JOURNAL OF PALLIATIVE MEDICINE
Volume 27, Number 7, 2024

DOI: 10.1089/jpm.2023.0675

Can We Make More Accurate Prognoses During Last Days of Life?

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Abstract

Background: Life expectancy prediction is important for end-of-life planning. Established methods (Palliative Performance Scale [PPS], Palliative Prognostic Index [PPI]) have been validated for intermediate- to long-term prognoses, but last-weeks-of-life prognosis has not been well studied. Patients admitted to a palliative care facility often have a life expectancy of less than three weeks. Reliable last-weeks-of-life prognostic tools are needed.

Objective: To improve short-term survival prediction in terminally ill patients.

Method: This prospective study included all patients admitted to a palliative care facility in Montreal, Canada, over one year. PPS and PPI were assessed until patients' death. Seven prognostic clinical signs of impending death (Short-Term Prognosis Signs [SPS]) were documented daily.

Results: The analyses included 273 patients (76% cancer). The median survival time for a PPS ≤20% was 2.5 days, while for a PPS ≥50% it was 44.5 days, for a PPI >8 the median survival was 3.5 days and for a PPI ≤4 it was 38.5 days. Receiver operating characteristic curves showed a high accuracy in predicting survival. Median survival after the first occurrence of any SPS was below one week.

Conclusions: This study demonstrated that the PPS and PPI perform well between one week and three months extending their usefulness to shorter term survival prediction. SPS items provided survival information during the last week of life. Using SPS along with PPS and PPI during the last weeks of life could enable a more precise short-term survival prediction across various end-of-life diagnoses. The translation of this research into clinical practice could lead to a better adapted treatment, the identification of a most appropriate care setting for patients, and improved communication of prognosis with patients and families.

Keywords: end-of-life communication; life expectancy; palliative care; prognosis; terminal cancer; terminal pathologies

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Accepted February 12, 2024.

Introduction

ESTIMATION OF LIFE EXPECTANCY in terminally ill patients is an important end-of-life care issue: patients and families expect that the prognosis estimated by the treating health care professional is as close to reality as possible to facilitate end-of-life planning activities and relieve patient and family/carer anxiety associated with prognostic uncertainty.[1] It is also important for transfer of patients to appropriate alternative care settings for optimal end-of-life care (a shorter prognosis likely necessitates more intense palliative care support).

Survival prediction of terminally ill patients in the palliative care setting is generally difficult to do with accuracy. There are some established clinical methods for determining an intermediate- to long-term prognosis, but there are discrepancies in predicting the actual length of survival depending upon the studied patient population (cancer vs. noncancer; heterogeneous patient populations, patients still on chemotherapy/radiotherapy, etc.) and setting (hospice/residence vs. hospital vs. home).[2] Christakis and Lamont[3] have shown in a prospective study of more than 500 terminally ill patients that only 20% of their predictions were accurate, whereas 63% were optimistic.

The most used validated tool for prognostication is the Palliative Prognostic Index (PPI). The PPI has shown usefulness in cancer patients with more than three weeks of life expectancy in various care settings.

The Palliative Performance Scale (PPS) developed at the Victoria Hospice Society in Canada was not specifically established as a prognostic tool, but it has been used to categorize patients into groups and to contribute to the understanding of patient status for better determination of the patient's prognosis.[4] The PPS is the most studied in a variety of versions and various patient populations.[5]

The PPI was validated in hospice cancer inpatients by Morita et al.[6] The PPI relies on the assessment of performance status using the PPS, oral intake, edema, dyspnea at rest, and delirium. The resulting score allows determination of predicted survival shorter than three weeks (PPI score >6), shorter than six weeks (PPI score >4), or more than six weeks (PPI score ≤4). Morita et al. concluded that the sensitivity and specificity of their method were, respectively, 80% and 85% for a 3-week survival prediction and 80% and 77% when the survival estimation was six weeks. They concluded that the PPI permitted acceptable prediction of survival longer than three and six weeks in cancer patients.

Mean life expectancy of patients admitted in palliative care facilities is often less than a few weeks. The PPI scale has not been validated as a prediction tool for a survival shorter than three weeks. A shorter prognosis requires more accurate and reliable end-of-life tools.

When patients are approaching the end of life, one can observe various specific signs illustrating the progressive deficiency of the neurologic, respiratory, and circulatory systems: for example, rattling (agonic rale), apnea, agitation, hallucinations, and skin changes. Hui et al.[7] have identified physical signs associated with death within three days in cancer patients with a specificity of 95% and a positive likelihood ratio (>5). However, that study only included cancer patients who were assessed in an acute palliative care unit where patients may be quite different from the ones typically admitted to other settings.

Porcu et al.[8] recently developed a new predictive multivariable model to evaluate short-term survival probability for advanced cancer patients in home palliative care. There are presently no reliable tools permitting evaluation of prognosis in patients in the hospice-based palliative care population when life expectancy is less than three weeks, including patients with advanced cancer or other terminal pathologies. The study presented here is intended to evaluate the usefulness of the PPS and PPI for an intermediate- and a short-term prognostic evaluation in patients with cancer or other terminal pathologies in a hospice setting. Furthermore, it evaluates the prognostic utility of assessing seven clinical signs, usually observed during the last weeks of life, which we have designated Short-Term Prognosis Signs (SPS).

It is our hypothesis that tracking of the PPS, PPI, and SPS will permit a more accurate short-term prognostic evaluation and a better prediction of life expectancy of terminally ill patients in the hospice setting where patients can live from a few days to a few weeks.

