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ORIGINAL COMMUNICATION

Validation of the scored Patient-Generated Subjective Global Assessment Short Form as a prognostic tool for patients with incurable cancer

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Abstract

Background: The Patient-Generated Subjective Global Assessment Short Form (PG-SGA SF) is a standardized tool for assessing nutrition risk in patients with cancer. The aim of this study was to propose and validate a cutoff point for the PG-SGA SF related to the prognosis of patients with incurable cancer in exclusive palliative care.

Methods: This is a prospective cohort study of patients with incurable cancer at the National Cancer Institute in Brazil. A total sample (n = 2,144) was randomly divided into groups: (1) training (n = 1,072), to determine the most accurate PG-SGA SF cutoff, and (2) validation (n = 1,072), to test the predictive accuracy of this cutoff point. The receiver operating characteristic curve was plotted to determine the best cutoff point of the PG-SGA SF related to death. Concordance statistics (C statistic) were used to test the predictive accuracy of the models. Kaplan-Meier curve and the Cox hazard model were used to verify a prognostic value of the cutoff point.

Results: PG-SGA SF score ≥15 was found to be the best cutoff based on 90-day mortality with good accuracy discrimination (C statistic ≥ 0.74). Patients whose PG-SGA SF score was ≥15 had a shorter survival of 32 (interquartile range [IQR], 12–75) vs 83 days (IQR, 31–90) (p-value < .001) and higher risk of death (hazard ratio: 2.20; 95% CI, 1.64–2.95).

Conclusions: The proposed PG-SGA SF cutoff score is valid and, alongside its usefulness in nutrition triage, could provide prognostic value for patients with incurable cancer.

KEYWORDS
malnutrition, nutrition assessment, palliative care, Patient-Generated Subjective Global Assessment, prognostic, validation studies

CLINICAL RELEVANCY STATEMENT

Patients with incurable cancer in palliative care are often undernourished and have reduced survival expectancy. As nutritional status in usually evaluated in these patients, tools commonly used for this purpose could also have prognostic value, broadening their applicability. The Patient-Generated Subjective Global Assessment is a validated tool for patients with cancer, and alongside its usefulness in screening for nutrition risk, it proved useful to evaluete the prognosis, guiding interventions better suited to each patient.

INTRODUCTION

Management of care for patients with incurable cancer requires accurate prognostic information.[1] Prognostic factors are central to establishing a supportive care plan, guiding decisions about treatment options and priorities to be offered, timing the referral to palliative care, and planning for death.[2] Oncology patients are at risk of malnutrition throughout the course of the disease and its treatment. Nutrition status impairment increases with the progress of the disease and is considered one of the main factors in poor prognoses, resulting in reduced overall survival (OS) and poorer quality of life.[3–5]

Nutrition status in cancer patients is frequently evaluated by the Patient-Generated Subjective Global Assessment (PG-SGA), a subjective method validated for this population, which aims to provide a standardized approach for nutrition assessment.[6,7] The short-form version (PG-SGA SF) consists of a four-part questionnaire based on patient-reported history of weight change, food intake, nutrition impact symptoms, and performance status.[7] As 80%–90% of the score results from the first four parts, the short version demonstrates high sensitivity and specificity when compared with the full-length assessment.[8,9]

The PG-SGA SF provides a continuous-range scoring system that can detect nutrition risk and help prioritize patients who need urgent interventions, besides monitoring changes in nutrition risk.[10] Because it is easy to use and can be completed in a few minutes, its use is suggested in clinical practice in palliative care settings.[7,11] PG-SGA SF is recommended by the Brazilian Consensus of Oncologic Nutrition as the standard for the nutrition screening of palliative cancer patients.[12]

A higher PG-SGA SF score indicates an increased risk of deterioration in nutrition status, and according to this tool, the cutoff point of ≥9 indicates a critical need for nutrition intervention and/or symptom management.[7] This cutoff is significantly associated with adverse outcomes in patients with cancer.[7,13] However, one of the limitations of using this cutoff point is that most patients with incurable cancer present high nutrition risk and a poor probality of survival; therefore, although a score of ≥9 indicates nutrition risk, in a palliative care setting this cutoff does not necessarily indicate the viability of specialized nutritional intervetions such as nutrition support, because it does not discriminate, among these patients, those with longer survival—that is, who would probably have time to benefit from this type of support.

