Medical Research Council Scale Predicts Spontaneous Breathing Trial Failure and Difficult or Prolonged Weaning of Critically Ill Individuals

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BACKGROUND: Handgrip strength is an alternative measure to assess peripheral muscle strength and is correlated with the Medical Research Council (MRC) scale, with promising values for diagnosing ICU-acquired weakness (ICUAW). Because ICUAW has been associated with delayed weaning from mechanical ventilation, we hypothesized that ICUAW evaluated with both the MRC scale score and handgrip strength are associated with failure of a spontaneous breathing trial (SBT) and duration of mechanical ventilation weaning. METHODS: We conducted a prospective observational study in 3 general ICUs with a total of 54 beds at 2 academic hospitals. Adult subjects with > 48 h of mechanical ventilation who were eligible for weaning were included in the study. RESULTS: In the evaluation before the first SBT, the MRC score (*P* < .001) and handgrip strength (*P* < .001) were significantly different between subjects extubated after a successful first SBT (simple weaning) and those extubated any time after a failed first SBT (difficult weaning). Only the MRC score discriminated between first SBT success or failure (*P* < .001); in multivariate analysis, the MRC score was significantly associated with first SBT failure (odds ratio 0.91, 95% CI 0.88–0.97, *P* < .001) and difficult weaning (odds ratio 0.91, 95% CI 0.87–0.96, *P* < .001). Handgrip strength exhibited good accuracy in identifying ICUAW. CONCLUSIONS: MRC score was independently associated with SBT failure and difficult or prolonged weaning. *Key words: MRC scale; handgrip dynamometry; ICU-acquired muscle weakness; mechanical ventilation; weaning.* [Respir Care 2021;66(5):733–741. © 2021 Daedalus Enterprises]

Introduction

Critically ill patients often develop generalized muscle weakness involving the respiratory and peripheral muscles.[1-3] Muscle weakness occurs early, and patients subjected to a spontaneous breathing trial (SBT) after 24 h on mechanical ventilation already present diaphragmatic or peripheral muscle dysfunction.[3] ICU-acquired weakness (ICUAW) is associated with short-term[4] and long-term[5] functional abnormalities and delayed weaning and extubation failure.[6,7]

The Medical Research Council (MRC) scale is recognized by many as a standard assessment tool for diagnosing ICUAW.[8] ICUAW evaluated with the MRC scale after 7 d of mechanical ventilation appears to be an excellent predictor of prolonged weaning.[6,9]

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Handgrip strength as measured by using hand dynamometry is simple, objective, and easy to apply, and it has been widely used in neuromuscular diseases.[10,11] When used with critically ill patients, it has shown good reliability.[12] Ali et al[13] found that in handgrip strength was correlated to MRC score in critically ill subjects, rendering handgrip strength a potential alternative measure to MRC for diagnosing ICUAW. Although both parameters were correlated with ICU and hospital length of stay and mortality, only MRC correlated with duration of mechanical ventilation.

Recently, 2 studies evaluated handgrip strength as a parameter to predict the outcome of weaning from mechanical ventilation.[14,15] Cottereau et al[14] evaluated ICUAW via handgrip strength prior to initiating the SBT in subjects on mechanical ventilation for at least 48 h and demonstrated that handgrip strength was independently associated with difficult and prolonged weaning as well as length of stay in the ICU. In a pilot study, Mohamed-Hussein et al[15] reported a negative correlation between baseline handgrip strength and duration of mechanical ventilation in subjects with COPD.

Given that these studies together have shown that ICUAW evaluated by the MRC scale score and handgrip strength are associated with the duration of mechanical ventilation, we hypothesized that these same measurements could in addition predict SBT failure. The primary objective of our study is thus to evaluate the association of both the MRC scale score and handgrip strength with SBT failure and to confirm their association with duration of mechanical ventilation weaning. The secondary objective is to define handgrip strength cutoff points indicative of ICUAW for men and women.

QUICK LOOK

Current knowledge

ICU-acquired weakness (ICUAW) is a common complication in critically ill patients and is associated with delayed weaning from mechanical ventilation. The assessment of peripheral muscle strength with the Medical Research Council (MRC) scale score and with handgrip strength has not been described as predictors of failure of a spontaneous breathing trial (SBT) and the duration of weaning from mechanical ventilation.