Methods

Study design

This noninterventional prospective study has the objective of providing clinical information regarding intermediate- and short-term prognosis with the aim of improving the accuracy of survival predictions in terminally ill patients admitted to a palliative care hospice. It was planned to include all patients admitted at the Teresa Dellar Palliative Care Residence (TDPCR) for up to one year after the first patient entry date. The TDPCR is an accredited facility that provides symptom management and end-of-life care to patients with end-stage diseases who have an estimated prognosis of less than or equal to three months. No imaging or major investigations are performed; complications requiring simple actions (such as bladder infections) are treated if the patient is still able to take medication. Patients are followed by dedicated multidisciplinary teams, who apply the standards of the Canadian Hospice Palliative Care association.[9]

Participants

Any patient with a cancer or other terminal pathology admitted to the TDPCR, in Montreal, Canada, between June 2021 and July 2022 was eligible for inclusion in the study. Patients who died the day of admission, or before full admission assessments could be performed, were excluded.

Ethics. This protocol was granted approval by the McGill Institutional Review Board (IRB) in March 2021, before the start of study procedures. The study was conducted in accordance with the Declaration of Helsinki.[10]

Patient consent was not obtained from patients, as the study did not involve any changes in the usual/standard treatment/care and only routinely documented clinical data were collected. No patient identifiers were documented during data collection.

Study evaluations. Patients in the study were evaluated using the PPS, PPI, and SPS. PPI and PPS scores were assessed at admission (day zero), week one, week two, week

three, month one, and then monthly thereafter until patient death or completion of the study. PPS and PPI were evaluated by physicians with experience using these scales; specific training was provided for utilization of the scales in the study to maintain rater uniformity.

The revised version of the PPS (PPSv2) comprises five parameters (ambulation, activity and evidence of disease, self-care, intake, and level of consciousness (LOC).[4]

The PPI combines the PPS and other clinical signs (oral intake, edema, resting dyspnea, and delirium) permitting evaluation of prognosis of three weeks or longer.

Seven SPS observed anytime during the study were systematically documented throughout patients' stay at the hospice. They were identified based on the literature[11,12] and verified through a search of the last two years' patient charts at TDPCR as well as clinical experience/internal discussion. The designated SPS are as follows:

- Complete cessation of oral intake (food and liquid) (excluding mouth care)
- Totally bedbound (unable to weight-bear to transfer and pivot)
- Agitation and/or hallucinations
- Severe decrease of LOC: no response to verbal or tactile stimuli
- Presence of rattling (terminal secretions/agonic rales)
- Mottled skin (marble appearance)
- Occurrence of end-of-life apnea: pause in breathing pattern (excluding known sleep apnea)

During the study, health care professionals (nurses or physicians) documented the date of first occurrence of each of the SPS items during the entire stay of the patient at the hospice.

Statistical analyses. The primary endpoint of the study was death. We compared the prognosis determination using the PPI and PPS score at every time point in the assessment schedule following admission to the actual survival time and determined the number of days between occurrence of each SPS and the actual date of death.

Sample size was determined by the number of patients presenting to the hospice within the 1-year time frame of the study. Three patient populations were analyzed: all patients included in the study, patients with cancer, and patients with other terminal pathologies. Demographic and other baseline characteristics were summarized for each patient population, and descriptive statistics (mean, median, interquartile range, frequencies, and proportions) were used to summarize the characteristics of the three populations. Data were censored for patients who could not be followed up until death due to relocation to other institutions; for patients who had not died by the end of the study follow-up (end of September 2022); and patients who received Medical Aid in Dying (MAID) (since the purpose of the study was to evaluate prognosis in case of death due to natural causes).

The patients who opted for MAID contribute data to the analysis before they received MAID as their survival experience before this is relevant to the research question: it provides information on that if they had not opted for MAID, they would have still been alive by that point (they remain eligible to die from natural causes). Once they receive MAID, they are no longer able to experience natural death so their data are censored after that point. A similar approach was used for patients who transferred out.

Patients who died on the same day as admission were excluded from the analysis because of inutility in making prognosis for patients with an anticipated survival of <24 hours and lack of time between admission and death for completion of the full first visit evaluations. We assumed deaths occurred midway through each day by adding 0.5 days to all survival times in analyses. This was done because many patients died on days where new patient assessments were performed, leading to zero days of follow-up between the new assessment and death. This addition of a small-time difference between assessment and death allows us to integrate the prognostic value of these new assessments on survival probability, which otherwise could not have been accounted for as survival models are not able to handle null follow-up times.

Continuous variables were expressed as median (range). Categorical variables were reported as number (n) or proportion (%). Statistical significance was defined as $p < 0.05$. Analyses were performed using Stata software version 17 (College Station, TX: StataCorp LLC).

PPI and PPS score analyses: The Kaplan–Meier product limit estimate was used to calculate the probability of overall survival by time from patients' admissions to the palliative care hospice by PPS and PPI scores at admission. The log-rank test was used to compare the survival time between diagnosis groups. We assessed the time-varying predictive performance of PPI and PPS scores using time-dependent cumulative receiver operating characteristic (ROC) curves to assess the ability of these scores to predict death by time since admission (death within less than one week, less than two weeks, less than three weeks, less than four weeks, less than six weeks, and less than three months), covariates, and updated at each assessment.[13,14] The ROC curve displays the sensitivity and specificity of different cutoff values for predicting an outcome at some point in the future.

