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Original Article

Weaning from mechanical ventilation: a cross-sectional study of reference values and the discriminative validity of aging

Camilo Corbellini, MSc, PT[1, 2], Cristiane Brenner Eilert Trevisan, Msc, PT[1], Jorge Hugo Villafañe, PhD, MSc, PT[3]*, Alexandre Doval da Costa, Msc, PT[1], Silvia Regina Rios Vieira, PhD, MD[4]

[1] *Postgraduate Program in Medical Sciences, Medical School, Universidade Federal do Rio Grande do Sul, Brazil*
[2] *Casa di Cura Villa Serena, Italy*
[3] *IRCCS Don Gnocchi Foundation: Milan, Italy*
[4] *Hospital de Clinicas de Porto Alegre, Universidade Federal do Rio Grande do Sul, Brazil*

Abstract. [Purpose] To evaluate pre-extubation variables and check the discriminative validity of age as well as its correlation with weaning failure in elderly patients. [Subjects and Methods] Two hundred thirty-nine consecutive patients (48% female) who were on mechanical ventilation and had undergone orotracheal intubation were divided into four subgroups according to their age: <59 years, 60–69 years, 70–79 years, and >80 years old. The expiratory volume (V_E), respiratory frequency (f), tidal volume (V_T), and respiratory frequency/tidal volume ratio (f/V_T) were used to examine differences in weaning parameters between the four subgroups, and age was correlated with weaning failure. [Results] The rate of weaning failure was 27.8% in patients aged >80 years and 22.1% in patients aged <60 years old. Elderly patients presented higher f/V_T and f values and lower V_T values. The areas under the receiver operating characteristic curves for f/V_T ratio were smaller than those published previously. [Conclusion] Our results indicate that aging influences weaning criteria without causing an increase in weaning failure.

Key words: Weaning, Mechanical ventilation, Aging

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INTRODUCTION

Assessment of spontaneous breathing is a routine procedure carried out in all mechanically ventilated patients. Many different techniques are used to decide if a patient is able to breathe independently[1]. Pre-extubation respiratory parameters (also known as weaning predictors) and weaning strategies have been studied previously, and their relevance has been found to vary according to the center where the studies were carried out[3].

The management of ventilatory support and its discontinuation in elderly patients remain controversial issues. Advanced age is thought to be an import associated factor in the intensive care unit, but its effect on weaning failure is unclear and there is a lack of information regarding the influence of aging on pre-extubation respiratory parameters[2, 4].

Aging is associated with a progressive decrease in lung performance. Physiological changes take place in the parenchyma and chest wall that decrease static elastic recoil, chest wall compliance, and the strength of the respiratory muscles, leading to changes in pulmonary function[5].

The strict utilization of weaning predictors to prevent weaning failure is not universally accepted[3, 6]. The first report on the most commonly used weaning predictor, the ratio of respiratory frequency (f) to tidal volume (V_T) or f/V_T[2], considered this parameter to be highly sensitive and specific[7]. However, other studies seem to disagree and have associated this ratio with a longer duration of mechanical ventilation. Meanwhile, other authors have suggested different cutoff values to avoid weaning failure in specific populations, such as the elderly[3, 6, 8]. Many studies have investigated the best method or index to predict weaning success, and several parameters have been described[9, 10]. Although the association between weaning and age has been demonstrated, no studies have found evidence of the influence of aging on conventional weaning parameters[6, 11, 12]. Therefore, the purpose of this study was to evaluate pre-extubation variables in a consecutive sample of elderly patients, and to check the discriminative validity of age as well as its correlation with weaning failure.

