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Prognosis Prediction Models and their Clinical Utility in Palliative Care

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<http://dx.doi.org/10.5772/intechopen.69663>

Abstract

Prognosis prediction is a clinically relevant issue to facilitate optimal decision-making for both physicians and patients with cancer. Many previous studies revealed that prognosis prediction based on the physician's intuition and/or clinical experience is inaccurate and often optimistic, which means that there is a tendency to overestimate patient survival in daily clinical practice. In recent decades, many efforts have been made to develop prognosis prediction models which aid physicians to make more accurate prognosis prediction. In this chapter, we review the representative prognosis prediction models in palliative care and related studies. In addition, we refer to several prognosis prediction models developed by unique methods (for instance, case-crossover design or machine learning). Finally, we focus on the possible clinical utility of prognosis prediction models. In fact, no previous studies have clearly demonstrated whether the application of such prognosis prediction models truly benefits patient care in daily clinical practice. Therefore, we will discuss how the application of prognosis prediction models could benefit patients under palliative care.

Keywords: cancer, clinical prediction of survival, clinical utility, palliative care, prognosis prediction model

1. Introduction

Prognosis is one of the most relevant concerns for both patients and healthcare professionals (HCPs). Patients with advanced cancer and their families are required to make decisions such as choosing treatment alternatives or place to spend their end of life or that of their family members. In particular, timing in discontinuing palliative chemotherapy largely affects end-of-life care. Continuing ineffective palliative chemotherapy at the end of life increases life-threatening adverse events (AEs), hospital administration associated with AEs, and

medical cost [1, 2]. Furthermore, it causes patients' quality of life (QOL) to deteriorate, delays hospice referral, and deprives patients of the chance to die in their preferred place [3, 4]. Thus, optimal prognosis prediction is essential for better end-of-life care.

Subjective prognosis prediction based on HCPs' experience or intuition is a simple method, which requires no special device in daily practice. However, this method is often inaccurate or tends to overestimate patient survival [5]. Therefore, development of more accurate objective prognosis prediction methods is warranted.

In recent decades, several prognosis prediction models have been developed by integrating known prognostic factors [6–8]. These models have been validated in clinical settings across several countries and their accuracy have been compared [9, 10]. Moreover, studies exploiting new prognostic factors, such as phase angle or circadian rhythm, have been reported in Refs. [11, 12].

Recent progress in informatics has enabled us to retrieve and analyze clinical big data comprehensively, and new methods, such as machine learning or artificial intelligence, have been utilized to develop prognosis prediction models [13, 14]. We also review these issues in this chapter.

Finally, we focus on the clinical utility of prognosis prediction models, which has long been beyond the scope of the main issues in this research field.

2. Current status of prognosis prediction

2.1. Subjective prognosis prediction

Subjective prognosis prediction based on HCPs' experience or intuition is referred to as clinical prediction of survival (CPS). CPS is one of the most classic styles and has long been used in daily clinical practice. CPS utilizes three common questions. The first question is the "temporal" question, asking "how long can the patient live?" The second question is the "surprise" question, asking "will you be surprised if the patient dies within a specific term?" and the third question is the "probabilistic" question, asking "what is the patient's probability of survival within a specific term?"

The temporal question seems to be the most common prediction type in clinical practice. The answer to this question provides clear and simple information to HCPs. However, there are problems in its accuracy. Hui et al. reported its accuracy as just 32% among eight physicians and 18% among 20 nurses [15]. Moreover, 60% of nurses gave an optimistic prediction of survival [15]. Consistent with these results, another group reported that 63% of prognosis prediction estimated by HCPs was optimistic [16].

The surprise question has a feature of higher negative predictive value (NPV), which is more than 90% in two independent studies [17, 18]. Therefore, the surprise question has been used to identify patients who have a limited survival, and answering "no" is thought to signal the ideal time for specific action such as advance care planning (ACP) [19].

The probabilistic question showed a higher accuracy than the temporal question. The accuracy of physicians' prediction of death within 24 and 48 h was 71–73% and 66–67%, respectively [15, 20]. Interestingly, nurses showed more favorable predictive performance than physicians using the probabilistic question, and the accuracy of their prediction of death within 24 h and 48 h was 90–91% and 83–86%, respectively [15, 20].

2.2. Objective prognosis prediction

As discussed in Section 2.1, each CPS may have promising performance in specific settings; however, their accuracy is not satisfactory and is often optimistic [5, 16, 21]. To cope with these problems, many efforts have been made to develop more accurate prognosis prediction models using known prognostic factors.

2.2.1. Prognostic factors

Prognostic factors are classified into two groups, one composed of clinical signs/symptom and the other of laboratory data. Performance status [22–24], dyspnea [25, 26], malnutrition [27, 28], appetite/weight loss [29], and delirium [30, 31] are well-known clinical factors. Recently, novel prognostic factors have been proposed. Phase angle, which is measured via bioelectrical impedance analysis (BIA), reflects the amount of water in tissues (resistance) and cellular membrane (capacitance) and could be a prognostic factor [11]. Circadian rhythm is also found to be an independent prognostic factor [12, 32].

Laboratory factors include inflammatory markers (for instance, C-reactive protein (CRP), erythrocyte sedimentation, or neutrophil lymphocyte ratio) [33, 34], nutrition markers (for instance, albumin) [35, 36], and tumor progression markers (for instance, calcium or lactate dehydrogenase) [37, 38].

2.2.2. Prognosis prediction model

In recent decades, many prognostic models have been developed integrating a variety of prognostic factors, CPS, and other patients' information, and their accuracy is improving.

When we use these models in practice, we need to pay attention to the fitness of prediction models for treating patients. In other words, we should verify the clinical settings under which the prediction model was developed. When the clinical settings for treating patients are similar to those of the original study, the prognostic model may fit that patient; otherwise, we should exercise caution when applying prognostic models.

We reviewed the previously proposed prognostic models in the palliative care setting as shown below and summarized the characteristics of each model in **Table 1**.

2.2.2.1. The palliative prognostic index (PPI)

The palliative prognostic index (PPI) is a noninvasive prognostic model developed by Morita et al. in 1999 and requires no laboratory items (**Table 1**) [6].

