

Original Article

Change in Palliative Performance Scale (PPS) Predicts Survival in Patients with Terminal Cancer

Jee Hye Oh, M.D., Yong Joo Lee, M.D., Min Seok Seo, M.D.,
Jo Hi Yoon, M.D., Chul Min Kim, M.D. and Chung Kang, M.D.

Department of Family Medicine, The Catholic University of Korea College of Medicine, Seoul, Korea

Purpose: The Palliative Performance Scale (PPS) is a widely used prognostic tool in patients with advanced cancer. This study examines the association between changes in PPS score and survival in patients with advanced cancer. **Methods:** We identified a cohort of 606 inpatients who died at a Korean university hospital's hospice/palliative care center. For each patient, the PPS score was measured twice according to a standard procedure: 1) upon admission, and 2) three days after admission (D3). "Change on D3" was defined as a difference between initial PPS and PPS on D3. We used a Cox regression modeling approach to explore the association between this score change and survival. **Results:** The changes in scores were associated with survival. A score change of $>30\%$ yielded a hazard ratio for death of 2.66 (95% CI 2.19~3.22), compared to a score change of $\leq 30\%$. PPS of ≤ 30 on D3 also independently predicted survival, with a hazard ratio of 1.67 (95% CI 1.38~2.02) compared to PPS of >30 . **Conclusion:** A change of over 30% in PPS appears to predict survival in hospitalized patients with terminal cancer, even after adjustment for confounders. Changes in PPS may be a more sensitive indicator of impending death than a single PPS measured on the day of admission in terminal cancer patients. Further prospective study is needed to examine this important finding in other populations.

Key Words: Palliative care, Hospice care, Prognosis, Survival

INTRODUCTION

Prognostication in terminally ill patients is one of the major subjects in the palliative care study. Many objective and subjective prognostic factors were examined to evaluate prognostic value to the patients. To date, patient's performance status, diverse physical symptoms, biochemical markers, and other various subjective parameters were known as significant prognostic factors (1-9). Such prognostic factors provide more accurate clinical information about patients to their physicians. Among them, Palliative Performance Scale (PPS) is one of most commonly used tool to evaluate patient' (10), numerous studies showed prognostic value of PPS (7,11-15). PPS con-

sisted of five parameters (ambulation, activity and evidence of disease, self-care, intake, and level of consciousness) which are mainly focused on patient's physical function. While most studies concerned PPS at first time, recent study showed another possibility of PPS's prognostic value. Not only the PPS scale itself, but the changes of the PPS also showed prognostic value to terminally ill patients (16). In the study, the magnitude of change in PPS during the terminal stage is also significantly associated with patient's survival. Because physicians usually predict patients' survival time by the changes or declining pace of performance status, changes of PPS also contains possibility as an objective prognostic tool. The aim of this study is to evaluate the prognostic value of PPS changes and degree of PPS changes in terminal cancer inpatients.

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Correspondence to: Yong Joo Lee

Department of Family Medicine, The Catholic University of Korea College of Medicine, 222 Banpo-daero, Seocho-gu, Seoul 06591, Korea

Tel: +82-2-2258-6298, Fax: +82-2-2258-1903, E-mail: sharp1003@catholic.ac.kr

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METHODS

1. Study population

This is a retrospective cohort study of inpatients from Jan 2010 to Dec 2012 who died at a tertiary hospice/palliative care center in South Korea. Among the 800 patients, we reviewed medical record of 606 patients who were eligible to obtain demographic and clinical data including PPS scores at day 1 and day 3. One patient's data had absent information of age, sex, and type of cancer. The institutional review boards at Seoul St. Mary's Hospital has approved this study (IRB no. KC14RISI0074).

2. Study method

In this study, age, sex, type of cancer, PPS, and survival time were collected by the review of medical record. Survival time was defined as the duration between admission and expired date. PPS is a modified Karnofsky performance index that evaluates patients' performance status. It reflects five functional statuses: ambulation, degree of disease, self-care, oral intake, and consciousness. PPS ranged from 0% to 100% in 10% increment, with 100% defined as a normal and healthy state whereas 0% defined as death (10). PPS scores were measured twice as part of standard care: 1) on admission, and 2) after three days in the hospital (D3). 'Change at D3' was defined as the difference between initial PPS and PPS at D3, divided by initial PPS.

3. Statistical analysis

Frequencies and medians of clinical data were measured by descriptive statistics. Kaplan-Myer survival analyses for age, sex, type of cancer, PPS at admission, PPS at D3, PPS change at D3 were examined. Multivariate Cox regression analysis was performed to explore the association between PPS at D3, PPS changes at D3 and survival time adjusting for the influence of age, sex and primary cancer type. Statistical Package for Social Science ver. 16.02 (SPSS Inc., Chicago, IL, USA) was used for all statistical analyses. The significance level was a P value of <0.05 in all tests.

