New Symptom-Based Predictive Tool for Survival at Seven and Thirty Days Developed by Palliative Home Care Teams

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Abstract

Aim: This study sought to develop models to predict survival at 7 and 30 days based on symptoms detected by palliative home care teams (PHCTs).

Materials and methods: This prospective analytic study included a 6-month recruitment period with patient monitoring until death or 180 days after recruitment. The inclusion criteria consisted of age greater than 18 years, advanced cancer, and treatment provided by participating PHCTs between April and July 2009. The study variables included death at 7 or 30 days, survival time, age, gender, place of residence, type of tumor and extension, presence of 11 signs and symptoms measured with a 0–3 Likert scale, functional and cognitive status, and use of a subcutaneous butterfly needle. The statistics applied included a descriptive analysis according to the percentage or mean $\pm$ standard deviation. For symptom comparison between surviving and nonsurviving patients, the χ^2 test was used. Classification and regression tree (CART) methodology was used for model development. An internal validation system (cross-validation with 10 partitions) was used to ensure generalization of the models. The area under the receiver operating characteristics (ROC) curve was calculated (with a 95% confidence interval) to assess the validation of the models.

Results: A total of 698 patients were included. The mean age of the patients was 73.7 ± 12 years, and 60.3% were male. The most frequent type of neoplasm was digestive (37.6%). The mean Karnofsky score was 51.8 ± 14 , the patients' cognitive status according to the Pfeiffer test was 2.6 ± 4 errors, and 8.3% of patients required a subcutaneous butterfly needle. Each model provided 8 decision rules with a probability assignment range between 2.2% and 99.1%. The model used to predict the probability of death at 7 days included the presence of anorexia and dysphagia and the level of consciousness, and this model produced areas under the curve (AUCs) of 0.88 (0.86–0.90) and 0.81 (0.79–0.83). The model used to predict the probability of death at 30 days included the presence of asthenia and anorexia and the level of consciousness, and this model produced AUCs of 0.78 (0.77–0.80) and 0.77 (0.75–0.79).

Conclusion: For patients with advanced cancer treated by PHCTs, the use of classification schemes and decision trees based on specific symptoms can help clinicians predict survival at 7 and 30 days.

Introduction

DOCTORS INVOLVED IN CLINICAL CARE, especially those working in palliative care, often face questions related to prognosis. For example, pharmacologic, psychotherapeutic, and interventionist measures can change depending on

whether patient survival is estimated at days, weeks, or months. Thus, proper access to objective prognostic data can reduce anxiety when informing patients and their families.¹

Survival predictions made by health care professionals are imprecise and have been shown to be optimistic.^{2–4} However, many studies have identified clinical and laboratory variables

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that can help better inform survival prognosis for patients with advanced cancer.⁵⁻⁷ Some of these tools include survival estimations made by clinicians,^{8,9} whereas others are associated with laboratory data obtained from blood samples¹⁰⁻¹² or based on the patient's signs and symptoms. A number of models have been developed using competent patients,^{1,13,14} while very few tools focused on disoriented patients have reached large-scale development. In addition, few models have been developed and validated in home care settings.

Until now, the methodology used in palliative care prognostic models has been based on multiple logistic regression. However, the recent development of more powerful mathematical applications such as classification trees can better adapt to the complexity of survival prognosis estimation. These classification tree models have acquired greater importance due to the immediate interpretation of the decision rules they generate and have been readily accepted by professionals in clinical practice. Classification tree programs include variables according to their relative importance and set variable breakpoints to establish the correct endpoint. These models also use a validated learning process for widespread application.¹⁵

The present study sought to develop prognostic models for the probability of death at 7 and 30 days based on symptoms detected by palliative home care teams (PHCTs).

Materials and Methods

This was a prospective analytical study with a 6-month recruitment period. The follow-up period continued until death or 180 days after recruitment.

Population

Patients over 18 years of age with advanced cancer who were treated during an initial visit by participating PHCTs in the regions of Aragon and Catalonia between April 1, 2009 and July 31, 2009 were included in the study. Patient recruitment was consecutive. A visit was considered valid when the state of the patient (survivor or nonsurvivor) could be verified within the time interval used in the design of the models (time from the previous first visit to 7 days or 30 days). Visits that did not fulfill this criterion were disregarded.

Procedure

Each new patient with cancer treated by PHCTs was assessed according to palliative care standards. At each visit, the patient's symptoms (asthenia, anorexia, cachexia, dry mouth, dysphagia, dyspnea, edema, and level of consciousness) were recorded using a 0-3 Likert scale (none, slight, moderate, or severe). Functional and cognitive status assessments were also recorded. Delirium was assessed using the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV)* criteria, and pressure sores were classified using the criteria of Cullum et al.¹⁶ (0-IV). The need for a subcutaneous butterfly needle was considered. The variables and assessment system are shown in Table 1.

