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## Aged patients with respiratory dysfunction: epidemiological profile and mortality risk factors

*Perfil epidemiológico e fatores de risco para mortalidade em pacientes idosos com disfunção respiratória*

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### ABSTRACT

**Objectives:** To describe the population of aged as compared to young patients under mechanical ventilation and to analyze the mortality risk factors of this group in an intensive care unit.

**Methods:** This was a prospective observational trial in patients over 18 years of age, admitted in an intensive care unit and under mechanical ventilation, during one year. Patients were divided into two groups according to age: Group 1 – patients over 65 years old; and Group 2, 65 years old or younger.

**Results:** eighty one mechanic ventilation patients were included, 62 aged and 18 younger, mean ages from aged was 76 years, while in the younger it was 56 years. As compared to the control, aged patients had longer mechanic ventilation time, higher intensive care unit and hospital mortality: 63.1% versus 26.3% and 74.2% versus

47.4% ( $P<0.05$ ), respectively. In addition, the aged under mechanic ventilation had increased desintubation failures, difficult ventilatory weaning and deaths directly related to respiratory dysfunction. The mechanic ventilation time was an independent risk factor for death in the intensive care unit in aged patients (OR= 2.7,  $p=0.02$ ). The area under the ROC curve of mechanic ventilation about intensive care unit death was 0.92 (95% CI 0.85-0.97,  $p$  (area 0.5)=0.0001), cutoff point of 4 days, sensitivity 89.4% and specificity 77.1%.

**Conclusions:** Mechanic ventilation patients over 65years of age have a worse prognosis than the younger, and the longer the mechanic ventilation time, the higher will be intensive care mortality.

**Keywords:** Aged; Mortality rate; Intensive care units; Respiration, artificial; Risk factors

### INTRODUCTION

The population of aged patients is steadily growing worldwide. Within the United States, the group above 65 years of age went from 12 million (8%) in 1950 to 36 million (12%) in 2002. The population above 85 years of age increased significantly, and it is estimated that in 2020 it will reach 7 million, and in 2040 14 million Americans.<sup>(1)</sup> In Brazil, a recent review by the Instituto Brasileiro de Geografia e Estatística (IBGE) has shown that in 2000 30% of Brazilians were within the zero to 14 years of age group, while those above 65 years were 5% of the total population. In a projection for 2050, these age groups are going to be similar, each representing 18% of the Brazilian population.<sup>(2)</sup>

In 40 institutions in the United States and 36 in France, the propor-

tion of patients over 65 years of age admitted to the intensive care unit (ICU) was of 48% and 36%, respectively.<sup>(3,4)</sup> Incidence of respiratory failure increases almost exponentially with age,<sup>(5)</sup> and in patients over 65 years of age it was two times higher as compared to patients between 55 and 65 years, and three times higher than in younger patients.

Advanced age affects prognosis, as aged patients have no functional reserve and evolved unfavorably when affected by severe illnesses.<sup>(6)</sup> Studies have shown that advanced age is an important independent mortality predictor.<sup>(6,7)</sup> Short time survival in patients over 65 years of age is significantly lower than in younger patients. Finally, after hospital discharge, deaths occur predominantly within the first 3 months.<sup>(8)</sup> Also, ageing itself is a risk factor for long term mortality, as risk of death increases with the number of comorbidities, lower cognitive function and difficulty to perform routine activities.

Ray et al. evaluated a population of aged respiratory failure patients from an emergency ward, and observed that 29% of them needed ICU admission within the first 24 hours, and mortality rates were higher in the inappropriately treated patients. In this trial, partial CO<sub>2</sub> pressure (PaCO<sub>2</sub>), creatinine clearance, increased natriuretic peptide levels, and paradoxical breathing were independent death-associated predictors.<sup>(9)</sup>

In this context, evaluation of mechanic ventilation (MV) impact in ICU aged patients is relevant, in addition to consider possible complications associated to this very common procedure in current medical practice.

