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SCIENTIFIC ARTICLE

Respiratory Rate as a Predictor of Weaning Failure from Mechanical Ventilation

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Abstract

Background and objective: There is not an ideal predictor of weaning from mechanical ventilation (MV). In a large meta-analysis, despite methodological limitations, respiratory rate (RR) was considered a promising predictor. The aim of this study was to evaluate RR as a predictor of weaning failure from MV.

Methods: We prospectively evaluated 166 patients scheduled for weaning from MV. RR and other essential criteria for weaning were evaluated at an early stage of screening. Patients who met the essential screening criteria for weaning underwent spontaneous breathing trial. RR was compared with the following outcomes: weaning success/failure or extubation failure.

Results: Weaning success was present in 76.5% and weaning failure in 17.5% of patients. There were 6% of reintubations. The predictive power for RR weaning failure, RR best cut-off point > 24 breaths per minute (rpm), was: sensitivity 100%, specificity 85%, and accuracy 88% (ROC curve, $p < 0.0001$). Of the patients with weaning failure, 100% were identified by RR during screening (RR cut-off > 24 rpm). There were 15% false positives, weaning successes with RR > 24 rpm.

Conclusion: RR was an effective predictor of weaning failure. The best cut-off point was RR > 24 rpm, which differed from those reported in the literature (35 and 38 rpm). Only 6% of patients were reintubated, but RR or other weaning criteria did not identify them.

Introduction

According to the 6th International Consensus Conference in Intensive Care Medicine, patients who meet the essential criteria for weaning from mechanical ventilation (MV) – particularly improvement of the cause of respiratory failure, oxygenation, appropriate respiratory mechanics, and hemodynamic stability – should be evaluated for the possibility of

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weaning. In this context, a predictor, such as the rapid shallow breathing index (RSBI), is initially used as screening and if the result is positive for weaning success, a spontaneous breathing trial (SBT) is started. If the patient passes this test, MV is discontinued and followed by extubation [1]. The problem is that, despite all systematization of the weaning process, backed by different studies that establish the various steps of this process, the average rate of weaning failure is 30%, which is associated with increased morbidity and mortality [1-7]. According to Epstein et al. [6], weaning failure, particularly extubation failure, is associated with 43% mortality compared to 12% among those with weaning success.

In addition to the previous problem, there is not an ideal predictor of successful weaning. In the largest systematic review of predictors of successful weaning conducted by Meade et al. [8] and involving 65 studies, the studied indices' predictive ability was considered modest, with RR and RSBI considered promising (sensitivity 88%/specificity 47% and sensitivity 96%/specificity 73%, respectively). In most of the 65 analyzed studies, methodological flaws, such as less than 50 patients per study and statistical deficiencies, decreased the results' accuracy [8]. In a recent publication, a new predictor resulting from the integration of three other predictors was presented: oxygen saturation (SaO_2), RSBI (obtained by dividing RR by tidal volume: RR/V_T), and static compliance (Cst). However, the study's major limitation was the measurement of this last variable with the patient without sedation and breathing spontaneously, which usually hinders Cst measurement [9].

The aim of this study was to evaluate RR as a predictor of weaning failure from MV.

Method

After approval by the Ethics Committee (025/2006), this prospective study was conducted from March 2009 to August 2011, during which we analyzed the weaning of 166 patients admitted to the Intensive Care Unit (ICU) - with eight beds - of the Hospital Geral de Camaçari (BA). All patients (or their guardians) included in the study signed an informed consent form (ICF).

Patients underwent discontinuation of MV, according to the ICU medical staff guidance.

The study included 166 patients aged over 18 years who met the essential criteria for weaning, according to the 6th International Consensus Conference in Intensive Care Medicine:

a) Improvement of the condition that lead to VM;
b) Discontinuation of sedatives and neuromuscular blockers;
c) Patient vigil and without agitation;
d) Absence of fever or new infection;
e) Hemodynamically stable;
f) Absence of metabolic and/or electrolytic disorders;
g) Effective cough;
h) Patient with an inspired oxygen fraction less than or equal to 40% ($FiO_2 \leq 40\%$) and positive end-expiratory pressure less than or equal to 5 cm H_2O (PEEP ≤ 5 cm H_2O) with $SaO_2 > 90\%$ and ratio of arterial oxygen pressure by the fraction of inspired oxygen greater than 200 ($PaO_2/FiO_2 > 200$);
i) Tidal volume greater than 5 $mL.kg^{-1}$ ($V_T > 5$ $mL.kg^{-1}$);
j) Maximum inspiratory pressure less than 20 cm H_2O (MIP < 20 cm H_2O);
l) $RR/V_T < 105$ $breaths.min^{-1}.L^{-1}$;
m) RR ≤ 35 breaths per minute (rpm).

