Acute Respiratory Distress Syndrome: Case Series, Two Years at an Intensive Care Unit

ARTIGO ORIGINAL

Síndrome de Dificuldade Respiratória Aguda: Casuística de Dois Anos numa Unidade de Cuidados Intensivos

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Acta Med Port 2014 Mar-Apr;27(2):211-217

ABSTRACT

Introduction: Acute Respiratory Distress Syndrome has a significant incidence and mortality at Intensive Care Units. Therefore, more studies are necessary in order to develop new effective therapeutic strategies. The authors have proposed themselves to characterize Acute Respiratory Distress Syndrome patients admitted to an Intensive Care Unit for 2 years.

Material and Methods: This was an observational retrospective study of the patients filling the Acute Respiratory Distress Syndrome criteria from the American-European Consensus Conference on ARDS, being excluded those non invasively ventilated. Demographic data, Acute Respiratory Distress Syndrome etiology, comorbidities, Gravity Indices, PaO2/FiO2, ventilator modalities and programmation, pulmonary compliance, days of invasive mechanical ventilation, corticosteroids use, rescue therapies, complications, days at Intensive Care Unit and obits were searched for and were submitted to statistic description and analysis.

Results: A 40 patients sample was obtained, with a median age of 72.5 years (interquartile range = 22) and a female:male ratio of ≈1:1.86. Fifty five percent of the Acute Respiratory Distress Syndrome cases had pulmonary etiology. The mean minimal PaO2/FiO2 was 88mmHg (CI 95%: 78.5–97.6). The mean maximal applied PEEP was 12.4 cmH2O (Standard Deviation 4.12) and the mean maximal used tidal volume was 8.2 mL/ Kg ideal body weight (CI 95%: 7.7–8.6). The median invasive mechanical ventilation days was 10. Forty seven and one half percent of the patients had been administered corticosteroids and 52.5% had been submitted to recruitment maneuvers. The most frequent complication was Ventilator Associated Pneumonia (20%). The median Intensive Care Unit stay was 10.7 days (interquartile range 10.85). The fatality rate was 60%. The probability of the favorable outcome 'non-death in Intensive Care Unit' was 4.4x superior for patients who were administered corticosteroids and 11x superior for patients < 65 years old.

Discussion and Conclusions: Acute Respiratory Distress Syndrome is associated with long hospitalization and significant mortality. New prospective studies will be necessary to endorse the potential benefit of steroid therapy and to identify the subgroups of patients that warrant its use.

Keywords: Adrenal Cortex Hormones; Critical Care; Prognosis; Respiratory Distress Syndrome, Adult; Respiration, Artificial.

RESUMO

Introdução: A Síndrome de Dificuldade Respiratória Aguda apresenta incidência e mortalidade significativas em Cuidados Intensivos, justificando estudos adicionais, nomeadamente para definição de novas abordagens terapêuticas. Os autores propuseram-se caracterizar os casos duma Unidade de Cuidados Intensivos em dois anos.

Material e Métodos: Procedeu-se a um estudo observacional retrospectivo dos casos admitidos numa Unidade de Cuidados Intensivos, cumprindo os critérios diagnósticos da American-European Consensus Conference on ARDS, tendo sido excluídos os não ventilados invasivamente. Pesquisados e submetidos a tratamento estatístico: dados demográficos, etiologia do Síndrome de Dificuldade Respiratória Aguda, comorbilidades, Índices de Gravidade, PaO2/FiO2, modalidades e parâmetros ventilatórios, *compliance* pulmonar, dias de ventilação mecânica invasiva, corticoterapia, terapêuticas de resgate, complicações, duração do internamento, óbitos.

