Prospective clarification of the utility of the Palliative Prognostic Index for advanced cancer patients in the home care setting

Introduction

Making prognostic predictions is one of the core skills of physicians engaged in end-of-life care,[1] and is a component of approaches to multidisciplinary palliative care.[2] In addition, patients with advanced cancer face difficult decisions regarding their treatment and choices related to end-of-life care.[3,4] Accurately predicting prognosis is therefore helpful not only for patients and their families, but also for healthcare professionals who support their decision making,[5] especially those in the home care setting.

In general, it is difficult to predict the prognosis of advanced cancer patients, especially those in the home care setting, because of limitations in the number of blood tests and radiological evaluations performed. Clinicians usually predict prognoses based on their own experience. A previous study revealed that prognostic prediction tools improved the accuracy of physicians' predictions.[6] Several prognostic prediction tools have been examined for cancer patients, for example the Palliative Prognostic Index (PPI),[7] Cancer Prognostic Scale,[7] Palliative Performance Scale,[8] Palliative Prognostic Score (PaP score),[9] Palliative Prognostic Score with Delirium (D-PaP score),[10] Japan Palliative Oncology Study-Prognostic Index (J-POS-PI),[11] and Prognosis in Palliative Care Study model,[12] and each was properly validated. These tools are intended for use in assessing inpatient and ambulatory patients, and the appropriateness of their application to advanced cancer patients in the home care setting is uncertain.

The PPI, which resulted in significant improvement in prognostication,[6] was defined

based on performance status assessment using the Palliative Performance Scale (PPSv2),[8] oral intake, and the presence or absence of dyspnea at rest, edema, and delirium. The PPI was developed and successfully validated for cancer patients in palliative care units by Morita et al in Japan.[13]

The PPI does not require blood tests or radiological evaluation, and would therefore be very useful for cancer patients in the home care setting as compared to other validated prognostic prediction tools. Each PPI component is assigned an individual score, and these are added to derive the overall score. The final PPI score classifies patients into 1 of 3 groups: those with survival predicted to be shorter than 3 weeks (PPI ≥6), shorter than 6 weeks (PPI ≥4), or longer than 6 weeks (PPI <4).

Previous studies[14] were performed prospectively and did not clarify the usefulness of the PPI in the home care setting. The aims of this study were thus to prospectively determine the sensitivity and specificity of the PPI in the home care setting and to evaluate the association of each PPI component with 3 and 6 weeks' prognostic prediction.

Methods

Our study population included all advanced cancer patients who received home visiting services regularly from Yamato Clinic between April 2010 and June 2012, and who died at home or in the hospital. Yamato Clinic provides ambulatory care and home visiting services for community residents, with 3 doctors (including one researcher: JH) specialized in family medicine and palliative care. The 3 doctors (including one researcher: JH) had trained to assess the PPI components and used the PPI in their usual practice. We recorded patients' background information and prospectively assessed the

components of the PPI at the first home visit: PPS score, oral intake, and the presence or absence of dyspnea at rest, edema, and delirium. One researcher (JH) calculated the PPI score and actual survival time when each patient died. Subsequently, we calculated overall sensitivity, specificity, and area under the curve (AUC) of the PPI. Survival predictions were defined as mentioned above: less than 3 weeks for PPI ≥6, and less than 6 weeks for PPI ≥4. In addition, we conducted univariable analyses to assess significant differences between 3- or 6-week survival and each PPI component.

To determine the association of each PPI component with 3 and 6 weeks' prognostic prediction, we used Student's t-test for continuous variables and Pearson's chi-square test or Fisher's exact test for categorical variables. All analyses were conducted using SPSS-J, ver.21.0, IBM, Tokyo, Japan.

This study was not confirmed by the institutional review board, but our study was performed according to the ethical guidelines for Epidemiological Research by the Ministry of Health, Labour and Welfare of Japan, and written informed consent was not necessary.

This study was conducted in conformity with the Declaration of Helsinki and was carried out with special regard for the protection of individual data.

Results

Sixty-six patients (48 males) were included in this study. Table 1 shows patient background information in detail. The mean patient age was 75.6 years, with 28 patients (42.4%) in their 70s and 15 patients (22.7%) in their 80s. The primary cancer site was the lung in 17 patients (15.8%), the stomach/esophagus in 12 patients (18.2%), and the colon/rectum/anus in 10 patients (15.2%).

The mean survival time after the first home visit was 72.9 days. Survival time was shorter than 3 weeks in 20 patients (30.3%) and shorter than 6 weeks in 34 patients (51.5%). Table 2 shows PPI scores and 3-week survival, and Table 3 shows PPI scores and 6-week survival. Eighteen patients (27.3%) had PPI scores ≥6, while 33 (50%) had PPI scores ≥4. Twelve patients with PPI scores ≥6 survived for less than 3 weeks, while 24 patients with PPI scores ≥4 survived for less than 6 weeks.

