



## ORIGINAL ARTICLE

## Epidemiology of mechanical ventilation in Argentina. The EpVAR multicenter observational study<sup>☆,☆☆</sup>



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### KEYWORDS

Mechanical ventilation;  
Intensive Care Unit;  
Epidemiology;  
Weaning mechanical ventilation;  
Mortality

### Abstract

**Objective:** To describe mechanical ventilation (MV) practices in Argentina, and to explore factors associated with ICU mortality in this population.

**Design:** A prospective, multicenter, observational study was carried out.

**Setting:** Intensive Care.

**Patients:** We enrolled patients above 18 years old admitted to any of the participating ICUs requiring invasive MV for at least 12 h since the admission to the healthcare institution, including MV initiation in emergency department, operating room or other hospitals.

**Interventions:** None.

**Variables:** All variables were classified into three categories: variables related to demographic and clinical factors before the MV, factors related to the first day on MV, and factors related to events happening during the MV (complications and weaning from MV). Mechanical ventilation weaning and mortality were classified according to WIND.

**Results:** The primary analysis included 950 patients. The main indication for MV was acute respiratory failure (58% of patients). Initial ventilation mode was volume control-continuous mandatory ventilation in 75% of cases. ICU and hospital mortality were 44.6% and 47.9%

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respectively. The variables identified as independent predictors of mortality in ICU were age (OR 3.48 IC 95% 1.22–11.66;  $p = 0.028$ ), failure to implement NIV before MV (OR 2.76 IC 95% 1.02–7.10;  $p = 0.038$ ), diagnosis of sepsis (OR 2.46 IC 95% 1.09–5.47;  $p = 0.027$ ) and extubation failure (OR 4.50 IC 95% 2.05–9.90;  $p < 0.001$ ).

**Conclusions:** The present study allowed us to describe the characteristics and clinical course of the patients who received mechanical ventilation in Argentina, finding as the main result that mortality was higher than that reported in international studies.

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## PALABRAS CLAVE

Ventilación mecánica;  
Unidad de Cuidados  
Intensivos;  
Epidemiología;  
Destete de la  
ventilación mecánica;  
Mortalidad

## Epidemiología de la ventilación mecánica en Argentina. Estudio observacional multicéntrico EpVAr

### Resumen

**Objetivo:** Describir las prácticas relacionadas a ventilación mecánica (VM) en Argentina y explorar los factores asociados a la mortalidad en UCI en esta población.

**Diseño:** Se realizó un estudio observacional, prospectivo, multicéntrico.

**Ámbito:** Unidad de Cuidados Intensivos.

**Pacientes:** Incluimos pacientes mayores de 18 años ingresados en las UCI participantes que requirieron VM invasiva durante al menos 12 horas desde el ingreso a la institución de salud.

**Intervenciones:** Ninguna.

**Variables:** Todas las variables se clasificaron en tres categorías: variables relacionadas con factores demográficos y clínicos antes de la VM, factores relacionados con el primer día de VM y factores relacionados con los eventos ocurridos durante la VM (complicaciones y destete de la VM). El destete de la ventilación mecánica y la mortalidad se clasificaron según WIND (Weaning according to a New Definition).

**Resultados:** El análisis primario incluyó a 950 pacientes. La principal indicación de VM fue insuficiencia respiratoria aguda (58% de los pacientes). El modo de ventilación inicial fue ventilación mandatoria continua con control de volumen en el 75% de los casos. La mortalidad en UCI y hospitalaria fue del 44,6% y 47,9% respectivamente. Las variables identificadas como predictoras independientes de mortalidad en UCI fueron edad (OR 3,48 IC 95% 1,22–11,66;  $p = 0,028$ ), fracaso en la implementación de VNI antes de VM (OR 2,76 IC 95% 1,02–7,10;  $p = 0,038$ ), diagnóstico de sepsis (OR 2,46 IC 95% 1,09–5,47;  $p = 0,027$ ) y fracaso de la extubación (OR 4,50 IC 95% 2,05–9,90;  $p < 0,001$ ).

**Conclusiones:** El presente estudio permitió describir las características y evolución clínica de los pacientes que recibieron ventilación mecánica en Argentina, encontrando como principal resultado que la mortalidad fue mayor a la reportada en estudios internacionales.

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## Introduction

Invasive mechanical ventilation (MV) is a fundamental tool for the management of patients with acute respiratory failure (ARF). The existing evidence shows that a number of interventions designed to prevent ventilator-associated lung injury and optimize weaning have a strong impact upon the duration of mechanical ventilation and mortality.<sup>1–5</sup> Several epidemiological studies have investigated the different tendencies in the use of mechanical ventilation throughout the world.<sup>6–8</sup> In addition, these studies have afforded useful information leading to updates in routine clinical practice referred to patients subjected to MV.