Resultados: Obtiveram-se 40 doentes, com uma mediana de 72,5 anos (amplitude interquartil 22) e um *ratio* feminino:masculino ≈1:1,86. Cinquenta e cinco por cento dos Síndrome de Dificuldade Respiratória Aguda tiveram etiologia pulmonar. A média do PaO2/FiO2 mínimo foi 88mm Hg (IC 95%: 78,5-97,6). A média da PEEP máxima aplicada foi 12,4 cmH2O (Desvio Padrão 4,12) e a média do Volume Corrente máximo utilizado foi 8,2 mL/Kg peso ideal (IC 95%: 7,7-8,6). A mediana dos dias de ventilação mecânica invasiva foi 10. Em 47,5% dos doentes foram administrados corticóides. Em 52,5% foi executado recrutamento alveolar. A complicação mais frequente foi a Pneumonia Associada a Ventilação (20%). A mediana da duração do internamento foi 10,7 dias (amplitude interquartil 10,85). Faleceram 60% dos doentes. A probabilidade de *outcome* favorável 'não óbito na Unidade de Cuidados Intensivos' foi 4,4x superior nos doentes sob corticoterapia e 11x superior nos doentes com idade < 65 anos.

Discussão e Conclusões: A Síndrome de Dificuldade Respiratória Aguda associa-se a internamentos prolongados e significativa mortalidade. Novos estudos prospectivos serão necessários para confirmar o benefício dos corticóides, bem como identificar o/(s) subgrupo/(s) de doentes que mais justificam a sua utilização.

Palavras-chave: Síndrome de Dificuldade Respiratória no Adulto; Ventilação Mecânica; Corticosteroides; Prognóstico; Portugal.

INTRODUCTION

Acute Respiratory Distress Syndrome (ARDS) is characterized by an acute lung injury associated either to primary lung pathology (such as pneumonia or aspiration of gastric contents, among others, with subsequent damage to the alveolar epithelium) or to extra-pulmonary involvement (secondary to sepsis and/or Systemic Inflammatory Response Syndrome (SIRS), resulting in damage to endothelial cells of the alveolar-capillary membrane).

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Recebido: 28 de Junho de 2013 - Aceite: 06 de Novembro de 2013 | Copyright © Ordem dos Médicos 2014

The definition in use until 2012 was established in 1994, at the American-European Consensus Conference on ARDS[1], and the condition was characterized by the following: Acute onset; $PaO_2/FiO_2 \leq 200$ mmHg; Bilateral Pulmonary Infiltrates on Chest X-ray, Pulmonary Artery Wedge Pressure (PAWP) ≤ 18 mmHg and no clinical evidence of left atrial hypertension. However, following a proposal presented by M Ranieri to the ESCIM 24th Annual Congress in 2011[2] and a Consensus between European and North-American representatives (The ARDS Definition Task Force), a new definition has been proposed in 2012 (The Berlin Definition)[3], focusing on: 1) acute onset over 1 week or less than a week following a known clinical event, *de novo* respiratory symptoms or worsening of previous respiratory symptoms; 2) Bilateral opacities not fully explained by pleural effusions, pulmonary/lobar collapse or nodules detected on Chest X-ray or CT; 3) Respiratory failure not fully explained by Cardiac Failure or fluid overload; 4) ARDS categorized as being mild (200 mmHg < $PaO_2/FiO_2 \leq 300$ mmHg with PEEP ≥ 5 cmH_2O), moderate (100 mmHg < $PaO_2/FiO_2 \leq$ 200 mmHg with PEEP ≥ 5 cmH_2O) and severe ($PaO_2/FiO_2 \leq$ 100 mmHg with PEEP ≥ 5 cmH_2O).[3] ARDS incidence (3.5-58.7 / 100,000 people/year, according to different studies)[4] and mortality (40-60%)[4-6] are significant, justifying additional studies to improve understanding of this syndrome and a definition of new therapeutic approaches.

