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Characteristics Of Patients Weaning From Invasive Mechanical Ventilation. A Multicenter Study

Correspondence to:
María Lucía Giménez.
Lic. Kinesióloga Fisiatra
Dirección postal: San Luis 3139 8 A CP 1186 CABA. Argentina.
e-mail: gimenezmarialucia@hotmail.com
Teléfono: 1131391682

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Authors: María Lucía Giménez[1], Gabriel Alejandro Verde[2], Iris Gloria Salvati[3], Walter Ariel Tozzi[1, 2], Adriano Javier Cura[2], Silvina Borello[3], Paola Bustamante[1], Sacha Alexis Virgilio[2], Marco Bezzi[3]

[1]Hospital de Clínicas José de San Martín, Ciudad Autónoma de Buenos Aires, Argentina.
[2]Hospital General de Agudos Parmenio Piñero, Ciudad Autónoma de Buenos Aires, Argentina.
[3]Hospital General de Agudos Donación Francisco Santojanni, Ciudad Autónoma de Buenos Aires, Argentina.

Abstract

The weaning process includes the release from the ventilatory support and endotracheal tube. It is classified into simple, difficult and prolonged, according to its difficulty and duration.

The purpose was to describe the epidemiological characteristics of patients successfully weaned from invasive mechanical ventilation and establish associations between the different types of weaning and the variables influencing the evolution of these characteristics associated with mortality.

We conducted a multicenter, prospective, longitudinal, analytical cohort study in three intensive care units of the Autonomous City of Buenos Aires, Argentina. We included patients who required invasive mechanical ventilation for more than 12 hours and were successfully weaned from it.

The variables to be analyzed were: type of weaning, amount of days the patients received invasive mechanical ventilation, extubation failure and length of stay and mortality in the intensive care unit.

The prevalence of simple, difficult or prolonged weaning was 52.2% (95/182), 25.8% (47/182) and 22% (40/182), respectively. The average of days the patients received invasive mechanical ventilation increased to 3.5 every time the category changed (*B Coefficient*: 3.5; *SE [standard error]* = 0.6). Patients with extubation failure presented a higher risk of prolonged weaning (*OR [odds ratio]* = 23; *CI [confidence interval]* = 95%: 3.55-149.45). No association was found between mortality and type of weaning (OR = 0.68; 95% CI: 0.31-1.51).

In conclusion, the type of weaning was not associated with mortality in the intensive care unit. The extubation failure, tracheostomy and presence of delirium were associated with a larger amount of days receiving invasive mechanical ventilation.

Key words: epidemiology, invasive mechanical ventilation, mortality, weaning

Introduction

Mechanical ventilation (MV) is one of the therapeutic pillars of intensive care medicine[1]. The generalized use of invasive mechanical ventilation (IMV) was first considered after the sudden decrease in mortality during the poliomyelitis epidemic of 1952. From that moment until now, MV has become the most common procedure for the management of critically ill patients[2]. Golingher et al predict an 80% increase in the incidence of IMV for 2026, in comparison with the prevalence obtained in 2004[1].

The weaning process is essential to the care of critically ill patients. It includes the process of

releasing the patient from the ventilatory support and endotracheal tube, and usually represents between 40 and 50% of the duration of the IMV[3, 4].

In 2007, the International Consensus Conference on Weaning suggested a new classification based on the difficulty and duration of the weaning period, considering it as simple, difficult and prolonged[3].

This new classification is exclusively based on expert opinion, and until now only few studies have used it[3-6].

In 2010, Funk et al reported an increase in hospital mortality within patients with prolonged weaning (32%), as compared with patients with simple weaning (13%). On the other hand, no associations have been established when comparing the mortality rate in the intensive care unit (ICU) between simple and difficult weaning[5, 6].

There are few published studies that address this topic with the new classification[4-6]. No published data are known about patients weaning from IMV in our country.

The purpose of this study was to describe the epidemiological characteristics of patients who successfully weaned from IMV in three intensive care units (ICUs) of the Autonomous City of Buenos Aires (Ciudad Autónoma de Buenos Aires, CABA). To a lesser extent, associations were established between the types of weaning according to the new classification and the variables that influenced their evolution in relation to mortality.

Materials and Methods

We conducted a multicenter, prospective, longitudinal, analytical cohort study using daily registration of patients admitted to adult ICUs of three CABA hospitals during the period between August 1, 2013 and January 31, 2014.

