Prognostic assessment in palliative cancer care: is there a difference between adult and older patients?

Avaliação prognóstica em cuidados paliativos oncológicos: Há diferença entre pacientes adultos e idosos?

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ABSTRACT

OBJECTIVE: To compare factors associated with death in adults and older people with advanced cancer who were hospitalized in a palliative care unit (PCU). **METHODS:** Case-control study with patients (adults vs older people) admitted to a PCU of National Cancer Institute José Alencar Gomes da Silva (INCA), in Rio de Janeiro, Brazil. Logistic regressions (odds ratio [OR] and 95% confidence interval [95%CI]) were used to identify factors associated with death. **RESULTS:** The study included 205 patients, most of which were aged over 60 years old (60.5%). Among the adult patients, a Karnofsky Performance Status ≤ 40% (OR 2.54 [95%CI 1.11–3.45]) and neutrophil-to-lymphocyte ratio (NLR) (OR 1.09 [95%CI 1.02–1.24]) were risk factors for death, while albumin (OR 0.30 [95%CI 0.12–0.78]) was a protective factor. Among older patients, NLR (OR: 1.13 [95%CI 1.02–1.24]), C-reactive protein (CRP) (OR 1.09 [95%CI 1.02–1.17]), modified Glasgow Prognostic Score (mGPS) 1 and 2 (OR 4.66 [95%CI 1.35–16.06]), CRP-to-albumin ratio (CAR) (OR 1.27 [95%CI 1.03–1.58]), and nutritional risk (OR 1.11 [95%CI 1.03–1.19]) were risk factors, whereas albumin (OR 0.23 [95%CI 0.09–0.57]) was a protective factor against death. **CONCLUSIONS:** Prognostic factors differed between groups. The NLR was a risk factor, and albumin was a protective factor regarding death in both groups. Additionally, CRP, mGPS, CAR, and nutritional risk were associated with an increased risk of death only among older people.
KEYWORDS: palliative care; prognosis; inflammation; nutritional status.

RESUMO

OBJETIVO: Comparar os fatores associados ao óbito entre adultos e idosos com câncer avançado internados em uma Unidade de Cuidados Paliativos (UCP). **METODOLOGIA:** Estudo de caso-controle com pacientes (adultos versus idosos) internados em uma UCP do Instituto Nacional do Câncer José Alencar Gomes da Silva (INCA), no Rio de Janeiro, Brasil. Regressões logísticas (*Odds Ratio* [OR] e intervalo de confiança de 95% [IC95%]) foram utilizadas para identificar os fatores associados ao óbito. **RESULTADOS:** Participaram 205 pacientes, com predomínio de idosos (60,5%). Entre os adultos, o *Karnofsky Performance Status* ≤ 40% (OR 2,54 [IC95% 1,11 – 3,45]) e a razão neutrófilo-linfócito (RNL) (OR 1,09 [IC95% 1,02 – 1,24]) foram fatores de risco, e a albumina (OR 0,30 [IC95% 0,12 – 0,78]) foi fator de proteção para o óbito. Nos idosos, a RNL (OR 1,13 [IC95% 1,02 – 1,24]), a proteína C-reativa (PCR) (OR 1,09 [IC95% 1,02 – 1,17]), o escore prognóstico de Glasgow modificado (EPGm) 1 e 2 (OR 4,66 [IC95% 1,35 – 16,06]), a razão PCR-albumina (RPA) (OR 1,27 [IC95% 1,03 – 1,58]) e o risco nutricional (OR 1,11 [IC95% 1,03 – 1,19]) foram fatores de risco, e a albumina (OR 0,23 [IC95% 0,09 – 0,57]) foi fator de proteção para o óbito. **CONCLUSÕES:** Os fatores prognósticos diferiram entre os grupos. A funcionalidade e a RNL foram fatores de risco e a albumina foi fator de proteção para o óbito em ambos os grupos. Adicionalmente, somente nos idosos, a PCR, o EPGm, a RPA e o risco nutricional foram associados ao aumento do risco de mortalidade.
PALAVRAS-CHAVE: cuidados paliativos; prognóstico; inflamação; estado nutricional.

