ramr
Revista Americana de Medicina Respiratoria

ORIGINAL ARTICLE

RAMR 2017;1:63-70
ISSN 1852 - 236X

Mechanical ventilation in patients with acute hypoxemic respiratory failure

Correspondence:
Gustavo Plotnikow.
gplotnikow@gmail.com

Received: 09.08.2016
Accepted: 11.14.2016

Authors: Plotnikow Gustavo[1], Pratto Romina[1], Tiribelli Norberto[2], Ilutovich Santiago[2], Andrich Emilia[1], Gómez Ramiro[1], Quiroga Corina[1], D'Annunzio Pablo[1], Vasquez Daniela[1], Intile Dante[1], Avaca Graciela[2], García Andrea[2], Noval Diego[2], Desmery Pablo[1]

[1]Sanatorio Anchorena. Ciudad Autónoma de Bs. As.
[2]Sanatorio de la Trinidad Mitre. Ciudad Autónoma de Bs. As.

Abstract

Objective: To describe the clinical characteristics of patients with AHRF (without ARDS) hospitalized in the ICU who require IMV. To evaluate the association between mortality and different variables.

Design: Inception cohort.

Scope: This study was conducted in two Argentine ICUs from the private health sector between 07/01/2013 and 12/31/2014.

Patients: From a consecutive sample of 2526 patients, 229 individuals aged 18 and upwards were included in the study; they were admitted to the ICU requiring IMV for over 24 hours and developed AHRF (without ARDS).

Primary endpoints: Demographic variables and variables associated with the number of days with IMV and at the ICU were documented, as well as the initial setting of the respirator, monitoring variables and evolution at discharge. Likewise, the number and type of complications developed during the period of IMV were documented.

Results: 70.7% of admissions were for medical reasons. SAPS II score was 42. The period of IMV and at the ICU was higher in patients with delirium ($p<0.0001$ in both).

In the logistic regression model adjusted by the severity of hypoxemia, age (OR 1.02; 95% CI 1.002-1.04: $p = 0.033$) and shock (OR 2.37; 95% CI 1.12-5: $p = 0.023$) acted as independent predictors of mortality.

Conclusions: In this group of patients who required IMV for over 24 hours and who developed AHRF (without ARDS) there was a demographic distribution similar to that described in other reports. Mortality was not associated with the severity of hypoxemia, whereas shock and age were independent predictors of mortality.

Key words: mechanical ventilation; acute respiratory failure; acute hypoxemic respiratory failure; intensive care unit

Introduction

Invasive mechanical ventilation (IMV) is an essential tool to assist patients with acute respiratory failure and is one of the distinctive procedures at intensive care units (ICUs). In this regard, current clinical trials have evidenced that procedures aimed at preventing lung injury induced by IMV[1, 2], and to improve weaning strategies[3, 4, 5], have a significant impact on mortality and the length of time with IMV.

Acute hypoxemic respiratory failure (AHRF) requires IMV, which is not exclusive to patients with acute respiratory distress syndrome (ARDS). ARDS is a clinical syndrome characterized by the emergence of bilateral pulmonary infiltrates, new respiratory symptoms or the aggravation of these symptoms and a partial pressure of O_2 / fraction of inspired O_2 ($PaO2/FiO_2$) ratio with values below 300[6]. It can be assumed that the "AHRF (without ARDS)" diagnosis, a condition many patients with IMV present with, can be arrived at with the same criteria, excluding radiographic criteria[7]. Acute respiratory failure is a frequent condition that approximately 56% of the patients at the ICU have; it is associated with a significant amount of extrapul-

monary factors and a high rate of mortality among critical patients[8]. However, the information linked to IMV implementation in patients with AHRF in our country is limited.

This study was created to describe the characteristics and clinical evolution of patients hospitalized at the ICU with AHRF (without ARDS) who require IMV and, at the same time, to evaluate the association between population mortality globally and by age groups according to the severity of hypoxemia, the length of time with IMV, the length of stay at the ICU, the reason for IMV, the number and type of complications presented, the driving pressure within the first 24 hours (DP24hs) and the evolution of the PaO_2/FiO_2 ratio during the first 72 hours.