In Latin America, the epidemiological data on the implementation patterns referred to MV are limited. To our knowledge, no studies to date have provided epidemiological information on a general population of

patients subjected to invasive mechanical ventilation in Argentina.<sup>9,10</sup> To address this issue, we have described the mechanical ventilation practices in this country and explored the factors associated with mortality in the Intensive Care Unit (ICU) in patients of this kind.

## Material and methods

A prospective, multicenter observational study was carried out between 1 September 2019 and 31 December 2019 in different ICUs in Argentina. The original study protocol was approved by the Ethics Committee of the *Sociedad Argentina de Terapia Intensiva* (ref. no. 1 2019) and was registered with clinicaltrials.gov (no. NCT04107467). Each participating center in turn received the corresponding approval from its own local Ethics Committee. The study was carried out following the Strengthening the Reporting of Observational

Studies in Epidemiology (STROBE) guidelines for observational cohort studies.<sup>11</sup>

We included patients over 18 years of age admitted to any of the participating ICUs and who required invasive MV during at least 12 h from the time of admission to the participating institution; patients having started mechanical ventilation outside the ICU in a different Department (emergency or operating room); and patients admitted from a different institution and transferred to the ICU of one of the centers participating in the study. We excluded patients admitted to pediatric ICUs, anesthesia recovery or resuscitation wards, or coronary units. The patients were only enrolled in the study on the occasion of their first admission to the ICU. Patients with more than 10% of missing data referred to key study parameters used to generate the predictive model were excluded from the analysis.

### Data collection and processing

The data were collected on a daily basis between 8:00 a.m. and 11:00 a.m. by the co-investigator of the study assigned to each participating Unit, or by any member of the study team, using customized case report forms (CRFs). The information obtained was entered into an online database using the REDCap application (Research Electronic Data Capture, Vanderbilt University, TN, USA) at Centro del Parque (Buenos Aires, Argentina) to guarantee data protection and confidentiality according to the recommendations of the Declaration of Helsinki.<sup>12,13</sup> All those in charge at the participating centers had access to the website containing all the study documentation, including the operational definition of the variables, the operations manual, and the corresponding links to facilitate calculation of the patient severity scores.

In order to minimize missing information, a mobile offline data loading application was habilitated. The patients were followed-up until day 28 from enrollment or until hospital discharge or death – whichever occurred first.

All the principal investigators of the study (GAP, EG, MA, EN and JHD) provided support and feedback via e-mail to the local co-investigators of the participating centers, and a telephone line was made available for consultations and immediate support.

The local co-investigators were in charge of training their teams in data compilation and quality control. Data consistency was assessed on a daily basis (missing information, atypical values, data entry error) by one of the principal investigators (EN). Whenever further information was needed, the rest of the members of the research team (GAP, EG, MA, EN and JHD) contacted the investigators of the participating centers as required.

### Statistical analysis

The primary endpoint was mortality in the ICU. All the variables were classified into three categories: variables related to demographic and clinical factors before MV; variables related to the first day of MV; and variables related to the events occurring during MV (complications and weaning from MV). Weaning from mechanical ventilation and mortality were classified according to the definition of the

WIND study.<sup>14</sup> Continuous variables were reported as the mean and standard deviation (SD), or as the median and interquartile range (IQR 25–75), as required. Normal data distribution was assessed with the Shapiro-Wilk test. Categorical variables in turn were reported as absolute values and percentages. The Student t-test or Mann-Whitney U-test was used to compare continuous variables as required. The chi-square test or Fisher exact test was used to compare categorical variables. In order to identify mortality predictors, we adjusted a logistic regression model with key predictors as independent variables and mortality in the ICU as dependent variable. Relationships between outcome and exposure were initially explored by univariate analysis. The variables selected for the multivariate analysis were those considered to be relevant by the authors and/or which obtained  $p < 0.1$  in the univariate analysis. Linearity between the numerical covariables and the dependent variable was evaluated.<sup>15</sup> In the absence of linearity, stratification was carried out as described in the literature.<sup>6,9,10</sup> In the case of multilevel categorical variables, the level of reference was selected according to the least probability related to the dependent variable. Sensitivity testing was performed using different criteria to select the final model (best-subset, backward, recursive feature elimination).<sup>15,16</sup> The model with the smallest value of the Akaike information criterion (AIC) was selected. All the selected variables were reported with their corresponding odds ratio (OR) and 95% confidence interval (95%CI). The goodness of fit of the final model was analyzed using the Hosmer-Lemeshow test, and its discriminating capacity was assessed based on the area under the curve (AUC) and 95%CI. Lastly, the predictive capacity of the model was evaluated through K-fold cross-validation (10-fold).<sup>16</sup> As this was an observational study, we decided to include as many patients as possible, with no pre-established sample size. The data were analyzed using the R version 3.6.2 package.<sup>17</sup>

## Results

### Participating Units and included patients

A total of 142 Units in 22 provinces and the city of Buenos Aires (Fig. 1) participated in the study. This represented 14% of all the ICUs in the country. Of the participating Units, 48.5% belonged to public hospitals ( $n = 461$ ) and 51.5% to private institutions ( $n = 489$ ).<sup>18</sup> The primary analysis comprised 950 patients, of which 41.1% ( $n = 390$ ) were females; the mean age was  $58.1 \pm 18.5$  years, and the mean SAPS II score was  $46.8 \pm 16.7$ . The main indication of MV was acute respiratory failure (58%;  $n = 555$ ). The baseline characteristics are described in Table 1.

