Nononcological Advanced Chronic Disease and Palliative Needs: Survival Analysis

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Abstract

Background: Professionals who care for patients with advanced chronic nononcological disease need accurate prognostic tools. There are validated prognostic indices for nononcological pathology in the fields of internal medicine (PALIAR and PROFUND indices) and palliative care (PPI indices, PaP score, ECOG, PPS, KI). The objective of this study is to describe survival and analysed factors associated with mortality in advanced chronic nononcological disease patients in palliative care services in the Community of Madrid.

Methods: Multilongitudinal observational study of a prospective cohort with a 6-month follow-up. Sociodemographic, clinical, analytical, service use, functionality, and prognostic indices were measured. Survival was analysed at 3 and 6 weeks and at 1, 2, 3, 4, 5, and 6 months through Kaplan–Meier curves. After the bivariate analysis, a Cox proportional-hazards multivariate regression analysis was performed.

Results: 217 patients were included. The mean age (SD) was 78.8 (12.6), and 47.5% were women. Some 129 patients died. Mean survival (SD) at 6 months was 146.12 (130.14) days, median (IQR) survival 111.5 (17.50-254.50). All prognostic indices (PALIAR $p < 0.001$, PROFUND $p < 0.005$, PPI $p < 0.016$, PaP Score $p < 0.001$, ECOG $p < 0.002$, PPS $p < 0.018$, and KI $p < 0.016$) predicted mortality at 6 months. The variables that explained survival at less than 3 months were PPS (HR (CI) 0.96 (0.95-0.98), $p < 0.000$), leukocytes (HR (CI) 1.06 (1.02-1.10), $p < 0.000$), delirium at the last admission (HR (CI) 1.79 (1.02-3.09) $p < 0.030$), and ≥ 4 hospitalization in the last year (HR (CI) 1.82 (1.16-2.88) $p < 0.010$). The variables that explained 6-month survival were PPS (HR (CI) 0.96 (0.94-0.97), $p < 0.000$), leukocytes (HR (CI) 1.06 (1.03-1.09), $p < 0.000$), and haemoglobin (HR (CI) 0.88 (0.82-0.97) $p < 0.005$).

Conclusions: Clinical and resource use variables were predictors of mortality in survivals shorter than 3 months, but not in survivals longer than 3 months.

Background

The progressive ageing of the population and the growing number of people with chronic diseases represent an emerging health problem (1). In the European Union, the percentage of people over 65 years of age will increase from 16.1% in 2000 to 27.5% in 2050. Spain, Italy, and Japan will lead this ageing process worldwide; by 2050, approximately 35% of our population will be over 75 years old (2).

The World Health Organization estimates for the year 2030 worldwide indicate that the total number of deaths will increase from 58 to 74 million and that advanced chronic diseases and complications of extreme clinical, functional, and cognitive deterioration will be responsible for most of this increase. Thus, approximately 75% of people who will die will do so because chronic diseases (mainly cardiovascular, oncological, respiratory, and dementias) that have evolved for many years (they will be older than 75 years) and that these people will have a high need for care, frequenting health and social services, in addition to the fact that they will have to make important and complex clinical decisions (3).

In our country, the percentage of people over 65 years of age has doubled in only four decades, going from 7.2% in 1950 to 18.5% in 2015. According to the epidemiological projections of the National Institute of Statistics, population growth will decrease, and it is estimated that in 2050, 37% of the population will be older than 64 years (4,5). The results of a recent population prevalence study show that 1.4% of the general population, 26-40% of those in acute hospitals, and 60-70% of those in nursing homes are in a situation of advanced chronic disease and palliative needs (6,7).

Currently, health professionals who care for patients with advanced chronic nononcological diseases who are in a final phase of the disease with an uncertain life prognosis need to predict, with greater or lesser accuracy, the time their patients have left to live. This need responds to the desire of the patient and the family to have adequate information about the real situation and the desire of the professionals to have tools that allow them to better adapt their decisions about the treatment, special care, or social and health resources necessary to improve their patients' quality of life, as well as to achieve proper advance planning of care. In the field of palliative care, predictive survival tools are available that, although they were created for oncological patients, were subsequently validated for the care of nononcological patients, such as palliative performance scale (PPS) indices (8–15), the Karnofsky index (KI) (16), the Eastern Cooperative Oncology (ECOG) score (17,18), the Palliative Prognostic Index (PPI) (19,20), and Palliative Prognostic (PaP score) (16,21). In the field of internal medicine, the PALIAR scale (22–24) and PROFUND (25–28) have been validated as predictors of nononcological survival at 6 and 18 months, respectively, for hospitalized patients, but their usefulness in the field of palliative care is unknown.

The objective of this study is to describe survival and analysed factors associated with mortality in advanced chronic nononcological disease patients in palliative care services in the Community of Madrid.

Methods

This is a multicentre longitudinal observational study of a prospective cohort of 6 months' duration. The study period was from October 15, 2018 to November 1, 2019. The scope of study included the different palliative care units of the Community of Madrid in acute hospitals, in mid-stay hospitals, and hospital and home palliative support teams.

