Original Article

Are Prognostic Scores Better Than Clinician Judgment? A Prospective Study Using Three Models

Yusuke Hiratsuka, MD, PhD, Sang-Yeon Suh, MD, MPH, PhD, David Hui, MD, MSc, FRCPC, Tatsuya Morita, MD, Masanori Mori, MD, Shunsuke Oyamada, PhD, Koji Amano, MD, Kengo Imai, MD, Mika Baba, MD, PhD, Hiroyuki Kohara, MD, PhD, Takayuki Hisanaga, MD, Isseki Maeda, MD, PhD, Jun Hamano, MD, PhD, and Akira Inoue, MD, PhD

Department of Palliative Medicine (Y.H.), Takeda General Hospital, Aizuwakamatsu, Japan; Department of Palliative Medicine (Y.H., A.I.), Tohoku University School of Medicine, Sendai, Japan; Department of Family Medicine (S.Y.S.), Dongguk University Ilsan Hospital, Goyang-si, South Korea; Department of Medicine (S.Y.S.), Dongguk University Medical School, Seoul, South Korea; Department of Palliative Care (D.H.), Rehabilitation and Integrative Medicine, The University of Texas MD Anderson Cancer Center, Houston, Texas, USA; Division of Palliative and Supportive Care (T.M., M.M.), Seirei Mikatahara General Hospital, Hamamatsu, Japan; Department of Biostatistics (S.O.), JORTC Data Center, Tokyo, Japan; Department of Palliative Medicine (K.A.), National Cancer Center Hospital, Tokyo, Japan; Seirei Hospice (K.I.), Seirei Mikatahara General Hospital, Hamamatsu, Japan; Department of Palliative Medicine (M.B.), Suita Tokushukai Hospital, Suita, Japan; Department of Internal Medicine (H.K.), Hatsukaichi Memorial Hospital, Hatsukaichi, Japan; Department of Palliative Medicine (T.H.), Tsukuba Medical Center Hospital, Tsukuba, Japan; Department of Palliative Care (I.M.), Senri Chuo Hospital, Toyonaka, Japan; Division of Clinical Medicine (J.H.), Faculty of Medicine, University of Tsukuba, Tsukuba, Japan

Abstract

Context. Several prognostic models such as the Palliative Performance Scale (PPS), Palliative Prognostic Index (PPI), Palliative Prognostic Score (PaP) have been developed to complement clinician's prediction of survival (CPS). However, few studies with large scales have been conducted to show which prognostic tool had better performance than CPS in patients with weeks of survival.

Objectives. We aimed to compare the prognostic performance of the PPS, PPI, PaP, and CPS in inpatients admitted to palliative care units (PCUs).

Methods. This study was part of a multi-center prospective observational study involving patients admitted to PCUs in Japan. We computed their prognostic performance using the area under the receiver operating characteristics curve (AUROC) and calibration plots for seven, 14-, 30- and 60-day survival.

Results. We included 1896 patients with a median overall survival of 19 days. The AUROC was 73% to 84% for 60-day and 30-day survival, 75% to 84% for 14-day survival, and 80% to 87% for seven-day survival. The calibration plot demonstrated satisfactory agreement between the observational and predictive probability for the four indices in all timeframes. Therefore, all four prognostic indices showed good performance. CPS and PaP consistently had significantly better performance than the PPS and PPI from one-week to two-month timeframes.

Conclusion. The PPS, PPI, PaP, and CPS had relatively good performance in patients admitted to PCUs with weeks of survival. CPS and PaP had significantly better performance than the PPS and PPI. CPS may be sufficient for experienced clinicians while PPS may help to improve prognostic confidence for inexperienced clinicians. J Pain Symptom Manage 2022;64:391−399.

Key Words

Prognostication, end of life, advanced cancer, palliative care unit, discrimination, calibration

Address correspondence to: Sang-Yeon Suh, MD, PhD, Department of Medicine, Dongguk University Medical School, Pildong 1-30, Jung-gu, Seoul, South Korea. E-mail: lisasuhmd@hotmail.com

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Key Message

All four models -the Palliative Performance Scale (PPS), Palliative Prognostic Index (PPI), Palliative Prognostic Score (PaP), and clinician's prediction of survival (CPS)-showed good performance in predicting survival of patients in our study in their last weeks. Notably, CPS and PaP had better performance than PPS and PPI.

