Clinicians’ Prediction of Survival and Prognostic Confidence in Patients with Far- Advanced Cancer in Three East Asian Countries

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Research Article

Keywords: Clinicians' prediction of survival, accuracy, prognosis, advanced cancer, palliative care

Posted Date: April 7th, 2022

DOI: https://doi.org/10.21203/rs.3.rs-1512099/v1

Abstract

Purpose: This study aims to examine accuracy of CPS for 7-, 21-, and 42-day survival of inpatients with far-advanced cancer in 37 palliative care units in Japan, Korea, and Taiwan and its association with prognostic confidence.

Methods: In this study, discrimination of CPS was investigated through sensitivity, specificity, overall accuracy, and area under the receiver operating curves (AUROCs) according to 7-, 21-, and 42-day survival. The accuracies of CPS were compared with those of Performance Status-based Palliative Prognostic Index (PS-PPI) in three timeframe prediction. Clinicians were instructed to rate confidence level for each prediction on a 0–10-point scale.

Results: A total of 2,571 patients were analyzed. Among the three time-frames, the specificity was highest at 93.2–100.0% for the 7-day CPS and sensitivity was highest at 71.5–86.8% for the 42-day CPS. The AUROCs of the 7-day CPS were 0.88, 0.94, and 0.89 while those of PS-PPI were 0.77, 0.69, and 0.69 for JP, KR, and TW, respectively. In all timeframe, CPS was more accurate than the PS-PPI. As for 42-day prediction, sensitivities of PS-PPI were higher than those of CPS. Clinicians' confidence was strongly associated with the accuracy of prediction in all three countries (all p values <0.01).

Conclusions: CPS accuracies were highest (0.88 -0.94) for the 7-day survival prediction. CPS was more accurate than PS-PPI in all timeframe prediction. Meanwhile, PS-PPI can be a screening tool in 42-day survival prediction which may be supplementary to CPS. Prognostic confidence was significantly associated with the accuracy of CPS.

Introduction

Accurate prognostication is vital for patients with advanced cancer and their families in palliative care. It allows them to prepare themselves by sharing an appropriate clinical decision-making or reallocating their resources in a limited time. Palliative clinicians can play a dynamic role in the communication and realignment of palliative care goals based on patients' expected survival. Successful prognosis-based hospice palliative care depends on the clinician's ability to accurately estimate survival [1–3]. Prognostication is one of the most challenging tasks for palliative care clinicians because of its inherent uncertainty. Clinicians may predict the survival of patients with far-advanced cancer using clinician prediction of survival (CPS) or well-known prognostic tools.

However, most clinicians have used CPS as a quick prognostic indicator in the palliative care field despite the availability of validated prognostic tools [4, 5]. Asking the temporal question (TQ) "How much time will this patient have?" [1] is the most common approach among the three types of CPS: TQ, surprise question (SQ), and probabilistic question (PQ). However, previous studies have reported that CPS is likely to be significantly optimistic in estimating patient survival [6, 7]. The TQ type of CPS is known to be approximately 20–30% of accuracy compared to the actual survival [8–10]. The accuracy of CPS has been influenced by clinician-related factors, such as lack of knowledge on survival of patients under palliative care, duration of the doctor-patient relationship, and training status on prognostication [11]. Palliative clinicians are trained and experienced in predicting patient survival. More experienced clinicians are less likely to commit an error in prognostication than less experienced clinicians [12, 13]. However, a study investigating whether the clinician's prognostic confidence in predicting survival can influence CPS has not been conducted yet. To date, most studies assessing the accuracy of prognostication using CPS have been conducted in Western countries [1, 10]. Little is known about CPS in East Asian countries.

The time frame of the prognosis, such as the last days or 6-month survival, affects the overall accuracy. Usually, limiting the specific time frame has been found to be influenced the accuracy of PQ. Previously, CPS was known to be inaccurate in preceding studies[7, 8, 14, 15]. However, a recent study showed that CPS was accurate in patients with weeks of survival under palliative care [16]. It is under-investigated whether various timeframes influence TQ in palliative care setting.

The Performance Status-Based Palliative Prognostic Index (PS-PPI) is a simplified version to assess performance status of the original PPI. It is an easy-to-use scoring system for survival prediction since it does not require CPS and laboratory data, either. A previous study reported that the PS-PPI was as accurate as the original PPI in patients with advanced cancer [17]. Till now, Palliative Prognostic Score (PaP) is the most commonly used tool and regarded as one of gold standards in prognostication. However, PaP requires CPS, thus it would be hard to compare PaP with CPS due to its subjective nature. Since we sought an objective tool to complement the limitation of CPS. Therefore, we chose PS-PPI as a simple and objective tool according to our aim. We aimed to investigate the accuracy of TQs for 7-, 21-, and 42-day survival of inpatients with far-advanced cancer in Japan (JP), Korea (KR), and Taiwan (TW). Also the accuracies of TQs for 21-, and 42-day survival prediction were compared to PS-PPI.

Methods

Participants

The present study was a part of the East Asian collaborative cross-cultural Study to Elucidate the Dying process (EASED), which aimed to investigate the dying process and end-of-life care of patients admitted in palliative care units (PCUs) nationwide in JP, KR, and TW. All observations were performed in routine clinical practice. We followed up discharged patients for 6 months from PCU admission in JP and TW and from PCU discharge in KR. Eligible patients were consecutively enrolled in the study if they had been newly admitted to participating PCUs during the study period. The inclusion criteria were: a diagnosis of far-advanced cancer, aged ≥ 18 years in JP and KR and > 20 years in TW, and new admission to participating PCUs. Patients planning to be discharged within 1 week and those who refused to participate in this study were excluded.

