtained few minutes after disconnection. If the patients maintained the spontaneous breathing with normality they were extubated, if not, they were reconnected. When the patients still maintained the spontaneous breathing after 48 h, the weaning trial process was considered successful, if not, the patients were reintubated. The patients were classified into three groups: group S, 94 patients (61 male, 33 female, aged 65±17

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years) with successful weaning; group F, 38 patients (24 male, 15 female, aged 67±15 years) that failed to maintain spontaneous breathing; and group R, 21 patients (11 male, 10 female, aged 68±14 years) who had successful weaning trials, but required reintubation in less than 48 h.

B. Measurements of ventilation

Respiratory flow signal was acquired using a pneumotachograph (Datex-Ohmeda monitor with a Variable-Reluctance Transducer) connected to an endotracheal tube. The signals were recorded at 250 Hz sampling rate, during 30 min. The time series used in the characterization of the respiratory pattern were: T_I, T_E, T_{Tot}, V_T, T_I/T_{Tot}, V_T/T_I, respiratory rate (f) and f/V_T.

C. Modeling techniques

– *Autoregressive model (AR).* The autoregressive (AR) model of an order p can be written as AR(p), and is defined as

$$x(n) = a_1 x(n-1) + \cdots + a_p x(n-p) + e(n) \tag{1}$$

where $x(n)$ is the series under investigation, $a_1, \ldots, a_p$ are the autoregressive coefficients, and $e(n)$ is a zero-mean white noise with variance λ^2. The coefficients a_p and the variance λ^2 are estimated using Levinson-Durbin recursion. The model order determination has been based on the Akaike Final Prediction Error (FPE) [7], [8], and is defined as

$$FPE = s^2 p \frac{N+p+1}{N-p-1} \tag{2}$$

where p is the order of the model, N the number of data and s^2p the total square error, which is given by [9]

$$s^2 p = \frac{1}{N} \sum_{p}^{N-1} e^2(n) \ . \tag{3}$$

– *Autoregressive moving-average model (ARMA)*. The power of ARMA models is that they can incorporate both autoregressive and moving average terms. The use of ARMA models was popularized by Box and Jenkins [9]. ARMA(p, q) model is given by

$$\begin{aligned} x(n) + a_1 x(n-1) + \cdots + a_p x(n-p) = \\ e(n) + b_1 e(n-1) + \cdots + b_q e(n-q) \end{aligned} \tag{4}$$

where p and q are the orders of the process estimated by the Akaike criterion, and $a_1,\ldots,a_p$ and $b_1,\ldots,b_q$ are the coefficients of the model [9].

– *Autoregressive model with exogenous input (ARX).* This model is defined with an exogenous input $u(n)$ and output $x(n)$, by

$$\begin{aligned} x(n) + a_1 x(n-1) + \cdots + a_p x(n-p) = \\ b_1 u(n-1) + \cdots + b_q u(n-q) + e(n) \end{aligned} \tag{5}$$

since p and q the orders of the model, and $a_1, \ldots, a_p$ and $b_1, \ldots, b_q$ their coefficients [10].

For each time series the following parameters were calculated: model order, first coefficient of the model and final prediction error. Non-parametric Kruskal-Wallis statistical test was applied when comparing the three groups of patients, and Mann-Whitney U-test when comparing two groups.

D. Classification methods

After obtaining the most relevant parameters with the models presented before, the next classification methods were applied. The leave-one-out procedure was used.

– *Logistic regression* is an approach to prediction, like ordinary least square regression. However, with logistic regression, the research is predicting a dichotomous outcome [11], [12]. This method is given by

$$p = \frac{1}{1 + e^{-(\alpha_0 + \alpha_1 X_1 + \alpha_2 X_2 \cdots \alpha_k X_k)}} \tag{6}$$

where p is the occurrence probability of an event x of the data series X, and α_k the weight of the parameters.

– *Linear discriminant analysis* can be used only for classification (i.e., with a categorical target variable), not for regression. The target variable may have two or more categories [13], [14]. It has been defined as

$$Y = \mu_0 + \mu_1 X_1 + \ldots \mu_p X_k \tag{7}$$

where X_i and μ_0 are the independent parameters and independent term, respectively, and μ_1 are the discriminant function coefficient.

– *Support vector machines* (SVM) are based on transforming data into a higher dimensional space since they may convert a complex classification problem into a simpler one that can be solved by a linear discriminant function, known as an hyperplane, defined by [15]

$$f(x) = w \cdot \mathrm{z} + \mathrm{b} = \sum_{i=!}^{L} \alpha_i y_i K(x_i, x_j) + b \tag{8}$$

where α_i and b are determined for solving a large scale quadratic programming problem, for which efficient algorithms exist that guarantee global optimum values [16]-[18].