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Received on: 05/19/2021. Accepted on: 09/03/2021.

How to cite this article: Sampaio SGSM, Oliveira LC, Rosa KSC. Prognostic assessment in palliative cancer care: is there a difference between adult and older patients? Geriatr Gerontol Aging. 2021;15:e0210044. https://doi.org/10.53886/gga.e0210044
https://doi.org/10.53886/gga.e0210044

INTRODUCTION

The global cancer incidence is estimated to be of 28.4 million cases in 2040, which is 47% higher than that in 2020.[1] In Brazil, for each year between 2020 and 2022, 625 thousand new cases are estimated for this disease.[2] Cancer is responsible for 28.2% of the demand for palliative care, where 44% of patients are aged between 50 and 60 years and 42% are over 70 years old.[3]

Palliative care is defined as an approach that aims for an improvement in the quality of life of patients and their families facing a life-threatening disease via the prevention and alleviation of suffering and the early identification, assessment, and treatment of pain and other physical, psychosocial, and spiritual symptoms.[4] In the context of oncological palliative care, considering patients with usually reduced survival, the precise determination of prognosis becomes imperative for care planning.[5,6]

According to scientific evidence on different types and stages of oncological diseases, prognostic assessment may consider clinical data, the presence of symptoms (such as delirium, dyspnea, anorexia, fatigue, and dysphagia),[7,8] nutritional and functional status, altered laboratory examinations and inflammatory biomarkers (such as hypoalbuminemia, hypercalcemia, hyponatremia, and increased C-reactive protein [CRP],[9-12] neutrophil-to-lymphocyte ratio [NLR], platelet-to-lymphocyte ratio [PLR], and CRP-to-albumin ratio [CAR]),[8,9,13-18] the modified Glasgow Prognostic Score (mGPS),[19] and prognostic models such as the Palliative Prognostic Score (PAP Score)[20] and Palliative Prognostic Index (PPI).[21]

However, different publications regarding this theme have considered the population as a whole, without the intention of separating patients with cancer according to age group and therefore without studying prognostic characteristics that may be specific to the older population, which could result in less accurate prognostic estimations in this group. In face of the physiological alterations inherent to aging, we perceive a knowledge gap regarding whether the use of prognostic tools should be differentiated in the older population. Therefore, the aim of this work is to compare factors associated with death in adults and older patients in oncological palliative care hospitalized at a national referral center.

METHODS

Study design and participants

This is a case-control study nested within a larger prospective cohort study, with data from patients cared for at the Palliative Care Unit (PCU) of National Cancer Institute José Alencar Gomes da Silva (INCA), in Rio de Janeiro, Brazil. Patients were recruited for the larger study in their first ambulatory visit or within 48 hours of their first hospitalization in this unit, between October 2019 and March 2020, and none of them were being actively treated with chemotherapy. The study was approved by INCA's Research Ethics Committee (protocol No. 3 550 658; 2019).

The inclusion criteria were: (i) having histologically or clinically confirmed locally advanced cancer or with distant metastasis; (ii) not receiving any antineoplastic treatments with curative intentions; (iii) being aged ≥ 20 years; (iv) Karnofsky Performance Status (KPS)[22] ≥ 30% at recruitment; (v) agreeing to participate in the research and signing the free and informed consent form. Since this case-control study only considered hospitalized patients, those who were followed-up on an outpatient basis were excluded (exclusion criterium).

Variables

The sample was divided into two groups according to the age retrieved from the electronic medical record: patients aged less than 60 years (adults) vs patients aged 60 years or more (older people).