What this paper contributes to our knowledge

ICUAW defined by the MRC scale score obtained before the first SBT was an independent prognostic factor for SBT failure and difficult or prolonged weaning. Although handgrip strength may serve as an alternative tool for diagnosing ICUAW, due to the ease of application, more studies are needed to evaluate handgrip strength as a first step to predict SBT failure and difficult or prolonged weaning.

Methods

Study Design and Research Protocol

This prospective observational study was conducted from March 2016 to March 2017 in 3 ICUs, with a total of 54 beds, at 2 hospitals in Porto Alegre, Rio Grande do Sul, Brazil. The study protocol was approved by the Research Ethics Committee of the Clinical Hospital Porto Alegre (n. 1,300,414), and written informed consent was obtained from all subjects or surrogates.

Adult subjects (> 18 y old) who were on mechanical ventilation for > 48 h and who were ready to be submitted to a SBT at the discretion of the medical intensivist in charge were included.[16] Subjects needed to be awake and cooperative to perform the tests (ie, −1 to +1 on the Richmond Sedation and Agitation Scale). Patients unable to perform the handgrip strength test or the MRC scale test due to rheumatologic or neuromuscular conditions or amputation of the dominant hand were excluded.

Demographic data (ie, sex, age), comorbidities and the severity of critical illness according to the Acute Physiology and Chronic Health Evaluation II (APACHE II) score,[17] as well as the reasons for hospitalization and mechanical ventilation, were collected from medical records.

When a subject failed the SBT or required re-intubation, the reason was verified and another muscle strength assessment was performed prior to the next SBT. When a subject passed the SBT, the decision to extubate was made at the discretion of the caregiver team. The caregiver team was not aware of muscle strength assessment results.

Muscle Strength Assessment

When the subjects were considered able to perform the SBT by the clinical team, they were evaluated for muscle strength by previously trained physical therapists using the MRC scale and the handgrip strength of the dominant hand prior to performing the SBT.

The evaluation with the MRC scale consisted of analyzing 6 specific movements bilaterally (ie, shoulder abduction, elbow flexion, wrist extension, hip flexion, knee extension, and ankle dorsiflexion) using the manual muscle test, with the score ranging from 0 points to 5 points.[2,18] The dorsal decubitus position was adopted, with the headboard between 45° and 60° and symmetrical posture. First, free-form movement was requested; then, according to the result, manual resistance was imposed or the action of gravity was eliminated (see the supplementary materials at http://www.rcjournal.com).

Immediately after application of the MRC scale, the same examiner asked the subjects to perform dynamometry of the dominant hand (E.clear dynamometer EH101, Camry, Hong Kong, China) 3 times, with a 1-min interval between each measurement, and the maximum value of the 3 measurements was used. Subjects were positioned with the headboard high, the shoulder in neutral rotation, and the elbow at 90° whenever possible,[13] and the test instructions were standardized.[12]

ICUAW was defined as a score on the MRC scale < 48 points (see the supplementary materials at http://www.rcjournal.com).[2] The MRC scale served as the accepted standard in the discrimination tests. Because handgrip strength cutoff points to identify ICUAW (<11 kg/force for men and < 7 kg/force for women)[13] were validated in a single study,[19] we used sensitivity and specificity analyses to establish the handgrip strength thresholds for identifying ICUAW.

Outcomes

The main explanatory variable was diagnosis of ICUAW, and the secondary explanatory variable was handgrip strength. The primary outcomes were failure on the SBT and the duration of mechanical ventilation weaning. Secondary analyses were performed to define handgrip strength cutoff points indicative of ICUAW for men and women.