Introduction

The success of prognosis-based palliative care can be affected by the ability of clinicians to predict patient survival.[1-3] The clinician's prediction of survival (CPS) is often used,[4,5] but CPS can sometimes be inaccurate and optimistic.[6-10] In fact, the accuracy of CPS is reported to be around 20% to 30% compared to actual survival.[9-11]

Several prognostic models have been developed to complement CPS, including the Palliative Performance Scale (PPS),[12] Palliative Prognostic Index (PPI),[13] and Palliative Prognostic Score (PaP).[14] The accuracy of the prognostic models has been reported to range between 65% and 85% and differ according to patient populations, clinical settings, and clinicians.[15-18] Investigators demonstrated that these prognostic models were more accurate than CPS.[4,16,18,19] However, previous studies were conducted predominantly in patients with months of survival. A single study focused on patients with only days of remaining survival. The study reported that CPS and PPS alone were as accurate as the PaP and PPI.[20] However, it should be considered a preliminary report since it was a single-center study in an acute palliative care unit with relatively small sample size.

Thus, we thought that the prognostic models should be compared in a multicenter study on a larger scale. The aim of our investigation was to compare the prognostic performance of the PPS, PPI, PaP, and CPS in Japanese inpatients admitted to palliative care units (PCUs) with far-advanced cancer.

Methods

Participants

This study was conducted as a secondary analysis of a multicenter prospective cohort study. The cohort study was a sub-study of the East-Asian collaborative cross-cultural Study to Elucidate the Dying Process, which examined the dying process and end-of-life care of inpatients with advanced cancer in PCUs nationwide in Japan. We enrolled eligible inpatients consecutively admitted to the participating PCUs during the study period. All observations were done in the range of routine clinical practice. The inclusion criteria for the patients in this study were: 1) adults (≥18 years old), 2) with locally extensive or metastatic cancer, 3) admitted to PCUs. We excluded subjects who planned to be discharged within one week of enrollment (to reduce follow-up loss) and those (or families when the patients lacked communicating capacity) who did not consent to participate in the study.

Data Collection

The palliative care physicians recorded all variables prospectively on the first day of admission on structured data collection sheets. We collected baseline patient demographics, including age, sex, primary cancer site, the highest level of education, living with family, children under the age of 20, and marital status. Mortality was defined to include all deaths in and outside of the PCUs. We followed patients who were discharged up until six months after enrollment. Thus, survival time was calculated by subtracting the admission date from the death date. Patients alive at the last follow-up were dealt with as censored data. The PPS, PPI, PaP, and CPS were calculated and recorded by the palliative care physicians at enrollment.

Measurements

The PPS includes five domains, including ambulation, activity level, evidence of disease, self-care, intake, and level of consciousness. Each of these domains is observer-rated from 0% (dead) to 100% (normal function) in 10% increments.[21] The reliability of the PPS was reported to be high,[22] and the PPS was significantly associated with survival.[23]

The PPI was developed[13] and validated[24] in Japan. Five variables are measured by the PPI, oral intake, edema, dyspnea at rest, delirium, and performance status based on the PPS.[13] The PPI generates a numerical score between 0 and 15. The score divides the patients into three groups: predicted survival of less than three weeks (PPI >6), less than six weeks (PPI: 5−6), and more than six weeks (PPI: 0−4).

The PaP was developed in Italy and is comprised of CPS, Karnofsky Performance five Status, dyspnea, anorexia, leukocyte count, and lymphocyte percentage.[14] The PaP aims to predict 30-day survival[14] and was validated in Japan in various clinical settings.[15] The maximum PaP score is 17.5 points. According to the total score, the 30-day survival probability is judged to be over 70% for 0 to 5.5 points, 30% to 70% for 5.6 to 11.0 points, and less than 30% for 11.1 to 17.5 points.[14]

CPS is used as a quick prognostic indicator in the palliative care field despite the progression of validated prognostic tools.[4,5] CPS was obtained from the palliative care physician based on the temporal question "How long do you think this patient will live (days)?" upon enrollment.

