Age, invasive ventilatory support and outcomes in elderly patients admitted to intensive care units

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Abstract

Background: although advancing age is associated with worse outcomes on mechanically ventilated elderly patients admitted to intensive care units (ICU), this relation has not been extensively investigated on patients not requiring invasive ventilatory support.

Objective: to determine the relationship between age and in-hospital mortality of elderly patients, admitted to ICU, requiring and not requiring invasive ventilatory support.

Design: prospective observational cohort study conducted over a period of 11 months.

Setting: medical-surgical ICU at a Brazilian university hospital.

Subjects: a total of 840 patients aged 55 years and older were admitted to ICU.

Methods: in-hospital death rates for patients requiring and not requiring invasive ventilatory support were compared across three successive age intervals (55–64; 65–74 and 75 or more years), adjusting for severity of illness using the Acute Physiologic Score.

Results: age was strongly correlated with mortality among the invasively ventilated subgroup of patients and the multivariate adjusted odds ratios increased progressively with every age increment (OR = 1.60, 95% CI = 1.01–2.54 for 65–74 years old and OR = 2.68, 95% CI = 1.58–4.56 for ≥75 years). For the patients not submitted to invasive ventilatory support, age was not independently associated with in-hospital mortality (OR = 2.28, 95% CI = 0.99–5.25 for 65–74 years old and OR = 1.95, 95% CI = 0.82–4.62 for ≥75 years old).

Conclusions: the combination of age and invasive mechanical ventilation is strongly associated with in-hospital mortality. Age should not be considered as a factor related to in-hospital mortality of elderly patients not requiring invasive ventilatory support in ICU.

Keywords: age, intensive care unit, prognosis, invasive ventilatory support, elderly

Introduction

The ageing process results in a higher rate of hospitalisation and admission to intensive care units (ICU) [1–3]. Intensive care is a costly intervention and, although the number of ICU beds increases in Brazil as it does in other countries, the offer does not meet the rising demand. Additional research is needed to optimally determine the prognostic factors related to ICU outcomes and hence making the best selection of patients. This is especially crucial in developing countries where financial resources allocated to healthcare are limited.

Although recent studies have investigated the factors related to outcomes of elderly patients in the ICU, conflicting results were observed, especially regarding the role played by age as a factor influencing mortality [4–14]. It is commonly acknowledged that elderly patients are more likely to die in the ICU than younger ones. Nonetheless, it is yet to be determined whether mortality of the elderly is independently determined by age or by other factors. When admitted to an ICU, elderly patients suffer from a relatively higher degree of physiological impairment and from certain co-morbid conditions that increase the risk of death [5–9].
Recent studies of patients requiring invasive mechanical ventilation show that age is independently and positively associated with mortality of elderly patients admitted to ICUs but have not provided precise quantitative descriptions on how this association varies along with age [15–21]. Earlier literature excluded non-ventilated patients from the studies or included them together with mechanically ventilated patients in mixed cohort populations. As patients not submitted to invasive ventilatory support have not been studied previously as an isolated subgroup, the relationship between age and mortality for this population remains unknown.

The aim of the current study is to examine prospectively the relationship between age and in-hospital mortality of elderly patients admitted to ICUs and to investigate the degree to which this relationship may vary across the age brackets within both subgroups of patients requiring and not requiring invasive ventilatory support.

Methods

This prospective observational study consecutively recruited patients over a period of 11 months (from 1 December 2000 to 31 October 2001) who were admitted to one of the ICUs located at the ‘Central Institute’ of the Hospital das Clínicas, University of São Paulo Medical School, a tertiary university hospital with 900 beds, 87 of which are ICU beds divided into 12 different units (42% used exclusively for surgical patients, 36% for medical admission and the remaining 22% used for both purposes). The sample of our study was defined as the elderly population aged 65 years and over. Those aged 55 and over were used as a reference population.

Patients who either died or were discharged within 24 h after admission were excluded from the study to avoid potential bias resulting from the inclusion of terminally ill patients and individuals submitted to elective surgery just recovering from anesthesia. If, within the same hospitalisation, a patient was readmitted to the ICU, only data from the first ICU-admission were analysed. The patients with coronary and orthopedic emergencies requiring intensive therapy were admitted to other areas of the hospital. The local ethics committee approved this study and, due to its observational nature, informed consent was not required.

The following data were recorded using a predefined form within the first 24 h of admission: age, gender, date of admission to hospital and ICU, primary cause for admission and co-morbidity (according to the Simplified Acute Physiology Score—SAPS II criteria [22]), need for invasive mechanical ventilation required for more than 24 h.

