Use of handgrip dynamometry for diagnosis and prognosis assessment of intensive care unit acquired weakness: A prospective study

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ABSTRACT

Objectives: To test the agreement between handgrip dynamometry and Medical Research Council (MRC) criteria for the diagnosis of intensive care unit acquired weakness (ICUAW) and to evaluate if dynamometry findings are associated with morbidity and mortality.
Methods: A prospective single center cohort study was conducted in a Brazilian ICU. Adults requiring at least 5 days of critical care were included. Primary outcome was the agreement between ICUAW diagnosis as assessed by the MRC score and the handgrip strength dynamometry. Exploratory outcomes were in-ICU, in-hospital, 6-month and one-year mortality, days of mechanical ventilation, length of ICU and hospital stay (in the present hospitalization and during the 6-month follow-up) and ICU readmission in six months.
Results: We included 45 consecutive subjects, of which 18 of them had ICUAW according to MRC criteria. Using sex specific thresholds, handgrip strength had high agreement with MRC criteria for ICUAW diagnosis (100% accuracy; Kappa coefficient = 1; $p < 0,001$). ICUAW was associated with more days of mechanical ventilation, longer length of ICU stay and hospital stay in six months. There were no differences regarding mortality.
Conclusions: Handgrip dynamometry may provide a simple and accurate alternative to the MRC examination for the diagnosis of ICUAW. ICUAW is associated with longer ICU and hospital stay and more requirement of mechanical ventilation.

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Introduction

Intensive care unit acquired weakness (ICUAW) is an important and common problem among individuals that survive the initial insult of a critical illness.[1,2] ICUAW prevalence is rising most likely due to increasing numbers of subjects that had multiple organ dysfunctions and survived.[2]

Various terms have been used to describe the weakness that develops after recovery from a critical illness. In 2009, Stevens et al proposed a simple definition and classification for this condition. The term ICUAW designates clinically detected weakness in critically ill patients in whom there is no plausible etiology other than critical illness. Patients with ICUAW and documented polyneuropathy and/or myopathy are classified in one of three subcategories, as following, critical illness polyneuropathy (CIP), critical illness myopathy (CIM) and critical illness neuromyopathy (CINM), which is reserved for patients who have electrophysiological and/or histologic findings of coexisting CIP and CIM.[3]

Sepsis, hyperglycemia and multiorgan system failure seem to be the most important risk factors for ICUAW development.[1,2,4,5] Corticosteroid use, neuromuscular blocking agents and aminoglycosides have also been considered risk factors.[1,6] There is no specific treatment for ICUAW, and early mobilization is the most important strategy for ICUAW prevention.[1,7] ICUAW is associated with high morbidity and mortality.[1,8] Subjects diagnosed with ICUAW usually have longer ICU and hospital stays when compared to individuals with normal strength. Delayed weaning from mechanical ventilation is also a problem for patients with ICUAW.[9−11] Two ongoing trials are currently testing specific physical therapy protocols for ICUAW prevention and treatment.[12,13]

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Strength assessment using the six-point Medical Research Council (MRC) score is the recommended method for diagnosing ICUAW. A MRC sum score of less than 48 for 12 muscle groups (or a mean MRC of less than 4 per muscle group) is used as the cutoff for defining ICUAW.[1,3,14] However, performing MRC score assessments in ICU patients is time consuming and requires adequate training. Handgrip strength dynamometry has been proposed as a simple and easy diagnostic method for ICUAW.[11,15] Moreover, handgrip strength seems to predict the outcome of intensive care patients regardless of ICUAW diagnosis.[11]

In this context, we performed a single center study to test the agreement between handgrip dynamometry and MRC criteria for the diagnosis of ICUAW and to evaluate if dynamometry findings are associated with morbidity and mortality in critically ill patients hospitalized in a Brazilian ICU. Moreover, we tested the baseline characteristics associated with development of ICUAW.