Materials and methods

A retrospective case series study conducted in two health centers from Ciudad Autónoma de Bs. As. (two monovalent, referral ICUs from the private health sector with a total of 32 beds) between July 1st, 2013 and December 31st, 2014. For this study, AHRF was defined as the emergence of new respiratory symptoms 24 hours after starting IMV, or the aggravation of these symptoms, PaO_2/FiO_2 ratio with values below 300, absence of new infiltrates in front chest X-rays and absence of echocardiographic evidence of left ventricular failure. All patients aged 18 and upwards who were admitted to the ICU during this period and who required IMV for over 24 hours and developed AHRF (without ARDS) were included.

Patients with incomplete daily monitoring records on ventilation and those who at the beginning of or during IMV developed ARDS were excluded.

– Once the first 24 hours of IMV had elapsed, the following variables were prospectively documented for each patient in a specially designed database: age, gender, severity s*core* during the first 24 hours after admission (*Simplified Acute Physiology Score II* [SAPS II]), type of admission to de ICU, reason for IMV, length of time with IMV, length of stay at the ICU, evolution at discharge (weaned "YES-NO" during ICU stay, survived "YES-NO"), initial setting variables of the respirator (tidal volume [TV] and positive end-expiratory pressure [PEEP]) and monitoring variables (DP24hs and PaO_2/FiO_2 evolution during the first 72 hours). At the same time, the number and type of complications developed during the period of IMV were documented in this datasheet, which were the following:
– Pulmonary thromboembolism (PTE) diagnosed by computed axial tomography angiography.
– Acute myocardial infarction (AMI) diagnosed by changes in the electrocardiogram and in cardiac enzymes (high-sensitivity troponin >15.6 pg/mL).
– Cardiac arrest (CA). Asystole or atrial fibrillation with an effective response to cardiopulmonary resuscitation.
– ICU-acquired weakness (ICUAW), defined as a *Medical Research Council scale*[9] (MRC) value < 38/60.
– ARDS development defined according to the Berlin definition[6].
– Barotrauma, defined as the presence of pneumothorax in the front chest X-ray.
– Multiple organ dysfunction[10] (MOD), defined as the presence of two or more of the following:
  a. Respiratory dysfunction: PaO_2FiO_2 ratio ≤ 400.
  b. Hematological dysfunction: Platelets (platelet count/mm^3) ≤ 150000.
  c. Liver dysfunction: Bilirubin (mg/dL) between 1.2-1.6.
  d. Cardiac dysfunction: mean blood pressure < 70mmHg.
  e. Neurological dysfunction: *Glasgow coma scale* between ≤14.
  f. Renal dysfunction: Creatinine (mg/dL) ≥1.2.
– Unprogrammed extubation.
– Delirium was defined by positive scores using the *Confusion Assessment Method for the ICU* (CAM-ICU)[11].
– Shock: mean blood pressure <70mmHg despite of adequate fluid resuscitation, with perfusion alterations that can include lactic acidosis, oliguria or acute altered mental status, but that are not necessarily limited to these[12].
– Severe renal failure, defined as those patients who required dialysis.
– Ventilator-associated pneumonia (VAP), defined as the presence of a new infiltrate in front X-rays, fever, increased level of leukocytes, changes in the characteristics of secretions, and bacterial culture of tracheal aspirate $>10^5$ CFU[13].

Continuous data are presented as mean and standard deviation (SD), or as median and interquartile range [IQR_{25-75}], depending on their

frequency distribution. Categorical data are presented as absolute values and/or percentages. The association between potential risk factors and outcome variables was assessed using the chi-square test, the Kruskal-Wallis test or the Mann-Whitney test. Factors linked to severity were included in a logistic regression model using mortality as an outcome variable. The power of association was presented as Odds Ratio and 95% Confidence Interval. For the analysis, the sample was classified into 3 severity groups according to the PaO_2/FiO_2 ratio from the first 24 hours (severe: $PaO_2/FiO_2 \leq 100$; moderate: $PaO_2/FiO_2 > 100$ and ≤ 200 and mild: $PaO_2/FiO_2 > 200$ and ≤ 300). A $p < 0.05$ value was considered significant. For the statistical analysis we used IBM's SPSS software 20.0.

Ethical considerations: the study was approved by the teaching and research committee from both institutions and informed consent forms were not required since it was a retrospective study of data prospectively collected at the ICU as part of the daily management of patients. In any case, patient data was codified in order to achieve anonymity.