MATERIAL AND METHODS

We carried out an observational retrospective study of the patients with ARDS admitted to the Intensive Care Unit (ICU) at *Hospital de Cascais Dr José de Almeida* from the 20th February 2010 to the 24th February 2012. The inclusion criteria were established based on the diagnostic criteria defined at the American-European Consensus Conference on ARDS and patients were excluded in the absence of invasive mechanical ventilation (IMV). This study was approved by the Hospital Ethics Committee. Hospital medical records (written and digitalized) were analysed, including demographic data, patient's referral origin, ARDS aetiology, comorbidities, Severity Scores (APACHE II and SAPS II within the first 24h and estimated mortality by SAPS II), maximum SOFA score and maximum number of organ system failures, minimum PaO_2/FiO_2 ratio and dynamic compliance (by spirometry), maximum PEEP (positive end-expiratory pressure) and Tidal Volume (Vt), maximum Plateau Pressure (*Pplateau)*, days of IMV, predominant ventilation modality used, corticosteroid administration according to the ARDS protocol (adapted from Meduri GU *et al.*),[7,8] salvage therapies [alveolar recruitment manoeuvers, ventral decubitus position, high frequency oscillatory ventilation (HFOV)], complications, length of stay in the ICU, ICU mortality and finally survival after30 days, 2 and 6 months. In addition, the worst Lung Injury Score (LIS) was calculated[9] for each patient. MedCalc – version 12.2.1.0 software was used for data statistical processing. The D'Agostino-Pearson Test for Normal Distribution and Logarithmic Transformation was applied to the variables with a positive asymmetry coefficient, when appropriate. Grubbs' - *double-sided* (significance level: α=0.05), Tukey's tests or the Generalized Extreme Studentized Deviate test (significance level: α=0.05) were used for outlier detection. Appropriate correlations were established between variables, using the Pearson or Spearman correlation, according to variable distribution with respect to normality distribution. Univariate Logistic Regression was applied to the different independent and dependent variables 'death/survival at the ICU', 'length of stay ≤ 10 / > 10 days' and 'IMV ≤ 10 / > 10 days'. For comparison between samples the following were used: Student's t-test and Signed Rank Sum test for continuous variables with normal distribution and Chi-square test for binary and nominal variables. A $p < 0.05$ was considered as significant.

RESULTS

We studied a group of 40 patients according to the above-mentioned inclusion and exclusion criteria (Fig. 1), from which 65% were male and 62.5% were aged above 65. The complete characterization of our group of patients

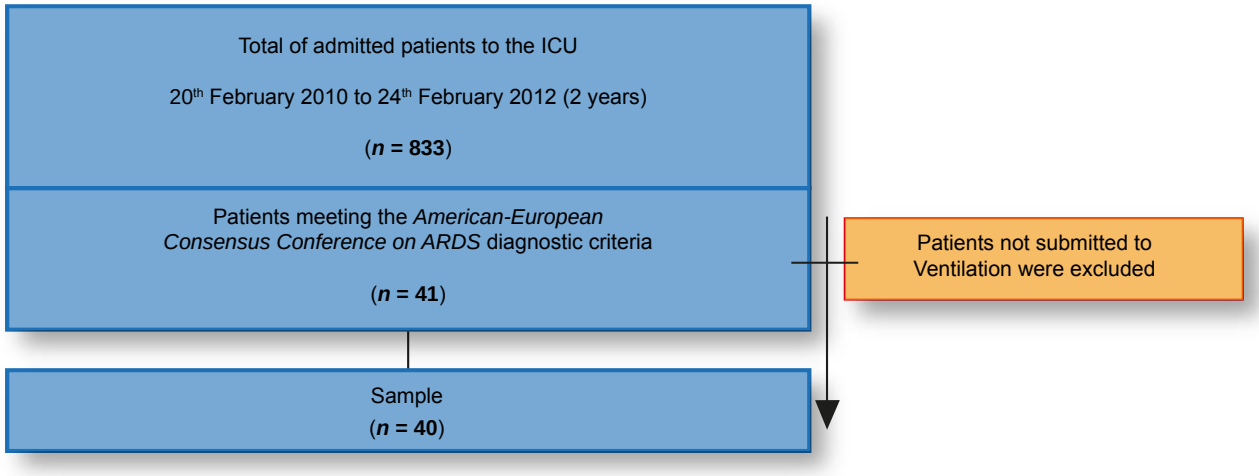

Figure 1 - CONSORT flow diagram

is shown in Table 1 and 2.

We should remark that in 27.5% of patients ARDS occurred as a result of an in-hospital-related occurrence/ complication.

As regards ARDS severity, 72.5% of the patients presented with a minimum PaO_2/FiO_2 ≤ 100 mmHg and 95% of the patients with a Lung Injury Score (LIS) > 2.5.

