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Risk factors for death among critically ill elderly patients

Fatores de risco para óbito em pacientes idosos gravemente enfermos

ABSTRACT

Background: The elderly population is increasing all over the world. The need of intensive care by the elderly is also increasing. There is a lack of studies investigating the risk factors for death among critically ill elderly patients. This study aims to investigate the factors associated with death in a population of critically ill elderly patients admitted to an intensive care unit in Brazil.

Methods: This is a retrospective cohort study including all elderly patients (>60 years) admitted to an intensive care unit in Fortaleza, Brazil, from January to December 2007. A comparison between survivors and nonsurvivors was done and the risk factors for death were investigated through univariate and multivariate analysis.

Results: A total of 84 patients were included, with an average age of 73 ± 7.6 years; 59% were female. Mortality was 62.8%. The main cause

of death was multiple organ dysfunction (42.3%), followed by septic shock (36.5%) and cardiogenic shock (9.7%). Complications during intensive care unit ICU stay associated with death were respiratory failure (OR=61, $p<0.001$), acute kidney injury (OR=23, $p<0.001$), sepsis (OR=12, $p<0.001$), metabolic acidosis (OR=17, $p<0.001$), anemia (OR=8.6, $p<0.005$), coagulation disturbance (OR=5.9, $p<0.001$) and atrial fibrillation (OR=4.8, $p<0.041$). Independent risk factors for death were age (OR=1.15, $p<0.005$), coma (OR=7.51, $p<0.003$), hypotension (OR=21.75, $p=0.003$), respiratory failure (OR=9.93, $p<0.0001$) and acute kidney injury (OR=16.28, $p<0.014$).

Conclusion: Mortality is high among critically ill elderly patients. Factors associated with death were age, coma, hypotension, respiratory failure and acute kidney injury.

Keywords: Aged; Intensive care units; Mortality; Prognosis; Risk factors

INTRODUCTION

The elderly population is increasing all over the world. It is estimated that the population older than 80 years-old will increase 40% between 1995 and 2015.⁽¹⁾ The US census estimates that by 2050, approximately 20.1% (88.5 million) of the US population will be older than 65, and 4.3% (19.04 million) will be older than 85 years of age.⁽²⁾ The consequence is an increase in chronic diseases and corresponding expectations of eventual decline in function.^(3,4) Many investigators have reported rising numbers of elderly patients admitted to intensive care units (ICUs).⁽⁵⁻⁷⁾

In the last years some studies regarding mortality in elderly patients have

been done, and the main causes of death in this population were cardiovascular diseases, neoplasms, respiratory diseases, gastrointestinal diseases, endocrine, nutritional or metabolic diseases and others.^(5,7-9) The analysis of risk factors for death in elderly patients showed that advanced age was the strongest prognostic factor. Male gender is also considered a risk factor for death in the elderly.^(8,9) There is a lack of studies investigating risk factors for death among critically ill elderly patients. The present study was conducted to investigate the factors associated with death in a population of critically ill elderly patients admitted to an ICU in Brazil.

METHODS

Study design and subjects

This is a retrospective cohort study conducted at the General Hospital of Fortaleza, in Northeast of Brazil. The records of all the patients admitted to the ICU from January to December 2007 were evaluated. Data were collected from the medical records by the authors. All patients older than 60 years-old admitted in the study period were included. Diagnosis at ICU admission, co-morbidities and complications during ICU stay presented by each patient, as well as length of ICU stay, need of surgery, need of dialysis and the cause of death were evaluated.

The protocol of this study was approved by the Ethical Committee of the Institution.