Results

Out of the 2526 patients admitted to the participating ICUs during the study period, 229 were included (see algorithm 1) for analysis: 58.1% (n=133) were males, with an average age of 62.8 (± 18.2) years, and 70.7% (n=162) of the admissions were for medical reasons. Median SAPS II score was 42 [31-57]. The main reasons for IMV were: pneumonia 20.5% (n = 47), shock 20.1% (n = 46) and postoperative ARF 18.3% (n = 42). The length of time with IMV was 7 [3-15] days, and the length of stay at the ICU was 14 [6.2-24] days (table 1).

The initial setting for IMV was with a 7.79 [7-8] ml/kg TV and with a PEEP of 7 [5-8] cmH_2O. After 24 hours of starting IMV, the DP24hs was 12 [10-15] cmH_2O and the PaO_2/FiO_2 ratio was 225 [187.4-261] (table 2).

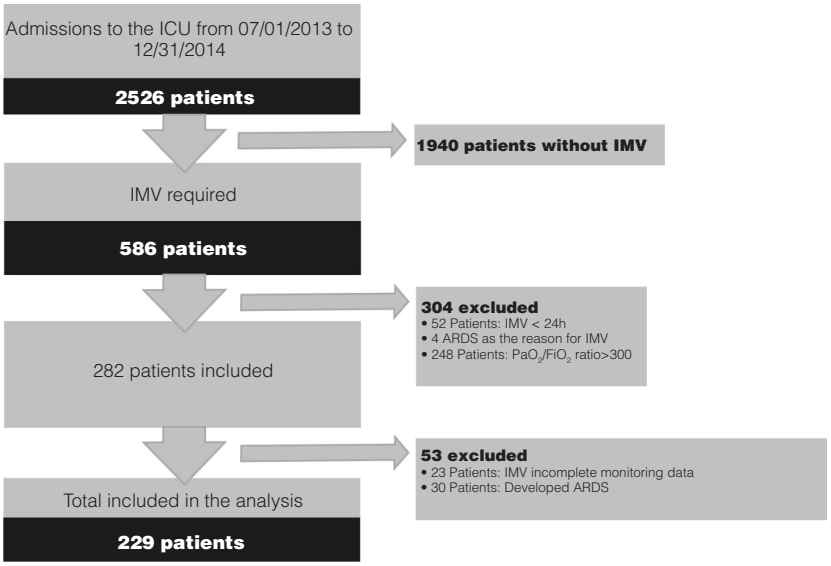
From the patients included, 61.6% (n = 141) could be weaned, 14.8% (n = 34) required reintubation and 22.7% (n = 52) required a tracheostomy. Mortality at the ICU was 36.7% (n = 84) (figure 1).

Age (60 ± 18 vs. 67 ± 18; p = 0,002), SAPS II (39 [26-53] vs. 49 [37-61]; p < 0,0001) and DP24hs (12 [9,9-14,5] vs. 13 [11-16]; p < 0,02) were higher in deceased patients than in survivors.

81% (n = 185) of the patients had at least one complication (table 3), delirium being the most frequent one (45.9%; n = 105).

An univariate analysis was conducted to assess the connection between the development of complications and mortality in the ICU. In this analysis, the variables associated with mortality were: multiple organ dysfunction (p = 0.05), cardiac arrest (p = 0.006), and shock (p < 0.0001).

In patients with delirium, the period of IMV and the stay at the ICU were longer (10 [6-16] vs. 5 [2-14] and 18 [12-30] vs. 9 [4-18] days respectively, p < 0.0001 for both) than in those who did not develop it (Figure 2).