### Ventilatory parameters

The initial ventilation mode was continuous demand ventilation with volume control (VC-CMV) in 75% of the cases ( $n = 677$ ) (Fig. 2). Independently of the ventilation mode used, the tidal volume ( $V_t$ ) was  $<8$  ml/kg of predicted body weight in 75.1% of the cases ( $n = 663$ ), with a positive end-expiratory pressure (PEEP) of  $<8$  cmH<sub>2</sub>O in 64.8% of the cases ( $n = 585$ ). The plateau pressure was measured in over 80% of

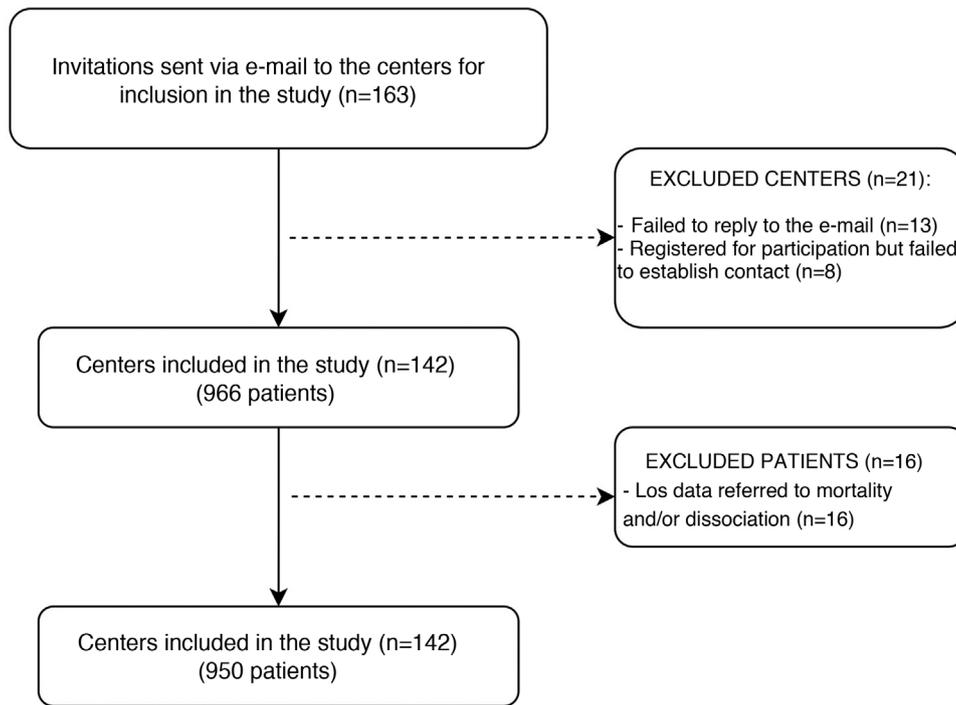


Figure 1 Study flowchart.

### Ventilation mode used on each day during mechanical ventilation

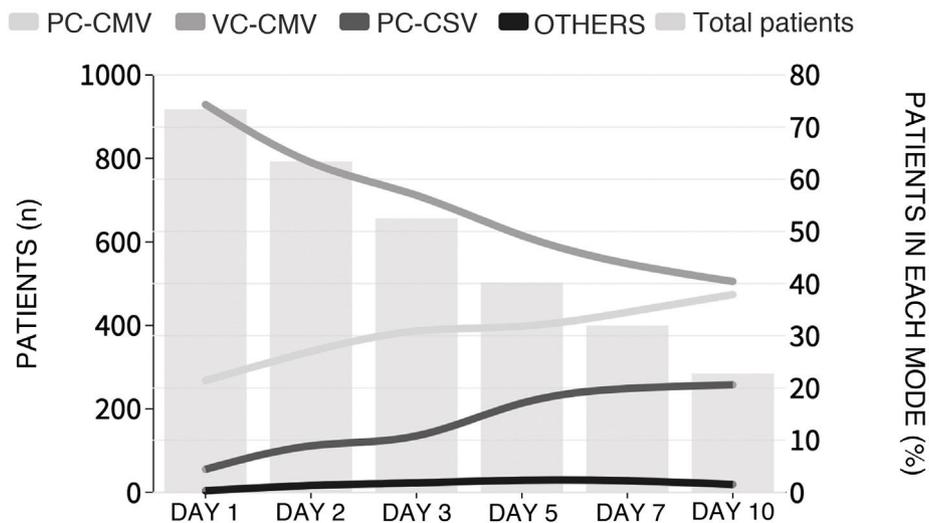


Figure 2 Proportion of patients subjected to mechanical ventilation according to selected mode during admission to the ICU. Each line represents the proportion of patients in each mechanical ventilation mode over follow-up. The height of the bars represents the number of patients each day in the ICU. PC-CMV: Pressure control-Continuous mandatory ventilation; VC-CMV: Volume control-Continuous mandatory ventilation; PC-CSV: Pressure control-Continuous spontaneous ventilation.

