Original Article

Clinical outcomes of neurological patients with and without prolonged mechanical ventilation

Desfechos clínicos de pacientes neurológicos com e sem ventilação mecânica prolongada

Lucas Lima Ferreira[1]
Anna Carolina Macedo Sousa[2]
Lilian Cristina Ascencio Sanchez[3]

[1]Corresponding author. União das Faculdades dos Grandes Lagos (São José do Rio Preto), São Paulo, Brazil. lucas_lim21@hotmail.com
[2-3]Faculdade de Medicina de São José do Rio Preto (São José do Rio Preto). São Paulo, Brazil. carolina.macedo.sousa@hotmail.com, lilian.sanchez_@hotmail.com

ABSTRACT | INTRODUCTION: Patients with neurological diseases on mechanical ventilation (MV) are at increased risk of prolonged MV (PMV) due to lowered level of consciousness, abnormal breathing patterns, and inability to protect the airways caused by neurological damage. **OBJECTIVE:** To compare clinical outcomes of neurological patients with or without PVM. **MATERIALS AND METHODS:** This was a retrospective observational documentary study carried out in the neurological ICU of a teaching hospital. The following were collected: age, gender, the pathology that led to hospitalization, presence of comorbidities, simplified acute physiology score (SAPS III), the incidence of PMV, length of stay on MV, length of stay in the ICU, and outcome discharge or death in the unit. Patients were divided into two groups according to the duration of MV, the PMV group and the non-PMV group. **RESULTS:** A total of 212 patients were included, the most prevalent diagnosis in the PMV group was brain tumor resection (27.5%), and in the group without PMV, it was traumatic brain injury (18%). It was found that 10% of these evolved to PMV. There was a prevalence of males in both groups. The PMV group had a significantly higher SAPS III score (p=0.003) than the group without PMV. The PMV group remained significantly longer (p<0.0001) in MV and ICU stay in days than the group without PMV. There was no significant difference (p=1.00) in the ICU outcome of discharge or death between the groups with and without PMV. **CONCLUSION:** The group of patients under PMV spent more time on invasive ventilatory support and remained in the ICU longer than those without PMV. There were no statistical differences in the ICU mortality outcome.

KEYWORDS: Artificial Respiration. Intensive Care Units. Respirator. Weaning.

RESUMO | INTRODUÇÃO: Pacientes com doenças neurológicas sob ventilação mecânica (VM) apresentam maior risco de VM prolongada (VMP) devido ao rebaixamento do nível de consciência, padrões respiratórios anormais e incapacidade de proteção de vias aéreas causados pela lesão neurológica. **OBJETIVO:** Comparar desfechos clínicos de pacientes neurológicos com ou sem VMP. **MATERIAIS E MÉTODOS:** Tratou-se de um estudo observacional documental retrospectivo, realizado na UTI neurológica de um hospital escola. Foram coletados: idade, sexo, patologia que motivou a internação, presença de comorbidades, valor do *simplified acute physiology score* (SAPS III), incidência de VMP, tempo de permanência em VM, tempo de permanência na UTI e desfecho alta ou óbito na unidade. Os pacientes foram divididos em dois grupos, de acordo com a duração da VM: o grupo VMP e o grupo sem VMP. **RESULTADOS:** Foram incluídos 212 pacientes. O diagnóstico mais prevalente no grupo VMP foi a ressecção de tumor cerebral (27,5%) e no grupo sem VMP foi o traumatismo cranioencefálico (18%). Verificou-se que 10% desses evoluíram para VMP, houve prevalência do sexo masculino em ambos os grupos. O grupo VMP apresentou escore SAPS III significativamente maior (p=0,003) que o grupo sem VMP. O grupo VMP permaneceu tempo, em dias, significativamente maior (p<0,0001) em VM e em internação na UTI que o grupo sem VMP. Não houve diferença significativa (p=1,00) no desfecho alta ou óbito da UTI entre os grupos com e sem VMP. **CONCLUSÃO:** O grupo de pacientes sob VMP esteve mais tempo em suporte ventilatório invasivo e permaneceu mais tempo internado na UTI que o grupo sem VMP. Não houve diferenças estatísticas no desfecho mortalidade na UTI.

PALAVRAS-CHAVE: Respiração Artificial. Unidades de Terapia Intensiva. Desmame do Respirador.