Definitions

Acute kidney injury (AKI) was defined as serum creatinine ≥ 1.5 mg/dL or increase of more than 50% on baseline creatinine. Hypotension was defined as mean arterial blood pressure (MAP) < 60 mmHg, and therapy with vasoactive medication was initiated when the MAP remained lower than 60 mmHg despite fluid administration. Sepsis was defined according to the American College of Chest Physicians/Society of Critical Care Medicine (ACCP/SCCM) as "the systemic response to infection, manifested by two or more of the following conditions as a result of infection: (1) temperature $>38^{\circ}\text{C}$ or $<36^{\circ}\text{C}$; (2) heart rate >90 beats per minute; (3) respiratory rate >20 breaths per minute or $\text{PaCO}_2 < 32$ mmHg; and white blood cell count $> 2000/\text{mm}^2$, $<4000/\text{mm}^2$ or $>0\%$ immature (band) forms".⁽¹⁰⁾ Hypovolemic shock was differentiated from septic shock when a patient without sepsis, i.e., those who did not fill the criteria for sepsis by ACCP/SCCM developed hypotension,

and in which cardiogenic shock was excluded. Coma was defined according to the Glasgow coma scale. Respiratory insufficiency was defined as the need for mechanical ventilation; metabolic acidosis as $\text{pH} < 7.35$ and arterial bicarbonate <20 mEq/L; and coagulation abnormalities as when the platelet count was $< 100 \times 10^3/\text{mm}^3$ or prothrombin time (PT) $<65\%$. Anemia as hemoglobin <13 g/dL for men and <12 g/dL for women.

Patients' subgroups

Patients were divided in two subgroups: survivors and non-survivors. We compared these subgroups in order to investigate the differences in clinical manifestations and laboratory features. Factors presented at admission and complications during ICU stay were investigated as possible risk factors for death.

Statistical analysis

The results were expressed through tables and summary measures (mean \pm standard deviation) in the cases of quantitative variables and median when appropriate. Univariate and multivariate analysis was conducted with SPSS version 10.0 (SPSS Inc. Chicago, IL). Comparison of parameters of the two subgroups (survivors and non-survivors) was done with Fischer's exact test. Analysis of associations between death and categorized risk factors was done with Fischer's exact test and Pearson's chi-square test. Adjusted odds ratios (ORs) and 95% confidence intervals (CIs) were calculated. A multivariate logistic regression was performed to analyze the possible risk factors for death. The factors included in the multivariate model were those that showed a significant level $<20\%$ in the univariate analysis (Mann-Whitney test and chi-square test), and "p" values < 0.05 were considered as statistically significant.

RESULTS

Demographic data and co-morbidities

A total of 84 patients were included in the analysis. The mean age was 73 ± 7.6 years (range 60-89, median 74 years) and 50 (59.5%) were female. The length of ICU stay was 17 ± 14.8 days (range 1-85, median 13 days). Co-morbidities identified were hypertension (75%), diabetes (40.5%), coronary artery disease (8.4%), chronic pulmonary obstructive disease (8.4%), chronic kidney disease (6%), obesity (6%), dementia (4.8%), dyslipidemia (4.8%) and heart failure (3.6%). Past history of stroke was observed in 18

cases (21.4%), smoking in 18 (21.4%) and ethylism in 4 (10.7%). The diagnosis at ICU admission were post-surgery, stroke, neoplasm and septic shock, as summarized in table 1.

Table 1 - Diagnosis at admission among critically ill elderly patients in an intensive care unit at Fortaleza, Brazil, in 2007

Diagnosis	N	%
Post-surgery	18	21.4
Stroke	16	19
Neoplasm	13	15.4
Septic shock	10	11.9
Hypovolemic shock	8	9.5
Respiratory failure	7	8.3
Cardiogenic shock	3	3.6
Other	9	10.7
Total	84	100

Complications during ICU stay

The main complications developed during ICU stay were anemia (86.9%), respiratory failure (77.4%), coma (66.7%), sepsis (57.1%), metabolic acidosis (53.6%), hypertension (51.2%), AKI (47.6%), coagulation disturbances (47.6%), hypotension (39.3%), atrial fibrillation (17.9%), hepatic dysfunction (16.7%), acute myocardial infarction (9.5%), delirium (9.5%), gastrointestinal bleeding (7.1%) and pancreatitis (6%). During ICU stay, surgery was required for 29 patients (34.5%), vasoactive drugs for 51 (60.7%) and dialysis for 23 (27.4%).