The area under the curve (AUC) summarizes the combined sensitivity and specificity of the characteristic over all possible cutoff values; characteristics with higher discriminatory abilities will have values closer to 1, while characteristics with poorer discriminatory abilities will have values closer to 0.5. These ROC curves were estimated by fitting Cox regression models to survival times using nearest neighbor estimation, where PPI and PPS scores were treated as time-varying. Nearest neighbor estimation is a method for estimating the time-dependent ROC curves accounting for the fact that some observations are censored.[13] SPS analyses: The probability of survival for the time from the incident occurrence of each SPS after admission to death was calculated using the Kaplan–Meier method.

Because we wanted to assess the predictive performance of a new SPS after admission, we did separate analysis for each SPS restricted to the population of patients who did not have that specific SPS at admission, to capture the first occurrence and true duration of the SPS. If they had occurrence of other SPS after admission, they could contribute to the analyses for other SPS.

Descriptive statistics were used to characterize the mean, median, and interquartile range for time to death for each of the SPS and to summarize the occurrence of SPS in the overall population and stratified by diagnosis of cancer or other terminal pathologies. The time from SPS occurrence to

death does not necessarily reflect its prognostic value as SPS might be coincidental. To assess the prognostic value of SPS, we used Cox regression model with each SPS considered a time-varying predictor of death hazard. The hazard ratios (HRs) from these models compare the relative hazard of death in a patient who newly presents an SPS to a patient who does not yet present the SPS by the same day since admission, and are a measure of the strength of the association between each SPS and risk of death.

Results

Baseline characteristics

A total of 285 patients were admitted to the TDPCR during the period of the study; data from 273 patients were included in the study analyses (Fig. 1).

The overall median survival duration from admission was nine days; median survival time was slightly longer in patients with cancer (10 days) compared with those with other terminal pathologies (seven days). The overall median age at enrollment, including both patients with cancer and with other terminal pathologies, was 83 years (Table 1). The median age was lower in patients with cancer (80 years) versus other pathologies (90 years). There were more women (57%) in the population. Patients consisted primarily of Caucasians (96%).

Most patients (76%) had a cancer diagnosis with the largest percentage diagnosed with gastrointestinal cancer (28%) followed by lung cancer (21%); most patients had metastases (81%). Twenty-three percent of patients with other terminal pathologies were admitted with a diagnosis of cardiac insufficiency.

Probability of survival by PPS score at admission

For patients admitted with a PPS score of 10%: the probability of survival was 1% by week two after admission, with only one patient still alive at this time (Fig. 2). The survival probability for a PPS score of 20% was also close to nil after 20 days. In the group of patients admitted with a PPS score <20%, nil survival probability was not reached during the two months after admission. However, a significant decline in survival probability was shown: a 50% survival probability was seen by week two for PPS scores of 30% and 40%, while for a PPS score of 50% or more, a 50% probability of survival was not evident until week 7.

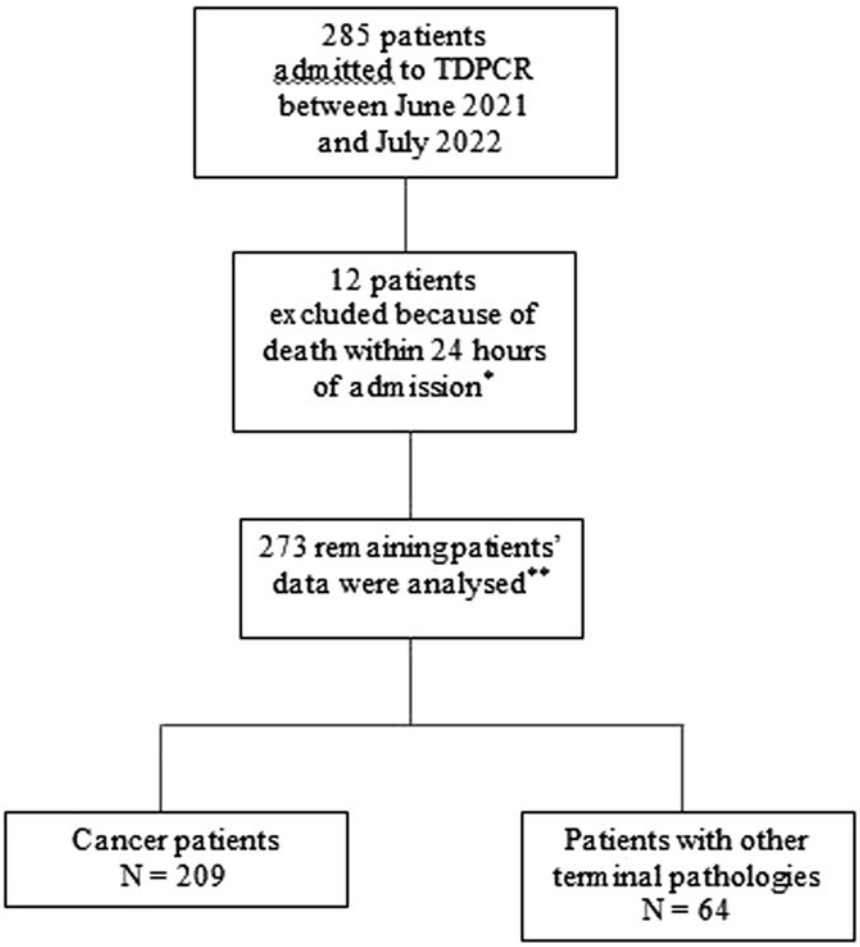

FIG. 1. Patient disposition. *Patients dying during the day of admission were excluded from the analysis due to rapid deterioration (few hours after admission) and lack of time to fully evaluate. **Data were included and censored for 14 patients for the following reasons: 4 patients received Medical-Assistance-in-Dying; 9 were stabilized and transferred to long-term care facilities; 1 patient did not die before the end of the study.

