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Original Article

Mortality and Prognostic Factors in Patients over 90 Years of Age Admitted in Internal Medicine: A Spanish Prospective Cohort Study

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SUMMARY

Background: The prevalence of multimorbidity and the number of chronic pathologies increases with age, and hospitalization rates are higher in very elderly patients.
Aims: To identify predictors of mortality in patients aged 90 years or more at 6 and 12 months after admission to the internal medicine ward.
Materials and methods: Prospective cohort study in patients aged 90 years or older who were admitted to the internal medicine ward of Alicante General University Hospital from November 2018 to March 2019. We collected data for patient scores on the Barthel, Lawton-Brody, and Short Portable Mental Status Questionnaire; a nutritional questionnaire; the Charlson index; PALIAR and PROFUND prognostic indexes; and mortality at 6 and 12 months.
Results: In the bivariate analysis adjusted for gender and comorbidity, malnutrition was associated with mortality at 6 and 12 months (odds ratio [OR] 5.17, 95% confidence interval [CI] 1.30, 20.50; OR 7.78, 95% CI 1.47, 40.9, respectively), as were moderate-severe cognitive impairment (6 months: OR 12.0, 95% CI 2.79, 52.0; 12 months: OR 10.73, 95% CI 2.40, 47.8) and high-risk scores on the PALIAR (6 months: OR 9.18, 95% CI 1.99, 42.27; 12 months: OR 11.7, 95% CI 2.62, 51.60) and PROFUND (6 months: OR 10.7, 95% CI 1.68, 68.80; 12 months: OR 20.9, 95% CI 3.15, 139.0) prognostic indexes. The Barthel index was associated with mortality only at 6 months (OR 6.16; 95% CI 1.69, 22.4).
Conclusions: In nonagenarian inpatients, a worse score on the comprehensive assessment and a higher score on prognostic indexes were associated with increased risk of mortality at 6 and 12 months.

1. Introduction

As in other high-income countries, the population in Spain is gradually aging. The proportion of people aged 90 years or more has more than doubled in the past two decades, from 0.49% in 2000 to 1.15% in 2019, and there are now about a half million people in this age bracket in the country.[1] Because the prevalence of multimorbidity and the number of chronic pathologies increases with age,[1,2] hospitalization rates are higher in very elderly patients, especially in the internal medicine service.[3]

Several studies have reported an association between comorbidity and in-hospital mortality in patients aged over 90 in the internal medicine ward.[4–8] The Charlson index is the most widely used instrument to evaluate comorbidities,[9] but to ensure proper management of very old patients, clinicians must consider functional impairment as well. Comprehensive geriatric assessments (CGAs) evaluate four domains: medical, mental, social, and functional, which together provide a holistic vision of the patient's condition.[10] The CGA includes a clinical history, physical examination, and specific assessment scales to detect and monitor problems.[10] The most common scales are the Barthel index (assessing dependence), the Lawton-Brody index (instrumental activities of daily living), the Short Portable Mental Status Questionnaire (SPMSQ, dementia), and different nutritional assessment questionnaires, for example the Mini Nutritional Assessment (MNA).

The growing population of people with multimorbidity and advanced chronic diseases has increased the demand for healthcare in Spain, which has in turn driven the development of the PALIAR and PROFUND prognostic scales. The PALIAR index is focused on patients with chronic, advanced, non-oncological pathologies,[11,12] while the PROFUND index is aimed at patients with multimorbidity (including cancer) and predicts the probability of death within 12 months.[13] However, these two prognostic scales have not been studied in people aged 90 years or older. The main function of comorbidity indexes, CGAs, and prognostic scales resides in their power to help clinicians make diagnostic and treatment decisions in older patients with numerous pathologies.

This study aims to evaluate the prognostic power of PALIAR and PROFUND indexes as well as other scales for predicting mortality at 6 and 12 months in people aged 90 years or older.