TABLE 1. VARIABLES AND ASSESSMENT SYSTEMS

Result variable		Survival at 7 or 30 days after the assessment visit
Independent variable	Survival time	
Dependent variables		Assessment system
Demographic variables	Age	Years
	Gender	Man/Female
	Place of residence	Urban/rural
	Tumor type	ICD 10
	Type of extension	I-IV
Clinical Variables	Asthenia	Likert scale 0-3
	Anorexia	Likert scale 0-3
	Cachexia	Likert scale 0-3
	Dry mouth	Likert scale 0-3
	Dysphagia	Likert scale 0-3
	Dyspnea	Likert scale 0-3
	Edema	Likert scale 0-3
	Level of consciousness	Likert scale 0-3
	Delirium	Yes/No by <i>DSM IV</i> criteria
	Pressure ulcers	Cullum scale 0-4
	Performance status	Karnofsky Index ECOG Index Barthel Index
	Cognitive state	Pfeiffer test
	Comorbidity	Charlson Scale
	Use of subcutaneous butterfly	Yes/No

CIE, ; *DSM IV*, *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*; ECOG, Eastern Cooperative Oncology Group.

TABLE 2. CLINICAL-DEMOGRAPHIC CHARACTERISTICS OF PATIENTS (N=698)

Age (years) ^a	73.7 ± 12
Gender, male (%)	60.3
Urban (%)	69.8
Metastasis (%)	62.5
Neoplasm (%)	
Head and neck	3.2
CNS	25.3
Upper gastrointestinal	17.7
Colon	19.9
Lung	15.6
Genitourinary	6.9
Breast	1.8
Blood	2.3
Others	3.8
Unknown	3.5
Source (%)	
General practice	55.0
Oncology	22.6
Other hospital service	13.3
Palliative care unit	4.6
Number of follow-up visits ^a	7 ± 4
Time in program ^a	65 ± 64
Status (%)	
Death	74.4
Out program	16.9
Survivor	8.7
Karnofsky Performance Score ^a	51.8 ± 14

^aMean ± standard deviation.

CNS, central nervous system.

TABLE 3. PREVALENCE OF SYMPTOMS AT VISITS INCLUDED FOR SEVEN- AND THIRTY-DAY SURVIVAL ASSESSMENT

Symptoms and signs	Prevalence of symptoms in survivors and nonsurvivors at 7-day follow-up (n=2893)			Prevalence of symptoms in survivors and nonsurvivors at 30-day follow-up (n=2720)		
	Survivors ^a (n=2461)	Nonsurvivors ^b (n=432)	p value ^c	Survivors ^a (n=1592)	Nonsurvivors ^b (n=1128)	p value ^c
Anorexia (%)			<0.001			<0.001
0	32.8	4.2		39.4	11.6	
1	32.5	6.9		33.7	21.8	
2	27.0	27.3		23.4	32.1	
3	7.6	61.6		3.5	34.5	
Asthenia (%)			<0.001			<0.001
0	17.1	1.4		21.5	4.5	
1	29.9	3.9		33.9	14.2	
2	35.0	16.7		33.3	31.4	
3	18.0	78.0		11.3	49.5	
Dry mouth (%)			<0.001			<0.001
0	44.7	12.3		51.1	23.2	
1	34.4	20.8		33.7	30.2	
2	17.5	37.0		13.1	30.9	
3	3.5	29.9		2.1	15.6	
Edema (%)			<0.001			<0.001
0	44.7	12.3		71.0	50.3	
1	34.4	20.8		21.2	24.9	
2	17.5	37.0		6.1	19.0	
3	3.5	29.9		1.7	5.9	
Level of consciousness (%)			<0.001			<0.001
0	87.3	35.4		90.7	61.8	
1	9.6	26.2		8.0	18.6	
2	2.4	18.3		1.1	10.5	
3	0.8	20.1		0.3	9.1	
Dyspnea (%)			<0.001			<0.001
0	59.7	35.0		65.2	43.5	
1	18.9	16.4		17.1	20.4	
2	14.4	19.4		13.0	19.3	
3	6.0	20.8		4.1	13.2	
4	1.0	8.3		0.6	3.5	
Dysphagia (%)			<0.001			<0.001
0	75.3	28.9		80.8	50.0	
1	13.5	15.0		11.1	17.8	
2	5.3	14.1		3.7	10.5	
3	4.1	16.2		3.1	10.1	
4	1.9	25.7		1.3	11.6	
Cachexia (%)			<0.001			<0.001
0	51.8	30.8		56.8	36.6	
1	27.4	23.4		27.7	26.2	
2	16.0	25.7		13.5	23.2	
3	4.8	20.1		2.1	14.0	
Pressure ulcers (%)			<0.001			<0.001
0	88.2	69.4		91.7	76.8	
1	8.4	20.1		6.4	15.4	
2	2.3	5.8		1.3	4.7	
3	0.7	2.6		0.3	2.0	
4	0.3	2.1		0.3	1.2	
Delirium (%) Yes/No	4.8	19.4	<0.001	4.0	12.1	<0.001
Subcutaneous butterfly (%) Yes/No	7.8	49.8	<0.001	4.3	29.2	<0.001

^aSurvivor was considered the patient alive 7 days or 30 day after the assessment visit.^bNonsurvivor was consider the patient who died at 7 or 30 days after the assessment visit.