SUBJECTS AND METHODS

In this cross-sectional study, informed consent was ob-

*Corresponding author. Jorge Hugo Villafañe (E-mail: mail@villafane.it)

Table 1. Causes of respiratory failure, gasometric values, and ventilatory settings before the weaning protocol

Age Group	Up to 60 years	61 to 70 years	71 to 80 years	Over 80 years	Total
n (% female)	113 (45%)	61 (52%)	49 (49%)	18 (55%)	239 (48%)
Cause of respiratory failure					
COPD/asthma exacerbation	33 (29.3%)	17 (28.8%)	15 (30.7%)	7 (38.9%)	72 (30.1%)
ALI/ARDS	27 (23.9%)	18 (30.5%)	13 (26.5%)	4 (22.2%)	38 (15.9%)
Pneumonia	19 (16.8%)	8 (13.5%)	5 (10.3%)	3 (16.7%)	35 (14.6%)
Surgery	18 (15.9%)	6 (10.2%)	7 (14.2%)	3 (16.7%)	34 (14.2%)
Others	11 (9.7%)	5 (8.5%)	4 (8.1%)	1 (5.5%)	21 (8.8%)
Cardiac arrest	3 (2.6%)	4 (6.7%)	4 (8.1%)	0	11 (4.6%)
Coma	2 (1.8%)	1 (1.7%)	1 (2%)	0	4 (1.7%)
Gasometric values					
pH	7.42±0.06	7.43±0.06	7.42±0.07	7.41±0.07	7.43±0.07
PCO_2	37.51±10.31	37.08±9.82	37.84±11.22	38.64±11.27	36.16±7.9
HCO_3	24.23±6.81	24.25±5.92	24.34±7.78	24.34±8.24	23.52±4.48
PO_2	115.9±37.5	112.7±39.1	106±35.7	115.5±36	107.2±30.8
Oxygen saturation (%)	96.98±4.71	96.98±6.13	96.57±3.39	97.51±2.22	96.84±2.84
Mechanical ventilator settings					
PEEP (cmH_2O)	5.17±0.84	5.17±0.88	5.06±0.76	5.2±0.88	5.44±0.78
PIP (cmH_2O)	18.51±3.64	18.4±3.64	18.17±2.95	19.2±3.39	18.39±5.87
Tidal volume (mL)	508±236	520±239	486±235	498±220	530±139
FiO_2	0.36±0.03	0.37±0.03	0.36±0.03	0.36±0.03	0.36±0.02
PaO_2/FiO_2	319±109	338±114	292±102	318±95	304±95
Days of MV					
Mean (± SD)	8.5±7.4	6.8±4.5	7.5±5.8	9±6	7.9±6.5
Median	6	5	5	8.5	
25th percentile	3	3	3	3	
75th percentile	12	9	9.5	13.2	

COPD: chronic obstructive pulmonary disease; ALI: acute lung injury; ARDS: acute respiratory distress syndrome; PCO_2: carbon dioxide pressure; HCO_3: bicarbonate; PO_2: oxygen pressure; PEEP: positive end expiratory pressure; PIP: positive inspiratory pressure; FiO_2: fraction of inspired oxygen; PaO_2/FiO_2: arterial oxygen partial pressure/fraction of inspired oxygen; MV: mechanical ventilation

tained from all participants and procedures were conducted according to the Declaration of Helsinki. Prior to participation in the study, all patients signed an informed consent form. The protocol (No. 196/96 of the National Research Board) was approved by the Ethical Committee of the Hospital de Clinicas de Porto Alegre, Brazil.

Two hundred thirty-nine patients (mean age, 57 ± 20 years; 48% female) who were mechanically ventilated and had undergone orotracheal intubation for at least 48 hours were recruited for the study from January 2004 to December 2006. To be enrolled in the study, patients had to show an improvement in or resolution of the cause of respiratory failure. Patients were enrolled when they were in the process of discontinuing mechanical ventilation. The inclusion criteria were as follows: arterial oxygen partial pressure (PaO_2)/fraction of inspired oxygen (FiO_2) ≥200 or oxygen saturation >90% at FiO_2 ≤0.4, positive end expiratory pressure (PEEP) ≤5 cmH_2O, mean arterial pressure ≥60 mmHg without vasopressor agents, and body temperature <38 °C. In addition, the patients had to be awake or easily aroused with adequate coughing and able to remove pulmonary secretions[3, 13]. The exclusion criteria were: accidental extubation, reintubation after glottis edema, and an inability to acquire informed consent[14]. Data were collected for each patient after the physician had made a decision regarding readiness for weaning. The characteristics of the subjects are presented in Table 1.