Kernels like linear, quadratic, polynomial, radial basis function and multilayer perceptron were evaluated, and finally, the linear kernel was selected.

TABLE I
MEAN ± STANDARD DEVIATION OF THE TIME SERIES THAT CHARACTERIZED THE BREATHING PATTERN FOR EACH GROUP OF PATIENTS: S, F AND R

Series	S	F	R	*p-value*
T_{Tot} (s)	2.79±0.73	2.25±0.80	2.69±0.10	<0.0005
T_I (s)	1.09±0.31	0.99±0.59	1.20±0.86	<0.0005
T_E (s)	1.69±0.52	1.26±0.35	1.48±0.26	<0.0001
V_T (mL)	622±492	565±484	780±709	ns
T_I/T_{Tot}	0.39±0.06	0.42±0.08	0.41±0.07	ns
V_T/T_I(mL/s)	629±493	687±539	800±524	ns
f/V_T(breath/min/L)	70.7±73.7	96.5±88.6	62.3±53.9	<0.005

III. RESULTS

The most relevant parameters are selected in order to classify patients in weaning process. The characterization of the respiratory pattern is evaluated considering the following three groups of patients: group S (patients with successful weaning), group F (patients with failed weaning), and group R (patients reintubated).

Table I presents the mean and standard deviation of the most relevant series that characterized the breathing pattern. The most statistically significant parameters were T_{Tot} T_I, T_E and f/V_T. The mean of the T_{Tot} T_I, T_E are lower in patients of group F than patients of group S and R.

Table II presents, for AR model, the mean, standard deviation, and *p*-value of the most relevant parameters for the model order (*p*) in the three groups of patients. The mean and standard deviation of patients group F are lower than the other two groups.

TABLE II
AR MODEL ORDER OBTAINED IN THE TIME SERIES OF THE RESPIRATORY PATTERN IN GROUPS S, F AND R (MEAN ± STD.)

Series	S	F	R	*p-value*
T_{Tot} (s)	36±38	26±38	42±43	<0.001
T_I (s)	39±37	30±28	36±39	<0.001
T_E (s)	40±39	37±29	46±36	<0.001
V_T (L)	37±36	35±33	47±38	<0.001

Table III presents, for AR model, the mean, standard deviation, and *p*-value of the most relevant parameters for the first coefficient of the model in the three groups of patients. The mean and standard deviation of group F is higher than in the other two groups. On the other hand, the group R presents the lower values.

FPE of AR model, presented significant differences between groups S and F in T_E and T_{Tot} series. The mean values of order *p* estimated with ARMA model, tend to be higher in group S than in Group F, with T_{Tot}, T_I and T_E. The most relevant parameter obtained is T_E (p =0.02). No one of the parameters of group R presented statistical significant differences with this model. When comparing the order *q*, T_I, T_E and T_{Tot} were higher in group S than in group F.

TABLE III
AR FIRST COEFFICIENT OF THE MODEL OBTAINED IN THE TIME SERIES THE RESPIRATORY PATTERN IN GROUPS S, F Y R (MEAN ± STD.)

Series	S	F	R	*p-value*
T_{Tot} (s)	0.409±0.168	0.430±0.228	0.387±0.154	<0.005
T_I (s)	0.323±0.173	0.358±0.182	0.323±0.183	<0.005
T_E (s)	0.361±0.162	0.382±0.185	0.312±0.131	<0.005
V_T (L)	0.477±0.178	0.482±0.213	0.402±0.168	<0.005

Table IV presents, for ARMA model, the FPE mean, standard deviation, and *p*-value of the most relevant parameters. Additionally, the mean of the order *p* tends to be higher in group S, suggesting greater variability in the time series of this group.

TABLE IV
FPE OF THE ARMA MODEL IN THE TIME SERIES OF THE RESPIRATORY PATTERN IN GROUPS S, F AND R (MEAN ± STD.)

Series	S	F	R	*p-value*
T_{Tot} (s)	0.31±0.70	0.21±0.43	1.45±6.043	<0.01
T_I (s)	1.00±6.77	0.21±0.37	0.21±0.23	<0.005
T_E (s)	1.34±6.79	0.44±0.68	1.75±6.24	<0.01
V_T (L)	80.80±20.80	60.12±14.624	17.33±57.03	<0.01

When applying ARX(*p,q*) models, the results of the order *p* tend to higher in group F than in group S, in all time series (Table V). In the group R the values of the four basic respiratory series are higher than in the group S.