the patients (n = 781). The mean plateau pressure (SD) and the driving pressure were  $18 \pm 4.6$  and  $11.2 \pm 3.9$  cmH<sub>2</sub>O, respectively. On the first day of mechanical ventilation, the peak pressure, the plateau pressure and the driving pressure were significantly lower among the survivors ( $p < 0.001$ ) (Fig. 3 and Appendix B Electronic Supplementary material A).

#### Variables related to complications during mechanical ventilation

Sepsis was recorded in 29.7% of the cases (n = 281), ventilator-associated pneumonia (VAP) in 17.6% (n = 166) and acute respiratory distress syndrome (ARDS) in 12.9% (n = 122). Sedation was administered as a continuous infusion

**Table 1** Characteristics of the patients admitted to the ICU. Demographic parameters and variables referred to the start of mechanical ventilation.

Variables	Total (n = 950)	Live (n = 526)	Deceased (n = 424)	OR (95%CI)	p-Value	Missing data n (%)
Female gender, n (%)	390 (41.1)	221 (42.0)	169 (39.9)	0.91 (0.70–1.19)	0.502	0 (0)
Age, mean (SD)	58.1 (18.5)	55.0 (19.3)	62.1 (16.6)	1.02 (1.01–1.03)	<0.001	0 (0)
BMI, mean (SD), kg	27.8 (6.8)	27.9 (6.9)	27.7 (6.6)	1.00 (0.97–1.02)	0.681	0 (0)
Charlson index, median [IQR] (n = 892)	4 [1–6]	3 [1–5]	4 [2–6]	1.19 (1.13–1.25)	<0.001	58 (6.1)
SAPS II, mean (SD) (n = 879)	46.8 (16.7)	44 (17.2)	50 (17.6)	1.02 (1.01–1.03)	<0.001	71 (7.5)
Geographical region*	-	-	-	-	-	-
CABA, n (%)	268 (28.2)	167 (31.7)	101 (23.8)	1 (1.09–2.15)	N/A	
PBA, n (%)	289 (30.4)	150 (28.5)	139 (32.8)	1.53 (1.09–2.15)	0.013	
Center, n (%)	186 (19.6)	93 (17.7)	93 (21.9)	1.65 (1.13–2.42)	0.009	0 (0)
Cuyo, n (%)	57 (6.0)	37 (7.0)	20 (4.7)	0.89 (0.48–1.61)	0.713	
North, n (%)	105 (11.1)	57 (10.8)	48 (11.3)	1.39 (0.88–2.20)	0.155	
Patagonia, n (%)	45 (4.7)	22 (4.2)	23 (5.4)	1.73 (0.91–3.28)	0.091	
Type of institution	-	-	-	-	-	-
Public	461 (48.5)	254 (54.7)	210 (45.3)	1 (0.74–0.24)	N/A	0 (0)
Private	489 (51.5)	273 (55.8)	216 (44.2)	0.96 (0.74–0.24)	0.769	
Time to admission to the ICU from hospital admission, days, median [IQR]	0 [0-2]	0 [0-1]	0 [0-3]	1.04 (1.02–1.07)	<0.001	0(0)
NIV failure before MV, n (%)	102 (10.7)	43 (8.2)	59 (13.9)	1.82 (1.20–2.77)	0.005	0 (0)
Reasons for MV, n (%)	-	-	-	-	-	-
ARF	555 (58.4)	296 (31.1)	260 (27.3)	1 (0.73–1.88)	NA	0 (0)
ARF in CLD	79 (8.3)	39 (4.1)	41 (4.3)	1.17 (0.73–1.88)	0.509	
Coma	301 (1.7)	182 (19.1)	120 (12.6)	0.76 (0.57–1.01)	0.056	
NMD	15 (1.6)	10 (1)	5 (0.5)	0.57 (0.18–1.63)	0.313	
PaO <sub>2</sub> /FIO <sub>2</sub> prior to MV, mean (SD) (n = 312)	236.7 (136.0)	265.0 (142.0)	208.0 (123.6)	0.99 (0.98–0.99)	<0.001	638 (67.1)