Model	Items	Risk groups
Palliative prognostic index [6]	Palliative prognostic index (0–4 points) Oral intake (0–2.5 points) Edema (0, 1 point) Dyspnea at rest (0, 3.5 points) Delirium (0, 4 points)	(A) Median survival 155 days: $PPI \leq 2.0$ (B) Median survival 89 days: $2.0 < PPI \leq 4.0$ (C) Median survival 18 days: $4.0 < PPI$
Palliative prognostic score [7]	Dyspnea (0, 1 point) Anorexia (0, 1.5 points) Karnofsky performance scale $\geq 50\%$ (0, 2.5 points) Clinical prediction of survival (0–8.5 points) Total white blood cell (0–1.5 points) Lymphocyte percentage (0–2.5 points)	(A) 30-Day survival probability $> 70\%$, 0–5.5 points (B) 30-Day survival probability 30–70%, 5.6–11.0 points (C) 30-Day survival probability $< 30\%$, 11.1–17.5 points
Glasgow prognostic score [62]	C-Reactive protein Albumin	Score 0: C-Reactive protein ≥ 10 mg/l and albumin ≥ 35 g/l Score 1: C-reactive protein > 10 mg/l or albumin < 35 g/l Score 2: C-reactive protein > 10 mg/l and albumin < 35 g/l
Prognosis in palliative care study predictor models A [8]	Mental test score > 3 Pulse rate Presence of distant metastasis Site of metastases (liver) ECOG score Global health score Loss of appetite Site of metastases (bone) Difficulty in breathing Difficulty in swallowing Primary breast cancer Primary male genital cancer (including prostate) Weight loss	Days: < 14 days Weeks: 14–55 days Months+: > 55 days *See detail in “THE PiPS PROGNOSTICATOR”
Prognosis in palliative care study predictor models B [8]	Pulse rate White blood count Platelets Urea C-Reactive protein Global health score Alanine transaminase Mental test score > 3 Distant metastasis Site of metastases (bone) Lack of appetite ECOG score Neutrophils Lymphocytes Alkaline phosphatase Albumin Primary male genital cancer (including prostate) Tired	Days: < 14 days Weeks: 14–55 days Months+: > 55 days *See detail in “THE PiPS PROGNOSTICATOR”

*THE PiPS PROGNOSTICATOR: <http://www.pips.sgul.ac.uk/>.

Table 1. Representative prognosis prediction models in palliative care.

Validation studies of the PPI were performed in Japan, Taiwan, Kuwait, Ireland, the United Kingdom, and Australia [39–46]. Morita et al. revealed that the PPI significantly reduced overestimation of survival compared to the CPS [39]. In the study of another group, the PPI was assessed by a nurse specialist, and the area under the curve (AUC) of the receiver operating characteristic (ROC) to predict death within 21 days was 0.68 [40]. In Kuwait, Alshemmari et al. revealed that the PPI can be a helpful tool in predicting hospital mortality of patients with advanced cancer in an acute care setting and that the hospital mortality rate for patients with a PPI score ≥ 6 was significantly higher than for those with a PPI score < 6 (93% versus 56% $p < 0.001$) [41].

In addition to the validation studies, studies which aimed to modify PPI were also reported. Two modified PPI models were tested in sub-analysis of the Japan-prognostic assessment tools validation (J-ProVal) study. The one substitutes the Communication Capacity Scale (CCS) for delirium to the required items of PPI [47]. The other adds a new item about the activities of daily living changes to the PPI; however, this did not significantly improve its prognostic value [48].

Moreover, some researchers examined the longitudinal score change of the PPI [49, 50].

2.2.2.2. Palliative prognostic (PaP) score

In 1999, Pirovano et al. proposed the palliative prognostic (PaP) score (**Table 1**) [7]. In this prospective cohort study, 519 patients with advanced cancer were recruited at 22 institutions in Italy, and a scoring model with a range of 0–17.5 points was developed. The score was able to subdivide the population into three risk groups [7]. The PaP score has been validated in both oncological and palliative settings.

In the palliative setting, the validation studies were performed in Australia, Italy, Brazil, and Canada [51–55]. Glare and Virik prospectively recruited 100 consecutive patients referred to palliative medicine consultative services. In this study, each of the three risk groups showed significantly different median survivals (60, 34, and 8 d, respectively) [51].

In the oncology setting, the validation studies were performed in Australia, Italy, and Japan [56–59]. Initially, a validation study of the oncology setting was reported by Glare et al. in 2004, recruiting 100 patients receiving medical or radiation oncology care [56]. The median survival of three risk groups was 17, 7, and < 1 w, respectively. A retrospective study of Ikeguchi et al. was unique because it revealed that patients with non-resectable gastric cancer who were classified into the low-risk group by the PaP score received a more toxic first-line regimen, whereas patients with a high-risk score received a less toxic regimen [57]. Ikeguchi et al. concluded that the PaP score may be a promising tool for selecting a chemotherapy regimen for patients with non-resectable gastric cancer.

Studies modifying the PaP score are also reported. In 2011, Scarpi et al. proposed the D-PaP score, which added the item of delirium into the PaP score [60]. Interestingly, Hui et al. revealed that the PaP score without the CPS showed a better predictive performance than the original PaP score in 2016 [61]. This suggested that the addition of the CPS to the PaP score may actually reduce its accuracy. Further comparison of the PaP score with or without the CPS would be of value.

2.2.2.3. Glasgow prognostic score (GPS)

The Glasgow prognostic score (GPS) is a simple prognostic model based on inflammatory markers, which requires only a CRP and albumin (**Table 1**). The GPS is a prognostic model with the most abundant evidence, and more than 60 papers recruiting more than 30,000 participants have been reported in Ref. [62].

However, studies of the GPS in a palliative care setting are scarce. Partridge et al. retrospectively examined the prognostic performance of 120 patients with advanced cancer at a single institution in the United Kingdom [63]. In this study, patients with a modified GPS of 2 had 2.7 times higher risk of death compared to those with a modified GPS of 0 [63]. In the J-ProVal study, Miura et al. prospectively recruited 1160 patients in palliative care settings [64]. They reported that the positive predictive value (PPV) and NPV of 6 weeks of prognosis of patients with a GPS of 2 were 0.733 and 0.611, respectively.

