Original Article

Survival of Women With Cancer in Palliative Care: Use of the Palliative Prognostic Score in a Population of Brazilian Women

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Abstract
The objective of this study was to estimate the survival time of patients referred to the palliative care unit of the National Cancer Institute of Brazil (INCA), using the Palliative Prognostic (PaP) score, and thereby evaluate this tool in a location and population different from that in which the instrument was originally developed. In this prospective study, the instrument, after translation and adaptation to Brazilian Portuguese, was applied to 250 women consecutively referred to the palliative care unit of INCA, who had been followed up as outpatients between June 2005 and August 2006. The PaP score subdivided a heterogeneous population into three homogeneous risk groups with respect to survival time, and the differences between groups were statistically significant. The median overall survival time, calculated using the Kaplan-Meier method, for the three groups was 142 days (95% confidence interval [CI]: 118—172) for Group A, 39 days (95% CI: 28—52) for Group B, and nine days (95% CI: 1—24) for Group C. The percentage survival at 30 days for the three groups was 91.4%, 57.1%, and 0%, respectively. The longer survival time found in the first group in this study would appear to reflect the referral of patients in better clinical condition for outpatient follow-up in this institute. These data suggest that the PaP score is a consistent and easily applied instrument that allows more accurate prognostication in advanced cancer patients with no possibility of cure, irrespective of the geographical location. J Pain Symptom Manage 2010;39:69—75.

Key Words
Palliative care, neoplasia, terminal patient, prognosis, survival time

Introduction

The importance of prognosis of patients with advanced cancer and other fatal diseases has been widely recognized. Meticulous prediction of the survival time of patients in the terminal stage of cancer is difficult but

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important.[1] Accuracy in the prediction of survival is necessary for clinical, ethical, and organizational reasons, particularly in planning care strategies and avoiding futile therapies and harming of vulnerable patients.[2,3]

In the past, prognostication received sparse attention in palliative medicine. Much effort was expended on the need to take the natural history of the disease into account and to predict the future consequences of a therapeutic act or omission.[4] Nevertheless, with the progress made in palliative medicine, including studies into the specialized care of patients with incurable diseases, some aspects of prognostication were identified while training professionals in this specialty.[5,6] Because of the particular characteristics of terminally ill patients and the difficulty in defining homogeneous groups, prognosis cannot be based on the criteria normally used for oncological patients in the initial stages of the disease. The histology and initial localization of the tumor do not appear to have predictive values in terms of the survival of these patients, making their prognosis one of the most difficult tasks in oncology and in palliative care.[3,7,8]

It also should be remembered that the physicians who care directly for these patients are frequently imprecise in their estimates of prognosis, which may be affected by an extensive doctor-patient relationship and by the physician's level of professional experience.[9–14] With the objective of improving prognostic estimates, some investigators have worked toward identifying particular variables related to prognostication. A potential was found in the combination of some simple clinical and laboratory parameters that are easily evaluated and measured in patients with terminal cancer.[3,15–18]

With the objective of improving prognostic accuracy in these patients, many studies were developed to determine the association between prognostic factors and survival;[1,14,19–22] however, few tested the predictive accuracy of their final models, a key step in the construction of a prognostic model. Maltoni et al.[23] were the first to publish details of a prognostic scoring system called the Palliative Prognostic (PaP) score. This prognostic tool classifies heterogeneous terminally ill patients with advanced cancer into homogeneous risk groups with respect to survival, based on a combination of clinical and laboratory parameters. This instrument was developed in a population of 519 patients in a palliative care program and validated in an independent sample of 451 patients using six prognostic factors that included both clinical and laboratory components. A score was given for each one of the factors, which, when added together, classify the patients into one of three homogeneous risk groups.

This method was subsequently validated in 14 Italian palliative care centers and in other countries, such as Australia, illustrating its usefulness in clinical practice, where it is helpful in defining appropriate therapeutic planning and optimizing use of available resources.[3,7,22] The authors recommended that studies should be carried out to evaluate the PaP score in other cultures and countries. To the best of our knowledge, no such evaluation has yet been carried out in Brazil on the PaP score or on any other method developed for prognostication in adult patients with advanced terminal cancer. Therefore, the objective of this study was to apply the PaP score to a population of Brazilians and to estimate the survival of patients referred to the palliative care unit of the National Cancer Institute of Brazil (INCA).