We excluded patients accidentally extubated (n = 4), tracheostomized (n = 24), and those who did not meet the essential criteria for weaning (n = 6).

Clinical and demographic data (Table 1) were collected from medical records and, in dubious cases, from doctors and physiotherapists.

Patients who presented with improvement of the condition that lead to VM, hemodynamic stability, oxygenation parameters mentioned above and absence of fever were subjected to the following screening measures, using the ventilator Vela (Viasys, USA) for monitoring:

1) Static compliance (Cst), with sedated patient, in volume control mode, and performing an inspiratory pause;
2) Minute volume (VE) and RR, with unsedated patient, awake and on PSV mode of 7 cm H_2O, $FiO_2 \leq 40\%$ and PEEP = 5 cm H_2O for one minute;
3) V_T: resulted from the division of VE by RR;

Table 1 Clinical Characteristics of 166 Patients on Mechanical Ventilation.

Clinical Characteristics	
Age (years ± DP)	53 ± 22
Female, n	72
Male, n	94
Death, n (%)	29 (17.5)
Discharge, n (%)	137 (82.5)
Duration of MV before weaning (days ± DP)	4 ± 3.6
Weaning success, n (%)	127 (76.5)
Weaning failure (SBT failure), n (%)	29 (17.5)
Extubation failure, n (%)	10 (6)
MV cause, n (%)	
Pneumonia	23 (13.8)
Nonrespiratory sepsis	13 (7.8)
Coma	17 (10.2)
Chronic obstructive pulmonary disease	4 (2.4)
Asthma	3 (1.8)
Postoperative	43 (25.9)
Acute Pulmonary Edema	16 (9.6)
Shock	5 (3.0)
Bronchoaspiration	8 (4.8)
Convulsion	7 (4.2)
Exogenous intoxication	12 (7.2)
Drowning	3 (1.8)
Metabolic acidosis	4 (2.4)
Arrhythmias	3 (1.8)
Stridor	1 (0.6)
Traumatic brain injury	1 (0.6)
Miscellany	3 (1.8)

SD: standard deviation; n: number of occurrences; SBT: spontaneous breathing trial.

4) RR/V_T: resulted from the division of RR by V_T in liters;
5) MIP was measured from the inspiratory occlusion valve.

During screening measurements, patients who had Cst > 25 mL.cm H_2O^{-1}; RR ≤ 35 bpm; V_T > 5 mL.kg^{-1}, f/V_T < 105 breaths.min^{-1}.L^{-1}; MIP < -20 cm H_2O underwent SBT for 30 minutes on PSV mode of 7 cm H_2O, FiO_2 ≤ 40% and PEEP = 5 cm H_2O. RR, VE, and V_T were recorded during SBT, minute by minute, using the respirator monitor. Additionally, vital signs data and pulse oximetry were recorded continuously on a multiparameter monitor. Throughout the test, the physiotherapist and/or doctor on duty constantly monitored the patient looking for signs of SBT failure [1], namely:

a) RR > 35 bpm;
b) RR/V_T > 105 breaths.min^{-1}.L^{-1};
c) SaO_2 < 90%;
d) Tachycardia > 140 bpm or ≥ 20% increase;
e) Systolic blood pressure < 90 mm Hg or > 180 mm Hg or ≥ 20% increase;
f) Arrhythmias;
g) Psychomotor agitation and/or reduced level of consciousness;
h) Dyspnea.

In the presence of any signs described, SBT was interrupted and the patient placed in a ventilation mode that would provide comfort. Data collection was performed by the investigators or by a previously trained physiotherapy team.

Outcomes

a) Weaning success: the patient underwent SBT, was extubated, and without mechanical ventilation for more than 48 hours;
b) Weaning failure: the patient had signs of SBT failure;
c) Extubation failure: the patient underwent SBT and was extubated, but returned to MV within 48 hours after extubation.

All patients were followed-up until discharge or death in the ICU.

Statistical Analysis

Continuous variables were expressed as mean and standard deviation and categorical variables as frequency and percentage. Mann-Whitney test and Fisher's exact test were used to compare nonparametric variables and Student's t-test to compare parametric variables. The following parameters were used to assess the predictive power of RR: sensitivity (SE), specificity (SP), positive predictive value (PPV), negative predictive value (NPV), likelihood ratio for a positive test (LR+), likelihood ratio for a negative test (LR-), accuracy, and area under the ROC curve. The statistical programs used were MedCalc version 11.5.1.0 and BioEstat version 5.0 [10,11]. A p-value < 0.05 was considered significant.

