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Abstract

Objective: To develop predictive criteria for successful weaning from mechanical assistance to ventilation based upon simple clinical tests using discriminant analyses and neural network systems.

Design: Retrospective development of predictive criteria and subsequent prospective testing of the same.

Setting: Medical intensive care unit of a 300-bed teaching veterans administration hospital.

Patients: Twenty-five ventilator-dependent elderly patients with acute respiratory failure.

Interventions: Routine measurements of negative inspiratory force (NIF), tidal values (VT), minute ventilation (VE), respiratory rate (RR), vital capacity (FVC), and maximum voluntary ventilation (MVV), followed by weaning trial. Success or failure in 21 efforts analyzed by linear and quadratic discriminant model and neural network formulas to develop prediction criteria. The criteria so developed were tested for predictive power prospectively in nine trials in six patients. The analyses thus obtained predicted the success or failure of weaning within 90–100% accuracy.

Conclusion: Use of quadratic discriminant and neural network analyses could be useful in developing accurate predictive criteria for successful weaning based upon simple bedside measurements.

Introduction

"Weaning" or discontinuing respiratory support to patients on mechanical assistance ventilation (MAV) requires identification of patients able to sustain unassisted breathing without clinical or physiological deterioration; extensive literature exists on the tests and measurements for the above purpose[1–10] . However, none of the criteria based on these tests consistently separate success from failure of the weaning efforts in clinical practice.[11–15] At present, weaning is instituted mostly on a trial and error basis after making a best guess based upon one or more of the published criteria. This method leads to unsuccessful trials in almost half of the patients, exposing them to the risks of worsening respiratory failure and related complications.[16] On the other hand, many patients continue to receive unnecessary MAV when these criteria fail to identify their readiness to sustain unassisted breathing.[17] Clearly, there is a need for the development of more reliable criteria for prediction of weaning outcomes.

The ability to breathe normally depends upon many independent physiological variables and a battery of tests for all these variables would be too cumbersome to be used clinically. We hypothesized that the capability of correctly predicting weaning outcomes based upon simple and routinely available tests could be improved by using computer analyses involving neural network (we use the phrase "neural networks" only to mean connectionist computational systems, not the biological systems from which they draw inspiration), and statistical classification techniques.

In this paper, we report the results of investigating the ability of statistical and neural network analyses in predicting success or failure of weaning efforts in patients dependent upon MAV.

Methods and Material

Twenty-one weaning efforts in sixteen patients were made and prospectively studied to develop criteria for predicting weaning outcomes. The variables used in developing the criteria were: peak negative inspiratory pressure (NIF), respiratory rate (RR), unassisted minute ventilation (VE), and tidal volume (VT). Maximum voluntary ventilation (MVV) and vital capacity (VC) were also measured, but were not used for analysis because not all patients could perform the VC or MVV maneuvers, and reproducible values were not obtained in many of the remaining patients. Weaning predictions were prospectively studied in eight more subjects based on the criteria obtained from the analysis of the data on the above mentioned 21 patients. In each patient, weaning effort was initiated after: (i) the underlying disease showed improvement, (ii) the patient was hemodynamically stable, (iii) the patient was conscious and able to cooperate with the weaning effort, (iv) arterial to alveolar PO_2 ratio, (a/A PO_2) was 0.45 or greater, and (v) the patient's weight had stabilized. Selected clinical data on patients are given in Table 1 and Table 2.

After the decision to wean a patient was made based upon these observations, measurements used in the present study were obtained by respiratory therapy staff trained to follow the established measurement procedures previously described.[17] MAV was discontinued within 48 hours of making the above measurements. Trials in which unfavorable clinical status within 48 hours of making measurements prevented weaning were considered failures, as were trials which necessitated reinstitution of MAV within 72 hours of weaning. Weaning was considered successful if patients were able to continue breathing unassisted for at least 72 hours after MAV was discontinued.

The weaning procedure and measurements obtained are established routine clinical practice at our institution and the patient care team in charge of the patients' management made the decisions to institute unassisted breathing, reinstitute MAV, continue unassisted breathing, or extubation. The pulmonary service did not participate in these decisions. Furthermore, the data collected by the respiratory therapists were not communicated to the investigators until after the success or failure of the weaning trial was determined.

The parameters NIF, RR, VE, VT, and success or failure of the weaning attempt were used to investigate the suitability of the statistical and neural network analysis techniques. The data in 21 weaning trials given in Table 3 of the appendix, constitute the "training set." Of these, weaning attempts had been successful in nine instances and unsuccessful in 12. This training set was used to obtain a quadratic statistical discrimination procedure as well as to train a neural network. Both procedures are described in the appendix. A linear classification procedure is inappropriate for these data.