Algorithm 1. patient flow

TABLE 1. Demographic and severity characteristics of the 229 patients

Variables¶	n = 229	Survivors	
		Yes (n = 145)	No (n = 84)
Age	62.8 (18.2)	60.2 (17.8)*	67.3 (18)*
Gender F/M (%)	41.9 / 58.1	42.7 / 57.3	40.4 / 59.6
SAPS II	42 [31-57]	39 [26-52.2]*	49 (37-61)*
SAPS II Mort Risk	28.5 [11.6-64]	22.9 [7.2-53]	43.7 (19.6-70.2)
Clinical admissions (%)	70.7	64.8	80.9
Surgical admissions (%)	29.3	35.2	19.1
Reason for IMV (%):			
Pneumonia	20.5	20.6	17.8
Postoperative ARF	18.3	20	13
S/Non-S coma	16.2	18.6	11.9
Shock	20.1	15.8	25
COPD exacerbation	5.7	4.1	8.3
Cardiac arrest	6.1	4.1	7.1
Others reasons	13.1	16.5	16.6
Days with IMV	7 [3-15]	7 [3-15.2]	7.5 [3-14.2]
Stay at the ICU (days)	14 [6.25-24]	15 [9-25]	12 [4-19]

¶Data presented as average (±DS), median [IQR25-75] or percentage, as appropriate. F: females; M: males; SAPS II: Simplified Acute Physiology Score II; S/Non-S coma: structural / non-structural coma; Days with IMV: Days with invasive mechanical ventilation. *p<0.05

TABLE 2. Ventilatory and monitoring variables of the 229 patients

Variables¶	Total of patients n = 229	Survivors (n = 145)	Non-survivors (n = 84)
Initial TV (ml/kg)	7.7 [7-8]	7.7 [7-8]	7.8 [7-8]
Initial PEEP (cmH_2O)	7 [5-8]	7 [5-8]	7 [5-8]
24-hour PEEP (cmH_2O)	8 [6-10]	8 [6-9.5]	8 [6-10]
Pplat (cmH_2O)	20 [17-24]	20 [17-23]	20 [18-26]
DP24hs (cmH_2O)	12 [10-15]	12 [9.9-14]*	13 [11-16]*
24-hour PaO_2/FiO_2 ratio	225 [187.4-261]	225.5 [190-256,6]	222.5 [180.6-275]
72-hour PaO_2/FiO_2 ratio	252.4 [204.7-325.5]	257.5 [207.6-323]	250.2 [195.5-332.5]

¶Data presented as median [IQR25-75]. Initial TV: initial tidal volume; PEEP: positive end-expiratory pressure; Pplat: Plateau Pressure. *p < 0.05

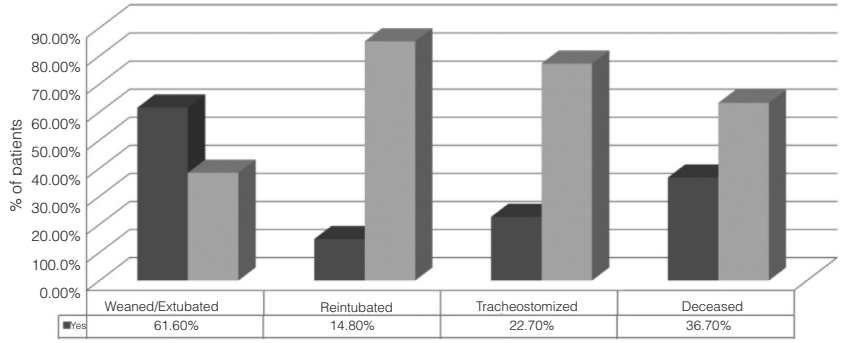


Figure 1. ICU evolution of the 229 patients.

When the sample was classified according to the severity of hypoxemia, differences were found in the settings of ventilation parameters; in the "mild" group, the initial TV was higher and the initial PEEP was lower compared to the other 2 groups (table 5). In the univariate analysis, there was a link between the days of IMV and the severity of hypoxemia (p = 0.013); however, the stay at the ICU was similar (Table 4). The percentage of tracheostomized patients was

TABLE 3. Complications developed during the stay at the ICU of the 229 patients

Complications	Total (n = 229) Count	Survivors (n = 145) Count	Non-survivors (n = 84) Count
Delirium	105	77	28
Shock	76	36	40
Sev. renal fail.	21	10	11
MOD	13	5	8
VAP	9	6	3
Cardiac arrest	7	1	6
ICUAW	6	5	1
Unprogr. EXTUB.	5	4	1
PE	4	3	1
Barotrauma	3	2	1
AMI	2	2	0
N° of complications	Count	Count	Count
0	42	31	11
1	76	47	29
2	62	38	24
3	49	29	20

Data presented as n (%). MOD: multiple organ dysfunction; VAP: ventilator-associated pneumonia; CA: cardiac arrest; ICUAW: ICU-acquired weakness; PE: pulmonary embolism; AMI: acute myocardial infarction.