This study was conducted in accordance with the Declaration of Helsinki Ethical Principle and Good Clinical Practices. Informed patient consent was waived in JP because of the observational nature of the study. Informed consent was obtained from the patients or their families (if the patient lacked the capacity to make decisions) in KR and TW. The study obtained approval from the local institutional review boards of all participating institutions.

Measurements

The CPS was evaluated using the TQ at study enrollment. The palliative care physicians formulated the CPS by asking the TQ “What is the approximate survival for this patient (in days)?,” which was answered by a specific time frame (e.g., 7 days and 28 days). The performance-based Palliative Prognostic Index (PS-PPI)[17] score was calculated to compare the accuracy for survival prediction. The range of PS-PPI scores is from 0 to 15. The PS-PPI score was calculated by summing the scores of the Eastern Cooperative Oncology Group Performance Status (ECOG PS) scores instead of Palliative Performance Scale in PPI, oral intake, delirium, dyspnea at rest, and edema. A PS-PPI score of more than 6 predicts survival of less than 21 days, and a score of more than 4 predicts survival of less than 42 days. We defined survival time as mortality in and outside of hospitals, and it was calculated from death date minus admission date in case of death or last follow-up date minus admission date in patients who were alive at follow-up. Clinicians were instructed to rate their level of confidence for each survival prediction on a

0–10-point scale (0: not at all, 10: very confident). Additionally, we collected clinician's characteristics as follows[18]: clinician's sex, clinical experiences (years), clinical experience in palliative care (years), number of far-advanced cancer patients treated in a year, and specialty (internal medicine, surgery, anesthesiology, palliative care, family medicine, or others [multiple choices were allowed]). We also recorded patients' demographic and clinical characteristics, including age, sex, primary cancer site, highest educational level, living arrangement, marital status, and religion.

Data analysis and statistics

Descriptive analyses were performed to summarize patients' baseline characteristics. The median survival time and 95% confidence interval (CI) were calculated using the Kaplan-Meier method. The CPS was categorized into three timeframes, 7-, 21-, and 42-day survival. The PS-PPI score was categorized as risk groups according to the validation study ($\leq$ 4.0, 4.5-6.0, $\geq$ 6.5)[17]. We calculated the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), overall accuracy to compare the performance of CPS and PS-PPI in 21-day and 42-day survival. Since PS-PPI aimed to predict 21-day and 42-day survival, it was impossible to compare performance of CPS and PS-PPI for 7-day timeframe. However, area under the receiver operating characteristics curves (AUROCs) were yielded in all three timeframes for CPS and PS-PPI. As for AUROCs, CPS and PS-PPI were dealt as continuous variables. Spearman's correlation was used to explore relationship between CPS and actual survival according to the level of prognostic confidence in the three countries. All statistical analyses were performed using International Business Machines (IBM) Statistical Package for the Social Sciences Statistics Program for Windows (version 21.0; IBM Corp., Armonk, NY, USA), and a p-value < 0.05 was considered statistically significant.

Results

A total of 2,685 patients with cancer were recruited across 38 PCUs (23 in JP, 11 in KR, and 4 in TW) from January 2017 to September 2018. However, 2,638 patients' data were available because a small portion of data were lost (JP: 30, KR; 17). Of these, 55 patients were excluded because of insufficient follow-up data (JP: 16, KR: 29, TW: 10), and 12 patients were excluded because of missing data on death date (JP: 6, KR: 1, TW: 5). Thus, 2,571 (JP: 1,874, KR: 305, TW: 392) patients were evaluated. Patients' baseline characteristics are summarized in Table 1. The study subjects included 1,332 men (JP: 951 [50.7%], KR: 166 [54.4%], TW: 215 [54.8%]) and 1,239 women (JP: 923 [49.3%], KR: 139 [45.6%], TW: 177 [45.2%]). The median survival times were 18 (95% confidence interval (CI): 16.9–19.4), 22 (95% CI 19.0–25.0), and 14 (95% CI 12.1–15.9) days in JP, KR, and TW, respectively. Among the 2,571 patients, 2,465 (95.9%) died at 6 months after discharge (JP: 1,808 [96.5%], KR: 296 [97.0%], TW: 361 [92.1%]).

Table 1
Baseline and Clinical Characteristics of the Patients (n = 2571)