Material and methods

We conducted a prospective single center cohort study from November 2016 through June 2017 at a mixed medical and surgical ICU in Brazil.[16,17] The study was approved by the Institutional Ethics Review Board. Written informed consent was obtained from all participants.

Adult patients (18 years or older) requiring at least 5 days of critical care were eligible for screening, being thereafter assessed daily for awakening. When subjects were found to be both awake and calm (Richmond Agitation Sedation Scale [RASS] -1 to +1)[18] they were enrolled in the study. Exclusion criteria included patients with previous diagnoses of diseases marked by regional or generalized weakness (e.g., myasthenia gravis, myopathies, muscular dystrophies), previous stroke with known motor deficits, neurosurgery at admission, patients unable to follow commands or to consent to be enrolled (e.g., delirium or dementia) during the ICU stay.

We collected baseline data on the day of initial screening including demographics (age and sex), comorbidities (diabetes mellitus, hypertension, liver cirrhosis, solid cancer, hematologic neoplasm, heart failure and chronic obstructive pulmonary disease), outpatient medication use (statins and corticosteroids), severity of illness (Simplified Acute Physiology Score [SAPS] 3),[19,20] presence of organ failure (Stage 3 acute kidney injury and Sequential Organ Failure Assessment [SOFA]),[21,22] routine laboratory results (complete blood count, urea, C-reactive protein, creatinine, creatine kinase, albumin, bilirubin, glucose and lactate), history of sepsis during current hospital stay and sepsis at ICU admission. We assessed reasons for ICU admission through the review of medical charts.

On the enrollment day, we collected retrospective data since ICU admission regarding mechanical ventilation support, hyperglycemia and clinical treatments (including any use of neuromuscular blocking agents, fentanyl, midazolam and corticosteroids). We also collected the same data prospectively until ICUAW diagnosis or ICU discharge.

Study procedures

After enrollment, subjects were clinically assessed by the same physician using the standard muscle strength examination (Medical Research Council Scale).[23] Twelve muscle groups in the upper (wrist extension, elbow flexion, and shoulder abduction) and lower extremities (dorsiflexion of the foot, knee extension, hip flexion) were tested in all patients.

Immediately after the MRC exam, the examiner asked the subjects to perform dominant hand dynamometry (Jamar Handgrip Dynamometer; Sammons Preston Rolyan, Bolingbrook, IL) three consecutive times. The instructions during testing were similar to that previously described in the ICU literature.[11,14] Subjects were positioned as close to sitting upright with elbows at 90°as possible. The total MRC score and the maximum handgrip result were registered.

ICUAW was defined as an MRC score of less than 48.[3] The cutoff values used to identify ICUAW using handgrip dynamometer were a force value of less than 11 kg-force for males and less than 7 kg-force for females, as previously suggested by Ali et al.[11]

Patients who did not meet MRC-based diagnostic criteria for ICUAW were submitted to strength assessment using MRC criteria and hand dynamometry every 72−96 h until ICUAW diagnosis or ICU discharge. This interval was arbitrarily defined based on logistic issues and on clinical plausibility.

Statistical analysis

The normality test of Kolmogorov-Smirnov was used to evaluate the distribution of the continuous variables. Data obtained from continuous variables are expressed as either mean and standard deviation, if they have normal distribution, or median and interquartile range (25th and 75th percentiles) if they have non-normal distribution. Data concerning categorical variables are expressed as absolute numbers and proportions. Clinical characteristics of patients with and without ICUAW diagnosis were compared using Student *t* test, Mann−Whitney test, chi-squared and exact Fisher test according to the type and the distribution of the variable.

The agreement between ICUAW diagnosis as assessed by the MRC score and the handgrip strength dynamometry was evaluated using the Cohen's Kappa coefficient. Finally, survival curves showing the length of ICU and hospital stay of patients with and without ICUAW were compared using the Log-Rank test, and a time dependent proportional hazards model was proposed in case of need of adjusting for confounding variables to explain this outcome.