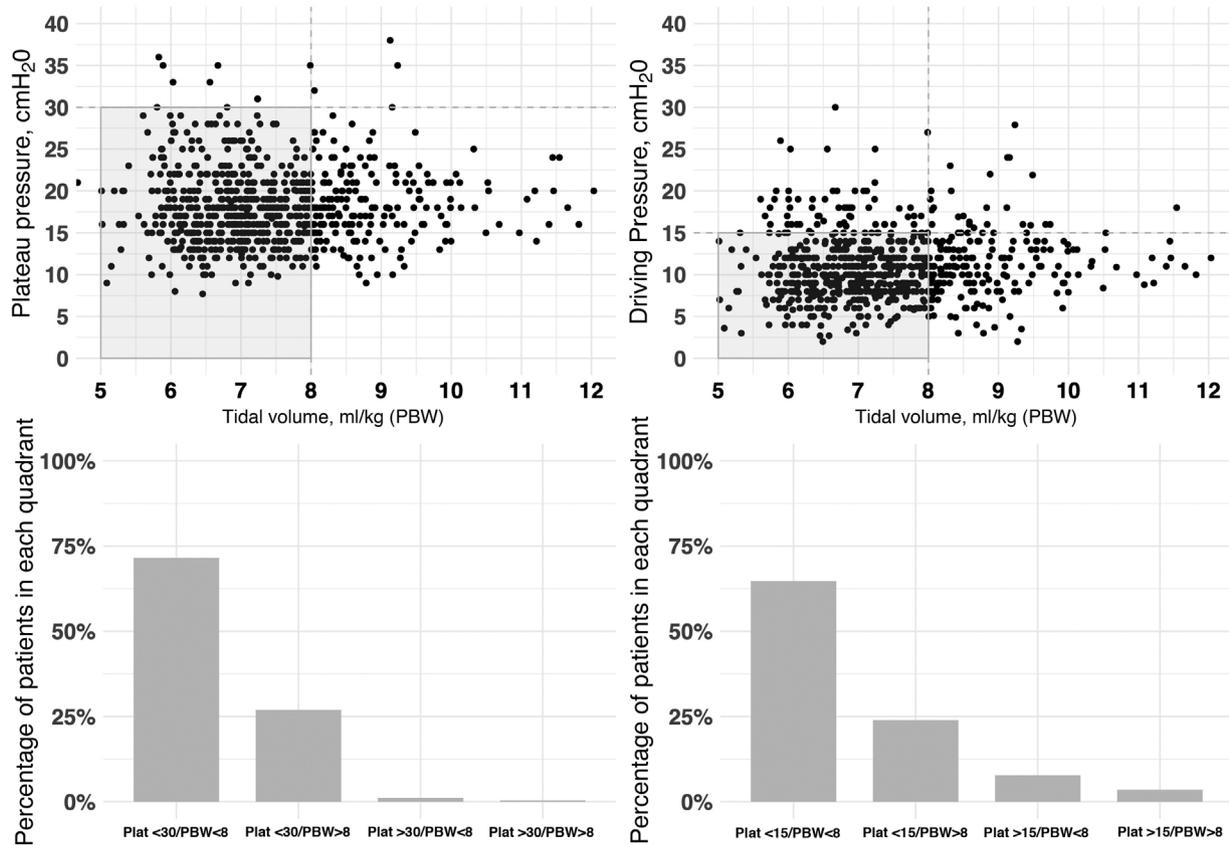
BMI: body mass index; SAPS II: Simplified Acute Physiology Score; ICU: Intensive Care Unit; NIV: noninvasive mechanical ventilation; MV: mechanical ventilation; ARF: acute respiratory failure; CLD: chronic lung disease; NMD: neuromuscular disease.

\* Geographical regions: CABA: city of Buenos Aires; PBA: province of Buenos Aires; Center: Cordoba, Santa Fe and Entre Rio; Cuyo: Mendoza, San Luis and San Juan; North: Tucuman, Salta, Misiones, Chaco, Corrientes, Santiago del Estero, Jujuy, Formosa, Catamarca and La Rioja; Patagonia: Rio Negro, Neuquen, Chubut, La Pampa, Santa Cruz and Tierra del Fuego.

in 86% of the patients (n = 815), and neuromuscular block (NMB) was used in 11.4% (n = 108). Fifty-seven percent of the patients (n = 540) presented the failure of at least one organ, with cardiovascular failure being the most frequent presentation (37.8%; n = 359) (Table 2).

### Weaning from mechanical ventilation and endpoints

With regard to weaning from MV, a total of 38.5% (n = 365) of the patients were weaned within the first 24 h after their



**Figure 3** Relationship between plateau pressure, driving pressure and tidal volume (ml/kg) expressed according to predicted body weight (PBW), during the first day of ventilatory support. The figure represents the distribution of tidal volume corresponding to day 1 versus the plateau pressure (left: figure at top and bottom) and tidal volume versus driving pressure (right:) for each patient. Most of the patients were within the limits of protective ventilation, defined as plateau pressure  $\leq 30$  cmH<sub>2</sub>O, driving pressure  $\leq 15$  cmH<sub>2</sub>O and tidal volume  $\leq 8$  ml/kg predicted body weight. The data are referred to the first day of mechanical ventilation.

first spontaneous breathing test (SBT) (Fig. 4). The median [IQR] number of days of MV was 6 [2–13]. The T-tube test was used as SBT in 72.5% (n = 419) of the cases. Extubation failed in 16% (n = 75) of the patients. Noninvasive ventilation (NIV) was used to prevent extubation failure in 6.8% of the cases (n = 65). The proportion of patients subjected to tracheostomy was 22.4% (n = 213) (Appendix B Electronic Supplementary material B).

