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Locating of the required Key-Variables to be employed in a Ventilation Management Decision Support System

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Abstract*—The aim of the paper is to identify the key physiological variables and ventilator settings involved in ventilation management, and required for an appropriate Clinical Decision Support System (CDSS). Based on the results of a questionnaire designed for the purpose of the research, 70 hours of physiological and ventilation data were recorded. Recorded data were classified by clinicians into three major lung pathologies and were further statistically analyzed for identifying strong relationships between monitored and controlled ventilator parameters. Correlation analysis was evaluated by Intensive Care Unit (ICU) clinicians. Based on the evaluators' majority voting the number and type of participating variables in a CDSS was drastically decreased. The number and type of monitored variables ranged from a single one to six, depending on the patient's lung pathology, and the controlled ventilator setting. Evaluation results were successfully applied to Neural Network models for providing suggestions on Tidal Volume and the Fraction of inspired Oxygen.

I. Introduction

Mechanical ventilation support is provided to ICU patients in critical condition, who are unable to maintain adequate gas exchange. ICU Clinicians continuously monitor and evaluate cardio-respiratory related physiological variables, in order to evaluate adequacy of mechanical ventilation. This ongoing process is known as ventilation management.

The strategy of applying changes on drug administration and ventilation settings could be based first on medical expertise and experience, secondly, on appropriate available guidelines and protocols, or, finally, on a combination of both.

The need of protocols and guidelines is due to the multifarious nature of the ventilation management process. Carson et al [1] focuses on the need of converting measured data into information for clinicians. Since humans have limited ability to estimate covariance between multiple variables [2], support tools are necessary.

A different strategy is suggested according to patient pathology. Although protocols and guidelines have been developed, there are diverse methodologies for dealing with the problem [3] – [5].

Automating the ventilation management process has been the 'holy grail' of research in the field. The driving forces for supporting ventilation decisions are the patients' safety, the improvement and measurement of the quality of care, and the resources limitations. Background information on historical and recent approaches on intelligent and expert systems on ventilation management could be found in a survey published by the authors [6].

II. Aims & Methods

The present paper aims to identify the key variables of the ventilation management process and employ them into a Neural Network (NN) model for providing suggestions on ventilator settings. The project aims adult ICU patients ventilated in control mode.

The number and types of participating variables in a CDSS establish the basic architecture of the system. Simplification of the basic architecture is important in order to make the system comprehensive and efficient. However oversimplification may result into suboptimal architectures for the task. Since ventilation strategies adapt to lung pathologies, the proposed basic architectures are pathology specific.

The identification of significant variables in ventilation management was performed into four steps:

Step 1: The first step was the ranking of physiological variables and ventilator settings based on their relative significance in the process of ventilation management, according to ICU medical staff. For this purpose a questionnaire was developed and circulated to ICUs doctors of three General Hospitals (GH) in Athens (Greece) urban area; namely Konstantopouleio Complex in Nea Ionia GH, Thriasio GH and Nikaia GH.

The questionnaire was designed to identify the relative significance of cardio-respiratory physiological variables and ventilator settings in the process of ventilation management of adult patients, ventilated in control mode. Five groups of ventilation related parameters have been

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identified with the assistance of the ICU clinician personnel of Konstantopouleio GH.

Parameters were grouped according to the acquisition methodology, and the physiology principle they describe (Table I, parameter groups: lines 5 – 9, Noninvasive parameters: lines 10 – 14, Volume, pressure parameters: lines 15 – 19, Lung mechanics: lines 20 – 22, Blood gases: lines 23 – 29, Hemodynamic parameters: lines 30 - 35).

The questionnaire was designed with closed questions, using an analog rating scale from 0 to 10. In total 26 physiological variables and 10 ventilator settings (Table I, lines 36 - 45) have been include in the questionnaire. Parameters that were ranked high by ICU clinicians were candidates for the recording process.

