BMJ Open Association of the mobility level of critically ill adult patients with the success of extubation: protocol for a cohort study

Camila Pal ^{1,2}, Carolina Fu,³ Carlos Roberto Ribeiro Carvalho,⁴ José Otávio Costa Auler Júnior,⁵ Liria Yuri Yamauchi¹

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¹Human Movement Sciences, Universidade Federal de São Paulo, São Paulo, Brazil

²Hospital Sírio-Libanês, São Paulo, Brazil

³Department of Physiotherapy, Speech Therapy and Occupational Therapy, Universidade de São Paulo, São Paulo, Brazil

⁴Discipline of Pulmonology, Heart Institute (InCor), Hospital das Clínicas, Faculty of Medicine, University of São Paulo, São Paulo, Brazil

⁵Surgery Department, Universidade de São Paulo, São Paulo, Brazil

Correspondence to
Professor Camila Pal;
camila.pal@hsl.org.br

ABSTRACT

Introduction Several factors contribute to the reduction of the mobility in ICU, such as the use of sedatives, severity, invasive devices, acute clinical instability, lack of resources, the culture of immobility, architectural barriers and the own weakness developed in the ICU. The need for ventilatory support is common in most of patients, and weaning from mechanical ventilation (MV) is an arduous process that requires the commitment of the entire team. Instruments that objectively assess the mobility of patients admitted to the ICU can be useful to identify the existence or not of an association between mobility and prognosis. **Objective** To estimate the association between the level of mobility and successful extubation.

Methods and analysis Prospective cohort study with the beginning of follow-up when the patient completes 24 hours of invasive MV in the ICU and ends on the date the patient's hospital discharge. Adult patients (≥18 years old) admitted to the ICU will be included in the first invasive MV event in this hospitalisation. Patients should be independently able to mobilise before current hospital admission. Predictor variables will be collected (age, sex, body mass index, Simplified Acute Physiological Score III (SAPS III), ICU admission type: clinic, elective or emergency surgery postoperative, Charlson Index, number of physiotherapists per patient in each ICU, use of sedation, vasoactive drugs and neuromuscular blocker, ICU mobility scale, time of invasive MV, ICU admission and hospital admission, and outcome. The primary outcome is the result of extubation (success or failure).

Ethics and dissemination This study was approved by the Ethics Committee, certificate number 92878218.1.0000.5505. The protocol was registered on the *Registro Brasileiro de Ensaios Clínicos* (ReBEC) (registration number RBR-8k4f68). The results will be published in specialised journals and disseminated to the medical society and the general public.

INTRODUCTION

The mobility of patients admitted to intensive care units (ICUs) is a topic of interest for the different areas of care for critically ill patients due to the deleterious effects in the short, medium and long term, such as decreased muscle protein synthesis, muscle

Strengths and limitations of this study

- We believe that it is one of the first prospective cohort studies that associate the level of mobility with the outcome of extubation.
- The exclusion of patients most severely affected (neurological, palliative and lower limb amputees) can reduce the generalisation of results for the entire critical patient population.
- Another limitation may be the lack of objective measurement of muscle strength such as the Medical Research Council (MRC) scale.
- It will not be possible to collect the participants' previous functionality.

atrophy and decreased lean muscle mass, decreased muscle strength and exercise capacity, increased likelihood of atelectasis, pneumonia, decreased maximal inspiratory pressure, decreased venous compliance of the lower limbs, orthostatic intolerance, decreased cardiac output, stroke volume and peripheral vascular resistance, among others.¹ However, several factors contribute to the reduction of the mobility of these patients, such as the use of sedatives, severity, the use of invasive devices, acute clinical instability, lack of equipment and human resources, the culture of immobility, architectural barriers and the own weakness developed in the ICU.^{2–4} This weakness, in turn, is also multifactorial and has immobility as its main risk factor.⁵ Therefore, it is clear that immobility and weakness are part of a cyclical process and that both have several associated factors in common. One of the main factors associated with immobility and weakness is the use of invasive mechanical ventilation (MV). According to Hodgson *et al*,⁶ about 25%–60% of patients who need MV for more than 7 days have neuromuscular weakness acquired in the ICU. Neuromuscular weakness develops early