The aim of this study were to compare an aged patients population to younger MV patients, analyzing risk factors for mortality rates in this group.

## METHODS

This was a prospective, observational cohort study of adult patients, developed in the ICU of a tertiary hospital from February 2007 to February 2008, after approval by the Institution's Ethics Committee, and was exempted an informed term of consent as observational study. This ICU takes care of critically ill adult patients, has 20 beds and data collection was carried out by respiratory assistance experienced physiotherapists.

Patients in the ICU and under Invasive Mechanic Ventilation (IMV) for longer than 24 hours and over 18 years of age were included. Were excluded chronic obstructive pulmonary disease patients, those with low

life expectancy or refusing to take part in the study. Two groups were established, according to patients' age: group 1 – over 65 years old and group 2 – 65 years old or less.

The sample size calculation was made considering 80% sample power, alpha error 5%, and death risk for aged patients under IMV 60% and 20% for younger IMV patients. For this purpose, 40 patients would be necessary, i.e. 20 aged IMV patients and 20 younger IMV patients. However, in order to assess the independent predictors of death in IMV aged patients, the group 1 sample size was tripled, thus reaching 81 patients.

For all included patients identification data, demographics, clinical evaluation and physiological and laboratory variables used for the calculation of Acute Physiologic Chronic Health Evaluation II (APACHE II)<sup>(10)</sup> and Sequential Organ Failure Assessment (SOFA)<sup>(11)</sup>, were collected. For calculation of scores the worst results of patient evolution in the 24h of ICU were used.

All patients were followed until hospital discharge, checking for organ dysfunction during stay. For sepsis definition the Society of Critical Care Medicine/American College of Chest Physicians (SCCM/ACCP) 1991 Consensus<sup>(12)</sup> was used, and for ventilator associated pneumonia the Center for Disease Control (CDC) criteria were used.<sup>(13)</sup> Polyneuropathy was diagnosed by electromyography. Difficult weaning was defined when, after undergoing more than two times, 24 hours apart, a 30-minutes spontaneous breathing trial with 7 cm-H<sub>2</sub>O pressure ventilation support, patients had worsening in the ventilatory mechanics evaluated, e.g., by an increase in respiratory rate and reduction in tidal volume that hamper ventilator withdrawn.

In the ICU where the study was developed, sedation is withheld daily for neurology evaluation and speeding respiratory mechanic ventilation withdrawal, according to the previously established study protocol.

The data were entered into an electronic databank (Excel - Microsoft®) and analyzed using statistical software (SPSS 13.0). Demographic, clinical and physiological aspects of the included patients were described. For the categorical variables description, frequencies were calculated. Quantitative variables were described using measures of central tendency and of dispersion.

Aged patients (Group 1) were compared to those under 65 years old (Group2). Choice of theme statistical method for each variable evaluation was based on

the distributions standard; the t Student test was used for continuous variables with normal distribution, the Kruskal Wallis for continuous variables with irregular distribution, and the Chi-square test for categorical variables. All statistics were two sided, and a 0.05 significance level was used.

Also a multivariate analysis was used by enter analysis, aiming to identify independent ICU death risk predictors, and control confounding effects (mutually adjustable variables). Variables with lower than 0.2 significance probability (p value) in the univariate analysis of ICU mortality were considered candidates for the multiple regression model.

To test discrimination power of MVI time to predict ICU clinical development (the ability to correctly rate survivors and non-survivors) and identify the best cutoff point for this parameter, the receiver operating characteristic (ROC) curve was used.

## RESULTS

Eighty one patients were included in the study, 62 in Group 1 and 19 in Group 2. Although this ICU admits monthly around 100 patients, in most cases mechanic ventilation withdrawal was before 24 hours, as the prevalent population was of surgical patients. In ad-

dition, aged patients had a higher incidence of previous pulmonary disease, and many were excluded.