Comparison between the subgroups: survivors x non-survivors

The comparison between survivors (n=31) and non-survivors (n=52) showed a higher prevalence of coma at admission among non-survivors (51.9% vs. 12.9%, $p<0.001$), as well as hypotension (40.4% vs. 12.9%, $p=0.012$), respiratory failure (82.7% vs. 29%, $p<0.001$), AKI (36.5% vs. 3.2%, $p<0.001$), infection (48.1% vs. 22.6%, $p=0.035$), sepsis (53.8% vs. 25.8%, $p=0.021$), anemia (80.8% vs. 54.8%, $p=0.023$) and atrial fibrillation (17.3% vs. 0%, $p=0.023$). Age was similar in both subgroups (survivors: 75 ± 7.0 years, non-survivors: 69 ± 7.0 years, $p=0.29$), as well as length of hospital stay (survivors: 18 ± 16 days, non-survivors: 13 ± 11 days, $p=0.73$).

The comparison of complications during ICU stay between survivors and non-survivors showed a higher incidence of coma among non-survivors (92.3% vs. 25.8%, $p<0.001$), as well as hypotension (55.8%

vs. 12.9%, $p<0.001$), respiratory failure (98.1% vs. 45.2%), AKI (71.2% vs. 9.7%, $p<0.001$), infection (78.8% vs. 41.9%, $p=0.001$), sepsis (78.8% vs. 22.6%, $p<0.001$), metabolic acidosis (76.9% vs. 16.1%, $p<0.001$), anemia (96.2% vs. 74.2%, $p=0.005$), coagulation disturbances (63.5% vs. 22.6%, $p=0.001$), atrial fibrillation (25% vs. 6.5%, $p=0.041$), need of dialysis (43.3 vs. 3.2%, $p<0.001$) and need of vasoactive drugs (80.8% vs. 29%, $p<0.001$).

Death occurred in 62.8% of the cases. The main causes of death were multiple organ dysfunction (42.3%), septic shock (36.5%), cardiogenic shock (9.7%), respiratory failure (5.8%), stroke (3.8%) and AKI (1.9%).

Risk factors for death

The univariate analysis found the following factors presented at ICU admission to be associated with death: coma, hypotension, respiratory failure, acute kidney injury, infection, sepsis and anemia, as can be seen in table 2. Multivariate analysis found as independent risk factors for death (factors present at ICU admission): coma, hypotension, respiratory failure, acute kidney injury and age, as summarized in table 3.

Table 2 - Risk factors for death in critically ill elderly patients in an intensive care unit at Fortaleza, Brazil, 2007 (univariate analysis)

Risk factors	OR	95% CI	P value
Factors present at admission			
Acute kidney injury	17.27	2.18-136.99	<0.001
Respiratory failure	11.68	4.06-33.62	<0.001
Coma	7.29	2.23-23.79	<0.001
Hypotension	4.57	1.4-14.99	0.012
Anemia	3.46	1.29-9.29	0.023
Sepsis	3.35	1.27-8.86	0.021
Infection	3.18	1.17-8.65	0.035
Factors observed during hospital stay			
Respiratory failure	61.9	7.57-506.57	<0.001
Coma	34.5	9.41-126.47	<0.001
Acute kidney injury	23	6.06-87.33	<0.001
Need of dialysis	22	2.78-173.81	<0.001
Metabolic acidosis	17.3	5.46-54.9	<0.001
Sepsis	12.7	4.36-37.37	<0.001
Need of vasoactive drugs	10.2	3.63-28.98	<0.001
Anemia	8.9	1.71-44.2	0.005
Hypotension	8.5	2.6-27.81	<0.001
Coagulation disturbances	5.9	2.16-16.40	0.001
Infection	5.1	1.94-13.69	0.001
Atrial fibrillation	4.8	1.01-23.10	0.041

OR - odds ratio; 95% CI - 95% confidence interval; Significant $p<0.05$.

Table 3 - Risk factors for death in critically ill elderly patients in an intensive care unit at Fortaleza, Brazil, 2007 (multivariate analysis)

Risk factors	OR	95% CI	P value
Factors present at admission			
Hypotension	21.75	2.03-27.79	0.003
Acute kidney injury	16.28	2.92-161.70	0.003
Respiratory failure	9.93	3.2-30.29	<0.001
Coma	7.51	1.75-150.80	0.014
Age	1.15	1.04-1.26	0.005
Factors observed during hospital stay			
Acute kidney injury	11.46	2.61-50.32	0.001
Metabolic acidosis	5.31	1.31-21.38	0.019

*OR - odds ratio; 95% CI - 95% confidence interval; Significant $p < 0.05$.