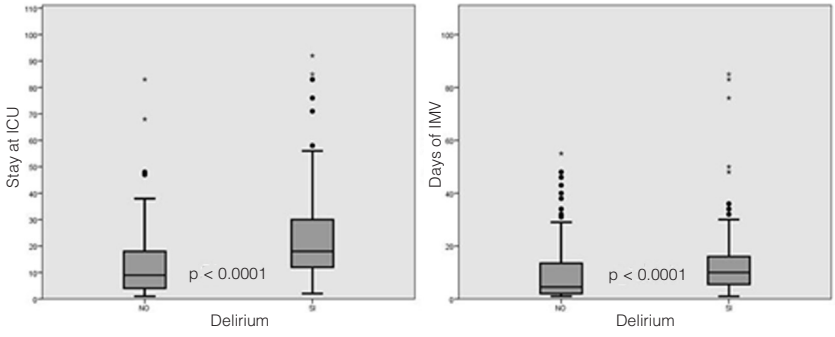


Figure 2. Stay at the ICU and days of IMV in patients with delirium vs. patients without delirium.

higher in the "severe" group than in the other two groups (table 5).

In the logistic regression model adjusted by the severity of hypoxemia, with mortality at the ICU as an outcome variable, the age (OR 1.02; 95% CI 1.002-1.04: p=0.033) and shock (OR 2.37; 95% CI 1.12-5: p=0.023) acted as independent predictors of mortality (table 6).

Discussion

According to the bibliography consulted, only a study by a Korean group led by Won-II Choi[7] assessed mortality in patients who developed AHRF (without ARDS) during invasive ventilatory support, classifying the sample by the severity of hypoxemia. In this regard, this is the second study that assesses mortality in this group of patients.

The main findings of our bicentric study, which included 229 patients who required IMV for over 24 hours and who developed AHRF (without ARDS), were that mortality was not associated with the severity of hypoxemia, and that only shock and age were independent predictors of mortality.

In comparison to other studies that assessed the characteristics and evolution of critical patients who required IMV, the severity of the disease determined by the SAPS II score at admission, the gender distribution and the age[14, 15] were similar. However, the median of the initial PaO_2/FiO_2 ratio

TABLE 4. Ventilatory and monitoring variables, classified by the severity of hypoxemia

Variables¶	Severe PaO_2/FiO_2 ratio ≤ 100 (n = 8) Median [IQR25-75]	Moderate PaO_2/FiO_2 ratio > 100 and ≤ 200 (n = 73) Median [IQR25-75]	Mild PaO_2/FiO_2 ratio > 200 and ≤ 300 (n =148) Median [IQR25-75]	p
Initial TV (ml/kg)	7 [7-8]	7 [7-8]	8 [7-8]	0.037*
Initial PEEP (cmH_2O)	8 [5-8]	7 [5-8]	5 [5-6]	0.021*
Pplat (cmH_2O)	20 [17-28]	20 [17-23]	20 [18-24]	0.969
24-hour PEEP (cmH_2O)	12 [8-12]	8 [6-10]	8 [6-10]	0.219
DP 24hs (cmH_2O)	13 [9.4-19.8]	13 [10-15.5]	12 [10-15]	0.746
24-hour PaO_2/FiO_2 ratio	71 [60-86]	172 [153-190]	253 [227-278]	<0.0001
72-hour PaO_2/FiO_2 ratio	103 [86-177]	217 [189-285]	289 [238-337]	<0.0001
Days of IMV	24 [13-40]	8 [4-17]	7 [3-13]	0.013#
Stay at ICU	26 [15-41]	15 [7-26]	13 [6-22]	0.13

¶Data presented as median [IQR25-75]. Initial TV: initial tidal volume; PEEP: positive end-expiratory pressure; Pplat: Plateau Pressure; DP24hs: 24-hour driving pressure; Days of IMV: Days of invasive mechanical ventilation; Stay at ICU: Stay at the Intensive Care Unit. *p = 0.037 for a PaO_2/FiO_2 ratio >200 and ≤ 300 regarding a PaO_2/FiO_2 ratio >100 and ≤ 200, and a PaO_2/FiO_2 ratio ≤100. #p = 0.013 for a PaO_2/FiO_2 ratio ≤100 regarding a PaO_2/FiO_2 ratio > 200 and ≤ 300 and a PaO_2/FiO_2 ratio > 100 and ≤ 200.