Aged patients had longer MV, in addition to higher ICU and hospital mortality versus group 2 (Table 1). Assessing the groups' development during ICU stay, aged patients had higher desintubation failure rates, need for non-invasive mechanic ventilation (NIMV), also higher number of deaths, directly respiratory-related (Table 2).

Analyzing only MV aged patients, it was perceived that in the ICU survivors and not-survivors univariate analysis, a higher death rate was found among patients from the emergency room and wards with high APACHE II, longer ICU stay and MV time, patients who developed mechanic ventilation associated pneumonia (MVP), sepsis, organ dysfunction, need of sedation and steroids, further, patients with difficult ventilatory weaning and critically ill patient polyneuropathy (Table 3).

Only univariate analysis  $p < 0.2$  variables underwent logistic regression, and only MV time was an independent ICU death predictor for aged MV patients (Table 4). Aged patients with longer than 4 days MV have increased ICU mortality as determined by the ROC curve, area 0.92, sensitivity 89.4% and specificity 77.1% (Figure 1).

**Table 1 - Groups characteristics**

Variables	Group 1 (N = 62)	Group 2 (N = 19)	Overall (N = 81)	P value
Age (years)	76.7±6.9	56.7±7.5	71.9±11.0	0.001
Female	50.0	52.6	50.6	0.841
Caucasian	69.4	63.2	67.9	0.851
Category				0.426
Clinical	9.3	21.4	12.3	
Surgery				
Urgency	32.6	21.4	29.8	
Elective	58.1	57.1	57.9	
APACHE II	22.9±7.4	19.9±6.2	22.6±7.2	0.105
SOFA	7.6±3.5	7.6±4.7	7.6±3.8	0.969
Weight (Kg)	69.3±12.6	70.3±16.3	69.5±13.5	0.770
Height (m)	1.64±0.1	1.65±0.1	1.64±0.1	0.605
Hospital Stay (days)	31.0(16.0-53.0)	31.0(25.2-49.0)	31.0(16.5-52.5)	0.858
ICU stay (days)	11.5(6.0-25.0)	7.0(3.2-12.7)	10.0(5.0-24.5)	0.082
IMV time (days)	10.0(3.0-25.0)	3.0(1.0-10.5)	8.0(2.5-22.5)	0.045
ICU mortality	66.1	26.3	56.8	0.002
Hospital mortality	74.2	47.4	67.9	0.028

IMV – invasive mechanic ventilation; APACHE II - Acute Physiologic and Chronic Health Evaluation; SOFA - Sequential Organ Failure Assessment; ICU – intensive care unit. Results expressed in % or mean ± standard deviation or median (25%-75%).

**Table 2 – Groups outcomes during intensive care unit stay**

Variables	Group 1 (N = 62)	Group 2 (N = 19)	Overall (N = 81)	P value
Sepsis	46.8	57.9	49.4	0.396
MVP	19.4	21.1	19.8	0.871
Organic dysfunction	58.1	42.1	54.3	0.222
Cardiovascular	25.8	26.3	25.9	0.965
Respiratory	33.9	15.8	29.6	0.131
Renal	17.7	10.5	16.0	0.453
Coagulation	6.5	5.3	6.2	0.851
Metabolic acidosis	4.8	10.5	6.2	0.367
Neurological	25.8	10.5	22.2	0.161
Liver	1.6	5.3	2.5	0.370
NET need	90.3	89.5	90.1	0.914
Sedation need	41.0	68.4	47.5	0.073
Steroids use	38.7	31.6	37.0	0.213
Psychomotor agitation	14.5	10.5	13.6	0.657
Blood components transfusion	40.3	42.1	40.7	0.890
MV withdrawal failure	38.7	10.5	32.1	0.021
NIMV need	25.8	0.0	17.9	0.013
Desintubation failure	41.9	15.8	35.8	0.038
Tracheotomy need	24.2	10.5	21.0	0.201
Critically ill patient polyneuropathy	27.4	10.5	23.5	0.110
Respiratory cause death	24.6	0.7	19.7	0.046

MVP = mechanic ventilation-associated pneumonia; IMV - invasive mechanic ventilation; NIMV - non-invasive mechanic ventilation; NET - Naso-enteral tube. Results expressed as %.