SBT failure was defined as the inability to maintain an acceptable respiratory pattern, gas exchange, hemodynamic stability and adequate comfort during the test: breathing frequency > 35 breaths/min; $S_{aO_2} < 90\%$; heart rate > 140 beats/min; systolic blood pressure > 180 mm Hg or < 90 mm Hg; uncontrollable psychomotor agitation; reduced level of consciousness; and excessive sweating and cyanosis.[16]

Weaning failure was defined as the need for re-intubation within 48 h related to cardiovascular dysfunction or inability of the respiratory pump to support the load of breathing (ie, $P_{aO_2} < 50$–60 mm Hg and $F_{IO_2} > 0.5$; $S_{aO_2} <$ 88–90%, and $F_{IO_2} > 0.5$; $P_{aCO_2} > 50$ mm Hg or increased by > 8 mm Hg; pH < 7.32 or reduced by > 0.07; breathing frequency > 35 breaths/min or increased by > 50%; heart rate > 140 beats/min or increased by > 20%; systolic blood pressure > 180 mm Hg or < 90 mm Hg; uncontrollable psychomotor agitation; reduced level of consciousness; excessive sweating and cyanosis; and evidence of increased respiratory muscle effort), in addition to upper airway involvement, including laryngospasm, abundant secretion, and ineffective cough (ie, revealing orotracheal tube dependence).[20]

Based on the total duration of weaning, as well as the number of SBT attempts required to disconnect the subject from the mechanical ventilation, weaning was categorized into 2 groups: simple versus difficult (ie, difficult or prolonged weaning).[20] Weaning was simple when the subject was successfully extubated after the first SBT. Difficult weaning was documented when the initial attempt failed and the subject was extubated after 2 SBTs up to 7 d after the first attempt. For prolonged weaning, the subject had failed at least 3 SBTs and needed > 7 d after the first SBT to be successfully weaned.[20]

Statistical Analysis

Based on data from previous studies dichotomized for simple versus difficult weaning on patients subjected to the SBT and local data suggesting a higher rate of difficult weaning after requiring mechanical ventilation for > 48 h, we estimated a difference between simple versus difficult weaning (36% vs 64%).[14,21] We estimated that ~ 102 subjects would be necessary to provide 80% power to detect a difference with a 2-tailed alpha level of 0.05. The sample size calculation was performed in WinPepi 11.43.

Normality was tested using the Kolmogorov-Smirnov test. Continuous data were described by the mean and standard deviation or the median and interquartile range and were compared with the Mann-Whitney test. Categorical variables were presented as a percentage and were compared with the chi-square test or Fisher exact test as appropriate. To identify factors associated with SBT failure and difficult or prolonged weaning, the significantly different variables among the subgroups were first analyzed using a univariate logistic regression model; the clinically relevant variables in literature and those with significant associations in the univariate analysis ($P < .10$) were then included in a multivariate logistic regression model. Multicollinearity was assessed comparing correlation between variables and with variance inflation factor in the model. The specificities and sensitivities of the MRC scale and handgrip strength were calculated, and the area under the receiver operating characteristic (ROC) curve and the best handgrip strength absolute threshold were determined using medCalc statistical software (https://www.medcalc.org). Other data were analyzed with SPSS 20.0 (IBM, Armonk, New York), and a 0.05 alpha level was adopted.

Results

Population

A total of 102 subjects were evaluated during the study period. The indications for initiating mechanical ventilation, type of SBT, and baseline characteristics of the subjects are presented in Table 1.

Table 1. Subject Characteristics

Age, y	58.0 ± 18.0
Sex, female	56 (55)
Body mass index, kg/m^2	26.6 ± 5.9
Dominant hand, right	88 (86)
Type of SBT	
T-tube	98
Pressure spontaneous ventilation	4
APACHE II	24.8 ± 8.7
Mechanical ventilation indication	
Pneumonia	27 (26)
Shock	18 (18)
ARDS	17 (17)
Postsurgical	15 (15)
Neurological	8 (8)
COPD	6 (6)
Other	11 (11)
COPD	22 (22)
Sepsis	69 (68)
Neuromuscular blocker	25 (24)
Daily caloric intake, kcal/kg/d*	22.8 ± 5.9
Mechanical ventilation duration before the first SBT, d	5 (2–8)
Mechanical ventilation duration, d	6 (3–10)
Length of ICU stay, d	1.5 (6–17)
ICU death	10 (10)
Handgrip strength on the first SBT, kg/force	5.9 (3.1–9.5)
MRC score on the first SBT	36 (30–42)
Muscle weakness according to handgrip strength†	70 (69)
Muscle weakness according to the MRC scale†	91 (89)