Data Analysis and Statistics

The sample size justification was previously reported, and the validation data used for the risk models are recommended to have at least 100 events based on a minimum of 10 events per predictor.[25,26] There is no guidance on calculating the sample size for multicenter prognostic model comparison studies. Because we aimed to compare CPS to three prognostic models (PPS, PPI, and PaP), we assumed that more than 400 deaths would be sufficient for the analysis (100 for each). Thus, this study had over 1,800 death cases, and our sample size fulfilled the criteria for statistical power.

First, descriptive analyses were performed to summarize the baseline patient and clinician characteristics.

Second, we classified the patients into three groups according to each prognostic score cutoff preestablished in the literature.[15,27] In the PPS, the patients were classified into low (10−30), intermediate (40−50), and high groups (60−100). Regarding the PPI, the patients were classified into the low-risk (0−4 points), intermediate (4.5−6 points), and high-risk groups (6.5−15 points). In terms of the PaP, the patients were classified into the low-risk (0−5.5 points), intermediate (6−11 points), and high-risk groups (11.5−17.5 points). In CPS, the patients were categorized into groups of days (0−14 days), weeks (15−42 days), and months (≥43 days). We calculated the median overall survival and 95% confidence intervals (CI) in each group and constructed survival curves for the risk groups classified by each prognostic score using the Kaplan-Meier method.

Third, to assess the discrimination ability of the PPS, PPI, PaP, and CPS, we used the area under the receiver operating characteristics curve (AUROC), an approach similar to that used in previous studies.[4,19] AUROC is the probability of classifying binary outcomes as its threshold varies and ranges from 0.5 (no discriminatory ability) to one (perfect discriminatory ability). We dealt with the PPS, PPI, PaP, and CPS as continuous variables to calculate the AUROCs. Additionally, χ^2 tests were performed to compare the AUROCs of all four indices in all timeframes.

Fourth, we used a calibration plot (observed vs. predicted graphs) to assess calibration.[28] We also dealt with the PPS, PPI, PaP, and CPS as continuous variables in the calibration assessment.

All analyses were performed using JMP version 16 for Windows (SAS, Cary, NC) and IBM Statistical Package for Social Science Statistics for Windows, version 21.0 (IBM Corp., Armonk, NY). A *P*-value of <0.05 was considered statistically significant.

Ethics

The present study was conducted in accordance with the ethical standards of the Declaration of Helsinki and the ethical guidelines for medical and health research involving human subjects presented by the Ministry of Health, Labor, and Welfare in Japan. This study was approved by the Institutional Review Board of each participating institution and by the Independent Ethics Committee of Tohoku University School of Medicine (approval no. 2016-1-689). Japanese law does not require individual informed consent from participants in a non-invasive observational trial such as the present study. Therefore, we used an opt-out method rather than obtaining written or oral informed consent. All patients could receive information on the study through the instructions posted on the ward or institutional website and had the opportunity to decline participation.

Results

Patient and Clinician Characteristics

A total of 1896 patients, including 965 men (50.9%) and 931 women (49.1%) (mean [standard deviation, SD] age, 72.4 [12.3] years), were enrolled across 22 PCUs in Japan between January 2017 and December 2017. The overall median survival was 19 days (95% CI: 2−140.2 days, mean [SD]: 37.4 [49.1] days), and 1842 patients (96.2%) died within six months of enrollment. The patient characteristics are shown in Table 1.

A total of 87 clinicians participated in the study, of which 76% were male (66/87), and 70% of the clinicians' specialties (60/87) were palliative care. The mean [SD] length of clinical experience was 11.2 [6.6] years, and the mean clinical experience in palliative care was 5.5 [5.1] years. The mean [SD] number of patients with far-advanced cancer treated in a year was 101.3 [104.7] (Supplementary Table 1).