2. Material and methods

We designed a prospective cohort study with one year of fol-

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low-up in the general internal medicine service of the Alicante General University Hospital. The hospital covers a catchment area of 268,000 inhabitants in metropolitan Alicante. The hospital does not have a geriatric unit, but it does have a general internal medicine ward (45 beds) and palliative care unit (10 beds). In 2019, 1735 patients were admitted to the general internal medicine ward.

Participants were recruited through convenience sampling over a five-month period, from 1 November 2018 to 28 March 2019. Inclusion criteria were: aged 90 years or older; admitted in the internal medicine ward; and signed informed consent. Exclusion criteria were: unaccompanied by a family member for informed consent; refusal to sign informed consent; admission to the palliative care unit; and death in the first 48 hours of admission.

We collected sociodemographic variables for each participant (gender, age, and residence type [home/institution]) along with information on functional, cognitive, and nutritional status and comorbidities. We used the age-adjusted Charlson comorbidity index[9] and the following scales, dichotomizing scores as indicated:

- MNA short form (MNA-SF) to evaluate nutritional state: normal nutrition/risk of malnutrition (8–14 points) versus malnutrition (0–7 points).
- Barthel index to assess functional capacity for activities of daily living. This ordinal scale measures different degrees of dependence on a scale from 0 to 100: total or severe dependence (≤ 60 points) versus moderate to no dependence (≥ 61 points).
- Lawton-Brody index to evaluate functional capacity for instrumental activities of daily living: total dependence (women, 0 or 1 point; men, 0 points) versus autonomous and mild to severe dependence (women, 2–8 points; men, 1–5 points).
- SPMSQ for cognitive impairment, adjusted for education: mild to no cognitive impairment (0–4 errors) versus moderate to severe cognitive impairment (5–10 errors).
- PALIAR prognostic index to assess the probability of death within 6 months in patients with advanced, chronic, non-oncological diseases. The scale assesses demographic, clinical, analytical, and functional dimensions and includes the following variables (Supplementary material). Scores range from 0 to 21 points: low-intermediate and intermediate-high risk (0–7 points) versus high risk (≥ 7.5 points).[11,12]
- PROFUND prognostic scale to evaluate the probability of death at one year in patients with multimorbidity, based on demographic, clinical, analytical, and functional dimensions (Supplementary material). Scores of 0 to 30 points indicate: low, intermediate, and high risk (0–10 points) versus very high risk (11–30 points).[13]

Moderate-to-severe renal disease was defined in (Supplementary material).

At 6 and 12 months, patients' electronic health records (Orion Clinic v11.0, Valencian Community, Spain) were used to assess mortality, readmissions, and use of healthcare services (home and emergency care).

2.1. Statistical analysis

We tested the association between 6- and 12-month mortality and the different instruments and variables, using the student's t test for the Charlson index and age, and the chi-squared test for dichotomized scores on the rest of the assessment and prognostic scales. A bivariate analysis, adjusted for gender and Charlson index, was performed using binomial logistic regression, and the Hosmer-Lemeshow test was used to assess goodness-of-fit for the logistic regression models. Analyses were undertaken with SPSS software, version 22.0 (SPSS Inc. Chicago, IL, USA).

2.2. Ethical aspects

The ethics committee of the Alicante General University Hospital approved the study (PI2016/40). All participants or family members signed informed consent.

3. Results

Figure 1 shows the patient flow chart. Of the 50 included participants, 34 (68%) were women and 16 (32%), men. Their median age was 92 years (interquartile range [IQR] 91–94), and 18% lived in nursing homes. The main comorbidities at baseline were dementia (n = 31, 62%), moderate-to-severe chronic kidney disease (n = 30, 60%), and heart failure (n = 28, 56%); the prevalence of the latter comorbidity rose to 66% at 6 months. Two-thirds of the patients (66%) were readmitted at least once during follow-up, and 70% visited the emergency department at least once (Table 1).