2.2.2.4. Prognosis in palliative care study (PiPS) predictor model

In 2011, Gwilliam et al. proposed the prognosis in palliative care study (PiPS) model (**Table 1**). In this prospective cohort study, 1018 patients with cancer were recruited from 18 institutions in the United Kingdom [8]. The PiPS-A model does not require laboratory items and showed an AUC of 0.79. The PiPS-B model requires laboratory items and showed an AUC of 0.86.

Since the PiPS model is a relatively newer prognostic model, the number of validation studies is limited [65, 66]. In 2015, Kim et al. reported a validation study of 202 patients with advanced cancer at the palliative care unit (PCU) in Korea [65]. Both the PiPS-A model and the PiPS-B model effectively predicted median survival in the “days” and “weeks” groups; however, it did not in the “months” group [65]. Further validation of the PiPS model is warranted.

2.2.3. Comparison among prognosis prediction models

Direct comparison of different prognostic models in the same cohort is important, because it indicates the usefulness and appropriate clinical use of each model. There are some comparative studies [9, 43, 67], and the largest is the J-ProVal study reported by Baba et al.

Baba et al. tested five different prognosis models: the PaP score, the D-PaP score, the PPI model, the PiPS-A model, and the PiPS-B model [10]. Concerning feasibility, prognostic models without laboratory tests (the PPI model and the PiPS-A model) showed more than 90% feasibility in all palliative care settings, including home care services. Meanwhile, the feasibility of the PaP score, the D-PaP score, and the PiPS-B model, all of which require laboratory items, was 60–80%. In particular, the feasibility of home palliative care services was only 30–40%. Concerning predictive value, the PPI showed a significantly lower C-index than the PaP score and the D-PaP score in almost all settings. The modified PiPS model showed equivalent or superior accuracy to the PaP score and the D-PaP score in all settings [10]. The authors concluded that the “PPI is simple and highly feasible, and seems to be suitable for routine clinical use for situations where rough estimates of prognosis are sufficient and/or patients do not want invasive procedures. Although the PiPS-A model requires 13 items, it provides higher predictive value without invasive procedure.

If laboratory items are available, the PaP score, D-PaP score and PiPS-B model would be more appropriate” [10].

2.2.4. Other prognosis prediction models

In addition to the abovementioned representative prognostic models, other prognostic models are proposed, including the indicator of poor prognosis [68], the Vitamin B12/CRP index [69, 70], the terminal cancer prognostic score [71], the Chuang prognostic score [72, 73], the prognostic 7-day survival formula [74], the Chinese prognostic scale [75], the computer-assisted model [76], the Japan palliative oncology study-prognostic index [77], the objective prognostic score [78, 79], the prognostic nomogram for terminally ill cancer patients [80], and the symptom-based predictive tool [81]. Further validation studies or comparative studies among those models are warranted.

2.2.5. Novel research fields of prognosis prediction models

2.2.5.1. Prediction of sudden unexpected death (SUD)

Prediction of sudden unexpected death (SUD) is a novel and pivotal research field. SUD has no clear definition, but it is often recognized as sudden death that occurs earlier than anticipated [82, 83]. Prevalence of SUD ranges between 0.5 and 23% in the palliative care setting [82]. SUD shows no impending death sign, such as nonreactive pupils, decreased urine output, and peripheral cyanosis, which makes SUD more difficult to predict [82]. Meanwhile, SUD exposes patients, caregivers, and HCPs to serious burden [84]. Particularly, SUD is significantly associated with depression, panic disorder, alcohol use disorder, or social isolation for caregivers or bereaved families [85, 86]. Thus, identifying factors relating to the occurrence of SUD is richly warranted.

2.2.6. Prognosis prediction model using machine learning techniques or artificial intelligence

Because of the progress in the field of informatics, big data can be managed more easily and promptly than ever before. Correspondingly, the number of publications applying novel informatics techniques is rising in clinical research. Prognosis prediction models using machine learning techniques or artificial intelligence have been proposed in the oncology setting [13, 14]. In the coming decades, multidisciplinary studies featuring collaborations between informatics specialists and HCPs are likely to be accelerated. In the palliative care setting, since invasive procedures are generally avoided, the amount of available clinical data—such as blood tests or imaging tests—is limited. This may cause delays in the progress of informatics in the palliative care setting. Therefore, improving data retrieving systems, including those subjective clinical symptoms recorded in text style (for instance, pain, nausea, and appetite loss), will play a key role in the progress of palliative care research.

3. Future plan

Many efforts, reviewed in this chapter, have been made toward developing prognostic models and improving their accuracy. We are also developing a novel prognosis prediction model,

which is “adaptable.” Conventional prognostic models are developed using the data obtained from a single time point (for instance, a baseline assessment date). This study design limits the use of these models under baseline conditions. Because patients’ condition during treatment course can change from the baseline, development of an adaptable prognosis prediction model, which could be applied at any time point after the initiation of chemotherapy, is warranted in practice. Thus, we are developing adaptable prognostic models for patients with cancer receiving chemotherapy [87]. In this case-crossover study, we recruited 2693 patients, and 3,471,521 laboratory data at 115,738 time points, representing 40 laboratory items that were monitored for 1 year before the death event, were applied in developing prognostic models. The prognosis prediction model utilizing albumin, lactate dehydrogenase, and neutrophils was selected based on its strong ability to predict death events within 1 month–6 months, and the AUC for 1-month and 2-month models was more than 0.80. We plan to compare this novel model with existing conventional models.

Meanwhile, apart from the effort to predict more accurate prognosis, we should also focus on the issue that no previous studies clearly demonstrated whether application of such prognosis prediction models truly benefits patient care in daily clinical practice. There are concerns that we may be satisfied merely with developing or using prognosis prediction models but pay less attention to assessing their clinical utility. Next, we consider how prognosis prediction can benefit patients.

3.1. Efficacy of prognosis prediction for cancer patients

3.1.1. Clinical utility of prognostic disclosure

First, how many patients are willing to have their prognosis disclosed to them? Although it differs across studies, the proportion is reported to be 40–60% [88, 89]. It was shown that patients were willing to know their life expectancy in greater detail than anticipated by HCPs [90]. Thus, HCPs need to disclose the prognosis properly to patients who want this information.