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Introduction

According to the literature, 40% of patients admitted to the intensive care unit (ICU) undergo invasive mechanical ventilation (MV)[1], of these, 20% are patients with acute neurological disorders, such as central nervous system dysfunction, trauma or coma, these being the main reasons for the need for invasive ventilatory support.[2]

Most patients under MV need short periods of ventilatory support, but a minority demand prolonged MV (PMV), defined as a period longer than 24 hours or more than 96 consecutive hours[3], or even more than seven days.[4] Loss et al.[5] and Chelluri et al.[6] used the definition of PVM as greater than or equal to six hours/day for 21 days. Thus, there is heterogeneity of definitions of PMV in the literature. Therefore, for the present study, the definition of PMV was used as greater than seven days in neurosurgical patients. PMV is directly associated with increased early mortality and, in the long term, worse quality of life, greater demands, and expenditures on health care.[7]

The incongruity in the definitions and criteria of PMV generates a variation in the literature regarding epidemiological data and clinical outcomes.[8] Some literary evidence indicates an incidence of PVM between 3-14%.[9,10] There is an important gap of robust epidemiological data of patients in PVM admitted to Brazilian ICUs, mainly due to the lack of specialized weaning units.[4]

Furthermore, patients with neurological diseases undergoing MV are at increased risk of ventilator-associated pneumonia (VAP), tracheotomies, prolonged time on ventilatory support and have a worse outcome in the ICU.[11,12] These risk factors in neurological patients occur due to anatomical lesions of the central nervous system, which can cause changes in cerebral compliance, resulting in a lowered level of consciousness, abnormal breathing patterns and inability to protect the airways.[11]

In this context, identifying the prevalence and the results of patients under PMV in a neurological ICU becomes preponderant to outline prevention and coping strategies for this condition. Thus, this study aimed to compare clinical outcomes of neurological patients with or without PMV. Moreover, as a specific objective, to assess the incidence of PMV. The present study hypothesizes that neurological patients who remain in PMV will have worse clinical outcomes, such as longer hospital stays and higher mortality in the ICU.

Material and Methods

A retrospective observational documentary study was carried out at the Neurological ICU on the 7th floor of the Hospital Base of the Regional Medical School Foundation (FUNFARME), in the city of São José de Rio Preto - SP, Brazil, with data for the period of June 2014 to April 2020.

Data were collected from the Ventilatory Weaning Book of the Physiotherapy Service and from electronic clinical records via the MVPEP® system of patients in the neurological ICU of that hospital. Data collection was carried out in May and June 2020. The primary clinical outcome was mortality in the unit, and the secondary outcome was the length of stay in the ICU.

Data from patients aged 18 years or over who had been under MV for more than 24 hours in the ICU were included in the study. However, medical records of patients with known neuromuscular disease, in addition to those with incomplete or inaccurate data on the duration of ventilation before admission to the ICU or who had restriction or suspension of therapeutic measures during the ICU stay, were excluded from the study.

For this study, PMV was defined as invasive ventilatory support for more than seven days, based on evidence from the literature that indicates that for surgical patients, a time longer than 48 hours can already be defined as PMV.[13] Patients were divided into two groups, based on the duration of MV, the group with prolonged ventilation, that is, the group that remained on MV for seven days or more and the group without prolonged ventilation, that is, the group that remained for less than seven days in MV.

Data such as age, gender, the pathology that led to hospitalization, presence of comorbidities such as hypertension, diabetes mellitus, alcoholism, smoking, among others, simplified acute physiology score (SAPS III), length of stay in days in MV, length of stay in the ICU in days, and outcomes at the unit such as discharge or death, in a form structured by the researchers.

The SAPS III score is a tool consisting of 20 assessment components when the patient is admitted to the ICU. The score components are demographic information, admission reasons, physiological variables, and health conditions before hospitalization. For each component, a value is assigned according to the gravity of the physiological system. The total score ranges from 16 to 217 points.[14,15]

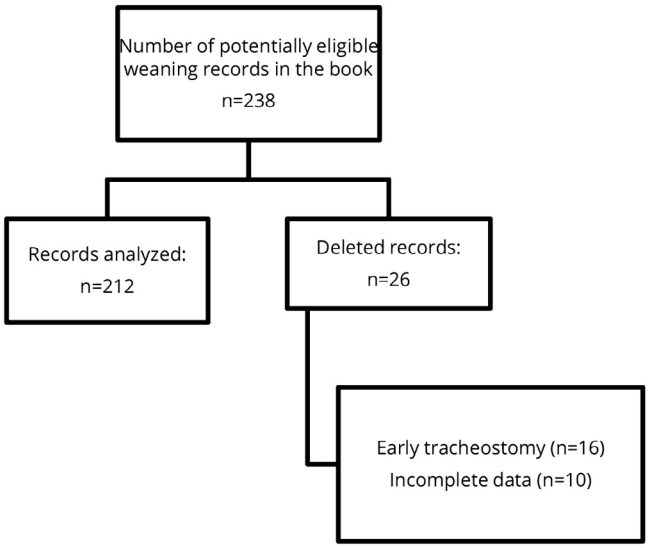
The work followed the ethical principles established in Resolution n.º 466/2012 of the National Health Council and was submitted to the Research Ethics Committee of the União das Faculdades dos Grandes Lagos – UNILAGO (CAAE: 31914620.8.0000.5489) and approved under opinion n.º 4,062,514. Furthermore, the waiver of the free and informed consent form was requested and authorized by the ethics committee, given the methodological documental design of the study.