RESULTS

1. Demographic and clinical characteristics

Patient's age was divided into three groups as below 64, 65 to 74, and over 75 years. The number of patients below 64 year old were 345, 65 to 74 were 184, and over 75 were 76.

Table 1. Demographic and Clinical Characteristics (N=606).

Characteristic	N	%
Age (y)		
≤64	345	56.9
65~74	184	30.4
75≥	76	12.5
Missing	1	0.2
Sex		
Female	313	51.7
Male	292	48.2
Missing	1	0.2
PPS at admission		
10	15	2.5
20	21	3.5
30	71	11.7
40	178	29.4
50	188	31.0
60	99	16.3
70	34	5.6
PPS at D3		
0	81	13.4
10	27	4.5
20	40	6.6
30	73	12.0
40	170	28.1
50	125	20.6
60	65	10.7
70	25	4.1
Cancer type		
Lung	88	14.5
Stomach	121	20.0
Colorectal	95	15.7
Ovary/Cervix	41	6.8
Hepatobiliary	71	11.7
Pancreas	48	7.9
Esophagus	10	1.7
Head & Neck	23	3.8
Soft tissue	40	6.6
Renal/Bladder	13	2.1
Others	55	9.1
Missing	1	0.2
Survival days	9 (1, 65)	

PPS: Palliative Performance Scale.

The number of males was 292 and female was 313. The number of each PPS score at admission from 10% to 70% showed 15, 21, 71, 178, 188, 99, 34 and PPS at D3 from 0 to 70% showed 81, 27, 40, 73, 170, 125, 65, and 25 each. The most common cancer type was stomach cancer with 121 patients following 95 colorectal cancer, 88 lung cancer, 71 hepatobiliary cancer, 48 pancreas cancer, 41 ovary/cervix cancer. Median survival time of the patients was 9 day (Table 1).

2. Comparison of survival time of patients' age, sex, type of cancer, PPS at admission, PPS at D3, and changes in PPS at D3

Differences of survival time were analyzed by grouping age, sex, type of cancer, PPS at admission, PPS at D3, PPS changes at D3. Age, PPS at admission showed no significant differences of survival time. Sex, type of cancer, PPS at D3, and PPS changes at D3 showed significant differences of survival time. Female revealed 9 days of survival time which is longer than 8 days of male. Lung cancer and stomach/colorectal cancer had 9 days of median survival time while hepatobiliary/pancreas cancer showed 7 days of relatively shorter survival time. PPS at D3 below 30%, 40%, over 50% showed each 8.57, 12.68, and 13.02 days of different survival time. PPS changes at D3 over 30% showed 3.57 days of survival time while PPS changes below 30% showed 12.55 days of survival time.

3. Multivariate Cox proportional hazard model

Multivariate Cox regression analyses were examined to evaluate hazard ration of PPS at D3 and PPS changes at D3. Adjusting age, sex, and type of cancer, PPS at D3 below 30% showed significant higher hazard ratio of 1.67 and 40% showed insignificant hazard ratio compared with PPS at D3 50%. PPS changes at D3 over 30% showed significant higher hazard ratio of 2.66 compared with PPS changed at D3 below 30% (Table 2).

4. Kaplan-Meier estimates of overall survival of patients

Kaplan-Meier estimates of overall survival of patients were analyzed by grouping PPS at D3 and changes at D3. Patients

Table 2. Hazard Ratio Adjusted for Sex, Age and Cancer Type.

	Model 1 PPS at D3		Model 2 change at D3	
	Hazard ratio (95% CI)	P value*	Hazard ratio (95% CI)	P value*
PPS at D3				
≤30%	1.67 (1.38, 2.02)	<0.001	-	
40%	1.04 (0.85, 1.28)	0.699		
≥50%	Ref			
Change at D3				
>30%			2.66 (2.19, 3.22)	<0.001
≤30%			Ref	

PPS: Palliative Performance Scale.

*P value was derived from cox proportional hazard model using a standardized variable.