Median Survival Time of Each Risk Group According to Prognostic Score

The prognostic model and CPS scores are shown in Table 2. The median survival predicted by the PPS was nine days (95% CI: 8−10 days) in the low group, 26 days (95% CI: 24−29 days) in the intermediate group, and 49 days (95% CI: 43−59 days) in the high group. The median survival predicted by the PPI was 38 days (95% CI: 35−42 days) in the low-risk group, 22 days (95% CI: 19−25 days) in the intermediate group, and 10 days (95% CI: 9−11 days) in the high-risk group. The PaP predicted a median survival of 63 days (95% CI: 54−71 days) in the low-risk group, 25 days (95% CI: 23−27 days) in the intermediate group, and nine days (95% CI: 8−9 days) in the high-risk group, and CPS predicted a median survival of seven days (95% CI: 7−8 days) in the groups of days, 23 days (95% CI: 21−24 days) in the groups of weeks, and 53 days (95% CI: 50−62 days) in the groups of

Table 1
Baseline Characteristics of the Participants (n =1896)

Characteristics	Number (%)
Age [years, mean ± SD]	72.4 ± 12.3
Sex	
Male	965 (50.9)
Female	931 (49.1)
Primary cancer site	
Hepatobiliary/pancreas	363 (19.1)
Lung	319 (16.8)
Gastroesophageal	265 (14.0)
Colorectal	254 (13.4)
Urological	141 (7.4)
Breast	131 (6.9)
Gynecological	119 (6.3)
Head/neck	76 (4.0)
Others	228 (12.0)
Highest level of education	
< High school	58 (3.1)
High school/some college	184 (9.7)
≥ College degree	127 (6.7)
Unknown	1527 (80.5)
Living with family	
Yes	1376 (72.6)
No	498 (26.3)
Unknown	22 (1.2)
Children under the age of 20	
Yes	74 (3.9)
No	1799 (94.9)
Unknown	23 (1.2)
Marital status	
Married	1151 (60.7)
Widowed	403 (21.3)
Unmarried	205 (10.8)
Separated	113 (6.0)
Unknown	24 (1.3)
Survival time [days (95% CI), mean ± SD]	19 (2.0−140.2) [37.4 ± 49.1]
Deceased persons within six months of enrollment	1842 (96.2)

CI = confidence interval; SD = standard deviation.

Table 2
Categories of Prognostic Models and Median Survival Time (n = 1896)

Prognostic Model	n (%)	Median Survival Time (Days, 95% CI)
Palliative performance scale (PPS)		
Low (10−30)	721 (38.0)	9 (8−10)
Intermediate (40−50)	991 (52.2)	26 (24−29)
High (60−100)	184 (9.7)	49 (43−59)
Palliative prognostic index (PPI)		
Low risk (0−4)	648 (34.2)	38 (35−42)
Intermediate risk (4.5−6)	424 (22.4)	22 (19−25)
High risk (6.5−15)	821 (43.3)	10 (9−11)
Missing value	3 (0.2)	-
Palliative prognostic score (PaP)		
Low risk (0−5.5)	259 (13.7)	63 (54−71)
Intermediate risk (6−11)	619 (32.6)	25 (23−27)
High risk (11.5−17.5)	470 (24.8)	9 (8−9)
Missing value	548 (28.9)	-
Clinicians' prediction of survival (CPS)		
Days: 0−14 days	661 (34.9)	7 (7−8)
Weeks: 15−42 days	746 (39.3)	23 (21−24)
Months: ≥43 days	489 (25.8)	53 (50−62)

The categories of the above three scores were based on pre-established cutoffs in the literature. Patients with lower PPS, higher PPI and PaP scores, and shorter CPS typically have the highest risk for mortality.
CI = confidence interval.

months. Fig. 1 shows the survival curves from the time of enrollment for each prognostic score. A prominent discrimination in the Kaplan-Meier (KM) plots according to cutoff values was shown in the PPS ($P < 0.01$), PPI ($P < 0.01$), PaP ($P < 0.01$), and CPS ($P < 0.01$).

Discrimination and Calibration

Table 3 shows the AUROCs of the PPS, PPI, PaP, and CPS. The AUROCs of the four indices ranged from 73% to 84% at 60 days, 73% to 84% at 30 days, 75% to 84% at 14 days, and 80% to 87% at seven days. Thus, all four prognostic tools showed moderate-to-high discriminatory power. The AUROC of the PaP and CPS was statistically significantly higher than that of the PPS and PPI at all four timeframes (Table 3). Fig. 2 shows the ROC curves for the four prognostic scores.