Table 1. Baseline Characteristics of Patients Who Survived the Day of Admission (Day Zero), Stratified by All Patients, Patients With Cancer, and Patients With Other Terminal Pathologies

	Cancer		*Other terminal pathologies*		*All*	
Characteristics[a]	*Median*	*IQR*	*Median*	*IQR*	*Median*	*IQR*
Age (years)	80	68–88	90	80–94	83	71–90
Time to death (days)	10	5–25	7	3–13	9	4–21
	n	%	n	%	n	%
Total	209	76	64	24	273	100
Female	121	58	35	55	156	57
Male	88	42	29	45	117	43
Cancer types						
Gastrointestinal	59	28			59	22
Lungs/bronchi	44	21	—	—	44	16
Genitourinary	35	17	—	—	35	13
Breast	20	10	—	—	20	7
Brain	14	7	—	—	14	5
Hematological	11	5	—	—	11	4
ENT	7	3	—	—	7	3
Others	19	8	—	—	18	7
Other terminal pathologies						
Cardiac insufficiency	—	—	15	23	15	5
Dementia/Alzheimer	—	—	10	16	10	4
COPD/pulmonary fibrosis/others	—	—	7	11	7	3
Vasculopathy/severe diabetes	—	—	6	9	6	2
Renal insufficiency	—	—	6	9	6	2
Hepatic insufficiency (cirrhosis)	—	—	5	8	5	2
Neurodegenerative disorders	—	—	2	3	2	1
Others	—	—	15	23	15	6
Cancer metastases	170	81	0	0	170	62

[a]Caucasians 95.7%; Asians 2.5%; Black 1.8%.
COPD, chronic obstructive pulmonary disease; ENT, ear, nose, throat; IQR, interquartile range.

There is a significant ($p < 0.001$) difference in the survival probability between patient groups of different admission PPS scores.

Probability of survival by PPI score at admission

At week three, more than 50% of patients with a PPI score of four or less were still alive, whereas almost all patients with a PPI score <6 were dead (Fig. 2).

There is a significant ($p < 0.001$) difference in survival probability between patient group admission PPI scores.

Median survival by PPS and PPI score

Table 2 shows the median survival time by PPS and PPI score at admission for the total population, patients with cancer and patients with other terminal pathologies. For the total population and cancer patients, a PPS score of 20%

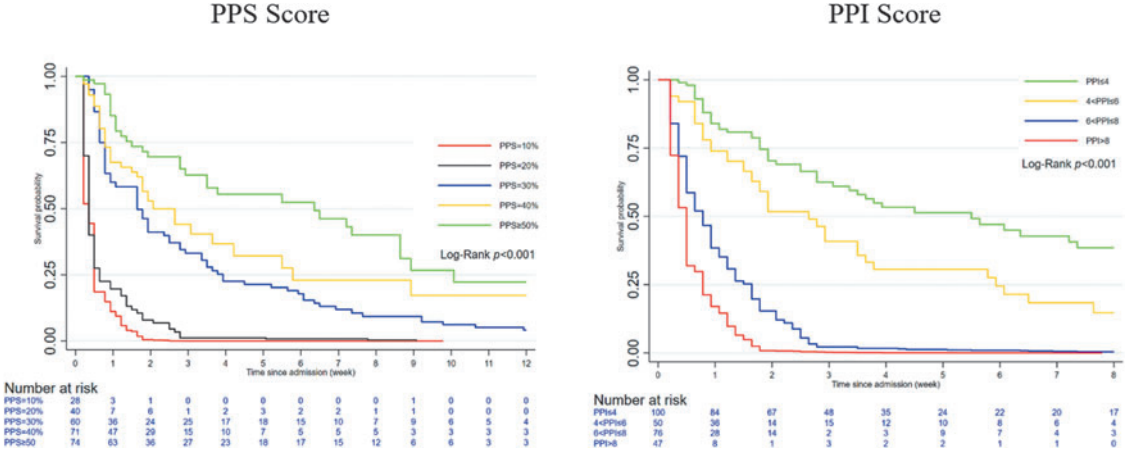

FIG. 2. Kaplan–Meier estimates of survival probability from admission by PPS and PPI score: all patients. PPI, Palliative Prognostic Index; PPS, Palliative Performance Scale.

Table 2. Median Survival Time Based on Palliative Performance Scale and Palliative Prognostic Index Scores: All Patients, Patients With Cancer, and Patients With Other Terminal Pathologies

Median survival time (days)									
All				*Cancer*			*Other terminal pathologies*		
	n	*Median*	*95% CI*	n	*Median*	*95% CI*	n	*Median*	*95% CI*
PPS score									
10%	67	2.5	1.5–3.5	49	1.5	1.5–3.5	18	3.5	1.5–6.5
20%	61	2.5	2.5–3.5	39	2.5	1.5–3.5	22	2.5	2.5–3.5
30%	103	11.5	5.5–17.5	81	13.5	5.5–19.5	22	6.5	4.5–26.5
40%	97	14.5	11.5–29.5	83	14.5	6.5–29.5	14	12.5	8.5–NR
≥50%	83	44.5	20.5–60.5	72	50.5	24.5–62.5	11	20.5	6.5–NR
PPI score									
PPI ≤4	122	38.5	23.5–60.5	104	42.5	24.5–60.5	18	19.5	4.5–NR
4 < PPI ≤6	77	18.5	10.5–25.5	59	19.5	11.5–25.5	18	8.5	4.5–53.5
6 < PPI ≤8	115	5.5	3.5–6.5	88	5.5	3.5–7.5	27	5.5	2.5–7.5
PPI >8	74	3.5	2.5–3.5	54	3.5	1.5–3.5	20	2.5	2.5–5.5