The bivariate analysis showed a relationship between mortality at 6 and 12 months, respectively, and: score of 60 or less on the Barthel index (p = 0.002 and p = 0.034); malnutrition (p = 0.010 and p = 0.006), moderate-severe cognitive impairment on the SPMSQ (p < 0.001 and p = 0.001), a high risk score on the PALIAR (p = 0.001 and p < 0.001) and PROFUND (p = 0.001 and p < 0.001) prognostic indexes, and comorbidities on the Charlson index (p = 0.050) (Table 2). No association was observed for age, gender, or the Lawton-Brody index.

The bivariate analysis was adjusted for gender and comorbidity and then repeated, as shown in Table 3. Significant associations for mortality at 6 and 12 months were seen for the nutrition questionnaire, SPMSQ, and PALIAR and PROFUND prognostic indexes. The Barthel index was independently associated with mortality only at 6 months.

4. Discussion

The mortality of the patients over the age of 90 years who were admitted to the internal medicine ward was 56% at 6 months and 66% at 12 months. The proportion of patients who died within a year was higher than in other studies; for example, in the Danish 1905 study, mortality was 25.7% in a cohort of 2249 nonagenarians at 15 months' follow-up,[14] while in the NonaSantfeliu study, it was 19.3% at 12 months and 36.2% at 24 months.[8,15] In that study, the mean Charlson index was 1.4 (standard deviation: 1.7), somewhat lower

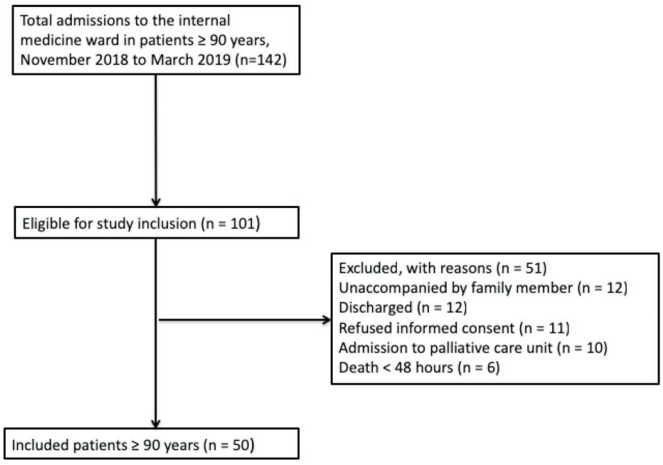

Figure 1. Patient flow chart.

Table 1
Patient characteristics and outcomes (N = 50).

Variables	N	%
Gender		
Women	34	68
Men	16	32
Living situation		
Home	41	82
Nursing home	9	18
Diagnosis on admission		
I13.0 Hypertensive heart and chronic kidney disease	8	16
J69.0 Pneumonitis due to inhalation of food and vomit	7	14
J22 Acute lower respiratory infection	5	10
J20.9 Acute bronchitis	5	10
N39.0 Urinary tract infection	4	8
I11.0 Hypertensive heart disease with heart failure	4	8
J18.9 Pneumonia	3	6
J10.1 Flu	3	6
A41.9 Sepsis	2	4
J96.01 Acute respiratory failure with hypoxia	2	4
Others*	6	12
Comorbidities		
Dementia	31	62.0
Moderate chronic kidney disease	30	60.0
Heart failure	28	56.0
Chronic respiratory disease	19	38.0
Atrial fibrillation	19	38.0
Stroke	13	26.0
Diabetes with organ damage	10	20.0
Acute myocardial infarction	9	18.0
Peripheral arterial disease	7	14.0
Peptic ulcer	7	14.0
Solid tumor without metastasis	7	14.0
Uncomplicated diabetes	6	12.0
Connective tissue disease	4	8.0
Others†	3	6.0
Mortality		
In-hospital mortality	3	6.0
Mortality at 6 months	28	56.0
Mortality at 12 months	33	66.0
Readmissions at 12 months		
≥ 1	33	66.0
Emergency health care at 12 months		
≥ 1	35	70.0
Home health care at 12 months		
≥ 1	19	38.0

