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ORIGINAL ARTICLE

Association between time to weaning from mechanical ventilation and presence of physical and mental health disabilities in survivors of critical illness: a multicenter prospective cohort study

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KEYWORDS
Mechanical ventilation;
Weaning;
Anxiety;
Depression;
Physical disabilities

Abstract
Objective: To evaluate the association between weaning time from invasive mechanical ventilation (IMV) and occurrence of physical and mental health disabilities in ICU survivors.
Design: Prospective, multicenter cohort study.
Setting: 10 Brazilian ICUs (May 2014-December 2018).
Patients or Participants: Adult survivors with an ICU stay >72 h for emergency medical and surgical admissions or >120 h for elective surgical admissions and who used IMV. Classification into 3 groups: simple, difficult, and prolonged weaning.
Interventions: Follow-up through structured telephone interviews
Main variables of interest: Outcomes included moderate to severe functional physical dependence (Barthel Index score $\leq$75) at 3 months post-ICU discharge, symptoms of anxiety and depression (Hospital Anxiety and Depression Symptom Scale scores >7 in the anxiety or depression subdomains) and post-traumatic stress (Impact Event Scale-6 > 9) at 6 months post-ICU discharge and all-cause post-ICU mortality (categorized as early [0–30 days] and late [>30 days]).
Results: Of the 804 patients, 492 (61.2%) presented simple weaning, 60 (7.5%) difficult weaning and 252 (31.3%) prolonged weaning. In total, 670 (83.3%) and 630 (78.3%) patients were alive at 3 and 6 months. Early post-ICU mortality (13.1% vs. 7.1%; p = 0.01) and 3-month physical dependence (55.9% vs. 37.6%; p < 0.001) were both higher in the prolonged weaning group than in the simple weaning group. At 6 months, difficult weaning patients were more anxious (55% vs 23.6% vs 21.4%; p = 0.02) and depressed (50% vs 24.7% vs 17.1%; p = 0.04) compared to simple and prolonged weaning groups, respectively, with no differences regarding post-traumatic stress.

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Conclusion: ICU survivors who experienced prolonged weaning had higher early post-ICU mortality and greater rates of moderate to severe physical functional dependence at three months after discharge, whereas those with difficult weaning showed higher rates of anxiety and depression at six months.
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PALABRAS CLAVE
Ventilación mecánica;
Destete;
Ansiedad;
Depresión;
Discapacidades físicas

Asociación entre el tiempo hasta el destete de la ventilación mecánica y la presencia de discapacidades físicas y mentales en supervivientes de enfermedades críticas: un estudio de cohorte prospectivo multicéntrico

Resumen
Objetivo: Evaluar la asociación entre tiempo de destete de la ventilación mecánica invasiva (VMI) y aparición de discapacidades físicas y mentales en supervivientes a la UCI.
Diseño: Estudio de cohorte, prospectivo, multicéntrico.
Ámbito: 10 UCI brasileñas (mayo 2014-diciembre 2018).
Pacientes: Adultos supervivientes, estancia >72 horas por ingresos médicos/quirúrgicos urgentes o >120 horas tras cirurgia electiva, que requirieron VMI. Tres grupos: destete simple, difícil o prolongado.
Intervenciones: Seguimiento mediante entrevistas telefónicas estructuradas
Variables de interés principales: Dependencia física funcional moderada a grave (Índice de Barthel $\leq$75) en 3 meses del alta de la UCI, síntomas de ansiedad y depresión (puntuaciones >7 en la Escala de Síntomas de Ansiedad y Depresión Hospitalaria-subdominios de ansiedad o depresión) y estrés postraumático (Escala de Impacto de Evento-6 > 9) a los 6 meses tras alta de la UCI y mortalidad post-UCI por todas las causas (clasificada como temprana [0 a 30 días] y tardía [>30 días]).
Resultados: Entre 804 pacientes, 492 (61.2%) presentaron destete simple, 60 (7.5%) destete difícil y 252 (31.3%) destete prolongado. Sobrevivieron 670 (83.3%) en 3 meses y 630 (78.3%) en 6 meses. La mortalidad temprana posterior a la UCI (13.1% vs. 7.1%; p = 0.01) y la dependencia física a los 3 meses (55.9% vs. 37.6%; p < 0.001) fueron mayores en el grupo con destete prolongado que en el grupo con destete simple. En 6 meses, pacientes con destete difícil presentaron más ansiedad (55% vs. 23.6% vs. 21.4%; p = 0.02) y depresión (50% vs. 24.7% vs. 17.1%; p = 0.04) en comparación con los grupos de destete simple y prolongado, respectivamente, sin diferencias em cuanto a estrés postraumático.
Conclusiones: Supervivientes de la UCI con destete prolongado han presentado mayor mortalidad temprana y major dependencia funcional física moderada/severa a los tres meses, mientras que aquellos con destete difícil apresentam más sintomas de ansiedad y depresión a los 6 meses tras alta de la UCI.
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Introduction