Nine weaning efforts on eight more patients were made and data are given in Table 4. The collection of this data is called the "test set" because it was used only to measure the performance of the trained neural network and the statistical classification procedure already determined by the training data.

Results

Statistical analysis led to a quadratic classification procedure which performed well (90.5%) on the training data, making only two errors (cf. Table 5). The neural network approach successfully solved the desired classification task using a network with one "hidden layer," making no errors on the training data (cf. Table 6).

In the test set, there were three patients on whom weaning attempts were unsuccessful, and the other six cases were weaned successfully. As shown in Table 7, the statistical method makes no error on these test data (100% performance), whereas the previously trained neural network made one error (88.9% performance), as shown in Table 8.

Discussion

Our analyses have shown that it is possible to obtain excellent predictive performance in determining whether a patient can be successfully weaned from MAV on the basis of a small number of simple, readily available measurements. On the 30 training and test data (combined), the statistical classification method correctly predicted 93.3% of the times, while the neural network technique yielded a performance of 96.7%.

With conventional statistical methods, using contingency tables and Bayesian analysis, prediction of the success or failure of weaning efforts has been disappointing. Sahn and Lakshminarayan[5] have reported a success rate of 81% using their criteria which are widely used. A major advantage of their prediction method is the use of tests which are widely available and are simple to use. However, in their study almost two-thirds of the patients were post-operative, a group that is easy to wean. Furthermore, these patients had received MAV for a mean duration of only 37 hours. Their criteria has much poorer predictability in patients with a longer history of MAV dependence. For example, Tahvanainen[11] has reported false positive and false negative rates of 63% and 11% respectively using Sahn and Lakhaminarayan's criteria. Using MVV alone the false positive and negative rate were 5% and 76% respectively, with an overall success rate of only 59.5%.

Many other tests have been proposed as better predictors of successful weaning. Some of these are: passive expiratory volume in one second (PEV_1),[16] mouth occlusion pressure (P.1),[18] CROP index based on compliance, rate, oxygenation and pressure[17] and estimates of work of breathing as a power spectral shift in the recordings of diaphragmatic electromyograms (EMG).[19] Although these tests reflect important physiological principles and may improve our ability to predict successful weaning, the cumbersome equipment and maneuvers needed to make these measurements preclude their widespread clinical use. Some of the newer ventilators incorporate equipment and automated programs which may lead to their wider application if larger studies confirm their usefulness. The cost effectiveness of this equipment will also need to be carefully studied. By contrast, success rates of 90–100% can be achieved with even a small number of readily available parameters by utilizing quadratic classification and neural network procedures.

It may be possible to build an "expert system" consisting of a set of rules to capture the knowledge relevant to weaning. In many applications, however, all that is available is some idea as to which parameters are relevant to decision-making; very little is known about the complex interrelationships between the relevant variables and the decision to be made. In such situations, a decision support system can utilize statistical analyses, or the more recent connectionist computational paradigm, "artificial neural systems" or "neural networks."

These methodologies can be used to model problems of classification of samples into groups based on past available cases, thereby establishing criteria to discriminate new cases and place them into the appropriate category. These methods are more reliable than subjective decision-making, and can be used at least to assist the decision-making process. When the nature of the data may be such that perfect performance (classification) is impossible, possibly due to noisy or partially unavailable data inputs, "case-based reasoning" (nearest neighbor classification) approaches could be used for decision support tasks with somewhat reduced chances of success.

We recognize the need for extensive analysis on more data to confirm our results. The exact mathematical formulas developed by us may not be equally successful in correctly predicting weaning outcomes in other centers because patient population, etiologies responsible for MAV dependence, and weaning practices differ between different institutions and often even within the same institution. However, we believe that our methods can be adapted and used in a wide variety of situations. We have demonstrated that mathematical and computational analyses involving nonlinear statistical and neural network methods can impart a greater accuracy and reliability to the predictive power of simple tests and these could enable clinicians to care for patients more cost effectively and with greater confidence than resorting to more expensive equipment or greater expenditure of time.

We conclude that statistical classification procedure and neural network analyses can assist in developing more accurate and reliable criteria for prediction of weaning in an institution with stable and well-understood mix of patients dependent upon MAV.

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Appendix

Statistical method

Given two populations P_1 and P_2, how do we decide whether an object belongs to P_1 or P_2 on the basis of k variables on the object? The values of these k variables $x_1, \ldots, x_k$ are collectively written as $X = (x_1, \ldots, x_k)$. For example, for Patient number 1 in the training set $X = (-24, 6.7, 300, 24)$, and these are the NIF, VE, VT, RR values, respectively, of the patient. The Linear Discriminant method, developed by Fisher,[21] addresses this question as follows. Suppose that the covariance matrices of the two populations are equal. Then, for each object a one-dimensional score (y)

$$y = w_1 x_1 + w_2 x_2 + \ldots + w_k x_k$$

is obtained and the weights $w_1, \ldots, w_k$ are determined such as to maximize the separation between P_1 and P_2 in the score variable y.