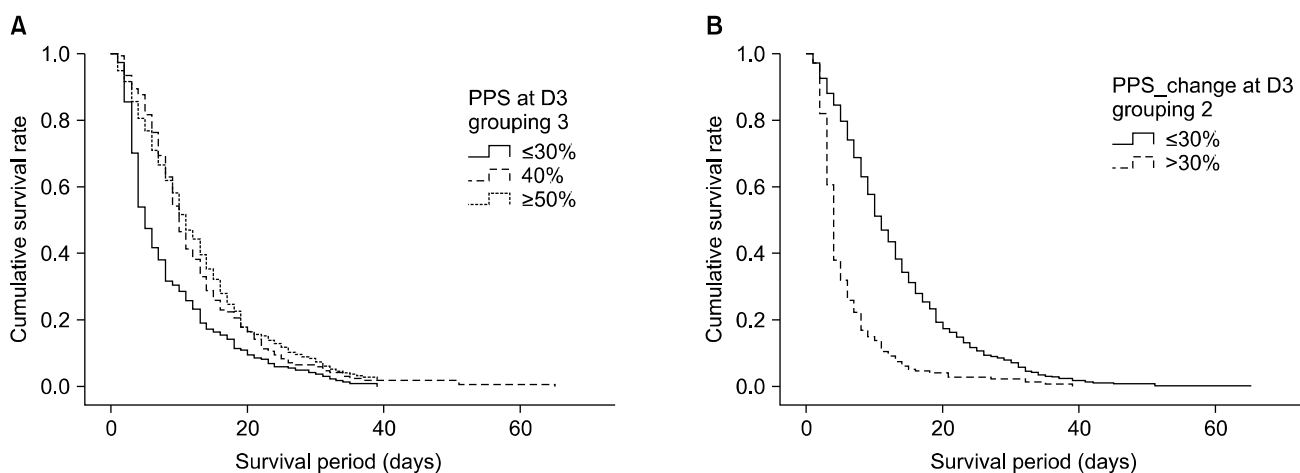


Figure 1. Kaplan-Meier estimates of overall survival of patients (A) PPS at D3 grouped by ≤30%, 40%, ≥50%; (B) PPS change grouped by ≤30% and >30%.

PPS: Palliative Performance Scale.

having PPS at D3 over 50% had significantly longer survival than those with PPS at D3 40% and below 30%. In addition, PPS changes at D3 over 30% showed shorter survival than those with changes below 30% (Figure 1).

DISCUSSION

Cross-sectional PPS were commonly used for evaluating patient's prognosis. However, pace of declining patient's condition often provide crucial information to predict appropriate prognosis. In this study, both change of PPS at D3 below 30% and degree of PPS changes at D3 over 30% were independent predictors of survival time when we adjusted for sex, age, and cancer type. Among the significant prognostic factors, degree of changes in PPS in D3 showed strongest hazard ratio. Our study also showed similar result with a previous study. Although PPS at admission was a strong predictor of survival, scores of PPS 10% through PPS 50%

also led to distinct survival curves that meant a larger increment in PPS change was associated with poorer survival time (16,17). However, PPS at admission showed no significant differences of survival time in each three PPS groups (Table 3). It is because of very short survival time that the mean survival time was lowest from 10.55 to highest 11.74 days in this study. The median survival time of all patients was even shorter than the Korea's nationwide median survival time of 18 days (18). These late referral to hospice and palliative care is one of the important issues of palliative care system in Korea (18) which result in relatively short duration of palliative care services than other countries (19). Moreover, admissions at impending death status, unexpected death, and long admission waiting times are thought to be other reasons of short survival time in this study.

Previous studies demonstrated that changes of performance status such as palliative prognostic index (PPI), Eastern Cooperative Oncology Group (ECOG), and PPS showed as an

Table 3. Survival Time by PPS at D3 and Change at D3 (N=606).

Variable	N	%	Survival time (days) median (95% CI)	Log rank P-value
Age (y)				0.54
≤ 64	345	56.9	8.00 (6.93, 9.07)	
65 ~ 74	184	30.4	9.00 (7.58, 10.42)	
≥ 75	76	12.5	9.00 (8.22, 9.79)	
Sex				0.02
Female	313	51.7	12.16 (11.00, 13.32)	
Male	292	48.2	10.40 (9.50, 11.30)	
Cancer type				0.02
Lung	88	14.5	9.00 (6.96, 11.04)	
Stomach+Colorectal	216	35.6	9.00 (7.73, 10.27)	
Hepatobiliary+Pancreas	119	19.6	7.00 (5.47, 8.53)	
Others	182	30.0	10.00 (8.24, 11.76)	
PPS at admission				0.43
≤ 30	107	17.7	10.55 (8.82, 12.28)	
40	178	29.4	10.96 (9.63, 12.29)	
≥ 50	321	53.0	11.74 (10.69, 12.79)	
PPS at D3				<0.001
≤ 30	221	36.5	8.57 (7.50, 9.64)	
40	170	28.1	12.68 (11.22, 13.13)	
≥ 50	215	35.5	13.02 (11.73, 14.32)	
Change at D3*				<0.001
≤ 30	522	86.1	12.55 (11.74, 13.36)	
> 30	84	13.9	3.57 (3.20, 3.94)	

PPS: Palliative Performance Scale.