**Table 3 – Comparison between survivor and non-survivor mechanic ventilation aged patients during intensive care stay – univariate analysis**

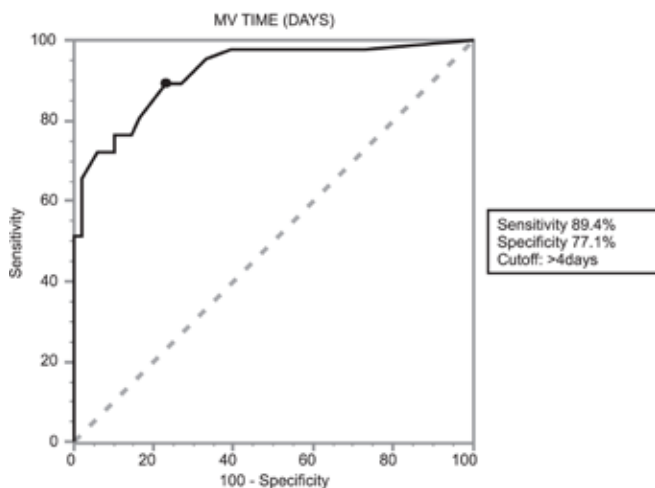
Variable	Non-survivors (N = 41)	Survivors (N = 21)	P value
Age (years)	77.7±7.2	74.7±5.9	0.109
Female gender	51.2	47.6	0.500
Caucasian	68.3	71.4	0.472
Origin			0.020
Operating room	51.3	85.7	
ER/Ward	48.7	14.3	
Category			0.943
Clinical	8.7	10.0	
Surgical			
Urgency	34.8	30.0	
Elective	56.5	60.0	
Prevalent Surgery			0.934
Gastrointestinal	34.8	35.0	
APACHE II	24.7±7.8	19.7±5.6	0.012
SOFA	8.2±3.5	6.7±3.2	0.083
Weight (Kg)	68.7±13.3	70.4±11.3	0.625
Height (m)	1.64±0.1	1.64±0.1	0.888
Hospital Stay (days)	27.0 (14.7-54.0)	38.0 (19.5-51.5)	0.297
ICU stay (days)	18.0 (8.0-32.5)	7.0 (4.0-11.0)	0.001
MV time (days)	18.0 (8.0-32.2)	2.0 (1.0-5.5)	0.000
MV-associate	26.8	4.8	0.034
Pneumonia			
Sepsis	63.4	14.3	0.000
Organ dysfunction	70.7	33.3	0.005
Sedation need	53.7	15.0	0.004
Steroids use	51.2	14.3	0.004
Psychomotor agitation	14.6	14.3	0.644
Blood components transfusion	36.6	47.6	0.285
MV withdrawal failure	41.5	33.3	0.367
NIMV need	26.8	23.8	0.526
Difficult ventilatory weaning	43.9	9.5	0.005
Desintubation failure	34.1	33.3	0.590
Tracheotomy need	34.1	4.8	0.009
Critical ill patient polyneuropathy	36.6	9.5	0.021

IMV - invasive mechanical ventilation; NIMV – non-invasive mechanical ventilation; ICU - intensive care unit; ER - emergency room; APACHE II - Acute Physiologic and Chronic Health Evaluation; SOFA - Sequential Organ Failure Assessment. Results expressed as % or mean± standard deviation.