The linear discriminant would be inappropriate for our study as the covariance matrices of the the two populations were statistically unequal. The estimates of these covariances (Σ_i) are

$$\Sigma_1 = \begin{pmatrix} 133.111 & -18.444 & -1989.472 & 40.875 \\ -18.444 & 29.625 & 1183.888 & -7.425 \\ -1989.472 & 1183.888 & 69698.444 & -1035.000 \\ 40.875 & -7.425 & -1035.000 & 31.000 \end{pmatrix}$$

and

$$\Sigma_2 = \begin{pmatrix} 39.060 & 3.137 & -317.636 & 4.621 \\ -3.137 & 4.022 & 5.463 & 6.094 \\ -317.636 & 5.463 & 10417.636 & -462.636 \\ 4.621 & 6.094 & -462.636 & 60.628 \end{pmatrix}$$

Quadratic discriminant analysis is used in cases of unequal covariances. In the quadratic discriminant analysis inter class distance is maximised via a generalized square distance function: [20]

$$D_j^2(X) = (X - \overline{X}_j)' Cov_j^{-1} (X - \overline{X}_j) + \log |Cov_j|$$

where Cov_j represents the covariance matrix and $\overline{X}_j$ represents the mean vector of the j^{th} class. The classification procedure calculates the posterior probability of a given X to class j by

$$Prob(j) = \exp(-0.5 D_j^2(X)) / \sum_k \exp(-0.5 D_k^2(X)).$$

If this probability is greater than 0.5 then X is classified in the j^{th} class. These probabilities are given in Tables 3 and 4 for the training and test sets.

Neural Networks

Neural networks belong to the class of *data-driven* approaches, as opposed to model-driven approaches. The analysis depends on available data, with little rationalization about possible interactions. Relationships between variables, models, laws and predictions are constructed *post-facto* after building a neural network whose behavior simulates the data being studied. The process of constructing such a machine based on available data is addressed by certain general-purpose algorithms like "back-propagation."[22] Artificial neural networks are computing systems containing many simple non-linear computing units or nodes interconnected by links. In a "feedforward" network, the units can be partitioned into layers, with links from each unit in the k^{th} layer being directed (only) to each unit in the $(k+1)^{th}$ layer. Inputs from the environment enter the input layer, and outputs from the network are obtained from the output layer. A neural network with one hidden layer is shown in Figure 1. A weight or "connection strength" is associated with each link, and a network "learns" or is trained by modifying these weights, thereby modifying the network function which maps inputs to outputs.

For the classification problem a neural network without any hidden layer is equivalent to a linear discriminant. The best possible linear discriminant for the present problem is .483 NIF + 1.5487 VE − 0.0223 VT +0.0223 VT + 0.3201 RR < 5.652.

A neural network with one hidden layer is nonlinear. For the present problem the classification formula given by one hidden-layer network works as follows. Suppose we define

$$D = \frac{12.26}{1+\exp(a)} + \frac{7.83}{1+\exp(b)},$$

where

$$a = -(0.276 \text{ NIF } + 0.945 \text{ VE } - 0.0123 \text{ VT} + 0.172 \text{ RR } - 4.97)$$

and

$$b = -(0.0715 \text{ NIF } - 0.432 \text{ VE} + 0.00455 \text{ VT } - 0.076 \text{ RR } + 4.55).$$

If the value of D is < 4.16, then the patient belongs to the success group, else to the failure group.

Table 1: Clinical data on the patients used to develop weaning criteria [2]

Variable	Number	Mean	St. Dev
Age(years)	16	70.5	5.8
Duration on MAV (days)		14.9	11.9
Clinical Diagnosis			
COPD	4		
CHF	4		
NM	1		
PO	1		
Pneum	4		
MI	2		
Cancer	3		

Table 2: Clinical data on the patients tested with developed weaning criteria

Variable	Number	Mean	St. Dev
Age(years)	8	63.4	7.6
Duration on MAV (days)		8.4	5.1
Clinical Diagnosis			
COPD	2		
CNS	2		
NM	1		
PO	5		
Pneum	2		
Cancer	2		

[2] COPD=Chronic Obstructive Pulmonary Disease
CHF = Congestive Heart Failure
NM = Neuromuscular disease
PO = Post Operative
Pneum = Pneumonia
MI = Myocardial Infarction
CNS = Central Nervous Disease