All patients with nononcological advanced chronic diseases who were treated in the different palliative care teams of the Community of Madrid during the study period were included. Severe mental disorders, amyotrophic lateral sclerosis, and AIDS were excluded. Sociodemographic variables were collected (age, sex, whether they lived alone, their need for a primary caregiver, and their relationship with the primary caregiver); disease variables according to the National Hospice Organization (NHO) criteria, (heart failure with dyspnoea of New York Heart Association (NYHA) class III-IV, chronic respiratory failure with baseline dyspnoea of Medical Research Council (MRC) grade ≥ 3 , chronic renal failure in stage 5, chronic liver disease with a

Child-Pugh score >7, chronic neurological diseases such as dementia, and cerebrovascular and other neurodegenerative diseases such as multiple sclerosis, myasthenia gravis, and Duchenne muscular dystrophy); clinical variables (anorexia, pressure ulcers, presence of active neoplasia, dementia, delirium in the last hospitalization, and number of drugs taken); analytical variables (Hb (g/dL), albumin (g/dL), leukocytes ($\times 10^3/\text{mm}^3$) and lymphocytes ($\times 10^3/\text{mm}^3$)); variables of service use (place of death and ≥ 4 hospitalizations in the last year); functionality (Barthel index); and the prognostic index (PALIAR, PROFUND, PPI, PaP Score, ECOG, PPS and KI).

Survival was evaluated taking the date of registration in the clinical history as the start date and the date of the death or last follow-up as the end date. Mortality from any cause recorded in the clinical history was included.

Qualitative variables, expressed as absolute frequency (n) and percentage (%), and quantitative variables, expressed as mean and standard deviation (SD) or median and interquartile range (IQR), are described, depending on whether the variable follows a normal distribution. Qualitative variables were compared by the chi-squared test with Yates's correction or by Fisher's exact test. Quantitative variables were compared by Student's t test.

Survival was analysed at 3 and 6 weeks and at 1, 2, 3, 4, 5, and 6 months with Kaplan–Meier curves, as performed by Morita et al. with the PPI index (20) at 3 and 6 weeks and the PaP score of Pirovano et al. (16) at 1 month and as done by Bernabeu-Wittel M et al. with the PALIAR index (22–24) at 6 months. To identify factors associated with mortality, a multivariate Cox proportional-hazards regression analysis was performed, with survival time as the dependent variable and as independent variables those that had $p < 0.20$ and/or were considered of clinical relevance. The hazard ratio (HR) and its 95% confidence interval (CI) were calculated.

For the statistical treatment and graphical representation of the data, the statistical package SPSS v.26.0. and Microsoft Office Excel 2007 were used. The confidentiality and privacy of the data were rigorously maintained, the data extraction was independent of the analysis, and an anonymized database was built. The study was approved by the Clinical Research Ethics and Medications of the San Carlos Clinical Hospital (code 18/123) and the Central Research Commission of Primary Care Management (Protocol code 25/18).

Results

Characteristics of the study participants

217 patients were included. The mean age was 78.8 (SD: 12.6), and 47.5% were women. Tables 1, 2, and 3 show the sociodemographic characteristics, disease according to NHO criteria, clinical and analytical variables, service use, and functional and prognostic indices stratified according to 6-month survival.

Primary Outcomes

Table 1. Description of sociodemographic, clinical, and analytical characteristics according to 6-month survival.

	Total N (%)	Survival ≥6 months	Survival <6 months	p
Sociodemographic variables	N=217	N=75 (34.5%)	N=129 (59.4%)	
Age, mean (SD)	78.8 (12.6)*	75.9 (12.6)*	80.7 (12.3)*	0.008
Sex				
Male	103 (47.5)	33 (44.0)	62 (48.1)	0.570
Female	114 (52.5)	42 (56.0)	67 (51.9)	
Lived alone	26 (12.0)	9 (12.0)	16 (12.4)	0.930
Required primary caregiver (Barthel index <60)	194 (89.4)	63 (84.0%)	119 (92.2)	0.067
Relationship with primary caregiver				
Spouse	78 (35.9)	34 (45.3)	39 (30.2)	
Other	120 (55.3)	32 (42.7)	81 (62.8)	0.020
(None)	19 (8.8)	9 (12.0)	9 (7.0)	
Disease variables according to NHO criteria				
CHF, NYHA class III-IV	53 (24.4)	19 (25.3)	34 (26.4)	0.870
Respiratory Insuf. MRC grade ≥3	76 (35.0)	24 (32.0)	49 (38.0)	0.390
CKD stage V	23 (10.6)	5 (6.7)	18 (14.0)	0.110
Chronic liver disease Child-Pugh >7	11 (5.1)	4 (5.3)	4 (3.1)	0.430
Dementia, ACVA	50 (24.0)	17 (22.7)	33 (20.2)	0.670
Others: MS, MG, Duchenne	4 (1.8)	2 (2.7)	2 (1.6)	0.580
Clinical and analytical variables				
Active neoplasia	17(7.8)	3(4.0)	13(10.1)	0.120
Delirium last hospitalization	42 (21.7)	10 (13.3)	35 (27.1)	0.022
Number of drugs	10.2 (4.7)*	10.7 (4.2)*	9.8 (4.5)*	0.200
Anorexia	128 (59.0)	35 (46.7)	84 (65.1)	0.010
Pressure ulcers	38(17.5)	12(16.0)	21(16.3)	0.960
Hb (g/dL)	11.9 (2.0)*	12.4 (2.1)*	11.8 (1.9)*	0.039
Albumin (g/dL)	3.3 (0.7)*	3.5 (0.6)*	3.3 (0.8)*	0.041
Leukocytes (×103/mm3)	8.6 (5.1)*	7.7 (3.6)*	8.9 (5.8)*	0.100
Lymphocytes (×103/mm3)	18.8(13.2)*	20.3 (11.4)*	17.2 (13.4)*	0.093

* mean ± standard deviation (SD). NHO: National Hospice Organization; CHF: congestive heart failure. NYHA: New York Heart Association. Insuf: insufficiency; MRC: Medical Research Council; CKD: chronic kidney disease; ACVA: acute cerebrovascular accident; MS: multiple sclerosis; MG: myasthenia gravis; Hb: haemoglobin.