	Japan (n = 1874)	Korea (n = 305)	Taiwan (n = 392)
Age (years, mean ± SD)	72.4 ± 12.3	68.2 ± 12.3	66.7 ± 13.7
Gender			
Male	951 (50.7)	166 (54.4)	215 (54.8)
Female	923 (49.3)	139 (45.6)	177 (45.2)
Primary cancer site			
Lung(small cell), Lung(non-small cell)	316 (16.8)	47 (15.4)	75 (19.2)
Stomach, Esophagus, Colon, Rectum, Small intestine,	513 (27.4)	86 (28.2)	80 (20.4)
Liver/ intrahepatic/cholangiocarcinoma, Gallbladder/bile duct, Pancreas	358 (19.1)	89 (29.2)	95 (24.3)
Peritonium, Lymph node, Blood, Myeloma, Thyroid, Bone/soft tissue, Thymus, Mesothelioma, Skin, Unknown, Other, Brain	233 (12.3)	31 (10.3)	38 (10)
Breast, Cervix, Uterine, Ovary	248 (13.2)	31 (10.2)	34 (8.7)
Kidney, Renal pelvis/Ureter, Bladder, Prostate	139 (7.4)	14 (4.6)	26 (6.6)
Head/ neck (excluding thyroid)	67 (3.6)	7 (2.3)	44 (11.2)
Highest level of education			
≤Junior high	57 (3.1)	140 (46.0)	217 (55.0)
High school	138 (7.4)	106 (34.8)	88 (22.4)
≥ Some college	167 (8.9)	52 (17.0)	80 (20.4)
Other	2 (0.1)	0 (0)	1 (0.3)
Unknown	1510 (80.6)	7 (2.3)	5 (1.3)
Living with family			
No	493 (26.3)	36 (11.8)	30 (7.7)
Yes	1359 (72.5)	269 (88.2)	362 (92.3)
Missing	22 (1.2)	0 (0)	0 (0)
Data were expressed as numbers (%)			
Abbreviation: SD, Standard deviation; CI, Confidence Interval; ECOG Eastern Cooperative Oncology Group; PS-PPI, Performance-Status based Palliative Prognostic Index			

	Japan (n = 1874)	Korea (n = 305)	Taiwan (n = 392)
Marital status			
Unmarried/widowed/divorced	713 (38.0)	98 (32.2)	151 (38.4)
Married	1137 (60.7)	207 (67.9)	241 (61.5)
Missing	24 (1.3)	0 (0)	0 (0)
Religion			
No religion	809 (43.2)	109 (35.7)	52 (13.3)
Buddhism	203 (10.8)	67 (22.0)	109 (27.8)
Christianity	37 (2.0)	123 (40.3)	24 (6.1)
Others	26 (1.4)	6 (2.0)	204 (52.2)
Unknown	777 (41.5)	0 (0.0)	3 (0.8)
Missing	22 (1.2)	0 (0)	0 (0)
Survival status			
Mortality at 6-month follow up	1808/1874 (96.5)	296/305 (97.0)	361/392 (92.1)
Median survival time (days, 95% CI)	18 (16.6–19.4)	22 (19.0–25.0)	14 (12.1–15.9)
ECOG performance status			
0–1	23 (1.2)	21 (6.9)	11 (2.8)
2	154 (8.2)	60 (19.7)	23 (5.9)
3–4	1697 (90.6)	224 (73.4)	358 (91.3)
Oral intake			
Normal	330 (17.6)	56 (18.7)	111 (28.3)
Reduced but more than mouthfuls	976 (52.1)	157 (52.3)	152 (38.8)
Mouthfuls	566 (30.2)	87 (29.0)	129 (32.9)

Data were expressed as numbers (%)

Abbreviation: SD, Standard deviation; CI, Confidence Interval; ECOG Eastern Cooperative Oncology Group; PS-PPI, Performance-Status based Palliative Prognostic Index

	Japan (n = 1874)	Korea (n = 305)	Taiwan (n = 392)
Edema			
Absent	905 (48.3)	174 (58.0)	196 (50.0)
Present	968 (51.7)	126 (42.0)	196 (50.0)
Dyspnea at rest			
Absent	1530 (81.6)	264 (89.8)	280 (71.4)
Present	344 (18.4)	30 (10.2)	112 (28.6)
Delirium			
Absent	1571 (83.8)	264 (86.8)	275 (70.2)
Present	303 (16.2)	40 (13.2)	117 (29.8)
PS-PPI risk groups			
≤ 4.0	220(11.8)	72(24.5)	51(13.0)
4.5-6.0	756(40.4)	114(38.8)	87(22.2)
≥ 6.5	895(47.8)	108(36.7)	254(64.8)
Data were expressed as numbers (%)			
Abbreviation: SD, Standard deviation; CI, Confidence Interval; ECOG Eastern Cooperative Oncology Group; PS-PPI, Performance-Status based Palliative Prognostic Index			

The sensitivity, specificity, PPV, NPV, and accuracy of the 7-, 21-, and 42-day time frames of the responses of TQ form of CPS and PS-PPI are listed in Table 2. The sensitivity, specificity, PPV, NPV, and overall accuracy of the responses of CPS TQs were different by time frame. The sensitivities were highest (71.5–86.8%) for the 42-day prediction of CPS and specificities were highest (93.2–100.0%) for the 7-day prediction of CPS. The sensitivities were higher (83.9–93.0%) for the 42-day prediction of PS-PPI. The overall accuracies for the 7-, 21-, and 42-day CPS were 81.6–85.9%, 71.6–75.5%, and 71.5–80.4%, respectively. The overall accuracies for the 21- and 42-day PS-PPI were 60.2%-67.0% and 75.1%-79.1%, respectively. The AUROCs in CPS of the 7-day were 0.88 (95% CI 0.85–0.90), 0.94 (95% CI 0.91–0.97), and 0.89 (95% CI 0.85–0.93) in JP, KR, and TW, respectively. The AUROCs in PS-PPI of the 7-day were lower than those of CPS as 0.77 (95% CI 0.74–0.79), 0.69 (95% CI 0.62–0.77), and 0.69 (95% CI 0.64–0.75) in JP, KR, and TW, respectively. The AUROCs in CPS of the 21-day in JP, KR, and TW were 0.84 (0.82–0.86), 0.80 (0.75–0.85), and 0.81 (0.77–0.85) and those of the 42-day were 0.84 (0.82–0.86), 0.79 (0.73–0.84), and 0.80 (0.75–0.85), respectively. The AUROCs in PS-PPI of the 21-day were 0.73 (95% CI 0.70–0.75), 0.65 (95% CI 0.59–0.72), and 0.70 (95% CI 0.64–0.75) in JP, KR, and TW, respectively. The AUROCs in PS-PPI of the 42-day in JP, KR, and TW were 0.71 (0.68–0.74), 0.65 (0.57–0.73), and 0.74 (0.67–0.80).