Regarding Mechanical Ventilation, a maximum Vt of 8 mL/ ideal body weight in Kg and a maximum *Pplateau* of 30 cmH_2O was exceeded in 50% and 37.5% of the patients,

Table 1 – Demography and ARDS characterization (*n* = 40)

Variable		Value
Age (years) **Median (P25-P75 interquartile range)**		72.5 (22.00)
Gender **Female/male ratio**		14:26 (≈ 1:1.86)
Most frequent comorbidities **Relative frequency % (Absolute frequency)**	Arterial Hypertension Diabetes *Mellitus*	50.0 (20) 20.0 (8)
Referral Origin **Relative frequency % (Absolute frequency)**	Emergency Department	47.5 (19)
	Intermediate Care Unit	15.0 (6)
	Operating Room	10.0 (4)
	Surgical ward	7.5 (3)
	Medical ward	5.0 (2)
	Orthopedics ward	2.5 (1)
	Other Hospitals	12.5 (5)
Severity scores	APACHE II first 24h (*n* = 38) † Mean (Standard Deviation)	23.6 (9.10)
	SAPS II first 24h (*n* = 38) † Median (P25-P75 interquartile range)	54.5 (27,00)
	Maximum SOFA score Median (P25-P75 interquartile range)	11.0 (5.50)
Estimated Mortality by SAPS II score (%) (n = 38) † **Median (P25-P75 interquartile range)**		56.40 (52.400)
Nº Organ System failures **Median (P25-P75 interquartile range)**		5.0 (1.00)
Length of ICU stay (days) **Median (P25-P75 interquartile range)**		10.70 (10.850)
Aetiology **Relative frequency % (Absolute frequency)**	Pneumonia	52.5 (21)
	Aspiration of gastric contents	2.5 (1)
	Sepsis	37.5 (15)
	Acute pancreatitis	5.0 (2)
	Severe non-thoracic injury	2.5 (1)
Minimum PaO_2/FiO_2 (mmHg) **Mean (Standard Deviation)**		88.0 (29.91)
Minimum dynamic compliance (mL/cmH_2O) (n = 20)‡ **Median (P25-P75 interquartile range)**		18.5 (9.00)
Worst Lung Injury Score **Mean (Standard Deviation)**		3,415 (0.4703)

Demographic characterization of our group of patients. Note: † APACHE II or SAPS II (within the first 24h) scores could not be found in in the medical records of 2 patients; ‡ Only 20 patients had dynamic compliance serial records in their medical records

Table 2 – Therapy and mechanical ventilation approaches (n = 40)

Variable		Value
Duration of IMV (days) Median (P25-P75 interquartile range)		10.0 (9.50)
Predominant ventilation modality Relative frequency % (Absolute frequency)	Pressão Controlada	87.5 (35)
	Volume Controlado	5.0 (2)
	PRVC	5.0 (2)
	Pressão Assistida	2.5 (1)
Maximum PEEP (cmH_2O) Mean (Standard Deviation)		12.4 (4.12)
Maximum Vt (mL/ideal weight in Kg) Mean (Standard Deviation)		8.2 (1.34)
Maximum *Pplateau* (cmH_2O) Median (P25-P75 Interquartile range)		30.5 (6.50)
Steroid therapy in ARDS Relative frequency % (Absolute frequency)		47.5 (19)
Use of Muscle Relaxants (Rocuronium bromide) Relative frequency % (Absolute frequency)		52.5 (21)
Alveolar Recruitment Manoeuvers Relative frequency % (Absolute frequency)		52.5 (21)
Ventral Decubitus Relative frequency % (Absolute frequency)		10.0 (4)
HFOV use Relative frequency % (Absolute frequency)		5,0 (2)

Characterization of our group of patients regarding therapy and mechanical ventilation approaches (n = 40). PRVC – pressure-regulated volume control; HFOV – high-frequency oscillatory frequency.

respectively.

Regarding therapy, corticosteroid were started on an early stage of ARDS (≤ 72 h) in 14 patients (73.7%)) and at a late stage (> 72h) in five patients (26.3%). Survival was improved in patients in patients who were started on early versus late steroid therapy (35.7% *vs.* 60.0% mortality), but the difference was not statistically significant (p = 0.677).