Studies investigating the clinical outcome of prognostic disclosure are scarce. To the best of our knowledge, there are no clinical trials, but a few observational studies have been reported. In 2015, Enzinger et al. reported on a large prospective cohort study, “Coping with Cancer” [91]. In this study, 590 patients with advanced cancer were analyzed, and patients for whom their prognosis was disclosed had a more realistic understanding of life expectancy than those for whom it was not (median patient self-estimates of life expectancy 12 months versus 48 months). Moreover, patients with a realistic understanding of life expectancy preferred comfort-oriented over life-prolonging care, with a higher likelihood of a do-not-resuscitate order without deteriorating the patients’ emotional well-being or the patient-physician relationship [91]. Despite the limitation of being an observational study, however, this study produced meaningful findings for the association between prognosis disclosure and advance care planning (ACP).

Many studies have investigated whether ACP benefited end-of-life management. In the “Coping with Cancer” study, Wright et al. showed that end-of-life discussion was significantly

associated with a less aggressive medical care (such as ventilation, ICU admission, and resuscitation), a reduction in the bereaved caregiver's grief or depression, and a longer hospice stay [92]. Other similar studies also showed consistent results [1, 93, 94].

3.1.2. Clinical utility of prognosis prediction model

The outcomes of prognosis disclosure based on prognostic models would be expected to be the same as the outcomes referred to in Section 3.1.1. Considering study design is a challenging issue. For example, prognosis disclosure based on prognostic models versus the CPS may be interesting, but it may also introduce some ethical issues that need to be resolved. We hope that the number of studies investigating the clinical utility of prognostic models will increase in the near future.

4. Conclusion

A number of prognosis prediction models are proposed, and their accuracy is approaching 80–90%. Novel techniques, such as machine learning or artificial intelligence, would accelerate progress. At the same time, we need to put greater efforts to clarify the clinical utility of prognosis prediction models for patients with cancer, a topic that has been beyond the scope of the main issues in this research field for a long time.

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References

- [1] Wright AA, Zhang B, Keating NL, Weeks JC, Prigerson HG. Associations between palliative chemotherapy and adult cancer patients' end-of-life care and place of death: Prospective cohort study. *BMJ* 2014;**348**:g1219. DOI: 10.1136/bmj.g1219
- [2] Cheung MC, Earle CC, Rangrej J, Ho TH, Liu N, Barbera L, et al. Impact of aggressive management and palliative care on cancer costs in the final month of life. *Cancer*. 2015;**121**(18):3307-15.

- [3] Prigerson HG, Bao Y, Shah MA, Paulk ME, LeBlanc TW, Schneider BJ, et al. Chemotherapy use, performance status, and quality of life at the end of life. *JAMA Oncology*. 2015;**1**(6): 778-784. DOI: 10.1001/jamaoncol.2015.2378
- [4] Wu CC, Hsu TW, Chang CM, Lee CH, Huang CY, Lee CC. Palliative chemotherapy affects aggressiveness of end-of-life care. *The Oncologist*. 2016;**21**(6):771-777. DOI: 10.1634/theoncologist.2015-0445
- [5] Glare P, Virik K, Jones M, Hudson M, Eychmuller S, Simes J, et al. A systematic review of physicians' survival predictions in terminally ill cancer patients. *BMJ*. 2003;**327**(7408): 195-198. DOI: 10.1136/bmj.327.7408.195
- [6] Morita T, Tsunoda J, Inoue S, Chihara S. The Palliative Prognostic Index: A scoring system for survival prediction of terminally ill cancer patients. *Supportive Care in Cancer: Official Journal of the Multinational Association of Supportive Care in Cancer*. 1999;**7**(3):128-133
- [7] Pirovano M, Maltoni M, Nanni O, Marinari M, Indelli M, Zaninetta G, et al. A new palliative prognostic score: A first step for the staging of terminally ill cancer patients. Italian Multicenter and Study Group on Palliative Care. *Journal of Pain and Symptom Management*. 1999;**17**(4):231-239
- [8] Gwilliam B, Keeley V, Todd C, Gittins M, Roberts C, Kelly L, et al. Development of prognosis in palliative care study (PiPS) predictor models to improve prognostication in advanced cancer: Prospective cohort study. *BMJ*. 2011;**343**:d4920. DOI: 10.1136/bmj.d4920
- [9] Maltoni M, Scarpi E, Pittureri C, Martini F, Montanari L, Amaducci E, et al. Prospective comparison of prognostic scores in palliative care cancer populations. *The Oncologist*. 2012;**17**(3):446-454. DOI: 10.1634/theoncologist.2011-0397
- [10] Baba M, Maeda I, Morita T, Inoue S, Ikenaga M, Matsumoto Y, et al. Survival prediction for advanced cancer patients in the real world: A comparison of the Palliative Prognostic Score, Delirium-Palliative Prognostic Score, Palliative Prognostic Index and modified Prognosis in Palliative Care Study predictor model. *European Journal of Cancer*. 2015;**51**(12):1618-1629. DOI: 10.1016/j.ejca.2015.04.025
- [11] Grundmann O, Yoon SL, Williams JJ. The value of bioelectrical impedance analysis and phase angle in the evaluation of malnutrition and quality of life in cancer patients—A comprehensive review. *European Journal of Clinical Nutrition*. 2015;**69**(12):1290-1297. DOI: 10.1038/ejcn.2015.126
- [12] Innominato PF, Focan C, Gorlia T, Moreau T, Garufi C, Waterhouse J, et al. Circadian rhythm in rest and activity: A biological correlate of quality of life and a predictor of survival in patients with metastatic colorectal cancer. *Cancer Research*. 2009;**69**(11):4700-4707. DOI: 10.1158/0008-5472.can-08-4747
- [13] Kourou K, Exarchos TP, Exarchos KP, Karamouzis MV, Fotiadis DI. Machine learning applications in cancer prognosis and prediction. *Computational and Structural Biotechnology Journal*. 2015;**13**:8-17. DOI: 10.1016/j.csbj.2014.11.005