* Other diagnoses on admission: diarrhea (2%), acute and subacute infective endocarditis (2%), malignant neoplasm of the ascending colon (2%), respiratory syncytial virus (RSV) as a cause of disease (2%), acute lung edema (2%), acute myocardial infarction with ST segment elevation (2%).
† Other comorbidities: solid tumor with metastasis (4%) and leukemia (2%).

than in ours;[8,15] the high burden of comorbidities in our participants may explain the difference in mortality compared with the NonaSantfeliu cohort.

In the bivariate analysis, severe dependence in the basic activities of daily living (Barthel ≤ 60 points) was significantly associated with mortality at 6 and 12 months, and in the multivariate analysis at 6 months, which is consistent with findings reported elsewhere.[6,7] As Socorro García et al.[7] described, the most important predictors of post-discharge mortality due to acute disease in both the short and long term are the loss of function at admission

In our study, severe dependence for instrumental activities of daily living (Lawton-Brody index) was not related to mortality at 6 or 12 months. This result is in keeping with the results of Formiga et al.'s NonaSantfeliu study,[8,15] wherein the Lawton-Brody index was the most important predictor of mortality at two years, but not at five years.

Malnutrition, as measured by the MNA-SF, and moderate-severe cognitive impairment, as measured by the SPMSQ, were also associated with higher mortality at 6 and 12 months. Similarly, this scale showed its predictive value in the NonaSantfeliu study in the bivariate analysis at two and five years and in the multivariate analysis at five years,[8,15] as well as in the study by Zafrir et al.[26] and in a systematic review.[27]

Our participants had higher scores on the Charlson index (mean 5.1 in participants who died at 6 months and 5.0 in those who died at 12 months) than in the study by Formiga et al.,[15] where Charlson scores were not especially high (1.7 in those who died and 0.7 in survivors at five years). In our study, we did not find a statistically significant association between the Charlson index and mortality at 6 and 12 months, unlike Conde-Martel et al.,[6] who observed an independent relationship between survival at five years and both the Charlson and Barthel indexes. For their part, Formiga et al.[8,15] found an independent association between the Charlson index and mortality at two and five years of follow-up; however, our multivariate analysis showed no such relationship. The reasons for this difference may reside in the fact that chronic diseases are worse predictors of mortality than frailty and functional capacity in people aged 80 or older. These latter two variables may be modified, unlike age, gen-

Table 2
Bivariate analysis of mortality at 6- and 12-months' follow-up.