Data are presented as *n* (%), mean ± SD, or median (interquartile range).
* Mean values observed in 97 subjects; 5 subjects were not receiving a diet on the day of the first SBT.
† Muscle weakness was defined according to previous cutoff points for the MRC scale[2] and handgrip strength.[13]
SBT = spontaneous breathing trial
APACHE II = Acute Physiology and Chronic Health Disease Classification System II
MRC = Medical Research Council

Muscle Strength Assessment

The percentages of subjects diagnosed with ICUAW by the MRC scale and by handgrip strength in the first SBT are shown in Table 1. A strong correlation (r = 0.747, $P <$ .001) was found between the 2 tools. The accuracy of the handgrip strength thresholds in the diagnosis of ICUAW was compared with the MRC scale score (< 48 of 60 points) (Fig. 1). The handgrip strength presented good diagnostic performance. Using the previously published cutoff points (ie, < 11 kg/force for men and < 7 kg/force for women),[13] the overall sensitivity was 77%, the specificity was 100%, the positive predictive value was 100%, and the negative predictive value was 34%. Based on the cutoff points proposed in the present study (ie, < 14 kg/force for men and < 8 kg/force for women), the overall sensitivity was 87%, the specificity was 100%, the positive predictive value was 100%, and the negative predictive value was 48%.

Risk Factors for SBT Failure

The failure rate for the first SBT was 29% (30 subjects). The reasons for failure were use of accessory muscles in 17 (56.7%) subjects, desaturation in 6 (20%), tachypnea and tachycardia in 4 (13.3%) and inadequate sensory (ie, reduction in Glasgow Coma Scale) in 3 (10%). The duration of mechanical ventilation, length of ICU stay, MRC score, and ICUAW rate differed significantly between the SBT failure and success groups (Table 2).

In the univariate analysis, handgrip strength (odds ratio [OR] 0.88, 95% CI 0.78–0.96, $P <$ .001) and MRC score (OR 0.92, 95% CI 0.87–0.96, $P <$ .001) were significantly associated with SBT failure. After a collinearity analysis, only MRC score was included in the multivariate models, and it was significantly associated with SBT failure (OR 0.91, 95% CI 0.88–0.97, $P <$ .001) (Table 3).

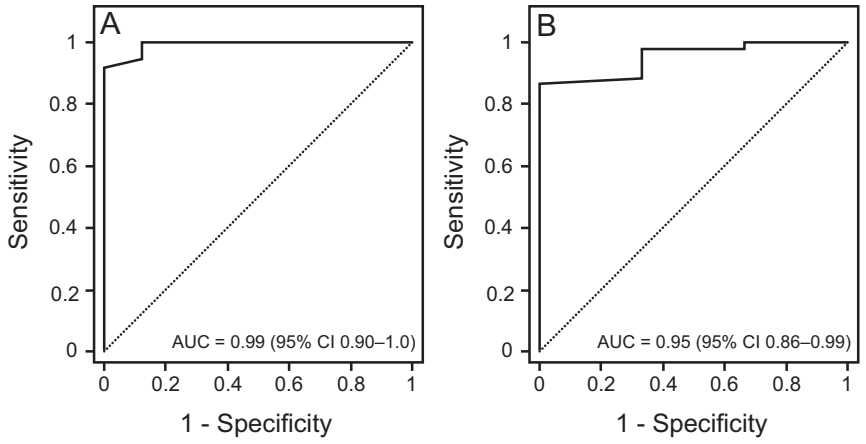
When the accuracy of ICUAW diagnosis by the MRC scale in predicting SBT failure was analyzed, the ROC curve was 0.57, the sensitivity was 100%, the specificity was 15%, the positive predictive value was 33%, and the negative predictive value was 100%. Diagnosis of ICUAW by handgrip strength using the cutoff points (ie, < 11 kg/force for men and < 7 kg/force for women) as defined by Ali et al[13] presented a ROC curve of 0.60, a sensitivity of 83%, a specificity of 38%, a positive predictive value of 36%, and a negative predictive value of 84% for predicting failure on the SBT.