CI, confidence interval; NR, not reached; PPI, Palliative Prognostic Index; PPS, Palliative Performance Scale.

showed a median survival of 2.5 days; for a PPS score of 30% it was 11.5–13.5 days; and for a PPS score of 40% it was 14.5 days. When the PPS score was 50% or more, median survival was 44.5–50.5 days. However, median survival days were lower in patients with other terminal pathologies for PPS scores of 50% or more (20.5 days).

For the total population, a PPI score of 4 or less, median survival was 38.5 days; for a PPI score between 4 and 6, median survival was 18.5; and when the PPI score was between 6 and 8, it was 5.5 days. A PPI score greater than 8 showed a median survival of 3.5 days. The median survival time was similar for the total population and cancer patients. Patients with other terminal pathologies showed similar median survival time for PPI scores greater than 6.

Performance of PPS as a classification model (ROC)

When PPS scores were considered a time-varying predictor, the ROC curves for PPS scores for the total population (cancer and other terminal pathologies for predicting death at various time points show that all areas under the curves (AUCs) are between 0.71 and 0.74 (highest at week one), thus reflecting a moderate predictive accuracy for the PPS score (Fig. 3).

Performance of PPI as a classification model (ROC)

When PPI scores were considered a time-varying predictor, the ROC for PPI scores for the total population (cancer and other terminal pathologies) for predicting death at various time points shows that all AUCs are between 0.79 and 0.82 (highest at weeks two and three), thus reflecting a high predictive accuracy for the PPI score (Fig. 3).

Frequency of SPS

For analyses of SPS, if patients already presented an SPS at admission, that particular sign was excluded: only presentation of a new SPS since admission was considered. The most

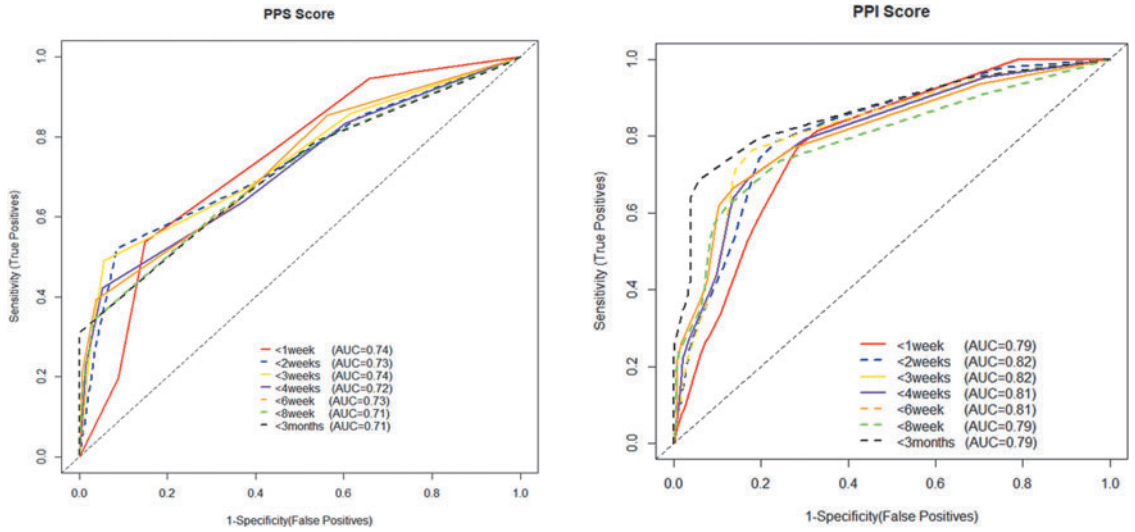

FIG. 3. ROC for the time-varying predictive value for cumulative risk of death by different time points for PPS and PPI scores: all patients. ROC, receiver operating characteristic.

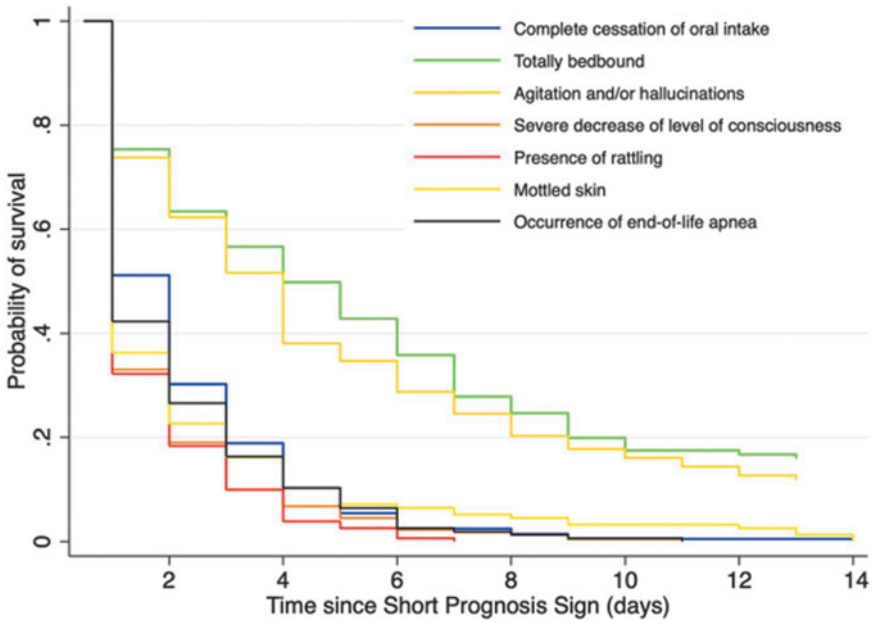

FIG. 4. Survival probability by SPS for all patients who developed SPS during their stay at the palliative care hospice. SPS, Short-Term Prognosis Signs.