Methods

This prospective study was conducted in the palliative care unit of the INCA between June 2005 and August 2006. The palliative care unit of INCA, located in the city of Rio de Janeiro, Brazil, provides follow-up care for a monthly average of 1,100 patients with advanced cancer no longer responsive to curative treatment. The mean survival time is 2.8 months. In accordance with their clinical conditions, the patients are initially enrolled for outpatient follow-up (44%) or directly for home care (39%) or hospitalization (17%) when performance status is more severely impaired. Historically, the unit enrolls an average of 60 women with advanced cancer and no possibility of cure per month, and of these, a mean of 26 women are enrolled for outpatient follow-up.[24]

For the present study, 250 women older than 18 years were enrolled and referred to the palliative care unit. All had a solid malignant tumor no longer responsive to primary

treatment. The presence of hematological or renal neoplasias or multiple myeloma constituted the exclusion criteria because of the possible effect of these conditions on some laboratory parameters. Comorbidities, such as chronic obstructive pulmonary disease, cardiopathies, and infections, which were unable to be treated or controlled, constituted additional exclusion criteria. At admission to the study, personal data (age, race, and education level) were collected in addition to data regarding topographical and histopathological diagnoses; current status of the disease; clinical assessment of the terminal phase, including clinical prediction of survival (CPS), Karnofsky Performance Status (KPS), and evaluation of the presence of symptoms (dyspnea and anorexia); and data on laboratory parameters (leukocyte count and percentage of lymphocytes), comprising the PaP score prognostic instrument.

The PaP score was determined for each individual patient at her first contact with the palliative care specialist during admission, after signing the informed consent form. As noted, this instrument consists of four clinical and two laboratory parameters that may be evaluated during the first outpatient consultation: 1) presence or absence of dyspnea, 2) presence or absence of anorexia, 3) KPS, 4) CPS, 5) total white blood cell count, and 6) percentage of lymphocytes. The presence or absence of the first two parameters was evaluated by asking the patients directly.

Performance status, evaluated according to the Karnofsky Scale as 50% or more, 30%–40%, or 10%–20%, and CPS, which contains five categories dividing survival into periods of less than 12 weeks and one category of survival of more than 12 weeks, were assessed based on the clinical experience of the investigators. The last two parameters were obtained by carrying out a full blood count using standardized laboratory measurements classified in three categories. A leukocyte count of 4,600–10,200 cells/mm^3 was considered normal, whereas leukocytosis with levels higher than 10,200 and lower than 15,000 cells/mm^3 was considered high, and counts of 15,000 cells/mm^3 or more were classified as very high. The percentage of lymphocytes was considered normal when values were between 20% and 40% of total leukocyte count, low for values less than 20% and 12% or more, and very low when values were less than 12%. A partial score is given for each one of the six parameters, which, when added together, provide a final score that classifies the likelihood of each individual patient surviving the next 30 days as high, intermediate, or low (Table 1). All the clinical parameters were recorded by the same investigators, who were experienced physicians in this specialty, and all the laboratory parameters were analyzed in the same laboratory.

Statistical Analysis

Survival time of the patients was evaluated using Kaplan-Meier survival curves. Curves for the three prognostic risk groups were compared using the log-rank test, and significance was defined at 5%. The analyses were performed using the SAS statistical software program, version 9.1.3 (SAS Institute, Inc., Cary, NC).

Table 1
PaP Score and Classification of Patients in Three Risk Groups

Parameters	Partial Scores
Dyspnea	
No	0
Yes	1
Anorexia	
No	0
Yes	1.5
KPS	
≥50	0
30–40	0
10–20	2.5
Clinical prediction of survival (weeks)	
>12	0
11–12	2
7–10	2.5
5–6	4.5
3–4	6
1–2	8.5
Total white blood cells	
Normal (4,600–10,200/mm^3)	0
High (>10,200 and <15,000/mm^3)	0.5
Very high (≥15,000/mm^3)	1.5
Lymphocyte percentage	
Normal (20%–40%)	0
Low (12%–20%)	1
Very low (<12%)	2.5
Risk Groups	**Total Score**
A: 30 days' survival probability >70%	0–5.5
B: 30 days' survival probability of 30–70%	5.6–11.0
C: 30 days' survival probability of <30%	11.1–17.5

Results

Of a total of 330 female patients admitted to INCA's palliative care unit during the study period, 250 (75.7%) were considered eligible for admission to the study. Eighty women were excluded, as they presented with one or more of the exclusion criteria. The sociodemographic characteristics of the patients are shown in Table 2, and the clinical and biological parameters are shown in Table 3. The median age of patients was 55 years (range 21–99 years). The most frequent diseases were gynecological cancer (86; 34.4%), cancer of the head and neck (49; 19.6%), breast cancer (44; 17.6%), gastrointestinal cancer (32; 12.8%), and lung cancer (23; 9.2%). In approximately three-quarters of the patients (74.4%), the disease was locally advanced; visceral metastases were present in 137 patients (54.8%). In 67.1% of cases, KPS was more than 50%. Only four patients (1.6%) were clearly in the "end-of-life care" phase, as characterized by KPS of 20% or lesser. Anorexia was present in 65.2% of cases and dyspnea in 13.2%. According to the criteria defined by the PaP score, hematological parameters were frequently abnormal—around 50% of patients having an abnormal leukocyte count and more than 70% having a low or very low lymphocyte count (Table 3).