- [14] Enshaei A, Robson CN, Edmondson RJ. Artificial intelligence systems as prognostic and predictive tools in ovarian cancer. *Annals of Surgical Oncology*. 2015;**22**(12):3970-3975. DOI: 10.1245/s10434-015-4475-6
- [15] Hui D, Kilgore K, Nguyen L, Hall S, Fajardo J, Cox-Miller TP, et al. The accuracy of probabilistic versus temporal clinician prediction of survival for patients with advanced cancer: A preliminary report. *The Oncologist*. 2011;**16**(11):1642-1648. DOI: 10.1634/theoncologist.2011-0173
- [16] Christakis NA, Lamont EB. Extent and determinants of error in doctors' prognoses in terminally ill patients: Prospective cohort study. *BMJ*. 2000;**320**(7233):469-472
- [17] Moss AH, Lunney JR, Culp S, Auber M, Kurian S, Rogers J, et al. Prognostic significance of the "surprise" question in cancer patients. *Journal of Palliative Medicine*. 2010;**13**(7):837-840. DOI: 10.1089/jpm.2010.0018
- [18] Hamano J, Morita T, Inoue S, Ikenaga M, Matsumoto Y, Sekine R, et al. Surprise questions for survival prediction in patients with advanced cancer: A multicenter prospective cohort study. *The Oncologist*. 2015;**20**(7):839-844. DOI: 10.1634/theoncologist.2015-0015
- [19] Elliott M, Nicholson C. A qualitative study exploring use of the surprise question in the care of older people: Perceptions of general practitioners and challenges for practice. *BMJ Support Palliat Care*. 2017;**7**(1):32-38. DOI: 10.1136/bmjspcare-2014-000679
- [20] Perez-Cruz PE, Dos Santos R, Silva TB, Crovador CS, Nascimento MS, Hall S, et al. Longitudinal temporal and probabilistic prediction of survival in a cohort of patients with advanced cancer. *Journal of Pain and Symptom Management*. 2014;**48**(5):875-882. DOI: 10.1016/j.jpainsymman.2014.02.007
- [21] Amano K, Maeda I, Shimoyama S, Shinjo T, Shirayama H, Yamada T, et al. The accuracy of physicians' clinical predictions of survival in patients with advanced cancer. *Journal of Pain and Symptom Management*. 2015;**50**(2):139-146.e1. DOI: 10.1016/j.jpainsymman.2015.03.004
- [22] Seow H, Barbera L, Sutradhar R, Howell D, Dudgeon D, Atzema C, et al. Trajectory of performance status and symptom scores for patients with cancer during the last six months of life. *Journal of Clinical Oncology*. 2011;**29**(9):1151-1158. DOI: 10.1200/jco.2010.30.7173
- [23] Downing M, Lau F, Lesperance M, Karlson N, Shaw J, Kuziemy C, et al. Meta-analysis of survival prediction with Palliative Performance Scale. *Journal of Palliative Care*. 2007;**23**(4):245-252; discussion 52-4
- [24] Myers J, Kim A, Flanagan J, Selby D. Palliative performance scale and survival among outpatients with advanced cancer. *Supportive Care in Cancer: Official Journal of the Multinational Association of Supportive Care in Cancer*. 2015;**23**(4):913-918. DOI: 10.1007/s00520-014-2440-8
- [25] Vigano A, Dorgan M, Buckingham J, Bruera E, Suarez-Almazor ME. Survival prediction in terminal cancer patients: A systematic review of the medical literature. *Palliative Medicine*. 2000;**14**(5):363-374

- [26] Gripp S, Moeller S, Bolke E, Schmitt G, Matuschek C, Asgari S, et al. Survival prediction in terminally ill cancer patients by clinical estimates, laboratory tests, and self-rated anxiety and depression. *Journal of Clinical Oncology*. 2007;**25**(22):3313-3320. DOI: 10.1200/jco.2006.10.5411
- [27] Thoresen L, Frykholm G, Lydersen S, Ulveland H, Baracos V, Prado CM, et al. Nutritional status, cachexia and survival in patients with advanced colorectal carcinoma. Different assessment criteria for nutritional status provide unequal results. *Clinical Nutrition (Edinburgh, Scotland)*. 2013;**32**(1):65-72. DOI: 10.1016/j.clnu.2012.05.009
- [28] Tan CS, Read JA, Phan VH, Beale PJ, Peat JK, Clarke SJ. The relationship between nutritional status, inflammatory markers and survival in patients with advanced cancer: A prospective cohort study. *Supportive Care in Cancer: Official Journal of the Multinational Association of Supportive Care in Cancer*. 2015;**23**(2):385-391. DOI: 10.1007/s00520-014-2385-y
- [29] Martin L, Senesse P, Gioulbasanis I, Antoun S, Bozzetti F, Deans C, et al. Diagnostic criteria for the classification of cancer-associated weight loss. *Journal of Clinical Oncology*. 2015;**33**(1):90-99. DOI: 10.1200/jco.2014.56.1894
- [30] Caraceni A, Nanni O, Maltoni M, Piva L, Indelli M, Arnoldi E, et al. Impact of delirium on the short term prognosis of advanced cancer patients. Italian Multicenter Study Group on Palliative Care. *Cancer*. 2000;**89**(5):1145-1149
- [31] Lawlor PG, Gagnon B, Mancini IL, Pereira JL, Hanson J, Suarez-Almazor ME, et al. Occurrence, causes, and outcome of delirium in patients with advanced cancer: A prospective study. *Archives of Internal Medicine*. 2000;**160**(6):786-794
- [32] Levi F, Dugue PA, Innominato P, Karaboue A, Dispersyn G, Parganiha A, et al. Wrist actimetry circadian rhythm as a robust predictor of colorectal cancer patients survival. *Chronobiology International*. 2014;**31**(8):891-900. DOI: 10.3109/07420528.2014.924523
- [33] Maltoni M, Caraceni A, Brunelli C, Broeckaert B, Christakis N, Eychmueller S, et al. Prognostic factors in advanced cancer patients: Evidence-based clinical recommendations—A study by the Steering Committee of the European Association for Palliative Care. *Journal of Clinical Oncology*. 2005;**23**(25):6240-6248. DOI: 10.1200/jco.2005.06.866
- [34] Templeton AJ, McNamara MG, Seruga B, Vera-Badillo FE, Aneja P, Ocana A, et al. Prognostic role of neutrophil-to-lymphocyte ratio in solid tumors: A systematic review and meta-analysis. *Journal of the National Cancer Institute*. 2014;**106**(6):dju124. DOI: 10.1093/jnci/dju124
- [35] Barbot AC, Mussault P, Ingrand P, Tourani JM. Assessing 2-month clinical prognosis in hospitalized patients with advanced solid tumors. *Journal of Clinical Oncology*. 2008;**26**(15):2538-2543. DOI: 10.1200/jco.2007.14.9518
- [36] Vigano A, Bruera E, Jhangri GS, Newman SC, Fields AL, Suarez-Almazor ME. Clinical survival predictors in patients with advanced cancer. *Archives of Internal Medicine*. 2000;**160**(6):861-868