Thus, given the fact that survival time is usually lower in patients with incurable cancer, awareness of these nutrition resources requires more promotion. It is necessary to use tools with adequate predictive discrimination. Therefore, the refinement of existing assessment tools, such as the PG-SGA SF, in search of their best prognostic power enables a better standardization of criteria for care. With a view toward getting the best clinical utility out of the PG-SGA SF tool for patients with incurable cancer, our objective was to propose and validate a cutoff point for the score that related to prognosis in these patients upon referral to palliative care.

METHODS

Patients and data collection

This is a data analysis from a prospective cohort study carried out in patients with incurable cancer referred to the Palliative Care Unit (PCU) of the José Alencar Gomes da Silva National Cancer Institute (INCA) in Rio de Janeiro, Brazil. The INCA Ethics Committee approved the study (protocol number 1.407.458, 2016), and written informed consent was obtained from all the participants. The study population has been described in more detail elsewhere.[5,14–17]

Eligible inpatients (hospitalized) and outpatients (ambulatory) were evaluated on their first visit to the PCU by trained researchers between July 2016 and March 2020 and followed for mortality events after inclusion. The researchers were trained on the application and interpretation of the PG-SGA SF under the supervision of the research coordinators, and whenever a new researcher joined the research group, new training was carried out. Inclusion criteria were having incurable cancer (locoregional advanced or metastatic cancer proven by histological, cytological, or radiological evidence); not receiving any antineoplastic treatment with curative intent; being ≥20 years old; having a Karnofsky Performance Status (KPS) ≥30% (ranges from 0 [death] to 100 [full function]) at the moment of recruitment, assigned according to patient-reported physical function; and having the ability to answer the necessary information. Patients with KPS of 10%–20% were not evaluated due to the aproaching of the end of life and inability to apply the PG-SGA-SF. The patients had generalized malignant disease or advanced local tumor growth and were not receiving any antineoplastic treatment with curative intent. Clinical characteristics such as type of tumor, cancer stage, and date of death were collected from the patients' electronic medical records.

PG-SGA SF

The validated Brazilian Portuguese version of the PG-SGA (FD Ottery, 2005, 2006, 2015), available at pt-global.org, was completed with the assistance of trained researchers, and only the first four parts of the questionnaire were applied. PG-SGA SF consists of these first four parts (boxes 1–4) of the questionnaire, which are based on patient-reported weight, food intake, symptoms, and function. Scores are attributed per box, with the total score ranging from 0 (no problems) to 36 (worst problems): (1) change in body weight, score from 0 to 5; (2) food intake, score from 0 to 4; (3) presence of nutrition impact symptoms, score from 0 to 24; and (4) performance status, score from 0 to 3. The total score is the sum of the scores from the patient-generated component; the higher the score, the higher the nutrition risk.[8]

Although the weight worksheet gives the option of reporting weight loss in 1 month or 6 months before inclusion in the study, 1-month weight loss was used whenever possible. Food intake in the last month was reported using the descriptors "unchanged" compared with normal intake, "less than usual and more than usual," "little solid

food," "only liquids/nutritional supplements," "very little of anything," and "only tube feedings or only nutrition by vein." Nutrition impact symptoms in the last 2 weeks were described as present or absent. Activities and function data in the last month were reported as "normal with no limitations"; "not my normal self, but able to be up and about with fairly normal activities"; "not feeling up to most things, but in bed or chair less than half the day"; "able to do little activity, and spend most of the day in bed or chair"; and "pretty much bedridden, rarely get out of bed."

Anthropometry

To complete the first PG-SGA SF box, with the intent of avoiding memory biases about current weight and height, body weight (kg) was obtained with a calibrated portable Wiso W905 digital scale (with 180-kg capacity; São José, Santa Catarina, Brazil). For those patients who were unable to stand, an in-bed scale system was used (GoBed II Stryker; Athens, Michigan, USA). Height (m) was measured using a tape stadiometer on the wall. When the patient was unable to stand, knee height was used, measured with the knee and ankle joints flexed at 90°, using a measuring tape or an anthropometer. Estimated height was calculated using the equations proposed by Chumlea et al.[18]

Overall survival

The date of death was obtained from electronic medical records. Patient OS (days) was defined as the time interval between date of recruitment to the PCU and the date of death from any cause.

