BRIEF REPORT

FACTORS ASSOCIATED WITH MORTALITY IN HOSPITALIZED ELDERS IN AN INTERNAL MEDICINE DEPARTMENT

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ABSTRACT

The aim of this prospective cohort study was to determine the factors associated with mortality in elders admitted to an Internal Medicine Department of a public hospital in Lima. During 2019, 360 patients over 60 years of age were consecutively evaluated by applying the Comprehensive Geriatric Assessment tools and reviewing their medical records. During hospitalization, 45 (12.5%) died. There was a higher frequency of anemia (p = 0.043), hypoalbuminemia (p = 0.006), pressure ulcers (p = 0.003), high comorbidity (p < 0.001), functional dependence (p < 0.001) and malnutrition (p = 0.002) among deceased patients compared to non-deceased. In the multivariate model, the presence of delirium on admission was associated with a higher risk of hospital mortality (RR = 3.64; 95% CI: 1.51 - 8.76, p = 0.004). Additional studies are required in our country to assess the prognostic value of delirium and other geriatric syndromes on mortality and other adverse outcomes.

Keywords: Elderly; Hospital Mortality; Risk Factors; Geriatric Assessment; Delirium; Aging, Hypoalbuminemia; Pressure Ulcer; Geriatrics; Internal Medicine (source: MeSH NLM).

INTRODUCTION

Previous studies have shown that the in-hospital mortality rate in older adults is approximately 12 to 14%, which is two to three times higher than mortality in people under 60 years of age; the most important causes of death being pneumonia, stroke, myocardial infarction, diabetes and cancer [1]. Different studies carried out in developed countries have shown that advanced age, poor functional and cognitive status, delirium, malnutrition, multiple comorbidities, frailty and severity of illness are factors independently associated with a higher risk of mortality and prolonged hospital stay [2,3].

The Comprehensive Geriatric Assessment (CGA) is a multidimensional and interdisciplinary diagnostic tool that identifies and quantifies the physical, functional, psychological and social problems that older adults may present [4]. Because of its diagnostic accuracy, the CGA has proven to be considerably useful in defining the type of care required

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by older adult patients with comorbidities, functional dependence and frailty. Its application in hospitalized patients has been proposed in order to reduce some adverse outcomes, such as mortality, prolonged hospital stay, functional deterioration, nosocomial infections, re-admissions and institutionalization [5,6].

Due to the lack of Peruvian studies on the subject, the aim of this study was to determine the factors associated with mortality in older adults admitted to an internal medicine department of a Peruvian hospital. For this purpose, we collected data from the medical records, including the components of CGA. The study will serve to design intervention strategies aimed at addressing the associated risk factors and to improve the quality of care for the older adult population, considered a vulnerable segment and generally at social risk.

KEY MESSAGES

Motivation for the study: In Peru there is little information on the factors associated with in-hospital mortality in older adults.

Main findings: Delirium on admission tripled the risk of mortality in older adults admitted to an internal medicine service. In most patients, the diagnosis of delirium was not registered in medical records.

Implications: In hospitalized patients, the application of the Comprehensive Geriatric Assessment allows for the timely detection of delirium and other geriatric syndromes. Further studies are needed to identify older patients at increased risk of mortality and other adverse outcomes.

THE STUDY

Study design and participants

We carried out a prospective study of older adult patients hospitalized in the Internal Medicine service of the Hospital Nacional Hipólito Unanue (HNHU) during 2019. Patients aged 60 years or older, of both sexes, with complete medical history and informed consent form were included. Patients who died within 24 hours of admission, with previous stays in other hospital services, those who died without having had an CGA, those hospitalized for end-of-life care, and those who requested voluntary discharge were excluded.

The sample size calculation was based on the search for factors associated with mortality with a relative risk (RR) of at least 2.0 [6]. Based on a confidence level of 95%, a power of 80%, and a proportion of unexposed individuals developing the event of interest of 12%, the sample size obtained was 352. However, in order to compensate for losses due to possible incomplete data, the number was increased by 10%, resulting in a final sample size of 387 patients. The calculations were carried out in the Open-Epi open-access program.