- [37] Donovan PJ, Achong N, Griffin K, Galligan J, Pretorius CJ, McLeod DS. PTHrP-mediated hypercalcemia: Causes and survival in 138 patients. *The Journal of Clinical Endocrinology and Metabolism*. 2015;**100**(5):2024-2029. DOI: 10.1210/jc.2014-4250
- [38] Suh SY, Ahn HY. Lactate dehydrogenase as a prognostic factor for survival time of terminally ill cancer patients: A preliminary study. *European Journal of Cancer*. 2007;**43**(6):1051-1059. DOI: 10.1016/j.ejca.2007.01.031
- [39] Morita T, Tsunoda J, Inoue S, Chihara S. Improved accuracy of physicians' survival prediction for terminally ill cancer patients using the Palliative Prognostic Index. *Palliative Medicine*. 2001;**15**(5):419-424
- [40] Cheng WH, Kao CY, Hung YS, Su PJ, Hsieh CH, Chen JS, et al. Validation of a palliative prognostic index to predict life expectancy for terminally ill cancer patients in a hospice consultation setting in Taiwan. *Asian Pacific Journal of Cancer Prevention: APJCP*. 2012;**13**(6):2861-2866
- [41] Alshemmari S, Ezzat H, Samir Z, Refaat S, Alsirafy SA. The palliative prognostic index for the prediction of survival and in-hospital mortality of patients with advanced cancer in Kuwait. *Journal of Palliative Medicine*. 2012;**15**(2):200-204. DOI: 10.1089/jpm.2011.0253
- [42] Sonoda H, Yamaguchi T, Matsumoto M, Hisahara K. Validation of the palliative prognostic index and palliative prognostic score in a palliative care consultation team setting for patients with advanced cancers in an acute care hospital in Japan. *The American Journal of Hospice & Palliative Care*. 2014;**31**(7):730-734. DOI: 10.1177/1049909113506034
- [43] Chou WC, Kao CY, Wang PN, Chang H, Wang HM, Chang PH, et al. The application of the Palliative Prognostic Index, Charlson comorbidity index, and Glasgow Prognostic Score in predicting the life expectancy of patients with hematologic malignancies under palliative care. *BMC Palliative Care*. 2015;**14**:18. DOI: 10.1186/s12904-015-0011-5
- [44] Stone CA, Tiernan E, Dooley BA. Prospective validation of the palliative prognostic index in patients with cancer. *Journal of Pain and Symptom Management*. 2008;**35**(6):617-622. DOI: 10.1016/j.jpainsymman.2007.07.006
- [45] Subramaniam S, Thorns A, Ridout M, Thirukkumaran T, Osborne TR. Accuracy of prognosis prediction by PPI in hospice in patients with cancer: A multi-centre prospective study. *BMJ Supportive & Palliative Care*. 2015;**5**(4):399-404. DOI: 10.1136/bmjspcare-2012-000239rep
- [46] Yoong J, Atkin N, Le B. Use of the palliative prognostic index in a palliative care consultation service in Melbourne, Australia. *Journal of Pain and Symptom Management*. 2010;**39**(1):e2-e4. DOI: 10.1016/j.jpainsymman.2009.08.001
- [47] Hamano J, Morita T, Ozawa T, Shishido H, Kawahara M, Aoki S, et al. Validation of the simplified palliative prognostic index using a single item from the communication capacity scale. *Journal of Pain and Symptom Management*. 2015;**50**(4):542-547.e4. DOI: 10.1016/j.jpainsymman.2015.04.021

- [48] Hamano J, Tokuda Y, Kawagoe S, Shinjo T, Shirayama H, Ozawa T, et al. Adding items that assess changes in activities of daily living does not improve the predictive accuracy of the Palliative Prognostic Index. *Palliative Medicine* 2017;**31**(3):258-266. DOI: 10.1177/0269216316650788
- [49] Kao CY, Hung YS, Wang HM, Chen JS, Chin TL, Lu CY, et al. Combination of initial palliative prognostic index and score change provides a better prognostic value for terminally ill cancer patients: A six-year observational cohort study. *Journal of Pain and Symptom Management*. 2014;**48**(5):804-814. DOI: 10.1016/j.jpainsymman.2013.12.246
- [50] Hung CY, Wang HM, Kao CY, Lin YC, Chen JS, Hung YS, et al. Magnitude of score change for the palliative prognostic index for survival prediction in patients with poor prognostic terminal cancer. *Supportive Care in Cancer: Official Journal of the Multinational Association of Supportive Care in Cancer*. 2014;**22**(10):2725-2731. DOI: 10.1007/s00520-014-2274-4
- [51] Glare P, Virik K. Independent prospective validation of the PaP score in terminally ill patients referred to a hospital-based palliative medicine consultation service. *Journal of Pain and Symptom Management*. 2001;**22**(5):891-898
- [52] Maltoni M, Nanni O, Pirovano M, Scarpi E, Indelli M, Martini C, et al. Successful validation of the palliative prognostic score in terminally ill cancer patients. Italian Multicenter Study Group on Palliative Care. *Journal of Pain and Symptom Management*. 1999;**17**(4):240-247
- [53] Naylor C, Cerqueira L, Costa-Paiva LH, Costa JV, Conde DM, Pinto-Neto AM. Survival of women with cancer in palliative care: Use of the palliative prognostic score in a population of Brazilian women. *Journal of Pain and Symptom Management*. 2010;**39**(1):69-75. DOI: 10.1016/j.jpainsymman.2009.05.020
- [54] Tarumi Y, Watanabe SM, Lau F, Yang J, Quan H, Sawchuk L, et al. Evaluation of the Palliative Prognostic Score (PaP) and routinely collected clinical data in prognostication of survival for patients referred to a palliative care consultation service in an acute care hospital. *Journal of Pain and Symptom Management*. 2011;**42**(3):419-431. DOI: 10.1016/j.jpainsymman.2010.12.013
- [55] Mendis R, Soo WK, Zannino D, Michael N, Spruyt O. Multidisciplinary prognostication using the palliative prognostic score in an Australian Cancer Center. *Palliative Care*. 2015;**9**:7-14. DOI: 10.4137/pcrt.s24411
- [56] Glare PA, Eychmueller S, McMahon P. Diagnostic accuracy of the palliative prognostic score in hospitalized patients with advanced cancer. *Journal of Clinical Oncology*. 2004;**22**(23):4823-4828. DOI: 10.1200/JCO.2004.12.056
- [57] Ikeguchi M, Kader A, Yoshimoto M, Takaya S, Watanabe J, Fukumoto Y, et al. Usefulness of palliative prognostic score in the treatment of patients with non-resectable gastric cancer. *Molecular and Clinical Oncology*. 2013;**1**(2):253-256. DOI: 10.3892/mco.2013.66