A two-level *P* value <0.05 was considered as significant for all analyses. All the statistical analyses were conducted in SPSS version 23 (SPSS Inc., Chicago, IL, USA).

Sample size

Based on Ali et al's[11] report of a Spearman's correlation coefficient of 0.9 between MRC score and dynamometry strength assessment, we expected a Spearman correlation coefficient of 0.7 in our study. In order to provide 90% power with a two-sided level of 0.05, we estimated that 34 examined subjects would be necessary to detect this correlation coefficient. Based on preliminary data, we expected an ICUAW prevalence of 50% in our population of critically ill patients. Accordingly, we planned to enroll 45 subjects.

Follow-up and outcomes

Subjects were followed for one year after enrollment. The primary outcome was the agreement between handgrip dynamometry and MRC criteria for the diagnosis of ICUAW.

Exploratory outcomes were in-ICU, in-hospital, 6-month and one-year mortality, days of mechanical ventilation (in the ICU and in 6 months), length of ICU and hospital stay (in the present hospitalization and during the 6-month follow-up) and ICU readmission in six months.

Results

One-hundred and two subjects were assessed for eligibility and 45 (44%) were included and examined for muscle strength (Fig. 1). Included and excluded subjects had similar age (55.3 [±16.3] versus 54.9 [±16.7], *P* = 0.9), sex (male sex 60% versus 40%, *P* = 0.07) and median SAPS 3 score (69 [59.5−73] versus 65 [50−79], *P* = 0.27).

The main characteristics of the included patients are shown in Table 1. There were no major differences in the demographics, comorbidities, previous outpatient medication use and organ failure (stage 3 acute kidney injury and Sequential Organ Failure Assessment
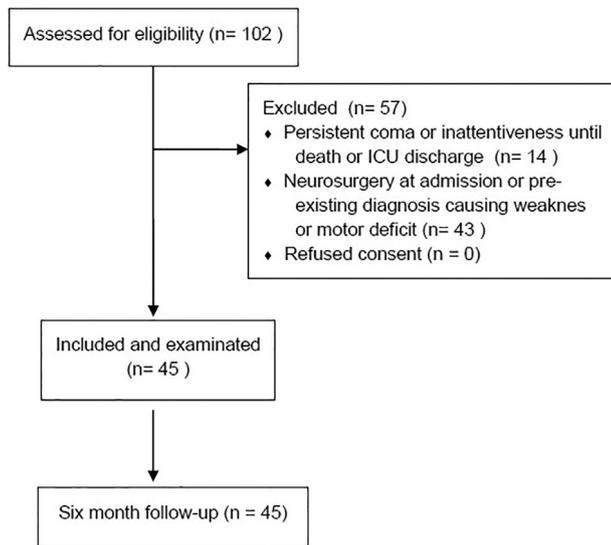
Fig. 1. Consort enrollment diagram.

Table 1
Cohort characteristics

Characteristic	Total	ICUAW	No ICUAW	P value
Subjects, %	45	18 (40%)	27 (60%)	
Age, mean ± SD	55,3 (±16.3)	55.6 (±15.9)	55.1 (±16.9)	0.91
Sex, % male	60 %	61.1 %	59.2 %	0.9
SAPS 3, median (IQR)	69 (59.5−79)	71.5 (65.7−84)	65 (54−77)	0.034
SOFA, median (IQR)	4 (2−8)	4.5 (2.75−8.25)	4 (2−8)	0.6
Stage 3 acute kidney injury, %	26.7	33.3	22.2	0.49
Lactate, mmol/L, median (IQR)	1.5 (1.1−2.2)	1.5 (1.2−2.3)	1.5 (1.1−1.2)	0.95
Sepsis at ICU admission, %	40	40.7	38.9	1
Previous sepsis within the same hospitalization, %	40	61.1	25.9	0.03
Comorbidity, %				
Diabetes mellitus, %	17.8	16.7	18.5	1.0
Hypertension, %	28.9	22.2	33.3	0.51
Liver cirrhosis, %	15.9	16.7	15.4	1.0
Hematological neoplasia, %	13.3	22.2	7.4	0.19
Solid cancer, %	24.4	27.8	24.4	0.73
Heart failure, %	22.2	16.7	25.9	0.71
COPD, %	6.7	11.1	3.7	0.55
Previous outpatient medication use, %				
Statins, %	15.6	5.6	22.2	0.21
Corticosteroids, %	11.1	22.2	3.7	0.14
ICU interventions				
Vasopressor, days median (IQR)	3 (1.5−6)	5 (1.75−8)	3 (1−5)	0.13
Fentanyl, days median (IQR)	3 (0−7)	5 (3−13.5)	1 (0−5)	0.002
Midazolam, days median (IQR)	2 (0−4.5)	3 (2−7.25)	0 (0−2)	0.004
Corticosteroid, days median (IQR)	6 (0−9.5)	5 (0−12)	6 (0−9)	0.75
Neuromuscular blocker, days median (IQR)	0 (0−0)	0 (0−0)	0 (0−0.5)	0.12

