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Review Article

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Prediction of Survival in Patients with Advanced Cancer: A Narrative Review and Future Research Priorities

Yusuke Hiratsuka, M.D., Ph.D.*,†, **Jun Hamano**, M.D., Ph.D.†, **Masanori Mori**, M.D., Ph.D.§, **Isseki Maeda**, M.D., Ph.D.‖, **Tatsuya Morita**, M.D., Ph.D.§ and **Sang-Yeon Suh**, M.D., Ph.D.¶,**

*Department of Palliative Medicine, Takeda General Hospital, Aizu Wakamatsu,
†Department of Palliative Medicine, Tohoku University School of Medicine, Sendai,
‡Department of Palliative and Supportive Care, Institute of Medicine, University of Tsukuba, Tsukuba,
§Department of Palliative and Supportive Care, Seirei Mikatahara General Hospital, Hamamatsu,
‖Department of Palliative Care, Senri Chuo Hospital, Toyonaka, Japan,
¶Department of Family Medicine, Dongguk University Ilsan Hospital, Goyang,
**Department of Medicine, Dongguk University Medical School, Seoul, Korea

This paper aimed to summarize the current situation of prognostication for patients with an expected survival of weeks or months, and to clarify future research priorities. Prognostic information is essential for patients, their families, and medical professionals to make end-of-life decisions. The clinician's prediction of survival is often used, but this may be inaccurate and optimistic. Many prognostic tools, such as the Palliative Performance Scale, Palliative Prognostic Index, Palliative Prognostic Score, and Prognosis in Palliative Care Study, have been developed and validated to reduce the inaccuracy of the clinician's prediction of survival. To date, there is no consensus on the most appropriate method of comparing tools that use different formats to predict survival. Therefore, the feasibility of using prognostic scales in clinical practice and the information wanted by the end users can determine the appropriate prognostic tool to use. We propose four major themes for further prognostication research: (1) functional prognosis, (2) outcomes of prognostic communication, (3) artificial intelligence, and (4) education for clinicians.

Key Words: Prognosis, Survival analysis, Decision making, Artificial intelligence, Education

Correspondence to
Yusuke Hiratsuka
ORCID:
https://orcid.org/0000-0003-2334-3893
E-mail: hiratsuka.med.t@gmail.com

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INTRODUCTION

Prognostic information is essential for patients, their families, and medical professionals to make end-of-life (EOL) decisions. Patients' life expectancy can directly affect their care because complex decisions such as systemic anticancer treatment and hospice care depend on prognostic information [1]. The clinician's prediction of survival (CPS) is often used, but this may be inaccurate and optimistic, with a reported accuracy of around 20~30% [2]. Inaccurate prognostication may contribute to more aggressive EOL care [3]. Therefore, clinicians are encouraged to supplement CPS with established prognostic tools such as the Palliative Prognostic Index (PPI) [4] and the Palliative Prognostic Score (PaP) [5]. However, few studies have investigated patients' outcomes according to prognostication. We aimed to summarize the current situation for prognostication in patients with an expected survival of a few weeks or months, and to clarify future research priorities.

1. Current prognostic models

1) CPS

CPS has been reported to be inaccurate and excessively optimistic, although heterogeneous methods have been used to formulate CPS and assess its accuracy [2]. A systematic review reported the accuracy of CPS in palliative care, with categorical estimates of survival between 23% and 78% and a probability estimate discrimination (evaluated by the c-index) between 0.74 and 0.78 [2]. Therefore, medical professionals should rethink how the accuracy of CPS should be interpreted. Recently, an international multicenter cohort study reported that CPS formulated by palliative care specialists showed good performance in predicting the weeks and days of survival among patients admitted to palliative care units [6]. However, it was suggested that experienced clinicians can use CPS, but should be aware of its limitations.

2) Surprise question

Clinicians can predict patients' prognosis using the "surprise question" (SQ), such as, "Would I be surprised if this patient were to die within the next year (or other specified time period)?" The SQ can be considered as a categorical form of CPS with two categories. The sensitivity and specificity of the 30-day SQ were reported as 95.6% and 37.0%, respectively, and that of the 7-day SQ as 84.7% and 68.0%, respectively [7]. These findings suggest that clinicians can screen patients for 30- and 7-day survival using the SQ.

3) Palliative performance scale (PPS)

The Palliative Performance Scale (PPS) [8] includes five domains: ambulation, activity level, evidence of disease, self-care, intake, and level of consciousness. The PPS was found to be as accurate as the PaP and PPI for patients with 60-, 30-, 14-, or 7-day survival [6,9]. Using the PPS may help to improve prognostic confidence among inexperienced clinicians.