A multi-parameter monitor (66S; Hewlett-Packard, Palo Alto, CA, USA) was used to collect data on heart rate (HR), arterial blood pressure, and oxygen saturation (SpO_2). Next, the positive inspiratory pressure (PIP), PEEP, V_T, and level of pressure support ventilation (PSV) were recorded from the mechanical ventilators used (Servo 300 and Servo 900; Siemens, Solna, Sweden). Once their baseline clinical characteristics had been collected, the patients underwent a spontaneous breathing trial (SBT). The trial involved 30 minutes of spontaneous breathing, with the T-piece connected in the orotracheal tube and the same level of supplementary oxygen that the patient had when on mechanical ventilation. At the beginning (T0) and end (T30) of the SBT, conventional weaning parameters were collected with a spirometer (Datex-Ohmeda Inc., Lousville, KY, USA). These parameters included expiratory volume (V_E), f, V_T, and f/V_T. V_E was measured in the first minute after ventilator

Table 2. Weaning failure and mean pre-extubation variables by age group

Age group	Up to 60 years (n=113)	61 to 70 years (n=59)	71 to 80 years (n=49)	Over 80 years (n=18)
Weaning failure (%)	22.1	25.4	22.4	27.8
Mean days of MV	8.5±7.4	6.8±4.5	7.54±5.8	9.0±6.1
Parameters				
V_E (L) T0	11.6±3.6	11.2±3.3	10.5±3.1	11.9±3.1
V_E (L) T30	11.7±3.2	11.4±3.4	11.3±2.8	11.4±3.4
V_T (mL) T0	534±195 †	499±173	441±143	447±144 †
V_T (mL) T30	520±196	505±163	473±128	498±251
f (bpm) T0	23±6†	23±5	24±4	28±7 †
f (bpm) T30	24±7	23 ±5	24±5	26±8
f/V_T ratio T0	50.8±27 †	52.5±22.6	61.6±24	68.5±28.4 †
f/V_T ratio T30	57.9±45.5	52.4±26.5	57.5±28	66.8±37

T0: time of first assessment of weaning parameters during spontaneous breathing trial; T30: 30 minutes after first measurements; V_E: expiratory volume; V_T: tidal volume; f: respiratory frequency; f/V_T: frequency to tidal volume ratio.
† indicates significant differences between age groups

discontinuation, and f was counted as breaths per minute. V_T was determined by the equation $V_T = V_E/f$, and f/V_T was then calculated. The trial was interrupted in cases of respiratory failure determined by tachypnea (f >35 breaths/min), hypoxemia (SpO_2 <90%), tachycardia (HR >140 beats/min), a sustained increase or decrease in HR of more than 20%, a systolic blood pressure above 200 or below 80 mm Hg, agitation, diaphoresis, or anxiety[15]. A V_E of 8 to 12 L/min, a f of <35 breaths/min, a V_T of >5 mL/kg, and a f/V_T of <105 were the criteria for patients to undergo the SBT. Weaning was classified as successful after 48 hours of spontaneous ventilation without any sign of respiratory failure.

The primary outcome of the study was the difference in weaning failure between four different age groups: up to 60 years old, 61 to 70 years old, 71 to 80 years old, and over 80 years old. The secondary variables analyzed were the differences in the mean weaning parameters measured during the weaning protocol between the age subgroups (i.e., V_E, f, V_T, and f/V_T). In order to determine the specificity and sensitivity of the f/V_T ratio at T0 and T30, receiver operating characteristic (ROC) curves for weaning failure were established. To compare the elderly to other adults we also analyzed our sample using a cutoff age of 65 years old[16] to divide the subjects into elderly and adult groups.

Data were analyzed using SPSS version 20.0 (SPSS Inc., Chicago, IL, USA). The results are expressed as means, standard deviations, and/or 95% confidence intervals. One-way ANOVA and multiple comparison Tukey tests were used to compare the four age subgroups (up to 60 years old, 61 to 70 years old, 71 to 80 years old, and over 80 years old). The elderly and adult groups were compared using an independent two-sample Student's t test for continuous data and the χ^2 test for categorical data. To compare the f/V_T ratio in the elderly and adult groups at T0 and T30, a repeated measures ANOVA was used. The area under the curve (AUC) of each ROC curve was calculated, and the sensitivity and specificity of the f/V_T ratio at T0 and T30 were calculated for the entire sample and for the elderly and adult groups separately, with the cutoff point = 100. Statistical analysis was conducted at a 95% confidence level and a p value of <0.05 was considered statistically significant.