Table 2
Performance and AUROCs of Clinicians' Prediction of Survival and Performance Status-Based Palliative Prognostic Index for 7-day, 21-day and 42-day Survival in Three Countries

Time Frame	Variable/ Country	Prevalence (n, %)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Overall Accuracy (%)	AUROC
7-day prediction	CPS/Japan	467/1874 (24.9)	46.7 (42.1–51.3)	93.2 (91.7–94.4)	69.4 (64.7–73.8)	84.0 (82.9–85.2)	81.6 (79.8–83.3)	0.88 (0.85–0.90)
	PS-PPI/ Japan		-	-	-	-	-	0.77 (0.74–0.79)
	CPS/Korea	58/305 (19.0)	25.9 (15.3–39.0)	100.0 (98.5–100.0)	100.0 (-)	85.2 (83.2–87.0)	85.9 (81.5–89.6)	0.94 (0.91–0.97)
	PS-PPI/ Korea		-	-	-	-	-	0.69 (0.62–0.77)
	CPS/Taiwan	117/392 (29.8)	54.7 (45.2–63.9)	94.9 (91.6–97.2)	82.1 (72.8–88.7)	83.1 (80.1–85.8)	82.9 (78.8–86.5)	0.89 (0.85–0.93)
	PS-PPI/ Taiwan		-	-	-	-	-	0.69 (0.64–0.75)
21-day prediction	CPS/Japan	1027/1874 (54.8)	71.4 (68.5–74.1)	80.4 (77.6–83.0)	81.5 (79.3–83.6)	69.9 (67.7–72.0)	75.5 (73.4–77.4)	0.84 (0.82–0.86)
	PS-PPI/ Japan		63.6 (60.5–66.5)	71.2 (68.1–74.3)	72.8 (70.5–75.1)	61.7 (59.5–63.9)	67.0 (64.8–69.2)	0.73 (0.70–0.75)
	CPS/Korea	149/305 (48.9)	57.7 (49.4–65.8)	84.6 (78.0-89.9)	78.2 (70.8–84.2)	67.7 (63.2–71.9)	71.6 (66.1–76.5)	0.80 (0.75–0.85)

Data were presented % values with (95% confidence intervals) except prevalence.

Prevalence is defined death events in each time frame per total study population.

PPV: positive predictive value; NPV: negative predictive value; AUROC: Area under receiver operating characteristics curve

PS-PPI: Performance status-based Palliative Prognostic Index, calculated by Eastern Cooperative Group performance status + reduced oral intake + resting dyspnea + edema in lower extremities + delirium, range 0–15.

Time Frame	Variable/ Country	Prevalence (n, %)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Overall Accuracy (%)	AUROC
	PS-PPI/ Korea		47.1 (38.7–55.8)	72.7 (64.9–79.6)	62.3 (54.8–69.3)	58.9 (54.5–63.4)	60.2 (54.4–65.9)	0.65 (0.59–0.72)
	CPS/Taiwan	250/392 (63.8)	72.4 (66.4–77.9)	76.8 (68.9–83.4)	84.6 (80.1–88.2)	61.2 (55.9–66.3)	74.0 (69.3–78.3)	0.81 (0.77–0.85)
	PS-PPI/ Taiwan		74.4 (68.5–79.7)	52.1 (43.6–60.6)	73.3 (69.4–76.7)	53.6 (47.0-60.1)	66.3 (61.4–71.0)	0.70 (0.64–0.75)
42-day prediction	CPS/Japan	1405/1874 (75.0)	86.8 (84.9–88.5)	61.2 (56.6–65.6)	87.0 (85.7–88.3)	60.7 (57.0-64.2)	80.4 (78.5–82.1)	0.84 (0.82–0.86)
	PS-PPI/ Japan		93.0 (91.9–94.6)	26.9 (23.0-31.2)	79.3 (78.4–80.2)	57.3 (51.2–63.1)	76.7 (74.7–78.6)	0.71 (0.68–0.74)
	CPS/Korea	228/305 (74.8)	71.5 (65.2–77.3)	71.4 (60.0-81.2)	88.1 (83.8–91.4)	45.8 (39.7–52.1)	71.5 (66.1–76.5)	0.79 (0.73–0.84)
	PS-PPI/ Korea		83.9 (78.4–88.6)	48.7 (37.0-60.4)	82.9 (79.5–85.9)	50.5 (41.1–59.9)	75.1 (69.7–79.9)	0.65 (0.57–0.73)
	CPS/Taiwan	309/392 (78.8)	86.1 (81.7–89.7)	56.6 (45.3–67.5)	88.1 (85.2–90.5)	52.2 (43.9–60.5)	79.9 (75.5–83.7)	0.80 (0.75–0.85)
	PS-PPI/ Taiwan		91.9 (88.3–94.7)	31.3 (21.6–42.4)	83.3 (81.1–85.2)	51.0 (38.9–63.0)	79.1 (74.7–83.0)	0.74 (0.67–0.80)

Data were presented % values with (95% confidence intervals) except prevalence.