The calibration plot is shown in Fig. 3. In this plot, a perfect calibration should lie on the 45° line, and most plots lied near the reference line. Therefore, the calibration plot demonstrated satisfactory agreement between the observational and predictive possibility in all timeframes for all four prognostic models.

Discussion

The PPS, PPI, PaP, and CPS showed good performance for predicting the weeks of survival in inpatients admitted to PCUs in this study. Interestingly, CPS and PaP demonstrated significantly better performance than the PPS and PPI in patients with two months to ober week of survival.

Our results suggest that CPS performed better in patients with weeks of survival. CPS performance was highest in patients with weeks of survival in this study. Several studies have reported that the prognostic scales were more accurate than CPS.[4,13,29] In contrast, some studies revealed that CPS was equal to or more accurate than other prognostic tools.[30,31] Therefore, whether the established prognostic models are superior to CPS is controversial. Our findings showed that the performance of CPS could differ according to the patient population, physician's characteristics, and timeframes evaluated. The participating patients had a median survival time of weeks, so they could have more predictable trajectories.[8,32] It is well-known that the accuracy of CPS can be affected by clinician-related factors such as knowledge of the survival of the patients and training on prognostication.[6] In Japan, it is mandatory for all palliative care clinicians to complete a comprehensive educational program provided by the Japanese Society

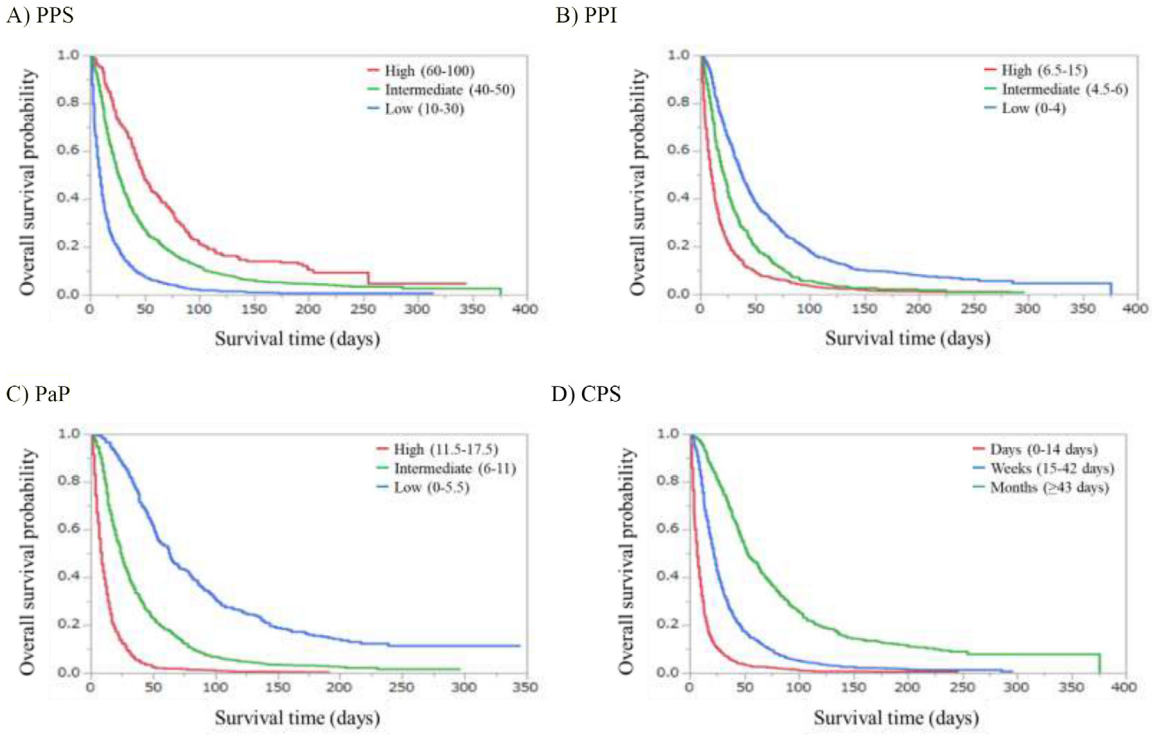

Fig. 1. Kaplan-Meier survival curves for overall survival according to prognostic model categories from the time of enrollment. CPS = clinicians' prediction of survival; PaP = palliative prognostic score; PPI = palliative prognostic index; PPS = palliative performance scale. The *P*-values were <0.01, <0.01, <0.01, and <0.01 for PPS, PPI, PaP, and CPS, respectively. The *P*-values were derived from log-rank tests.