frequent SPS clinical signs first observed after admission were ''totally bedbound'' (92% of patients not bedbound at admission), ''complete cessation of oral intake'' (90% of patients still eating at admission), and ''severe decrease of level of consciousness'' (89% of patients conscious at admission). The four other clinical signs (''agitation and/or hallucinations,'' ''presence of rattling,'' ''mottled skin,'' and ''end-of-life apnea'') each occurred in 52%–69% of patients who did not have these signs at admission. The percentage of postadmission occurrence of ''complete cessation of oral intake'' and occurrence of ''end-of-life apnea'' was similar between cancer patients and patients with other terminal pathologies.

Probability of survival and median survival for each SPS

Overall, the probability of survival declined most rapidly in patients demonstrating the following SPS after admission: ''rattling'' and ''severe decrease in level of consciousness,'' ''end-of-life apnea,'' and ''complete cessation of oral intake'' with the probability of survival becoming nil within six to nine days of the occurrence of these signs (Fig. 4). The decline in the probability of survival was slower for ''agitation and/or hallucinations'' and ''totally bedbound'' without reaching nil probability of survival by week two. The rate of decline in probability of survival for each of the SPS was comparable with the overall population in both cancer patients and patients with other terminal pathologies.

The clinical sign with the longest median survival time was ''totally bedbound'' (4 days (IQR 2 to 8) followed by ''agitation/hallucinations'' (3.5 days [IQR 1 to 7]) and ''complete cessation of oral intake'' (2 days [IQR 1 to 3]) (Table 3). The other clinical signs of the SPS show a median occurrence of only one day (IQR 0.5 to 3 days) before death.

All SPS were strong predictors of mortality in Cox models; HR in these models compared the hazard of death in patients newly presenting an SPS compared with patients who did not present the same SPS by the same time since admission. The

Table 3. Median Survival Time from Occurrence of Short-Term Prognosis Signs, All Patients, Patients With Cancer, and Patients With Other Terminal Pathologies

	Median survival time (days)											
	All				*Cancer*				*Other terminal pathologies*			
SPS	n	*Event*	*Median days*	*IQR*	n	*Event*	*Median days*	*IQR*	n	*Event*	*Median days*	*IQR*
Totally bedbound	134	130	4	2.0–8.0	114	110	4	1.0–9.0	20	20	2	2.0–6.5
Agitation and/or hallucination	122	120	3.5	1.0–7.0	98	96	3	1.0–8.0	24	24	4	1.5–6.0
Complete cessation of oral intake	215	213	2	1.0–3.0	168	166	2	1.0–3.0	47	47	1	1.0–2.0
Severe decrease of LOC	227	225	1	0.5–2.0	176	174	1	0.5–2.0	51	51	1	0.5–2.0
Presence of rattling	183	181	1	0.5–2.0	144	142	1	0.5–2.0	39	39	1	0.5–2.0
Mottled skin	156	155	1	0.5–2.0	124	123	1	0.5–2.0	32	32	1	0.5–2.0
Occurrence of end-of-life apnea	167	165	1	0.5–3.0	131	129	1	0.5–3.0	36	36	1	0.5–2.5

LOC, level of consciousness; SPS, Short-Term Prognosis Signs.

Table 4. Hazard Ratios of Short-Term Prognosis Sign Events After Admission, All Patients, Cancer Patients, and Patients With Other Terminal Pathologies

	All			*Cancer*			*Other terminal pathologies*		
SPS	n	*HR*	*95% CI*	n	*HR*	*95% CI*	n	*HR*	*95% CI*
Complete cessation of oral intake	240	233.1	122.8–442.7	188	228.8	111.8–468.6	52	147.5	35.5–612.9
Severe decrease of LOC	254	214.3	126.0–364.5	199	201.7	111.5–364.8	55	259.9	61.9–1090.4
Totally bedbound	146	82.8	30.5–224.3	123	91.2	28.9–287.7	23	65.1	8.3–513.4
Rattling	266	57.1	42.1–77.5	204	67.6	47.1–97.2	62	23.6	12.9–43.0
End-of-life apnea	256	36.8	27.3–49.7	198	41.0	29.0–58.2	58	19.2	10.4–35.6
Mottled skin	260	29.9	22.1–38.6	200	33.8	24.3–46.9	60	16.4	9.1–29.7
Agitation and/or hallucinations	234	7.8	5.9–10.4	179	8.7	6.2–12.1	55	4.7	2.5–8.6

HR, hazard ratio.

most predictive clinical signs are ''complete cessation of oral intake'' (HR = 233) followed by ''severe decrease of consciousness'' (HR = 214), ''totally bedbound'' (HR = 83), and ''rattling'' (HR = 57) (Table 4). The pattern is similar for cancer patients and patients with other terminal pathologies (Table 4).