Advances in intensive care have improved survival rates; however, many survivors experience new physical and mental health impairments, affecting up to half of patients with prolonged ICU stays.[1] This shift has redirected research in critical care toward long-term functional and mental health outcomes.[2] Among the most common mental health problems in ICU survivors are anxiety, depression and post-traumatic stress disorder (PTSD).[3] Factors such as depth and duration of sedation, length of mechanical ventilation and hospital stay are associated with the development of these conditions.[4] From a physical perspective, patients requiring mechanical ventilation for acute respiratory distress syndrome (ARDS) remain at increased risk of functional dependence for up to five years after discharge.[5]

Although the association between the duration of mechanical ventilation and adverse outcomes is well established, the impact of weaning process—particularly its difficulty and duration—on survivors' physical and mental health is less well understood. Most prior studies have focused on short-term outcomes, leaving a gap in knowledge regarding medium- and long-term effects. Our group has previously shown that physical decline is associated with the development of mental health impairments in ICU survivors,[6] yet the specific relationship between dif-

ficult or prolonged weaning and these disabilities remains underexplored. Thus, this study aims to address this gap by examining the association between weaning difficulty and duration and the occurrence of physical and mental health disabilities in survivors of critical illness.

Methods

Study design and ethical aspects

This ancillary analysis is part of a multicenter prospective cohort study conducted in 10 Brazilian ICUs from May 2014 to December 2018 (Post-ICU Quality of Life project).[7] Consecutive adult ICU survivors who had required invasive mechanical ventilation (IMV) were recruited while still hospitalized, within a predefined screening window (24–120 hours after ICU discharge) designed to standardize the timing of baseline assessments. Participants were followed through structured telephone interviews conducted by trained researchers not associated with patient care at 3, 6, and 12 months after ICU discharge. Telephone interviews were centralized, and investigators had a 30-day window (15 days before and 15 days after the target date) to complete them. An interview was considered lost if the participant's phone line was disconnected or nonexistent, or after 10 unsuccessful attempts made at different times on multiple days within the window period. The study was conducted in accordance with resolution 466/12 of the Brazilian National Health Council. The study protocol was approved by the Research Ethics Committee of the coordinating center (CAAE 04258312.4.1001.5330) and by the Research Ethics Committees of all participating institutions. Informed consent was obtained from all participants or their legal representatives.

Participants

The study included patients aged ≥18 years who were discharged from participating ICUs and remained in the ICU for 72 h or more for emergency medical or surgical admissions, or 120 h or more for elective surgical admissions and who required IMV. The following exclusion criteria were applied: (1) transfer from another hospital to the ICU; (2) discharge directly from the ICU to home (due to logistical constraints); (3) discharge from the ICU to another hospital; (4) need for respiratory isolation after ICU discharge (due to logistical constraints); (5) readmission to the ICU within 24 h after ICU discharge; (6) absence of a proxy for patients with communication difficulties; (7) refusal or withdrawal of consent to participate; (8) previous inclusion in the study; and (9) absence of available telephone contact.

Type of ventilatory weaning

Weaning procedures occurred in each center according to local protocols. The weaning classification was based on the 2005 International Consensus Conference, which categorizes ventilated patients into three groups according to the difficulty and duration of the weaning process: (1) simple weaning, defined as successfully completion of the first spontaneous breathing trial (SBT) followed by successful extubation on the first attempt; (2) difficult weaning, defined as requiring up to three SBTs or up to seven days from the first SBT to achieve successful weaning; and (3) prolonged weaning, defined as requiring more than three SBTs or more than seven days of weaning after the first SBT.[8]

Outcomes

Three months after ICU discharge, physical functional capacity was assessed using the Barthel Index,[9] which measures the degree of functional dependence in domains such as self-care, mobility, locomotion and elimination control. An overall score is obtained by assigning points to each category, depending on the time and assistance required for each patient. The score ranges from 0 to 100, in five-point intervals, with lower scores indicating greater dependence. Patients with scores ≤75 were classified as having moderate to severe functional dependence as previously performed in other studies.[10]

Six months after discharge from the ICU, symptoms of anxiety and depression were assessed using the Hospital Anxiety and Depression Scale (HADS[11] and PTSD symptoms using the Impact of Event Scale-6 (IES-6).[12] HADS scores range from 0 to 21 in the anxiety and depression domains, with higher scores indicating greater symptom burden. Patients with scores >7 were classified as having symptoms of anxiety or depression. IES-6 scores range from 0 to 24, with higher scores indicating greater symptom burden, and patients with scores >9 were classified as having symptoms of PTSD.