Diagnosis of ICUAW by handgrip strength using the cutoff points proposed in our study (ie, < 14 kg/force for men and < 8 kg/force for women) presented a ROC curve of 0.61, a sensitivity of 93%, a specificity of 29%, a positive predictive value of 35%, and a negative predictive value of 91% for predicting failure on the SBT.

Risk Factors for Difficult or Prolonged Weaning

The incidences of simple and difficult weaning were 58% and 42%, respectively. The lengths of mechanical ventilation and ICU stay, handgrip strength, MRC score, sepsis rate, and mortality rate differed significantly among these groups (Table 4).

In the univariate analysis, a diagnosis of sepsis (OR 3.21, 95% CI 1.31–8.53, $P = .01$), mechanical ventilation duration (OR 1.16, 95% CI 1.05–1.31, $P <$ .001), handgrip strength (OR 0.86, 95% CI 0.77–0.94, $P <$ .001), and MRC score before the first SBT (OR 0.91, 95% CI 0.86–0.95, $P <$ .001) were significantly associated with difficult or prolonged weaning. After a collinearity analysis, only MRC score was included in the multivariate models, and it remained significantly associated (OR 0.91, 95% CI 0.87–0.96, $P <$ .001) with difficult or prolonged weaning (Table 3).



Sex	Criterion	Sensitivity	95% CI	Specificity	95% CI
Males	<1.5	0	0–0.93	1.0	0.63–1.0
	≤14.6	0.92	0.79–0.98	1.0	0.63–1.0
	≤16.5	0.95	0.82–0.99	0.88	0.47–0.99
	≤20.4	1.0	0.91–1.0	0.88	0.47–0.99
	≤46.7	1.0	0.91–1.0	0	0–0.37
Females	<0.8	0	0–0.67	1.0	0.23–1.0
	≤8.1	0.87	0.75–0.95	1.0	0.23–1.0
	≤8.9	0.89	0.77–0.96	0.67	0.94–0.99
	≤12.8	0.98	0.90–1.0	0.67	0.94–0.99
	≤17.4	0.98	0.90–1	0.33	0.01–0.91
	≤17.5	1.0	0.93–1	0.33	0.01–0.91
	≤20.5	1.0	0.93–1	0	0–0.71

Fig. 1. Accuracy of handgrip strength and cutoff points in determining ICU-acquired weakness (ICUAW). Males (A) and females (B) were analyzed separately. The table shows each individually plotted cutoff point. At ≤ 14.6 kg/force (males) and ≤ 8.1 kg/force (females), the sensitivities were 92% and 87%, respectively, with a specificity of 1.0 for both. A cutoff point of 14 kg/force for males and 8 kg/force for females would therefore result in high sensitivity and specificity for diagnosing ICUAW. AUC = area under the curve.

The accuracy of ICUAW diagnosis with the MRC scale in predicting difficult or prolonged weaning showed a ROC curve of 0.57, a sensitivity of 98%, a specificity of 17%, a positive predictive value of 46%, and a negative predictive value of 91%. Diagnosis of ICUAW according to handgrip strength using the cutoff points as defined by Ali et al[13] (ie, < 11 kg/force for men and < 7 kg/force for women) showed a ROC curve of 0.61, a sensitivity of 81%, a specificity of 41%, a positive predictive value of 50%, and a negative predictive value of 75% for predicting difficult or prolonged weaning.

Diagnosis of ICUAW according to handgrip strength using the cutoff points proposed in our study (ie, < 14 kg/force for men and < 8 kg/force for women) resulted in a ROC curve of 0.63, a sensitivity of 93%, a specificity of 34%, a positive predictive value of 51%, and a negative predictive value of 87% for predicting difficult or prolonged weaning.

Weaning failure occurred in 18 (17.6%) subjects. Of these subjects, 15 used noninvasive ventilation as a rescue therapy during the first 48 h after extubation and all require re-intubation. Thirty-eight subjects (37%) who used preventive noninvasive ventilation just after extubation (high estimated risk of failure) were successfully weaned. Tracheostomy was performed in 2 subjects. The reasons for re-intubation were inability to maintain patent airways ($n = 7$), laryngeal edema ($n = 3$), aspiration ($n = 2$), cardiogenic pulmonary edema ($n = 2$), and other causes of acute respiratory failure ($n = 4$).