Table 4 shows the accuracy of the PPI for advanced cancer patients in the home care setting. Three-week survival was predicted with a sensitivity of 60% (95% CI, 39–78%), a specificity of 86.9% (95% CI, 74–94%), a positive predictive value of 66.7%, and a negative predictive value of 83.3%; the AUC was 74% (95% CI, 59–88%). Six-week survival was predicted with a sensitivity of 70.6% (95% CI, 54–83%), a specificity of 71.9% (95% CI, 55–84%), a positive predictive value of 72.7%, and a negative predictive value of 69.7%; the AUC was 67% (95% CI, 54–81%).

Table 5 shows the association of each PPI component with 3 and 6 weeks' prognostic prediction. We conducted univariable analyses concerning PPI components for patients who survived less than 3 weeks and less than 6 weeks. These analyses found that PPS, oral intake, dyspnea at rest, and delirium were statistically significant for patients who survived less than 3 weeks and less than 6 weeks.

Discussion

This study demonstrated three important findings. First, the sensitivity of the PPI for advanced cancer patients in the home care setting was lower than for advanced cancer patients in palliative care units. Morita et al[13] reported that the sensitivity of the PPI for advanced cancer patients in the hospice setting who survived less than 3 weeks and less

than 6 weeks was 83% and 79%, respectively. This finding is same as that of our previous retrospective study.[15] Maltoni et al[16] also reported a prospective comparison between several prognostic scores, including the PPI, in the hospice setting. They found that the sensitivity and specificity of PPI scores ≥5 in patients who survived for less than 3 weeks in the hospice setting were 73.7% and 67.1%, respectively. To the best of our knowledge, however, our study is the first to prospectively reveal the usefulness of the PPI for advanced cancer patients in the home care setting, while also pointing out the limitations of the utility of the PPI in this population and setting.

One possible reason for the discrepancy in PPI sensitivity between advanced cancer patients in the hospice setting and those in the home care setting is the differential prevalence of PPS ≤20 and delirium, which are the most heavily weighted scores in the PPI scoring system. In our study, the prevalence of PPS ≤20 in the home care setting was 4.5%, whereas Morita et al[13] and Maltoni et al[16] reported prevalence of 23% and 41.3%, respectively, in the hospice setting. This discrepancy suggests the possibility that home visiting services tend to be started at early stages for patients with advanced cancer, because whereas the median duration of survival was 40 days in our study, Morita et al[13] reported 27 days and Maltoni et al[16] reported 22 days in the hospice setting. Regarding the prevalence of delirium, our study revealed a prevalence of 18.2% in the home care setting, whereas Morita et al[13] and Maltoni et al[16] reported prevalence of 38% and 28.2%, respectively, in the hospice setting. This discrepancy may have two causes. First, we may have underdiagnosed delirium because we did not use routinely a specific assessment tool for its screening. Second, patients who have delirium may tend not to transfer from hospital to home care because management of delirium is commonly difficult in the home care setting. The prevalence of other symptoms in our

study, namely oral intake, edema, and dyspnea at rest, also differed compared to the hospice setting. In our study the prevalence of severely reduced oral intake, edema, and dyspnea at rest were 13.6%, 40.9%, and 16.7% respectively, although Morita et al[13] reported prevalence of 38%, 35.4%, and 18% and Maltoni et al[16] reported prevalence of 27.7%, 33%, and 24.4%, respectively. These discrepancies may suggest that patient background differs intrinsically between the home care setting and hospice setting. Therefore the low sensitivity of the PPI means that this instrument may not be suitable for detecting poor prognosis in patients with relatively good performance status, especially in the home care setting . In addition to the results above, we found that the specificity of PPI for advanced cancer patients in the home care setting was nearly 90% in our study for 3-week survival, the same as in our previous study.[15] These results support our previous suggestion that the PPI might not be useful as a screening tool for poor prognosis in the home care setting because of its low sensitivity, but might be useful with PPI scores <6, predicting survival longer than 3 weeks.

The second important finding of this study was that PPS, oral intake, dyspnea at rest, and delirium had statistically significant associations with survival durations of less than 3 weeks and less than 6 weeks for advanced cancer patients in the home care setting, while edema showed no significant correlation. This finding is in accordance with the EAPC recommendations regarding prognostic factors.[2] It is possible that no association was detected between edema and survival due to insufficient power resulting from the small sample size of this study. We must reevaluate this question using a larger sample size from this patient population before forming a definitive conclusion, because a previous study[11] showed that edema was significantly related to patient survival in the hospital setting.

The last important finding of this study was that all 14 patients with normal oral intake survived longer than 3 weeks. One possible reason may be that the nutritional status of the current study subjects with normal intake was maintained better than that of subjects in previous studies using inpatient settings. In the home care setting, patients can eat their favorite foods whenever they want, making it more likely that they can maintain a normal oral intake, which may lead to prolonged survival. A corollary to this is that there may be several disadvantages to using oral intake as a factor in predicting prognosis in the inpatient setting; for example, patients may not be served meals they like, and they may not express their meal preferences as easily as in the home care setting. Therefore we may mistakenly judge that patients in the inpatient setting may have decreased oral intake when in another setting they would in fact have normal oral intake.

