

RESEARCH COMMUNICATION

Validation of a Palliative Prognostic Index to Predict Life Expectancy for Terminally Ill Cancer Patients in a Hospice Consultation Setting in Taiwan

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Abstract

Background: The aim of our study was to assess the practical utility of the palliative prognostic index (PPI) as a prognostic tool used by nurse specialists in a hospice consultation setting in Taiwan. **Methods:** In total, 623 terminal cancer patients under hospice consultation care from one medical center in northern Taiwan were enrolled between January 1 and June 30, 2011. PPI was assessed by a nurse specialist at first hospice consultation and patients categorized into groups by prognosis (good, intermediate, poor). Patient survival was analyzed retrospectively to determine significance of between-group differences. **Results:** By PPI sum score, 37.2% of patients were in the good prognosis group, 18% in the intermediate prognosis group and 44.8% in the poor prognosis group. The death rates were 56%, 81.2% and 89.6% and median survivals were 76, 18 and 7 days, respectively. The hazard ratio was 0.19 (95% confidence interval [CI] 0.10-0.24, $p < 0.001$) for the poor versus good prognosis group and 0.54 (95% CI 0.43-0.69, $p < 0.001$) for the poor versus intermediate prognosis group. The sensitivity and specificity for the poor prognosis group was 66% and 71%; the positive predictive value and negative predictive value were 81% and 52%, respectively, to predict patient death within 21 days (area under the curve of the receiver operating characteristic was 0.68). **Conclusions:** Assessment by PPI can accurately predict survival of terminal cancer patients receiving hospice consultation care. PPI is a simple tool and can be administered by nurse members of hospice consultation teams.

Keywords: Terminal cancer patients - hospice consultation - palliative prognostic index - prognosis - palliative care

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Introduction

Predicting life expectancy in terminal cancer is important for clinicians and patients (Kutner et al., 1999; Steinhauser et al., 2000; Kirk et al., 2004). A realistic survival estimate helps clinicians decide on the appropriate medical interventions, discharge planning or timing of referral to palliative care services. Prognostic accuracy helps patients plan the rest of their lives, prepare for death and choose where they want to die (Steinhauser et al., 2001; Adams et al., 2009). Respect for the autonomy of those who wish to die at home was reported to help terminally ill cancer patients in Taiwan achieve a good death (Yao et al., 2007).

Members of the hospice consultation team observe that estimating survival is one of the greatest concerns of patients and their families. Proper prognostic determination helps members of the hospice team make clinical decisions about appropriate treatment. For example, the aim of hospice care is to avoid unnecessary treatment and help patient and their proxies prepare for

patients' imminent death.

A working group of the Research Network of the European Association for palliative care recommended that a prognostic correlation in advanced cancer patients be formulated for clinical prediction of survival (CPS) and prognostic scores (Maltoni et al., 2005). CPS is defined as a clinical prognostic judgment that depends on the clinician's subjective assessment of the individual patient. CPS is a generally useful tool, but its accuracy depends on the clinician's experience and training in end-of-life care. CPS was reported to be more than twice as likely to be over-optimistic than over-pessimistic and to over-estimate the length of actual survival by a factor of 3 to 5 (Glare et al., 2003). Clinicians seem better at estimating survival time using CPS for patients with either very bad or very good prognosis. CPS cannot produce a precise, reliable prognosis for other types of patients. Therefore, CPS should be used in combination with other prognostic scores to improve the accuracy of predicting life expectancy in terminal cancer patients (Maltoni et al., 2005).