TABLE 5. ICU evolution of the 229 patients classified by the severity of hypoxemia#

Variable	Severe PaO_2/FiO_2 ratio ≤ 100 (n=8) n (%)	Moderate PaO_2/FiO_2 ratio > 100 and ≤ 200 (n = 73) n (%)	Mild PaO_2/FiO_2 ratio > 200 and ≤ 300 (n = 148) n (%)	p
Weaned/Extubated	2 (25)	44 (60.2)	95 (64.1)	0.082
Reintubated	2 (25)	14 (19.1)	18 (12.1)	0.587
Tracheostomized	5 (62.5)	20 (27.3)	27 (18.2)	0.007*
Deceased	2 (25)	30 (41)	52 (35.1)	0.539

#Variable contingency tables vs. degree of severity. Chi-square contrast test. *p = 0.007 for a PaO_2/FiO_2 ≤100 ratio regarding a PaO_2/FiO_2 ratio > 200 and ≤ 300 and a PaO_2/FiO_2 ratio > 100 and ≤ 200

TABLE 6. Multivariate analysis adjusted by the severity of hypoxemia for the association between severity and mortality variables in the 229 patients

Variable	Severity and mortality Logistic regression	p
Age	OR 1.02 (95% CI 1.002-1.04)	0.033
SAPS II	OR 1.015 (95% CI 0.992-1.037)	0.199
MOD	OR 3.752 (95% CI 0.976-14.41)	0.054
Shock	OR 2.372 (95% CI 1.125-5.004)	0.023
DP24hs	OR 1.086 (95% CI 0.992-1.19)	0.07
Delta PaO_2/FiO_2 ratio	OR 0.999 (95% CI 0.996-1.003)	0.803
Days of IMV	OR 0.997 (95% CI 0.992-1.001)	0.127

SAPS II: Simplified Acute Physiology Score II; DP24hs: 24-hour driving pressure; Delta PaO_2/FiO_2 ratio: Differences between the 72-hour PaO_2/FiO_2 ratio and the 24-hour PaO_2/FiO_2 ratio; Days of IMV: Days of invasive mechanical ventilation

in our study was higher[7, 15], which could be associated with the fact that both Esteban et al.[14] study and Tomicic et al.[15] study included all patients with IMV, whereas our study only included those with AHRF (without ARDS), excluding patients with ARDS.

The reasons for IMV among our patients were similar to those in other epidemiological reports from Latin America[15], with pneumonia and postoperative respiratory failure within the main indications for IMV. Likewise, the reasons for IMV described by the Korean group led by Won-II Choi[7] concurred with the ones described in this study, and the percentage of pneumonia was similar in both cases. The frequency of postoperative ARF as a reason for IMV was similar to that described by Esteban et al. in the year 2010[14].

As for the initial ventilation setting variables, the selected TV was lower and the PEEP higher compared to Chile's epidemiological report, even when their sample only included patients with acute respiratory failure[15]. The PEEP selected for our patients was also higher to the one described in the group of patients with AHRF from the study by Won-II Choi[7].

Even though temporary criteria is difficult to compare with other reports[14, 15], both the length of

time with IMV and the length of stay at the ICU were higher in our sample. Severity scores used in our study and in the Korean study were different (SAP II and SAPS III, respectively); therefore, it is impossible to determine if a potential higher severity at admission in our group could explain the longer length of time with IMV and at the ICU. On the other hand, ICUs from our study have an intermediate care unit, which certainly prolongs the stay of these type of patients at the closed unit, a situation that could be solved taking into account the hospital stay, although we do not have that information.