Table 3. Success and failure rates after weaning trial

Group	AG	EG
Success	83 (74.8%)	100 (78.1%)
Failure	28 (25.1%)	28 (21.9%)
Total	128	111

AG: adult group; EG: elderly group

RESULTS

The study enrolled 239 patients (mean age, 57 ± 20 years; 48% female), who were divided into four subgroups classified according to age: <60 years old (n=111), 60–69 years old (n=61), 70–79 years old (n=49), and >80 years old (n=18). The most common causes of respiratory failure were chronic obstructive pulmonary disease (COPD), acute lung injury/acute respiratory distress syndrome (ALI/ARDS), and pneumonia. Before the weaning trial, the gasometric characteristics and ventilatory settings were statically and clinically similar among the groups (Table 1).

Differences in weaning failure among the age groups were not statistically significant. Although weaning parameters showed statistically significant differences among the age groups, these differences were not clinically important. Respiratory frequency increased with age while tidal volume decreased. Therefore, the f/V_T index was higher in older patients (Table 2).

Using a cutoff age of 65 years old, there were 111 patients in the elderly group and 128 patients in the adult group. The difference in weaning failure between these two groups was not statistically significant (p=0.552) (Table 3). Differences in the f/V_T ratio between adults and the elderly are shown

Table 4. Comparisons of mean f/VT ratio between adults and the elderly

Group	Elderly		Adult	
n (% female)	111 (47%)		128 (48%)	
Weaning Parameter	T 0	T 30	T 0	T 30
f/V_T ratio [a] (mean ± SD)	59.31±23.66*	58.03±29.66	50.81±27.69*	56.35±43.43
Median	56.09	50.44	45.73	49.22
25th percentile	42	40.36	28.57	33.61
75th percentile	68.57	66.22	65.59	66.75

T0: time of first assessment of weaning parameters during spontaneous breathing trial; T30: 30 minutes after first measurements; f/V_T: ratio of respiratory frequency to tidal volume.
a: non-significant ANOVA for repeated measures of time, group, and interaction. *****: $p < 0.05$ in t test for independent samples

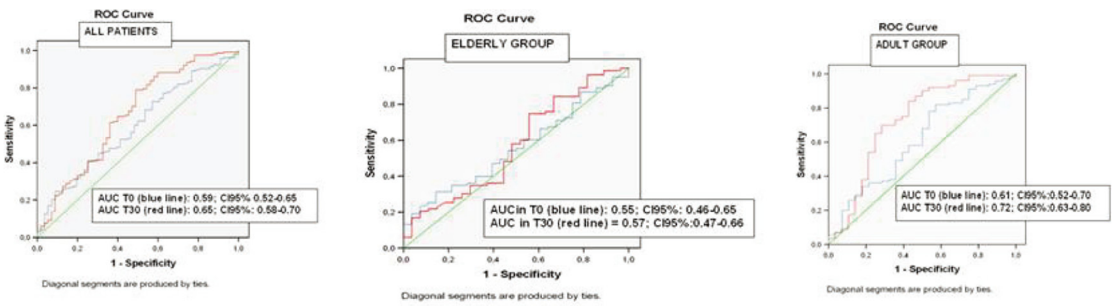

Fig. 1. ROC curves for f/V_T ratio in all patients (n=239), the adult group (n=128), and the elderly group (n=111)
Blue line: T0; red line: T30. AUC: area under the curve; CI: confidence interval

