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**CLINICAL SCIENCE**


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**PREDICTORS OF IN-HOSPITAL MORTALITY AMONG OLDER PATIENTS**

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doi: 10.1590/S1807-59322009000700002

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Silva TJA, Jerussalmy CS, Farfel JM, Curiati JAE, Jacob-Filho W. Predictors of in-hospital mortality among older patients. Clinics. 2009;64(7):613-8.

**OBJECTIVE:** The objective of this study was to determine predictors of in-hospital mortality among older patients admitted to a geriatric care unit.

**INTRODUCTION:** The growing number of older individuals among hospitalized patients demands a thorough investigation of the factors that contribute to their mortality.

**METHODS:** This was a prospective observational study implemented from February 2004 to October 2007 in a tertiary university hospital. A consecutive sample of 922 patients was evaluated for possible inclusion in this study. Patients hospitalized for palliative care, those who declined to participate, and those with incomplete data were excluded, resulting in a group of 856 patients aged 60 to 104 years. Bivariate and multivariate analyses were performed to determine associations between in-patient mortality and gender, age, length of stay, number of prescribed medications and diagnoses at admission, history of heart failure, neoplastic disease, immobility syndrome, delirium, infectious disease, and laboratory tests at admission (serum albumin and creatinine).

**RESULTS:** The overall mortality rate was 16.4%. The following factors were associated with higher in-hospital mortality: delirium (OR=4.13, CI=2.65-6.44,  $P<.001$ ), neoplastic disease (OR=3.38, CI=2.11-5.42,  $P<.001$ ), serum albumin levels at admission  $<3.3\text{mg/dL}$  (OR=3.23, CI=2.03-5.13,  $P<.001$ ), serum creatinine levels at admission  $\geq 1.3\text{mg/dL}$  (OR=2.39, CI=1.53-3.72,  $P<.001$ ), history of heart failure (OR=1.97, CI=1.20-3.22,  $P=.007$ ), immobility (OR=1.84, CI=1.16-2.92,  $P=.009$ ), and advanced age (OR=1.03, CI=1.01-1.06,  $P=.019$ ).

**CONCLUSIONS:** This study strengthens the perception of delirium as a mortality predictor among older inpatients. Cancer, immobility, low albumin levels, elevated creatinine levels, history of heart failure and advanced age were also related to higher mortality rates in this population.

**KEYWORDS:** Aged; Death; Risk factors; Delirium; Serum albumin.

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## INTRODUCTION

In Brazil, as in more developed countries, the impact of population aging is becoming increasingly evident.<sup>1</sup> The need to allocate resources to the care of older people is steadily growing; thus, public health care measures aimed at the management of their specific morbidities are necessary. Further understanding of older individuals' mortality

risk factors at various levels of health care would allow patients, families and multidisciplinary teams to better plan therapeutic approaches and more efficiently allot available resources.

In Brazil, from January 2002 to December 2007, over 13 million patients aged 60 years and over were admitted to public hospitals, accounting for 19.4% of total admissions. More than 1.2 million of these patients died while they were in the hospital, corresponding to 56.4% of total deaths during that period and a mortality rate of 9.2%. It is known, however, that elderly medical inpatient mortality rates can be as high as 20%.<sup>2,3</sup> It is also important to note that more than 6 billion dollars (25.9% of total expenditures) were spent on those hospital stays.<sup>1</sup>

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Received for publication on February 05, 2009

Accepted for publication on April 01, 2009

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Despite the size of the problem, few studies have been dedicated to determining mortality predictors among hospitalized older patients. Most studies focus on intensive care unit patients or mortality rates at 6 to 12 months following discharge.<sup>4-9</sup> Poor nutrition, functional decline, cognitive deficits, illness severity, male gender and polypharmacy have all been correlated to higher mortality rates after discharge.<sup>4,10</sup> In the intensive care environment, age plays an important role in the elderly mortality rate, but the degree of physiological dysfunction resulting from the severity of an acute illness is more significant in determining the final outcome.<sup>2,11</sup> Impaired levels of consciousness and infections have also been correlated to intensive care unit mortality.<sup>2</sup>

This study thus aimed to determine the predictors of in-hospital mortality among older patients admitted to a geriatric ward.