The sex and clinical data (primary tumor localization, distant metastasis, comorbidity — systemic arterial hypertension [SAH] and diabetes mellitus [DM]) were retrieved from electronic medical records. The KPS (varying from 0% [death] to 100% [complete functional capacity]) was evaluated and recorded by trained researchers according to the patient's functional status at assessment.[22]

Data regarding routine laboratory examinations performed at the PCU were obtained from electronic medical records, including CRP, serum albumin, and some hemogram data. The following indices were calculated: NLR, PLR, and CAR. The mGPS was based on the combination of 2 biomarkers (serum albumin and CRP), being scored as 2 when albumin < 3.5 g/dL and CRP > 10 mg/L; as 1 when albumin ≥ 3.5 g/dL and CRP > 10 mg/L; and as 0 when CRP ≤ 10 mg/L,[15,19,23] as described on Table 1.

Table 1. Modified Glasgow Prognostic Score.

CRP (mg/L)	Albumin (g/dL)	Classification
≤ 10	-	0
> 10	≥ 3.50	1
> 10	< 3.50	2

CRP: C-reactive protein.
Source: McMillan et al.[19]

Nutritional risk was assessed by trained researchers by using the Patient-Generated Subjective Global Assessment (PG-SGA) Short Form, made available by Ottery in pt-global.org.[24] This is a questionnaire comprising 4 domains: 1) body weight history; 2) alterations in food intake; 3) nutrition impact symptoms; and 4) functional status. The sum of scores obtained in all domains resulted in a total numerical score (0–36 points). The higher the score, the higher the nutritional risk.[24-26] Another nutritional risk variable assessed in this study was involuntary weight loss in up to 6 months, which was categorized as ≤ 5% vs > 5%.

The outcome considered in this study was death within 90 days of the beginning of palliative care (yes or no), being retrieved from medical records.

Statistical analysis

Analyses were performed using Stata Data Analysis and Statistical Software v. 13.1 (Stata Corp., College Station, TX, USA). Statistical significance was established with $p < 0.050$.

The Kolmogorov-Smirnov test was used for assessing variable distribution. We used median, interquartile range (IQR; 25th and 75th percentiles), and the Mann-Whitney U test for non-parametric data; mean, standard deviation (SD), and Student's t-test for parametric data; absolute (n) and relative (%) frequencies and the chi-squared or Fisher's exact tests for categorical variables.

Uni and multivariate logistic regressions were used for identifying factors associated with death in both age groups. All variables with p-values > 0.20 in the univariate analysis were selected as candidates for the final model. We employed backward selection for a saturated model, that is, all variables of the same level were included and then eliminated, one by one, from the saturated model when $p \geq 0.05$. Only variables with $p < 0.05$ remained in the final model.

RESULTS

Two hundred and five patients were included in the study, with a median age of 63 (IQR: 54 – 72) years. In the total sample, most individuals were from the older population (60.5%), were female (59.0%), and had mostly gynecological (18.5%) and head and neck (17.1%) primary tumor sites. The death rate was 65.8%, not differing between age groups. The prevalence of SAH was 39.5%, reaching higher values in the older patient group (50.8%; $p < 0.001$) (Table 2).

In general, patients with advanced cancer in palliative care presented altered median values of laboratory parameters. Moreover, older patients had lower median CRP concentrations (6.4 [2.5 – 13.1]; $p = 0.04$) and a higher prevalence of mGPS 0 ($p = 0.04$) when compared to adult patients (Table 3).

In the total sample, the mean PG-SGA Short Form score was 11.4 (0.4) points, and the percentage of patients with weight loss > 5% within 6 months was high (70.1%), characterizing a striking presence of nutritional risk in patients with advanced cancer. However, no difference was observed between age groups (Table 3).

According to the multiple logistic regression model for the adult patient group, a KPS ≤ 40% (odds ratio [OR] 2.54; 95% confidence interval [95%CI] 1.11 – 3.45) and NLR (OR 1.09; 95%CI 1.02 – 1.24]) were risk factors, whereas albumin (OR 0.30; 95%CI 0.12 – 0.78) was a protective factor against death. In the older population, NLR (OR 1.13; 95%CI 1.02 – 1.24), mGPS 1 and 2 (OR 4.66 95%CI 1.35 – 16.06), CAR (OR 1.27; 95%CI 1.03–1.58), and nutritional risk (OR 1.11; 95%CI 1.03 – 1.19) were risk factors for death, while albumin (OR 0.23; 95%CI 0.09 – 0.57) was a protective factor (Table 4).