Step 2: The second step was the recording of real patient data, as identified by the first step. Two hospitals were chosen for the data collection process, based on availability of digital communication interfaces, namely the University Hospital of Heraklion (PAGNH), Crete and Veterans Hospital of Athens (NIMITS). For the collection of patient physiology data, the ethics committee of the PAGNH Hospital granted the approval. Monitor and ventilator data were automatically collected, while blood gases were manual recorded from the patients' charts. Approximately 70 hours of patient data were collected. Two databases were developed. The first included all recordings at 5 minute sample rate, while the second included only the recordings at the time that the clinician was applying changes on ventilator settings. Three patients with Chronic Obstructive Pulmonary Disease (COPD), three patients with Acute Lung Injury – Acute Respiratory Distress Syndrome (ALI-ARDS) and two Normal lungs patients were recorded; recordings were performed approximately for 43, 16 and 11 hours respectively.

Step 3: In order to identify the strength of relationship between inputs (monitored physiological variables) and outputs (ventilator settings), correlation analysis and statistical significant tests on the analysis ($p<0.05$) were performed.

Step 4: Three ICU doctors evaluated the correlation coefficients. Based on a voting process the variables participated in the model when the majority of evaluators accepted the correlation.

Evaluators' (*E*) results were used for establishing the basic architecture of a NN model in terms of input and output variables. Two feed-forward back propagation Neural Network (NN) models were designed. The first NN was designed for providing suggestions on V_T and the second for providing suggestions on F_iO_2 ventilator settings for COPD patients. The NN was trained with 60% (randomly allocated) of the available data sets. Models' evaluation was performed against the clinical decisions (40% of the training set). The measure of performance was the root mean square error (*rmse*) between model's suggestions and clinical decisions.

TABLE I
QUESTIONNAIRE PARAMETERS SCORING (**IN BOLD**: PARAMETERS CHOSEN AS CANDIDATES FOR THE MODELS)

No	Questionnaire Parameters	AVG	Mdn	SD
1	Age	6,11	7,00	3,16
2	Weight	8,83	10,0	1,98
3	Height	7,44	8,00	2,59
4	Sex	4,94	5,00	3,62
5	***Non Invasive group***	8,28	9,00	1,99
6	***Volume Flow Pressure group***	8,89	10,0	1,57
7	***Lung mechanics group***	8,61	9,00	1,54
8	***Blood gases group***	9,72	10,0	0,67
9	Hemodynamic group	7,72	8,00	1,71
10	***Arterial Oxygen Saturation SaO_2***	9,56	10,0	1,15
11	End Tidal Capnography E_TCO_2	7,17	7,50	2,31
12	***Heart Rate HR***	7,61	8,50	2,55
13	Core Temperature	5,89	6,00	3,07
14	Extremes Temperature	3,39	3,00	3,03
15	***Expired Volume Ve***	8,94	10,0	1,63
16	Mean airway pressure P_{MEAN}	8,28	8,00	1,93
17	***Peak Inspiratory Pressure PIP***	9,28	10,0	1,02
18	***End-Inspiratory Pause Pressure $P_{PLATEAU}$***	9,72	10,0	0,67
19	Intrinsic PEEP Auto PEEP	4,44	1,50	4,83
20	***Lung Compliance C***	8,89	10,0	1,68
21	***Airway Resistance R***	8,78	9,00	1,35
22	Work of breathing WOB	8,17	8,50	2,07
23	***Partial Pressure of Oxygen in Arterial blood PaO_2***	9,50	10,0	1,15
24	***Partial Pressure of Carbon Dioxide in Arterial blood $PaCO_2$***	9,56	10,0	1,15
25	***Hydrogen Ions Concentration in blood pH***	9,06	9,50	1,35
26	***Concentration of H_2CO_3 in blood HCO_3***	8,33	9,00	1,71
27	Oxygen Saturation of Central Vein blood S_VCO_2	6,17	7,00	2,31
28	O_2 Oxygen in Venous blood PvO_2	5,78	6,00	2,56
29	Partial Pressure of CO_2 in Venous blood $PVCO_2$	4,72	5,00	2,67
30	Cardiac Output C.O.	7,22	7,00	2,02
31	***Oxygenation Index OI***	8,83	10,0	2,07
32	Mean airway Pressure MPAP	6,28	6,50	2,76
33	Variation of Syst. Arterial Pressure	7,06	7,50	2,29
34	Central Venous Pressure CVP	6,67	7,00	2,83
35	Pulmonary Capillaries Wedge Pressure PCWP	6,67	7,00	2,93
36	Minute Ventilation V_E	9,44	10,0	1,25
37	***Tidal Volume V_T***	9,44	10,0	1,15
38	***Respiration Rate RR***	9,17	10,0	1,72
39	***Positive End Expiratory Pressure PEEP***	9,11	10,0	1,75
40	***Fractional Inspired Oxygen FiO_2***	9,56	10,0	1,04
41	***Maximum allowed airway Pressure P max***	9,50	10,0	0,71
42	Inspiration Time / Expiration Time I/E	8,00	9,00	2,70
43	***Maximum Inspiratory Flow Peak Flow***	8,17	9,00	2,46
44	Inspiratory Pause	3,39	0,00	4,02
45	Inspiration Flow Pattern	8,00	9,00	2,70