Prevalence is defined death events in each time frame per total study population.

PPV: positive predictive value; NPV: negative predictive value; AUROC: Area under receiver operating characteristics curve

PS-PPI: Performance status-based Palliative Prognostic Index, calculated by Eastern Cooperative Group performance status + reduced oral intake + resting dyspnea + edema in lower extremities + delirium, range 0–15.

Table 3 shows the characteristics of 180 clinicians (JP: 87, KR: 29, TW: 64) participating in this study. The study included 106 male clinicians (JP: 66 [75.9%], KR: 8 [27.6%], TW: 32 [50.0%]). Clinicians' clinical backgrounds, such as specialty, clinical experiences, and clinical experience in palliative care, varied in the three countries. The most common specialty of Japanese clinicians was palliative care, but it was family medicine for Korean and Taiwanese clinicians. The clinical and palliative care careers of Taiwanese clinicians were slightly shorter than those of Japanese or Korean clinicians because nearly 50% of Taiwanese physicians were resident physicians in this study. There were no differences in the number of patients with far-advanced cancer treated in one year among clinicians in the three countries.

Table 3
General Characteristics of the Participating Clinicians in Three Countries (n = 180)

	Japan (n = 87)	Korea (n = 29)	Taiwan (n = 64)
Gender (male)	66 (75.9)	8 (27.6)	32 (50.0)
Specialty			
Internal medicine	13 (15.1)	5 (17.2)	1 (1.6)
Palliative care	60 (69.8)	0 (0.0)	18 (28.1)
Family medicine	4 (4.7)	22 (75.9)	51 (79.7)
Others	9 (10.5)	2 (6.9)	11 (17.2)
Clinical experiences (years)	11.2 ± 6.6	12.7 ± 7.8	5.8 ± 3.5
Clinical experiences of palliative care (years)	5.5 ± 5.1	6.8 ± 5.5	2.8 ± 3.1
Number of patients with far advanced cancer seen in a year	101.3 ± 104.7	129.3 ± 151.9	111.1 ± 141.3
Level of prognostic confidence (0–10)	4.59 ± 1.80	5.94 ± 1.26	6.03 ± 1.40
Data were expressed as numbers (%) or mean ± standard deviation.			

Although there were some variations in the clinician's prognostic confidence in predicting survival in the three countries, clinician's prognostic confidence was strongly associated with accuracy of prediction ($p < 0.01$) in all countries. Additionally, clinicians showed a stronger correlation between the estimated survival and actual survival time of the patients when they had a higher level of prognostic confidence in CPS (Table 4). Participated clinicians had significantly higher levels of prognostic confidence in patients with lower KPS (0–20) compared than higher KPS (30–40, ≥ 50) (all p values < 0.001) (Fig. 1). And prognostic confidence was significantly higher when patients had shorter survival (< 3-week) compared than patients with longer survival (3–6 weeks, ≥ 6-week) (all p values < 0.001) (Fig. 2).

Table 4
Spearman's Correlation of Clinicians' Prediction of Survival and Actual Survival according to Level of Confidence in Three Countries.

Country	Level of Confidence	n	Correlation coefficient	P value
Japan	Low tertile	643	0.63	< 0.01
	Mid tertile	668	0.67	< 0.01
	High tertile	563	0.76	< 0.01
	Total	1874	0.70	< 0.01
Korea	Low tertile	131	0.51	< 0.01
	Mid tertile	68	0.61	< 0.01
	High tertile	106	0.70	< 0.01
	Total	305	0.61	< 0.01
Taiwan	Low tertile	121	0.48	< 0.01
	Mid tertile	142	0.65	< 0.01
	High tertile	129	0.76	< 0.01
	Total	392	0.65	< 0.01

Clnicians' confidence was measured by numeric rating scale from 0 (not at all) to 10 (full of confidence).

Tertile was grouped by dividing numeric rating scale 0–3/4–5/6–10 for Japan, NRS 0–5/6/7–10 for Korea and Taiwan, respectively.

Discussion

This study showed that the CPS was more accurate as the PS-PPI in predicting patients' survival at 7 days, 21 days and 42 days. Interestingly, the specificities of the TQ form of CPS were better than those of PS-PPI at 21-day prediction, whereas the sensitivities of PS-PPI were better than those of CPS at 42-day prediction. The CPS showed highest accuracy in 7-day prediction. As a novel finding, clinicians' confidence in CPS was strongly associated with accuracy in all three countries. Also prognostic confidence was higher when performance status is lower (KPS ≤ 20) and survival is shorter (< 3 weeks).