## METHODS

A prospective observational study was implemented in the infirmary of the Geriatric Service of the Hospital das Clinicas da Faculdade de Medicina da Universidade de São Paulo (HC-FMUSP) and was approved by the Ethics Committee for Analysis of Research Projects of the Clinical Board of Hospital das Clinicas da Faculdade de Medicina da Universidade de São Paulo.

Hospital das Clinicas da Faculdade de Medicina da Universidade de São Paulo is a tertiary university hospital with 1,076 beds designed for the care of medical cases with high complexity. Its geriatric infirmary has 17 beds and admits patients aged 60 years and older whose illnesses at admission are non-surgical and do not require intensive care. Patients are treated by a multidisciplinary healthcare team including geriatric physicians and residents, and healthcare professionals that specialize in gerontology such as nurses, nutritionists, physical therapists, speech pathologists and audiologists, psychologists and social workers. Patients are either admitted directly from the emergency room (40.8%) and intensive care units (6.5%), or referred from the geriatric ambulatory (40.2%) and other hospital services (12.5%), such as the home care service and infirmaries belonging to other departments.

All 922 patients admitted to the geriatric care unit from February 2004 to October 2007 were evaluated for possible inclusion in this study. Patients hospitalized for palliative care, those who declined to participate, and those with incomplete data were excluded. Following these criteria, 66 patients (7.2%), mostly under palliative care, were not included in the final analysis. This resulted in a group of 856 patients.

Participants' data were collected by the multidisciplinary team using pre-defined questionnaires. At admission, the following factors were evaluated: gender, age, reason for

hospitalization (clinical treatment, diagnostic investigation or palliative care), number of diagnoses, number of drugs in use, heart failure history, neoplastic disease history, infectious disease diagnosis, urinary incontinence (defined as the involuntary loss of urine in quantity and frequency so as to be considered a health and/or social problem),<sup>12,13</sup> and immobility (defined as the incapacity to change position in bed without help).<sup>14</sup> It is important to note that deep venous thrombosis prophylaxis is routinely prescribed for the patients diagnosed with immobility. The occurrence of delirium, according to the criteria established by the Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV),<sup>15</sup> was also registered. Serum creatinine and albumin levels at admission were recorded because of their clinical importance.<sup>16-18</sup> Laboratory tests were taken only when there was a clear medical indication, and never for the exclusive purpose of generating data for this study. During hospitalization, patients were evaluated daily by the multidisciplinary health team and any presence of delirium and infections was reported. In-hospital mortality and length of stay were registered at the end of hospitalization. Whenever possible, information was obtained from the patients themselves, and otherwise from their surrogate respondents.

Statistical analysis was carried out comparing data obtained from patients who were discharged and patients who died during hospitalization, searching for parameters that correlated to higher mortality rates. Student's *t*-tests, or non-parametric tests when necessary, were employed for quantitative variable analysis, and Pearson Chi-square tests were used for categorical variable analysis. An alpha error of 5% was admitted. Tests were performed using the statistical software MINITAB version 14.0 (Minitab, Inc., State College, PA). Multivariate analysis and identification of the independent factors associated with in-hospital mortality was achieved through the adjustment of a logistic regression model by the statistical software Statistics Package for Social Scientists version 11.0 (SPSS, Inc., Chicago, IL). Only the variables associated with mortality that yielded *P* values lower than 0.10 in the initial analysis were input in the stepwise logistic regression analysis. Odds ratios (OR) and 95% confidence intervals (95% CI) were used to estimate the association between death and the independent determinants of hospital mortality. Cutoff values for the continuous variables identified as independent mortality predictors were established through Receiver Operating Characteristic (ROC) curves.