III. RESULTS

The questionnaire was circulated among three ICUs in Athens Greece, and it was answered by eighteen (18) doctors with a mean working experience in the ICU of 8.5 years.

Responses were statistically analyzed in terms of average (AVG), median (Mdn) and Standard Deviation (SD). The final selection of variables was based on those ones that exhibit the highest average and median score. Based on group scores, eleven (11) variables were included (Table I, parameters described in lines 10, 12, 15, 17, 18, 20, 21, 23, 24, 25, 26, 31), as well as one calculated variable; namely the oxygenation index (OI= F_iO_2/ P_aO_2).

The groups with the higher scores contributed with more variables to our model. This approach resulted in utilizing four variables from the blood gases group, three from the volume-pressure group, two from the lung mechanics group and two from the non-invasively acquired variables group.

The decaying number of variables reflects the group's importance to the ventilation management process. Hemodynamic blood pressure variables were excluded based on their low scoring and on the need of catheterization prior to monitoring, which is not always available or applied.

Six output ventilator settings were chosen, based on their scoring as system's outputs (Table I**,** lines 37 – 41 and 43). Although minute ventilation (V_E) scored very high it was excluded from the development process since in control ventilation mode its value is equal to the product of tidal volume multiplied by the respiration rate. Similarly flow pattern setting (Flow Pattern) was excluded on the ground that is not available in all commercial ventilator equipment.

The reduction of the number of ventilation related variables simplified the recording phase and reduced the complexity of the problem.

Correlation (*r*) and significance tests were performed on the recorded data, between monitored physiological variables and ventilator settings. The analysis was performed separately for each lung's pathology. Table II presents the average correlation analysis results (*r*), for COPD, ALI-ARDS and physiological (normal) lung categories. Average correlation is the average value derived from the two databases (5 minute and applied changes database). Correlation between two variables is accepted when it is above a set threshold (0.5) in one of the two databases, P value is bellow or equal to 0.05 and it is accepted by the majority of the evaluators. In Table II, fields which are blank do not satisfy the correlation criteria.

Evaluators' voting process rejected 28%, 29% and 31% of correlation coefficients for the Normal, COPD and ALI-ARDS category respectively. Although some of the rejected relationships are easily justified, since there is no apparent cause and effect relationship (e.g. COPD F_iO_2 correlation with R and PIP), this is not true for other since there is a documented relationship (e.g. P max and $P_{PLATEAU}$ in COPD category).