Mortality from any cause one year after discharge from the ICU was categorized into early mortality (0–30 days after discharge) and late mortality (>30 days after discharge).

Covariates

Baseline data included sociodemographic variables, health status prior to ICU admission, and characteristics of acute critical illness. Comorbidity burden was assessed using the Charlson Comorbidity Index[13] and patients with a score ≥2 were categorized as having a high comorbidity burden. Critical illness severity was assessed by the risk of death on ICU admission, defined as the predicted risk of in-hospital death derived from the Acute Physiology and Chronic Health Evaluation II (APACHE II[14] or Simplified Acute Physiology Score 3 (SAPS 3).[15] Organ dysfunction was defined as the presence of any of the following factors during the ICU stay: need for mechanical ventilation, need for vasopressors, need for renal replacement therapy (except for patients on chronic dialysis), need for parenteral nutrition, need for blood transfusion or blood products, and delirium (measured according to the Confusion Assessment Method for the ICU[16].

Statistical analysis

Quantitative variables were described as mean and standard deviation (SD) or median and interquartile range (IQR), while categorical variables were described as absolute and relative frequencies. Baseline variables were compared according to the weaning category using the Kruskal-Wallis test for quantitative variables and Pearson's Chi-Square test for categorical variables using the Bonferroni correction as needed. Physical functional dependence and mental health

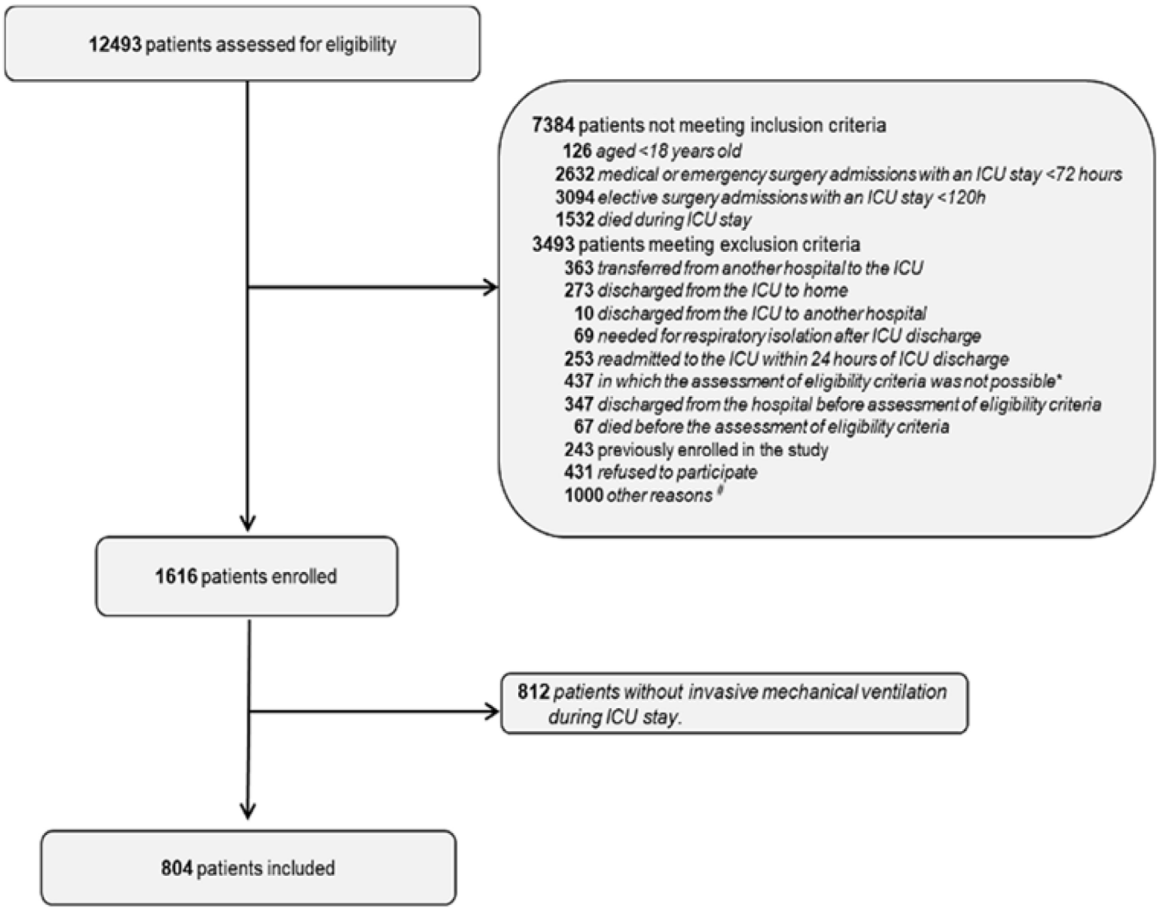

Figure 1 Study Flowchart.
* Patient was not assessed or found in the ward after five attempts (screening failures).
# No available telephone contact, or absence of a proxy for patients with communication difficulties, or previous inclusion in the study.