This study has three limitations. First, our report may not be representative of advanced cancer patients in the home care setting because it was carried out in only one institution. Second, the population of this study was relatively small. These limitations restrict the generalizability of our results. Third, as we have already described above, we may have underdiagnosed delirium because we did not screen using a standardized specific assessment tool such as CAM (Confusion Assessment Method[17]). This may affect the accuracy of the PPI in the current study. To overcome these limitations, we should carry out a large multicenter study for advanced cancer patients using standard symptom assessment tools in the home care setting.

In conclusion, this study showed that the PPI had a lower sensitivity for advanced cancer patients in the home care setting than for those in palliative care units, though the specificity of the PPI for advanced cancer patients in the home care setting was nearly

90% for 3-week survival. Further research is needed to develop more accurate prognostic prediction tools for use in the home care setting.

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Table 1 Patient background (n=66)

		All patients (n=66)
		n (%)
Gender	Male	48 (72.7)
	Female	18 (27.3)
Mean age (years ± SD †)		75.6 ± 11.3
Range (years)		41–94
Age distribution	35–49	3 (4.5)
	50–59	1 (1.5)
	60–69	12 (18.2)
	70–79	28 (42.4)
	80–89	15 (22.7)
	90–	7 (10.6)
Primary cancer site	Lung	17 (25.8)
	Stomach/Esophagus	12 (18.2)
	Colon/rectum/anus	10 (15.2)
	Kidney/bladder	6 (9.1)
	Liver/Biliary system	6 (9.1)
	Pancreas	4 (6.1)
	Prostate	3 (4.5)
	Brain	3 (4.5)
	Breast	1 (1.5)
	Blood	1 (1.5)
	Others	3 (4.5)

† Standard Deviation

Table 2 PPI scores and 3-week survival

	< 3 weeks' survival	≥3 weeks' survival	Total
PPI ≥ 6	12 †	6	18
PPI < 6	8	40	48
Total	20	46	66

† Number of patients surviving <3 weeks with PPI scores >6

Table 3 PPI scores and 6-week survival

	< 6 weeks' survival	≥ 6 weeks' survival	Total
PPI ≥ 4	24 †	9	33
PPI < 4	10	23	33
Total	34	32	66

† Number of patients surviving <6 weeks with PPI scores >4

Table 4 Accuracy of PPI for advanced cancer patients in home care settings

	< 3 weeks (%)	< 6 weeks (%)
Sensitivity	60.0	70.6
Specificity	87.0	71.9
Positive Predictive Value	66.7	72.7
Negative Predictive Value	83.3	69.7
Area under the curve	74	67

Table 5 Univariable analyses for patients surviving <3 weeks and 6 weeks (n = 66)

Variable		< 3 weeks' survival (n = 20)	≥ 3 weeks' survival (n = 46)		< 6 weeks' survival (n = 34)	≥ 6 weeks' survival (n = 32)	
		n (%)	n (%)	P value	n (%)	n (%)	P value
Mean age (years ± SD †)		73.1 ± 10.7	76.6 ± 11.5	0.25[a]	72.4 ± 10.4	78.9 ± 11.4	0.019[a]
Sex	male	15 (75.0)	33 (71.7)	0.785[b]	26 (76.5)	22 (68.8)	0.482[b]
	female	5 (25.0)	13 (28.3)		8 (23.5)	10 (31.3)	
Palliative Performance Scale(PPSv2)[8)]	10–20	3 (15.0)	0	0.01[c]	3 (8.8)	0	0.001[c]
	30–50	16 (80.0)	36 (78.3)		30 (88.2)	22 (68.8)	
	60–	1 (5.0)	10 (21.7)		1 (2.9)	10 (31.3)	
Oral intake	Severely reduced	8 (40.0)	1 (2.2)	P<0.01[c]	8 (23.5)	1 (3.1)	0.006[c]
	Moderately reduced	12 (60.0)	31 (67.4)		23 (67.6)	20 (62.5)	
	Normal	0	14 (30.4)		3 (8.8)	11 (34.4)	
Edema	Present	11 (55.0)	16 (34.8)	0.125[b]	17 (50.0)	10 (31.3)	0.122[b]
	Absent	9 (45.0)	30 (65.2)		17 (50.0)	22 (68.8)	
Dyspnea at rest	Present	8 (40.0)	3 (6.5)	0.002[c]	9 (26.5)	2 (6.3)	0.028[b]
	Absent	12 (60.0)	43 (93.5)		25 (73.5)	30 (93.8)	
Delirium	Present	8 (40.0)	4 (8.7)	0.005[c]	11 (32.4)	1 (3.1)	0.002[b]
	Absent	12 (60.0)	42 (91.3)		23 (67.6)	31 (96.9)	

a:Student's t-test
b:Pearson's chi-square test
c:Fisher's exact test
† Standard Deviation