in patients with MV for 24 hours or more.⁷ In addition, the weakness is independently associated with an increase in the duration of MV, an increase in ICU and hospital stay days, low quality of life among survivors and high cost generated by hospitalisation.^{8–10} According to the review by Hashem *et al*,¹¹ most patients with MV did not make any form of mobilisation out of bed. These results were compiled from studies in the USA, Germany, Australia and New Zealand. Early mobilisation in intensive care has been the subject of a common study in recent years. In a systematic review by Tipping *et al*,¹² they concluded that early active mobilisation and rehabilitation in the ICU did not have consistent effects on the duration of MV, length of hospital stay and in the ICU. Another important aspect is the standardisation of the mobility assessment of these patients. Parry *et al*¹³ reported the existence of 26 scales to assess function in patients admitted to the ICU. These instruments make it possible to assess the effects of different levels of mobility in relation to some outcomes in the ICU, in the hospital and after returning home. Our hypothesis is that higher levels of mobility are associated with extubation success.

METHODS AND ANALYSIS

Study objectives

The primary objective of this study is to estimate the association between the level of mobility and successful extubation of adult patients admitted to the ICU.

Secondary objective

The secondary objective of this study is to perform a survival analysis of adult patients admitted to the ICU with MV, according to the level of mobility (higher or lower).

Design

We are conducting a prospective cohort study of adult patients under MV for at least 24 hours. We started in January 2020 and the final assessments including follow-up will be made in January 2021.

Study location

This study will be conducted in the ICUs of a large university hospital in the city of São Paulo. Nine ICUs will be studied, including four clinical units (35 beds), three surgical units (46 beds), a mixed neurological ICU (9 beds) and an ICU for burned patients (4 beds), a total of 94 beds. These ICUs have multidisciplinary teams to provide comprehensive patient care. This team is composed of members who work in different areas, but which complement each other for comprehensive patient care. This team includes doctor, nurses, physiotherapist, nutritionist, pharmacist, psychologist and social workers. These professionals can work through interconsultations or in joint work with the others, according to what is standardised by each unit.

Study population

Inclusion criteria

Adult patients (≥18 years old) will be included in the first event of invasive MV for >24 hours.⁷ Patients should

independently be able to mobilise prior to current hospital admission (this included patients who needed assistance from someone else or a walking device, such as a cane or walker).

Exclusion criteria

Patients will be excluded if they have one or more of the following criteria: neurological disease (vascular, tumour or infectious), neuromuscular disease, degenerative muscle disease, brain or spinal cord trauma, inability to communicate in Portuguese, severe cognitive impairment before ICU stay, unstable fractures, burns or any other injury that requires a prescription for rest, patients in palliative care, lower limb amputation or readmission to the ICU in the last 6 months.^{4,14}

Procedure

In Brazil, most patients are discharged directly to home, as there are no rehabilitation hospitals for post-ICU patients or long-term MV weaning units. Therefore, patients will be followed up during the ICU stay until hospital discharge. The data will be obtained daily in the ICUs at pre-established times, from medical records and with the multidisciplinary teams of the units, by trained researchers and according to the procedures manual carried out for the study. The information will be stored in REDCap (Research Electronic Data Capture) software for later statistical analysis. Standard forms will be used, prepared within the REDCap platform. All decisions regarding weaning from MV, extubation, reintubation, tracheostomy, mobilisation and other interventions will be made by the multidisciplinary care team of the units studied in accordance with institutional protocols, as follows. Patients hospitalised and submitted to MV will undergo daily assessment in order to identify possible conditions to initiate weaning and interruption of ventilatory support, according to the following criteria: reversion or control of the clinical condition that led to intubation; haemodynamic stability without the use of vasopressors or with the use of low doses or values acceptable by the team; presence of ventilatory drive; $\text{PaO}_2/\text{FIO}_2$ ratio greater than or equal to 150 (for patients with previous lung disease, modify this cut-off value on a case-by-case basis); $\text{PaO}_2 \geq 60$ with $\text{FIO}_2 \leq 0.4$ and positive end expiratory pressure (PEEP) less than or equal to 8 cm H_2O (differentiated cases must be evaluated by the team and modified cut-off value); adequate level of consciousness (Glasgow ≥ 8); normal acid–base and electrolyte balance, or values acceptable by the team; patient without scheduling examinations or surgical procedures that use general anaesthesia in the next 24 hours; hydric balance assessment.