Statistical analysis

Statistical analysis was conducted using the software Stata, version 13.1 (Stata Corp, College Station, TX, USA). Statistical significance was set at $p < .05$.

After the data were collected, the cohort (n = 2,144) was randomly divided into two equal groups for two purposes: (1) training (n = 1,072), when the data were used to determine the most accurate cutoff point of the PG-SGA SF score to predict mortality, and (2) validation (n = 1,072), when the data were used to test the predictive accuracy of this cutoff point in relation to prognosis. Only six patients were excluded (because they had incomplete PG-SGA SF data) (Figure 1)

The Kolmogorov-Smirnov test was used to assess distribution symmetry. The descriptive statistics characterizing the patient groups were presented in percentages (count/frequency, %) for the categorical variables and as means ± SD or medians with interquartile ranges (IQRs, 25th–75th percentile) for continuous variables. Comparisons between the training and validation groups were evaluated using the chi-squared test for categorical variables, independent-samples *t*-test for normally distributed continuous variables, and the Mann-Whitney *U* test for nonnormally distributed variables.

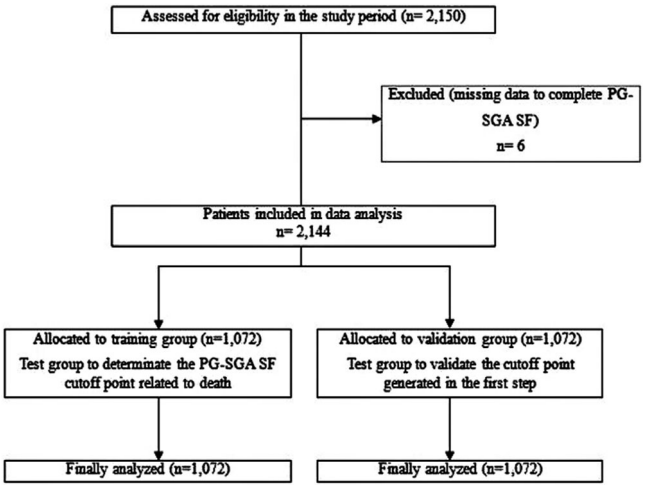

FIGURE 1 Flow diagram. KPS, Karnofsky Performance Status; n, number of observations; PG-SGA SF, Patient-Generated Subjective Global Assessment Short Form

Receiver operating characteristic (ROC) analysis was performed to compare the area under the curve (AUC) for the PG-SGA SF score in predicting 30-day, 90-day, and 180-day mortality. Statistical significance was set at AUC ≥0.70,[19] and sensitivity and specificity of the best cutoff point for the PG-SGA SF score were analyzed. Specificity is the ability of a tool to correctly identify true negatives. Because we wanted to identify patients with a better prognosis—that is, ones with >90 days' survival—a cutoff point with higher sensitivity and specificity was selected, prioritizing a higher degree of specificity. When false-positive results can lead to patients not being given potentially beneficial treatment, tests with higher specificity are required. We also tested the standardized cutoff point (≥9) to compare both groups.

In addition, a concordance statistic (C statistic) was used to evaluate the discrimination of the PG-SGA SF score cutoff point to predict prognosis in the training and validation groups. The C statistic reflects the probability of an event (ie, death) occurring more in a participant in the event group than in a participant from the non–event group.[20] A C statistic of 0.50 indicates that the model predicts the outcome as well as chance (ie, equal numbers of true and false positives); 0.70–<0.80 indicates good discrimination; 0.80–<0.90 indicates excellent discrimination; 0.90–<1.00 is outstanding discrimination; and 1.00 is perfect prediction.[21]

Finally, we validated the capacity of the cutoff point of the PG-SGA SF score to predict OS. Kaplan-Meier curve was used to evaluate OS probability, and the log-rank test was used to compare survival curves according to PG-SGA SF score. Additionally, the Cox proportional hazard model was used to assess whether the predictive ability of the cutoff point proposed for the PG-SGA SF was able to predict death. The stepwise selection method was used, in which variables with $p < .05$ in the univariate regressions were included in the final model.

