



Survival prediction in advanced cancer patients – a narrative review

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Purpose of review

The exploration for accurate ways to predict survival for advanced cancer patients continues to be a significant theme despite the advent of objective criteria and their combination with clinical criteria. The purpose of this article was to review some of the latest studies relating to prognostication and the capacity to predict survival during the terminal cancer stage.

Recent findings

Recent studies show notable prognostication approaches using genetic tests and advanced computation methods such as machine learning, which we will summarize.

Summary

Significant effort has been made to improve the accuracy of survival estimation for advanced cancer patients. The main goals are to optimize individualized patient management and uses of resources. Advanced techniques, including genetic markers and machine learning techniques, may improve the accuracy of prediction.

Keywords

cancer, palliative care, prediction, prognosis, prognostic factors, survival

INTRODUCTION

Accurate estimation of prognosis and survival time is of critical importance in patients with cancer. Prognostic information is often requested by the patients or their families so that they can make informed plans, including handling certain legal matters such as wills, financial arrangement, and even funeral preparation [1]. Even if they do not prefer to be explicitly informed of the timescale, prognostication is important for clinicians to manage patients in a personalized approach. The information is used to guide appropriate medical care and avoid overtreatment or undertreatment, and to better utilize healthcare resources.

The above purposes cannot be achieved by merely providing median survival estimates based on stage and histology at diagnosis, because those are the population average figures and neglect various prognostic factors, including specific clinical and psychosocial factors after diagnosis [2^a]. Additionally, the prognosis can change dynamically with clinical events such as intercurrent illness and disease progression, especially as the patient exhausts' treatment options. We argue that it is essential for oncologists to draw on a range of relevant clinical and nonclinical information in formulating survival estimates.

Traditionally, the first key step in defining prognosis is clinical judgement based on experience and knowledge. However, such an approach can be quite subjective and tends to be inaccurate if being used alone [3–5]. Additionally, it can be difficult to justify the estimates and rationales to colleagues, patients, and their family. In view of these concerns, this subjective judgement is often complemented by objective criteria and scales to improve the accuracy and efficiency [6].

This narrative review summarizes the recent literature on survival prediction in advanced cancer patients and discuss the latest development and future direction in clinical prognostication.

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KEY POINTS

- Survival prediction in advanced cancer patients has inherent uncertainty due to unexpected acute deterioration in the background of gradual decline.
- A variety of prognostic scoring systems are available so that clinicians may choose to employ them in addition to their clinical judgement.
- Judicious use with consideration of the applicability to individual patients and the limitations of the prediction is needed.

INSTRUMENTS AVAILABLE TO MAKE A PROGNOSIS

A total of 45 studies published in the past 2 years met the inclusion criteria and are listed in Table 1. The search was performed on 17 December 2022 in PubMed using the following search terms: ((score*[Title] OR tool*[Title] OR scale*[Title] OR instrument*[Title] OR model*[Title] OR assessment*[Title] OR index*[Title] OR performance*[Title]) AND ('life expectancy'[Title] OR 'survival'[Title] OR prognos*[Title])) AND (palliat*[Title] OR terminal*[Title] OR 'end of life'[Title] OR 'end stage'[Title] OR hospice[Title] OR 'advanced cancer'[Title]) AND (2021:2023 [pdat])). They were discussed below, with particular focus on the performance of prognostic tools, the applicable patient groups, and our summary, including the challenges and future directions. Two major areas of research among the literature were identified: (1) evaluation and validation of the existing predictive systems such as Palliative Performance Scale, Palliative Prognostic Score, Palliative Prognostic Index, and Glasgow Prognostic Scale; and (2) novel or emerging predictive tools.

Existing predictive methods

Sudden, unexpected death in advanced cancer patients is not uncommon [7^o]. Death is often precipitated by acute deterioration (e.g. pneumonia, sepsis, and pulmonary embolism), although there is a great degree of uncertainty surrounding the exact timing of death [8^o,9].

Clinicians often rely on their clinical intuition to formulate a prognosis. However, the lack of formal training in prognostication and systematic bias may contribute to inaccurate and sometimes overly optimistic or pessimistic survival estimates [10], which may have a negative impact on patient outcomes such as overtreatment or undertreatment, poorer quality-of-life and a higher symptom burden [10]. There has been increasing interest in employing laboratory parameters to complement clinical judge-

ment in order to improve the accuracy of survival prediction, as such parameters have been found to have independent prognosis value [11]. To improve prognostic certainty, multiple prognostic models have been developed and validated in the terminal stage setting to facilitate a well-informed shared decision making for patients with advanced cancer. While several prognostic scores, such as the Palliative Performance Scale [12], Palliative Prognostic Score [13], and Palliative Prognostic Index [14], have been developed and calibrated for patients with a short expected survival (i.e. median overall survival of ~1 month), a system such as the Glasgow Prognostic Score was designed for advanced cancer patients with an expected survival in the range of multiple months [15]. These models often stratify patients into good, moderate, and poor risk groups, which correspond to different survival times. These models have been validated to variable extent.