Table 2. Description of the characteristics of service use according to 6-month survival.

Service use variable	Total N (%)	Survival ≥ 6 months	Survival <6 months	p
Place of Death				
Address	56 (26.7)	3 (4.3)	51 (39.5)	<0.001
Acute hospitals	37 (17.6)	6 (8.6)	31 (24.0)	
PCU	53 (25.2)	6 (8.6)	41 (31.8)	
Residence	3 (1.4)	0 (0.0)	3 (2.3)	
Unknown	61 (29.0)	55 (78.6)	3 (2.3)	
≥ 4 hospitalizations in the last year	79 (36.4)	22 (29.3)	49 (38.0)	0.210

PCU: palliative care unit.

Table 3. Description of the functional characteristics and prognostic indices according to 6-month survival.

	Total N (%)	Survival ≥6 months	Survival <6 months	p
Functionality variables				
Barthel index	36.2 (30.4)	42.3 (32.9)	34.2 (28.7)	0.065
<20	74 (34.1)	23 (30.7)	43 (33.3)	0.250
20-35	38 (17.5)	10 (13.3)	27 (20.9)	
40-55	53 (24.4)	17 (22.7)	33 (25.6)	
≥60	49 (22.6)	24 (32.0)	24 (18.6)	
Variables of prognostic indices				
PALIAR index				
0 points	16 (7.4)	5 (6.7)	11 (8.5)	<0.001
3-3.5 points	40 (18.4)	23 (30.7)	16 (12.4)	
4-7 points	39 (18.0)	18 (24.0)	18 (14.0)	
≥7.5 points	122 (56.2)	29 (38.7)	84 (65.1)	
PROFUND index				
0-2 points	1 (0.5)	0 (0.0)	1 (0.8)	0.005
3-6 points	47 (21.7)	26 (34.7)	21 (16.3)	
7-10 points	60 (27.6)	23 (30.7)	33 (25.6)	
≥11 points	109 (50.2)	26 (34.7)	74 (57.4)	
PPI				
> 0 points	16 (7.4)	8 (10.7)	8 (6.2)	0.016
> 2 points	60 (27.6)	26 (34.7)	32 (24.8)	
> 4 points	55 (25.3)	22 (29.3)	27 (20.9)	
> 6 points	64 (29.5)	17 (22.7)	45 (34.9)	
> 9,5 points	22 (10.1)	2 (2.7)	17 (13.2)	
PaP Score				
0-5.5	133 (61.6)	59 (79.7)	67 (51.9)	<0.001
5.6-11	61 (28.2)	15 (20.3)	41 (31.8)	
11.1-17.5	22 (10.2)	0 (0.0)	21 (16.3)	
ECOG				
1	17 (7.8)	10 (13.3)	7 (5.4)	0.002
2	76 (35.0)	32 (42.7)	40 (31.0)	
3	88 (40.6)	29 (38.7)	52 (40.3)	
4	36 (16.6)	4 (5.3)	30 (23.3)	
PPS				
10	9 (4.1)	0 (0.0)	8 (6.2)	0.018
20	6 (2.8)	0 (0.0)	6 (4.7)	
30	26 (12.0)	6 (8.0)	17 (13.2)	
40	39 (18.0)	13 (17.3)	24 (18.6)	
50	109 (50.2)	41 (54.7)	63 (48.8)	
60	27 (12.4)	14 (18.7)	11 (8.5)	
70	1 (0.5)	1 (1.3)	0 (0.0)	

KI				
10	5 (2.3)	0 (0.0)	5 (3.9)	0.016
20	13 (6.0)	1 (1.3)	11 (8.5)	
30	34 (15.7)	9 (12.0)	21 (16.3)	
40	64 (29.5)	26 (34.7)	36 (27.9)	
50	74 (34.1)	24 (32.0)	46 (35.7)	
60	24 (11.1)	13 (17.3)	9 (7.0)	
70	2 (0.9)	2 (2.7)	0 (0.0)	
90	1 (0.5%)	0 (0.0%)	1 (0.8)	

* PPI: Palliative Prognostic Index; PaP Score: Palliative Prognostic Score; ECOG: Eastern Cooperative Oncology Group; PPS: Palliative Performance Scale; KI: Karnofsky Index.

The sociodemographic variables, disease characteristics according to NHO criteria, clinical variables, analytical variables, service use, and functional and prognostic indices stratified according to survival at 3 and 6 weeks and 1, 2, 3, 4, and 5 months can be found in the Supplementary Materials 1.

The mean survival of the patients during the 6 months of follow-up was 146.12 days (SD 130.14), with a median of 111.5 (IQR 17.50-254.50) and a range of 0-420 days. In this period, 129 patients died, for a mortality of 60.19% in men and 58.77% in women. Figure 1 shows the Kaplan–Meier survival curves according to the prognostic index.

The means and medians of survival according to each prognostic index can be visualized in Supplementary Materials 2.

Table 4 shows the prognostic factors of survival at 3 and 6 weeks and 1, 2, 3, 4, 5, and 6 months. PPS and haemoglobin were protective factors (HR<1), and leukocytes, 4 or more hospitalizations in the last year, and delirium in the last hospitalization were risk factors for mortality (HR>1).