Table 3
Discrimination of the Prognostic Models and Clinicians' Prediction of Survival

Predictor	PPS	PPI	PaP	CPS
AUC for seven-day survival (95% CI)	0.80 (0.77–0.82)[a]	0.80 (0.78–0.82)[a]	0.85 (0.83–0.88)[b]	0.87 (0.85–0.89)[b]
AUC for 14-day survival (95% CI)	0.75 (0.73–0.78)[a]	0.76 (0.74–0.78)[a]	0.83 (0.81–0.85)[b]	0.84 (0.83–0.86)[b]
AUC for 30-day survival (95% CI)	0.73 (0.70–0.75)[a]	0.74 (0.72–0.76)[a]	0.84 (0.82–0.86)[b]	0.84 (0.83–0.85)[c]
AUC for 60-day survival (95% CI)	0.73 (0.70–0.75)[a]	0.74 (0.71–0.76)[a]	0.84 (0.82–0.87)[b]	0.83 (0.80–0.85)[c]

AUC = area under the curve; CI = confidence interval; CPS = clinicians' prediction of survival; PaP = palliative prognostic score; PPI = palliative prognostic index; PPS = palliative performance scale.
Differing superscripts in two cells which are given below are indicate that the values in those two cells are significantly different by chi-square test.
[a, b, c]The absence of superscripts indicates that there are no significant differences among the values.

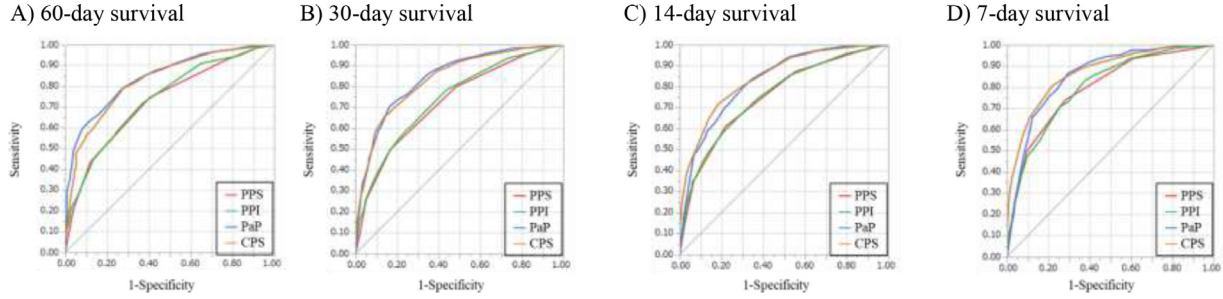

Fig. 2. Receiver operating characteristic (ROC) curves for four prognostic approaches for 60-day survival, 30-day survival, 14-day survival, and seven-day survival. CPS = clinicians' prediction of survival; PaP = palliative prognostic score; PPI = palliative prognostic index; PPS = palliative performance scale.