**Table 4 – Multivariate analysis for independent death predictors in aged patients requiring mechanic ventilation**

Variables	OR (95%CI)	P value
Age (years)	1.17 (0.90-1.52)	0.24
Origin	0.16 (0,00-20,62)	0.46
Surgery Center		
APACHE II	1.26 (0.72-2.10)	0.37
SOFA	0.96 (0.52-1.80)	0.90
ICU stay (days)	0.76 (0.51-1.13)	0.17
MV time (days)	2.70 (1.15-6.32)	0.02
MV-associated Pneumonia	8.46 (0.00-10.11)	0.66
Sepsis	0.95 (0.02-4.43)	0.98
Organ dysfunction	6.33 (0.19-2.16)	0.30
Sedation need	0.11 (0.00-13.15)	0.37
Steroids use	1.74 (0.16-18.95)	0.15
Difficult ventilation weaning	2.42 (0.02-3.12)	0.81
Tracheotomy need	0.02 (0.00-5.41)	0.23
Critically ill patient	0.41 (0.02-9.70)	0.74
polyneuropathy		

OR – odds ratio; CI - confidence interval; APACHE II - Acute Physiologic and Chronic Health Evaluation; SOFA - Sepsis-related Organ Failure Assessment; MV- mechanic ventilation; ICU – intensive care unit.



**Figure 1- ROC curve for mechanic ventilation time in relation to intensive care unit death. Area: = 0.92 (95%CI 0.85-0.97, p (Area 0.5)=0,0001).**

## DISCUSSION

This study shows that mortality rate among IMV aged patients both in ICU and hospital may be three- and two-fold higher, respectively, when compared to younger patients with similar clinical features.

Ely et al. evaluated 902 mechanically ventilated patients in a trial performed in the United States of America, where they observed that patients over 70 years of age had increased mortality and longer intensive care stay than a group below 70 years of age.<sup>(14)</sup>

Sophia E. et al. showed that the increased critically ill patients mortality rate is due to disease relevance and pre-disease functional status in these patients.<sup>(15)</sup> An example was the study in geriatric burned patients where pulmonary failure and dependence on IMV for more than 7 days largely contributed to these patients' morbidity and mortality.<sup>(16)</sup>

Indeed, aged patients had longer IMV. This group can be more difficult for mechanic ventilation withdrawal, causing increased incidence of severe infections and mortality, as observed in this sample.

Ageing is associated to decrease of cardiopulmonary and renal reserves and higher comorbidities rates, which in turn, increase the progressive risk of developing progressive organ failure.<sup>(17)</sup>

Both aged and young patients requiring mechanic ventilation had high rates of pneumonia, sepsis and organ dysfunction, as clearly seen in this analysis. The mortality among sepsis and septic shock patients who develop organ failures are comparable to those reported in literature. Age of more than 65 years and organ failure present an additionally increased mortality of 20% in hospital stay.<sup>(18)</sup> Evolution of aged patients under mechanic ventilation is much worse than that of young patients, as they had increased extubation failure and respiratory-related death rates.

Respiratory complications requiring mechanic ventilation for more than 10 days may have a mortality rate above 50%, and increases with age.<sup>(19)</sup> Thus, early extubation should be considered, to favor the patients evolution and to reduce the ICU stay, consequently reducing hospital costs,<sup>(20)</sup> as mechanic ventilation patients represent more than 50% of total costs in this institution.<sup>(21)</sup>

Additionally, aged IMV patients had increased polyneuropathy rates, suggesting that just need of IMV can be directly related to severe muscle strength loss in this population, and difficult respiratory weaning. Studies have shown that polyneuropathy begins early, within the first 72 hours in septic shock patients.<sup>(22)</sup> This muscle loss has a direct effect on respiratory muscle strength; the maximal diaphragm strength is reduced and intercostal muscles reduce their section area, resulting in an up to 50% decreased maximal inspiratory and expiratory strengths. This in the lungs means loss of

elasticity with collapsed small airways and irregular alveoli ventilation.<sup>(23)</sup> However, these patients need more sedation and steroids, which is also related to muscle loss as previously reported in literature. However, the comparison in this cohort with young patients also under IMV shows that this group received a similar or larger amount of these drugs during ICU stay, but their IMV withdrawal was faster than in aged patients.