Table 4. Multivariate analysis of Cox proportional hazards (n=217).

	3 weeks		6 weeks		1 month		2 months		3 months		4 months		5 months		6 months	
	HR (CI)	p	HR (CI)	p	HR (CI)	p	HR (CI)	p	HR (CI)	p	HR (CI)	P	HR (CI)	p	HR (CI)	p
PPS	0.96 (0.94-0.98)	0.00	0.96 (0.94-0.98)	0.00	0.96 (0.94-0.99)	0.00	0.96 (0.95-0.98)	0.00	0.95 (0.94-0.97)	0.00	0.95 (0.94-0.97)	0.00	0.96 (0.94-0.97)	0.00	0.96 (0.94-0.97)	0.00
Leukocytes	1.05 (1.01-1.10)	0.02	1.06 (1.02-1.10)	0.00	1.06 (1.02-1.10)	0.01	1.06 (1.02-1.10)	0.00	1.05 (1.01-1.09)	0.01	1.06 (1.03-1.09)	0.00	1.06 (1.03-1.09)	0.00	1.06 (1.03-1.09)	0.00
Delirium last admission	1.95 (1.01-3.76)	0.05	1.89 (1.05-3.39)	0.03	1.97 (1.06-3.66)	0.03	1.79 (1.04-3.09)	0.03								
≥4 admissions	1.77 (1.02-3.08)	0.04	1.96 (1.20-3.22)	0.01	1.93 (1.14-3.27)	0.01	1.82 (1.16-2.88)	0.01	1.61 (1.06-2.43)	0.02						
Haemoglobin											0.89 (0.82-0.97)	0.00	0.89 (0.82-0.97)	0.00	0.88 (0.82-0.97)	0.00

PPS: palliative performance scale; HR: hazard ratio,

Discussion

In our study, the average survival of nononcological advanced chronic disease patients in the Community of Madrid was 111 days. The predictive factors of mortality below 3 months have been the PPS scale, the number of leukocytes, having 4 or more hospitalizations in the last year and delirium in the

hospitalization. The PPS scale, the number of leukocytes, and haemoglobin were the factors that were associated with mortality, over 3 months.

This study reveals factors associated with mortality at 6 months, such as the PPS scale and the number of leukocytes. The PPS scale has powerful predictive value for survival in patients receiving palliative oncological care (8) and has been validated in noncancer patient care (8-15). It is an excellent tool to measure the functional status and progression of the patient, and our findings once again confirm it as an adequate index and predictor of mortality. In this study, for each 10-points increase in PPS, the probability of death decreased by 5% in all studied periods of survival: at 2 and 3 weeks and at 1, 2, 3, 4, 5, and 6 months.

The number of leukocytes was another predictor of long-term mortality, an effect that is well described for coronary disease (29–31) and cerebrovascular disease (32) but has also been associated with hypertension (33), glucose intolerance (34), and the risk of overall mortality (35). The systematic review of Asadollahi K et al. (36) provides evidence of an independent association between leukocytosis and mortality, particularly coronary and cerebrovascular mortality. Several associations with morbidity have also been reported, although the evidence is less strong than for mortality. Maltoni et al. (37) conducted a multicentre prospective study of 519 patients with advanced oncological disease and analysed the prognostic capacity of 11 variables, among which leukocytosis had independent prognostic value, showing that the immune system is closely involved in the prognosis of patients with advanced cancer (3).

The prevalence of delirium at the end of life approaches 85% in palliative care settings (38–40). During hospitalization, it is a strong risk factor for complications, a longer stay, and subsequent institutionalization (39,41–43). The prospective meta-analysis of Witlox J et al. (44) that included almost 3000 elderly patients with delirium followed for a mean of 22.7 months showed that delirium was independently associated with higher risks of death (OR [95% CI]: 2.0 [1.5-2.5]), institutionalization (OR [95% CI]: 2.4 [1.8-3.3]), and incident dementia (OR [95% CI]: 12.5 [11.9-84.2]). More recently, the meta-analysis of Aung Thein MZ et al. (45) found that mortality related to delirium has not decreased in the last 30 years and that delirium is associated with a higher risk of mortality from all causes in hospitalized elderly patients. Delirium has been recognized by different authors as a prognostic factor within the following survival indices: the PPI index. (20), Delirium-Palliative Prognostic Score (D-PaP score) (38), and PROFUND (25–28). In our study, delirium in the last hospitalization increased the probability of death by 95% at 3 weeks, 89% at 6 weeks, 96% at 1 month, and 79% at 2 months.

Presenting ≥ 4 hospitalization in the last year was a predictor of short-term mortality. Roig T et al. (46), in their prospective study of 101 patients in an acute geriatric unit, found that readmissions were associated with a higher risk of death at 1 year (OR [95% CI]: 3.53 [1.19-10.44], $p=0.023$). This model, like ours, emphasizes the prognostic weight of the care variables, and not only the clinical variables, to establish a prognosis with precision. In this study, having had ≥ 4 hospitalization in the last year, brought a 77% probability of dying at 3 weeks, 96% at 6 weeks, 93% at 1 month, 82% at 2 months, and 61% at 3 months.