The sample was selected by convenience by recruiting patients who met the eligibility criteria until the sample size was reached. A total of 387 patients were consecutively evaluated, of whom 377 were eligible. During follow-up, 17 patients dropped out of the study: 12 due to voluntary discharge and five due to transfer to other services. Therefore, the final sample consisted of 360 patients.

Variables

The dependent variable was the occurrence of in-hospital death. Independent variables were considered to be those that could be linked to this outcome, grouped into demographic, clinical, laboratory tests and CGA results.

Information was obtained on age, sex, marital status and educational level. The clinical variables were the main diagnosis on admission, number of drugs the patient was consuming on admission (polypharmacy ≥ 5 drugs per day), and history of hospitalizations and falls in the last year. The results of the following laboratory tests were collected: hemoglobin, glycemia, creatinine, albumin and C-reactive protein (CRP).

The components of CGA considered were the diagnoses of urinary incontinence and pressure ulcers, comorbidity using the Charlson Comorbidity Index (CCI) [7] (low < 3 points, high ≥ 3 points), functional status at admission with the Katz index (basic activities of daily living) [8] (independent 0-1 point, partial dependence 2-3 points and total dependence 4-6 points, dichotomized for analysis into total + partial dependent vs. independent), nutritional status with the Mini Nutritional Assessment Short Form (MNA-SF) [9] (normal 12-14 points, risk of malnutrition 8-11 points and malnutrition 0-7 points) and social condition with the socio-family assessment scale modified by Merino for Peru [10] (good social condition 5-9 points, social risk 10-14 points and social problem ≥ 15 points).

All patients were evaluated with the Confusion Assessment Method (CAM) to detect delirium [11]. In patients without delirium, cognitive function was immediately assessed with the Pfeiffer test [12] (normal 0-4 points, cognitive impairment ≥ 5 points) and affective state using the Yesavage Geriatric Depression Scale (GDS) (normal < 10 points, depression ≥ 10 points) [13]. For patients with delirium on admission, both tests were deferred until discharge.

Procedures and techniques

Within 24 hours of admission, a member of the research team collected data from the medical record, completing the required information by interviewing the patient or the responsible family member, after the signing of the informed consent form. The CGA tools were then applied. The participants in the study were followed up daily, recording the date of discharge or death, in the latter case noting the basic cause of death.

Statistical analysis

The data were analyzed with the statistical program STATA 15. We determined measures of central tendency and dispersion for quantitative variables.For qualitative variables, frequencies and percentages were calculated. To evaluate the association between mortality and the independent variables, the Student's t-test or Mann-Whitney U-test was used for continuous variables and the Chi-square test or Fisher's exact test for categorical variables. Associations were established by calculating relative risks (RR) with their respective 95% confidence intervals (95% CI).

Adjusted associations were calculated according to a Poisson regression model with robust variance for each of the groups of variables associated with the outcome of interest. Variables with p values < 0.20 were included in the multivariate model.

Ethical aspects

The study was approved by the Institutional Research Ethics Committees of the Universidad Peruana Cayetano Heredia and the Hospital Nacional Hipólito Unanue.

FINDINGS

A total of 360 patients were evaluated (median age 76 years, IQR: 67-83). Of the total, 54.2% were male; 57.8% had a stable partner (married or cohabiting); and 71.4% were illiterate or had primary education. Regarding clinical data, 7.2% were polymedicated patients, 53.1% were hospitalized, and 34.2% had a history of falls in the last year. The CGA showed that 44.4% had urinary incontinence, 15.8% had pressure ulcers, 50.6% had high comorbidity, 54.7% had total functional dependence, 60.8% had malnutrition, 47.5% had social problems and 38.6% had delirium at admission. Of a total of 238 patients evaluated who did not have delirium on admission or whose symptoms subsided during hospitalization, 33.2% had cognitive impairment and 12.2% depression (Table 1).

The median length of hospital stay was 9 days (IQR: 6-13). The most frequent diagnoses on admission were pneumonia in 15.8% and stroke in 14.4% (Table 2) of the patients. Of 360 patients studied, 45 died during their hospital stay, with a cumulative incidence of mortality of 12.5%. The main causes of death were sepsis (44.4%), multiorgan failure (35.6%), in-hospital pneumonia (8.9%) and acute renal failure (4.4%).