## RESULTS

Characteristics of the patients included in this study and results from the bivariate analysis are detailed in Table

**Table 1-** Comparison between the demographic, clinical and laboratory characteristics of patients who died and those who were discharged

|                                     | <i>Total</i> | <i>Deaths</i> | <i>Discharges</i> | <i>P</i> |
|-------------------------------------|--------------|---------------|-------------------|----------|
| <b>N</b>                            | 856          | 140           | 716               |          |
| <b>Age (years)</b>                  | 78.43 ±8.62  | 80.67 ±8.86   | 77.99 ±8.51       | .001     |
| <b>Gender</b>                       |              |               |                   | .153     |
| <b>Male</b>                         | 327 (38.2%)  | 61 (43.6%)    | 266 (37.2%)       |          |
| <b>Female</b>                       | 529 (61.8%)  | 79 (56.4%)    | 450 (62.9%)       |          |
| <b>Length of stay</b>               | 16.16 ±16.79 | 19.91 ±17.92  | 15.43 ±13.49      | .001     |
| <b>Admission motive</b>             |              |               |                   | <.001    |
| <b>treatment</b>                    | 545 (63.7%)  | 110 (78.6%)   | 435 (60.8%)       |          |
| <b>investigation</b>                | 311 (36.3%)  | 30 (21.4%)    | 281 (39.3%)       |          |
| <b>Number of diagnoses</b>          | 5.57 ±2.2    | 6.09 ±2.26    | 5.47 ±2.17        | .003     |
| <b>Number of drugs at admission</b> | 5.075 ±3.32  | 5.24 ±3.12    | 4.94 ±3.05        | .315     |
| <b>Urinary incontinence</b>         | 253 (29.7%)  | 51 (36.4%)    | 202 (28.2%)       | .055     |
| <b>Immobility</b>                   | 259 (30.3%)  | 72 (51.4%)    | 187 (26.1%)       | <.001    |
| <b>Heart failure</b>                | 186 (21.7%)  | 40 (28.6%)    | 146 (20.4%)       | .037     |
| <b>Cancer</b>                       | 207 (24.2%)  | 58 (41.4%)    | 149 (19.6%)       | <.001    |
| <b>Delirium</b>                     | 279 (32.6%)  | 97 (69.3%)    | 182 (25.4%)       | <.001    |
| <b>Infection</b>                    | 430 (50.2%)  | 109 (77.9%)   | 321 (44.8%)       | <.001    |
| <b>Albumin (mg/dL)</b>              | 3.35 ±0.7    | 2.79 ±0.62    | 3.45 ±0.67        | <.001    |
| <b>Creatinine (mg/dL)</b>           | 1.37 ±1.24   | 1.97 ±2.03    | 1.23 ±0.95        | <.001    |

1. In the study sample of 856 individuals, 140 deaths were reported, resulting in a mortality rate of 16.4%. Infectious complications of the respiratory and urinary tracts were the most common causes of death among these patients, followed by other conditions such as kidney failure complications, acute myocardial infarction, pulmonary embolism and liver failure complications. The patients ranged in age from 60 to 104 years old, with an average of 78.43 ± 8.62 years of age.

Most of the individuals were admitted for clinical treatment, and the mortality rate in this group was 20.2%. A high level of functional dependency was present, with approximately one third of the patients having a diagnosis of immobility. Among the immobile patients, the mortality rate reached 27.8%. The mortality rate was 34.8% among patients diagnosed with delirium, 28% among those diagnosed with cancer, and 21.5% among patients with a history of heart failure.

In terms of metabolic parameters, 370 (43.2%) patients presented with albumin levels lower than 3.3 mg/dL, and in that group there were 107 deaths (28.9%). The mortality rate among patients with albumin levels higher than that value was 6.8% (33 in 486). A total of 259 patients (30.3%) had admission creatinine levels equal to or higher than 1.3 mg/dL, and 65 of them died (25.1%). On the other hand,

of the 597 individuals with creatinine levels below this threshold, only 75 died (12.6%). The association between these laboratory test values and death was confirmed by ROC curves, which showed an area under the curve of 0.76 for albumin and 0.60 for creatinine.