We included patients older than 18 years old who had been admitted to the ICUs of the three participating hospitals and had required IMV for more than 12 hours, meeting the criteria for successful IMV weaning. Such criteria included: success in the spontaneous breathing trial (SBT), without requiring reintubation, and/or restoration of mechanical ventilation within the first 48 hours after extubation[3].

The hospitals that participated in the study were: Hospital General de Agudos "Parmenio Piñero", Hospital de Clínicas "José de San Martín" and Hospital General de Agudos "Donación Francisco Santojanni". They have polyvalent, medical-surgical intensive care units, on-staff physicians and nurses and 24-hour physician and physiotherapist on call. One of the intensive care units participating in this study belongs to a hospital that is a neurosurgical and trauma referral center.

For the epidemiological analysis, data from the following variables were defined and collected:

* Prevalence: The relationship between the amount of patients that were included and the total of patients requiring IMV for more than 12 hours.
* Birth data and personal history: Name and surname, age, gender and Acute Physiology And Chronic Health Evaluation II (APACHEII) score at ICU admission.

The following conditions were considered as indications for IMV:[7-9]

- Worsened chronic respiratory insufficiency (CRI) (chronic obstructive pulmonary disease [COPD], asthma or other).
- Acute respiratory insufficiency (ARI) (acute respiratory distress syndrome [ARDS], post-surgery [PS], congestive heart failure, aspiration, pneumonia, sepsis, multiple trauma, cardiac arrest or other).
- Coma (metabolic, intoxication, stroke, traumatic brain injury or other).
- Neuromuscular disease.

The following intercurrent conditions associated with IMV were recorded:

- *Barotrauma:* Presence of pneumoperitoneum, pneumomediastinum, subcutaneous emphysema, pneumothorax and pneumopericardium, associated with the implementation of IMV[7-9].
- *Delirium:* Evaluated on a daily basis, whenever the patient presented a value between < 3 and > 4, according to the Richmond Agitation and Sedation Scale (RASS). The Chilean validation of the Confusion Assesment Method Intensive Care Unit (CAM- ICU)[10] was used. Patients with history of mental illness documented in the medical record were excluded.11
- *Intensive care unit-acquired weakness (ICUAW):* Patients with more than 72 hours of IMV who were capable of responding to 5 instructions (eye opening, mouth opening, sticking out their tongue, squeezing their hand, eye tracking test) were assessed once a week using the Medical Re-

search Council (MRC) scale. ≤ 48 point-scores[12] were considered positive for ICUAW.

– *ARDS:* According to the criteria of the American-European Consensus Conference regarding the ARDS[13].
– *Ventilator-associated pneumonia (VAP):* Assessed through the Clinical Pulmonary Infection Score (CPIS), whenever it was suspected. ≥ 6 point- scores were considered compatible with VAP[14].

Weaning: Patients were classified into three groups. *Simple*: Those who started weaning until they achieved a successful extubation having undergone only one SBT. *Difficult*: Those requiring up to three SBTs or up to 7 days after the first SBT was conducted in order to achieve a successful extubation. *Prolonged*: Those who failed more than three SBT attempts or required more than 7 days after the first SBT was conducted in order to achieve weaning[3].

Regarding the chosen weaning method, the following was considered: Gradual reduction of ventilatory support, SBT (with T-piece, continuous positive airway pressure [CPAP] of 5 cmH_2O, PSV ≤ 7 cmH_2O with or without positive end-expiratory pressure [PEEP]) or a combination of both methods.

Weaning failure: Failure of the SBT or the need to reintubate and/or restore the patient´s ventilation within the first 48 hours after extubation.3

Tracheostomy (TQT): IMV rate and day in which it was performed. The following temporary variables and mortality values were recorded:

Length of stay in the ICU: The number of days was counted from the admission day (day 0) up to the day the patient was dismissed from the unit.

Hospital length of stay: From hospital admission (day 0) up to the day the patient was dismissed or referred to another institution or up to the patient´s death.

Total IMV days: Counted since it began to be used at our ICUs (day 0) up to successful weaning, referral to another institution or the patient´s death.

Weaning days: Counted from day 0 (zero) as the day in which the team of professionals decided to begin with the process until the day in which the patient was successfully weaned and extubated.5 Also the duration of IMV before weaning was counted, from the moment it was first provided at the ICUs (day 0) until the day the professionals decided to begin with the weaning process.

The time of IMV devoted to weaning was calculated by relating the weaning days with total IMV days.

In order to calculate mortality at the ICU and the hospital, patients who died both at the unit and the hospital were taken into account.