The univariate analysis found the following complications associated with increased risk for death: coma, hypotension, respiratory failure, acute kidney injury, infection, sepsis, anemia, atrial fibrillation, need of dialysis and need of vasoactive drugs, as summarized in table 2. The following complications were independent risk factors for death: acute kidney injury and metabolic acidosis (Table 3).

DISCUSSION

The present study evaluated the risk factors for death among critically ill elderly patients in a population in Northeast of Brazil. This study had some limitations, including the small number of patients and the retrospective design, but we believe the results achieved are important and can highlight some topics which could be taken into consideration for the clinical practice. Elderly patients currently account for 42-52% of ICU admissions and for almost 60% of all ICU days, so it is important to know the factors associated with a poor outcome. Aging is associated with decreased cardiopulmonary and renal reserve and with a high rate of comorbidities, increasing the risks of the elderly developing progressive organ failure.⁽¹⁰⁾

This is one of the few studies on this subject in our region.^(11,12) We included patients older than 60 years, according to the definition of elderly used by the Brazilian Ministry of Health, although in the majority of the studies use the cut-off of 65 years to define an elderly patient. In the present study, age varied from 60 to 89 years-old, and non-survivors were older than survivors, evidencing a significant association between advanced age and increased mortality. Age is generally thought to be strongly associated with intensive care outcomes, but

this relationship may be confounded with acute physiological impairment, age-related changes (lower functional reserve, co-morbidity).⁽¹³⁻¹⁵⁾ Other studies did not evidence gender as a risk factor for death also.^(7,14-16) Data from Brazilian Government (Ministry of Health) shows that 55% of all deaths occurred with people older than 70 years-old,⁽¹⁷⁾ but this association was not observed among critically ill elderly patients.^(7,16) It is believed that elderly patients present higher mortality when admitted to ICU, but age *per se* does not contribute to this, so investigation for risk factors for death is important.^(7,16)

Campion et al. showed that critically ill patients with higher length of ICU stay have worse prognosis.⁽¹⁸⁾ The length of ICU stay varied from 1 to 85 days in the present study. There was no difference among survivors and non-survivors. Although non-survivors presented a higher mean length of hospital stay (18 days) in comparison to survivors (13 days) the difference was not statistically significant. This could be due to the small size of the studied population. Maybe with a higher number of patients this difference would be significant.

Vosylius et al. found the following organ dysfunction during stay in ICU: shock, impaired level of consciousness, arterial hypoxaemia, uremia or oliguria, thrombocytopenia and hyperbilirubinemia.⁽¹⁹⁾ The main complications observed during ICU stay in the present study were anemia, respiratory failure, coma, sepsis, metabolic acidosis, hypertension, acute kidney injury, coagulation disturbances and hypotension. We did not observed patients with uremia because of prompt initiation of dialysis in the appropriate cases. The other complications found in the present study were attributed to the baseline disease.

Mortality was high in the present study (62%), which could be attributable to the severity of disease or by the delayed admission to the ICU (which occurs in our hospital due to the lack of sufficient number of ICU beds). Other studies found mortality between 6.4% and 40% of critically ill elderly patients.^(11,20) In a recent study performed in São Paulo, Brazil, including 840 patients older than 55 years admitted to an ICU, age was significantly associated with in-hospital mortality (OR=2.68 for patients older than 75 years and OR=1.60 for those between 65-74 years-old).⁽²¹⁾ Blot et al., in a study with 984 critically ill patients with bloodstream infection (134 aged ≥ 75 years), evidenced an increase in the number of elderly patients admitted in a period of 15 years, and mortality increased with age (42.9%, 49.1% and 56% for middle-aged - 45-64 years, old - 65-74 years and very old patients ≥ 75 years).⁽²²⁾