The accuracies of CPS in this study were higher than those in previous studies[8, 10]. Researchers have reported that the TQs of CPS had 23–78% accuracies with wide variation [10, 11, 19] and were comparable to well-validated tools, such as the Palliative Prognostic Score (PaP) or PPI [13]. A recent study showed a similar accuracy of the TQ compared to PaP and PPI [16]. In this study, TQ showed superior accuracies compared than those of PS-PPI in all time predictions in all three countries. The TQ has been suggested to be relatively accurate in patients with a more predictable trajectory and experienced clinicians [15, 20]. Considering that our study population comprised patients with far-advanced cancer with a short median survival time of a few weeks, they may have had a more predictable clinical course than in recent studies. Additionally, in this study, experienced clinicians estimated patient survival. The SQ or PQ is known to be more accurate than the temporal approach [1, 10]. However, this study proved the similar accuracy of the TQ by limiting the time frame.

PS-PPI had higher sensitivities than TQ in 42-day prediction. Attributed to the higher sensitivities in 42-day prediction, PS-PPI would be helpful in determining the time of the referral to palliative care. Especially for inexperienced clinicians, PS-PPI can aid clinical decision to refer to palliative care timely and may augment their prognostic confidence. For experienced clinicians, an objective approach such as PS-PPI may be useful to reduce subjective variations and enhance reproducibility. In the 21-day prediction, CPS showed better sensitivities than PS-PPI. This time frame could be helpful to determine when patients should admit to PCUs in three East Asian countries.

Our study showed that the TQ had the highest overall accuracy of approximately 83% for 7-day survival in the three countries. The highest accuracy of the 7-day prediction is related to the horizon effect [10]. The horizon effect means that imminently occurring events are easier to predict, and it is similar to weather broadcasting [20, 21]. The concept of the horizon effect is that clinicians can be more accurate in recognizing a shorter prognosis than a longer prognosis. We confirmed that CPS showed higher accuracies than those of PS-PPI in the 7-day prediction also. A previous study consistently reported that the TQ for 7-day survival is more accurate than other prognostic tools because of the physical signs of impending death [16]. Multiple highly specific tell-tale signs of impending death are pulselessness of the radial artery, Cheyne-Stokes breathing, respiration with mandibular movement, and death rattle [22]. The investigators reported that strong signs of impending death were observed relatively infrequently in the last 3 days of life. Clinicians often rely on these signs of impending death for prediction. This may explain why CPS had low sensitivity but high specificity for the 7-day time frame. Considering high specificity of CPS, clinicians can rule out death of patients in the last week of life more confidently. On the contrary, clinicians should pay attention to other prognostic tools such as Palliative Performance Scale to guide families and friends to prepare for loved ones' imminent death.

The accuracy of CPS was associated with clinicians' prognostic confidence in our study. To the best of our knowledge, this is the first study to evaluate the association between clinicians' prognostic confidence and the accuracy of CPS.

Interestingly, we found that the clinician's prognostic confidence significantly increased as survival duration was shorter (< 3 weeks) or the performance status was worse (KPS 0 ~ 20). It is well known that the accuracy of CPS is higher when survival is less than 3weeks and/or when performance status is low[10]. Performance status is the single most important factor which determines survival duration. And patients with advanced cancers suffers various symptoms in last weeks of life[23]. The increment of symptom burden and decline of function at that time make it easier for physicians to predict the patient's survival, thus accuracy of CPS can improve. However, no preceding studies related to the accuracy of CPS and prognostic confidence. Therefore, our study is the first one which revealed that prognostic confidence strengthened in proportion to accuracy of CPS.

Previous studies have reported that there was no difference in the accuracy of prognostication between Western and Eastern countries [8, 10, 24]. Until now, there has been insufficient information regarding the cultural differences in clinicians' prognostic confidence between Western and Eastern countries. It is known that East Asian countries have unique cultural characteristics in end-of-life care [25]. When clinicians are eager to provide an accurate estimate of the final day of life, they tend to experience more difficulties and have lower prognostic confidence [26].

Previous studies have reported that young clinicians with less clinical experience were more likely to have prognostic error in an optimistic direction than clinicians with more clinical experience[27]. Previous studies reported that clinicians' confidence increased according to clinical experience in predicting survivals in patients with advanced cancer [26, 28]. In TW, half of resident clinicians participated in this study in all institute. However, all of them received supervision from attending physicians in terms of CPS. The clinicians' prognostic confidence might be interrelated to the accuracy of CPS especially when patients lacked clinical signs or symptoms to predict survival. Further researches are necessary to evaluate the role of clinicians' prognostic confidence in the accuracy of survival prediction in various settings.

The strengths of this study are as follows: We enrolled a large number of patients from three East Asian countries. This study confirmed the superior accuracy of CPS by using time frames-such as 7 days,21 days and 42 days, as a common form of TQ. We also support the suggestion of Hui et al. that TQ may be relatively accurate under certain circumstances with short survival [16]. This study supported the usefulness of simple predictive tool such as PS-PPI, as an adjunctive tool to CPS. We proved that prognostic confidence was enhanced by the accuracy of CPS or given conditions (< 3-week survival, KPS 0–20) in the three countries.

This study has several limitations. First, this study was based on PCUs in three East Asian countries. These findings may not be applicable to other countries or other types of palliative care settings. Second, the median survival of our patients was relatively short (14–22 days). Because patient survival time is an important factor that influences the accuracy of CPS, we cannot guarantee that the accuracy of our CPS finding would be similar for patients with longer survival.