Based on evaluators' results (Table II), CDSSs for two ventilator settings were developed. Two NN models were designed and trained for producing advice on V_T and F_iO_2 settings for COPD patients. The NNs are feed-forward back propagation network with one hidden layer. The number of nodes in the input layer is equal to the number of input variables [7]. According to Table II, the COPD V_T NN model utilized as input variables the SpO_2, OI, PIP, $P_{PLATEAU}$ and R, while the F_iO_2 NN utilized SpO_2 and OI variables. Similarly the number of nodes for the output layer is equal to the number of the output variables; this number is equal to one (1). The number of nodes in the hidden layers satisfies Kolmogorov's theorem [7], [8] and is less than the available data sets. The NNs were trained for 1000 epochs with normalized data.

V_T NN performed with a *rmse* of 0.12 ml/Kgr, while F_iO_2 NN performed with 0.02 *rmse* (approximately 2% error in inspired O_2 concentration). A high percentage of models' suggestions followed closely clinical decisions; 98.1% of V_T NN and 95.2% of F_iO_2 NN suggestions exhibited less than 10% deviation from clinical decisions.

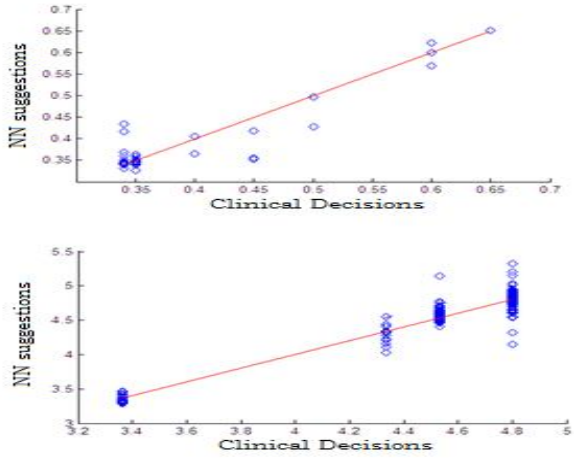

Fig. 1. Scatter diagrams, NN suggestions vs. clinical decisions; top F_iO_2 NN model, bottom V_T NN model (ml/Kgr)

IV. Conclusion

We approached the complex problem of identifying significant variables in ventilation management CDSSs based on statistical analysis of real patients data and evaluation of findings from clinical experts. The proposed approach minimizes the bias introduced by experts into the design of CDSSs with the assistance of statistical tools.

Since the process of ventilation management is pathology specific, the above process was applied to three major lung pathologies encountered in the ICU setting; namely COPD, ALI-ARDS and normal lungs.

Application of evaluation findings to the development of NNs models for supporting ventilation management has shown promising results. NN Models were shown to efficiently map the relationship between input variables and ventilator setting, as described by the evaluation process. However the application of NNs for the task has drawbacks.

The most important drawback is the transparency of the final architecture of the NN. Since NNs are black boxes to end users, a secondary operation of rule extraction is needed for identifying NN response to uncharted areas by the available data sets. Since NNs response is unknown, safeguarding algorithms should be in place prior to the application.

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REFERENCES

[1] E.R. Carson, J.J.L. Chelsom, R. Summers, "Progress with measurement, information and decision-making in critical care medicine", Measurement, 1991, vol 9(3), pp. 104-110.

[2] A.H. Morris, D.J. Cook, "Clinical trial issues in mechanical ventilation", In J.J. Marini, A.S. Slutsky, "Physiological basis of ventilatory support", Marchel Dekker Inc. 1998.

[3] L. Brochard, A. Rauss, S. Benito, G. Conti, J. Mancebo, N. Rekik, A. Gasparetto, F. Lemaire " Comparison of three methods of gradual withdrawal from mechanical support during weaning from mechanical ventilation", Am. J. Resp. Crit. Care Med., vol 150 (4), Oct 1994, pp. 896-903.

[4] R. Butter, S.P. Keenan, K.J. Inman, W.J. Sibbald, G. Block, " Is there a preferred technique for weaning the difficult-to-wean patient? A systematic review of the literature". Crit. Care Med., vol 27, 1999, pp. 2331-2336.

[5] H.M. Horst, D. Mouro, R.A. Hall-Jenssens, N. Pamukou, "Decrease in ventilation time with a standardized weaning protocol", Arch. Surg, vol 133, 1998, pp. 483-489.