4) PaP

The PaP comprises CPS, Karnofsky Performance Status, dyspnea, anorexia, leukocyte count, and lymphocyte percentage [5]. The PaP aims to predict 30-day survival and has been validated in various clinical settings [10]. Inexperienced clinicians may hesitate to use the PaP because it can be difficult for them to formulate CPS [11]. However, recent, large-scale cohort studies demonstrated that CPS enhanced the accuracy of the PaP [12].

5) PPI

The PPI [4] covers five variables: oral intake, edema, dyspnea at rest, delirium, and the PPS. The PPI aims to predict 3-week survival and has been validated in various clinical settings [13]. A laboratory test is not necessary to calculate a PPI score, meaning that this tool is easy to use in various settings. However, medical professionals often misdiagnose delirium, meaning the accuracy of the PPI may be lower among inexperienced clinicians.

6) Prognosis in palliative care study (PiPS) models

Prognosis in Palliative Care Study (PiPS) models were developed and validated in patients with advanced incurable cancer [14,15]. The PiPS score can be calculated using the website calculator (www.ucl.ac.uk/psychiatry/pips). The PiPS can predict probability estimates for 14- and 56-day survival in patients for whom blood results are not available (PiPS-A) or are available (PiPS-B). It has been reported that all PiPS models (PiPS-A14, PiPS-A56, PiPS-B14, and PiPS-B56) had excellent discrimination and were well-calibrated [15].

7) Objective prognostic score (OPS)

The Objective Prognostic Score (OPS) is a tool that does not require CPS and was developed through a multicenter study in Korea and validated in various settings [16]. The OPS covers anorexia, dyspnea, Eastern Cooperative Oncology Group Performance Status, leukocyte count, and serum total bilirubin, creatinine, and lactate dehydrogenase levels. The OPS is optimized to predict 3-week survival and may therefore be useful for inexperienced physicians who hesitate to estimate CPS.

2. How should clinicians carry out prognostication?

Recent studies suggested that expert CPS is as accurate as prognostic tools [6,9], although many different prognostic tools have been developed and validated. However, there are major methodological challenges in directly comparing the accuracy of prognostic tools with that of CPS [17]. The area

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under the receiver operating characteristic curve or c-index should be used to compare the accuracy of CPS with other prognostic tools [10], although this may not capture clinically significant and important differences [18]. The accuracy of CPS can be evaluated by an estimate of ±33% of actual survival within a maximum time window (e.g., 30 days) using a threshold range (e.g., 7~14 days) and an estimate of discrimination [2]. Therefore, clinicians should rethink how the accuracy of CPS should be interpreted. However, clinicians may value prognostic tools even if they are no better than CPS because they offer more objective and reproducible results, meaning these tools could be particularly helpful for inexperienced clinicians. To date, there is no consensus on the most appropriate methods of comparing tools that use different formats to predict survival. The most appropriate prognostic tool can be determined by the feasibility of prognostic scales used in clinical practice and the information that end users actually want. It has been suggested that clinicians could preferentially use validated prognostic models (e.g., the PaP or PiPS), and other prognostic tools (e.g., the PPI) may be considered in certain circumstances (e.g., difficulty in calculating scores or obtaining laboratory test results).

3. Future research priorities

1) Functional prognosis

Prognostic information about functional ability is essential alongside survival estimation to allow patients with serious illness and their families to consider and decide on a future care plan. As most patients want to maintain their physical independence, predicting their functional ability could help empower them to act toward achieving their wishes and goals [19]. A recent study indicated that patients with cancer wanted more information about their functional prognosis than about their life expectancy [19]. Hiratsuka et al. developed the Functional Palliative Prognostic Index (FPPI), which was the first scoring system for functional prognostication of patients with advanced cancer [20]. The FPPI can be used to predict functional ability for walking, eating, and communicating. In addition, that study revealed several factors that were related to functional survival, such as anorexia, a low ratio of lymphocytes, and low PPS scores. Further research is needed to clarify the real interests and concerns of patients with serious illnesses regarding the kind of functional prognosis they want and how this information should be shared with them to meet their individual needs.