After the 4th month, haemoglobin <10 g/dL was associated with mortality. For each 1 g/dL increase in haemoglobin, they were 11% more likely to be alive at 4, 5 and 6 months. In a Dutch cohort study of 1016 patients older than 85 years who lived in the community and were followed up for 10 years, Izaks GJ et al. (47) identified that the risk of mortality (95% CI) was 1.60 (1.24-2.06) ($p<0.001$) in women with anaemia and 2.29 (1.60-3.26) ($p<0.001$) in men. In both sexes, the risk of mortality increased with lower haemoglobin concentrations. The Leiden 85-plus prospective study (48), with a sample of 562 healthy people older than 85 years, identified that both prevalent and incident anaemia were associated with a higher risk of death, even after adjusting for sex, education level, and income, and predicted premature death in institutionalized elderly individuals (49). Multiple studies have shown an association between anaemia and increased mortality (47,48,50,51). Chaves et al. (52) identified, in a prospective study of 686 women older than 65 years with moderate to severe disability, that haemoglobin below 11.0 g/dL was associated with higher mortality (HR [95% CI]: 1.2 [1.1-1.4]), while levels of 13.0 and 14.0 g/dL were associated with a lower risk of death (HR [95% CI]: 0.6 [0.63-0.92]).

Strengths and limitations

This was a prospective multicentre study in which the different palliative care units of the Community of Madrid, acute care units, mid-stay units, and both hospital and home support teams participated. The study reflects the evolution of the disease in the context of routine clinical practice, since it was an observational study in which the only selection criterion was the authorization of the patient and/or their family to participate in the study by granting their informed consent. Having been able to consult the follow-up data of all the patients at 6 months minimized our losses of data. The different scales of functionality and prognosis were exhaustively studied, which allowed us to study many variables.

One of the limitations of this study is that its design could introduce great variability, although to reduce this possible bias, all the researchers went through in-person training, normalizing the data collection as well as making sure the study was carried out in conditions of routine clinical practice, which favoured the involvement of professionals, reduced losses, and ensured good data collection.

Applicability to clinical practice and research

In advanced chronic disease, the type of cardiac, respiratory, digestive, nephrological, and neurological pathology was not associated with an increased risk of mortality. This finding leads us to think that, as in advanced oncological disease, the type of tumour is not a predictor of mortality, nor is the type of chronic pathology, there being a common end of life in both cases.

Few prognostic scales allow us to define and estimate survival in patients with nononcological advanced chronic disease. We have specific prognostic indicators for pathologies, but the NHO criteria, without taking into account the specific pathology, were published in 1995 (53). They are still the most commonly used guidelines to determine the prognosis in advanced chronic nononcological diseases due to their simplicity. These medical guidelines

were developed based on expert opinions, and as demonstrated by Fox et al. (54), up to 70% of patients whose survival estimate was less than 6 months exceeded this period. Some studies even show that these criteria cannot be applied when life expectancy is very short. (55).

In our study, all the evaluated prognostic indices could classify the population into groups with significantly different survival at 3 and 6 weeks and at 1, 2, 3, 4, 5, and 6 months.

Conclusions

These findings support the recommendation of the European Association of Palliative Care to use a prognostic tool and avoid relying only on the clinical impression of the professional, with the aims of improving decisions for patients with advanced disease (56), communicating more realistic expectations, offering treatments tailored to the needs of each patient, avoiding futile therapies, and thereby optimizing the use of health resources (57–59).

Our study reflects the need to use prognostic scales in patients with nononcological advanced chronic diseases and demonstrates that the PPS scale, the number of leukocytes, delirium in the last hospitalization, and having ≥ 4 hospitalization in the last year are indicators that predict mortality within 2 months. The PPS scale, leukocyte count, and haemoglobin level predict mortality at 6 months. It would be of interest to develop a new line of research explaining why haemoglobin is only a factor associated with mortality after the 4th month and not earlier. Clinical and resource use factors were not predictor variables in the long term.

Abbreviations

ACKD: Advanced Chronic Kidney Disease

ACVA: Acute Cerebrovascular Accident

CHF: Congestive Heart Failure

CI: Confidence Interval

D-PaP score: Delirium Palliative Prognostic Score

ECA-NO: NonOncological Advanced Chronic Diseases

ECOG: Eastern Cooperative Oncology Group

Hb: Haemoglobin

HPST: Home Palliative Support Teams

HPST: Hospital Palliative Support Team

HR: Hazard Ratio

Insuf: Insufficiency

IQR: Interquartile Range

KI: Karnofsky Index

MG: Myasthenia Gravis

MRC: Medical Research Council

MS: Multiple Sclerosis

NHO: National Hospice Organization

NYHA: New York Heart Association

PaP Score: Palliative Prognostic Score

PCU: Palliative Care Unit

PCU-MSH: Palliative Care Unit, Mid-Stay Hospital

PPI: Palliative Prognostic Index

PPS: Palliative Performance Scale

SD: Standard Deviation

PU: Pressure Ulcers

Declarations

Ethics approval and consent to participate

The study was approved by the Clinical Research Ethics and Medications of the San Carlos Clinical Hospital (code 18/123) and the Central Research Commission of Primary Care Management (Protocol code 25/18). All methods were performed in accordance with the relevant guidelines and regulations.

Informed consent to participate was obtained from all subjects and/or their legal guardian(s).

Consent for publication

Not applicable

Availability of data and materials

The datasets generated and/or analysed during the current study are not publicly available **because contains sensitive clinical information about patients, so there are ethical and legal restrictions to sharing the data set**. The datasets used and analyzed during the current study are available from the author on reasonable request: cmiguel@salud.madrid.org.