The following variables were analyzed 28 days after admission to the ICU: Total IMV days, ICU mortality and length of stay.

Follow-up of patients was conducted from ICU admission until January 31, 2014, hospital discharge, referral or death.

Patients dismissed from the ICU who were readmitted to the unit requiring IMV were considered as new patients.

During 4 weeks before patient inclusion, records were implemented in order to prepare the work team.

According to the statistical analysis that was conducted, the variables presenting a normal distribution were informed as mean ± SD (standard deviation), whereas those presenting an asymmetrical distribution were expressed as median with minimum-maximum range.

An analysis was conducted comparing the 3 weaning groups. For the categorical variable analysis, the Pearson´s Chi-Squared Test was used, as appropriate. The APACHEII of this group of patients was compared with the Analysis of Variance (ANOVA) Test. The variable "total IMV days" was analyzed with the Median Test.

A multiple linear regression analysis was performed between the variables "type of weaning" and "total IMV days".

A stepwise multinomial logistic regression analysis was conducted, in order to analyze the type of weaning variable in relation to all those variables that obtained $p < 0.10$. Also, the confusion and interaction factors of each variable were assessed.

A value of $p \leq 0.05$ was considered a statistically significant difference. The program SPSS®, v17 was used.

The Ethics Committees of participating hospitals approved the performance of the study and considered it did not imply any risk for the patient or changes in the patient´s evolution. They also believed that due to the design and purpose of the study, the informed consent of participants was not necessary.

Results

57.6% (182/316) of patients finished the weaning process successfully (Figure 1), representing 44.9% of the total IMV days. The main demographic variables are described in Table 1.

The most prevalent indication for IMV was ARI, with 72.5% (132/182). PS was the main cause, with 30.2% (55/182), followed by sepsis/septic shock and pneumonia with 8.8% (16/182) each (Table 1).

As regards intercurrences registered during the study period, we found there was 20.8% (38/182) of mechanical ventilation associated pneumonia (MVAP), with late onset in 25 patients. 62% developed delirium, whereas 29.2% presented ICUAW.

85.2% (155/182) of patients were able to weave from IMV by means of SBT as the only method, 1.6% (3/182) through gradual reduction of the ventilatory support and 13.2% (24/182) through the combination of both methods. The prevalence of simple, difficult and prolonged weaning was 52.2% (95/182), 25.8% (47/182) and 22% (40/182), respectively.

Table 2 describes the epidemiological characteristics and main variables related to the type of weaning.

A multiple linear regression analysis was performed between the variables "type of weaning" and "total IMV days" and we found that the average of days increased to 3.5 every time the weaning category changed (*B Coefficient*: 3.5; SE: 0.6. $p \leq 0.01$).

A multinomial logistic regression analysis was performed using the simple weaning as a reference category. We did not find any statistical association between age and type of weaning (*OR* = 1.01; 95% CI: 0.99-1.04), or between the type of weaning and mortality variables at the ICU (*OR* = 0.68; 95% CI: 0.31-1.51). On the other hand, a statistically significant association was found between the TQT and the type of weaning (*OR* = 7.06*; p* = 0.04*),* that is to say, there is a greater risk every time it goes from simple to difficult weaning or from difficult