Results

In total, 166 patients were evaluated during weaning from MV from March 2009 to August 2011. The mean age of the study population was 53 ± 22 years, with 94 males and 72 females, and mean duration of MV before weaning was 4 ± 3.6 days. Postoperative period was the most common cause of MV (25.9%), followed by pneumonia (13.8%), coma (10.2%), acute pulmonary edema (9.6%), sepsis (7.8%), exogenous intoxication (7.2%), aspiration (4.8%), and seizures (4.2%) (Table 1).

At the end of the study, 137 (82.5%) patients were discharged from the ICU and 29 (17.5%) died in that unit. Weaning success occurred in 127 (76.5%); weaning failure in 29 patients (17.5%), and extubation failure in 10 patients (6%).

Of the patients with weaning failure, 100% presented with RR > 24 bpm during screening measurement and SBT (Graphic 1 and Table 2). This pattern of tachypnea remained throughout SBT up to suspension, with the onset of signs of SBT failure. The major cause of extubation failure was acute pulmonary edema (APE), present in five out of 10 patients (50%), followed by bronchospasm in three patients (30%). The two remaining cases of failure were laryngeal edema and respiratory infection (Table 3).

There was a lower mortality rate (12.6%) among patients with weaning success (16/127), followed by the rate (20.7%) among patients with weaning failure (6/29). Patients with extubation failure had the highest mortality rate (70%), and compared with that observed among the successes, the difference was statistically significant (p = 0.0001).

Considering the best cut-off point as RR > 24.19 bpm, the RR generated by the ROC curve presented the following predictive power for weaning failure: SE 100%, SP 85%, NPV 100%, PPV 60%; LR+ 6.68; LR- 0.00, and accuracy 88% (p < 0.0001; Table 2 and Graphic 1). During screening and SBT stages, RR behavior was characterized by increased weaning failure (RR = 31 ± 6 bpm) and normal among successes (RR = 19 ± 5 bpm) (p < 0.0001). There was no difference in RR behavior among patients with extubation failure (RR = 18 ± 6 bpm) compared to the success cases (RR = 19 ± 5 bpm); p = 0.7313.

Discussion

On average, 46% of the patients admitted to the ICU require MV as fundamental life support, but this procedure is associated with significant rates of morbidity and mortality, which are directly proportional to the duration of MV and weaning failure [5,6,12-16]. The need to develop new strategies to remove the patient from MV as early as possible is evident. According to Coplin et al. [7], delayed extubation was associated with a statistically significant increase in mortality (RR for death 2.2, 95% CI: 1.0-4.7). Boles et al. [1] have proposed the early investigation of weaning capacity to avoid its delay.

A systematic daily evaluation of the possibility of weaning is an independent predictor of successful extubation and survival [12]. In this context, the investigation of predictors that, combined with clinical experience, improve the success rates of weaning is essential and justified our study.

The rates of weaning success (76.5%) and failure (23.5%) in the present study are close to those reported in the literature (70% and 30%, respectively [1]). The causes of MV were similar to those found in the literature: postoperative (25.9%), pneumonia (13.8%), coma (10.2%), APE (9.6%), and sepsis (7.8 %) [17,18].

Table 2 Predictive Power of Respiratory Rate for Different Cut-off Points in 156 Patients during Weaning (127 weaning successes and 29 failures).