2) Outcomes of prognostic communication

Prognostic communication is usually embedded in EOL discussions and advance care planning (ACP), which occur throughout the disease trajectory [21]. Prognostic information entails several components, including life expectancy, possibility of further treatment, and anticipated changes in quality of life (QOL) and functional abilities [19,20,22]. This information could be delivered explicitly or implicitly and with some reassurance statements, depending on patients' preferences [23]. Therefore, the outcomes of prognostic communication and its components are difficult to distinguish from those of concurrent discussions about other topics and clinicians' support. The ultimate goal of prognostic communication is to help patients better understand their illness trajectory, facilitate goals-of-care discussions, make important decisions, and prepare for EOL.

Various outcomes can be measured to evaluate the effects of prognostic communication. The most direct outcome is prognostic awareness (PA) [24]. The accuracy of PA or illness understanding and uncertainty have previously been evaluated [24]. Given the importance of finding a balance between explicit communication and discomfort, other variables have been used, such as anxiety and satisfaction with communication [25].

When prognostic communication is included as part of EOL discussions, ACP, and specialist-level palliative care, the entire process may support more comprehensive outcomes. Short-term outcomes include patient-centered communication and patient-clinician relationships [26]. Long-term outcomes include those related to care (e.g., goal-concordant care), mental health (e.g., depression and hope), QOL, quality of death, place of care, and personal issues (e.g., unfinished business and preparation for death) [21,26]. Caregivers frequently participate in prognostic communication, talk about death with patients, engage in shared decision-making, and prepare patients for death. Caregiver outcomes may include regret, unfinished business, grief, and depression [27].

The most appropriate outcomes may vary depending on

clinical settings, estimated prognosis (e.g., months, weeks, or days), and culture. Further studies should elucidate the true clinical outcomes throughout the disease trajectory from both patients' and families' perspectives, and explore whether and how a comprehensive approach, including prognostic communication, can improve these outcomes.

3) Artificial intelligence (AI)

Sudden unexpected death (SUD) is reported to occur in 5~10% of terminally ill patients with cancer [28]. Because most prognostic models do not address the course of death separately, SUD may lead to underestimation in survival prediction. Although several factors have been reported as associated with SUD, predicting SUD is difficult because of its nature.

In addition, most classical prognostic models only use baseline data for prognostication; however, trends and patterns in the data could be useful for more accurate predictions. Prognostic accuracy may be improved by using static demographic and laboratory data, as well as data on dynamic changes and a wider range of data, such as imaging and genetic data. The use of artificial intelligence (AI) and big data is promising in constructing such complex models. Prognostication is an area in which AI technology works well, and this technology has been used for prognosis prediction in oncology [29]. More accurate prognosis prediction through further research will facilitate EOL discussions with patients and be useful for providing better goal-concordant care.

4) Education for clinicians

CPS plays a unique role, and education for clinicians is essential. Prognostication comprises two parts: "foreseeing" and "foretelling." Education relating to "foreseeing" may be delivered and updated through methods such as academic conferences and seminars. Specifically, this education should adopt small workshops and web-based programs to allow interactions. Clinicians can also learn through a web-based calculator (www.predictsurvival.com) by using various prognostic indices to complement their CPS. Empirically, a prognostication log is recommended to help clinicians recognize their own tendencies. This refers to recording the CPS in charts at the first encounter and then periodically making notes regarding CPS when new events occur. Finally, clinicians can compare the accuracy of CPS with actual survival after a patient dies. The second component of prognostication, "foretelling," inherently involves communication with patients and families. Education in this area will enhance clinicians' confidence, which is needed to initiate prognostic communication. In Asian countries, shared decision-making and a family-centered context are common patterns [30]. Education about CPS would be enriched by incorporating patients' preferences and providing good examples of realistic communication with families.

CONCLUSION

Further studies investigating whether education improves prognostic confidence and the accuracy of CPS are needed. Prognostication has inherent uncertainty; therefore, qualitative studies should explore those difficulties through in-depth interviews. In addition, a standardized education program is required. Experts can collaborate to develop such a program by sharing similar cultural characteristics and research experiences. Standardization of education can also be facilitated via AI, such as a web-based calculator, or an application for a prognostication log in the near future.

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CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

ORCID

Yusuke Hiratsuka, https://orcid.org/0000-0003-2334-3893
Jun Hamano, https://orcid.org/0000-0003-0304-9881
Masanori Mori, https://orcid.org/0000-0002-5489-9395
Isseki Maeda, https://orcid.org/0000-0002-0018-3359
Tatsuya Morita, https://orcid.org/0000-0002-7257-7429
Sang-Yeon Suh, https://orcid.org/0000-0002-6145-1150

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AUTHOR'S CONTRIBUTIONS

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