Table 2
Principal Sociodemographic Characteristics of 250 Patients

Variables	*n*	%
Median age 55 (range 21–99)	—	—
Race		
White	131	52.4
Mulatto	74	29.6
Black	45	18.0
Years of formal education		
No formal education	32	12.8
1–4 years	181	72.4
5–8 years	28	11.2
>9 years	9	3.6
Primary tumor site		
Gynecological	86	34.4
Cervix	66	
Ovary	13	
Uterus	6	
Vagina	1	
Head and neck	49	19.6
Breast	44	17.6
Gastrointestinal tract	32	12.8
Colorectal	17	
Stomach	12	
Esophagus	3	
Lung	23	9.2
Urinary tract	3	1.2
Liver and biliary tract	4	1.6
Melanoma	3	1.2
Central nervous system	1	0.4
Miscellaneous	5	2.0
Current status of the disease (metastases)		
Locally advanced	186	74.4
Viscera	137	54.8
Lymph nodes	79	31.6
Bone	34	13.6
Central nervous system	21	8.4

At the time of data analysis, 34 patients (13.5%) were still alive. The day on which data analysis was initiated was considered the cutoff date for the survival analysis of the entire study sample. The median survival time of the study group as a whole was 95 days (95% confidence interval [CI] 74–107 days). Figure 1 shows the overall survival curve for the study population. A considerable proportion of cases consisted of patients in good general condition when they were referred for palliative care, as shown by the finding of an estimated probability of surviving 30 days of approximately 78%.

Patients were subsequently classified into three homogeneous groups with respect to survival in accordance with their PaP scores (Table 2): Group A consisted of 162 women (64.8%) with more than 70% likelihood of surviving 30 days, whereas Group B consisted of 84 women (33.6%) in whom the likelihood of surviving 30 days was 30%–70%, and Group C consisted of four patients in whom the probability of surviving 30 days was less than 30%.

Kaplan-Meier survival curves for the three groups of patients are shown in Fig. 2. The three groups show different survival rates (log-rank = 125.25, $P < 0.0001$). The likelihood of

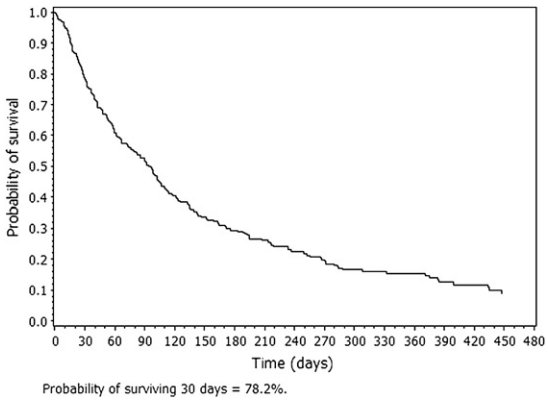

Fig. 1. Overall Kaplan-Meier survival curve.

Table 3
Main Clinical and Biochemical Characteristics of 250 Patients

Variables	*n*	%
Dyspnea		
Yes	33	13.2
No	217	86.8
Anorexia		
Yes	163	65.2
No	87	34.8
KPS (%)		
≥50	199	79.6
30–40	47	18.8
10–20	4	1.6
CPS (weeks)		
>12	60	24.0
11–12	86	34.4
7–10	55	22.0
5–6	10	4.0
3–4	33	13.2
1–2	6	2.4
Leukocyte count		
Normal (4,600–10,200 cells/mm^3)	130	52.0
High (10,201–15,000 cells/mm^3)	69	27.6
Very high (>15,000 cells/mm^3)	51	20.4
Percentage of lymphocytes		
Normal (20%–40%)	66	26.4
Low (12–<20%)	65	26.0
Very low (<12%)	119	47.6
Risk groups		
Group A	162	64.8
Group B	84	33.6
Group C	4	1.6

surviving 30 days in this series, as expected, was more than 70% for Group A (91.4%), 30%–70% for Group B (57.1%), and less than 30% for Group C (0%). The values of the median survival time and the relative 95% CIs for the three groups were 142 days (95% CI 118–172 days) for Group A, 39 days (95% CI 28–52 days) for Group B, and nine days (95% CI 1–24 days) for Group C.