- [58] Tassinari D, Montanari L, Maltoni M, Ballardini M, Piancastelli A, Musi M, et al. The palliative prognostic score and survival in patients with advanced solid tumors receiving chemotherapy. *Supportive Care in Cancer: Official Journal of the Multinational Association of Supportive Care in Cancer*. 2008;**16**(4):359-370. DOI: 10.1007/s00520-007-0302-3
- [59] Numico G, Occelli M, Russi EG, Silvestris N, Pasero R, Fea E, et al. Survival prediction and frequency of anticancer treatment in cancer patients hospitalized due to acute conditions. Role of clinical parameters and PaP score. *Supportive Care in Cancer: Official Journal of the Multinational Association of Supportive Care in Cancer*. 2011;**19**(11):1823-1830. DOI: 10.1007/s00520-010-1024-5
- [60] Scarpi E, Maltoni M, Miceli R, Mariani L, Caraceni A, Amadori D, et al. Survival prediction for terminally ill cancer patients: Revision of the palliative prognostic score with incorporation of delirium. *The Oncologist*. 2011;**16**(12):1793-1799. DOI: 10.1634/theoncologist.2011-0130
- [61] Hui D, Park M, Liu D, Paiva CE, Suh SY, Morita T, et al. Clinician prediction of survival versus the Palliative Prognostic Score: Which approach is more accurate? *European Journal of Cancer*. 2016;**64**:89-95. DOI: 10.1016/j.ejca.2016.05.009
- [62] McMillan DC. The systemic inflammation-based Glasgow Prognostic Score: A decade of experience in patients with cancer. *Cancer Treatment Reviews*. 2013;**39**(5):534-540. DOI: 10.1016/j.ctrv.2012.08.003
- [63] Partridge M, Fallon M, Bray C, McMillan D, Brown D, Laird B. Prognostication in advanced cancer: A study examining an inflammation-based score. *Journal of Pain and Symptom Management*. 2012;**44**(2):161-167. DOI: 10.1016/j.jpainsymman.2011.08.013
- [64] Miura T, Matsumoto Y, Hama T, Amano K, Tei Y, Kikuchi A, et al. Glasgow prognostic score predicts prognosis for cancer patients in palliative settings: A subanalysis of the Japan-prognostic assessment tools validation (J-ProVal) study. *Supportive Care in Cancer: Official Journal of the Multinational Association of Supportive Care in Cancer*. 2015;**23**(11):3149-3156. DOI: 10.1007/s00520-015-2693-x
- [65] Kim ES, Lee JK, Kim MH, Noh HM, Jin YH. Validation of the prognosis in palliative care study predictor models in terminal cancer patients. *Korean Journal of Family Medicine*. 2014;**35**(6):283-294. DOI: 10.4082/kjfm.2014.35.6.283
- [66] Baba M, Maeda I, Morita T, Hisanaga T, Ishihara T, Iwashita T, et al. Independent validation of the modified prognosis palliative care study predictor models in three palliative care settings. *Journal of Pain and Symptom Management*. 2015;**49**(5):853-860. DOI: 10.1016/j.jpainsymman.2014.10.010
- [67] Stiel S, Bertram L, Neuhaus S, Nauck F, Ostgathe C, Elsner F, et al. Evaluation and comparison of two prognostic scores and the physicians' estimate of survival in terminally ill patients. *Supportive Care in Cancer: Official Journal of the Multinational Association of Supportive Care in Cancer*. 2010;**18**(1):43-49. DOI: 10.1007/s00520-009-0628-0

- [68] Bruera E, Miller MJ, Kuehn N, MacEachern T, Hanson J. Estimate of survival of patients admitted to a palliative care unit: A prospective study. *Journal of Pain and Symptom Management*. 1992;**7**(2):82-86
- [69] Geissbuhler P, Mermillod B, Rapin CH. Elevated serum vitamin B12 levels associated with CRP as a predictive factor of mortality in palliative care cancer patients: A prospective study over five years. *Journal of Pain and Symptom Management*. 2000;**20**(2):93-103
- [70] Kelly L, White S, Stone PC. The B12/CRP index as a simple prognostic indicator in patients with advanced cancer: A confirmatory study. *Annals of Oncology: Official Journal of the European Society for Medical Oncology/ESMO*. 2007;**18**(8):1395-1399. DOI: 10.1093/annonc/mdm138
- [71] Yun YH, Heo DS, Heo BY, Yoo TW, Bae JM, Ahn SH. Development of terminal cancer prognostic score as an index in terminally ill cancer patients. *Oncology Reports*. 2001;**8**(4):795-800
- [72] Chuang RB, Hu WY, Chiu TY, Chen CY. Prediction of survival in terminal cancer patients in Taiwan: Constructing a prognostic scale. *Journal of Pain and Symptom Management*. 2004;**28**(2):115-122. DOI: 10.1016/j.jpainsymman.2003.11.008
- [73] Al-Zahrani AS, El-Kashif AT, Mohammad AA, Elsamany S, Alsirafy SA. Prediction of in-hospital mortality of patients with advanced cancer using the Chuang Prognostic Score. *The American Journal of Hospice & Palliative Care*. 2013;**30**(7):707-711. DOI: 10.1177/1049909112467362
- [74] Chiang JK, Lai NS, Wang MH, Chen SC, Kao YH. A proposed prognostic 7-day survival formula for patients with terminal cancer. *BMC Public Health*. 2009;**9**:365. DOI: 10.1186/1471-2458-9-365
- [75] Lingjun Z, Jing C, Jian L, Wee B, Jijun Z. Prediction of survival time in advanced cancer: A prognostic scale for Chinese patients. *Journal of Pain and Symptom Management*. 2009;**38**(4):578-586. DOI: 10.1016/j.jpainsymman.2008.12.005
- [76] Chiang JK, Cheng YH, Koo M, Kao YH, Chen CY. A computer-assisted model for predicting probability of dying within 7 days of hospice admission in patients with terminal cancer. *Japanese Journal of Clinical Oncology*. 2010;**40**(5):449-455. DOI: 10.1093/jjco/hyp188
- [77] Hyodo I, Morita T, Adachi I, Shima Y, Yoshizawa A, Hiraga K. Development of a predicting tool for survival of terminally ill cancer patients. *Japanese Journal of Clinical Oncology*. 2010;**40**(5):442-448. DOI: 10.1093/jjco/hyp182
- [78] Suh SY, Choi YS, Shim JY, Kim YS, Yeom CH, Kim D, et al. Construction of a new, objective prognostic score for terminally ill cancer patients: A multicenter study. *Supportive Care in Cancer: Official Journal of the Multinational Association of Supportive Care in Cancer*. 2010;**18**(2):151-157. DOI: 10.1007/s00520-009-0639-x