outcomes were analyzed with generalized linear models. Models for physical dependence were adjusted for age, gender, Charlson comorbidity index, prior moderate to severe functional dependence (1 month before ICU admission), and risk of death at ICU admission. Models for anxiety and PTSD symptoms were additionally adjusted for history of anxiety, and models for depression outcomes were additionally adjusted for history of depression. Mortality was assessed with mixed-effects Cox regression, adjusted for age, gender, Charlson comorbidity index, prior moderate-to-severe functional dependence, and risk of death at ICU admission. Mortality was also described by Kaplan-Meier curves. A significance level of 5% was considered and analyses were performed using R software, version 3.6.1. [R Core Team (2019). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL https://www.R-project.org/].

Results

Of the 1616 patients included in the Post-ICU Quality of Life Project, 804 (49.8%) were included in the present analysis (Fig. 1). Baseline characteristics are shown in Table 1. The median age was 64 years, 43.9% (n = 353) were female, and 56.0% (n = 450) had a Charlson Comorbidity Index of two or higher. A prior history of anxiety and depression was reported in 18.5% (n = 148) and 19.7% (n = 157) of patients, respectively. During the acute phase of critical illness, 78.2% (n = 629) received vasopressors, 42.2% (n = 339) had a diagnosis of sepsis, and 32.1% (n = 258) had delirium.

Regarding ventilatory weaning characteristics, 61.2% (n = 492) underwent simple weaning, 7.5% (n = 60) difficult weaning and 31.3% (n = 252) prolonged weaning. Compared to the other weaning groups, the simple weaning group had a higher median age, a greater proportion of patients aged over 65 years, higher household income per capita, and a greater frequency of elective surgical admissions. Baseline health status prior to ICU admission - including comorbidities, dementia, depression, and anxiety- was similar across the three weaning groups. The simple weaning group showed lower severity of critical illness across several parameters. Sepsis was less frequent compared with the difficult and prolonged weaning groups (35.4% vs. 53.3% vs. 52.8%), as was the need for renal replacement therapy (9.8% vs. 21.7% vs. 25.8%) and delirium (26.0% vs. 38.3% vs. 42.5%). ARDS was uncommon overall, but occurred less often in the simple weaning group (2.8%) compared with the difficult (13.3%) and prolonged (17.1%) groups. The incidence of ICU-

Table 1 Patient characteristics and type of ventilatory weaning.