Discussion

The objective of this study was to apply the PaP score, translated into Brazilian Portuguese, to a different population from which the instrument was originally developed. It was found that it was possible to subdivide a heterogeneous population into three homogeneous groups with respect to survival. These results are in agreement with those reported by Maltoni et al.[23] and Glare and Virik,[22] confirming the capacity of this prognostic tool to divide a heterogeneous population into three homogeneous risk groups with different survival characteristics.

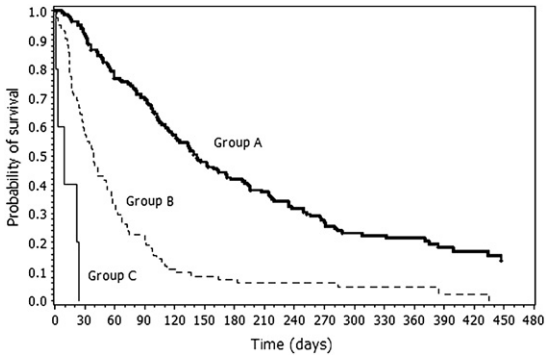

Fig. 2. Kaplan-Meier survival curves for the three groups of patients. Log-rank test = 125.5; $P < 0.0001$. Probability of surviving 30 days: Group A, 91.4%; Group B, 57.1%; and Group C, 0%.

This study evaluated a sample of Brazilian women with a median age of 55 years (range 21–99 years), few years of formal education (one to four years in 72.4%), and a predominant gynecological primary tumor site, characteristic of the female population in developing countries, such as Brazil. In this country, the prevalence of cervical cancer is high, and diagnosis is frequently made at an already advanced stage of the disease.

The median survival for the population as a whole was 95 days, which differs from the findings of other studies, in which they were reported as 32 and 30 days. This divergence reflects the differences in the characteristics of the patients included in the present study. One of the principal differences was the fact that the entire group was composed of patients referred for outpatient follow-up and, therefore, in a better general clinical condition compared with groups evaluated in previous studies. KPS values were higher, and dyspnea was less prevalent; nevertheless, hematological abnormalities were common. Consequently, although the survival times in the homogeneous risk groups B and C in this study were similar to those of the other studies, survival times were greater in the patients in Group A, suggesting that patients in better general condition are referred for outpatient palliative care in this institute.

It should be emphasized that, of the scales available, the PaP score is the instrument that

has been most frequently validated[25,26] and is most widely used. It was specifically identified as such in the European Association for Palliative Care evidence-based clinical recommendations on prognosis and may be considered the instrument of choice for predicting the future progression of the disease and, consequently, for taking decisions relevant to the type of care to be offered,[3] because in this category of patient, there may be no need for sophisticated prognostic tools, easily obtained parameters being sufficient. The PaP score achieves this objective, combining subjective clinical judgment with objective parameters,[23,25,26] thus contributing toward improving overall prognostic ability. One of the clinical parameters of the PaP score is the CPS, which is based on the physician's clinical experience. The CPS is a useful and valid tool that was found to have a definite correlation with prognosis.[3] However, its use alone is subject to factors that limit its accurac,y and it is recommended that it should be used in conjunction with other prognostic factors.[3] Although it is probable that "the prognosis of any individual shall be always either better or worse than the median of a group of patients at the same stage of the same disease,"[27,28] and that the question "How long have I got, doctor?"[29] still has no definite answer, it is undeniable that the individualization of groups of patients with more homogeneous prognoses leads to better-structured therapeutic interventions.[28]

Currently in Brazil, the ability of the physician to calculate the probable survival time of the patient constitutes the usual clinical means of estimating the survival of cancer patients in palliative care. Confirmation in the present study of the prognostic capability of the PaP score in a population of Brazilian women should contribute toward providing more adequate health care for this important group of patients. The agreement in the ability of these different data sets to differentiate groups of patients confirms the applicability of the PaP score in the prognostication of patients with terminal disease, irrespective of the location or characteristics of the population evaluated.

Although life expectancy is only one of many factors that influence clinical decision making, the importance of accurate prognostication in estimating life expectancy should not be underestimated. The systematic use of prognostic scores may assist health professionals in improving their care strategies and help patients and their families make more informed choices. Failure to prognosticate may, in some circumstances, be as harmful as a mistaken diagnosis or therapy, resulting in ethical considerations of fundamental importance. Moreover, in a developing country such as Brazil, where resources are limited, it may be argued that ensuring the appropriate use of resources is imperative, and a simple, reliable, and valid prognostic model, such as the PaP score, may be readily used for patients with cancer in palliative care, thereby contributing toward achieving this purpose.

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