To verify our sampling power, we calculated a post hoc test using an online tool (https://clincalc.com/Stats/Power.aspx) and considered dichotomous results for two independent groups, with an alpha error

TABLE 1 Patient characteristics according to training and validation groups

Variables	Group			*p*-value
	Overall, n = 2,144	Training, n = 1,072	Validation, n = 1,072	
Age,[a] years	61.9 (13.6)	61.7 (13.4)	62.1 (13.9)	.465
Gender[a]				
Male	888 (41.4%)	443 (41.3%)	445 (41.5%)	.895
Female	1256 (58.6%)	629 (58.7%)	627 (58.5%)	
Tumor type[b]				
Digestive system	625 (29.2%)	310 (28.9%)	315 (29.4%)	.148
Gynecological	382 (17.8%)	186 (17.3%)	196 (18.3%)	
Head and neck	294 (13.7%)	149 (13.9%)	145 (13.5%)	
Breast	245 (11.4%)	140 (13.1%)	105 (9.8%)	
Lung	217 (10.1%)	103 (9.6%)	114 (10.6%)	
Others	381 (17.8%)	184 (17.2%)	197 (18.4%)	
Cancer stage[b]				
Locally advanced	303 (14.1%)	150 (14.0%)	153 (14.3%)	.853
Metastatic	1841 (85.9%)	922 (86.0%)	919 (85.7%)	
Current medical situation[b]				
Inpatient	551 (25.7%)	287 (26.8%)	264 (24.6%)	.277
Outpatient	1593 (74.3%)	785 (73.2%)	808 (75.4%)	
KPS,[b] %				
30–40	887 (41.4%)	455 (42.4%)	432 (40.3%)	.460
50–60	957 (44.6%)	475 (44.3%)	482 (45.0%)	
≥70	300 (14.0%)	142 (13.3%)	158 (14.7%)	
PG-SGA SF,[a] score	14.4 (6.7)	14.5 (6.7)	14.2 (6.8)	.317
Survival,[c] days	51 (19–90)	53 (20–90)	50 (18–90)	.257

Abbreviations: KPS, Karnofsky Performance Status; PG-SGA SF, Patient-Generated Subjective Global Assessment Short Form.
[a]Mean/SD/Student *t*-test.
[b]Number of observations/frequency/chi-squared.
[c]Median/interquartile range/Mann-Whitney *U* test.

of .05. A sample power of 100% for the cutoff point of the PG-SGA SF score was found to predict OS in 90 days.

RESULTS

The mean age was 61.9 years (±13.6), and 58.6% (n = 1,256) of the sample were female . The most common cancer types were tumors of the digestive system (29.2%, n = 625) and gynecological tumors (17.8%, n = 382). Overall, 85.9% (n =1,841) presented metastatic cancer, and 86.0% (n = 1,844) of the sample had KPS ≤60%; median OS was 51 (IQR, 19–90) days. There were no statistical differences between the characteristics of the patients from the two groups (training and validation) (Table 1).

The AUCs for the PG-SGA SF score in predicting 30-day, 90-day, and 180-day mortality for the training group were, respectively, 0.671, 0.705, and 0.666 (data not shown). Figure 2 shows the PG-SGA SF score ≥15, which was the best cutoff value to predict 90-day mortality, as the end point of the ROC curve (with specificity >70% and sensitivity ~60%). The standardized cutoff point of ≥9 presented high sensitivity; however, it had poor specificity. The C statistic demonstrated good predictive accuracy when the cutoff point was ≥15 (0.74–0.75), and this cutoff was more accurate than a score of ≥9 (0.59–0.62) for predicting death (Table 2).

The Kaplan-Meier curves showed that the probability of survival was three times higher in the patients with PG-SGA SF score <15 than it was in the other patients (83 [IQR, 31–90] vs 32 [IQR, 12–75] days; *P*-value < .001). In addition, multivariate Cox regression demonstrated a significantly increased risk of 90-day mortality when the cutoff was ≥15 points (hazard ratio: 2.20; 95% CI, 1.64–2.95) (Table 3).