	Total n (%)*	Mortality 6 months			Mortality 12 months		
		Death (n = 28) n (%)†	Survival (n = 22) n (%)†	p	Death (n = 33) n (%)†	Survival (n = 17) n (%)†	p
Gender				0.21			0.78
Women	34 (68%)	17 (50%)	17 (50%)		22 (64.7%)	12 (35.3%)	
Men	16 (32%)	11 (68.8%)	5 (31.3%)		11 (68.8%)	5 (31.3%)	
Age in years				0.71			1
90–95	41 (82%)	22 (53.7%)	19 (46.3%)		27 (65.9%)	14 (34.1%)	
≥ 96	9 (18%)	6 (66.7%)	3 (33.3%)		6 (66.7%)	3 (33.3%)	
Barthel index				0.002			0.034
Moderate to no dependence	22 (44%)	7 (31.8%)	15 (68.2%)		11 (50%)	11 (50%)	
Total or severe dependence	28 (56%)	21 (75%)	7 (25%)		22 (78.6%)	6 (21.4%)	
Lawton-Brody index				0.25			0.13
Autonomous and mild to severe dependence	21 (42%)	12 (48%)	13 (52.0%)		14 (56.0%)	11 (44%)	
Total dependence	25 (50%)	16 (64%)	9 (36%)		19 (76%)	6 (24%)	
MNA-SF				0.010			0.006
Normal nutrition/risk of malnutrition	31 (62%)	13 (41.9%)	18 (58.1%)		16 (51.6%)	15 (48.4%)	
Malnutrition	19 (38%)	15 (78.9%)	4 (21.1%)		17 (89.5%)	2 (10.5%)	
SPMSQ				< 0.001			0.001
Mild to no cognitive impairment	22 (44%)	6 (27.3%)	16 (72.7%)		9 (40.9%)	13 (59.1%)	
Moderate to severe cognitive impairment	28 (56%)	22 (78.6%)	6 (21.4%)		24 (85.7%)	4 (14.3%)	
PALIAR index				0.001			< 0.001
Low-intermediate and intermediate-high risk	12 (24%)	4 (33.3%)	13 (76.5%)		5 (15.2%)	12 (70.6%)	
High risk	33 (66%)	24 (72.7%)	9 (27.3%)		28 (84.8%)	5 (15.2%)	
PROFUND index				0.002			< 0.001
Low, intermediate, and high risk	12 (24%)	2 (16.7%)	10 (83.3%)		2 (16.7%)	10 (83.3%)	
High risk	33 (66%)	26 (68.4%)	12 (31.6%)		31 (81.6%)	7 (18.4%)	
Charlson index, mean (SD)	4.62 (2.1)	5.1 (2.1)	3.9 (1.8)	0.050	5.0 (2.0)	3.8 (2.0)	0.050

n (%)*: column number and percentages; †: row number and percentage.
MNA-SF: Mini-Nutritional Assessment-Short Form; SD: standard deviation; SPMSQ: Short Portable Mental Status Questionnaire.

Table 3
Bivariate analysis of mortality at 6 and 12 months, adjusted for gender and comorbidities.

	Model 1 OR (95% CI)	Model 2 OR (95% CI)	Model 3 OR (95% CI)	Model 4 OR (95% CI)	Model 5 OR (95% CI)
Mortality 6 months					
Gender, woman	0.57 (0.13–2.43)	0.54 (0.13–2.22	0.58 (1.23–2.75)	0.34 (0.07–1.63)	0.37 (0.82–1.70)
Charlson index	1.29 (0.92–1.18)	1.31 (0.94–1.83)	1.46 (80.97–2.20)	1.45 (0.80–1.62)	1.08 (0.77–1.53)
Barthel index, total or severe dependence (≤ 60 points)	6.16 (1.69–22.4)*				
MNA-SF, malnutrition (0–7 points)		5.17 (1.30–20.50)*			
SPMSQ, moderate to severe cognitive impairment (5–10 errors)			12.0 (2.79–52.0)*		
PALIAR index, high risk (≥ 11 points)				9.18 (1.99–42.27)*	
PROFUND index, high risk (≥ 11 points)					10.7 (1.68–68.8)*
Hosmer-Lemeshow test (p value)	0.268	0.386	0.265	0.475	0.477
Mortality 12 months					
Gender, woman	1.24 (0.29–5.18)	1.16 (0.26–5.08)	1.45 (0.29–7.06)	0.75 (0.15–3.38)	0.73 (0.14–3.82)
Charlson index	1.36 (0.94–1.95)	1.37 (0.95–1.9)	1.55 (0.98–2.33)	1.18 (0.78–1.78)	1.04 (0.70–1.54)
Barthel index, total or severe dependence (≤ 60 points)	2.38 (0.94–12.07)				
MNA-SF, malnutrition (0–7 points)		7.78 (1.47–40.90)*			
SPMSQ, moderate to severe cognitive impairment (5–10 errors)			10.73 (2.40–47.8)*		
PALIAR index, high risk (≥ 11 points)				11.7 (2.62–51.6)*	
PROFUND index, high risk (≥ 11 points)					20.9 (3.15–139.0)*
Hosmer-Lemeshow test (p value)	0.044	0.013	0.250	0.167	0.173