Most of the previous studies which analysed the relationship between mortality and mechanical ventilation included only invasively ventilated patients. Esteban et al. included non-invasively ventilated subjects, but this subgroup represented only 4.9% of the sample [14]. In order to compare our results with those obtained in the previous literature, patients who were exclusively submitted to non-invasive ventilation were included on the group of patients not requiring invasive ventilatory support.

To assess the severity of illness on the first day of admission to the ICU, the Acute Physiology Score (APS) was calculated using only the 12 physiologic variables of the SAPS II. The APS was used instead of the SAPS II because age, type of admission and presence of co-morbidity were analysed as independent variables. The use of SAPS II could lead to biased results since it is partially based on these parameters. The APS scores from 0 to 115 points. Higher scores represent more severe illness. The organic dysfunction was assessed using the Logistic Organ Dysfunction Score (LODS) system. The score ranges from 0 to 22 points [23].

Advanced directives such as do not resuscitate or intubate were not analysed in the study. Usually, patients transferred to ICUs in our institution are candidates for all advanced measures needed, irrespective of their age. Withdrawal of care or terminal weaning is an ICU team decision in agreement with the family and was not influenced by researchers.

Lengths of ICU and hospital stay were recorded. The main measure of outcome used was survival status at the time of hospital discharge.

The statistical analysis was performed using the Statistical Package for Social Scientists (SPSS) version 13.0. The continuous variables were compared between groups using the Student $t$-test for equality of means and non-parametric similar tests when necessary, whereas categorical variables were analysed using the chi-square test and odds ratio (OR) with a 95% confidence interval (CI). The level of significance used was $P < 0.05$. The variables that had a significant association with mortality to a value of $P < 0.10$ on univariate analysis were entered into a logistic regression analysis performed for the whole sample and for the isolated subgroups of ventilated and non-mechanically ventilated patients in order to determine the relationship between age and in-hospital mortality for these groups. Rather than using a continuous variable for age, the relationship between age and in-hospital mortality was examined using a ‘dummy’ variable for three different age intervals (55–64, 65–74 and ≥ 75 years). The first category of patients aged 55 to 64 years was considered as a reference population for comparison. The three intervals of age were considered the best and clearest solution to show the evolution of mortality across the ageing process on an elderly population.

Results

During the period of investigation, 2,118 patients were admitted to the ICU, 975 being 55 years or older. From these, 135 (13.8%) stayed in the ICU for < 24 h or were discharged soon after this period not allowing enough time for data collection. A total of 840 subjects met the inclusion criteria and constituted the population of the present study. Table 1 illustrates the main characteristics of the sample across the four age intervals. The mean age ± standard deviation of the sample was 69.2 ± 8.7 years (range 55–99); there were 486 men
Invasive ventilation for Haematological cancer, Co-morbidity

Type of admission

Time between hospital admission and ICU (days), mean (SD) 6.5 (9.5) 6.8 (9.9) 6.0 (8.3) 0

Characteristics 55–64 65–74 ≥75 P-value

Number of patients (%) 284 (34) 326 (39) 230 (27) 0.001

Age, mean (SD) 59.9 (2.8) 69.5 (2.7) 80.4 (4.7) < 0.001

Female, n (%) 115 (40) 123 (38) 116 (50) 0.009

Time between hospital admission and ICU (days), mean (SD) 6.5 (9.5) 6.8 (9.9) 6.0 (8.3) 0.50

Type of admission

Medial, n (%) 122 (43) 134 (41) 97 (42) 0.90

Scheduled surgery, n (%) 119 (42) 134 (41) 70 (30) 0.013

Unscheduled surgery, n (%) 43 (15) 58 (18) 63 (27) 0.001

Co-morbidity

Solid cancer, n (%) 80 (28) 96 (29) 63 (27) 0.86

Metastatic cancer, n (%) 21 (7) 24 (7) 18 (8) 0.97

Haematological cancer, n (%) 10 (3) 13 (4) 6 (3) 0.68

Invasive ventilation for ≥24 h, n (%) 147 (52) 195 (60) 140 (61) 0.06

APS, mean (SD) 15.6 (12.5) 17.2 (12.5) 18.8 (13.0) 0.02

LODS, mean (SD) 3.1 (2.6) 3.6 (2.8) 3.9 (2.8) 0.003

Neurological, mean (SD) 0.3 (0.7) 0.2 (0.6) 0.3 (0.7) 0.37

Cardiovascular, mean (SD) 0.2 (0.5) 0.4 (0.8) 0.4 (0.8) 0.03

Pulmonary, mean (SD) 0.6 (0.8) 0.6 (0.7) 0.6 (0.8) 0.88

Renal, mean (SD) 1.8 (1.9) 2.2 (1.8) 2.4 (1.9) < 0.001

Haematological, mean (SD) 0.1 (0.3) 0.1 (0.3) 0.1 (0.2) 0.80

Hepatic, mean (SD) 0.1 (0.3) 0.1 (0.3) 0.1 (0.3) 0.72

Length of ICU stay (days), mean (SD) 10.8 (16.0) 11.4 (16.0) 10.4 (12.9) 0.75

Length of hospital stay (days), mean (SD) 26.3 (24.2) 25.0 (24.6) 24.0 (19.6) 0.49