[6] A. Tzavaras, P.R. Weller, "Classical approaches and intelligent systems in Ventilation Management: A Survey", Critical Reviews in Biomedical Engineering, vol 38(2), 2010, pp. 157-188

[7] A. Tzavaras, "Intelligent decision support systems in ventilation management" [PhD thesis]. Centre for Health Informatics. City University London UK. 2009.

[8] V. Kurkova, "Kolmogorov's theorem and multilayer neural networks", Neural Networks, vol 5, 1992, pp. 501-506.

TABLE II
CORRELATION COEFFICIENTS AND EVALUATOR'S VOTING RESULTS FOR LUNG CATEGORIES (**IN BOLD** ACCEPTED CORRELATION BY EVALUATORS)

	V_T (ml/kgr)		RR		PEEP		F_iO_2		Max Insp. P		Max Flow		
	r	*E*	*r*	*E*	*r*	*E*	*r*	*E*	*r*	*E*	*r*	*E*	
SpO_2	**-0.55**	**3/3**	**0.64**	**3/3**	**-0.55**	**3/3**	**-0.64**	**3/3**			**-0.58**	**3/3**	**COPD category**
PaO_2									-0.75	1/3			
$PaCO_2$									**0.90**	**2/3**			
pH									0.50	0/3			
O_2 Index	**0.87**	**2/3**	**-0.47**	**3/3**	**0.84**	**2/3**	**-0.87**	**3/3**			**-0.79**	**3/3**	
Ve (ml)													
PIP (mbar)	**-0.59**	**3/3**			**-0.81**	**2/3**	0.56	1/3	**0.59**	**2/3**	**0.68**	**3/3**	
Plateau	**-0.59**	**3/3**			**-0.79**	**2/3**	0.57	1/3	0.52	1/3	**0.66**	**2/3**	
C (l/bar)									-0.84	1/3			
R (mbar/L/s)	**-0.50**	**3/3**			**-0.71**	**2/3**	0.52	1/3	0.47	1/3	**0.58**	**3/3**	
HR			**0.55**	**2/3**									
HCO_3									0.89	0/3			
SpO_2													**Normal Lungs category**
PaO_2	**0.92**	**3/3**	**-0.61**	**3/3**			**-0.70**	**3/3**	**0.82**	**3/3**	**-0.72**	**3/3**	
$PaCO_2$	**-0.93**	**3/3**	**0.85**	**3/3**			0.89	1/3	**-0.93**	**3/3**			
pH	**0.91**	**2/3**	**-0.79**	**2/3**			-0.84	1/3	**0.89**	**3/3**			
O_2 Index	**1.00**	**3/3**	**-0.89**	**3/3**			**-0.94**	**3/3**	**0.99**	**3/3**			
Ve (ml)	-0.59	1/3	0.82	0/3			0.78	0/3	**-0.70**	**2/3**			
PIP (mbar)											**0.59**	**2/3**	
Plateau													
C (l/bar)			0.51	1/3			0.50	0/3					
R (mbar/L/s)													
HR	**0.52**	**3/3**	**-0.76**	**3/3**			-0.72	1/3	**0.64**	**3/3**			
HCO_3													
SpO_2	**-0.65**	**3/3**					**-0.68**	**3/3**					**ALI-ARDS category**
PaO_2													
$PaCO_2$			**0.91**	**3/3**					**0.90**	**2/3**	**-0.86**	**2/3**	
pH					0.75	0/3							
O_2 Index	**-0.84**	**3/3**			**-0.91**	**3/3**	**-0.98**	**3/3**					
Ve (ml)	**0.86**	**3/3**			**0.84**	**3/3**	0.92	1/3					
PIP (mbar)					**0.86**	**3/3**					**0.79**	**3/3**	
Plateau	**0.57**	**3/3**			**0.89**	**3/3**	0.72	1/3					
C (l/bar)													
R (mbar/L/s)													
HR													
HCO_3			0.76	0/3					0.86	0/3	-0.75	0/3	