DISCUSSION

Our results demonstrated that factors associated with death may vary with age. While growing NLR values were associated with an increase in the risk of death, and an increase in albumin concentration was associated with a reduction in this risk in both groups, CRP, mGPS, CAR, and nutritional risk were considered risk factors for death within 90 days only in older patients in oncological palliative care. These results are relevant because they may guide health professionals towards a more accurate prognostic assessment in patients of this age group.

Prognostic markers are valuable instruments in the routine of professionals working in oncological palliative care. In this context, tools that are not subject to biases regarding the professional's subjectivity and that can be used by the whole multi-professional team are being studied and have been shown to be valid, feasible, and extremely helpful when devising a care plan.[5,6]

The studied sample seems to adequately reflect the population normally cared for at PCUs. In a study performed in the same unit in 2016 that assessed all hospitalized patients, the median age and female majority were comparable to our results, and gynecological malignant neoplasms were the most prevalent.[27] The higher functional status verified in the present research can be explained by the inclusion of patients who had only recently been referred to the PCU and were therefore in the initial phase of palliative care.

The prevalence of SAH and distant metastasis was also higher among older people. The presence of SAH in older people reflects the increase in prevalence expected for this age group that has previously been reported in the scientific literature.[28] Although DM was a more common comorbidity among older patients, no statistically significant difference was observed between age groups.

As expected for the population cared for by the PCU, nutritional risk was observed with no statistically significant difference between age groups. Likewise, the rate of death within 90 days was similar in both groups. This observation confirms that age, separately, cannot be considered as an indicator in the prognostic assessment of patients with cancer.[29]

The results found in the present study showed that only CRP and mGPS values presented a statistically significant difference between the studied age groups, both being superior among older people. Since CRP is included in the mGPS classification, a decrease in the former may justify better results in this score. Moreover, worse functional status was associated with a higher risk of death within 90 days only in the group of adult patients. This finding deserves to be further studied in the future, with more robust samples.

Table 2. Demographic and clinical characteristics of patients with advanced cancer in palliative care, according to age (n = 205).

	Total	Age (years)		p-value
		< 60 (n = 81; 39.51%)	≥ 60 (n = 124; 60.49%)	
Sex[a]				
Male	84 (41.00%)	27 (33.33%)	57 (46.00%)	0.07
Female	121 (59.00%)	54 (66.67%)	67 (54.00%)	
Primary tumor site[a]				
Gynecological	38 (18.54%)	19 (23.46%)	19 (15.32%)	0.22
Head and neck	35 (17.07%)	14 (17.28%)	21 (16.94%)	
Breast	31 (15.12%)	16 (19.75%)	15 (12.10%)	
Gastrointestinal tract	28 (13.66%)	11 (13.58%)	17 (13.71%)	
Lung	22 (10.73%)	9 (11.11%)	13 (10.48%)	
Skin, bones, and soft tissues	17 (8.29%)	4 (4.94%)	13 (10.48%)	
Others[b]	34 (16.59%)	8 (9.88%)	26 (20.97%)	
Distant metastasis[b]				
No	40 (19.51%)	10 (12.35%)	30 (24.19%)	< 0.001
Yes	165 (80.49%)	71 (87.65%)	94 (75.81%)	
SAH[a]				
No	124 (60.49%)	63 (77.78%)	61 (49.19%)	< 0.001
Yes	81 (39.51%)	18 (22.22%)	63 (50.81%)	
DM[a]				
No	173 (84.39%)	72 (88.89%)	101 (81.45%)	0.15
Yes	32 (15.61%)	9 (11.11%)	23 (18.55%)	
KPS ≤ 40%[a]				
No	106 (51.71%)	42 (51.85%)	64 (51.61%)	0.97
Yes	99 (48.29%)	39 (48.15%)	60 (48.39%)	
Death within 90 days[a]				
No	70 (34.15%)	28 (34.57%)	42 (33.87%)	0.91
Yes	135 (65.85%)	53 (65.43%)	82 (66.13%)	

N: number of observations; SAH: systemic arterial hypertension; DM: diabetes mellitus; KPS: Karnofsky Performance Status. [a]Number of observations (frequency)/chi-squared or Fisher's exact test; [b]leukemia, lymphoma, myeloma, central nervous system, kidney and urinary tract, male genital organs, peritoneum, mediastinum, and unknown site.