Compared to non-deceased patients, deceased patients had a higher frequency of: anemia (46.7% vs. 31.4%, p = 0.043), hypoalbuminemia (88.9% vs. 69.2%, p = 0.006), pressure ulcers (31.3% vs. 13.7%, p = 0.003), high comorbidity (75.6% vs. 47.0%, p < 0.001), functional dependency at admission (93.3% vs. 49.2%, p < 0.001), malnutrition (84.4% vs. 57.5%, p = 0.002) and delirium (80.0% vs. 32.7%, p < 0.001) (Table 3).

We calculated adjusted associations using a multiple Poisson regression model with robust variance in the variables associated with the outcome of interest in the bivariate model. In the multivariate model, delirium was associated with a 3.64-fold increase in the risk of in-hospital mortality (RR = 3.64; 95% CI: 1.51-8.76, p = 0.004) (Table 4).

DISCUSSION

Delirium is characterized by an abrupt change in mental status, with altered attention and cognition, frequently accompanied by a disorder of consciousness, disorientation and inversion of the sleep-wake cycle [14]. This geriatric syndrome increases the risk of mortality, prolongs hospital stay, produces functional deterioration and institutionalization in older adults, which increases health care costs [15].

In our research, 38.6% of the patients had delirium at the time of admission and its presence was associated with

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Table 1. General characteristics of the patients (n = 360).

Variable	n	%
Age (years) [a]	76 (67-83)	
Sex		
Male	195	54.2
Female	165	45.8
Marital status		
No stable partner	152	42.2
With stable partner	208	57.8
Education level		
Illiterate/primary school	257	71.4
Secondary school	89	24.7
Technical/higher	14	3.9
Polypharmacy (≥ 5 drugs)	26	7.2
Hospitalizations in the last year	191	53.1
Falls in the last year	123	34.2
Hemoglobin (g/dL) [a]	11.3 (9.4-12.8)	
Glycemia (mg/dL) [a]	104.21 (89-136.9)	
Creatinine (mg/dL) [a]	0.95 (0.71-1.35)	
Albumin (g/dL) [a]	3.10 (2.66-3.60)	
C reactive protein (mg/dL) [a]	3.77 (1.98-6.44)	
Urinary incontinence	160	44.4
Pressure ulcers	57	15.8
High comorbidity (CCI ≥ 3)	182	50.6
Functional status at admission		
Independent	111	30.8
Partially dependent	52	14.4
Totally dependent	197	54.7
Nutritional status		
Normal	48	13.3
Risk of malnutrition	93	25.8
Malnutrition	219	60.8
Social status		
Good social status	40	11.1
Social risk	149	41.4
Social problem	171	47.5
Delirium	139	38.6
Cognitive impairment [b]	79	33.2
Depression [b]	29	12.2

[a] Median and interquartile range, [b] Data from 238 patients
CCI: Charlson comorbidity index.

Table 2. Main diagnoses at admission (n = 360).

Diagnostic	n	%
Pneumonia	57	15.8
Stroke	52	14.4
Decompensated DBM	51	14.2
Cancer	47	13.1
Sepsis	42	11.7
Heart failure	39	10.8
Respiratory failure	35	9.7
Delirium	27	7.5
Urinary tract infection	26	7.2
Cellulitis	25	6.9
Arterial hypertension	23	6.4
Liver cirrhosis	22	6.1
DILD	22	6.1
Upper gastrointestinal bleeding	16	4.4
Acute cholecystitis	14	3.9
Abdominal pain	11	3.1
COPD	10	2.8
Pancytopenia	9	2.5
Acute pancreatitis	8	2.2
Decompensated CKD	5	1.4
Hypothyroidism	5	1.4
Rheumatoid arthritis	4	1.1
Vitamin B12 deficiency	4	1.1
Tuberculosis	3	0.8
Deep vein thrombosis	3	0.8
Lower gastrointestinal bleeding	2	0.6

DBM: diabetes mellitus, DILD: diffuse interstitial lung disease, COPD: chronic obstructive pulmonary disease, CKD: chronic kidney disease.

an increased risk of death. Studies conducted in national hospitals have shown that 34.9 to 42.7% of older adults admitted to emergency services for medical conditions present delirium, which usually coexists with conditions of functional dependence, chronic cognitive impairment and dehydration [16]. Despite its high frequency, delirium is often not correctly diagnosed and, consequently, its treatment is not accurate, and it can be confused with dementia, depression or with the changes produced by aging [14]. According to the latter, only 27 (7.5%) of our patients had a diagnosis of delirium registered in their medical record.