Measures and outcomes

The demographic and clinical variables of the study are shown in table 1.

The primary outcome of this study is extubation failure, the need for reintubation within 48 hours after

Table 1 Study's variables

Variables	Variable's description
ICU admission data	
Date of inclusion in the study	Dd/mm/yyyy
Full name and register number:	
Age	Years
Sex	Biological (male/female)
Date of hospital admission	Dd/mm/yyyy
BMI	kg/m ²
Date of ICU admission	Dd/mm/yyyy
Saps III	Points
Ph	Arterial blood gas measurement
PaO ₂ /FiO ₂ ratio	Oxygenation index
Main cause of ICU admission	Neurological, cardiovascular, respiratory, gastrointestinal and others
Type of admission	Clinic, elective or emergency surgery
Comorbidities Charlson Index	Points
Main cause of MV	Decreased level of consciousness, ARF, cardiorespiratory arrest, surgery
MV data and times	
IMS scale	Highest level within 24 hours after intubation
Patient on MV—daily evaluation	
Sedatives	Yes or no
Neuromuscular blocker	Yes or no
Vasoactive drug	Yes or no
IMS scale	Highest level
Extubation data	
Extubation	Yes or no
Extubation date and time	
IMS scale	Highest level within 24 hours
Extubated patients' outcome	
Extubation outcome	Success or failure (reintubation <48 hours)
IMS	Highest level within 24 hours after extubation
Reintubation	
Date and time reintubation	Dd/mm/yyyy
Cause of reintubation	Check protocol
Final outcome	
Duration of invasive MV	Days
Invasive MV free time in the ICU	Days
ICU length of stay	Days
ICU mortality	N (%)
Hospital length of stay	Days
Hospital mortality	N (%)

ARF, acute respiratory failure; BMI, body mass index; ICU, intensive care unit; IMS, ICU Mobility Scale; MV, mechanical ventilation; SAPS, Simplified Acute Physiology Score.

extubation. In order to analyse the association between mobility level and extubation outcome, we have selected some independent variables, as follows:

- Demographic data: age, sex, body mass index (BMI).
- Severity of the disease assessed by the Simplified Acute Physiological Score III (SAPS III) score.
- Type of admission to the ICU: clinic, postoperative of elective or emergency surgery.
- Presence of comorbidities recorded by the Charlson Index.¹⁵
- Number of physiotherapists per patient in each ICU.
- Use of sedation, vasoactive drugs and neuromuscular blocker, as a binary variable (yes or no).
- Days of invasive MV.
- The ICU Mobility Scale (IMS)¹⁶ will be assessed from the first 24 hours of MV in the ICU and daily for 14 consecutive days. If the patient performs more than one level of mobility during the day, the highest level of mobility for the period in question will be noted. For the analysis of this variable, three main moments were considered: admission IMS, extubation IMS and post-extubation IMS. The IMS admission evaluates from the moment of intubation until the next day at the same time, for example, day 1 at 09:00, until day 2, 08:59; the extubation IMS assesses the day of extubation, from 12:00 to 23:59; and the post-extubation IMS, evaluates from the time of extubation up to 24 hours after. The IMS will be analysed in two ways: as a discrete continuous variable and as a categorical variable, in which participants will be classified as having a higher or lower level of mobility. Therefore, we will categorise patients with IMS less than or equal to 1 as low mobility group, and greater than or equal to 2 as high mobility group.
- Cause of reintubation: Reduced level of consciousness, ineffective cough associated with hypersecretion, respiratory rate >35, use of accessory muscles, peripheral oxygen saturation <90%, heart rate >140bpm or 20% increase in baseline; systolic blood pressure >180 mm Hg or 20% increase in baseline; <90 mm Hg; agitation, sweating and/or altered level of consciousness; signs of respiratory distress (use of accessory muscles, paradoxical pattern, flapping of the nose). Possible confounding variables: MV days, days of sedation, age, sex, severity score (SAPS III), comorbidities (Charlson Index), causes of MV.