TABLE V
ORDER P ESTIMATED FOR ARX MODEL IN THE TIME SERIES OF THE RESPIRATORY PATTERN IN GROUPS S, F AND R (MEAN ± STD.)

Series	S	F	R
T_{Tot} (s)	3.74±3.38	4.51±3.65	4.69±3.62
T_I (s)	3.78±3.25	4.33±3.23	3.81±3.75
T_E (s)	3.65±3.22	4.15±3.28	4.42±3.72
V_T (L)	3.82±3.19	4.36±3.37	4.19±4.14
T_I/T_{Tot}	5.28±3.52	7.41±4.62	7.14±5.20
V_T/T_I(mL/s)	4.07±3.67	4.41±3.16	3.42±2.59
f/V_T(breath/min/L)	2.66±2.42	3.64±2.83	2.61±2.43

Table VI presents the lists of parameters that showed higher statistically significant difference with the functions used for sorting with the logistic regression, linear discriminant analysis, and SVM. All possible combinations of parameters were analized.

TABLE VI
THE RELEVANT VARIABLES THAT CHARACTERIZED THE BREATHING PATTERN USED TO TRAIN THE LOGISTIC REGRESSION CLASSIFIERS, LINEAR DISCRIMINANT, AND SUPPORT VECTOR MACHINES

Name	Variables	Series	*p-value*
X_1	Mean	T_E	<0.0001
X_2	Mean	T_I	<0.0005
X_3	Mean	T_{Tot}	<0.0005
X_4	Mean	f/V_T	<0.005
X_5	AR model order	T_E	<0.001
X_6	AR model order	T_I	<0.001
X_7	AR model order	T_{Tot}	<0.001
X_8	AR model order	f/V_T	<0.001
X_9	First coefficient AR model	T_E	<0.005
X_{10}	First coefficient AR model	T_I	<0.005
X_{11}	First coefficient AR model	T_{Tot}	<0.005
X_{12}	First coefficient AR model	f/V_T	<0.005
X_{13}	ARMA model *FPE*	T_I	<0.005
X_{14}	ARMA model *FPE*	T_E	<0.01
X_{15}	ARMA model *FPE*	T_{Tot}	<0.01
X_{16}	ARMA model *FPE*	f/V_T	<0.01

The logistic regression function (Eq. 9) with the best classification rate (87%), was the average value of T_E variable (X_1), AR model order of T_E variable (X_5) and the first AR coefficient of T_E (variable X_9).

$$p = \frac{1}{1 + e^{\left(-1.633 + 4.443X_1 - 0.046X_5 - 8.138X_9\right)}} \tag{9}$$

The linear discriminant function (Eq. 10) with better classification rate (86%), combined the average variables T_E, order p in AR model for T_E and T_{Tot} series, and the first coefficient of the model for the same series.

$$\begin{aligned} 0 = -2.474 + 2.322X_1 - 0.013X_5 - 9.816X_7 + \\ + 0.022X_9 + 6.82X_{11} \end{aligned} \tag{10}$$

Finally, Table VII presents the best values of accuracy, sensitivity and specificity obtained with the proposed classification methods.

TABLE VII
RANKING FUNCTIONS PROPOSED FOR THE DISCRIMINATION OF PATIENT GROUPS IN THE PROCESS OF WEANING.

Method	*Accuracy*	*Specificity*	*Sensitivity*
Logistic regression	0.87	0.93	0.70
Linear discriminat	0.86	0.86	0.84
Support vector machines	0.87	0.95	0.70

IV. CONCLUSION

The breathing pattern in the three groups of patients can be characterized using the first coefficient and order p parameters of the model, through autoregressive models AR(p), when comparing T_I, T_E, and V_T time series.

Likewise, the final prediction error is a relevant parameter of models ARMA(p,q) when comparing the same time series (T_I, T_E, and V_T).

In addition to the differences found previously, when characterizing the respiratory pattern, with correlated, oscillatory and random fractions information [5], and variability by symbolic dynamics [4], present significant differences in mean, AR model order, first coefficient AR model, and FPE of the ARMA model, of some time series.

When classifying all groups of patients, using logistic regression, linear discriminant analysis, and support vector machines, the accuracy is higher than 86% in all case, with the best relation between specificity (86%) and sensitivity (84%) using the linear discriminant analysis classification.

As a preliminary study, these results suggest that the most relevant variables obtained by the characterization of the respiratory pattern using autoregressive modeling techniques, are a promising approach to evaluate differences between patients on weaning trials, in order to identify the optimal extubation moment.

Nevertheless, additional parameters and clinical information about the patients should be considered before the weaning trial for even greater discrimination between these three groups, and identification of reintubated patients in particular. The significance of the results, though being promising, needs to be further established on a larger set.

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