Variables	Total	Simple Weaning (n = 492)	Difficult Weaning (n = 60)	Prolonged Weaning (n = 252)	p-value
Sociodemographic characteristics					
Age, years – median (IQR)	64 (49.8–76)	66 (55–77)[A]	63 (50.8–72.5)[B]	60 (40.8–73)[C]	<0.001
Age ≥65 years – no./total n (%)	399/804 (49.6)	264/492 (53.7)[A]	29/60 (48.3)[A,B]	106/252 (42.1)[B]	0.011
Female gender – no./total n (%)	353/804 (43.9)	209/492 (42.5)	24/60 (40)	120/252 (47.6)	0.335
Educational level, years – median (IQR)	9 (5–11)	10 (5–11)	7 (5–11)	10 (4–11)	0.530
Higher education – no./total n (%)	160/801 (20)	104/491 (21.2)	12/59 (20.3)	44/251 (17.5)	0.499
Household income per capita, USD – median (IQR)	489.2(286.2–1075.8)	537.9(352.6–1482.2)[A]	331.7 (146.7–537.9)[B]	462.9 (266.1–806.9)[C]	<0.001
Health status prior to ICU admission					
Charlson Comorbidity Index median (IQR)	2 (0–3)	2 (0–3.2)	2 (0–3)	2 (0–3)	0.343
Charlson Comorbidity Index ≥2 no./total no. (%)	450/804 (56.0)	281/492 (57.1)	34/60 (56.7)	135/252 (53.6)	0.650
Physical dependence – no./total n (%)	158/804 (19.7)	90/492 (18.3)	13/60 (21.7)	55/252 (21.8)	0.46
History of dementia no./total no. (%)	58/804 (7.2)	33/492 (6.7)	3/60 (5.0)	22/252 (8.7)	0.474
History of depression no./total no. (%)	157/797 (19.7)	95/491 (19.3)	18/60 (30.0)	44/246 (17.9)	0.102
History of anxiety no./total no. (%)	148/799 (18.5)	82/491 (16.7)	13/59 (22.0)	53/249 (21.3)	0.244
Characteristics of Acute Critical Illness					
Type of ICU admission					<0.001
Medical – no./total no. (%)	510/804 (63.4)	273/492 (55.5)[A]	44/60 (73.3)[B]	193/252 (76.6)[C]	
Surgical, elective – no./total no. (%)	145/804 (18)	117/492 (23.8)[A]	10/60 (16.7)[B]	18/252 (7.1)[C]	
Surgical, emergency – no./total no. (%)	149/804 (18.5)	102/492 (20.7)[A]	6/60 (10.0)[B]	41/252 (16.3)[C]	
Risk of death on admission to ICU, % – median (IQR)	26.2 (14.6–49.7)	21 (14.1–42.4)[A]	31.5 (20.4–56)[B]	35.5 (21–53.3)[B]	<0.001
Sepsis – no./total no. (%)	339/804 (42.2)	174/492 (35.4)[A]	32/60 (53.3)[B]	133/252 (52.8)[B]	<0.001
ARDS – no./total no. (%)	65/804 (8.1)	14/492 (2.8)[A]	8/60 (13.3)[B]	43/252 (17.1)[B]	<0.001
Length of mechanical ventilation, days – median (IQR)	4.0 (2.0–9.0)	2.0 (1.0–4.0)[A]	7.0 (5.0–7.0)[B]	12.5 (9.0–21.8)[C]	<0.001
Organ dysfunction during ICU stay					
Number of organ dysfunctions – median (IQR)	1 (1–2)	1 (1–2)[A]	1 (1–2)[A]	2 (1–3)[B]	<0.001
Need for vasopressor – no./total no. (%)	629/804 (78.2)	372/492 (75.6)[A]	43/60 (71.7)[A]	214/252 (84.9)[B]	<0.001
Need for renal replacement therapy – no./total no. (%)	126/804 (15.7)	48/492 (9.8)[A]	13/60 (21.7)[B]	65/252 (25.8)[B]	<0.001
Need for parenteral nutrition – no./total no. (%)	55/804 (6.8)	32/492 (6.5)	1/60 (1.7)	22/252 (8.7)	0.134
Need for blood products transfusion – no./total no. (%)	172/804 (21.4)	83/492 (16.9)[A]	13/60 (21.7)[A,B]	76/252 (30.2)[B]	<0.001
Delirium – no./total no. (%)	258/804 (32.1)	128/492 (26.0)[A]	23/60 (38.3)[B]	107/252 (42.5)[B]	<0.001
Infection acquired in the ICU – no./total no. (%)	193/804 (24.0)	36/492 (7.3)[A]	10/60 (16.7)[B]	147/252 (58.3)[C]	<0.001

ARDS, acute respiratory distress syndrome; IQR, interquartile range; ICU, Intensive Care Unit; USD, United States dollar.
Groups sharing the same superscript letter (A, B, C, etc.) do not differ significantly from each other in post hoc pairwise comparisons. Groups with different letters differ significantly at $p<0.05$.

Table 2 Long-term outcomes after ICU discharge.