Criteria	Sensitivity	95% CI	Specificity	CI 95%	LR+	LR-
≥ 6.6022	100.00	88.1 – 100.0	0.00	0.0 – 2.9	1.00	
> 24.1935 *	100.00	88.1 – 100.0	85.04	77.6 – 90.7	6.68	0.00
> 24.7857	96.55	82.2 – 99.9	85.04	77.6 – 90.7	6.45	0.041
> 24.9806	96.55	82.2 – 99.9	86.61	79.4 – 92.0	7.21	0.040
> 25	93.10	77.2 – 99.2	86.61	79.4 – 92.0	6.96	0.080
> 25.4984	93.10	77.2 – 99.2	89.76	83.1 – 94.4	9.10	0.077
> 25.7016	89.66	72.6 – 97.8	89.76	83.1 – 94.4	8.76	0.12
> 25.8146	89.66	72.6 – 97.8	90.55	84.1 – 95.0	9.49	0.11
> 25.871	86.21	68.3 - 96.1	90.55	84.1 – 95.0	9.12	0.15
> 26.2581	86.21	68.3 - 96.1	92.91	87.0 – 96.7	12.16	0.15
> 26.4929	79.31	60.3 – 92.0	92.91	87.0 – 96.7	11.19	0.22
> 26.5565	79.31	60.3 – 92.0	94.49	89.0 – 97.8	14.39	0.22
> 26.6452	75.86	56.5 – 89.7	94.49	89.0 – 97.8	13.76	0.26
> 26.7271	75.86	56.5 – 89.7	95.28	90.0 – 98.2	16.06	0.25
> 27.2257	68.97	49.2 – 84.7	95.28	90.0 – 98.2	14.60	0.33
> 27.9091	68.97	49.2 – 84.7	96.06	91.1 – 98.7	17.52	0.32
> 28.6478	62.07	42.3 – 79.3	96.06	91.1 – 98.7	15.77	0.39
> 29.0862	62.07	42.3 – 79.3	96.85	92.1 – 99.1	19.71	0.39
> 29.7419	48.28	29.4 - 67.5	96.85	92.1 – 99.1	15.33	0.53
> 30.1121	48.28	29.4 – 67.5	98.43	94.4 – 99.8	30.66	0.53
> 32.9173	20.69	8.0 – 39.7	98.43	94.4 – 99.8	13.14	0.81
> 33.0968	20.69	8.0 – 39.7	99.21	95.7 - 100.0	26.28	0.80
> 33.1108	17.24	5.8 – 35.8	99.21	95.7 – 100.0	21.90	0.83
> 33.2673	17.24	5.8 – 35.8	100.00	97.1 – 100.0		0.83
> 48.8333	0.00	0.0 – 11.9	100.00	97.1 – 100.0		1.00

CI: confidence interval; LR+: likelihood ratio for a positive test; LR-: likelihood ratio for a negative test; *: best cut-off point.

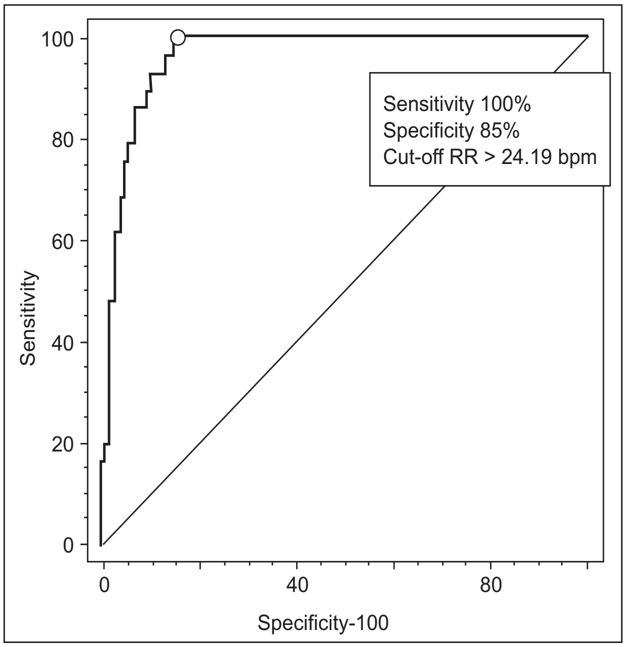
Table 3 Clinical Characteristics of 10 Reintubated Patients.

Sex	Age (years)	Intubation cause	Reintubation cause	Time interval for reintubation (hours)	Outcome	Observation
Male	72	AMI/APE	APE	12	Death	
Female	54	Sepsis/UTR	APE	6	Death	WBC 17200
Female	62	APE/SAH	APE	6	Death	WBC 31900
Male	65	Uremia	APE	24	Death	WBC 20300
Female	68	CHF	APE	4	Death	
Male	79	Sepsis	BESP	12	ICU discharge	
Male	75	Seizures	BESP	4	ICU discharge	
Female	64	PO	BESP		Death	WBC 15400
Female	29	Pneumonia	Stridor	6	ICU discharge	1 previous FE
Male	77	Aspiration	Pneumonia	24	Death	

AMI: acute myocardial infarction; APE: acute pulmonary edema, UTR: pneumonia; WBC: white blood cell count; SAH: systemic arterial hypertension, CHF: congestive heart failure; BESP: bronchospasm; EF: extubation failure.

Extubation failure (EF) was associated with higher mortality rate (70%). Several studies show that EF is associated with increased mortality [2,3,6,18-20]. According to Epstein et al. [6], the mortality rate in patients with EF was 43% compared to 12% among those with weaning success ($p < 0.0001$).