Definition of abbreviations: ICUAW = intensive care unit acquired weakness; COPD = chronic obstructive pulmonary disease; SOFA = Sequential Organ Failure Assessment; SAPS = Simplified Acute Physiology Score; IQR = interquartile range. Descriptive characteristics are displayed for the entire cohort and by the presence or absence of global weakness as defined by the Medical Research Council exam (ICUAW). All comparisons were performed with the chi-square or Student's *t* test as appropriate. *P* values reflect the significance of observed differences in values from ICUAW and no ICUAW patient groups.

[SOFA]) of subjects with or without a diagnosis of ICUAW. Conversely, severity of current illness as assessed by SAPS 3 score was significantly higher in the group with ICUAW. Subjects with ICUAW were also exposed to more days of fentanyl and midazolam. Corticosteroid and neuromuscular blocker use was similar between groups. There was no significant difference in the rates of sepsis at ICU admission between groups, but history of sepsis in the current hospitalization was more common among subjects with ICUAW. Finally, there were no relevant differences regarding routine laboratory data at baseline or episodes of hyperglycemia during ICU stay between groups (Table 2).

All patients were able to have all 12 muscle groups examined, and 18 subjects (40%) were diagnosed with ICUAW as assessed by MRC criteria. In these subjects with ICUAW, the maximum handgrip dynamometry was significantly lower than in those without this diagnosis [4 (±3) kg-force vs. 21.6 (±7.3) kg-force, p < 0.001].

Using sex specific thresholds (males, <11 kg-force; females, <7 kg-force), handgrip strength had perfect performance (100% accuracy; Kappa coefficient =1; p < 0,001) when compared to MRC criteria for the diagnosis of ICUAW.

Mortality rates in both groups, ICUAW and no ICUAW, were similar, considering the follow-up in the ICU, hospital, at 6-month and one-year.

Subjects with ICUAW assessed either by MRC examination or handgrip dynamometry had more days of mechanical ventilation during the first ICU stay and longer length of ICU stay. This difference persisted in the following six months, period in which the number of in-hospital days was also higher among the group with ICUAW when compared to the group without this diagnosis (Tables 3 and 4). Considering the whole sample of patients, 26,7% of subjects were readmitted to the ICU and 22% were intubated during the six-month follow-up period. There was no difference between groups regarding ICU readmission or intubation rates. The curves for ICU stay and mechanical ventilation comparing patients with and without diagnosis of ICUAW are presented in the Fig. 2 (P = 0.001).

Discussion

In this study, we found that 40% of the evaluated patients had ICUAW, and they required more days of mechanical ventilation support and had longer length of ICU stay during index hospitalization, as compared with those without ICUAW. We also showed that handgrip dynamometry had excellent test performance to detect ICUAW when compared to MRC examination. To the best of our knowledge, this is the first study testing the usefulness of handgrip dynamometry to diagnose ICUAW in a Latin American population.