In the Ely et al., study, patients with more than 70 years, after undergoing respiratory test needed one additional day when compared to younger patients to achieve spontaneous breathing.<sup>(14)</sup> Thus, effectively IMV apparently has an important negative influence on loss of muscle strength and consequently difficult IMV weaning in aged patients, constituting a vicious circle.

Thus, when independent ICU death features are analyzed, only for aged patients to avoid confounding factors, this study shows that in this population, the longer IMV, the larger will be the risk of death, with OR=2.7, i.e., for each additional IMV day, the death odds ratio is 2.7. However, although IMV duration is the factor associated to increased mortality, it may not necessarily be the cause.

Recent studies have shown a hospital mortality rate around 29.3% for 75 year or older patients, while patients developing acute pulmonary disease and/or acute respiratory distress syndrome have a 49.7% mortality rate.<sup>(14)</sup> This confirms the finding in this study, where it was shown that respiratory related deaths were higher in older patients.

Thus, aged patients requiring IMV should receive special attention during their ICU stay and IMV withdrawal should be considered as soon as possible, as delaying this procedure in this population is associated do increased risk of death.

However, some important limitations in this study are noteworthy. It followed an observational methodology, which can bias patients' selection. The sample was too small to allow definitive conclusions, although the sample size calculation showed enough statistical power for the study. Additionally, definition of the aged patient in this trial was based upon a chronology rather than on physiological aspects, i.e., rating as aged patient those with more than 65 years may not be the best approach, if the previous mental and physical status is not considered.

Thus, more studies, with larger samples and appropriate design are warranted to corroborate the findings of this study.

## CONCLUSION

In the studied population, aged patients under mechanic ventilation had increased mortality rate, longer MV time, and invasive mechanic ventilation weaning and desintubation failure, when compared to the control group.

The time under mechanic ventilation was an independent variable for increased

ICU risk of death among aged patients. The longer mechanic ventilation time, the higher was mortality, and MV time of more than 4 days was associated to poorer prognosis in ICU.

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## RESUMO

**Objetivos:** Descrever população de pacientes idosos em relação a jovens em ventilação mecânica e analisar fatores de risco para mortalidade na unidade de terapia intensiva neste grupo.

**Métodos:** Estudo prospectivo observacional, em pacientes com idade acima de 18 anos, admitidos na unidade de terapia intensiva em ventilação mecânica no período de um ano. Os pacientes foram divididos em dois grupos de acordo com a idade: Grupo 1- pacientes acima de 65 anos e Grupo 2 com idade menor ou igual a 65 anos.

**Resultados:** Foram incluídos 81 pacientes, 62 idosos e 19 jovens em ventilação mecânica. A média de idade dos idosos foi 76 anos, enquanto o grupo mais jovem apresentou média de 56 anos. Idosos em comparação aos controles, apresentaram maiores tempo de ventilação mecânica, mortalidade na unidade de terapia intensiva e no hospital: 63,1% versus 26,3% e 74,2% versus 47,4% ( $p < 0,05$ ), respectivamente. Além disso, idosos em ventilação mecânica apresentaram maiores taxas de falências de desintubações, desmame ventilatório difícil e óbitos diretamente relacionados à disfunção respiratória. O tempo de ventilação mecânica foi fator de risco independente de morte na unidade de terapia intensiva em pacientes idosos (OR= 2,7,  $p=0,02$ ). A área sob a curva ROC do tempo de ventilação mecânica em relação a óbito na unidade de terapia intensiva foi de 0,92 (IC95% 0,85-0,97,  $p$  (área 0,5)=0,0001), ponto de corte de 4 dias sensibilidade 89,4% e especificidade 77,1%.

**Conclusões:** Pacientes com idade acima de 65 anos em ventilação mecânica apresentam pior prognóstico que os pacientes mais jovens e quanto maior seu tempo de ventilação mecânica maior mortalidade na unidade de terapia intensiva.

**Descritores:** Idosos; Mortalidade; Unidades terapia intensiva; Respiração artificial; Fatores de risco

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