The Palliative Prognostic (PaP) score and the Palliative Prognostic Index (PPI) are the two most popular scores used worldwide to predict life expectancy in terminally ill cancer patients. The PaP score combines CPS with clinical symptoms (performance status, dyspnea and anorexia) and blood tests (total white count and lymphocyte percentage) (Pirovano et al., 1999). PPI is scored using presentations of clinical symptoms only (performance status, dyspnea, oral intake, edema and delirium) without CPS or laboratory tests (Morita et al., 1999). Both scores had been validated in various hospice settings with acceptable sensitivity and specificity for end-of-life prediction (Maltoni et al., 1999, 2001, 2012; Caraceni et al., 2000; Glare et al., 2001; Stone et al., 2008; Stiel et al., 2010; Yoong et al., 2010; Alshemmari et al., 2012). One study from Germany compared PaP score, PPI and CPS in terminally ill patients. The estimate of PPI and PaP scores correlate highly, but both had lower correlation with CPS. Again, CPS over-estimated survival time, on average, fourfold (Stiel et al., 2010). A recent published study compare prognostic scores between CPS, PPI, PaP and a variant of PaP score including delirium (D-PaP score) in hospice patients. The authors concluded that all four prognostic scores accurately predicted survival. All prognostic scores, except CPS, had a more than 70% positive prediction rate of a less than 21-days survival (Maltoni et al., 2012).

Compared to the PaP score, PPI is relative simple and noninvasive. All medical staffs involved in hospice care can use PPI to predict life expectancy in terminally ill cancer patients. PPI had been validated in smaller patient numbers in hospice wards and hospice consulting services in Japan and western countries (Stone et al., 2008; Stiel et al., 2010; Maltoni et al., 2012). However, the value of PPI in Taiwanese terminal cancer patients, especially in the hospice consultation setting, has not been determined. The aim of our study was to assess the practical utility of PPI as a prognostic tool for clinical decision making when used by nurse specialists in routine clinical practice in a hospice consultation setting in Taiwan.

Materials and Methods

Patient selection

A total of 623 patients were enrolled consecutively from those admitted to Chang Gung Memorial Hospital (CGMH) in Linkou who received hospice consultation care from January 1, 2011 to June 30, 2011. CGMH is a medical center with more than 3,000 acute care beds. All patients were diagnosed with metastatic or locally advanced cancer and were referred to hospice consultation care on the basis of their clinicians' judgment that they would benefit from hospice care and were unlikely to live for six months. Patients who were referred from the emergency room or were undergoing cancer treatments of curative intent were excluded. The study protocol was approved by the hospital Institutional Review Board.

Hospice setting and data collection

All participants were under the combined care of a primary care physician and a multidisciplinary palliative

care team consisting of physicians, specialist nurses, social workers and a Buddhist priest. Every patient was interviewed by a physician and a nurse specialist at first consultation, and then was followed weekly until the end of the service. The end-point of these services was patient death, transfer to a hospice ward or home hospice care, or discharge from the hospital under stable conditions.

The study results consisted of patients' demographic data (age, gender, tumor diagnosis and survival time) and PPI score. The PPI was constructed using the palliative performance scale (described below) and four clinical presentations: oral intake, edema, dyspnea at rest and delirium. The palliative performance scale is a modification of the Karnofsky Performance Scale Index (Anderson et al., 1996), which grades a patient's general condition on a scale from 0 (death) to 100 (normal). The clinical presentations were evaluated using a structured interview in which patients were asked about the presence or absence of each symptom. For patients who had difficulty with verbal communication, a nurse specialist assessed their status using proxy or caregiver response. Patients receiving total parental nutrition or having an enteral feeding tube were classed as having "normal" oral intake. Delirium was diagnosed based on the criteria of the Diagnostic and Statistical Manual of Mental Disorders, 4th edition. Delirium was judged absent if believed caused by medications, as in the original PPI study (Morita et al., 1999). All the nurse specialists involved in hospice consultation care had at least five years of clinical experience in patient care.

The sum PPI scores range from 0 to 15 points. In the original report in a Japanese palliative care unit, patients were categorized into three groups by PPI sum (0-4 good prognosis, 4.5-6 intermediate prognosis and >6 poor prognosis) to predict life expectancy. For this study, we used the same categories to test survival time by category. All demographic data and PPI scores were entered into an electronic database by a specialist nurse immediately after the first consultation. Survival time was defined as the difference between the day of the first hospice consultation and the day of death. Patients discharged to home, nursing home or hospice ward were followed by phone and day of death was elicited from family members until December 2011. All data were analyzed retrospectively from the electronic database.