* $p < 0.05$.
CI: confidence interval; MNA-SF: Mini-Nutritional Assessment-Short Form; OR: odds ratio; SPMSQ: Short Portable Mental Status Questionnaire.
Model 1: adjusted for gender, Charlson index, and Barthel index. Model 2: adjusted for gender, Charlson index, and MNA-SF. Model 3: adjusted for gender, Charlson index, and SPMSQ. Model 4: adjusted for gender, Charlson index, and PALIAR index. Model 5: adjusted for gender, Charlson index, and PROFOUND index.

der, and chronic diseases, as seen in the EPESE cohort study, which began in 1981.[18] Lu et al.[19] also indicated that geriatric conditions, more than multimorbidity, predict the development of incident disability and mortality in people aged 80 years or older.

The Charlson index has some limitations in the geriatric population: it does not capture the severity of the diseases affecting very old people with frailty or functional impairment; it excludes non-malignant hematological diseases and others that are very prevalent in this population; and it does not include geriatric syndromes. The Cumulative Illness Rate Scale for Geriatrics (CIRS-G)[20] was developed to measure the impact of chronic diseases according to their severity, and this instrument was revised further to reflect common problems in very old populations. It is easy to use and at least as useful as the more extensive comorbidity scales for rehospitalization and mortality outcomes.[20,21]

With regard to the PALIAR and PROFUND prognostic indexes, the high-risk groups defined by these instruments showed significantly higher mortality at both 6 and 12 months, as reported by previous studies.[12,13,22] The PALIAR index was associated with 6- and 12-month mortality only in the multivariate analysis. In a recent study, the PALIAR index had a higher predictive power for mortality at 6 months than the PROFUND index, but the two scales performed equally at 12 months.[22]

Cruz-Jentoft and Rexach[10] suggest that the search for tools to detect palliative problems and characterize end-of-life process may be useless, especially when authoritative evidence already shows that CGAs can detect needs and problems and inform the development of an effective care plan, tailored to each elderly patient throughout the course of their disease. According to our study, the PALIAR and PROFUND prognostic indexes were also associated with higher mortality in nonagenarians and could constitute an additional dimension of CGAs in this population.

In our cohort, malnutrition and moderate-severe cognitive impairment — both important geriatric syndromes — were associated with higher mortality at 6 and 12 months. This finding is consistent with other studies that have observed a high prevalence of undernutrition in elderly patients hospitalized in geriatric and general internal medicine wards and its association with increased 1-year mortality.[23] Moreover, cognitive impairment is considered a risk factor for mortality in elderly patients, probably due to its link with respiratory and urinary tract infections and sepsis.[24] Both of these geriatric syndromes should thus be monitored closely in elderly populations.

Strengths of the study include its novelty and relevance in a sample from a very old population, which in 2019 numbered 540,500, or 1.15% of the total population in Spain[1] — a 300% increase from 1990. The most important limitation is the small sample size and the convenience sampling method, which led to the inclusion of patients admitted only on certain days of the week. However, we did exclude patients who died within 48 hours of admission and those admitted to the palliative care unit in order to minimize the risk of selection bias. Secondly, in this study 51 individuals were excluded, so just 50 individuals were included in the final analysis. Although the age and sex were similar between groups, the outcomes were not recorded in excluded patients, constituting one limitation of the current study. Other limitations include the single-center design; the absence of biological data, measures of frailty, and information on functional loss (Barthel index) on admission or on discharge; and the failure to quantify geriatric conditions of interest, such as delirium, falls, polypharmacy, or dysphagia.

In our cohort study, severe dependence for basic activities of daily living, malnutrition, and moderate-severe cognitive impairment were associated with higher mortality at 6 and 12 months. Higher scores on the PALIAR and PROFUND prognostic indexes were also associated with higher mortality at these time points. However, more prospective cohort studies based on CGAs, comorbidity measures, and prognostic indexes like PALIAR and PROFUND are necessary to improve management of hospitalized patients aged 90 years and over.

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