The mortality rate in the ICU and in hospital was 44.6% (n = 424) and 47.9% (n = 455), respectively, with a median (IQR) of 10 [5–20] and 17 [9–30] days of stay in each case (Appendix B Electronic Supplementary material B). Among the patients with ARF as the main indication of MV, the highest mortality rates corresponded to sepsis (62.6%, n = 62), ARDS (60%, n = 15) and pneumonia (58%, n = 52). Of all the variables considered in the univariate model and entered in the multivariate model, those identified as independent predictors of mortality in the ICU were age (over 70 years), the implementation of NIV before MV, the diagnosis of sepsis, and extubation failure before 72 h (Table 3).

## Discussion

This multicenter study provides new epidemiological data on mechanical ventilation in Argentina. The key findings can be

summarized as follows: mortality in the ICU and in hospital among patients subjected to MV in this country is higher than reported at international level.<sup>6,8,10</sup> Both the days of MV and the need for reintubation were high. With regard to the potential predictors, patient age, the diagnosis of sepsis, the use of NIV before MV, and extubation failure were correlated to increased mortality.

In coincidence with the observations of international studies, the most frequent reasons for starting MV were acute respiratory failure and coma.<sup>6,7,19</sup>

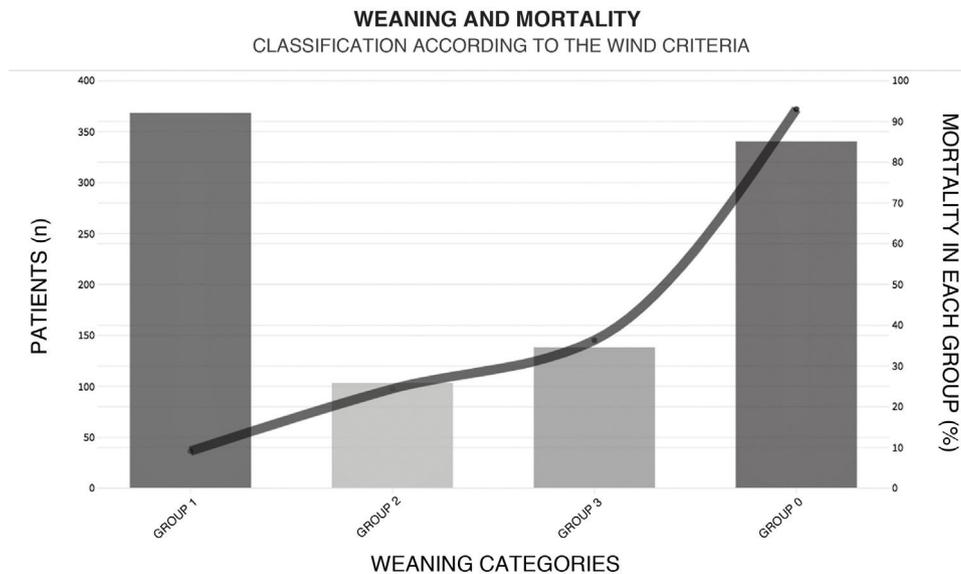
In their epidemiological study, Esteban et al.<sup>8</sup> found VC-CMV to be the most widely used ventilation mode at the start of MV. Our own results are consistent with this; however, the percentage use of VC-CMV doubled that reported in the aforementioned study (EpVar 2019: 74.9%; Esteban 2013: 38%).

Based on the results of our study, it can be concluded that the mortality rate among patients on MV for over 12 h is high in Argentina. Although the severity of the patients at the time of admission could explain this high percentage, other multicenter studies have revealed a mortality rate up to 15% lower in patient cohorts with similar characteristics in terms of variables such as age, SAPS II score upon admission and the reasons for MV.<sup>6,8,10</sup> In a population of similar characteristics, Peñuelas et al. attributed mortality in