Multivariate logistic regression analysis identified the following factors as independent predictors of in-hospital mortality: the occurrence of delirium, diagnosis of neoplastic disease, admission albumin levels lower than 3.3 mg/dL, admission creatinine levels equal to or higher than 1.3 mg/dL, history of heart failure, immobility, and age. These results are detailed in Table 2.

**Table 2-** Independent in-hospital mortality predictors of elderly patients admitted to a geriatric ward

|                             | <b>OR</b> | <b>95% CI</b> | <b>P</b> |
|-----------------------------|-----------|---------------|----------|
| <b>Age (years)</b>          | 1.03      | 1.01-1.06     | .019     |
| <b>Immobility</b>           | 1.84      | 1.16-2.92     | .009     |
| <b>Heart failure</b>        | 1.97      | 1.20-3.22     | .007     |
| <b>Neoplastic disease</b>   | 3.38      | 2.11-5.42     | <.001    |
| <b>Delirium</b>             | 4.13      | 2.65-6.44     | <.001    |
| <b>Albumin &lt;3.3mg/dL</b> | 3.23      | 2.03-5.13     | <.001    |
| <b>Creatinine ≥1.3mg/dL</b> | 2.39      | 1.53-3.72     | <.001    |

## DISCUSSION

Delirium, cancer and heart failure diagnoses, age, immobility, serum albumin levels lower than 3.3 mg/dL at admission and serum creatinine levels equal to or higher than 1.3 mg/dL at admission were identified in this study as independent factors related to higher mortality in hospitalized older patients.

The continuous growth of the geriatric population in recent decades has led to an increasing number of acute hospitalizations.<sup>19</sup> For many older patients, acute clinical conditions that demand hospital care are life-changing events that often result in functional decline, institutionalization, or even death. Such unfavorable outcomes are noticed not only during the hospital stay, but also in the year following discharge.<sup>19,20</sup>

Few authors have explored the many factors that contribute to mortality in the elderly during hospitalization. A multicenter study carried out in Europe that included 1,626 patients at least 65 years old verified that death was correlated both to functional and cognitive impairment and with the male gender.<sup>19</sup> A recent systematic review from the same group indicated that functional decline, illness severity, cognitive impairment, comorbidity scores, polypharmacy, age and male gender were all associated with higher mortality.<sup>5</sup> Physical function was a particularly strong mortality predictor, and a consistent correlation has been established by many studies.<sup>4,21,22</sup>

One of the main contributions of this study is to confirm the importance of delirium as a factor associated with death among elderly in-patients. Delirium has a great impact on the health of older patients. Those who are affected not only experience prolonged hospitalizations and functional decline,<sup>23</sup> but may also have persisting signs of delirium for 12 months or longer after discharge. This is particularly prevalent in those diagnosed with dementia.<sup>24</sup> Delirium was diagnosed in 32.6% of the individuals included in this study. It has been reported that up to 70% of patients older than 70 years arrive at the emergency room with some level of cognitive impairment, and that up to 25% are diagnosed with delirium.<sup>25</sup> Another study verified that 24% of community-originating patients and 64% of institutionalized patients were diagnosed with delirium on hospital arrival.<sup>26</sup> Additionally, delirium is one of the earliest clinical manifestations of older patients' acute ailments and has been associated with increased morbidity and mortality.<sup>27</sup>

The mortality associated with delirium is high. In agreement with previously reported data, we observed that 34.8% of our delirium-diagnosed patients died during hospitalization. According to the literature, older patients who develop delirium after admission have a 22% to

76% risk of dying before hospital discharge.<sup>27</sup> It is also estimated that after discharge, the 1-month and 6-month mortality rates are 14% and 22%, respectively; approximately twice that of patients without delirium.<sup>28</sup> The concomitant presence of dementia and severe physical illness probably influenced these results, but prospective observational studies that adjusted for such confounding factors still found that delirium was an independent marker of mortality at 6 or 12 months after hospitalization.<sup>29-31</sup> The importance this diagnosis as an indicator of poor prognosis and increased length of stay demands an assessment for delirium in geriatric patients who are agitated or have acutely impaired cognitive functions.<sup>32,33</sup> Additionally, the implementation of preventive measures and daily cognitive evaluations is also crucial to diminish the impact of delirium in patient outcomes.