*Change at D3=(PPS at admission-PPS at D3)/(PPS at admission)×100.

independent prognostic factor in patients with terminal cancer. Arai et al. (20) suggested that the change of PPI per day might be a useful marker to predict the survival of terminal cancer patient in palliative care unit. Another study reported that magnitude of PPI score change between day 1 and day 8 provided more accurate and reliable information related with survival predictions than day 1 PPI alone (21). Peng et al. (22) reported that sequential assessment of ECOG between day 1 and day 8 was more precise method for predicting survival time than initial assessment alone in terminal cancer patients who are receiving palliative care. Studies concerned with PPS also showed similar results with forementioned studies. Seow et al. (23) reported that the hazard ratio significantly increases 1.7 times with 10% decrease of PPS score in ambulatory cancer patients. Chan et al. (21) demonstrated that while PPS at admission showed no significant hazard ratio, the over 30% change of PPS showed significant hazard ratios by 3.14 and 7.66 at week 1 and with 2, respectively. Consistent with previous findings, our results revealed that PPS change even in 3 days assessment was significantly associated with survival in patients with terminal cancer.

There are few studies investigating prognosis of advanced cancer patients with rapid declining performance status. Studies are rather focused on associations between intractable symptoms and poor prognosis (24-27). Therefore, little is identified about the mechanisms or causal relationships between declining of performance status and prognosis. Limited data demonstrated that as the progression of primary cancer and metastasis gradually promote activation of inflammatory cytokines and interleukins, systemic symptoms such as fatigue, cachexia-anorexia, and decreased performance status are developing. Poor immune system and physical status are associated with complications such as severe sepsis, hemorrhage, embolism, and multiple organ failure which were known as major cause of death (28-36). By previous studies, rapid declining of patient's performance status appears to be a result of cancer progression, imbalanced immune system and unexpected complications. Rapid declining performance is also required both careful management of reversible factor and the possibility of death. Regular evaluation of PPS and PPS change may provide tailored information about the prognosis of impending death patients and enables physicians

establishing proper care plans. But it is uncertain that how often subsequent assessment is appropriate in terminal cancer patient. According to recent researchers, they agreed that it is optimal to reassess the functional status within 7 days (21,37). However, in practice physicians have to face more frequent and detailed assessment of numerous medical problems including PPS so that regular interval time may need more flexible consideration by medical environment and patient's survival time.

There are several limitations in this study. Because this study is performed in a single tertiary hospice/palliative hospital, the result cannot be a standard to general population. And we could not gain the whole data from the all patients admitted in same time due to a nature of retrospective studies. We could not analyze other prognostic factors (38-40). Prospective study needs longitudinal analyses of PPS changes among cancer type, cancer-related complication, and extension of metastasis are also required.

PPS changes, especially PPS changes more than 30% appears to be a prognostic factor in terminal cancer patients. Tailored estimation of PPS change is warranted to provide a useful prognostic tool in terminally ill patients.

요 약

목적: Palliative Performance Scale (PPS)는 진행성 암환자에서 널리 사용되는 예후도구이다. PPS 측정이 생존에 대한 예측을 의미하지만, 연속적인 PPS 측정에 대한 유용성은 추가적인 연구가 필요하다. 본 연구에서는 완화병동에 입원한 진행성 암환자를 대상으로 PPS score의 변화와 생존간의 연관성에 대해 진행한 연구이다.

방법: 2010년 1월부터 2012년 12월까지 서울성모병원 완화의학과에 입원한 환자 606에 대한 의무기록을 통하여 입원 당일의 PPS score와 입원 3일째의 PPS score 그리고, 두 score의 차이를 측정하여 점수의 변화와 생존간의 관련성을 분석하였다.

결과: PPS score의 변화와 생존과는 통계적으로 유의한 관련이 있었다. PPS score의 변화가 30% 이하인 군과 비교하였을 때, 30% 초과된 군에서 hazard ratio가 2.66 (95% CI 2.19~3.22)로 확인되었다. 입원 3일째 PPS score가 30% 이하인 경우 독립적으로 생존에 대한 예측이 가능하였으며, PPS score 30% 초과된 군과 비교했을 때 hazard ratio는 1.67 (95% CI 1.38~2.02)로 확인되었다. 입

원 당시의 PPS score는 생존과 독립적인 관련성은 없었다.

결론: 후향적으로 의무기록 분석을 통해 이루어진 본 연구에서 30% 이상의 PPS score 변화는 입원중인 말기 암환자의 생존과의 관련이 확인되었다. 입원 당시의 PPS score는 생존을 예측하지 못했다. PPS score의 변화는 말기암환자에서 단일 PPS score 측정보다 더 민감한 지표일 수 있다. 차후 더 많은 환자들에서 이에 대한 다기관, 전향적 연구가 필요하다.

중심단어: 완화의료, 호스피스, 예후, 생존

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