**Table 2** Variables referred to complications during mechanical ventilation.

Variables	Total (n = 950)	Live (n = 526)	Deceased (n = 424)	OR (95%CI)	p-Value	Missing data n (%)
VAP, n (%) (n = 945)	166 (17.6)	87 (16.6)	79 (18.7)	1.15 (0.82–1.61)	0.402	5 (0.5)
Sepsis, n (%) (n = 945)	281 (29.7)	108 (20.7)	173 (41.0)	2.67 (2.01–3.57)	<0.001	5 (0.5)
ARDS, n (%) (n = 945)	122 (12.9)	39 (7.5)	83 (19.7)	3.04 (2.04–4.60)	<0.001	5 (0.5)
Prone, n (%) (n = 945)	41 (4.3)	13 (2.5)	28 (6.6)	2.79 (1.45–5.63)	0.003	5 (0.5)
Sedation in CIP, n (%) (n = 945)	815 (86.2)	434 (83.0)	381 (90.3)	1.91 (1.29–2.85)	0.001	5 (0.5)
Use of NMB, n (%)	108 (11.4)	45 (8.6)	63 (14.9)	1.86 (1.25–2.81)	0.003	0 (0)
WAICU (n = 946)	–	–	–	–	–	–
Yes, n (%)	142 (15.0)	93 (17.8)	49 (11.6)	1	N/A	4 (0.4)
No, n (%)	361 (38.2)	276 (52.8)	85 (20.1)	0.58 (0.38–0.89)	0.013	
Delirium (n = 945)	–	–	–	–	–	–
Yes, n (%)	168 (17.8)	126 (24.1)	42 (10.0)	1	N/A	
No, n (%)	360 (38.1)	266 (50.9)	94 (22.3)	1.06 (0.70–0.63)	0.786	5 (0.5)
Without organ failure, n (%) (n = 950)	410 (43.2)	323 (61.4)	87 (20.5)	0.16 (0.12–0.22)	<0.001	10 (1)
Cardiovascular failure, n (%) (n = 950)	359 (37.8)	124 (23.6)	235 (55.4)	4.03 (3.06–5.33)	<0.001	10 (1)
Liver failure, n (%) (n = 950)	105 (11.1)	33 (6.3)	72 (17.0)	3.06 (2.00–4.77)	0.005	10 (1)
Renal failure, n (%) (n = 950)	302 (31.8)	86 (16.3)	216 (50.9)	5.31 (3.95–7.20)	<0.001	10 (1)
Hematological failure, n (%) (n = 950)	119 (12.5)	31 (5.9)	88 (20.8)	4.18 (2.74–6.4)	0.003	10 (1)
Neurological failure, n (%) (n = 950)	139 (14.6)	48 (9.1)	91 (21.5)	2.72 (1.88–3.99)	<0.001	10 (1)

VAP: ventilator-associated pneumonia; ARDS: acute respiratory distress syndrome; CIP: continuous infusion pump; NMB: neuromuscular blockers; WAICU: weakness acquired in the ICU (See electronic Supplement C).

**Figure 4** Weaning according to the WIND classification<sup>14</sup> and mortality within each group.

GROUP 0: Never entered weaning; GROUP 1: Weaning ended within 24 h after the first spontaneous breathing test (SBT); GROUP 2: Weaning ended between the second day and the first week after the first SBT; GROUP 3: No successful weaning 7 days after the first SBT.

This figure shows the number of patients (height of the bars) for the corresponding weaning group according to the WIND classification, and mortality (solid line).

the ICU to changes in clinical practice associated with the adoption of a protective ventilation strategy allowing the end-expiratory airway pressure to be maintained below the level considered to be harmful for the lungs.<sup>20</sup> However, ventilator adjustment during the first day does not appear to be associated with mortality. In the same way as in other inter-

national reports, we found variables such as Vt and PEEP to be within ranges that could be regarded as acceptable in terms of lung protection.<sup>6,7,10</sup> We also found that the values recorded for monitoring parameters such as driving pressure and plateau pressure were low.<sup>21–23</sup> A high plateau pressure recording rate was observed (90%); this percentage was far

**Table 3** Multiple logistic regression analysis for variables associated with mortality.

Predictors	Mortality		
	OR	95%CI	p-Value
Age			
Age <40 years	Ref	Ref	Ref
Age 40–70 years	0.98	0.33–3.33	0.972
Age >70 years	3.48	1.22–11.66	0.028
Renal failure	2.08	0.90–4.68	0.079
Use of NIV before MV	2.76	1.02–7.10	0.038
Sepsis	2.46	1.09–5.47	0.027
Liver failure	2.76	0.90–7.86	0.064
Extubation failure (72 h)	4.50	2.05–9.90	<0.001

NIV: noninvasive ventilation; MV: mechanical ventilation; CI: confidence interval; OR: odds ratio; area under the receiver operating characteristic (ROC) curve for predicting mortality (95%CI): 0.79 (0.71–0.87). Hosmer–Lemeshow  $\chi^2$ : 8.654 (df = 8); p = 0.3804.

higher than that recorded in the LUNG SAFE study (42%), and could reflect the interest in lung protection.<sup>23</sup> This could be explained in terms of increased adherence to the use of protective mechanical ventilation protocols.<sup>24</sup>