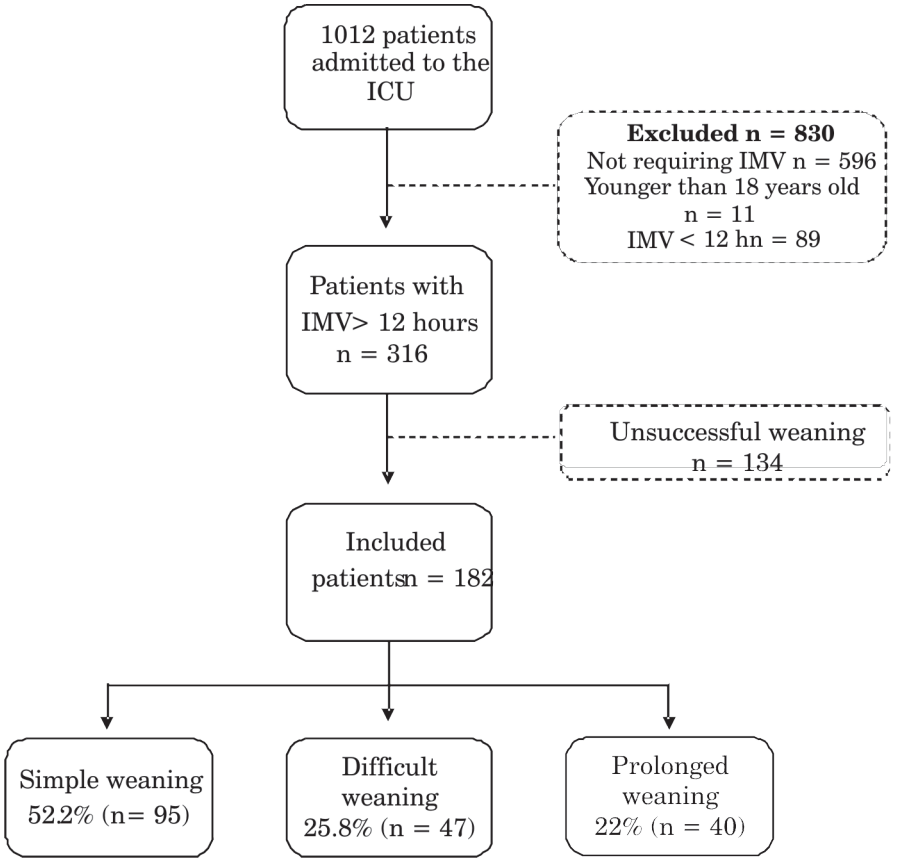

Figure 1. Flow Chart

TABLE 1. Epideiological Characteristics of Patients with IMV

Characteristics of patients with weaning = 182	
Age	
Mean ± SD	57,7 ± 22
Gender	
Female n (%)	97 (53,3%)
Male n (%)	85 (46,7%)
APACHE II	
Mean ± SD	21,25 ± 8,19
Reason for starting with IMV n (%)	
Acute chronic respiratory insufficiency	3,3%
COPD	4 (2,1%)
Asthma	1 (0,5%)
Oher	0
Acute respiratory insufficiency	72,5%
ARDS	3 (1,6%)
Ps	55 (30,2%)
Congestive heart failure	11 (6,5%)
Aspiration	5 (2,7%)
Pneumonia	16 (8,8%)
Sepsis	16 (8,8%)
Multiple trauma	9 (4,9%)
Cardiac arrest	5 (2,7%)
Other	12 (6,6%)
Coma	24,2%
Metabolic	5 (2,7%)
Intoxication/Overdose	2 (1,1%)
S	8 (4,4%)
TBI	15 (8,2%)
Other	15 (8,2%)
ND	0

IMV: invasive mechanical ventilation; APACHEII: Acute Physiology And Chronic Health Evaluation II; SD: standard deviation; COPD: chronic obstructive pulmonary disease; ARDS: acute respiratory distress; PS: post-surgery; S: stroke; TBI: traumatic brain injury; ND: neuromuscular disease.

to prolonged. Another statistical association that was obtained suggests that the risk of presenting difficult weaning increases every time the delirium event is present (OR = 3.2; 95% CI: 1.15-8.92).

The extubation failure variable presented a statistically significant association when it was compared with prolonged weaning (OR = 23; 95% CI: 3.55-149.45). Also, every time the extubation failure variable was present, an increase of 6.32 days was found in the average of IMV days (*B Coefficient:* 6.32; SE 1.28. $p \leq 0.01$). Finally, regarding the extubation failure associated with mortality, it was estimated that the mortality odds at the ICU in subjects who failed extubation was 17.32 times higher in comparison with those subjects who did not fail (OR: 17.32; 95% CI: 3.85-77.86).

Discussion

The prevalence of simple and difficult weaning was similar to the one reported by Funk et al,[5] whereas the prevalence of prolonged weaning was higher than the one reported in the literature[5, 6].

Age and APACHEII values found at the sample are similar among the three groups. However, the severity score reported at the prolonged weaning group was higher than the values published by Sellares in 2010[4]. When comparing median age with the values reported in the literature, it was observed that the statistical estimates that were used differ from those used in this work, thus this comparison is difficult[4-6].

In contrast with the data reported by various authors[5, 6], a statistically significant difference was obtained for the reintubation variable between the types of weaning, and a statistically significant association was found between reintubation and prolonged weaning.

Regarding the TQT rate in the prolonged weaning group, the results of this study contrast with the information reported by Peñuelas et al[6], but coincide with the data published by Funk et al[5].

The study of Frutos Vivar et al15 conducted in a cohort of tracheomized patients, established an OR = 8.77 (95% CI: 6.76-11.37) for TQT every time the reintubation event was present. This finding could be related to the comparisons found in this study, where reintubated patients have greater possibilities to undergo prolonged weaning, and a greater risk of requiring a TQT.