Outcome	Total (n = 804)	Simple Weaning (n = 492)	Difficult Weaning (n = 60)	Prolonged Weaning (n = 252)	Adjusted p-value
Physical dependence[1] at 3 months					
Respondents – no. (%)	564 (70.1)	351 (71.3)	43 (71.7)	170 (67.5)	0.50
Barthel Index score – median (IQR)	85 (30–95)	90 (50–100)^{A}	85 (40–95)^{AB}	67.5 (20–90)^{B}	<0.001
Moderate to severe functional dependence – no (%)	246 (43.6)	132 (37.6)^{A}	19 (44.2)^{AB}	95 (55.9)^{B}	<0.001
Anxiety[2] and depression[3] at 6 months					
Respondents – no. (%)	272 (33.8)	182 (37.0)	20 (33.3)	70 (27.8)	0.104
Anxiety symptoms – median (IQR)	5 (2–8)	4 (2–7)^{A}	8.5 (3–11.5)^{B}	4.5 (2–7)^{A}	0.01
Anxiety symptoms (HADSa >7) – no (%)	69 (25.4)	43 (23.6)^{A}	11 (55.0)^{B}	15 (21.4)^{A}	0.02
Symptoms of depression – median (IQR)	5 (1.8–7)	5 (2–7)	7.5 (3.8–10)	3 (1–6)	0.14
Symptoms of depression (HADSd >7) – no (%)	67/272 (24.6)	45/182 (24.7)^{A}	10 (50.0)^{B}	12 (17.1)^{A}	0.04
Post-traumatic stress disorder[2] at 6 months					
Respondents – no (%)	275 (34.2)	184 (37.4)	20 (33.3)	71 (28.2)	0.43
IES-6 score – median (IQR)	4 (1–8)	4 (1–8)	6 (4.5–13.2)	4 (1–8)	0.08
IES-6 score > 9 – no (%)	50 (18.2)	35 (19.0)	6 (30.0)	9 (12.7)	0.29
Post-ICU mortality					
Early (0–30 days after discharge) – no. (%)	72/804 (9.0)	35/492 (7.1)A	4/60 (6.7)AB	33/252 (13.1)B	0.01
Late (>30 days after discharge) – no. (%)	159/725 (21.9)	99/452 (21.9)	10/56 (17.9)	50/217 (23.0)	0.41

IES-6, impact event scale-6; IQR, interquartile range; HADS, Hospital Scale of Anxiety and Depression Symptoms; ICU, Intensive Care Unit.

Groups sharing the same superscript letter (A, B, C, etc.) do not differ significantly from each other in post hoc pairwise comparisons. Groups with different letters differ significantly at $p < 0.05$.

[1] Analyses adjusted by age, gender, Charlson comorbidity index, moderate to severe functional dependence 1 month before ICU admission, and risk of death at ICU admission.

[2] Analyses adjusted by age, gender, Charlson comorbidity index, moderate to severe functional dependence 1 month before ICU admission, risk of death at ICU admission, and history of anxiety.

[3] Analyses adjusted by age, gender, Charlson comorbidity index, moderate to severe functional dependence 1 month before ICU admission, risk of death at ICU admission, and history of depression.

acquired infection differed significantly across all groups, being highest in prolonged weaning (58.3%), followed by difficult (16.7%) and simple weaning (7.3%). Vasopressor use was common in all groups, but more frequent in prolonged weaning (84.9%) than in simple (75.6%) or difficult (71.7%) weaning. Overall, 670 (83.3%), 630 (78.3%), and 573 (71.3%) of patients were alive at 3, 6, and 12 months, respectively.

Outcomes

The occurrence of outcomes by ventilatory weaning type is shown in Table 2 and in Fig. 2 and Fig. 3. The proportion of respondents for Barthel index, HADS and IES-6 were 70.1%, 33.8%, and 34.2%, respectively. At 3 months post-ICU discharge, patients in the prolonged weaning group had lower median Barthel index scores (67.5 vs. 90.0 vs. 85.0; $p < 0.001$) and a higher occurrence of moderate to severe functional dependence (55.9% vs. 37.6% vs. 44.2%; $p < 0.001$) compared with those in the simple and difficult weaning groups, respectively. At 6 months, the difficult weaning group had higher median HADS scores for anxiety (8.5 vs. 4.0 vs. 4.5; $p = 0.01$) and higher occurrences of anxiety (55% vs. 23.6% vs. 21.4%; $p = 0.02$) and depression (50% vs. 24.7% vs. 17.1%; $p = 0.04$) compared to the simple weaning and prolonged weaning groups, respectively. There was no statistically significant difference between the ventilator weaning groups in HADS depression scores, IES-6 scores and in the occurrence of PTSD. Early mortality was significantly higher in the prolonged weaning group compared with the simple weaning group (13.1% vs. 7.1%, $p = 0.01$), with no significant difference between the difficult and prolonged weaning groups. Late mortality did not differ significantly among the three groups.

Discussion

The main findings of our study indicate that prolonged weaning was associated with early post-ICU mortality and higher prevalence of moderate to severe physical dependence at 3 months, whereas difficult weaning was associated with a higher prevalence of anxiety and depression at 6 months. While associations persisted after adjustment for age, sex,