We found that the 10 patients with EF showed behavior patterns similar to those of successful patients during both screening and SBT stages. RR remained normal in both groups; therefore, it had no predictive power.



Graphic 1 ROC Curve of Respiratory Rate and Best Cut-off Point in 156 patients (127 weaning successes and 29 failures). RR: respiratory rate; bpm: breaths per minute.

Identifying patients with the possibility of extubation failure remains a major challenge for all who study weaning. The current predictive indices do not distinguish patients who, after a satisfactory SBT, will be reintubated from those who will be successfully extubated [3,19].

In our series, the group of patients who were reintubated was characterized by elderly individuals (mean age 64 ± 15 years); 40% had severe comorbidities (AMI Killip class III, CHF, SAH, renal failure), and 40% had significant leukocytosis (over 15,000), which could indicate an underlying inflammatory process, a new or persistent infection. One patient had laryngeal edema after two tracheal intubations and another had pneumonia 24 hours after extubation (Table 3). According to Esteban et al. [3], respiratory failure leading to reintubation is due to conditions arising after extubation, such as bronchospasm, laryngeal edema, and pneumonia. In our patients, cardiovascular comorbidities (CHF, SAH, AMI) predispose the occurrence of APE, the most frequent cause of reintubation (50%). Study of conditions leading to reintubation should create strategies to reduce EF rates [3]. It is noteworthy that the rate of reintubation of 6% was lower than that reported in the literature (13%) [1], which may be due to the rigor of including only patients who met all essential criteria for weaning.

During analysis, RR proved to be a practical and efficient predictive index (SE 100%, SP 85%, and accuracy 88% for a cut-off point of RR > 24 bpm), able to identify 100% of patients with weaning failure during screening and SBT stages on PSV mode. In other words, all patients with weaning failure had a RR > 24 bpm during the screening stage and maintained it during SBT.

There were 15% of false positive cases of weaning success with RR > 24 rpm; in these patients, the response to mental suffering or adaptation to pathological conditions was identified (Table 4), with increased RR during screening and SBT stages, without cardiorespiratory involvement. In this context, the continuous monitoring of patients by the team that identified the conditions responsible for isolated tachypnea

Table 4 Conditions Related to Respiratory Rate (RR) > 24.19 bpm and Weaning Success (false positive) in 19 Patients.

RR (bpm)	Condition	Management during SBT
25	Attempted suicide/odynophagia	Analgesia and anxiolytic
26	ICH sequel/paresis	Observation
33	Pulmonary fibrosis	Observation
27	Pneumonia treatment	Observation
29	IS/CRF/AF sequel	Observation
25	Congestion	Diuretics and fluid restriction
26	Anxiety and agitation	Anxiolytic
25	Abdominal pain	Analgesia
25	IS sequel/coma vigil	Observation
26	CHF/EF = 34%	Observation
26	Anxiety and agitation	Anxiolytic
25	Pneumonia treatment	Observation
25	Congestion	Diuretics and fluid restriction
26	Anxiety and agitation	Anxiolytic
33	Anxiety and agitation	Anxiolytic
28	Chronic asthma/dehydration	Rehydration
30	Compensated metabolic acidosis	Observation
26	Anxiety and agitation	Observation
30	Attempted suicide	Anxiolytic

ICH: intracerebral hemorrhage; SBT: spontaneous breathing trial; IS: ischemic stroke; CRF: chronic renal failure, AF: atrial fibrillation, CHF: congestive heart failure, EF: ejection fraction.

and correctly chose weaning was important. Patients with psychiatric disorders characterized by psychomotor agitation were treated with doses of sedative for anxiety, which enabled the weaning process.

Conclusion

In this study population, RR was an efficient predictor of weaning failure easy to be recorded from the respirator, exempting calculations by the assistants. In the initial screening phase, RR > 24 bpm was present in 100% of patients who would have a weaning failure during SBT (sensitivity 100%). RR ≤ 24 bpm was found in the initial stage of screening in 85% of patients who would have a weaning success (specificity 85%). The 15% of false positive cases (successful weaning with RR > 24 bpm) are acceptable and were identified by clinical evaluation. A predictor of weaning failure has to have a sensitivity of 100%, even if it involves some loss of specificity, because it decreases the chance of early MV discontinuation and associated cardiorespiratory risks. In this study, the best cut-off point of 24 bpm generated by the ROC curve suggests that the cut-off points of 35 and 38, mentioned in the literature, are too high for our reality [1,8].

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