DISCUSSION

This was the first study to determine the validity of a specific PG-SGA SF cutoff point to assess nutrition risk with prognostic value in patients with incurable cancer. Our results demonstrated that ≥15 was the optimal cutoff point for the total score to predict 90-day mortality,

TABLE 2 Predictive accuracy of 90-day mortality according to the cutoff points of the Patient-Generated Subjective Global Assessment Short Form (PG-SGA SF) score in training and validation groups

	Group			
	Training		Validation	
	≥9 (n = 845; 78.8%)	≥15 (n = 526; 49.1%)	≥9 (n = 837; 78.1%)	≥15 (n = 517; 48.2%)
Sensitivity	85.4%	60.0%	86.8%	60.2%
Specificity	34.3%	71.3%	38.1%	70.1%
LR+	1.30	2.07	1.40	1.95
LR−	0.42	0.57	0.34	0.60
C statistic (CI 95%)	0.59 (0.51–0.73)	0.74 (0.70–0.82)	0.62 (0.52–0.73)	0.75 (0.67–0.80)

Abbreviations: CI, confidence interval; LR, likelihood ratio; n, number of observations.

TABLE 3 Cox proportional regression by Patient-Generated Subjective Global Assessment Short Form (PG-SGA SF) score in validation group

Variables	Univariate		Multivariate	
	HR (95% CI)	*p*-value	HR (95% CI)	*p*-value
PG-SGA SF (score) ≥15	1.80 (1.55–2.09)	<.001	2.20 (1.64–2.95)	<.001
Adjusting factors				
Age, years	0.99 (0.98–0.99)	<.001	0.99 (0.98–0.99)	.002
KPS, %	0.96 (0.96–0.97)	<.001	0.97 (0.96–0.98)	<.001
Primary tumor site (GI)	1.32 (1.12–1.72)	<.001	1.44 (1.10–1.88)	.007
Current healthcare setting (inpatient)	2.44 (2.07–2.87)	<.001	1.51 (1.24–1.84)	<.001

Abbreviations: HR, hazard ratio; CI, confidence interval; GI, gastrointestinal; HR, hazard ratio; KPS, Karnofsky Performance Status; PG-SGA SF, Patient-Generated Subjective Global Assessment Short Form.

demonstrating good accuracy in discrimination (C statistic ≥ 0.74). Its high prognostic predictive ability makes it potentially valuable in planning the nutrition care of patients referred to palliative care services.

Patients with incurable cancer commonly experience malnutrition with progressive weight loss, anorexia, and symptoms of nutrition impact, which impose additional challenges for nutrition planning.[22] Despite the recommendations that standardized and validated nutrition assessment protocols should be used for patients with cancer, nutrition status is often not systematically evaluated in palliative settings.[23] In patients with advanced cancer, it is important for the nutrition screening tools used in clinical practice to be related to prognosis, enabling a better standardization of risk groups and thus more-targeted decision making about nutrition interventions. The results of this study can help to implement screening protocols for this specific cancer population.

The findings of this study indicate that patients who have incurable cancer and are receiving palliative care are at high nutrition risk, which is consistent with previous studies that have demonstrated that the majority of patients in palliative settings have high PG-SGA scores.[11,24,25] The use of PG-SGA in these patients is highly recommended, indicating the point that symptom control and nutrition intervention should begin, as well as monitoring of intervention success, using the same tool over time.[7] Although several studies have shown the relationship between high PG-SGA scores and shortened OS,[3,26–29] no study has yet validated a clinically accurate cutoff point for patients with incurable cancer. We have proposed a score that could be useful for these patients, whose nutrition risk is known to be higher than that of patients with early-stage cancer.[24,30] For this reason, the proposed cutoff point to assess nutrition risk with prognostic value are limited to advanced-stage cancer patients with a probability of survival of a few months.

Our results show that a score of ≥15 was optimal for predicting 90-day mortality. Moreover, patients with this score were 2.2 times more likely to die within 90 days. As expected, a higher score was found to be appropriate for its use as a prognostic factor in patients in palliative care. When compared with the usual cutoff score of ≥9, this study demonstrated better predictive accuracy and calibration between the training and validation groups for a score of ≥15. In other words, we showed that our proposed cutoff is more accurate and could be more useful to improve decision making for patients with incurable cancer.