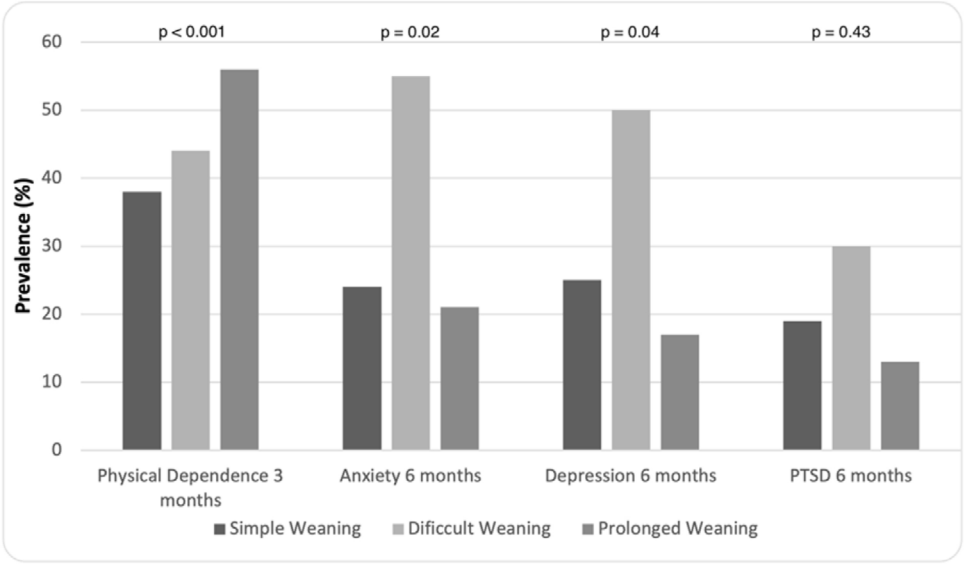

Figure 2 Prevalence of physical dependence at 3 months, anxiety, depression and post-traumatic stress disorder (PTSD) at 6 months for each type of weaning.

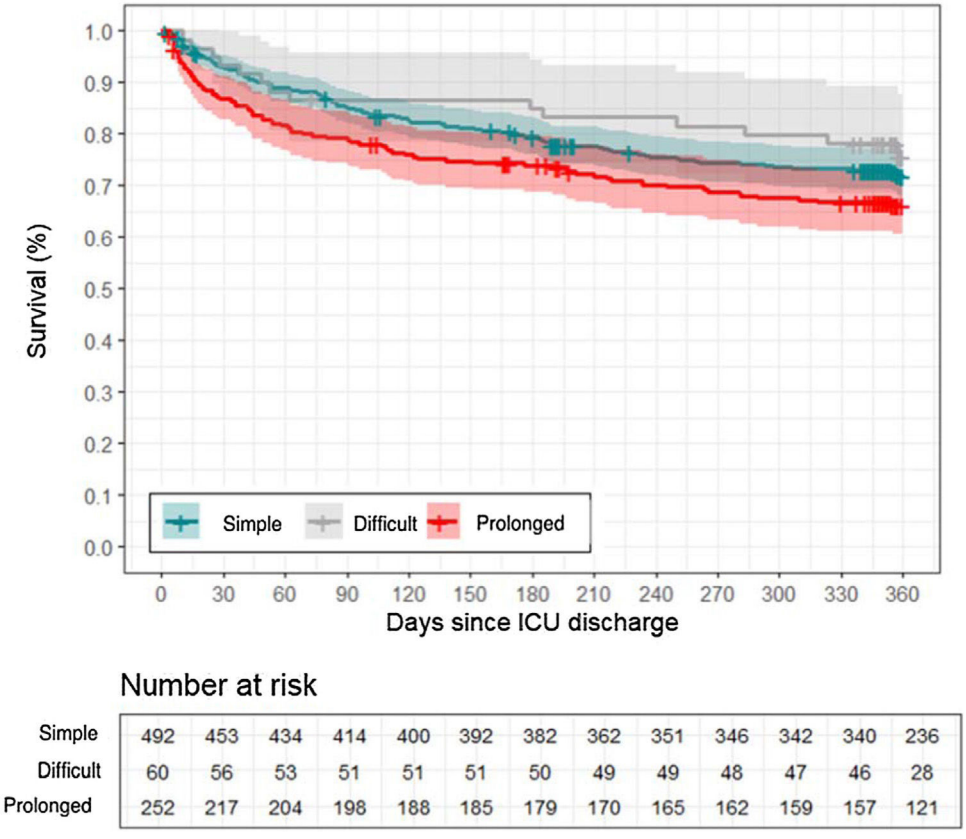

Figure 3 Survival curves according to type of weaning.

comorbidity burden, prior functional status, and risk of death at ICU admission, residual confounding remains possible.