Complications occurred in 32.5% of the patients, more frequently Ventilator-Associated Pneumonia in eight patients (20%), Ventilator-Associated Pneumothorax/Alveolar Recruitment Manoeuvers in five (12.5%) and Critical Illness Myopathy in 3 (7.5% of the patients). In all patients with a pneumothorax, the maximum PEEP that was used was ≥ 10 cmH_2O (median = 13, P25-P75 interquartile range = 4) and the maximum *Pplateau* was ≥ 28 cmH_2O (median = 32, P25 - P75 interquartile range = 5.25). In one of these patients, the maximum Vt was just 3 mL/ ideal body weight in Kg, although median was 6 (P25 - P75 interquartile range = 1.5). Despite not having shown statistical significance with respect to the 'presence/absence of complications' and to 'non-survival/survival at the ICU' parameters (χ^2 3.249; p = 0.071), the patients without complications presented a higher odds ratio for ≤ 10 days stay (odds ratio 24.556; 95% CI 2.752 to 219.091; p = 0.004) and IMV ≤ 10 days (odds ratio 54.600; 95% CI 5.722 to 520.991; p = 0.001) (Table 3).

Only one patient (2.5%) underwent a tracheostomy procedure during the stay, being on IMV for 38 days and surviving at 6 months upon discharge.

The mortality rate in ICU was 60% (24 patients).

The patients with ARDS and the need for IMV included in our study represented 4.8% of total ICU admissions and 8.1% of ventilated patients. Their median length of stay – 10.7 days – was higher in comparison to the global ICU mean length of stay – 6.1 days - (p < 0.0001) and mortality was much higher: 27.3% (p < 0.0001). However, their APACHE II score within the first 24h was not significantly different (ICU total admissions: mean 21.7; ARDS with IMV: mean 23.6; p = 0.1988).

After discharge from ICU survival at 30 days and 2 months was100% (n=16). Five surviving patients had been discharged from the ICU for less than six months at the time of data collection; out of the remaining 11 patients, one had died at four months and 10 were alive at six months.

A positive correlation was found between: maximum PEEP and days of IMV (Log) – Correlation Coefficient r = 0.3189 (p = 0.0449, 95% CI 0.008181 to 0.5734); LIS score and days of IMV days (Log) - Correlation Coefficient r = 0.3607 (p = 0.0222, 95% CI 0.05546 to

Table 3 – Variáveis independentes estudadas, como eventuais preditoras dos *outcomes* favoráveis 'Não óbito na UCI', 'VMI ≤ 10 dias' e 'Demora ≤ 10 dias'