Competing interests

The authors declare that they have no competing interests

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Authors' contributions

CMT, LSV, IDCG and CDMS conceived the study and participated in its design. CMT and LSV are executive coordinators of the project. PJD, PAF, JMCG, MBMC, EMSP, GDS, BSS, MSI contributed to data acquisition, and quality control at their respective palliative care units. Clinical investigators in clinical practice of the NOECA GROUP developed the field work in their palliative care units. CDMS, JCGM, and IDCG were in charge of statistical analyses, and with CMT are in charge of table and figure design. The first draft was initially written by CMT and CDMS with discussion with IDCG and JCGM. All authors contributed to data interpretation, critically reviewed the first draft, approved the final version, and agreed to be accountable for the work.

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References

1. Unidad de Pacientes Pluripatológicos Estándares y Recomendaciones [Internet]. Ministerio de Sanidad y Política Social. 2009 [Internet]. 2009. Available from: http://www.msc.es/organizacion/sns/planCalidadSNS/docs/EyR_UPP.pdf
2. Consejería de Salud de la Comunidad de Madrid. Estrategia de Atención a Pacientes con Enfermedades Crónicas [Internet]. 2013. 143 p. Available from: <http://www.madrid.org/bvirtual/BVCM017570.pdf>
3. Rexach Cano L. Atención al anciano con enfermedad oncológica o no oncológica que precisa cuidados paliativos. In: Tratado de Medicina Geriátrica. p. 640–9.
4. INE [Internet]. [cited 2020 Nov 26]. Available from: <https://www.ine.es/prensa/np587.pdf>
5. Zunzunegui MV, Béland F. Políticas intersectoriales para abordar el reto del envejecimiento activo. Informe SESPAS 2010. Gac Sanit. 2010;24(SUPPL. 1):68–73.
6. Gómez-Batiste X, Martínez-Muñoz M, Blay C, Amblàs J, Vila L, Costa X. Identificación de personas con enfermedades crónicas avanzadas y necesidad de atención paliativa en servicios sanitarios y sociales: elaboración del instrumento NECPAL CCOMS-ICO®. Med Clin (Barc). 2013;140(6):241–5.
7. Solano JP, Gomes B, Higginson IJ. A comparison of symptom prevalence in far advanced cancer, AIDS, heart disease, chronic obstructive pulmonary disease and renal disease. J Pain Symptom Manage [Internet]. 2006 Jan;31(1):58–69. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/16442483>
8. Downing M, Lau F, Lesperance M, Karlson N, Shaw J, Kuziemy C, et al. Meta-analysis of survival prediction with palliative performance scale. J Palliat Care. 2007;23(4):245–54.
9. Lau F, Maida V, Downing M, Lesperance M, Karlson N, Kuziemy C. Use of the Palliative Performance Scale (PPS) for end-of-life prognostication in a palliative medicine consultation service. J Pain Symptom Manage [Internet]. 2009 Jun;37(6):965–72. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/19232892>
10. Anderson F, Downing GM, Hill J, Casorso L, Lerch N. Palliative performance scale (PPS): a new tool. J Palliat Care [Internet]. 1996;12(1):5–11. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/8857241>
11. Olajide O, Hanson L, Usher BM, Qaqish BF, Schwartz R, Bernard S. Validation of the palliative performance scale in the acute tertiary care hospital setting. J Palliat Med [Internet]. 2007 Feb;10(1):111–7. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/17298259>
12. Virik K, Glare P. Validation of the Palliative Performance Scale for inpatients admitted to a palliative care unit in Sydney, Australia [5]. J Pain Symptom Manage. 2002;23(6):455–7.
13. Morita T, Tsunoda J, Inoue S, Chihara S. Validity of the palliative performance scale from a survival perspective. J Pain Symptom Manage [Internet]. 1999 Jul;18(1):2–3. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/10439564>
14. Head B, Ritchie CS, Smoot TM. Prognostication in hospice care: Can the palliative performance scale help? J Palliat Med. 2005;8(3):492–502.
15. Lau F, Downing M, Lesperance M, Karlson N, Kuziemy C, Yang J. Using the Palliative Performance Scale to provide meaningful survival estimates. J Pain Symptom Manage [Internet]. 2009 Jul;38(1):134–44. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/19171459>
16. Pirovano M, Maltoni M, Nanni O, Marinari M, Indelli M, Zaninetta G, et al. A new palliative prognostic score: A first step for the staging of terminally ill cancer patients. J Pain Symptom Manage. 1999;17(4):231–9.
17. Oken M M; Creech R H; Tormey D C; Horton J; Davis T E; McFadden E T; Carbone PP. Toxicity and response criteria of the Eastern Cooperative Oncology Group. Am J Clin Oncol. 1982;5:649–55.
18. Peng M-T, Liu C-T, Hung Y-S, Kao C-Y, Chang P-H, Yeh K-Y, et al. Sequential Assessments of the Eastern Cooperative Oncology Group Performance Scale Enhance Prognostic Value in Patients With Terminally Ill Cancer Receiving Palliative Care. Am J Hosp Palliat Care [Internet]. 2016 Jun;33(5):471–6. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/25552306>
19. Nieto Martín MD, Bernabeu Wittel M, de la Higuera Vila L, Mora Rufete A, Barón Franco B, Ollero Baturone M, et al. Adaptation of the Palliative Prognostic Index in patients with advanced medical conditions. Rev Clin Esp [Internet]. 2013 Oct;213(7):323–9. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/23725861>
20. Morita T, Tsunoda J, Inoue S, Chihara S. The Palliative Prognostic Index: a scoring system for survival prediction of terminally ill cancer patients. Support Care Cancer [Internet]. 1999 Apr 7;7(3):128–33. Available from: <http://link.springer.com/10.1007/s005200050242>
21. Maltoni M, Pirovano M, Scarpi E, Marinari M, Indelli M, Arnoldi E, et al. Prediction of survival of patients terminally ill with cancer. Results of an Italian prospective multicentric study. Cancer [Internet]. 1995 May 15;75(10):2613–22. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/7537625>
22. Bernabeu-Wittel M, Ruiz-Cantero A, Murcia-Zaragoza J, Hernández-Quiles C, Barón-Franco B, Ramos-Cantos C, et al. Precisión de los criterios definitorios de pacientes con enfermedades médicas no neoplásicas en fase terminal. Proyecto PALIAR. Rev Esp Geriatr Gerontol. 2010;45(4):203–12.
23. Bernabeu-Wittel M, Murcia-Zaragoza J, Hernández-Quiles C, Escolano-Fernández B, Jarava-Rol G, Oliver M, et al. Development of a six-month prognostic index in patients with advanced chronic medical conditions: The PALIAR score. J Pain Symptom Manage. 2014;47(3):551–65.
24. Hernández Quiles C, Bernabeu Wittel M, Praena Segovia J, Ternero Vega J, Díez Manglano J, Jarava Rol G, et al. Comparación de la pregunta sorpresa frente a un índice objetivo (Índice PALIAR) para la identificación de situación terminal en pacientes con enfermedades crónicas avanzadas. Rev Clin Esp. 2017;217(2):123–4.