Table 3. Laboratory and nutritional characteristics of patients with advanced cancer in palliative care, according to age (n = 205).

	Total	Age (years)		p-value
		< 60 (n = 81; 39.5%)	≥ 60 (n = 124; 60.5%)	
NLR[a]	6.21 (3.82 – 10.50)	7.5 (4.11 – 12.69)	5.9 (3.72 – 10.34)	0.10
PLR[a]	332.10 (204.81 – 488.39)	374.7 (234.33 – 522.48)	306.0 (195.50 – 444.42)	0.08
CPR (mg/L)[a,c]	7.14 (3.00 – 14.51)	8.6 (5.00 – 17.52)	6.4 (2.54 – 13.12)	0.04
Albumin (g/dL)[a,c]	3.36 (2.82 – 3.70)	3.1 (2.63 – 3.59)	3.4 (2.89 – 3.70)	0.17
CAR[a]	2.00 (0.81 – 5.42)	2.3 (1.21 – 7.00)	1.8 (0.61 – 3.91)	0.08
mGPS[b,c]				
0	90 (63.38%)	31 (53.45%)	59 (70.24%)	0.04
1 and 2	52 (36.62%)	27 (46.55%)	25 (29.76%)	
PG-SGA SF (pts)[d]	11.40 (0.40)	12.20 (0.60)	10.80 (0.60)	0.10
WL in 6 months (%)[b,c]				
≤ 5	35 (29.91%)	12 (24.00%)	23 (34.32%)	0.22
> 5	82 (70.09%)	38 (76.00%)	44 (65.68%)	

n: number of observations; NLR: neutrophil-to-lymphocyte ratio; PLR: platelet-to-lymphocyte ratio; CRP: C-reactive protein; CAR: CRP-to-albumin ratio; mGPS: modified Glasgow Prognostic Score; PG-SGA: Patient-Generated Subjective Global Assessment, Short Form; pts: points; WL: weight loss. [a]Median (interquartile range)/Mann-Whitney's U test; [b]number of observations (frequency)/chi-squared or Fisher's exact test; [c]variables with missing data; [d]mean (standard deviation)/Student's t-test.

Table 4. Logistic regression of factors associated with death within 90 days in patients with advanced cancer in palliative care, according to age (n = 205).

	Age (years)			
	< 60		≥ 60	
	Univariate OR (95%CI)	Multivariate OR (95%CI)	Univariate OR (95%CI)	Multivariate OR (95%CI)
Female sex	0.55 (0.20 – 1.52)	-	0.97 (0.45 – 2.02)	-
Primary tumor site at GIT	0.99 (0.79 – 1.25)	-	0.86 (0.74 – 1.01)	-
Distant metastasis	1.56 (0.79 – 3.06)[a]	-	0.79 (0.50 – 1.23)	-
SAH	1.07 (0.35 – 3.25)	-	1.05 (0.50 – 2.21)	-
DM	1.98 (0.38 – 10.23)	-	0.95 (0.37 – 2.46)	-
KPS ≤ 40%	2.75 (1.05 – 7.20)[b]	2.54 (1.11 – 3.45)[b]	2.56 (1.18 – 5.55)[b]	-
NLR	1.07 (0.99 – 1.17)[a]	1.09 (1.02 – 1.24)[b]	1.13 (1.03 – 1.24)[b]	1.13 (1.02 – 1.24)[b]
PLR	1.00 (0.99 – 1.01)	-	1.00 (0.99 – 1.01)	-
CRP (mg/L)	1.04 (0.99 – 1.10)[a]	-	1.10 (1.02 – 1.18)[b]	1.09 (1.02 – 1.17)[b]
Albumin (g/dL)	0.24 (0.10 – 0.58)[b]	0.30 (0.12 – 0.78)[b]	0.18 (0.07 – 0.42)[c]	0.23 (0.09 – 0.57)[b]
CAR	1.23 (1.03 – 1.48)[b]	-	1.29 (1.02 – 1.63)[b]	1.27 (1.03 – 1.58)[b]
mGPS 1 and 2	2.68 (0.88 – 8.14)[a]	-	4.14 (1.26 – 13.55)[b]	4.66 (1.35 – 16.06)[b]
PG-SGA SF (pts)	1.06 (0.98 – 1.16)[a]	-	1.11 (1.04 – 1.19)[b]	1.11 (1.03 – 1.19)[b]
WL > 5% in 6 months	2.17 (0.58 – 8.13)	-	2.05 (0.71 – 5.91)[a]	-