Table 3: The Training Set

				Weaning	Posterior Probability	
NIF	VE	VT	RR	Effort	Success	Failure
-24	6.7	300	24	success	0.815	0.185
-30	7.2	500	17	failure	0.858	0.142
-23	8.0	300	29	success	0.366	0.634
-26	11.4	265	44	failure	0.000	1.000
-18	12.1	370	32	failure	0.089	0.911
-22	10.6	350	30	failure	0.137	0.863
-10	10.1	320	29	failure	0.175	0.825
-60	7.8	650	16	success	1.000	0.000
-20	9.6	225	46	failure	0.000	1.000
-24	10.5	276	38	failure	0.001	0.999
-15	10.9	270	40	failure	0.000	1.000
-30	7.5	250	30	success	0.948	0.052
-42	14.9	950	13	success	1.000	0.000
-12	7.2	220	32	failure	0.065	0.935
-20	11.8	124	33	failure	0.006	0.994
-42	15.1	750	24	success	1.000	0.000
-32	9.3	530	21	success	0.893	0.107
-40	23.3	916	22	success	1.000	0.000
-30	9.6	500	19	success	0.663	0.337
-25	12.4	412	30	failure	0.258	0.742
-28	14.1	400	38	failure	0.002	0.998

Table 4: The Test Set

				Weaning	Posterior Probability	
NIF	VE	VT	RR	Effort	Success	failure
-40	10.6	465	23	success	0.967	0.033
-15	6.7	450	25	failure	70.003	0.997
-22	15.1	400	41	failure	0.001	0.999
-28	9.7	310	24	failure	0.114	0.886
-48	9.5	380	24	success	0.999	0.001
-34	11.6	530	28	success	0.528	0.472
-40	14.1	740	19	success	1.000	0.000
-42	14.1	550	27	success	0.984	0.016
-55	7.9	480	19	success	1.000	0.000

Table 5: Number of observations and Percentage of correct Classification

Results of Statistical Analysis on the Training Set

	Predicted Success	Predicted Failure	Total	Correctly Classified
Success	8	1	9	88.89%
Failure	1	11	12	91.67%
Total	9	12	21	90.5%

Table 6: Number of observations and Percentage of Correct Classification

Results of Neural Network Analysis on the Training Set

	Predicted Success	Predicted Failure	Total	Correctly Classified
Success	9	0	9	100%
Failure	0	12	12	100%
Total	9	12	21	100%

Table 7: Number of observations and Percentage of Correct Classification

Results of Statistical Analysis on the Test Set

	Predicted Success	Predicted Failure	Total	Correctly classified
Success	6	0	6	100%
Failure	0	3	3	100%
Total	6	3	9	100%

Table 8: Number of observations and Percentage of Correct Classification

Results of Neural Network Analysis on the Test Set

	Predicted Success	Predicted Failure	Total	Correctly Classified
Success	6	0	6	100%
Failure	1	2	3	66.6%
Total	7	2	9	88.8%

Table 9: The Training and Test Sets Statistics

	The Training Set		The Test Set	
Variable	Mean	St. Dev	Mean	St. Dev
NIF	-27.2857	11.5332	-36	12.6392
VE	10.9571	3.76664	11.0333	2.92788
VT	422.762	226.044	478.333	123.187
RR	28.9048	9.12636	25.5556	6.55956

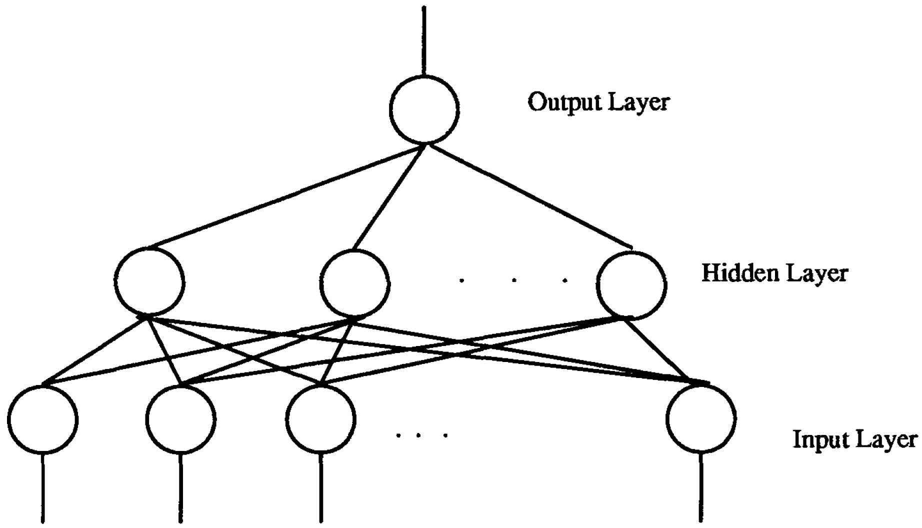

Figure 1: A Neural Network with One Hidden Layer
(For details see the appendix)