Outcome / Independent variables	'Survival to ICU stay'		
	LR Test	***OR***	**95% CI *OR***
Steroid therapy (yes *vs.* no)	χ^2 = 4.924, *p* = 0.026	4.4	1.134 - 17.069
Age (< 65 *vs.* ≥ 65 years)	χ^2 = 11.423, *p* = 0.001	11	2.438 - 49.627
Gender (male *vs.* female)	χ^2 0.891, *p* = 0.345	_____	_____
Aetiology (Pulmonary *vs.* Extra-pulmonary)	χ^2 0.269, *p* = 0.604	_____	_____
Minimum PaO_2/FiO_2 (≤ 100 *vs.* > 100)	χ^2 1.320, *p* = 0.251	_____	_____
***LIS* score** (≤ 2.5 *vs.* > 2.5)	χ^2 2.113, *p* = 0.146	_____	_____
Maximum PEEP (< 10 *vs.* ≥ 10 cmH_2O)	χ^2 1.151, *p* = 0.283	_____	_____
Maximum Vt (≤ 8 *vs.* > 8)	χ^2 0, *p* = 1.000	_____	_____
Maximum *Pplateau* (≤ 30 *vs.* > 30)	χ^2 1.680, *p* = 0.195	_____	_____
Nº days of IMV (≥ 10 *vs.* < 10)	χ^2 0.820, *p* = 0.365	_____	_____
Alveolar Recruitment Manoeuvers (yes *vs.* no)	χ^2 2.427, *p* = 0.119	_____	_____
Ventral Decubitus (yes *vs.* no)	χ^2 0.440, *p* = 0.507	_____	_____
HFOV (yes *vs.* no)	χ^2 2.113, *p* = 0.146	_____	_____
	'IVM ≤ 10 days'		
	LR Test	***OR***	**95% CI *OR***
Maximum PEEP (< 10 *vs.* ≥ 10 cmH_2O)	χ^2 = 6.088, *p* = 0.014	9.714	1.081 - 87.313
Complication (no *vs.* yes)	χ^2 = 22.389, *p* = < 0.001	54.600	5.722 - 520.991
Age (< 65 *vs.* ≥ 65 years)	χ^2 0.027, *p* = 0.870	_____	_____
Gender (male *vs.* female)	χ^2 0.040, *p* = 0.841	_____	_____
Aetiology (Pulmonary *vs.* Extra-pulmonary)	χ^2 0.004, *p* = 0.949	_____	_____
Minimum PaO_2/FiO_2 (≤ 100 *vs.* > 100)	χ^2 0.462, *p* = 0.496	_____	_____
LIS score (≤ 2.5 *vs.* > 2.5)	χ^2 2.477, *p* = 0.116	_____	_____
Maximum *VT* (≤ 8 *vs.* > 8)	χ^2 0.027, *p* = 0.870	_____	_____
Maximum *Pplateau* (≤ 30 *vs.* > 30)	χ^2 3.696, *p* = 0.055	_____	_____
Steroid therapy (yes *vs.* no)	χ^2 0.123, *p* = 0.726	_____	_____
Alveolar Recruitment Manoeuvers (yes *vs.* no)	χ^2 2.670, *p* = 0.102	_____	_____
Ventral Decubitus Positioning (yes *vs.* no)	χ^2 0.045, *p* = 0.833	_____	_____
HFOV (yes *vs.* no)	χ^2 3.323, *p* = 0.068	_____	_____
	"ICU stay ≤ 10 days"		
	LR Test	***OR***	**IC 95% *OR***
Maximum PEEP (<10 *vs.* ≥10 cmH_2O)	χ^2 = 5.192, *p* = 0.023	6.364	1.122 - 36.081
Complication (no *vs.* yes)	χ^2 = 14.304 , *p* = <0.001	24.556	2.752 - 219.091
Age (< 65 *vs.* ≥ 65 years)	χ^2 0.243, *p* = 0.622	_____	_____
Gender (male *vs.* female)	χ^2 0.040, *p* = 0.841	_____	_____
Aetiology (Pulmonary *vs.* Extra-pulmonary)	χ^2 0.496, *p* = 0.481	_____	_____
Minimum PaO_2/FiO_2 (≤ 100 *vs.* >1 00)	χ^2 2.134, *p* = 0.144	_____	_____
LIS score (≤ 2.5 *vs.* > 2.5)	χ^2 3.323, *p* = 0.068	_____	_____
Maximum *VT* (≤ 8 *vs.* > 8)	χ^2 0.243, *p* = 0.622	_____	_____
Maximum *Pplateau* (≤ 30 *vs.* >.30)	χ^2 3.696, *p* = 0.055	_____	_____
Steroid therapy (yes *vs.* no)	χ^2 0.854, *p* = 0.355	_____	_____
Alveolar Recruitment Manoeuvers (yes *vs.* no)	χ^2 0.854, *p* = 0.355	_____	_____
Ventral Decubitus Positioning (yes *vs.* no)	χ^2 0.045, *p* = 0.833	_____	_____
HFOV (yes *vs.* no)	χ^2 2.477, *p* = 0.116	_____	_____

Independent variables studied as possible favourable outcome predictors for 'Survival to ICU stay', 'IMV ≤ 10 days' and 'ICU stay ≤ 10 days'. In the case of variables without statistical significance as outcome predictive factors only the LR test is presented. [LR test = Likelihood ratio test; OR = odds ratio; 95% CI = 95% confidence interval].

0.6043) and maximum *Pplateau* and number of days of IMV - Spearman's rank correlation coefficient *(*rho*)* = 0.345 (*p* = 0.0294, 95% CI: 0.0371 to 0.593). The following correlations had no statistical significance (*p* > 0.05): minimum PaO_2/FiO_2 and days of IMV (Log); minimum PaO_2/FiO_2 and maximum PEEP; age and number of organ system failures; age and number of IMV days; age and length of stay at the ICU; maximum SOFA score and length of stay at the ICU; maximum SOFA score and number of days of IMV.