Table 2. Subject Characteristics According to the Results of the First SBT

Characteristics	Failure ($n = 30$)	Success ($n = 72$)	P‡
Age, y	55.2 ± 18.8	59.2 ± 17.8	.27
Sex, female	19 (63)	37 (51)	.26
Body mass index, kg/m^2	26.7 ± 5.7	26.5 ± 6.1	.78
APACHE II	25.6 ± 9.2	24.4 ± 8.6	.55
COPD, *n* (%)	5 (17)	17 (24)	.43
Sepsis	23 (77)	46 (64)	.20
Neuromuscular blocker	9 (30)	16 (22)	.40
Caloric intake, kcal/kg/d*	23.3 ± 4.5	22.6 ± 6.5	.52
Mechanical ventilation duration before first SBT, d	6 (3–9)	4 (2–7.7)	.09
Mechanical ventilation duration, d	7.5 (5–12)	5 (2–9.7)	< .001
Length of ICU stay, d	12 (7.7–19.5)	9 (5–15.7)	.042
ICU death	4 (13)	6 (8)	.43
Handgrip strength on the first SBT, kg/force	4.9 (2.9–7.2)	6.9 (3.2–12.6)	.060
MRC score on first SBT	30 (26.7–36.5)	40 (32.2–45.5)	< .001
Muscle weakness according to handgrip strength†	25 (83)	45 (62)	.039
Muscle weakness according to MRC scale†	30 (100)	61 (85)	.02
Weaning failure	2 (7)	16 (22)	.02
Preventive noninvasive ventilation	13 (43)	25 (35)	.32

Data are presented as *n* (%), mean ± SD, or median (interquartile range).
* Mean values observed in 97 subjects; 5 subjects were not receiving a diet on the day of the first SBT.
† Muscle weakness was defined according to previous cutoff points for the MRC scale[2] and handgrip strength.[13]
‡ Comparison of the 2 subgroups with the Mann-Whitney test or Fisher exact test.
SBT = spontaneous breathing trial
APACHE II = Acute Physiology and Chronic Health Disease Classification System II
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Table 3. Factors Associated With Spontaneous Breathing Trial Failure and Difficult or Prolonged Weaning

Variables	Univariate Analysis		Multivariate Analysis	
	Odds Ratio (95% CI)	*P*	Odds Ratio (95% CI)	*P*
Spontaneous breathing trial failure				
Mechanical ventilation duration before first SBT	1.08 (0.99–1.20)	.07	NA	NA
Handgrip strength on first SBT	0.88 (0.78–0.96)	< .001	NA	NA
MRC score on first SBT	0.92 (0.87–0.96)	< .001	0.91 (0.88–0.97)	< .001
Difficult or prolonged weaning				
Sepsis	3.21 (1.31–8.53)	.01	2.59 (0.96–7.04)	.060
Mechanical ventilation duration before first SBT	1.16 (1.05–1.31)	< .001	NA	NA
Handgrip strength on first SBT	0.86 (0.77–0.94)	< .001	NA	NA
MRC score on first SBT	0.91 (0.86–0.95)	< .001	0.91 (0.87–0.96)	< .001

SBT = spontaneous breathing trial
NA = not applicable
MRC = Medical Research Council

Discussion

The main finding of our study is that muscle weakness as defined by a low MRC score and poor handgrip strength before starting the SBT was associated with failure on the first SBT and difficult or prolonged weaning, as defined in this study. However, only the MRC score was independently associated with both mechanical ventilation-related outcomes.