Conclusion

We demonstrated that experts' CPS is highly accurate around 80% in and superior to PS-PPI in 7-day, 21-day and 42-day prediction. The accuracy of the temporal approach of CPS was highest for the 7-day prediction (0.88 ~ 0.94). Prognostic confidence was significantly associated with accuracy of CPS in all three countries. Considering its simplicity, PS-PPI can be useful as a screening tool to enter palliative care by supporting CPS. Future studies are needed to evaluate the effect of the level of clinicians' confidence in the accuracy of CPS in various palliative care settings.

Declarations

Acknowledgments

The authors appreciate all the EASED investigators for their contribution on the data collection.

Funding

This work was supported in part by a Grant-in-Aid from the Japanese Hospice Palliative Care Foundation (Grant Numbers 16H05212 and 16KT0007).

Ethics declarations

Ethics approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. This study was approved by the local Institutional Review Boards of all participating institutions in Korea and Taiwan. Also, the independent ethics committee of Inje Ilsan Paik Hospital (approval no. ISPAIK 2017-10-005) approved the study.

Consent to participate

According to the ethical guidelines for human research issued by the Ministry of Health, Labor, and Welfare in Japan, patients' informed consent was waived because of the completely observational nature of the study. In Korea and Taiwan, informed consent was obtained from the patients or their families (in case the patient lacked the capacity to decide).

Consent for publication

The authors affirm that all participants provided informed consent for the publication of the article.

Conflicts of interest

The authors have no related interests to disclose.

Availability of the data

The data that support the findings of this study are available from the corresponding author, Sang-Yeon Suh. All authors agreed to the journal to review the data if needed.

Author contributions

Eon Sook Lee: Conceptualization, investigation, methodology, project administration, writing—original draft, writing—review and editing

Yusuke Hiratsuka: Conceptualization, investigation, writing—original draft, writing—review and editing

Sang-Yeon Suh: Conceptualization, investigation, methodology, project implementation, supervision, writing—review and editing

Seon Hye Won: project administration, writing—review and editing

Sun-Hyun Kim: Investigation, writing—review and editing

Seok-Joon Yoon: Additional analysis, investigation, writing—review and editing

Sung Eun Choi: Formal analysis, writing—review and editing

Hana Choi: Data curation, Formal analysis, writing—review and editing

Hong-Yup Ahn: Formal analysis, writing—review and editing

Yoonjoo Kim: Data curation, project administration, writing—review and editing

David Hui: Supervision, writing—review and editing

Shao-Yi Cheng: Investigation, project administration, writing—review and editing

Ping-Jen Chen: Investigation, writing—review and editing

Chien-Yi Wu: Investigation, writing—review and editing

Masanori Mori: Funding acquisition, investigation, methodology,

project administration, resources, writing—review and editing

Tatsuya Morita: Funding acquisition, supervision, investigation, writing—review and editing