in Table 4. The mean values of the f/V_T ratio in the elderly group, while higher, were still on the edge of normality. The sensitivity and specificity of the f/V_T ratio at T0 and T30 were assessed in all patients, as well as separately in the elderly and adult groups. At T0 for all patients, the sensitivity was 0.95 (95% confidence interval [CI], 0.91–0.97) and the specificity was 0.08 (95% CI, 0.03–0.19). In the elderly group, the sensitivity was 0.95 (95% CI, 0.88–0.98) and the specificity was 0.07 (95% CI, 0.090.23). In the adult group, the sensitivity was 0.95 (95% CI, 0.88–0.98) and the specificity was 0.1 (95% CI, 0.02–0.28). At T30 for all patients, the sensitivity was 0.96 (95% CI, 0.93–0.98) and the specificity was 0.21 (95% CI, 0.11–0.35). In the elderly group, the sensitivity was 0.95 (95% CI, 0.88–0.99) and the specificity was 0.18 (95% CI, 0.06–0.38). In the adult group, the sensitivity was 0.98 (95% CI, 0.93–0.99) and the specificity was 0.25 (95% CI, 0.1–0.44). The ROC curves were calculated to estimate the success value for the f/V_T ratio ≤100 at T0 and T30 (Fig. 1).

DISCUSSION

The baseline characteristics of all patients were similar regardless of age. Comparisons according to age subgroup showed no statistically significant differences in weaning failure. Previous studies have demonstrated that conventional weaning criteria show differences between age subgroups[11], but these results were not associated with differences in weaning failure. Although weaning failure increased with age in the present study, the mean values of failure did not show significant differences. Therefore, when applying the same conventional weaning criteria as used in the literature[17, 18], the data from this study do not support the idea that elderly patients have a higher rate of weaning failure than adults[19, 20].

The differences observed in pre-extubation variables were expected and confirmed the effect of aging on the respiratory system[5, 11, 13, 21]. The aged lung shows a homogeneous increase in the distal air space and a tendency to close the small airways more readily, a fact that leads to a decreased expiratory flow and gas trapping. Theoretically, this may have affected the parameters measured in the present study. In fact, analysis of the pre-extubation variables showed that the measured values were in line with previous descriptions of changes in the aged lung[13, 14].

In the current study, the older subgroups had a lower tidal volume, higher respiratory frequency, and consequently higher f/V_T ratio values. While the f/V_T ratio was significantly higher in older patients, this result was clinically irrelevant and the mean f/V_T ratio was still adequate to wean these patients[15, 22, 23]. The mean f/V_T ratio in the group of patients aged over 80 years old was close to the limit established previously[7] in order to predict weaning failure. The influence of age on pre-extubation variables such as the f/V_T ratio has already been studied, and the previous finding that elderly patients present a higher respiratory frequency and lower tidal volume lead to the recommendation to change the cutoff value of this index from 105 to 130 for patients of 70 years of age or older[11]. Since all the enrolled patients displayed f/V_T ratios in the normal range in the current study, a failure incidence of lower than 5%, as published in the seminal paper on this index, was expected. However, the failure incidence varied from 22 to 28% in our sample[1, 7, 21].

In comparison to some previous studies, the failure rate found in the current study was normal, whereas others report rates of up to 20% as high[24–27]. In these studies, the criteria used to discontinue weaning were clinical signs such as respiratory frequency, cardiac frequency, and oxygen saturation[17, 28]. In contrast, our study used the f/V_T ratio to determine when to discontinue mechanical ventilation, and we did not achieve the success reported in other studies[21]. Therefore, when using the same conventional weaning criteria as found in the literature[17, 18], our data did not support the idea that success rates of weaning are lower for elderly patients than adults[20]. This result highlights whether the weaning predictor f/V_T should be used in daily clinical practice for elderly patients[6, 29–31].

Analysis of ROC curves showed that the sensitivity of the f/V_T ratio in the elderly group in the current study was similar to that found in a previous study that analyzed the same weaning predictor in elderly patients[6, 19]. The AUC for this predictor in our study was smaller than the first ROC curve which was published regardless of age[7] and similar to a study that analyzed 16 patients during a 60 minute SBT[32]. However, as our protocol was observational it was impossible to determine the necessary true negative results; therefore, we believe that the AUC of our sample was underestimated.

The main limitation of our study was the fact that it was an observational and single center study, using previously described parameters, which could have caused selection bias. Future investigations should be conducted prospectively. In addition, statistical and data analyses should be standardized, and the pretest probability should be taken into consideration.

The impact of aging should be the focus of future weaning studies because elderly populations are increasing worldwide and age may affect many clinical outcomes. The higher mean f/V_T ratio as well as the weaning failure incidence presented in older subjects in the present study may indicate a typical finding of this subset of patients.

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