Outcome variables

- Successful extubation (patients maintained on spontaneous ventilation for ≥48 hours).
- ICU and hospital mortality.

Planned statistical analyses

In the descriptive analysis, the quantitative variables will be expressed as mean and SD or median and IQR, according to their distribution. In the comparison between the extubation success and failure groups, the continuous variables will be compared with the t-test or

non-parametric equivalent. Categorical variables will be expressed as an absolute number and proportion. Comparisons between proportions will be made using the χ^2 test or Fisher's exact test. Logistic regression analysis will be performed to estimate whether the level of mobility is independently associated with the result of extubation. All possible confounding variables will be included in the initial model, and to check for the existence of multicollinearity, the variance inflation factors will be calculated. The Kaplan-Meier method will be used to determine the probability of death in the hospital for patients with different levels of mobility.

RESULTS

This research will record a wide range of demographic and medical variables. We will measure the IMS daily to identify the mobility pattern of patients on MV and analyse whether mobility has an independent relationship with the outcome of extubation. We will present the final multivariate statistical model with the success of extubation as the main outcome variable.

Sample size and power calculation

The sample size was determined using the calculation for comparison of means, in which the response variable was the level of mobility, measured as the ICU Mobility Scale (IMS), and considered as a numerical variable. Considering the study by Tipping *et al.*,¹⁷ it was determined that the minimum clinically significant difference between the success group and the extubation failure group is one point. The variability was determined by the value of the SD of the variable, obtained from a pilot study carried out between January and March 2020, for testing the collection instruments. The value obtained was 1.77. To have a power greater than 0.80 and a significance level of 0.05, the minimum sample size must be 102 participants, that is, 51 per group.

Ethics and dissemination

Ethical considerations

This study was approved by the Federal University of São Paulo Ethics Committee, certificate number 92878218.1.0000.5505. The protocol was registered on the *Registro Brasileiro de Ensaios Clínicos* (ReBEC) (registration number RBR-8k4f68).

As this is a large cohort study with a purely observational nature with data from medical records, the waiver of the free and informed consent form was approved, with a commitment to maintaining the confidentiality and anonymity of participants. The data collected daily will be stored in the RedCap software, a secure web platform to create and manage databases and online surveys. Within the software, we developed seven forms (patient admission to the project, daily assessment of the intubated patient, interruption of intubation, extubation outcome, reintubation data, final outcome, and complications) with appropriate variables for each moment of data collection.

Dissemination

This study follows the model of the Strengthening the Reporting of Observational Studies in Epidemiology initiative ('Strobe—Improving the Presentation of Results of Observational Studies in Epidemiology'), aiming to contribute to a more adequate report of the study and, consequently, to facilitate critical reading by editors, reviewers and readers in general.¹⁸

The results obtained will be disseminated to the scientific, medical and general public by publication in national and international peer-reviewed journals, as well as by presentations at conferences and meetings with clinicians dealing with critical patients in ICU.

DISCUSSION

This project will be one of the first studies with repeated measures with daily documentation of mobility level of patients under MV in ICU. This research will be developed over a year. Also, a wide range of demographic and medical variables will be measured to identify if the mobility pattern has an independent relationship with the result of extubation.

It seems to be more informative to analyse mobility systematically over a period with daily assessments. These data can offer a more detailed understanding of the dynamics of function recovery and a better understanding of the effect of these changes on important clinical outcomes of the ICU patient, for example, the result of extubation and ICU and hospital mortality. The present study will follow the patients from ICU admission to hospital discharge.

We highlight as positive aspects of the study the prospective design and the scarcity of publications that relate the level of mobility of patients with MV and the result of the withdrawal of support.

On the other hand, we consider some limitations such as the exclusion of neurological, palliative care and lower limb amputee patients. This approach can reduce the generalisation of results for the entire critical patient population. Another limitation may be the lack of objective measurement of muscle strength, such as the MRC scale, because it is not performed in the studied ICUs.

The results of this study will be relevant to researchers and clinical practice.

Correction notice This article published with an error. Dr Carvalho's institution has been updated.

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ORCID iD

Camila Pal <http://orcid.org/0000-0002-6373-8980>

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