Statistical analysis

Statistical analyses were performed using SPSS 15.0 statistics software (SPSS Inc, Chicago, IL). Basic demographic data were summarized as n (%) for categorical variables and median with the interquartile range (IQR) (Q1-Q3) for continuous variables, respectively. Overall survival was calculated using the Kaplan-Meier method. Hazard ratios were estimated for good and intermediate PPI sum scores (0-4 and 4.5-6, respectively) relative to poor PPI sum scores (>6) using unstratified Cox regression. Sensitivity, specificity, positive predictive value negative predictive value and accuracy were calculated for each PPI category separately. All statistical assessments were considered significant when $p < 0.05$.

Table 1. Basic Demographic Data of Patients

Patient characteristics (n=623)	Number (% or range)
Median age (IQR= interquartile range)	62 (52-73)
Gender	
Male	378 (60.7%)
Female	245 (39.3%)
Death at study end	471 (75.6%)
Cancer diagnosis	
Lung cancer	141 (22.6%)
Liver cancer	131 (21.0%)
Colorectal cancer	58 (9.3%)
Upper gastrointestinal tract cancer	62 (10.0%)
Head and neck cancer	56 (9.0%)
Breast cancer	42 (6.7%)
Other	133 (21.3%)

Table 2. Patient Performance Status and Clinical Symptoms by Palliative Performance Index (PPI) Score (n=623)

Clinical	Value	Score	Number (%)
PPI Score:	≥60	0.0	123 (19.7)
	30-50	2.5	160 (25.7)
	10-20	4.0	340 (54.6)
Dyspnea at rest:	No	0.0	297 (47.7)
	Yes	3.5	326 (52.3)
Delirium:	No	0.0	560 (89.9)
	Yes	4.0	63 (10.1)
Oral intake:	Normal	0.0	313 (50.2)
	Reduced but more than a mouthful		
		1.0	271 (43.5)
	A mouthful or less	2.5	39 (6.3)
Edema:	No	0.0	454 (72.9)
	Yes	1.0	169 (27.1)

Table 3. Survival and Death Rate by Palliative Performance Index (PPI) Category

Category	PPI score	No. (%)	Death (%)	Median survival days (95% CI)	Hazard ratio (95% CI)
Good prognosis*	0-4	232 (37.2)	130 (56)	76 (49.8-102)	0.2 (0.1-0.2)
	4.5-6	112 (18)	91 (81)	18 (15.3-21)	0.5 (0.4-0.7)
Intermediate prognosis*	6.5-8	112 (18)	91 (81)	18 (15.3-21)	0.5 (0.4-0.7)
	8.5-10	112 (18)	91 (81)	18 (15.3-21)	0.5 (0.4-0.7)
Poor prognosis	>6	279 (44.8)	250 (90)	7 (05.1-009)	reference
	Overall	623 (100)	471 (76)	19 (15.3-023)	

*P value ≤ 0.001, CI, confidence Interval

Results

Data from 623 patients were analyzed. Median patient age was 62 years (IQR 52-73 years). Males accounted for 60.7% of patients. Main cancer diagnoses are shown in Table 1. At the time of study end, 471 patients (75.6%) had died.

Patients' performance status and clinical symptoms by PPI score are summarized in Table 2. The distribution of PPI score was as follows: 16.4% had a score 0-2, 20.9% had a score of 2.5-4, 18% had a score of 4.5-6, 16.1% had a score of 6.5-8, 20.7% had a score of 8.5-10 and 7.9% had a score of 10.5 or more.

The PPI sum score gave a good prognosis to 37.2% of all patients (sum score 0-4), intermediate prognosis to

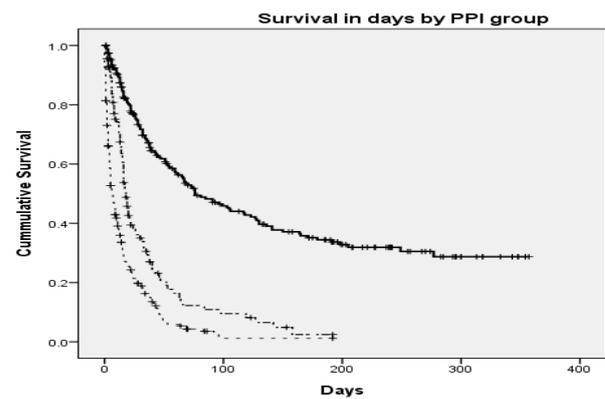


Figure 1. Legend: Kaplan-Meier Survival Curves for each Palliative Performance Index (PPI) Group. Good prognosis, PPI score 0-4; Intermediate prognosis, PPI score 4.5-6; Poor prognosis, PPI score >6