Died in ICU, n (%) 63 (24) 127 (39) 96 (42) < 0.001

Died in the hospital, n (%) 89 (31) 143 (44) 121 (53) < 0.001

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SD = standard deviation; SAPS II = Simplified Acute Physiology Score II; APS = Acute Physiology Score; LODS = Logistic Organ Dysfunction Score.

Of the subjects examined, 42.0% were medical, 38.5% had an elective surgery and 19.5% had an emergency surgery. The mean time between hospitalisation and ICU admission was 5.9 ± 2.3 points vs 4.9 ± 2.7, P < 0.001, and time between hospital and ICU admission (5.9 ± 8.2 days vs 7.2 ± 10.8, P = 0.05) were significantly associated with in-hospital mortality on the univariate analysis. Of the categorical variables, type of admission (57.5% mortality for medical admission, 47.6% for unscheduled surgery and 22.3% for scheduled surgery, P < 0.001) and invasive ventilation (63.3% of mortality, P < 0.001) were associated significantly with in-hospital mortality. The variables gender and presence of solid and metastatic cancer were not associated with mortality.

The results of multivariate analysis on the overall sample are shown in Table 2. Age, severity of the acute physiological impairment measured through APS, invasive mechanical ventilation, type of ICU admission and time between hospital and ICU admission were determined as independent risk factors for in-hospital mortality. When LODS replaced the APS in the analysis, it was determined as an independent factor associated with mortality, a factor that remained unobserved when it was introduced together with APS.

The relationship between age and in-hospital mortality rates was examined using multivariate analysis of the odds ratio of death for patients divided into three age brackets (55–64, 65–74, ≥75 years). The first category showed the lowest mortality rate and was used as a reference group. When adjusted for other variables, age remained strongly correlated with in-hospital mortality in all categories and the

<table>
<thead>
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<th>Variable</th>
<th>Odds ratio (95% CI)</th>
<th>P-value</th>
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<tr>
<td>Age (65–74 years)</td>
<td>1.68 (1.11–2.53)</td>
<td>0.013</td>
</tr>
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<td>Age (75–84 years)</td>
<td>2.44 (1.56–3.80)</td>
<td>&lt; 0.001</td>
</tr>
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<td>Medical admission</td>
<td>3.30 (2.17–5.00)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Unscheduled surgery</td>
<td>2.08 (1.27–3.39)</td>
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<tr>
<td>APS, points</td>
<td>1.05 (1.03–1.07)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Invasive ventilatory support</td>
<td>6.12 (4.04–9.29)</td>
<td>&lt; 0.001</td>
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<tr>
<td>Time hospital/ICU (days)</td>
<td>1.03 (1.01–1.05)</td>
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</tbody>
</table>

CI = confidence interval.
multivariate odds ratios increased progressively with every age interval.

To examine the consistency of the relationship between age and in-hospital mortality of elderly patients admitted to the ICU and to identify the need for invasive mechanical ventilation as a factor that could modify this relationship we conducted a stratified multivariate analysis separating patients requiring and not requiring invasive ventilatory support. The results are shown in Table 3 and indicated that age was an independent factor related to mortality for the invasively ventilated patients and the multivariate odds ratios increased progressively with every age interval. However, for the patients not requiring invasive ventilation, age was not correlated with mortality in any interval.

### Discussion

The results of our study suggest that the in-hospital mortality of elderly patients admitted to an ICU is elevated and furthermore affected by a variety of factors such as age, invasive mechanical ventilation, organ dysfunction, severity of impairment on admission, primary cause for admission and time between hospital and ICU admission. Although our results reinforce current evidence on predictive factors of mortality in older patients admitted to ICU [13, 14], this study could clearly reveal differences between patients receiving and not receiving invasive ventilatory support with respect to the relationship between age and in-hospital mortality.

This study evaluated the importance of the time interval between hospitalisation and admission to the ICU for the elderly population. The literature reports that patients admitted from the emergency department have better prognosis than those admitted from other hospital wards, probably because of the prompt transfer to the ICU [26, 27]. Our results showed that a delayed transfer to the ICU is correlated with higher rates of in-hospital mortality. The lack of vacant beds on ICU was the major reason for delayed transfer.