Within 30 days of ICU discharge, approximately 13% of patients in the prolonged weaning group had died—nearly twice the rate observed in the simple weaning group. At 3 months, more than half of these patients remained moderately to severely dependent in activities of daily living, with median Barthel Index scores markedly lower than those in the other groups. These results align with prior evidence linking prolonged ventilation and greater illness severity to post-ICU mortality and disability,[17–21] but they also suggest

that the weaning phase itself may be a critical determinant. The excess early mortality in the prolonged weaning group likely reflects a combination of greater baseline severity, higher rates of ICU-acquired complications, and sustained physiological stress during liberation from mechanical ventilation. Notably, late mortality did not differ significantly among groups, indicating that the vulnerability associated with prolonged weaning was concentrated in the immediate post-ICU period.

The prevalence rates of anxiety, depression and PTSD were similar to those reported in prior studies,[22–24] which have described anxiety in 24–28% of patients, depression in 16–23%, and PTSD in approximately 16% at 6 months post-ICU discharge. In a systematic review and meta-analysis, Rabiee et al[25] also reported suprathreshold in 29–30% of patients across studies. Notably, our study identified a significantly higher burden of anxiety and depression symptoms in the difficult weaning group compared with the other groups. Potential explanations for the finding of a higher occurrence of symptoms of anxiety and depression in the difficult weaning group compared to the prolonged weaning group include: (1) survival bias, as patients with prolonged weaning and more severe mental health impairment may have died before follow-up or been unable to respond; (2) a higher baseline prevalence of potential risk factors for mental health impairment in the difficult weaning group, such as lower household income and, although not statistically significant, a higher proportion of patients with prior history of depression. Accordingly, Davydow et al.[26] found rates of psychiatric history of 11−38% in patients prior to ICU admission, and Rabiee et al.[25] reviewed 15 studies reporting the prevalence of previous psychiatric problems before hospital admission with rates of 10–54%, and concluded that ICU survivors with comorbid psychopathology before and during hospitalization had a higher prevalence of depressive symptoms after discharge. In interpreting these mental health outcomes, we acknowledge that differences in delirium, ICU-acquired infection, ARDS, and baseline risk of death may partly account for observed associations despite multivariable adjustment.

Our study has several limitations. First, approximately two-thirds of eligible survivors did not provide HADS or IES-6 responses at 6 months. Although non-response was relatively balanced among groups, attrition could bias mental health estimates in either direction (e.g., sicker patients being unable to respond or healthier patients being less motivated); therefore, these results should be interpreted with caution. Second, because weaning strategies followed local protocols instead of a standardized study protocol, unmeasured center-level variation may have introduced heterogeneity in outcomes. Third, we did not assess mental health symptoms at 3 months, which could have provided a more comprehensive understanding of the early psychological impact of prolonged weaning. Similarly, functional status at 6 months was not evaluated using the Barthel Index, limiting our ability to track long-term physical recovery. Fourth, we did not collect SOFA scores, a validated and widely used measure of organ dysfunction. Instead, we relied on clinical proxies, which may not fully capture the severity or extent of organ failure. Fifth, we were unable to perform robust subgroup analyses comparing surgical vs. non-surgical patients or patients with and without ARDS, as the small number of patients in different weaning categories within each subgroup would likely preclude accurate statistical analyses and increase the risk of type II error. Finally, the study's eligibility criteria excluded a large proportion of patients (e.g., those with an ICU stay of less than 3 days), which limits the generalizability of findings to less severely ill populations. However, our findings are noteworthy given the scarcity of evidence on how weaning duration influences physical dependence, neuropsychiatric disorders, and mortality in ICU survivors.

Conclusion

ICU survivors who experienced prolonged weaning had higher early post-ICU mortality and greater rates of moderate to severe physical functional dependence at three months after discharge, whereas those with difficult weaning showed higher rates of anxiety and depression at six months. Although these associations may be influenced by survival bias, particularly for mental health outcomes in the difficult weaning group, these results highlight the potential role of standardized weaning protocols in reducing the proportion of difficult and prolonged weaning cases, which could, in turn, lessen their impact on long-term functional dependence and neuropsychiatric outcomes. Future research is still needed to correlate other variables with the presence of these neuropsychiatric disorders and to establish with greater certainty the risk factors and their impact on the outcome of ICU survivors, so that preventive interventions can be applied an also provide these patients with the necessary follow-up after discharge.

CRediT authorship contribution statement

Bruna B. Valer: Literature search, Study design, Analysis of data, and Manuscript preparation.

Cassiano Teixeira: Data collection, Study design, and Manuscript preparation.

Regis Rosa: Literature search, Data collection, Study design, and Review of manuscript

Daniel Sgarzela: Analysis of data.

Gilberto Friedman: Study design, Analysis of data, Manuscript preparation and Review of manuscript.

Declaration of Generative AI and AI-assisted technologies in the writing process

We declare non-use of AI.

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Declaration of competing interest

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