FIG. 1. Classification and regression tree (CART) model of probability of death 1 week later than the visit. VISIT-7: Valid visit with 7 days follow up. (%): Percentage of visits followed by patients death by 7 days. Symptoms were recorded using a Likert 0–3 scale (none, slight, moderate, or severe).

Statistical analysis

The variables were described as percentages or the mean $\pm$ standard deviation. Comparisons between the presence of symptoms for surviving and nonsurviving patients were performed using the χ^2 test. Statistically significant differences were established for values of $p < 0.05$.

Classification and regression tree (CART) methodology was used for model creation. The result variables in-

cluded mortality at 7 and 30 days after the visit. All available variables (full model) were initially incorporated, and the CART methodology automatically selected the variables and optimum cutoff points. An internal validation system (cross-validation with 10 partitions) was utilized to ensure generalization of the models. The sole stopping criterion for growing the trees was established with a minimum number of visits at terminal nodes greater than 50.¹⁵

FIG. 2. Classification and regression tree (CART) model of probability of death 30 days later than the visit. VISIT-30: Valid visit with 30 days follow up. (%): Percentage of visits followed by patients death by 30 days. Symptoms were recorded using a Likert 0–3 scale (none, slight, moderate or severe).

The area under the receiver operating characteristics (ROC) curve was calculated (with a 95% confidence interval) to assess the validation of the models.

The SPSS 18.0 (AnswerTree™ module; IBM SPSS, Armonk, NY) statistical software package was used for data analysis.

Results

A total of 698 patients were included, and these patients generated a total of 2997 visits. Data from 2893 visits fulfilled the criteria for the 7-day survival analysis, and data from 2720 visits were valid for the 30-day survival analysis.

The main characteristics of the patient sample have been described elsewhere^{17–19} and are summarized in Table 2. The overall mortality of the study group was 74%.

Table 3 shows the prevalence of symptoms at visits for the 7- and 30-day survival analysis. Symptoms were observed to be more severe at visits made by nonsurviving patients beyond the study time period.

Figures 1 and 2 show CART model estimates for the probability of death at 7 days and 30 days after visitation, respectively.

The 7-day model (with 6 variables) demonstrated a probability of death in the range between 2.2% and 83.6% and achieved an AUC of 0.88 (0.86–0.90). The 30-day model (with 6 variables) indicated a probability of death in the range between 16.9% and 96.5% and achieved an ABC of 0.78 (0.76–0.80).

For those patients who presented anorexia scores greater than 2 of 4, a low level of consciousness, and dysphagia, the probability of dying within 7 days reached 87%. However, patients with little or no asthenia and those without edema returned a probability of death within 30 days that was lower than 17%.

Discussion

This study focused on the presence or absence of specific signs and symptoms that could be easily perceived by any member of a palliative care team, including anorexia, dysphagia, edema, and the patient's level of consciousness.

The proposed models fulfill the criteria established by the European Association for Palliative Care (EAPC)⁶ for methodological quality and those defined by Justice et al.²⁰ for reproducibility and ease of use.

All parameters included in the proposed models are easy to assess, and the results are in agreement with the clinical experience of many professionals and many previous reports.^{15,21,22}

It is known that symptoms such as asthenia, anorexia, a low level of consciousness, and dyspnea are related to poor prognosis in palliative care.^{1,23,24} Our results are consistent with these previous findings, and by applying a different methodology, our findings confirm the roll of those symptoms as prognostic factors.

In addition, the prognostic model presented herein is easier to use than Maltoni's Palliative Prognostic Score (PaP)^{8,9} or the models proposed by Feliu et al.²⁵ or Suha et al.²⁶ because no blood sample is needed, no mathematics or conversion factors need to be used, and clinical survival estimation is avoided. Similar to the models described by

Narducci et al.,²³ Morita et al.,¹² and Gwilliam et al.,¹ our prognostic model only includes patient signs and symptoms, the particular sequence of which can be used to assess the probability of dying within 7 or 30 days. This approach is easy to remember and can help clinicians working in primary care to develop survival estimations based not only on their clinical experience.

The main strengths of our study include its prospective nature, sample size, close connection with palliative care activity, and consecutive recruitment. The selected variables are consistent with existing prognostic models and are easily detected in any clinical setting. Thus, these strengths support the generalization of our results and model.

Nevertheless, our work was not free of limitations. For example, our results were not assessed in an independent population. Additionally, our cohort was limited to a population receiving care at home. Thus, to corroborate our results, additional studies in different health care settings are required. In addition, our analysis did not include the degree to which prognosis would be modified when treatments proved to be effective. It would also be necessary to test the usefulness of our model in daily care before advocating its indiscriminate use.

There is significant clinical interest in palliative care prognostication, although the use of different methodologies and the absence of any consensus for describing patient samples hinder comparisons between methods. Therefore, we must consider the need for an international multicenter study to address the questions that remain unanswered.

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Author Disclosure Statement

No competing financial interests exist.

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