Discussion

Prognostication is of upmost importance for clinical decision making and care planning in patients with end-of-stage diseases. Efforts to develop effective end-of-life prognostic tools have been undertaken in patients with a variety of terminal diagnoses (mainly cancer) using various methodologies for more than 30 years and researchers in the field continue to work aiming to develop more accurate predictions.[15] Research shows that determination of prognosis in palliative care based solely on clinical judgment, although providing important contributions, tends to be inaccurate on its own and to overestimate survival.[16,17] Validated prognostic algorithms provide more objective prediction, discrimination, and reproducibility.[2,3] Previous prognostic studies in end-of-life care have validated PPS and PPI prognostic tools statistically and have reported their discrimination, calibration, and accuracy[4,6] mainly for medium-term survival in cancer patients.

In the hospice setting, patients have various terminal diseases, often with a less than 3-week life expectancy. Therefore, there is a need to validate the use of tools such as the PPS and PPI in these patients as well as identify clinical signs that can assist in making these prognostications more accurate.

We conducted this study with the aim of addressing this need. This study included 273 patients admitted to hospice, with various advanced cancers (76% with cancer; 81% with metastases) and other end-of-life pathologies, and evaluated the PPS, PPI, and SPS in these patients.

The PPS was not specifically established as a prognostic tool, but it is used to contribute to the understanding of patient status for better determination of the patient's prognosis.[4] In a large retrospective analysis ($n = 6066$) of referrals to a Canadian hospice service, Lau et al.[18] reported that the median survival of patients with a PPS of 20, 30, 40, and 50%–70% was 2, 5, 13, and 28–63 days, respectively; our study results were similar showing a median survival of 2 (2.5–3.5 days), 11.5 (5.5–17.5 days), 14.5 (11.5–29.5 days), and 44.5 (20.5–60.5 days).

The predictive validity of PPS at each week was evaluated using ROC curve plots with the AUC being above 0.7 in both cancer and noncancer patients, thus demonstrating an important link between PPS score and duration of survival in end-of-life palliative care patients. This further confirmed the utility of the PPS as a significant predictor for survival not only in cancer patients but also in patients with a variety of other end-of-life diagnoses (including cardiac diseases and dementia). This study supports and provides reproducibility of the PPS data observed in advanced cancer patients.[19]

The PPI scale was developed by Morita et al.[6] and studies have demonstrated that it has good discrimination, calibration, sensitivity, and specificity for a three-week survival prediction or more.[2] The PPS score is an integral part of the PPI scale: it is one of the five items included accounting for more than 25% of the total score. Patients with a PPI score of 4 or less are predicted to survive more than six weeks, while PPI scores <6 predict a survival of less than three weeks. It was, therefore, relatively straightforward to compare the accuracy of PPI predictions with the results we had in this study, which, in fact, confirm these survival estimations.

Moreover, this study not only confirmed the established validated prognostic group patients' stratification reported by Morita, but it allowed, for the first time, the extension and refinement of prognostication to a very short-term survival time: PPI >8 with median survival less than one week (between 2.5 and 3.5 days) in both cancer and other life-limiting diseases. These results constitute an extension of the use of already published prognostic predictions (shortest term prediction being PPI greater than 6 with a survival estimation of less than three weeks), providing information for use in predicting shorter term survival time.

With ROCs showing AUCs of 0.8 and above for each week, this study confirmed that the PPI is a significant survival predictor not only in cancer patients but also in a variety of other terminal diagnoses. It also demonstrated that the level of predictive precision and specificity is maintained and can be refined for very short-term survival (less than three weeks).

Furthermore, we found that both the PPS and PPI were able to significantly ($p < 0.001$) discriminate the duration of survival between patients with different levels of PPS or PPI scores, further establishing the utility of these scores for near-term end-of-life prognostication. In addition, this study shows that, according to the PPI and PPS tools, for most scores, the survival of patients with terminal diagnoses other than cancer is shorter than for the cancer patients.

This study provides information on the short-term survival prediction for cancer patients and patients with other terminal pathologies by documenting the occurrence of seven specific short-term prognosis clinical signs (SPS) in hospice setting. Previous studies[12,20] have identified and documented short-term survival in cancer patients in acute palliative care units using mainly symptoms that are subjective, treatable, and depend upon patient cooperation and ability to respond, which diminish or disappear as the patient approaches death. The SPS did not require patients' responses since they are clinical signs, as observed by the clinical health care professionals (nurses and physicians). This allowed us to gather results independently from the loss of ability to respond from the patient and a certain level of uniformity was preserved because of the nature of the clinical signs.

Among the seven targeted clinical signs, we selected two that were already part of the PPS (''totally bedridden'') and the PPI (''cessation of oral intake'') and five others were complementary to the known scales. At least one of the seven clinical signs was newly occurred in all patients after admission. Most patients presented ''severe decrease of level of consciousness (LOC),'' ''complete cessation of oral intake,'' and ''rattling.'' More than half patients presented ''mottled skin'' or ''end-of-life apnea'' and close to 50% became ''totally bedbound'' or experienced ''agitation/hallucinations.''