ICUAW incidence ranges from 25% to more than 60% according to the different inclusion criteria of the studies.[1] In our study, ICUAW was diagnosed in 40% of the included subjects.

Sepsis is a recognized risk factor for developing ICUAW.[2,24] Mitochondrial dysfunction and increased microvascular permeability in the endoneurium caused by sepsis may contribute to the development of ICUAW.[1,25] In accordance with that, ICUAW was more common in patients that had a previous episode of sepsis within the same hospitalization in our study.

Midazolam and fentanyl use may be associated with an increased risk of critical illness myopathy development.[26] Subjects that had ICUAW diagnosis in our study were exposed to more days of fentanyl and midazolam. It is possible that the use of these drugs is associated with an increased risk of ICUAW, but this conclusion might be imprecise since this finding may only reflect that these patients had more days of mechanical ventilation.

Our findings that patients with ICUAW as assessed by MRC exam or handgrip dynamometry required more days of mechanical

Table 2
Routine laboratory results

Characteristic	Total	ICUAW	No ICUAW	*P* value
Hemoglobin g/dL, mean±SD	8.3 (±1.5)	7.5 (±1)	8.8 (±1.65)	0.004
Absolute neutrophil count/microL, mean±SD	13,300 (±12,359)	15,867 (±16,252)	11,589 (±8842)	0.31
Platelets /microL, mean±SD	202,115 (±146,117)	244,722 (±168,795)	173,777 (±124,142)	0.13
Hyperglycemia during ICU stay, %	20	33.3	11.1	0.12
C-reactive protein mg/dL, median (IQR)	76 (53−198)	76 (55−185)	151 (40−206)	0.86
Urea mg/dL, mean±SD	67 (±36)	64 (±32)	69 (±38)	0.70
Creatinine, mg/dL, median (IQR)	0.7 (0.5−1.7)	0.6 (0.4−2.3)	0.8 (0.6−1.3)	0.12
Creatine kinase U/L, median (IQR)	42.5(0−111)	28 (0−51)	57.5 (17−122)	0.08
Morning blood glucose, mg/dL, mean±SD	145 (±54)	146 (±60)	145 (±50)	0.97
Total Bilirubin mg/dL, median (IQR)	0.88 (0.6−2.3)	0.86 (0.58−1.63)	0.88 (0.6−2.6)	0.73
Albumin g/dL, mean±SD	2.2 (±0.46)	2 (±0.4)	2.3 (±0.47)	0.06

Definition of abbreviations: ICUAW = intensive care unit acquired weakness; IQR = interquartile range. Hyperglycemia during ICU stay was defined as one episode of capillary blood glucose above 300 mg/dL or two episodes between 220 and 300 mg/dL in one day. Descriptive characteristics are displayed for the entire cohort and by the presence or absence of global weakness as defined by the Medical Research Council exam (ICUAW). All comparisons were performed with the chi-square or Student's *t* test as appropriate. *P* values reflect the significance of observed differences in values from ICUAW and no ICUAW patient groups.

Table 3
Short term clinical outcomes in pacients with (ICUAW) and without (NO-ICUAW) ICU acquired weakness

Characteristic	Total	ICUAW	No ICUAW	*P* value
Subjects, %	45	18 (40%)	27 (60%)	
Mechanical ventilation during index ICU stay, days median (IQR)	5 (0.2−9)	9 (6.5−20)	2 (0−5)	<0.001
Length of ICU stay during index ICU stay, days median (IQR)	10 (8−16)	15 (10.5−31.5)	9 (6−13)	<0.001
Length of hospital stay during index hospitalization, days median (IQR)	39 (19.5−77.5)	59.5 (31.2−94)	35 (16−61)	0.05
Hospital mortality, *n* (%)	12 (26.7)	6 (33.3)	6 (22.2)	0.49

Definition of abbreviations: ICUAW = intensive care unit acquired weakness; IQR = interquartile range. Descriptive characteristics are displayed for the entire cohort and by the presence or absence of global weakness as defined by the Medical Research Council exam (ICUAW). All comparisons were performed by use of the chi-square or Student's *t* test as appropriate. *P* values reflect the significance of observed differences in values from ICUAW and no ICUAW patient groups.