Previous studies have shown an association between delirium and a high risk of death, independent of the effect of other factors, such as advanced age, cognitive impairment, comorbidity, functional status and severity of illness [14,15]. In a study of 469 patients over 70 years of age belonging to Project Recovery, a controlled clinical trial for the prevention of delirium, Dharmarajan *et al.* [17] found that 15% of patients developed delirium during hospitalization. Those affected

Table 3. Factors associated with hospital mortality in older adults (n = 360).

Variables	Not deceased (n=315)	Deceased (n=45)	p value [a]
	n (%)	n (%)	
Age (years)			0.137
>80	98 (31.1)	19 (42.2)	
≤80	217 (68.9)	26 (57.8)	
Sex			0.162
Male	175 (55.6)	20 (44.4)	
Female	140 (44.4)	25 (55.6)	
Marital status			0.107
No stable partner	128 (40.6)	24 (53.3)	
With stable partner	187 (59.4)	21 (46.7)	
Educational level			0.386
Illiterate/primary school	221 (70.2)	36 (80.0)	
Secondary school	81 (25.7)	8 (17.8)	
Technical/higher	13 (4.1)	1 (2.2)	
Polypharmacy (≥5 drugs)	21 (6.7)	5 (11.1)	0.349
Hospitalizations in the last year	165 (52.4)	26 (57.8)	0.497
Falls in the last year	103 (32.7)	20 (44.4)	0.120
Hemoglobin < 10 g/dL	99 (31.4)	21 (46.7)	0.043
Glycemia > 140 mg/dL	75 (23.8)	8 (17.8)	0.781
Creatinine > 1,3 mg/dL	79 (25.1)	16 (35.6)	0.938
Albumin < 3,5 g/dL	218 (69.2)	40 (88.9)	0.006
CRP > 10 mg/dL	44 (14.0)	4 (8.9)	0.348
Urinary incontinence	137 (43.5)	23 (51.1)	0.336
Pressure ulcers	43 (13.7)	14 (31.1)	0.003
High comorbidity (CCI ≥ 3)	148 (47.0)	34 (75.6)	<0.001
Functional status at admission			<0.001
Independent	108 (34.3)	3 (6.7)	
Partially dependent	52 (16.5)	0 (0)	
Totally dependent l	155 (49.2)	42 (93.3)	
Nutritional status			0.002
Normal	47 (14.9)	1 (2.2)	
Risk of malnutrition	87 (27.6)	6 (13.3)	
Malnutrition	181 (57.5)	38 (84.4)	
Social status			0.126
Good social status	39 (12.4)	1 (2.2)	
Social risk	128 (40.6)	21 (46.7)	
Social problem	148 (47.0)	23 (51.1)	
Delirium	103 (32.7)	36 (80.0)	<0.001
Cognitive impairment [b]	76 (33.2)	3 (33.3)	0.623
Depression [b]	28 (12.2)	1 (11.1)	0.699

[a] Chi-square or Fisher's exact test were used to compare categorical variables, [b] data from 238 patients
CRP: high-sensitivity C-reactive protein, CCI: Charlson comorbidity index

had a higher frequency of falls, pressure ulcers; as well as use of mechanical restraint and complications during evolution, such as sleep disorders, malnutrition, dehydration and pneumonia. It has been proposed that the increased risk of death in delirious patients could be mediated by this cascade of adverse events.

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Table 4. Poisson regression model for factors associated with hospital mortality.