In patients with ARDS, the severity of hypoxemia determined by the PaO_2/FiO_2 ratio at the beginning of IMV is associated with an increase in mortality[16]. In the study by Won-Il Choi et al., mortality in patients who developed ARDS was compared to mortality in patients who developed AHRF without distress, and there were no significant differences between the groups, although there was a significant difference when the sample was classified by the severity of hypoxemia[7]. In our study, when we assessed the link between severity of hypoxemia and mortality, there were no differences in mortality between the moderate and mild groups, even excluding the severe group due to the reduced size of the sample. Moreover, severity of hypoxemia did not act as an independent predictor of mortality in the multivariate analysis. This finding could be associated with a higher level of hypoxemia reversibility in patients with AHRF (without ARDS) compared to patients with ARDS, with a lower temporary exposure to hypoxemia levels that would determine multiple organ dysfunction. On the other hand, in two-thirds of the patients the causes of AHRF (without ARDS) were extrapulmonary, and in only 20% of the patients AHRF emerged in the context of pneumonia; this could be associated with a quicker resolution of hypoxemia, which has a better prognosis.

Mortality risk factors in patients with ARDS have been extensively analyzed[17]; however, mortality risk factors in patients with AHRF and without ARDS were analyzed in only one study[7], which found thrombocytopenia acted as a predictor variable. In our study, age and shock acted as independent predictor variables of mortality in patients with AHRF (without ARDS). While it is easy to associate mortality with age and, additionally, evidence supports that patients with ARDS are older and have more complications than patients without ARDS[7, 17], in our study, age was higher among the patients who died, and at the same time it was higher than the age usually described in populations with ARDS[17]. The presence of shock could affect patient mortality, for instance, if it was linked to multiple organ dysfunction caused by the shock itself.

The length of time with IMV in AHRF could be associated with the severity of hypoxemia. While this could be expected in patients with ARDS[18], this finding was not described in populations with AHRF (without ARDS). We found that the length of time with IMV in the severe hypoxemia group was longer in comparison with the other two groups.

A study of patients with ARDS was recently published in the New England Journal of Medicine. In this study, the authors concluded that the use of a protective ventilation strategy associated with a lower DP24 hs provided increased chances of survival[19]. Even though our study population is characterized by the presence of AHRF (without ARDS), DP24 hs was higher in the group of deceased patients, with a median of 13 cmH_2O, where 25% of them had a DP24 hs ≥ 16cmH_2O. Therefore, DP24 hs could also be used in the group of patients with AHRF (without ARDS) as a prognostic marker, although this would require performing a study specifically designed to that end.

In the subgroup of patients who developed delirium as a complication, the length of time with IMV and at the ICU was longer. This finding is similar to the descriptions in other international publications in reference to the development of delirium[20, 21].

Among the limitations of this study, we can point out the possibility of data loss, or data inaccuracy, associated with the type of design (retrospective). However, we have a systematic and prospective database that included all patients receiving ventilation for over 24 hours. Data loading was performed by highly trained staff, which could minimize this limitation to a certain extent. As for the generalization of the findings, two private centers from the City of Buenos Aires were included, so it might not be suitable to generalize the findings in other populations of patients, although the sample was sufficiently heterogeneous regarding the reasons for admission so that conclusions could be extensive. Lastly, although there could

have been confounding factors associated with the type of study as well, we conducted a multivariate analysis to monitor them.

Conclusions

In this group of 229 patients who required IMV for over 24 hours and who developed AHRF (without ARDS) there was a demographic distribution similar to that described in other reports that included patients receiving ventilation. Mortality was not associated with the severity of hypoxemia, whereas shock and age were independent predictors of mortality. Only the severe hypoxemia group had a longer length of time with IMV in comparison with the moderate and mild groups. Development of delirium in these patients was associated with a significant increase in the length of time with IMV and at the ICU.

Taking into consideration the findings described in this study and the differences in evolution, we think it is very important to be able to determine early which of our patients have ARDS and which only have AHRF (without ARDS).

Acknowledgements: we appreciate the collaboration of Dr. Jose Luis Scapellato, Dr. Carla Sanchez and Dr. Lucia Carreras.

* This study was accepted to be presented for an award at the 25th Argentine Congress of Intensive Therapy. In December, 2015, this study received the "2015 Award for Best Scientific Study" from the Sanatorio Anchorena Teaching and Research Committee.

Conflict of interest: The authors declare that there is no conflict of interest associated with this publication.