Hui et al.[20] reported median time to death for 10 clinical signs in cancer patients in the hospital setting. Four of these were followed in our study and observed median time to death compared with Hui's results as follows: ''decrease LOC'': Hui: seven days (our study: one day [0.5–2]), ''PPS ≤20%,'' which includes totally bedbound'': four days (our study: four days in total and cancer population; two days in noncancer patients), ''apnea periods'': 1.5 day (our study: one day [0.5–3], ''rattle'': 1.5 days (our study: one day [0.5–2]). Except for ''decrease LOC'' that showed a lower median survival in our study, these results support the findings by Hui et al.,[20] suggesting that these clinical signs might be useful indicators both in cancer and other end-of-life diagnoses in palliative care settings.

Furthermore, our study contributes information regarding survival after occurrence of three other clinical signs: ''agitation/hallucinations,'' ''complete cessation of oral intake,'' and ''mottled skin'' with median survival of 3.5 days (1.0–7.0), 2 days (1.0–3.0), and 1 day (0.5–2.0), respectively, in the total population. The probability of survival declined most rapidly in patients with ''rattling,'' ''severe decrease in level of consciousness,'' ''end-of-life apnea,'' ''complete cessation of oral intake,'' and ''mottled skin'' with the probability of survival becoming nil (or close to nil) within six to nine days of the occurrence of these signs.

The decline in the probability of survival was slower for the two other short-term clinical signs: ''agitation and/or hallucinations'' and ''totally bed bound'' and did not reach nil probability of survival by week two. The rate of decline in probability of survival for each of the SPS was comparable with the overall population in both cancer patients and patients with other terminal pathologies.

To assess the prognostic value of these signs, we compared death rates in those who newly presented each sign to patients who did not and found that all the SPS strongly predicted the risk of death within the next few days. However, while it is not possible to say which sign is the strongest predictor, our findings clearly suggest that all these clinical signs might be useful in survival prediction both in cancer and other end-of-life diagnoses in the hospice setting.

In a recent large cancer population publication (2023), Porcu et al.[8] presented a new predictive multivariable model, including five predictors (including one SPS: rattling), to evaluate the short-term survival probability for advanced cancer patients in home palliative care. Although useful in that population, it provided suboptimal discrimination in hospice patients and no information on other terminal diseases.

This study presents, for the first time, an extension of the use of PPI to predict survival during the last three weeks of life and explores the contribution of seven clinical signs that can easily and objectively be documented in the hospice setting during the last weeks of life not only in patients with advanced cancer but also in patients with other end-of-life diagnoses.

Professionals need to have access to validate more precise and larger scope (including short-term) prognostic tools. A suite of tools that include the PPI items (which already include PPS) in addition to selected specific physical signs would have great utility. They can be used to provide a larger scope and more refined and precise ability to predict survival from medium-term to very short-term (last week of life) in all patients whether they have cancer or another terminal diagnosis. The findings of this study along with those reported in the literature pave the way for the development and validation of a more refined tool that includes more precise information on impending death.

Limitations and future work

This study had some limitations. Several patients died during the first hours of admission, therefore not permitting full evaluation and were excluded from our analyses. Our results therefore apply to those who survived the first day of admission only. We also right-censored the observations for patients who had to be relocated because they were clinically stable or requested MAID. This study was performed in one palliative care hospice in one country. Ninety-six percent of patients entered in the study were Caucasian as this was the demographic of patients admitted to our hospice during the year of study recruitment. This could limit the ability to generalize conclusions to other racial groups.

Future studies should include the use of the most predictive clinical signs along with the PPI to elaborate a versatile and more precise tool (for short- and medium-term prognosis) that will need to be validated in various patients (cancer and other end-of-life diagnoses) in various palliative care centers confirming its reproducibility and reliability.

What this study adds

This study has the potential to contribute to advancing short-term prognostication. As a result, it will enable more precise short-term survival prediction across various end-of-life diagnoses leading to translation into clinical practice and improving communication of prognostication to patients and their families.

Conclusions

This study provides additional evidence for the utility of the PPS and PPI in both cancer patients and patients with

other terminal pathologies. Furthermore, it supports the extension of their use for prognostic estimation for patients within the last three weeks of life. Moreover, it identifies seven clinical signs strongly associated with impending death and provides median survival duration in days for each one.

The determination of PPS, PPI scores, and SPS allows for prognostic determination over a wide duration between more than six weeks (PPI ≤4), more than one month (PPS ≥50%), and last days of survival (SPS occurrence). Therefore, the combination of PPS, PPI, and SPS can permit greater refinement and precision of prognostic predictions within the last days of life.

Finally, this work provides the groundwork for the development of an integrated tool that can be used by health providers to make more accurate end-of-life prognoses. These results hold utility for health professionals estimating survival permitting patients to orient toward appropriate services tailored to their needs. In addition, it permits communication of short-term prognosis with more confidence to families and appropriate care setting.

Acknowledgments

The authors wish to express their gratitude to Ms. D. Weil, Executive Director of the Montreal Institute for Palliative Care and the TDPCR, who supported the use of these facilities and gave us free access to clerical and coordination staff. The authors thank the nurses of the TDPCR who significantly contributed to reporting the SPS items and for their support. They also would like to thank Ms. N. Lapointe who monitored this study and made sure that all investigators were following the schedule properly. The authors are also grateful to the McGill University, Oncology Department, Division of Cancer Epidemiology, which provided us with full statistical support and gave us access to its Ethics Review Board.

Authors' Contributions

The authors confirm contributions to this article as follows: study conception and design: S.B., A.P.I., and E.N.; data collection: all investigators; statistical analysis: T.M. and S.J.; article preparation: S.B. and S.S.-R. All authors reviewed the results and approved the final version of the article.

Funding Information

No funding was received for this article.

Author Disclosure Statement

No competing financial interests exist.

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