Predicting both situations is important for the decision-making process of professionals involved in mechanical ventilation weaning because these outcomes are considered distinct in clinical practice. The SBT assesses tolerance of spontaneous breathing and is recommended before extubation.[20,22] Complete performance of the test (30–120 min) can predict 85% of the odds of successful weaning from mechanical ventilation[23]; however, approximately 15% of subjects do not

Table 4. Subject Characteristics According to Ventilatory Weaning

Characteristics	Simple ($n = 59$)	Difficult ($n = 43$)	P‡
Age, y	60.8 ± 16.3	54.4 ± 19.8	.13
Sex, female	31 (52)	25 (58)	.57
Body mass index, kg/m^2	26.8 ± 6.3	26.2 ± 5.5	.76
APACHE II	23.3 ± 8.5	26.7 ± 8.7	.059
COPD	15 (25)	7 (16)	.26
Sepsis	34 (58)	35 (81)	.01
Neuromuscular blocker	12 (20)	13 (30)	.25
Daily caloric intake, kcal/kg/d*	22.5 ± 6.7	23.2 ± 4.9	.37
Mechanical ventilation duration before first SBT, d	3 (2–6)	7 (3–10)	< .001
Mechanical ventilation duration, d	3 (2–6)	10 (7–15)	< .001
Length of ICU stay, d	8 (5–12)	14 (9–21)	< .001
ICU death	1 (2)	9 (21)	< .001
Handgrip strength on first SBT, kg/force	7.4 (3.5–14.6)	4.9 (2.6–7.2)	< .001
MRC score on the first SBT	40 (34–47)	30 (27–38)	< .001
Noninvasive ventilation 48 h after extubation	28 (47)	25 (58)	.28
Muscle weakness according to handgrip strength†	35 (59)	35 (81)	.01
Muscle weakness according to MRC scale†	49 (83)	42 (98)	.01
Weaning failure	0 (0)	18 (42)	.01
Preventive noninvasive ventilation	28 (47)	10 (23)	.12

Data are presented as *n* (%), mean ± SD, or median (interquartile range).
* Mean values observed in 97 subjects; 5 subjects were not receiving a diet on the day of the first SBT.
† Muscle weakness was defined according to previous cutoff points for the MRC scale[2] and handgrip strength.[13]
‡ Comparison of the 2 subgroups with the Mann-Whitney test or Fisher exact test.
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tolerate spontaneous ventilation during the 48 h following extubation[24] and require re-intubation, thus becoming subjects with difficult or prolonged weaning. In this sense, our data support the concern that the use of predictive indexes for mechanical ventilation weaning can identify only those subjects who may fail or successfully complete the SBT[25] but not those who will be unable to tolerate spontaneous breathing during the 48 h after extubation. Furthermore, predicting successful SBT and weaning is important for the decision-making process to start early mobilization as the prevalence of such strategy is low,[26] despite evidence supporting the safety, feasibility, and benefits of mobilization in mechanically ventilated patients.[27]

Application of the MRC scale requires training, and up to 30 min may be required to test the 6 muscle groups bilaterally. In addition, the MRC scale has a subjective component, particularly for categories 4 and 5, in terms of resistance according to the Oxford classification system,[18,28] which may introduce some variability into the measurement. Two studies comparing the MRC scale and handgrip strength suggest that handgrip strength measurement may serve as an alternative to identify ICUAW,[13,19] as evidenced in our study.

The comparison of handgrip strength and MRC has shown different results in several studies. Ali et al[13] reported that handgrip strength had lower predictive power compared to the MRC scale as a predictor of morbidity and mortality associated with ICUAW in mechanically ventilated subjects. However, both tests presented similar sensitivities and specificities, and the authors proposed that a manual dynamometer should be used to screen for ICUAW because of the ease of application for any professional working in the ICU. In a study in which handgrip strength was used in the context of mechanical ventilation weaning, handgrip strength was independently but weakly associated with difficult and prolonged weaning; however, the greatest limitation of the study was the lack of comparison with the MRC scale, as this scale is considered the standard method for evaluating ICUAW.[14] Our findings support previous studies reporting that ICUAW diagnosis with the MRC scale and handgrip strength before the SBT is associated with difficulty in definitive withdrawal from ventilatory support.[6,9,13,14] Although both tools presented moderate discriminatory power, as previously shown,[14] our data indicate that handgrip strength is not independently associated with failure on the SBT and difficult or prolonged weaning. Handgrip strength ICUAW sensitivity, specificity, and predictive values were similar to those with the MRC scale. The ease of measuring handgrip strength suggests that this test may be useful as a first step to predict failure on the SBT and difficult or prolonged weaning, followed by the MRC scale in select cases. Such an approach was also proposed by Parry et al[19] for diagnosing ICUAW.