Table 4. Accuracy of Life Expectancy in a Given Period by Palliative Performance Index (PPI) Cutoff Score

Predicted life expectancy	Cutoff PPI score	Sensitivity (%)	Specificity (%)	Positive Predictive	Negative Predictive	Accuracy (%)
				Value (%)	Value (%)	
Less than 1 week	≥4	91	40	49	87	63
	>5	81	58	55	83	71
	>6	79	64	58	83	74
Less than 3 weeks	≥4	86	53	77	62	75
	>5	71	68	81	56	74
	>6	66	71	81	52	72
Less than 6 weeks	≥4	80	62	90	42	79
	>5	65	76	93	34	73
	>6	61	79	92	32	69

AUC, area under curve of receiver operating characteristic

18% (sum score 4.5-6) and poor prognosis to 44.8% (sum score >6). The death rate was 56%, 81.2% and 89.6% and median survival was 76, 18 and 7 days for each group, respectively. The hazard ratio was 0.19 (95% confidence interval [CI] 0.10-0.24, p<0.001) when comparing the good prognosis with poor prognosis group and 0.54 (95% CI 0.43-0.69, p<0.001) when comparing the intermediate prognosis with poor prognosis group (Table 3).

The survival curve shows the cumulative survival for patients in the three categories. Chi-square analysis of the distribution of survival (Mantel-Cox) for the curves of the different categories was highly significant (p<0.001) (Figure 1).

The accuracy of life expectancy within a given period by PPI cutoff point is presented in Table 4. The sensitivity and specificity to predict life expectancy for those with poor prognosis was 66% and 71%; the positive predictive value and negative predictive value was 81% and 52%, respectively, to predict patient survival for those who died within 21 days. The accuracy of life expectancy to predict a given period varied from 63-79% by different PPI score. In general, the sensitivity, and negative predictive value drop as the PPI score cutoff point and predicted survival time increased. By contrast, the specificity and positive predictive value rose in the same manner.

Table 5. Comparison of the Accuracy Between Different Hospice Settings in Terminally Ill Cancer Patients of Palliative Prognosis Index Score > 6 to Predict a Less Than 21-days Survival

Author, published year	Patient No.	Medical setting	Sensitivity	Specificity	Positive predictive value	Negative predictive value
Morita, 1999,	245	Hospice ward	83	85	80	87
Stone, 2008	194	74% hospice consultation; 26% home hospice	56	94	86	76
Stiel, 2010	83	Hospice ward	51	94	92	64
aMaltoni, 2012	549	Hospice ward	74	67	68	73
Alshemmari, 2012	91	Acute cancer care setting	73	78	93	41
Yoong, 2010	80b	Hospice consultation	85	75	NA	NA
This study	623	Hospice consultation	66	71	81	52

^aaccuracy with palliative prognosis index score > 5 as cutoff; ^bincluding 35% non-cancer patients; N/A, non-available

Discussion

Patients in different PPI categories had significantly different lengths of survival in this study. The results showed that PPI was a reliable means to predict life expectancy for terminally ill cancer patients in a hospice consultation setting in Taiwan. To the best of our knowledge, this study was the largest study validating PPI as a prognosticator of life expectancy in terminal cancer patients in a hospice consultation setting. The method of PPI scoring is easy and objective. PPI requires neither blood test nor assistance from experienced clinicians; it is therefore easily administered by any healthcare worker or volunteer.