Factors	Bivariate model [a]			Multivariate model [b]		
	RR	95% CI	p value	RR	95% CI	p value
Anemia (Hb < 10 g/dL)	1.75	1.01-3.01	0.044	1.40	0.82-2.39	0.211
Hypoalbuminemia (albumin < 3.5 g/dL)	3.16	1.28-7.79	0.012	1.68	0.68-4.13	0.256
Pressure ulcers	2.41	1.36-4.22	0.002	0.93	0.52-1.66	0.813
High comorbidity (CCI ≥ 3)	3.02	1.58-5.78	0.001	1.55	0.77-3.08	0.212
Functional status at admission						
Total/partial dependent	6.24	1.97-19.73	0.002	2.08	0.58-7.48	0.258
Independent	1.00			1.00		
Nutritional status						
Malnutrition	8.33	1.17-59.34	0.034	2.57	0.32-20.25	0.370
Risk of malnutrition	3.10	0.38-25.06	0.289	1.47	0.17-12.50	0.724
Normal	1.00			1.00		
Delirium	6.36	3.16-12.81	<0.001	3.64	1.51-8.76	0.004

[a] Simple Poisson regression with robust variance.
[b] Multiple Poisson regression with robust variance; model adjusted for anemia, hypoalbuminemia, pressure ulcers, high comorbidity, functional status at admission, nutritional status and delirium.
RR: relative risk; 95% CI: 95% confidence interval.

Our study found a higher frequency of hypoalbuminemia, anemia, pressure ulcers, high comorbidity, functional dependence on admission, and malnutrition among the deceased patients. These factors have been associated in the international literature with a higher risk of death in hospitalized older adults, but did not reach statistical significance in the multivariate model of this study.

Akirov *et al.* [18] evaluated a cohort of 30,732 patients (mean age 67 years) and found an in-hospital mortality rate of 67% in patients with mild hypoalbuminemia (2.5-3.5 g/dL) and 83% in those with severe hypoalbuminemia (<2.5 g/dL). The association was present in all age groups, and significantly normalizing the albumin levels reduced the risk of death. Specifically, in older adults, an association has been found between hypoalbuminemia and an increased risk of death, prolonged hospital stay, and re-admission after discharge [5,6].

In a study of 17,030 older adults from Calgary (Canada), an increased risk of hospitalization and death was found among patients with anemia. The observed association was independent of age, sex, renal function, comorbidity or history of diabetes in the patients studied [19].

In older adults with pressure ulcers at the time of hospital admission, a shorter survival time has also been described when compared to patients without ulcers (94 vs. 414 days, p = 0.005), especially in patients with dementia, anemia or malnutrition [20].

De Gelder *et al.* [3] designed a predictive model of 90-day mortality after hospital admission in older adults. Six variables were included in the model: assessment of comorbidity by CCI, platelet count, oxygen saturation, CRP values, urea and plasma glucose. Of the total of 517 patients, 18.2% died during the observation period, which corresponds to a mortality of 53% in patients located in the highest risk decile.

On the other hand, the association between poor functional status on admission and high mortality in older adults is well known. Incalzi *et al.* [2], in their study of 308 older adults admitted to a hospital ward, reported an excess of death among patients with functional dependence determined with the Katz index. Possible explanations for this association have been proposed, such as a greater vulnerability of patients with functional dependence and a high frequency of comorbidity, immobility, cognitive impairment, depression, polypharmacy, social problems and malnutrition in these patients.

A higher mortality rate has been described in malnourished older adults. Avelino-Silva *et al.* [6] prospectively evaluated a group of 746 older adults admitted to the geriatrics service of a university hospital in Brazil. In their study, patients with a low MNA-SF score who had hypoalbuminemia were twice as likely to die as patients without this condition.

Our study has several limitations. First, since it considers patients from the third level of healthcare, its conclusions

cannot be generalized to other realities, as this would compromise its external validity. Second, a larger sample size could have improved the statistical power of the research. Third, we mainly focused on the evaluation of geriatric factors associated with higher in-hospital mortality rather than on the severity of the disease at admission. Fourth, we did not consider the frailty syndrome, which may have been present in a significant group of patients.

In conclusion, in older adult patients admitted to an internal medicine service, delirium on admission was independently associated with a 3.64-fold increase in the risk of in-hospital death.

Author contributions: JLV and AS conceived and designed the manuscript; JLV and AS analyzed and interpreted the data; JLV, LCR, and AS drafted the manuscript; LCR participated in the recollection of results. All authors participated in the critical revision of the article, approved the final version, and assume responsibility for the contents of the article.

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