Statistical analysis was performed descriptively, in which continuous variables were presented as mean ± standard deviation or median (interquartile range), and categorical variables were described as percentages and frequencies. Data normality was analyzed using the Kolmogorov-Smirnov test. Inferential statistical analysis was performed using the unpaired Student's t-test or the Mann-Whitney test to compare continuous variables and Fisher's exact test to compare categorical variables. For this, the Statistical Package for Social Sciences (SPSS) program was used, values of $p \leq 0.05$ were considered statistically significant.

Results

238 records of ventilatory weaning were found in the weaning book of the physiotherapy service, of which 212 were included (Figure 1).

Figure 1. Sample selection flowchart



There was a 10% incidence of PMV (n=21) and a prevalence of males in both groups with a statistically significant difference between the groups without PMV and with PMV (p=0.03) between males and females. In addition, the group with PMV had a significantly higher SAPS III score (p=0.003) than the group without PMV (Table 1). Among the most prevalent admission diagnoses, traumatic brain injury (18% / n=21) was found in the group without PMV and brain tumor resection (27.5% / n=11) in the group with PMV. In addition, there were other diagnoses in the groups without (21% / n=25) and with PMV (15% / n=6), which included spinal arthrodesis, septic shocks of meningococcal origin, hydrocephalus, etc. (Table 1).

Table 1. Sociodemographic and clinical characteristics of patients

Variable	Group without PMV	Group with PMV	p-valor
Sample	n=190 (90%)	n=22 (10%)	–
Sex – M/F	M=112 (59%)	M=18 (82%)	**0.03**†
	F=78 (41%)	F=04 (18%)	
Age (years)	51,1±15,7	48,9±16,3	0.53*
SAPS III	54,3±17,4	68,8±14,6	0.003*
Diagnosis			
Stroke	n=15 (13%)	n=8 (20%)	
Aneurysmal SAH	n=17 (14,5%)	n=7 (17,5%)	
Brain tumor resection	n=16 (13,5%)	n=11 (**27,5%**)	
Multiple injury	n=15 (13%)	n=3 (7,5%)	
Traumatic brain injury	n=21 (**18%**)	n=5 (12,5%)	
Drainage of brain hematoma	n=9 (8%)	–	
Others	n=25 (21%)	n=6 (15%)	

PMV: prolonged mechanical ventilation; M: male; F: female; SAH: subarachnoid hemorrhage; SAPS: Simplified acute physiology score; †Fisher's exact test; *unpaired t test.

Among the most prevalent comorbidities, systemic arterial hypertension was found in both groups without (36%) and with PMV (35%), followed by alcoholism and smoking (Table 2).

Table 2. Most prevalent comorbidities in patients in the groups with and without PMV

Comorbidities	Group without PMV		Group with PMV	
	n	%	n	%
Systemic arterial hypertension	43	**36**	14	**35**
Diabetes mellitus	13	11	4	10
Obesity	3	2,5	2	5
Dyslipidemias	6	5	-	-
Chronic kidney disease	3	2,5	2	5
Alcoholism	25	21	10	25
Smoking	25	21	12	30

PMV: prolonged mechanical ventilation.

It was found that the group with PMV remained a median MV time of seven days, while the group without PMV had a median of only one day. Regarding the outcome variable, length of stay in the ICU, the group with PMV remained significantly longer (p<0.0001) than the group without PMV (Table 3).

Table 3. Comparison of outcome variables for groups with and without PMV

Variable	Group without PMV	Group with PMV	p-valor
Length of stay in the ICU (days)	8 [2–40]	17,5 [8–49]	**<0.0001***
Weaning from MV	S=150 (79%)	S=14 (64%)	0.11†
(Success/Failure)	F=40 (21%)	F=8 (36%)	
Outcome in the ICU	Di=162 (85%)	Di=19 (86%)	1.00†
(Discharge/Death)	De=28 (15%)	De=3 (14%)	

MV: mechanical ventilation; PMV: prolonged mechanical ventilation. S: success; F: failure; Di: discharge; De: death. *Mann-Whitney test. †Fisher's exact test.

Discussion

In the present study, the incidence of PMV in patients with neurological diseases was low, and when comparing the outcome variables, there was no significant difference in mortality and high between the groups. However, it was identified that the PMV group had a longer stay in the ICU than the group without PMV.

The low incidence of PMV in neuropathic patients in the present study is similar to data described in other countries such as Argentina (14%), United Kingdom (6%)16, and Brazil (10%).[5,17,18] The cited incidences literature did not relate directly to neurological patients. Furthermore, in the evidence available in the literature, PMV was defined as MV greater than 21 days. These studies used heterogeneous samples in relation to clinical diagnoses.