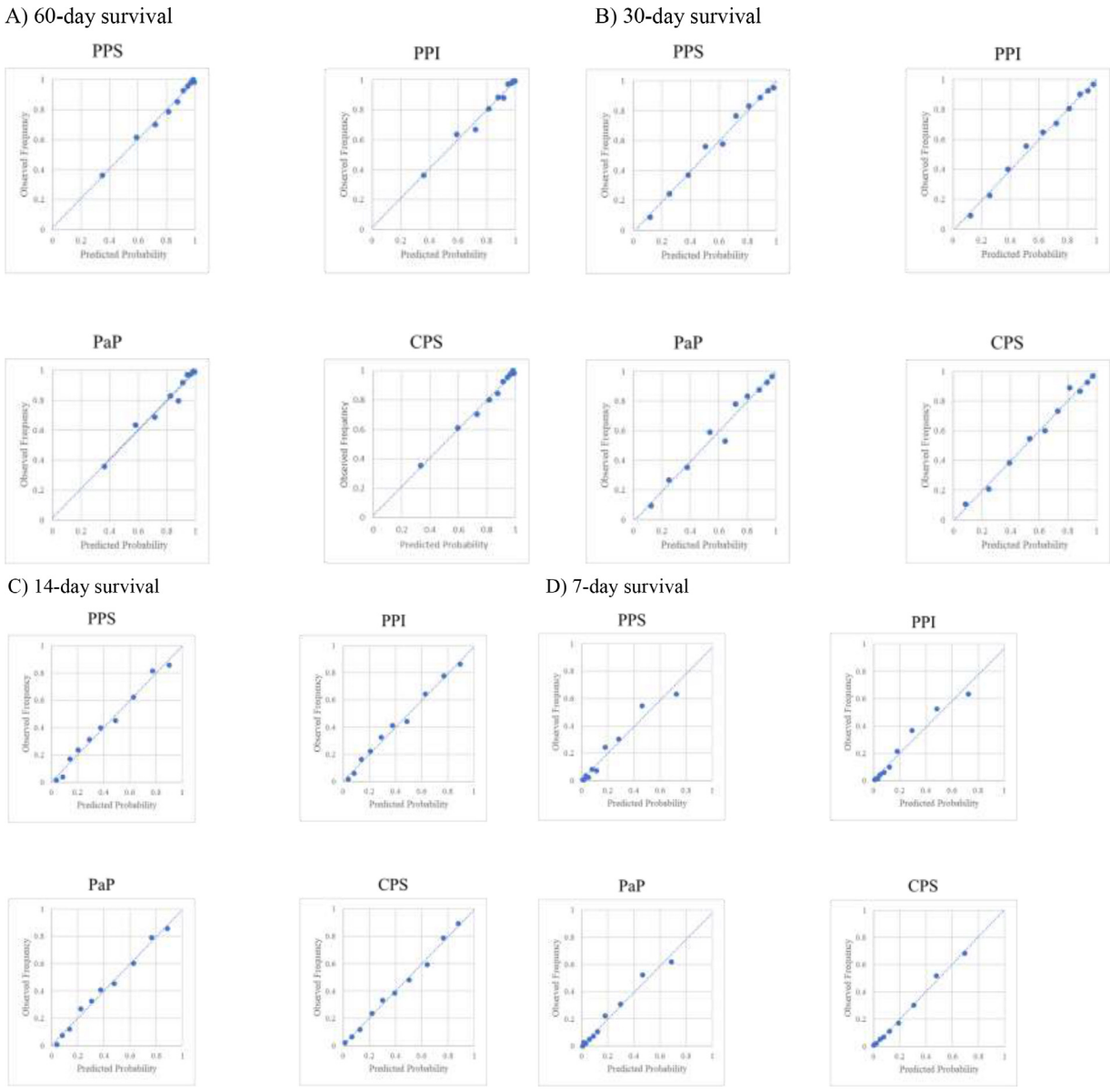

Fig. 3. Calibration plots for prognostic models. CPS = clinicians' prediction of survival; PaP = palliative prognostic score; PPI = palliative prognostic index; PPS = palliative performance scale. The decile on the x-axis is the observed frequency and the decile on the y-axis is the predicted probability. The reference line indicates a perfect model, in which the observed values equal the predicted values.

for Palliative Medicine.[33,34] It was reported that experienced clinicians could more accurately predict prognoses and had smaller errors in predictions than inexperienced clinicians.[6,35] Therefore, the accuracy of CPS in the current study could be highly influenced by the patient's predictable trajectory and the clinician's experience and educational background.[10] It is unique that CPS was more accurate here than in a previous study (AUROC, 75%−81%).[20] We assumed the different results were due to the following three reasons. First, our study was conducted in PCUs, whereas the previous study was performed in an acute PCU. Previous studies conducted in acute PCUs showed that the frequency of unexpected death ranged from 10% to 22.4%.[36,37] A recent study in Japan PCUs[38] reported that the frequency of unexpected death was 6% to 18%. We recognize that the frequency may vary depending upon the definition and timeline used. However, we assumed that unexpected deaths in acute PCUs might be more difficult to predict than those in PCUs since the aim of acute PCUs is the recovery of patients for discharge. Therefore, dynamic changes in an acute PCU may lower the accuracy of CPS. Second, the median survival time of the patients was different. In our study (19 days), the clinicians may have been able to use prognostic tools such as the PaP and PPI to

formulate and complement CPS.[13,14] However, using these tools may be less suitable for shorter median survival of patients (10 days) in the previous study.[20] Third, it is common for Japanese palliative physicians to see patients a few weeks before their admission to PCUs. Thus, the relatively longer observation period may allow Japanese physicians to recognize the patterns of decline in the patients.