CPS is widely used to predict life expectancy in terminally ill patients. However, CPS relies on a clinician's estimation, which is often incorrect. Christakis et al. (2000) reported that only 20% of predictions were accurate and 63% were over-optimistic by a factor of 5.3. Gripp et al. (2007) reported similarly that 71-96% of estimates of survival of patients who died within one month were over-optimistic. One head-to-head direct comparison of CPS and prognostic scores in terminally ill patients by Stiel et al. (2010) reported lower correlation with actual survival for CPS than for either PPI or PaP. Further detailed analysis showed that clinicians scored better for patients with either poor or good prognosis than for those with an intermediate prognosis. In our experience, CPS may accurately estimate survival in those patients who present with pre-dying signs; however, such information often comes too late to be useful for patients and their families. For other patients without signs of pre-dying sign, lifespan is often difficult to estimate accurately. Subjective estimation by clinicians creates most of the bias of CPS. Lack of experience in oncology and palliative care in a clinician or a stronger physician-patient relationship reduces CPS accuracy (Tanneberger et al., 2002). In contrast to CPS, PPI is an objective assessment. It may be accurately used by those with no experience in oncology or palliative care.

Some clinical presentations have proven to be prognostically significant in terminally ill cancer patients. The most important of these are performance, anorexia-cachexia, dyspnea, dysphagia and delirium or cognitive failure (Evans et al., 1985; Morita et al., 1995; 1999; Tamburini et al., 1996). Because these symptoms cluster in every dying patient whatever the underlying disease, they are often grouped into a clinical condition termed

the "common terminal pathway" (Viganò et al., 1999). Identifying the core symptoms of the "common terminal pathway" provide a simple, practical tool by which health care workers not experienced in oncology or palliative care may estimate life span. Other symptoms such as fever, pain, nausea, anxiety and hemorrhage have proved to be significant in less advanced stage cancer patients; however, their value for life span prognostication in terminal cancer patients is uncertain (Maltoni et al., 2005).

In different hospice settings, the sensitivity and specificity rates to predict patient mortality within three weeks range 51-85% and 67-94%, respectively, for patients with a PPI sum score ≥ 6 (Morita et al., 1999; Stone et al., 2005; Stiel et al., 2010). The sensitivity rate in this study (66%) was comparable to previous reports, but the specificity (71%) was far below that previously found (Table 5). The possible explanation for this phenomenon was the closely median survival between the poor prognosis and intermediate prognosis groups in this study (7 and 18 days, respectively). Since more than half of the patients in the intermediate prognosis group died in less than three weeks, the specificity and negative predictive value in our study was lower than for other reports. Another possible explanation was the difference in recruitment criteria between studies. All our patients were enrolled from the hospital hospice consultation setting. Hospice consultation care was designed to provide end-of-life care for terminally-ill patients by qualified multidisciplinary specialists (Higginson et al., 2003; Hunt et al., 2004) and it was enthusiastically promoted in Taiwan since 2005 (Taiwan Academy of Hospice Palliative Medicine, 2011). The service solved the hospice demand for terminally-ill patients either because their reluctance to be transferred to acute palliative unit, or the unavailability of the acute palliative unit, or the patient was just too sick to be transferred. Scoring accurate may be influenced by limited interview duration at first hospice consultation. Further studies are needed to evaluate the effect of clinical presentation or repetitive PPI scoring on PPI score in the hospice consultation setting.

Considering the highest accuracy of life expectancy by PPI score, the cutoff point of PPI > 4 gave a 79% accuracy used in prediction of survival less than six weeks in our study. Using the same PPI score as a cutoff point reduced the sensitivity and negative predictive value, while it raised the specificity and positive predictive value. This effect highlighted the fact that the PPI score was over-pessimistic in predicting survival in less than one week

and over-optimistic in predicting survival in 1-6 weeks in our study.

This study had some limitations. First, it was a retrospective study, so that some bias may have existed in the way in which the data were obtained. Second, while about 10% of patients referred for hospice consultation service in daily practice came from the emergency room, these patients were excluded from this study because their clinical course was unpredictable and their acute complications may transiently aggravate the PPI score. A prospective study to valid PPI scores for all patients referral to hospice consultation care should be conducted in the near future.

In conclusion, survival of terminal cancer patients receiving hospice consultation care can be predicted by PPI. PPI is an easy to use and objective tool that can be administered by nurse member of the hospice consultation team.

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Wei Hong Cheng et al

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