Takashi Yamaguchi: Investigation, writing—review and editing

Satoru Tsuneto: Supervision, writing—review and editing

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Figures

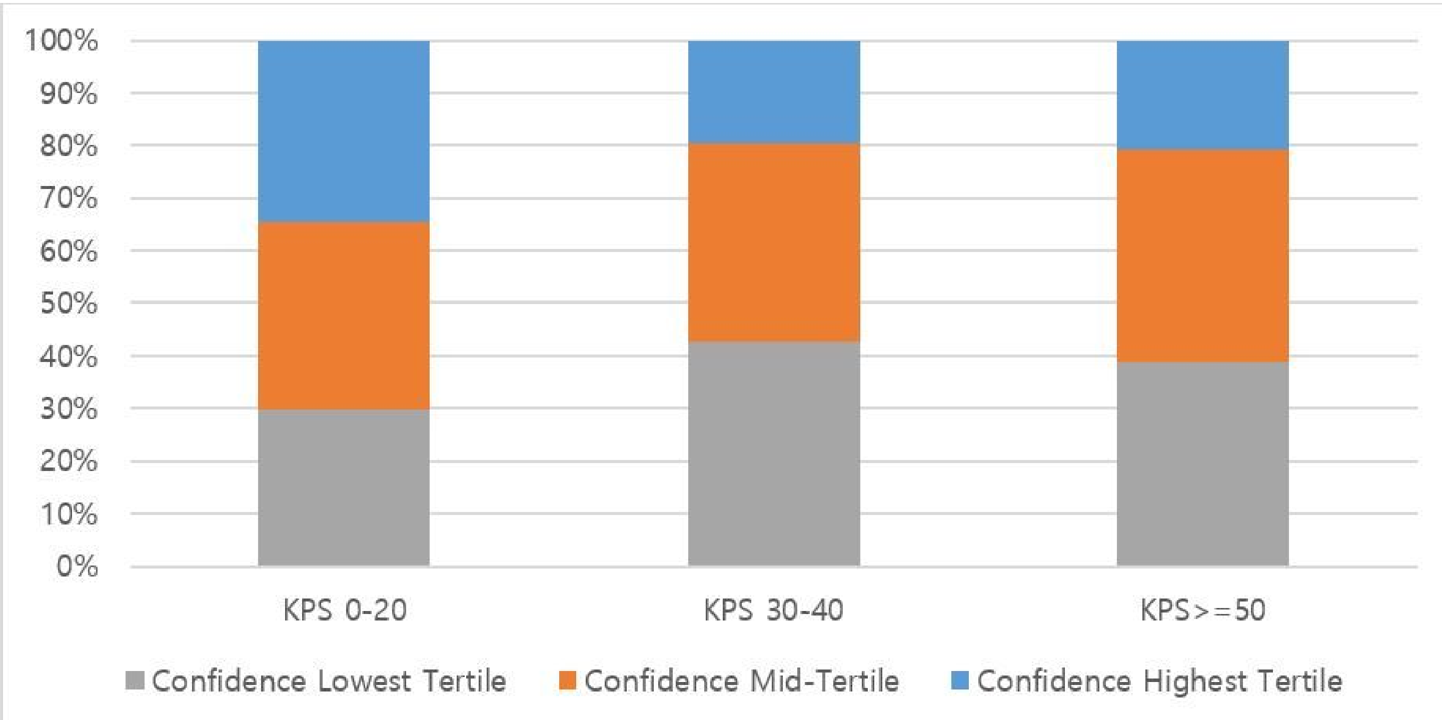

Figure 1

The Proportion of Prognostic Confidence by Performance Status

KPS: Karnofsky performance status

Clnicians' confidence was measured by numeric rating scale from 0 (not at all) to 10 (full of confidence).

Tertile was grouped by dividing numeric rating scale 0-3/4-5/6-10 for Japan, NRS 0-5/6/7-10 for Korea and Taiwan, respectively.

All p values were <0.0001, from Chi-Square tests and Kendall's tau-beta (ordinal) tests.

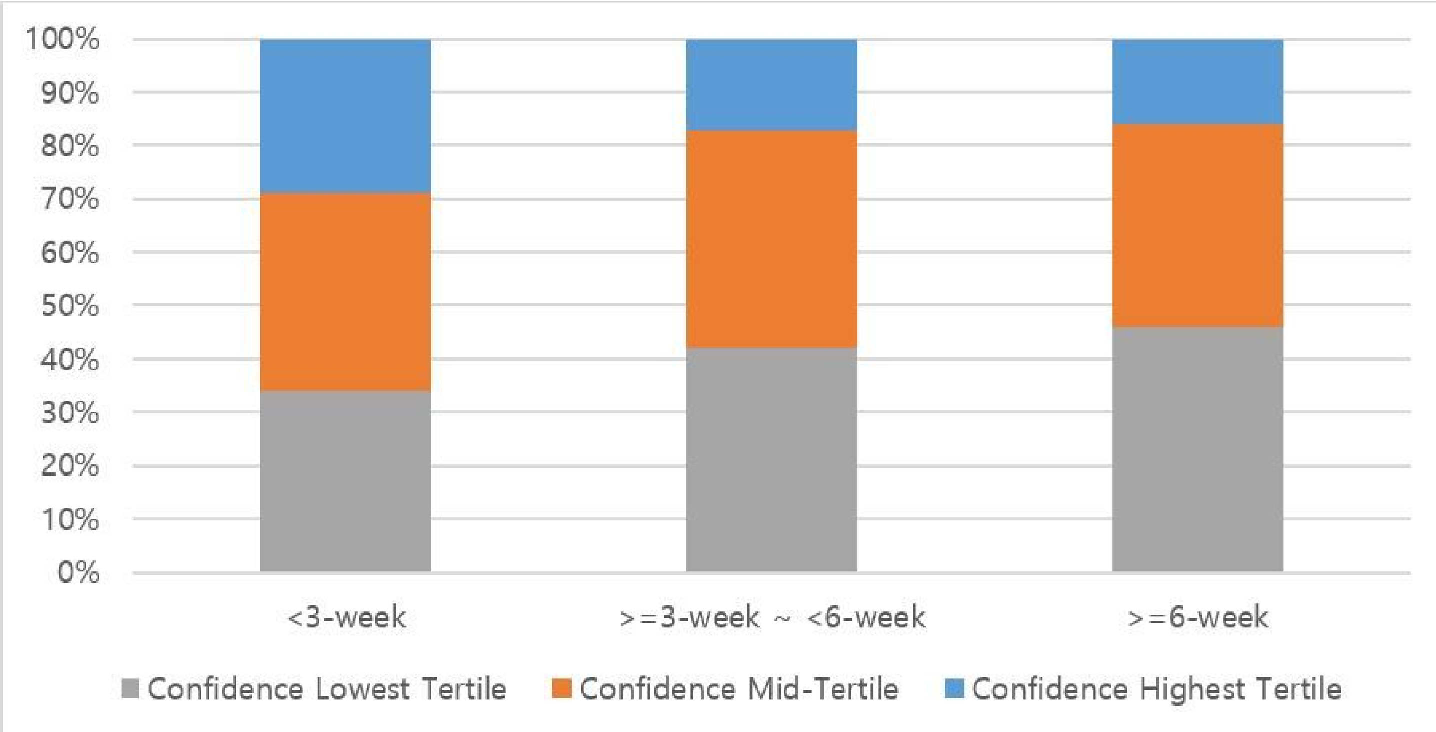

Figure 2

The Proportion of Prognostic Confidence by Survival Duration

Clinicians' confidence was measured by numeric rating scale from 0 (not at all) to 10 (full of confidence).

Tertile was grouped by dividing numeric rating scale 0-3/4-5/6-10 for Japan, NRS 0-5/6/7-10 for Korea and Taiwan, respectively.

All p values were <0.0001, from Chi-Square tests and Kendall's tau-beta (ordinal) tests.