In agreement with previous studies, the importance of functional status in the prediction of mortality was shown. A higher prevalence of immobility was observed among the patients who died, and, after multivariate analysis, this diagnosis was confirmed as an independent factor associated with higher mortality. Similar results were reported by another study that, after analyzing 353 elderly patients, verified that functional impairment at admission was strongly correlated to death.<sup>21</sup> The comparison of immobility with other widely employed functionality status measures is necessary. Further studies using the Functional Independence Measure (FIM)<sup>34</sup> and the Katz functionality scale<sup>35</sup> are being conducted to investigate this issue.

Our results confirmed the association between higher mortality rates and malnutrition, a common condition among hospitalized older patients. Poor nutritional condition has already been established as an independent predictor of bad prognosis at admission, and this association is not exclusively due to illness severity, comorbidities, or functional impairment.<sup>36</sup> More specifically, diminished levels of serum albumin, besides implying higher in-hospital mortality levels,<sup>37</sup> are also associated with death in the general elderly population.<sup>33</sup> In agreement with our findings, other authors<sup>37</sup> have described higher in-hospital mortality among geriatric patients with albumin levels lower than 3.3 mg/dL at admission. Additionally, other researchers have documented a correlation between mortality at one year following discharge and albumin levels lower than 3.5 mg/dL at admission.<sup>12</sup>

This study also showed that neoplastic disease diagnoses, whether already established at admission or given later during hospital stay, were associated with death. It is important to note that many of the patients diagnosed with cancer had metastases at admission, which could explain the elevated mortality rate in that population.

Having a history of heart failure was also associated with higher mortality. It is known that patients aged 70 years and over who suffer from heart failure have a poorer prognosis, with a greater number of them dying within a year, when compared to younger individuals.<sup>38</sup> Comorbidities are a key factor in mortality prediction among older in-patients, and heart failure has been described and corroborated by our study as one of the strongest influences on these individuals' outcomes.<sup>38</sup>

The evaluation of clinical severity by physiological criteria is essential when predicting the mortality of older hospitalized individuals. Our study verified that creatinine level at admission is an independent mortality predictor in this population.<sup>16</sup>

On the other hand, even though age was identified in our work and in other studies as an independent factor associated with death, other authors suggest that it is not such a significant predictor after clinical and functional status are considered.<sup>5</sup>

A limitation of this study is that the impact of dementia diagnoses in hospitalized elderly mortality was not evaluated. Cognitive impairment has already been identified as a predictor of immediate and late mortality among geriatric patients,<sup>4,12</sup> and its role should be studied more carefully in the future.

## CONCLUSIONS

Delirium, neoplastic diseases, immobility, congestive heart failure history, albumin levels lower than 3.3 mg/dL, creatinine levels higher or equal to 1.3 mg/dL and advanced age are all highly correlated to the mortality of hospitalized older patients admitted to a geriatric ward. The methodical evaluation of these factors might be useful for therapeutic planning, resource allocation and identification of potential candidates for specific geriatric interventions. For these reasons, such factors should be actively investigated and considered in the decision-making process in each case.

## ACKNOWLEDGEMENTS

None of the authors report a potential, real, or perceived conflict of interest or financial disclosure. No sponsors participated in or funded this research.

We thank the patients and their relatives for their participation. Also, we appreciate the support of all members of the multidisciplinary team from our unit. None of the acknowledged participants received any form of compensation for their contributions.

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