Bibliography

1. The Acute Respiratory Distress Syndrome Network. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. N Engl J Med 2000; 342: 1301-1308.
2. Protti A, Cressoni M, Santini A, et al. Lung stress and strain during mechanical ventilation: any safe threshold? Am J Respir Crit Care Med 2011; 183: 1354-1362.
3. Brochard L, Rauss A, Benito S, et al. Comparison of three methods of gradual withdrawal from ventilatory support during weaning from mechanical ventilation. Am J Respir Crit Care Med 1994; 150: 896-903.
4. Esteban A, Frutos F, Tobin MJ, et al. A comparison of four methods of weaning patients from mechanical ventilation. N Engl J Med 1995; 332: 345-350.
5. Esteban A, Alía I, Gordo F, et al. Extubation outcome after spontaneous breathing trials with T-tube or pressure support ventilation. Am J Respir Crit Care Med 1997; 156: 459-465.
6. Ranieri VM, Rubenfeld GD, Thompson BT, et al. Acute respiratory distress syndrome: The Berlin Definition. JAMA 2012; 307: 2526-2533.
7. Won-Il Choi, Shehu E, So Yeon Lim et al. Markers of poor outcome in patients with acute hypoxemic respiratory failure. Journal of Critical Care 2014; 29: 797-802.
8. Vincent JL, Akça S, de Mendonça A, et al. The Epidemiology of Acute Respiratory Failure in Critically Ill Patients. Chest. 2002; 121 (5): 1602-1609.
9. Kleyweg R, Van der Meché F, Schmitz P. Interobserver agreement in the assessment of muscle strength and functional abilities in Guillain-Barré syndrome. Muscle & Nerve 1991;14:1103-1109.
10. Vincent JL, de Mendonca A, Cantraine F, et al. Use of the SOFA score to assess the incidence of organ dysfunction/failure in intensive care units: results of a multicenter, prospective study. Working group on "sepsis-related problems" of the European Society of Intensive Care Medicine. Crit Care Med 1998; 26 (11): 1793-800.
11. Confusion Assessment Method for diagnosing delirium in ICU patients (CAM-ICU): cultural adaptation and validation of the Spanish version. Tobar E, Romero C, Galleguillos T, Fuentes P, Cornejo R, Lira MT, de la Barrera L, Sánchez JE, Bozán F, Bugedo G, Morandi A, Wesley Ely E. Med Intensiva. 2010 Jan-Feb;34(1):4-13.
12. Bone RC, Sprung CL, Sibbald WJ. Definitions for sepsis and organ failure. Crit Care Med 1992; 20 (6): 724-6.
13. Guidelines for the management of adults with hospital-acquired, ventilator-associated, and healthcare-associated pneumonia. Am J Respir Crit Care Med 2005; 171 (4): 388-416.
14. Esteban A, Frutos-Vivar F, Muriel A, et al. Evolution of mortality over time in patients receiving mechanical ventilation. Am J Respir Crit Care Med 2013; 188 (2): 220-230.
15. Tomicic V, Espinoza M, Andresen M, et al. Características de los pacientes que reciben ventilación mecánica en unidades de cuidados intensivos: primer estudio multicéntrico chileno. Rev Méd Chile 2008; 136: 959-67.
16. Brun-Buisson C, Minelli C, Bertolini G, et al. Epidemiology and outcome of acute lung injury in European intensive care units. Results from the ALIVE study. Intensive Care Med 2004; 30: 51-61.
17. Pierrakos C, Vincent JL. The changing pattern of acute respiratory distress syndrome over time: a comparison of two periods. Eur Respir J 2012; 40: 589-95.
18. Villar J, Fernández RL, Ambrós A, et al. A clinical classification of the acute respiratory distress syndrome for predicting outcome and guiding medical therapy. Crit Care Med 2015; 43: 346-353.
19. Amato M, Meade M, Slutsky A, et al. Driving pressure and survival in the acute respiratory distress syndrome. N Engl J Med 2015; 372: 747-55.
20. Mehta S, Cook D, Devlin JW, et al. Prevalence, risk factors, and outcomes of delirium in mechanically ventilated adults. Crit Care Med 2015; 43: 557-566.
21. Balas M, Vasilevskis E, Olsen K, et al. Effectiveness and Safety of the Awakening and Breathing Coordination, Delirium Monitoring/Management, and Early Exercise/Mobility Bundle. Crit Care Med 2014; 42: 1024-1036.