Several methods can be used to assess the accuracy of tools, including AUC and C statistic. In this study, the better AUC for the PG-SGA SF score in predicting 90-day mortality was 0.701 and therefore statistically significant.[19] A previous study evaluated the accuracy of other prognostic tools validated for patients with cancer in palliative care (Palliative Prognostic [PAP] Score, Objective Prognostic Score, and Palliative Prognostic Index [PPI]) in predicting 30-day OS in 334 patients with terminal cancer, demonstrating AUCs of 0.82, 0.70, and

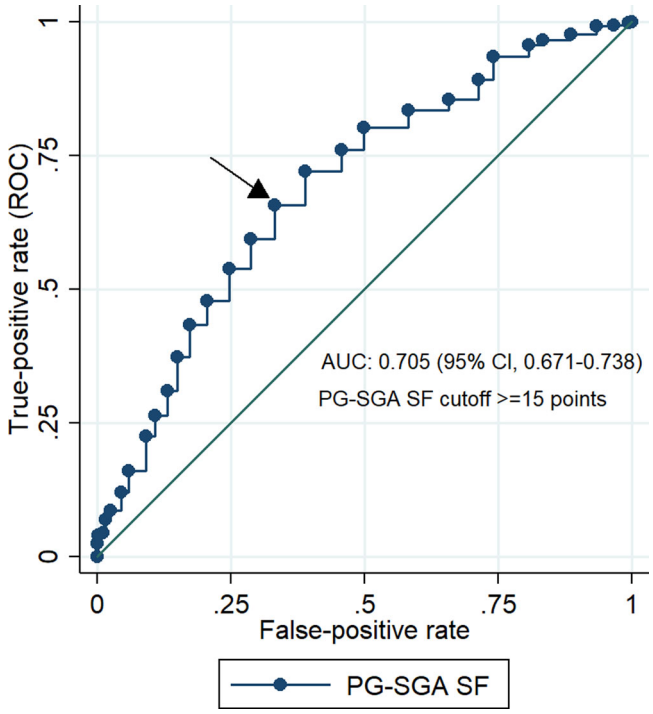

FIGURE 2 Receiver operating characteristic (ROC) curve of the scored Patient-Generated Subjective Global Assessment Short Form (PG-SGA SF) as a predictor of 90-day mortality according to training group. AUC, area under the curve; CI, confidence interval

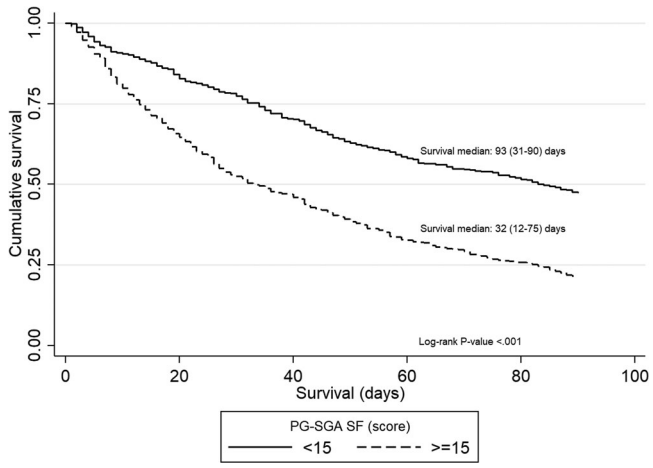

FIGURE 3 Kaplan-Meier survival curves in 90 days stratified by scored Patient-Generated Subjective Global Assessment Short Form (PG-SGA SF) in the validation group

0.72, respectively.[31] The PG-SGA SF's good accuracy in discriminating is also worth mentioning (C statistic ≥ 0.74). Studies that assessed the accuracy of prognostic tools by this method demonstrated that the PAP Score presented a C statistic ≥0.79 and PPI ≥0.75.[32] Thus, the PG-SGA SF has demonstrated an accuracy similar to that of prognostic tools that are widely validated and used in clinical practice.

The goal of nutrition care must be consistent with the stage of the disease and the patient's prognosis. It is important to reliably identify patients who are malnourished or at nutrition risk as the first step toward providing appropriate nutrition support, with the objective of improving modifiable nutrition risk factors and maintaining or delaying the compromise of the nutrition status.[33] The invasiveness of an intervention needs to be chosen and tailored, weighing the benefits and risks for each individual patient. This is of increasing importance with advancing disease and when approaching the end of life.[34] In this sense, the PG-SGA would help to screen patients to plan not only nutrition care but also the general care to be offered. In patients with an estimated survival longer than 90 days, the focus of care may include specialized interventions and potentially nutrition therapy, whereas the focus of care for patients with shorter survival is the relief of symptoms and suffering.