OR: odds ratio; 95%CI: 95% confidence interval; GIT: gastrointestinal tract; SAH: systemic arterial hypertension; DM: diabetes mellitus; KPS: Karnofsky Performance Status; NLR: neutrophil-to-lymphocyte ratio; PLR: platelet-to-lymphocyte ratio; CRP: C-reactive protein; CAR: CRP-to-albumin ratio; mGPS: modified Glasgow Prognostic Score; PG-SGA SF: Patient-Generated Subjective Global Assessment, Short Form; pts: points; WL: weight loss. [a]$p < 0.200$; [b]$p < 0.05$; [c]$p < 0.001$.

To the best of our knowledge, no studies have yet compared these prognostic factors in different age groups.

The PG-SGA Short Form scores were similar in both groups but were associated with a higher risk of death within 90 days only among older patients. Self-rated health has been defined as a part of the prognostic assessment of older people[30] and may be used as a valid instrument in advanced cancer. For the population in oncological palliative care with no age stratification, the ≥ 19 threshold is associated with death within 90 days,[9] and no studies comparing age groups have been found.

Our multiple logistic regression models revealed that CRP, mGPS, CAR, and nutritional risk were associated with risk of death within 90 days only among older people in oncological palliative care. Although these markers are extensively associated with prognosis in patients with advanced cancer,[8-19] they displayed distinct behaviors between groups. This highlights the need for further development of this type of investigation in order to reveal the most appropriate tools for different groups of patients in palliative care, leading to the optimization of care strategies.

The higher the serum albumin concentration, the lower the risk of death in both groups, with a stronger protective factor in the older people group. Various authors study the correlation between nutritional status deterioration and a worse prognosis.[5,6,8,9,13] When considering hypoalbuminemia as a marker for malnutrition, this finding may contribute to reinforce such a discussion.

We could not retrieve national studies that investigated prognostic factors in adult and older patients. Regarding international studies, we also did not find data regarding older people in palliative care. However, in studies with patients going through a curative treatment approach, similarly to our results, mGPS[31] and CAR[32] were found to be predictive factors for survival. Furthermore, other studies observed NLR to be a prognostic factor in these individuals.[33-36]

Nevertheless, some limitations of this study should be highlighted. As previously described, the reduced sample size and single-centered characteristic of our design may limit our results. The retrieval of some data from medical records may be the source of bias derived from possible inadequate or insufficient information records in the source document. Moreover, no prognostic models such as the PaP Score or PPI were used. In this sense, other studies should be performed, especially regarding the older age group and the inclusion of other instruments.

CONCLUSION

The findings of this study suggest that prognostic factors differ between age groups. Functional status and NLR were risk factors, and albumin was a protective factor regarding death in both groups. Additionally, only among older people, CRP, mGPS, CAR, and nutritional risk were associated with an increase in mortality risk. Therefore, the tools used for prognostic assessment in patients with advanced cancer should be differentiated for a better care planning considering different age groups.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

FUNDING

None.

AUTHORS' CONTRIBUTION

SMSMS: conceptualization, analysis and interpretation of data, preparation, review, supervision. LCO: conceptualization, analysis and interpretation of data, elaboration, review. KSCR: data collection, analysis and interpretation, preparation, review.

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