Similar to the preceding study, the performance of the PaP was as good as that of CPS in patients with weeks of survival. Because CPS comprises the greatest proportion of the PaP,[14] the performance of the PaP should be influenced by CPS. A previous study reported that the total PaP was more accurate than the PaP which did not include CPS.[39] Therefore, the performance of the PaP would be attributed to CPS since the PaP is heavily loaded with CPS elements. This finding is also consistent with that of another previous study.[40]

Interestingly, the discrimination of the PPS and PPI was a little bit lower (73%−80% of AUROC) than that of the PaP and CPS (83%−87% of AUROC), although both the PPS and PPI demonstrated good calibration. We assume that the difference between our study and that of Hui et al. arose from the proportion of patients in the low PPS (10−30) group. In the previous study, 61.3% of the patients were in the low PPS group, whereas 38.0% of our patients were in that group. The survival of our patients may be less predictable by the PPS because of their longer survival time. However, our findings showed that the discrimination of the PPS (and PPI) increased within a seven-day timeframe. And the discrimination was almost the same as that in a previous study (AUROC, 79% for PPS and 74% for PPI).[20] A PPS score of ≤20 was reported as an indicator of impending death (within three days).[41] Thus, it is reasonable that the individual scores of both the PPS and PPI (the overall score is heavily driven by the PPS elements) had the highest discrimination in the seven-day timeframe compared to other timeframes.

This was the first large-scale and multicenter study to compare the prognostic performance of the PPS, PPI, PaP, and CPS in inpatients with far-advanced cancer. A previous multicenter study[15] also compared various prognostic indices in Japanese PCUs. The distinction from our study is that CPS was not included in the previous study. However, we recognize several limitations to our study. First, this was a study conducted in PCUs in Japan. Therefore, our findings may not be generalizable to other countries or different palliative care settings, such as general wards or home hospice care. Second, this study required laboratory data to calculate the PaP. We used available bloodwork results obtained within the range of routine practice conducted from one week before to three days after study enrollment. Thus, if the timing of the laboratory data collection was different in other studies, the PaP total score may differ from ours. Third, considering the nature of the secondary analysis of this study, future prospective studies are needed to generalize our results.

In conclusion, the PPS, PPI, PaP, and CPS had relatively good performance in patients with weeks of survival. Notably, CPS and PaP had better performance than the PPS and PPI in our study. It may be sufficient for experienced clinicians to use CPS alone to estimate the short-term survival of PCU inpatients with far-advanced cancer. However, the PPS alone had a sufficiently good performance when death was within one to two weeks. Thus, the PPS may help to improve prognostic confidence for inexperienced clinicians and reduce subjective variation among experts.

Author Contributions

Y. H.: Conceptualization, data curation, formal analysis, investigation, methodology, project administration, writing-original draft, and writing-review and editing. S. Y. S.: Conceptualization, investigation, methodology, project implementation, supervision, and writing-review and editing. D. H.: Supervision and writing-review and editing

Tatsuya Morita: Investigation and writing-review and editing. M. M.: Conceptualization, funding acquisition, investigation, methodology, project administration, resources, supervision, and writing-review and editing. S. O.: Formal analysis and writing-review and editing. K. A.: Investigation and writing-review and editing. K. I.: Investigation and writing-review and editing. M. B.: Investigation and writing-review and editing. H. K.: Investigation and writing-review and editing. T. H.: Investigation and writing-review and editing. I. M.: Investigation and writing-review and editing. J. H.: Investigation and writing-review and editing. A. I.: Investigation, supervision, and writing-review and editing.

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The authors declare no conflicts of interest.

Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.jpainsymman.2022.06.008.

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