Muzaffar et al.[4] identified in a prospective cohort of one year, 49 patients (29%) who remained on PMV, with a mean age of 49.7 years, 63% male, with a median time on MV of 39 days and a 39-day ICU stay, and weaning from ventilation was successful in 87%. These findings are similar to those of the present research in some points, such as the prevalence of males and the age of the patients. However, they were contrary in others, such as the incidence of PMV, the length of stay on MV, the percentage of successes in weaning, and the length of stay at the unit, which were shorter than in the current study in the study mentioned above. This can be explained by the homogeneity of patients and pathologies included in the present study, where eligibility for neurological patients only showed similar epidemiological characteristics.

A multicenter prospective cohort study[5] identified an incidence of 10% of patients who required PMV, defined as greater than 21 days, with a significant increase in ICU mortality and longer hospital stay after ICU discharge.[5] This evidence is identical to the present study concerning the incidence of PMV. However, they were contrary about the period defined as PMV and the mortality outcome, as in our study PMV was defined as a need for MV greater than or equal to seven days, and there was no difference in ICU mortality between the groups with and without VMP. The lack of statistical significance in the mortality rates of the present study, compared to the study mentioned above, can be explained in part by the time defined as PMV between the two studies, making it clear that the longer the time spent on invasive ventilatory support, the greater the chances of worse outcomes.

Loss et al.[5] identified some complications associated with an increased risk of PMV, such as muscle weakness, pressure ulcers, nosocomial bacterial sepsis, candidemia, pulmonary embolism, and hyperactive delirium, but these were not evaluated in the current research.

A recent study[19] evaluated the association between extubation failure and functional outcomes in patients with acute neurological diseases. Patients had a median age of 58.5 years, 60.5% male. Extubation failure occurred in 12.8% of patients. Extubation failure was associated with longer ICU and hospital stays and worse functional outcomes at six months, as measured by the modified Rankin score.[17]

Piotto et al.[13] evaluated the predictors for PMV, defined as greater than 48 hours, in patients undergoing coronary artery bypass graft (CABG) surgery and identified an incidence of PMV in 3% of these patients. In addition, the authors identified age, chronic renal failure, chronic obstructive pulmonary disease, CABG associated with other procedures, and clamping time as independent predictors of PMV. These authors' findings contradict those found in the present study regarding the incidence of PMV, but comparisons are not plausible due to differences in the definition of PMV between studies and in the type of surgical patients included in each study.

According to previous studies, 38-68% of patients on PMV successfully evolve in ventilatory weaning.[20-22] Damuth et al.[16] conducted a systematic review with meta-analysis of 124 studies of patients with respiratory failure on PMV, defined as MV greater than 14 days, of which 50% were successfully weaned. These pieces of evidence corroborate the present study in which 64% of patients under PMV successfully completed ventilatory weaning.

Weaning protocols for patients under conventional MV do not apply to patients under PMV.[23] There is some evidence on weaning strategies in patients undergoing PMV.[4,22,24,25] There is no uniformity of protocols and the time required to complete the ventilatory weaning, which demonstrates the difficulty in predicting the success of weaning from MV. This fact demonstrates the gap present in the current literature and the need for further studies on the subject.

Some limitations inherent in this study refer to the lack of long-term follow-up of patients to identify important clinical outcomes such as post-discharge mortality, the absence of stratification of the use of medications such as sedatives, vasoactive drugs and neuromuscular blockers, as they are they directly interfere in the evolution of weaning, as well as the retrospective methodological design of the study, which allowed failures in the inclusion of data, due to incomplete systems and did not include specific statistical analyzes to identify predictors associated with PMV in neurological patients. In addition, another limitation refers to the variety of definitions of PMV in the literature, which makes comparisons between studies difficult.

One can mention as clinical implications or strengths of the present study, the design of the epidemiological profile of patients with neurological diseases that progress to PMV, in order to outline intervention strategies aimed at this group of patients in order to accelerate the weaning process ventilatory and reduce the incidence of morbidity and mortality.

Conclusion

The incidence of PMV was 10% in patients with neurological diseases included in this study. The group of patients under PMV remained in the ICU longer than the group without prolonged ventilatory support. Nevertheless, there were no statistical differences in the outcome of mortality and discharge from the ICU.

Authors' contributions

Ferreira LL, Sousa ACM, and Sanchez LCA participated in the conception, design, search, and statistical analysis of research data, interpretation of results, writing of the scientific article.

Conflicts of interest

No financial, legal, or political conflicts involving third parties (government, companies, and private foundations, etc.) have been declared for any aspect of the submitted work (including, but not limited to grants and funding, advisory board participation, study design, preparation manuscript, statistical analysis, etc.).

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