Factors associated with death in the present study were coma, hypotension, respiratory failure, acute kidney injury and age. The values of confidence intervals were large which evidence the small sample size. The results could differ if the sample were larger. However, these data are in accordance with other studies. In a recent study with 856 patients aged 60 to 104 years admitted to a tertiary hospital in Brazil, found a mortality rate of 16.4%, and the factors associated with death were delirium, neoplastic disease, serum albumin levels at admission $< 3.3\text{mg/dL}$, serum creatinine level at admission $\geq 1.3\text{mg/dL}$, history of heart failure, immobility and advanced age.⁽²³⁾ In a recent study with patients older than 80 years in an ICU after surgery the factors associated with death were need of vasoactive drugs in the first and second 24h.⁽²⁴⁾ In a recent study with critically ill patients aged > 80 years showed that the most important determinants of ICU mortality were emergency (versus elective) admission, non-operative (versus post-operative) source of admission and a higher age-adjusted APACHE II score.⁽²⁵⁾ Esteban et al. reported that variables associated with mortality of patients aged ≥ 75 years receiving mechanical ventilation were acute renal failure, shock and arterial blood oxygenation index.⁽²⁶⁾ In a study performed in Australia and New Zealand with critically elderly patients, old patients (> 80 years) accounted for 13% of ICU admissions. ICU and hospital mortalities were higher among old patients (ICU: 12% vs. 8.2%, $p < 0.001$; hospital: 24% vs. 13%, $p < 0.001$). Age > 80 years was associated with higher ICU and hospital death compared with younger patients. Factors associated with lower survival included admission from a chronic care facility, co-morbid illness, nonsurgical admission, greater illness severity, mechanical ventilation, and longer stay in the ICU.⁽²⁷⁾

CONCLUSION

In summary, mortality among elderly critically ill patients is high. Age, coma, hypotension, respiratory failure and AKI are factors associated with death. Some factors can be preventable, such as AKI and anemia, so

we should adopt measures to decrease the incidence of these complications to try to reduce mortality. The better comprehension of factors associated with death in the elderly can improve medical care to these patients.

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RESUMO

Objetivo: A população idosa está aumentando em todo o mundo, assim como a necessidade de cuidados intensivos para os idosos. Existem poucos estudos que investiguem os fatores de risco para óbito em pacientes idosos gravemente enfermos. Este estudo teve o objetivo de investigar os fatores associados ao óbito em uma população de pacientes idosos gravemente enfermos admitidos a uma unidade de terapia intensiva no Brasil.

Métodos: Estudo retrospectivo de coorte que incluiu todos os pacientes idosos (idade ≥ 60 anos) admitidos a uma unidade de terapia intensiva em Fortaleza, Brasil, de janeiro a dezembro de 2007. Foi realizada uma comparação entre os sobreviventes e os não sobreviventes, e os fatores de risco para óbito foram investigados por meio de análise univariada e multivariada.

Resultados: Foi incluído um total de 84 pacientes, com uma média de idade de $73 \pm 7,6$ anos, sendo 59% do gênero feminino. A mortalidade foi de 62,8%. A principal causa de morte foi disfunção de múltiplos órgãos (42,3%), seguido por choque séptico (36,5%) e choque cardiogênico (9,7%). As complicações durante a permanência na unidade de terapia intensiva associadas com óbito foram insuficiência respiratória (OR = 61; $p < 0.001$), lesão renal aguda (OR = 23, $p < 0.001$), sepse (OR = 12; $p < 0.001$), acidose metabólica (OR = 17; $p < 0.001$), anemia (OR = 8,6; $p < 0.005$), distúrbios da coagulação (OR = 5,9; $p < 0.001$) e fibrilação atrial (OR = 4,8; $p < 0.041$). Os fatores de risco independentes para óbito foram idade (OR = 1,15; $p < 0.005$), coma (OR = 7,51; $p < 0.003$), hipotensão (OR = 21,75; $p = 0.003$), insuficiência respiratória (OR = 9,93; $p < 0.0001$), e lesão renal aguda (OR = 16,28; $p < 0.014$).

Conclusões: A mortalidade é elevada em pacientes idosos gravemente enfermos. Os fatores associados ao óbito foram idade, coma, hipotensão, insuficiência respiratória e lesão renal aguda.

Descritores: Idosos; Unidades de terapia intensiva; Mortalidade; Prognóstico; Fatores de risco

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