25. Bernabeu-Wittel M, Ollero-Baturone M, Moreno-Gaviño L, Barón-Franco B, Fuertes A, Murcia-Zaragoza J, et al. Development of a new predictive model for polypathological patients. The PROFUND index. *Eur J Intern Med*. 2011;22(3):311–7.
26. Díez-Manglano J, Cabrerizo García JL, García-Arilla Calvo E, Jimeno Saínz A, Calvo Beguería E, Martínez-Álvarez RM, et al. External validation of the PROFUND index in polypathological patients from internal medicine and acute geriatrics departments in Aragón. *Intern Emerg Med*. 2015;10(8):915–26.
27. Díez-Manglano J, del Corral Beamonte E, Ramos Ibáñez R, Lambán Aranda MP, Toyas Miazza C, Rodero Roldán M del M, et al. Utilidad del índice PROFUND para predecir la mortalidad a los 4 años en pacientes pluripatológicos. *Med Clin (Barc)*. 2016;147(6):238–44.
28. Colombo PB, Nieto Martín MD, De La Pisa BP, Lozano MJG, Camúñez MÁO, Wittel MB. Validación de un modelo pronóstico para pacientes pluripatológicos en atención primaria: Estudio PROFUND en atención primaria. Vol. 46, *Atencion Primaria*. 2014. p. 41–8.
29. A Amaro 1, J R Gonzalez-Juanatey, C Iglesias, L Martinez-Sande, R Trillo, J García-Acuña MG de la P. Leukocyte count as a predictor of the severity ischaemic heart disease as evaluated by coronary angiography [Internet]. Available from: <https://pubmed.ncbi.nlm.nih.gov/8305243/>
30. Barron H V, Harr SD, Radford MJ, Wang Y, Krumholz HM. The association between white blood cell count and acute myocardial infarction mortality in patients > or =65 years of age: findings from the cooperative cardiovascular project. *J Am Coll Cardiol* [Internet]. 2001 Nov 15;38(6):1654–61. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/11704377>
31. Cannon CP, McCabe CH, Wilcox RG, Bentley JH, Braunwald E. Association of white blood cell count with increased mortality in acute myocardial infarction and unstable angina pectoris. *Am J Cardiol*. 2001;87(5):636–9.
32. Kaźmierski R, Guzik P, Ambrosius W, Kozubski W. Leukocytosis in the first day of acute ischemic stroke as a prognostic factor of disease progression. *Wiad Lek* [Internet]. 2001;54(3–4):143–51. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/11436679>
33. Tatsukawa Y, Hsu WL, Yamada M, Cologne JB, Suzuki G, Yamamoto H, et al. White blood cell count, especially neutrophil count, as a predictor of hypertension in a Japanese population. *Hypertens Res*. 2008;31(7):1391–7.
34. Fritsche A, Häring H, Stumvoll M. White blood cell count as a predictor of glucose tolerance and insulin sensitivity. The role of inflammation in the pathogenesis of type 2 diabetes mellitus. *Dtsch Med Wochenschr* [Internet]. 2004 Feb 6;129(6):244–8. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/14750050>
35. White blood cell count as a predictor of mortality: Results over 18 years from the normative aging study.
36. Asadollahi K, Beeching NJ, Gill G V. Leukocytosis as a predictor for non-infective mortality and morbidity. *QJM* [Internet]. 2010 May;103(5):285–92. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/20056764>
37. Maltoni M, Pirovano M, Nanni O, Marinari M, Indelli M, Gramazio A, et al. Biological indices predictive of survival in 519 Italian terminally ill cancer patients. Italian Multicenter Study Group on Palliative Care. *J Pain Symptom Manage* [Internet]. 1997 Jan;13(1):1–9. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/9029856>
38. Scarpi E, Maltoni M, Miceli R, Mariani L, Caraceni A, Amadori D, et al. Survival prediction for terminally ill cancer patients: revision of the palliative prognostic score with incorporation of delirium. *Oncologist* [Internet]. 2011;16(12):1793–9. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/22042788>
39. Inouye SK, Westendorp RGJ, Saczynski JS. Delirium in elderly people. *Lancet (London, England)* [Internet]. 2014 Mar 8;383(9920):911–22. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/23992774>
40. Marcantonio ER. Delirium in Hospitalized Older Adults. *N Engl J Med* [Internet]. 2017 Oct 12;377(15):1456–66. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/29020579>
41. Marcantonio ER. In the clinic. Delirium. *Ann Intern Med* [Internet]. 2011 Jun 7;154(11):ITC6-1, ITC6-2, ITC6-3, ITC6-4, ITC6-5, ITC6-6, IT. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/21646553>
42. Marcantonio ER. Postoperative delirium: a 76-year-old woman with delirium following surgery. *JAMA* [Internet]. 2012 Jul 4;308(1):73–81. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/22669559>
43. Gleason LJ, Schmitt EM, Kosar CM, Tabloski P, Saczynski JS, Robinson T, et al. Effect of delirium and other major complications on outcomes after elective surgery in older adults. Vol. 150, *JAMA Surgery*. 2015. p. 1134–40.
44. Witlox J, Eurelings LSM, de Jonghe JFM, Kalisvaart KJ, Eikelenboom P, van Gool WA. Delirium in elderly patients and the risk of postdischarge mortality, institutionalization, and dementia: a meta-analysis. *JAMA* [Internet]. 2010 Jul 28;304(4):443–51. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/20664045>
45. Aung Thein MZ, Pereira J V, Nitchingham A, Caplan GA. A call to action for delirium research: Meta-analysis and regression of delirium associated mortality. *BMC Geriatr* [Internet]. 2020 Sep 7;20(1):325. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/32894065>
46. Roig T, Márquez MÁ, Hernández E, Pineda I, Sabartés O, Miralles R, et al. [Geriatric assessment and factors associated with mortality in elderly patients with heart failure admitted to an acute geriatric unit]. *Rev Esp Geriatr Gerontol* [Internet]. 48(6):254–8. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/24099900>
47. Izaks GJ, Westendorp RG, Knook DL. The definition of anemia in older persons. *JAMA* [Internet]. 1999 May 12;281(18):1714–7. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/10328071>
48. den Elzen WPJ, Willems JM, Westendorp RGJ, de Craen AJM, Assendelft WJJ, Gussekloo J. Effect of anemia and comorbidity on functional status and mortality in old age: results from the Leiden 85-plus Study. *CMAJ* [Internet]. 2009 Aug 4;181(3–4):151–7. Available from:

<http://www.ncbi.nlm.nih.gov/pubmed/19635749>

49. Kikuchi M, Inagaki T, Shinagawa N. Five-year survival of older people with anemia: variation with hemoglobin concentration. *J Am Geriatr Soc* [Internet]. 2001 Sep;49(9):1226–8. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/11559383>
50. Patel K V, Harris TB, Faulhaber M, Angleman SB, Connelly S, Bauer DC, et al. Racial variation in the relationship of anemia with mortality and mobility disability among older adults. *Blood* [Internet]. 2007 Jun 1;109(11):4663–70. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/17284526>
51. Mindell J, Moody A, Ali A, Hirani V. Using longitudinal data from the Health Survey for England to resolve discrepancies in thresholds for haemoglobin in older adults. *Br J Haematol* [Internet]. 2013 Feb;160(3):368–76. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/23151145>
52. Chaves PHM, Xue Q-L, Guralnik JM, Ferrucci L, Volpato S, Fried LP. What constitutes normal hemoglobin concentration in community-dwelling disabled older women? *J Am Geriatr Soc* [Internet]. 2004 Nov;52(11):1811–6. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/15507056>
53. Medical guidelines for determining prognosis in selected non-cancer diseases. The National Hospice Organization. *Hosp J* [Internet]. 1996;11(2):47–63. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/8949013>
54. Fox E, Landrum-McNiff K, Zhong Z, Dawson N V, Wu AW, Lynn J. Evaluation of prognostic criteria for determining hospice eligibility in patients with advanced lung, heart, or liver disease. SUPPORT Investigators. Study to Understand Prognoses and Preferences for Outcomes and Risks of Treatments. *JAMA* [Internet]. 1999 Nov 3;282(17):1638–45. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/10553790>
55. Life I of M (US) C on C at the E of, Marilyn J. Field, Christine K. Cassel E. *Approaching Death: Improving Care at the End of Life*. 1997. 358–62 p.
56. Stevinson C, Preston N, Todd C, Cancer Experiences Collaborative (CECo). Defining priorities in prognostication research: results of a consensus workshop. *Palliat Med* [Internet]. 2010 Jul;24(5):462–8. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/20501513>
57. Conill C, Verger E, Garrigós A. Prognostic accuracy of survival in patients with advanced cancer. *Med Clin (Barc)* [Internet]. 2003 Nov 8;121(16):635. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/14636543>
58. Weeks JC, Cook EF, O'Day SJ, Peterson LM, Wenger N, Reding D, et al. Relationship between cancer patients' predictions of prognosis and their treatment preferences. *JAMA* [Internet]. 1998 Jun 3;279(21):1709–14. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/9624023>
59. Glare P, Virik K, Jones M, Hudson M, Eychmuller S, Simes J, et al. A systematic review of physicians' survival predictions in terminally ill cancer patients. *BMJ* [Internet]. 2003 Jul 26;327(7408):195–8. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/12881260>

Figures

Figure 1

Survival curves as a function of the prognostic index

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