This is the first study to analyze ICUAW and delirium in patients with IMV according to the new weaning classification. Although we couldn´t find any statistical association between these variables regarding the type of weaning, we did find differences among the three groups.

Significant differences regarding mortality have been established in this study between the simple and difficult weaning groups as compared to the prolonged weaning group. The reason for the highest mortality rate found in the prolonged weaning group could be the median weaning days (10.5 days, minimum-maximum range: 7-15). In relation to this, Peñuelas et al[6] report that the probability to die is kept constant regardless of

TABLE 2. Epidemiological Characteristics According to the Weaning Classification

Variable	Simple waning n = 95	Difficult weaning n = 47	Prolonged weaning n = 40	*p* value
Age				
Median (minR-maxR)	53.5 (18-96)	64 (18-88)	62 (18-88)	0.09
Gender				
Female n (%)	51 (53.7)	23 (48.9)	23 (57.5)	0.72
APACHE II				
Mean ± SD	20.8 ± 8.19	19.9 ± 7.11*	22.9 ± 8.5≈∞	N/S
Reason for IMV n (%)				
CRI	2 (2.1)	2 (4.3)	2 (5)	
ARI	66 (69.5)	36 (76.6)	30 (75)	0.61
Coma	27 (28.4)	9 (19.1)	8 (20)	
Median IMV days (IQR)				
IMV total days	2 (1-4)	7 (3-10)	18 (13-24)	
IMV days before weagning				
Weaning days	0	2 (1-4)	10.5 (7-15)	
Intercurrences				
MVAP n (%)	6 (6.3)	12 (25.5)	20 (50)	
Early	4 (4.2)	4 (8.5)	5 (12.5)	
Late	2 (2.1)	8 (17)	15 (37.5)	
ICUAW (n = 106) n (%)	3 (6.1)	11 (39.3)	17 (58.6)	
DeliRIUM (n = 134) n (%)	30 (42.9)	28 (77.8)	25 (89.3)	< 0.01
Extubation failure n = 156				
n (%)	0	7 (16.3)	14 (66.7)	< 0.01
TQT				
n (%)	1 (1.1)	4 (8.5)	25 (62.5)	< 0.01
Mortality				
n (%)	12 (12.63)	6 (12.7)	12 (30)	0.01

MinR-MaxR: minimum range - maximum range; APACHE II: Acute Physiology And Chronic Health Evaluation II; SD: standard deviation; IMV: invasive mechanical ventilation; IQR: interquartile range; CRI: chronic respiratory insufficiency; ARI: acute respiratory insufficiency; MVAP: mechanical ventilation associated pneumonia; DAUCI: intensive care unit-acquired weakness: polyneuropathy in critically ill patients; TQT: tracheostomy.∞ p value of intergroup.*Simple weaning vs. difficult weaning p = 0.54.≈Difficult weaning vs. prolonged weaning p = 0.08. ∞Simple weaning vs. prolonged weaning p = 0.17.

the type of weaning until the seventh day after it began, which is the moment the mortality risk increases. In contrast to various authors[5, 6] and despite the differences found in this study between the groups as regards mortality, we were not able to establish a statistical association.

The mortality rate that was found is lower than the aforementioned one according to the APACHEII value obtained in each weaning group. This finding could be related to the fact that such score is an objectivation of the severity at ICU admission, but maybe it does not take into account the difficulty of the weaning process or the evolution of the patient during his stay at the unit.

In this study we were able to establish an association between extubation failure and mortality at the ICU. These results are related to the findings of Sellares et al,4 which establish that the risk of dying at the ICU increases every time the patient fails extubation with an OR = 5.34 (95% CI: 3.14-9.09). To sum up, we may conclude that this study allowed us to know the characteristics and evolution of patients who underwent IMV for more than 12 hours and were able to wean successfully

in three ICUs of the Autonomous City of Buenos Aires, Argentina.

We haven´t found any association between mortality and type of weaning. The reasons for starting to use IMV do not impact on the type of weaning to be developed, whereas the risk of being tracheomized increases every time the type of weaning changes category. Extubation failure, TQT and delirium are associated with an increase in IMV days.

So, it is necessary to extend this study with the purpose of increasing the number of analyzed patients and establishing associations between ICUAW and delirium among the different weaning subgroups, given the fact that, as of today, this information has not been reported in the literature.

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