Table 4
Long term clinical outcomes in pacients with (ICUAW) and without (NO-ICUAW) ICU acquired weakness

Characteristic	Total	ICUAW	No ICUAW	*P* value
Subjects, %	45	18 (40%)	27 (60%)	
ICU readmission in 6 months, %	26.7	27.8	25.9	1
Six-month mortality, *n* (%)	13 (28.9)	7 (38.9)	6 (22.2)	0.31
ICU stay in 6 months, days median (IQR)	14 (9−22.5)	18.5 (11−40)	10 (8−16)	0.004
Mechanical ventilation in 6 months, days median (IQR)	7 (2.5−14)	13.5 (7−31.7)	4 (0−8)	<0.001
Length of hospital stay in 6 months, days median (IQR)	49 (27−82)	68 (36.5−99.5)	37 (21−63)	0.029
One-year mortality, *n* (%)	14 (31.1)	7 (38.9)	7 (25.9)	0.5

Definition of abbreviations: ICUAW = intensive care unit acquired weakness; IQR = interquartile range. Descriptive characteristics are displayed for the entire cohort and by the presence or absence of global weakness as defined by the Medical Research Council exam (ICUAW). All comparisons were performed by use of the chi-square or Student's *t* test as appropriate. *P* values reflect the significance of observed differences in values from ICUAW and no ICUAW patient groups.

ventilation support and had longer length of ICU stay are in agreement with data previously published in the literature.[9,11,27] The longer need for mechanical ventilation and the longer ICU and hospital stay observed among patients with ICUAW extended to the following six months, suggesting that ICUAW is related to sustained morbidity as previously described by Wieske et al.[28] However, the difference between the two groups did not increase significantly in this period, contradicting our hypothesis that ICUAW could further impact on these outcomes during the follow-up of six months.

Previous studies have reported higher mortality rates for patients with ICUAW.[2,3,10,11,29] In our study, we did not find statistically significant increased mortality in subjects with ICUAW. This discrepancy might be partially explained by the small number of subjects included in our study. Additionally, the frequency of ICUAW in our cohort was lower than expected and the mortality rate of subjects without ICUAW was higher than expected.

Handgrip strength dynamometry had excellent performance when compared to MRC criteria for the diagnosis of ICUAW. This finding corroborates the use of handgrip strength dynamometry as a surrogate for MRC strength examination for ICUAW diagnosis. Ali and colleagues found the best cutoff scores for diagnosing ICUAW using handgrip dynamometry to be less than 11 kg-force for males and less than 7 kg-force for females.[11] Our results reinforce that these cutoffs are accurate. Parry et al proposed a two-tier approach to diagnosing ICUAW that first tests handgrip dynamometry with subsequent strength assessment using MRC strength testing if handgrip strength falls below these cutoff scores.[14] Considering that we did not have any false positive results using handgrip dynamometry this second step may not be necessary.

This is an important finding for clinical practice since handgrip strength dynamometry is easier and quicker to perform when compared to MRC examination and the use of this diagnostic tool may save time and increase ICUAW recognition. Moreover, these attractive characteristics make handgrip dynamometry a potential gold standard diagnostic tool in future studies on the management and outcome of ICUAW.