We found four variables to be independently associated with increased mortality: age (over 70 years), the diagnosis of sepsis, the use of NIV before MV, and extubation failure. In coincidence with the study published by Estenssoro et al. in 2018,<sup>25</sup> the need for mechanical ventilation in patients diagnosed with sepsis was an independent predictor of mortality. Unfortunately, we were unable to obtain information on the implementation of NIV as the first ventilatory support strategy, since the patients with successful initial NIV were not documented. Furthermore, in relation to extubation failure, the patients did not seem to have been prematurely extubated, since our median days on MV were similar to that reported by Esteban in 2013.<sup>8</sup> However, the percentage of patients that were extubated in the first 24 h of the first SBT was lower than the figure reported in the WIND study (38.5% versus 57%).<sup>14</sup> The T-tube SBT was used in a large proportion of patients (72.5%), despite the latest publications in relation to the process of weaning from MV, which point to this strategy as being more demanding than others for patients subjected to MV.<sup>26–29</sup> It is known that sedation can have a negative impact upon ventilation-free days and on the days of ICU stay.<sup>30,31</sup> According to the variables recorded by our investigators, many of the patients were subjected to deep sedation at some time during MV, even though almost half of the subjects had no organ failure. This may indicate an excessive use of sedation in our population – a fact that could have influenced the outcomes. Furthermore, another aspect that could indicate excessive use of sedatives is the fact that in our study the VC-CMV mode was the most frequently used ventilation mode, even on the tenth day of MV – while other studies report the use of spontaneous modes in preference to other modes before the end of the first week of MV.<sup>7–9</sup>

Although a confirmatory study specifically designed for the purpose would be needed, we believe that the high percentage of mortality recorded in our study could reflect

the obstacles found throughout Argentina regarding the routine implementation of protocols referred to general patient care, such as those described in the PADIS guides.<sup>32</sup> However, these results in relation to mortality could also be explained by differences in human and technological resources that were not considered in our study, or may reflect the findings of the LUNG SAFE and ICON studies, in which medium to low-income countries showed greater mortality due to sepsis and ARDS than high-income countries.<sup>33,34</sup> Complex organizational and economic factors in medium to low-income countries account for the poorer outcomes in patients admitted to the ICU. Profound inequities, defined as systematic, unfair and avoidable differences in health determinants such as socioeconomic level, demographics and geography, can generate differences in access to healthcare services among different population groups – a situation which in turn has an impact upon health-related outcomes.<sup>35</sup> Furthermore, in medium to low-income countries, the health systems tend to be divided into public and private sectors, and this sustains the differences based on socioeconomic level, affecting healthcare – particularly in the critical care setting.<sup>36</sup> Of note in our study is the fact that we did not observe differences in mortality between these two healthcare sectors. This is possibly because we also did not observe structural differences in terms of human resources – with a similar distribution in the proportions physician/patient, nurse/patient and ventilatory assist specialist/patient in the two the mentioned sectors (unpublished data).

Our study has limitations. Firstly, this is an analysis of prospectively compiled clinical data corresponding to a large range of ICUs in our country, with different conditions regarding the patients and clinical practices – some of which could have influenced the results obtained. However, our analysis took this into account in the model to minimize possible bias related to the variables. Nevertheless, although use was made of multivariate models, the presence of unmeasured confounding factors cannot be discarded. Secondly, missing data are a problem in studies of this kind, since they may lead to misinterpretation of the results. To reduce this impact, we eliminated those records with over 10% missing data referred to the relevant study variables. Lastly, the data compiled in Argentina might not be representative of other medium to low income countries or other regions.

## Conclusions

The present study describes the characteristics and clinical evolution of patients subjected to mechanical ventilation in Argentina. The main finding was a mortality rate higher than that reported in the international literature. Patient age, the diagnosis of sepsis, the use of noninvasive mechanical ventilation as an initial support measure, and extubation failure, were identified as independent mortality risk factors – some of them being potentially modifiable. The information obtained in this study is essential for our specialty and constitutes the basis for the development of care protocols seeking to optimize the management of patients on MV and thus improve the care outcomes in our country.

## Conflicts of interest

GAP has received funding for teaching programs from Medtronic Argentina and for teaching programs from Vapotherm Inc., USA.

EG is currently employed by Medtronic Argentina.

The mentioned sponsors had no role in the designing of the study, data collection and analysis, or in preparation of the manuscript.

## Contributions of the authors

GAP conceived and designed the study; collected, interpreted and analyzed the data; conducted the literature search; and drafted the manuscript. EG, MA and JHD designed the study; collected the data; and conducted a critical review of the manuscript. EN designed the study, collected and analyzed the data; and conducted a critical review of the manuscript.

All the authors approved the final version of the manuscript and assumed responsibility for all aspects of the study in order to guarantee that the issues referred to the accuracy and integrity of any part of the study were reviewed and adequately resolved.

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## Appendix B. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:<https://doi.org/10.1016/j.medine.2022.05.002>.

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