The favourable outcome 'ICU survival' odds ratio was 4.4 times higher (95% CI 1.1342-17.0693; *p* = 0.0265) in patients on steroid therapy and 11 times higher (95% CI 2.4381-49.6282; *p* = 0.0007) in patients aged above 65 (Table 3). Age-adjusted (≥ 65 / < 65) favourable outcome odds ratio was 6.4 times higher (95% CI 1.1179-36.2707; *p* = 0.0002) in patients on steroid therapy.

In addition, patients submitted to a maximum PEEP < 10 cmH_2O had 9.7 times higher odds ratio of 'IMV ≤ 10 days' (odds ratio 9.714; 95% CI 1.081 – 87.313; χ^2 4.118, *p* = 0.042) and approximately 6.4 times higher of 'ICU stay ≤ 10 days' (odds ratio 6.364; 95% CI 1.122 – 36.081; χ^2 4.370, *p* = 0.037) (Table 3).

We did not find any statistically significant association between a favourable outcome and other independent variables, as shown in Table 3.

DISCUSSION AND CONCLUSIONS

This retrospective study aimed to characterize the patients with ARDS admitted to an Intensive Care Unit at a regional hospital whose area of influence comprises a population of about 200,000 people.

Over this two-year period, as described, the patients with ARDS and the need for IMV represented approximately 5% of all ICU admitted patients and about 8% of ventilated patients. Generally speaking, in this group of patients, length of admission was longer and mortality rates were much higher than global values for these parameters in this ICU.

Our group of patients included a large percentage of elderly patients and severe ARDS situations (minimum PaO_2/FiO_2 ≤ 100 mmHg), which may explain a significant mortality (nevertheless, within the 40-60% interval described in literature).[4-6] In fact, an age below 65 was associated with a higher odds ratio of survival during ICU stay. However, we did not find any statistical significance in the association between a PaO_2/FiO_2 > 100 mmHg and a favourable outcome.

In line with other studies, we found a male predominance[4,10] and major ARDS aetiologies were pneumonia and sepsis.[4,10,11]

The most frequent comorbidities might be explained by their significant prevalence in the general population, but we recognize that other type of studies would be required in order to support the latter statement.

Although protective ventilation is recommended in ARDS[12] (with a maximum Vt of 6-8 mL/ ideal body weight in Kg and maximum *Pplateau* of 30 cmH_2O), this may not always allow for adequate gas exchanges, explaining the need to exceed these limits in a significant percentage of the patients described in the present study. However, we did not find any statistically significant association with a worse outcome in this particular subset of patients.

Approximately half of our patients underwent steroid therapy according to the established ARDS protocol.[7,8] Due to the retrospective nature of this study we were unable to determine the justification or criteria for starting steroid therapy in every patient, having assumed that this decision was based on disease severity and physician's judgement.

Several published reports in ARDS have been unable to find benefit from steroid use administered either early or late in the course of disease. In contrast, Meduri et al.[7,8] obtained a significant ICU mortality reduction, particularly with the early steroid administration in patients with severe ARDS.

In our group of patients, which included a high percentage of severe situations, steroid therapy was associated to a higher odds ratio of survival during the ICU stay. However, it did not have any influence on statistical significance regarding IMV duration and on length of stay at ICU.

This study had as major limitations its observational and retrospective nature. Additionally, it was difficult to analyse some variables due to the absence of standardized medical records. Furthermore, despite early steroid therapy in most, patients in whom it was delayed were also included in the study. Due to the small number of patients who underwent ventral decubitus positioning and HFOV, this study does not allow for valid conclusions to be reached regarding these two salvage therapies.

We wish to emphasize that the scarcity of nationally published studies on ARDS motivated our commitment to carry out this study.

The authors conclude that ARDS is associated to long ICU stays (with higher costs) and to a significant mortality. The questions that we raise should prompt future prospective studies aimed to confirm the proposed benefit of steroid therapy in ARDS and identify those patient's subgroups that may benefit the most.

CONFLICTS OF INTEREST

The authors declare the absence of conflicts of interest.

FINANCIAL SOURCES

The authors declare there was no financial support for writing this manuscript.

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Acta Med Port 2014:27:211-217

Publicado pela **Acta Médica Portuguesa**, a Revista Científica da Ordem dos Médicos

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ISSN:0870-399X | e-ISSN: 1646-0758