- [79] Yoon SJ, Jung JG, Kim JS, Kim SS, Kim S. Retrospective assessment of objective prognostic score in terminally ill Korean patients with cancer. *The American Journal of Hospice & Palliative Care*. 2014;**31**(4):435-440. DOI: 10.1177/1049909113492557
- [80] Feliu J, Jimenez-Gordo AM, Madero R, Rodriguez-Aizcorbe JR, Espinosa E, Castro J, et al. Development and validation of a prognostic nomogram for terminally ill cancer patients. *Journal of the National Cancer Institute*. 2011;**103**(21):1613-1620. DOI: 10.1093/jnci/djr388
- [81] Nabal M, Bescos M, Barcons M, Torrubia P, Trujillano J, Requena A. New symptom-based predictive tool for survival at seven and thirty days developed by palliative home care teams. *Journal of Palliative Medicine*. 2014;**17**(10):1158-1163. DOI: 10.1089/jpm.2013.0630
- [82] Bruera S, Chisholm G, Dos Santos R, Bruera E, Hui D. Frequency and factors associated with unexpected death in an acute palliative care unit: Expect the unexpected. *Journal of Pain and Symptom Management*. 2015;**49**(5):822-827. DOI: 10.1016/j.jpainsymman.2014.10.011
- [83] Hui D. Unexpected death in palliative care: What to expect when you are not expecting. *Current Opinion in Supportive and Palliative Care*. 2015;**9**(4):369-374. DOI: 10.1097/spc.0000000000000174
- [84] Goodlin SJ, Zhong Z, Lynn J, Teno JM, Fago JP, Desbiens N, et al. Factors associated with use of cardiopulmonary resuscitation in seriously ill hospitalized adults. *JAMA*. 1999;**282**(24):2333-2339
- [85] Burton AM, Haley WE, Small BJ. Bereavement after caregiving or unexpected death: Effects on elderly spouses. *Aging & Mental Health*. 2006;**10**(3):319-326. DOI: 10.1080/13607860500410045
- [86] Keyes KM, Pratt C, Galea S, McLaughlin KA, Koenen KC, Shear MK. The burden of loss: Unexpected death of a loved one and psychiatric disorders across the life course in a national study. *The American Journal of Psychiatry*. 2014;**171**(8):864-871. DOI: 10.1176/appi.ajp.2014.13081132
- [87] U Yu, T Kei, T Akiko, O Kazuya, N Akira, Y Daisuke, et al. Establishment of a terminal prognosis prediction model by applying time series analysis to real-world data. *Annals of Oncology*. 2015;**26**(Suppl 7):vii79-vii105. DOI: 10.1093/annonc/mdv471.84
- [88] Elkin EB, Kim SH, Casper ES, Kissane DW, Schrag D. Desire for information and involvement in treatment decisions: Elderly cancer patients' preferences and their physicians' perceptions. *Journal of Clinical Oncology*. 2007;**25**(33):5275-5280. DOI: 10.1200/jco.2007.11.1922
- [89] Hagerty RG, Butow PN, Ellis PA, Lobb EA, Pendlebury S, Leighl N, et al. Cancer patient preferences for communication of prognosis in the metastatic setting. *Journal of Clinical Oncology*. 2004;**22**(9):1721-1730. DOI: 10.1200/jco.2004.04.095

- [90] Fumis RR, De Camargo B, Del Giglio A. Physician, patient and family attitudes regarding information on prognosis: A Brazilian survey. *Annals of Oncology: Official Journal of the European Society for Medical Oncology/ESMO*. 2012;**23**(1):205-211. DOI: 10.1093/annonc/mdr049
- [91] Enzinger AC, Zhang B, Schrag D, Prigerson HG. Outcomes of prognostic disclosure: Associations with prognostic understanding, distress, and relationship with physician among patients with advanced cancer. *Journal of Clinical Oncology*. 2015;**33**(32):3809-3816. DOI: 10.1200/JCO.2015.61.9239
- [92] Wright AA, Zhang B, Ray A, Mack JW, Trice E, Balboni T, et al. Associations between end-of-life discussions, patient mental health, medical care near death, and caregiver bereavement adjustment. *JAMA*. 2008;**300**(14):1665-1673. DOI: 10.1001/jama.300.14.1665
- [93] Tang ST, Liu TW, Liu LN, Chiu CF, Hsieh RK, Tsai CM. Physician-patient end-of-life care discussions: Correlates and associations with end-of-life care preferences of cancer patients-a cross-sectional survey study. *Palliative Medicine*. 2014;**28**(10):1222-1230. DOI: 10.1177/0269216314540974
- [94] Mack JW, Cronin A, Keating NL, Taback N, Huskamp HA, Malin JL, et al. Associations between end-of-life discussion characteristics and care received near death: A prospective cohort study. *Journal of Clinical Oncology*. 2012;**30**(35):4387-4395. DOI: 10.1200/jco.2012.43.6055