This study had some limitations that deserve commentary. We did not perform electrophysiological studies to classify patients with ICUAW into the three subcategories (CIM, CIP and CINM).[3] Although this classification is important it is unpractical due to costs and limited availability of electroneuromyography in the ICU. Due to the small number of patients included the association between handgrip strength results and mortality was investigated as exploratory analysis. Despite this limitation we were able to find important results regarding ventilator use and length of ICU and hospital stay. A strong point that should be remarked in our study is that we had no loss of follow-up in the one year period.
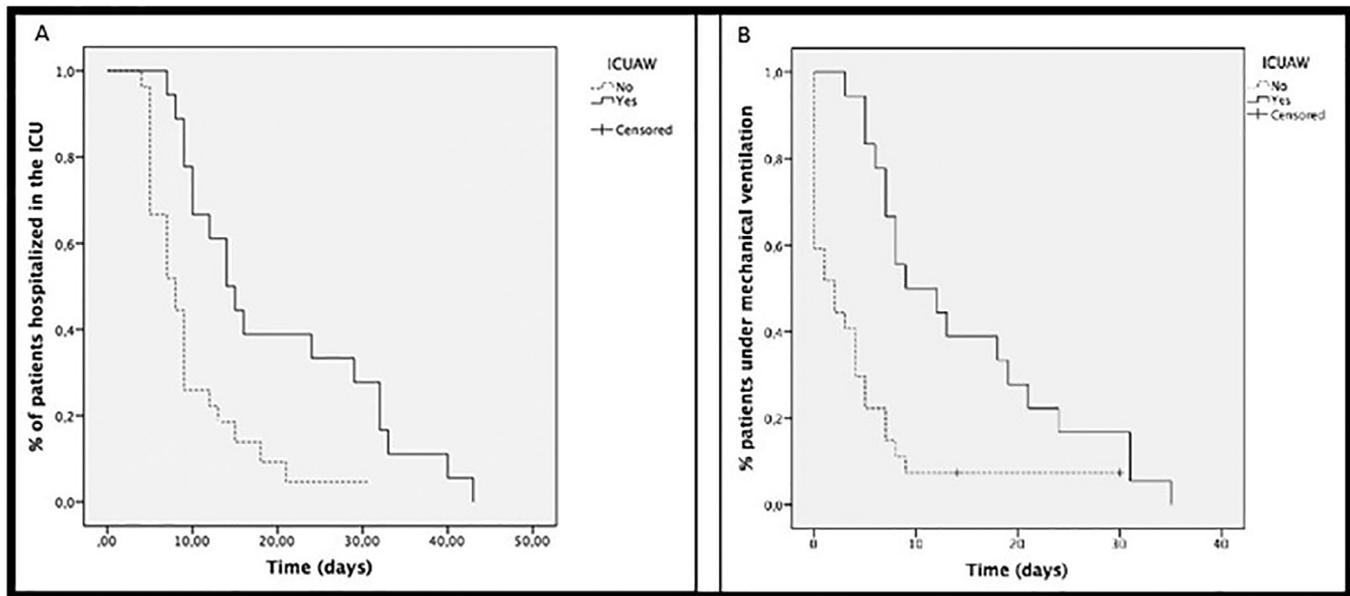
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Fig. 2. (A) Curves comparing the length of ICU stay between patients with and without ICUAW during index ICU stay ($p < 0.001$). (B) Curves comparing the length of mechanical ventilation support between patients with and without ICUAW during index ICU stay ($p < 0.001$). Definition of abbreviations: ICUAW = intensive care unit acquired weakness.

Conclusions

ICUAW is associated with longer ICU and hospital stay and delayed weaning from mechanical ventilation throughout a period of at least six months, suggesting that this condition is related to long term consequences.

Handgrip dynamometry may provide a rapid, simple and accurate alternative to the MRC examination for the diagnosis of ICUAW.

Future prospects

Although ICUAW is a common condition, several important questions remain unanswered. More studies evaluating nutrition support, early mobilization, biomarkers, new diagnostic methods (e.g., muscle ultrasound) and possible treatments are needed. Handgrip strength dynamometry will certainly contribute to accurately identify patients for these future investigations.

We intend to begin a new cohort study of patients with ICUAW, including electroneuromyography, biomarkers and ultrasonography evaluation. The patients included in this cohort will be submitted to a long-term clinical follow-up to evaluate aspects such as time to strength recovery, functional status and long-term morbidity.

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Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.hrtlng.2019.07.001.

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