In this sense, a cutoff point <15 indicates to the health professional that although the patient is currently malnourished, the prognosis is better. By the same token, a cutoff point ≥15 would indicate not only poor nutrition status but also a limited prognosis. In this case, patients should be monitored closely and receive dietary counseling to provide comfort-directed care, mitigate multiple nutrition impact symptoms, and relieve eating-related distress.

This cutoff does not mean that other factors should not be taken into consideration in planning nutrition support, as recommended in situations of expected survival of longer than 3 months, but merely that it could a be helpful objective guide for making such decisions. Ruggeri et al,[35] in a cohort study with 43,474 patients receiving palliative oncology care in Italy, found that those who started specialized nutrition support with KPS ≥40%, prognosis >6 weeks, and precachexia or cachexia had improved KPS and longer survival during the follow-up period. As discussed by Cotogni et al,[36] even when the disease can no longer be cured, some patients (especially those with longer survival) can benefit from specialized nutrition support if it is well indicated.

Another important aspect is the fact that most of the prognostic tools validated in palliative care vary in their complexity and subjectivity and need to be evaluated by a physician.[2,32] When it comes to patients with incurable cancer, however, interdisciplinary care must be given. In such circumstances, PG-SGA offers a simple nutrition assessment method that can be administered by any trained health professional.[7] Its advantages are that it is a multidimensional screening tool that provides a nutrition risk assessment that has been used in several clinical settings to assess important prognostic factors in patients with advanced cancer,[30] facilitating proactive screening, assessment, monitoring, and interdisciplinary intervention triage.[7] In addition, it should be noted that the PG-SGA SF provides an opportunity for the entire multidisciplinary team to identify earlier the need to optimize symptom control, by screening for the presence of constipation, vomiting, dysphagia, and pain, among others, in the past 2 weeks.

Our findings confirm that PG-SGA SF can be used for both nutrition screening and prognostic evaluation. It could help inform decisions about what approach will best meet the patients' needs. Our study suggests that the majority of patients with incurable cancer who first enter palliative care would benefit from nutrition care for symptom management and nutrition counseling and should be screened and referred

to a nutrition team for further evaluation to enable specialized intervention and nutrition support. An important element in cancer care is adjusting treatment as the patient's status changes over time, part of which involves identifying the degree of malnutrition, so that adequate nutrition intervention strategies can be devised to improve patient outcomes.

The challenge is to implement the right tool at the right stage in the cancer patient's journey. Finding the right tool is still an open question and one that is likely to require a combination of mixed methodologies. Other easy-to-use prognostic tools, such as the modified Glasgow Prognostic Score,[26] could be used in conjunction with this and other approaches.

The generalizability of our results might be limited in this study. The patients were treated at the same specialized tertiary center and might not be representative of patients with incurable cancer elsewhere, but the sample size is the main strength of the study. The suggested cutoff point must undergo external validation to be extrapolated to populations other than the one studied. Future investigations are needed to assess whether the proposed total PG-SGA SF score is capable of predicting which patients are at risk for adverse clinical outcomes, including lower quality of life, and how well it serves to monitor nutrition interventions, especially for patients with incurable cancer.

CONCLUSION

Our findings suggest that a PG-SGA SF score ≥15 is an accurate tool that is easily applied in clinical practice. The proposed cutoff score is valid, and alongside its usefulness in screening for nutrition risk, it has the added advantage of providing prognostic value for patients with incurable cancer in palliative care. Our results suggest that patients below this cutoff point will probably present reduced impairment of nutrition status and a better prognosis, indicating the best group to target for specialized nutrition assistance, whereas patients with worse prognosis could benefit mostly from symptom palliation to promote quality of life and death.

CONFLICT OF INTEREST

None declared.

FUNDING INFORMATION

None declared.

AUTHOR CONTRIBUTIONS

Emanuelly Varea Maria Wiegert, LarissaCalixto Lima, and Livia Costa de Oliveira contributed to conception and design; Marcela Souza Cunha, Emanuelly Varea Maria Wiegert, Larissa Calixto Lima, and Livia Costa de Oliveira contributed to acquisition, analysis, and interpretation of data; Marcela Souza Cunha, Emanuelly Varea Maria Wiegert, Larissa Calixto Lima, and Livia Costa de Oliveira drafted and critically revised the manuscript. All authors critically revised the manuscript, agree to be fully accountable for ensuring the integrity and accuracy of the work, and read and approved the final manuscript.

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