Since the publication by Ali et al,[13] the same handgrip strength threshold for identifying ICUAW has been used in studies that implemented this tool as a form of ICUAW detection. For handgrip strength, our cutoff points demonstrated sensitivity, specificity, and predictive values higher than those reported by Ali et al,[13] indicating that although the established cutoff points have been validated in an independent sample,[19] these values may not accurately describe ICUAW in different populations of critically ill patients. The handgrip strength cutoff points indicating ICUAW in our study require validation in different populations.

The rate of ICUAW in our study was higher than that reported by Cottereau et al[14] (31%) and Parry et al[19] (42%) based on handgrip strength, and that reported by Ali et al[13] (26%) and De Jonghe et al[9] (25%) based on the MRC scale. Considering that muscle weakness develops early, the rates of ICUAW reported by Ali et al[13] and De Jonghe et al[9] should be higher because previous studies examined subjects starting on the fifth and seventh day of ventilation, respectively. The rates of ICUAW vary mainly according to the characteristics of the subjects evaluated; however, the profile of the subjects included in our study was similar to other studies.[9,13,14] In our study, ICUAW was associated with a greater severity of critical illness per APACHE II, longer duration of mechanical ventilation, longer ICU stay, and higher sepsis rate, which is consistent with previous studies.[13,14]

Our study also indicates that the presence of sepsis was a factor associated with difficult or prolonged weaning, although it was not independently associated with this outcome. Weakness and muscle loss are common complications that may be more severe in patients with sepsis.[29-31] Such complications may occur asymmetrically in these subjects and may be more noticeable in the peripheral muscles than in the diaphragm.[31]

Our study has some limitations. First, the ICU teams did not prescribe noninvasive ventilation to allow earlier extubation in selected subjects who did not successfully complete the SBT, but to prevent weaning failure in high-risk subjects or to rescue a failed weaning after a successful SBT. Interestingly, when noninvasive ventilation was indicated to prevent weaning failure immediately after extubation because of the high estimated risk of failure, including ICUAW as a risk, all subjects succeeded ($n = 38$ subjects). On the contrary, whenever noninvasive ventilation was used as a rescue support during the 48 h period, all subjects were re-intubated ($n = 15$ subjects). This could have played a role in our results. Although noninvasive ventilation is becoming more and more effective in the postextubation period,[32,33] its use as a rescue therapy is discouraged and re-intubation should not be delayed if noninvasive ventilation is not immediately successful.[33,34]

Second, we did not implement a standardized weaning protocol and criteria for SBT failure, but 98 (96%) subjects were submitted to a T-tube. Third, in observational studies it is impossible to rule out external causal effects and to isolate the true independent variable, making it tricky to identify cause-and-effect relationships. Fourth, although ICUAW and diaphragmatic dysfunction show some overlap, the correlation is limited and we did not measure diaphragm strength.[3,35,36] The GRIPWEAN trial (ClinicalTrials.gov registration NCT02946502) is exploring the association between grip strength, diaphragmatic tests, and mechanical ventilation weaning. Fifth, our study was underpowered to detect an association between COPD with difficult or prolonged weaning. Sixth, although the MRC score and handgrip strength before starting the SBT is associated with SBT failure and difficult or prolonged weaning, the odds ratio for these factors is so close to 1 as to render these not useful clinically. Lastly, the definition of ICUAW was based on the study of De Jonghe et al,[2] who evaluated subjects starting on the seventh day of mechanical ventilation, whereas we studied subjects starting on the second day of mechanical ventilation.

Conclusions

Our findings indicate that muscle weakness as defined by a low MRC score before the first SBT is an independent prognostic factor for SBT failure and difficult or prolonged weaning. Although handgrip strength may serve as an alternative tool for diagnosing ICUAW, due to the ease of application, more studies are needed to evaluate handgrip strength as a first step to predict SBT failure and difficult or prolonged weaning in routine clinical practice. Finally, further studies are needed to confirm these findings and to determine the validity of the cutoff points identified for handgrip strength and the roles of handgrip strength and the MRC scale in predicting difficulty to wean from mechanical ventilation.

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