Similar to other studies, age was strongly associated with the severity of illness scores [8, 9, 24], but even when adjusted for the degree of physiological impairment, age remained a strong predictor of mortality. This finding is consistent with previous studies, which evaluated the severity of illness upon admission to the ICU through the APS application and differs from many others that found no association between age and mortality [5, 9, 10]. Most of these studies used the SAPS II or the Acute Physiology and Chronic Health Evaluation III (APACHE III) [6, 8, 24, 25]. The use of these two scales could lead to biased results since they are partially based on age. In our study, the use of SAPS II in multivariate analysis instead of APS removed age from the list of factors independently related to mortality.

In the current study, the mortality rates verified for the subgroup of invasively ventilated patients in all age groups were slightly more elevated than those observed in other similar studies. Although the severity of disease measured by APS was comparable to that found in the literature, other factors not measured such as functionality or previous cognitive status could have influenced our results [6]. Methodological aspects like the inclusion of patients requiring non-invasive ventilatory support in this subgroup could explain the lower mortality found in other studies [16].

Although age has frequently been examined as a prognostic factor related to mortality of patients admitted to the ICU, few prior studies have provided quantitative estimates of increased risk associated with specific age intervals. Most of these studies adopted different selection criteria when defining an elderly population, mainly ranging from 60 to 85 years of age and not differentiating between various age intervals [5–12]. Our study defined an elderly population following the most widely used criteria which considers elderly every patient aged 65 and over and analysed the relationship between age and in-hospital mortality in three intervals of age (55–64, 65–74 and > 75 years).

Esteban et al. created a different model to determine a threshold of age that could best discriminate for ICU survival [19]. A higher mortality for older patients, compared with the younger according to Esteban cut points was found in our sample for both subgroups of patients requiring and not requiring invasive ventilatory support. However, our goal was not to compare an older and a younger...
subgroup of ICU patients, but to compare in-hospital mortality occurring at different age stages in an elderly population.

Different from the prior literature that contains a variety of studies on invasively ventilated patients [15–21], the present study evaluated the relationship between age and in-hospital mortality for both patients receiving and not receiving invasive ventilatory support. We found that age is strongly related to mortality of invasively ventilated patients and that this relationship strengthens along with decades of age. However, this effect was not observed among patients not requiring invasive ventilatory support, an important subgroup of ICU admitted patients, which represented 42% of our sample. On this subgroup of patients, there was no age-related increase in mortality both in the individuals between 65–74 years old and in the individuals aged 75 years or older when compared to the reference group, although a large sample was included in the three age brackets.

Although there was a greater mortality on the group of patients not requiring mechanical ventilation aged 65 years and over (including those aged 75 years and over) when compared to younger individuals, this comparison was not the main objective of the current study, as stated before. Furthermore, the age-related mortality found in the group aged 75 years or more was even lower than that in the group between 65 and 74 years old, showing that age should not be considered as a factor related to in-hospital mortality in elderly patients not requiring invasive ventilatory support in ICUs.

The association of age and invasive mechanical ventilation is strongly related to mortality. These results constitute additional evidence for the liberal indication of non-invasive mechanical ventilation and for the development of novel and particular strategies of invasive mechanical ventilation for elderly patients admitted to the ICU with respiratory acute failure.

Some limitations of this study must be addressed. First, although previous studies have shown relationship of in-hospital mortality with other variables such as cognitive and functional impairment and nutritional status prior to admission, these factors were not analysed in our study and could affect the age-related impact in the outcome [6]. Second, we did not examine the aggressiveness or appropriateness of care, factors that could vary across different age groups (as previously shown [28–30]) and could be responsible for some of the difference in age-related mortality. Nevertheless, there were no statistical differences observed between the three age groups regarding the need for invasive mechanical ventilation, showing that the same procedures were indicated, irrespective of the patient’s age. The demand for ICU beds is higher than the offer in our institution and the selection of candidates for admission results from general physicians or general surgeons referral and acceptance by the intensivists. The researchers did not interfere on this decision and a possible age-related bias of selection could have occurred both on the referral and on the acceptance processes. Third, our study was conducted at a single university institution with a specific sample excluding primary cardiologic and orthopedics admissions.

Key points

- Age worsens outcomes in elderly submitted to invasive mechanical ventilation.
- Age is not related to mortality in elderly not submitted to invasive mechanical ventilation.
- Severity of acute illness is a predictor of mortality in elderly admitted to ICU.
- Age is associated with severity of illness in elderly admitted to ICU.

Acknowledgements


Conflicts of interest

None.

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References