Clinical prediction of survival and performance status

Five articles that assessed the performance of a clinical prediction of survival in advanced cancer have been published in the past 2 years [10,16^o–19]. Overall, the performance of 'clinical prediction of survival' had a similar discriminative accuracy in predicting short-term survival (e.g. 30-day survival) compared with established scores such as palliative prognostic score [16^o–18] and palliative prognostic index [19] in various settings, including outpatient radiation therapy and palliative clinic [16^o], palliative care service [17,18], outpatient medical oncology [10], and patients with head and neck cancer at their end-of-life [19]. The clinical survival prediction C-indices generally ranged from 0.7 to 0.8, demonstrating a reasonable correlation with the aforementioned predictive scores. Kim and colleagues have shown that clinician overestimation of survival is associated with poorer quality-of-life, shorter survival times, and a higher symptom burden for patients. Performance status was originally applied to determine functional capacity and clinical deterioration. One recent study has shown that it remains strongly associated with the overall survival of a contemporary cohort of cancer patients who attend palliative care services [20]. Furthermore, a Karnofsky Performance Score greater than or equal to 70 is an independent predictor of better survival for palliative irradiation of sinonasal cancer [21].

The latest evidence has shown that clinical judgment is still an important tool for survival prediction for advanced cancer patients and should be part of the training for clinicians caring for these patients. An objective prognostic score can be used

Table 1. Summary of recent clinical prognostication studies

First authors	Methods of prognostic prediction						Other predictive models
	Clinical prediction	Performance status	Palliative performance scale	Palliative prognostic score	Palliative prognostic index	Glasgow prognostic score	
Promptantakorn P			+				
Yoon SJ	+			+			
Kim YJ	+						
Zaorsky NG							METSSS based on Metastases location, Elderly (> 65 years), Tumor primary, Sex, Sickness/comorbidity, and Site of radiotherapy
Yang HJ					+ (Simplified)		
Kishino T					+	+	
Shatri H					+		
Lee GJ			+ (and its trend)				
Miyagi T							Combination of routine blood test values
Turrillas P							NECPAL prognostic factors
Stone P			+	+	+		Feliu prognostic nomogram
Hiratsuka Y	+			+			
Rades D							New tool (performance, Hb level, tumor site)
Vankun P			+				
Rades D		+					
Hiratsuka Y				+			Objective prognostic score
Momokita M							Prognostic nutritional index (PNI)
Koyama N							Patient-reported European Organization for Research and Treatment of Cancer Quality-of-Life Questionnaire Core 15 Palliative scores and blood inflammatory markers
Lund JL							Geriatric assessment model
Nieder C							LabBM (which is based on objective lab tests)
Allende-Pérez S		+					
Goh ZNL							Shock index
Nieder C							METSSS model
Lee SH				+	+		Prognosis in palliative care study and objective prognostic score (OPS)
Kishino T	+				+		
Nagasako Y						+	

Table 1. (continued)

First authors	Methods of prognostic prediction						Other predictive models
	Clinical prediction	Performance status	Palliative performance scale	Palliative prognostic score	Palliative prognostic index	Glasgow prognostic score	
Ieda S							CRP/albumin, PNI, fibrosis-4 index, albumin-bili score (ALBI)
Maltoni M	+			+			Survival prediction score, TEACHH
Iizuka-Honma H					+		
Ueshima J							Cachexia Staging Score
Fernandes M					+		
Lee SH					+		
Oyama K							Prognostic nutritional index
Ikari T							One-day surprise question
Feng C							Neutrophil-albumin ratio and patient generated subjective global assessment (PG-SGA)
Howdon D							Self-care dimension of EQ-5D
Onishi K							Laboratory prognostic score for gynecologic malignancy (G-LPS)
Stone PC							Prognosis in palliative care study models
Feng Y							Liver chemistry score
Lojanapiwat N							'Modified' Glasgow prognostic score
Kuijper SC							Source beyond first-line model
De Giglio A				+			LIPI score
Nagai H							Laboratory prognostic score for GI malignancy (GI-LPS)
Tanaka M							Laboratory prognostic score for respiratory malignancy (R-LPS)
Mori N							SARC-F

CRP, C-reactive protein; Hb, hemoglobin, SARC-F, Strength, Assistance with walking, Rise from a chair, Climb stairs, and Falls, LIPI, Lung immune prognostic index, G-LPS, Laboratory prognostic score for gynecologic malignancy, GI-LPS, Laboratory prognostic score for gastrointestinal malignancy, R-LPS, Laboratory prognostic score for respiratory malignancy, NECPAL, NECesidades PALiativas, METSSS, (Metastases location, Elderly (>65 years), Tumor primary, Sex, Sickness/comorbidity, and Site of radiotherapy), LabBM, Laboratory test for brain metastasis.

to complement clinical prediction and assist in decision making for patients approaching end-of-life.

Palliative Performance Scale

The Palliative Performance Scale was modified from the Karnofsky Performance Scale to measure the changing functional status of patients receiving palliative care, and it rates patients based on ambulatory status, activity level, evidence of disease, self-care, oral intake, and level of consciousness [12]. The system categorizes patients from 0% (dead) to 100% (healthy and mobile) in 10% increments and has been used in various healthcare settings in different countries [22]. Although the scale was not shown to be more accurate than clinical prediction of survival [23], it was useful for predicting survival time among a contemporary advanced cancer cohort [24,25]. Furthermore, the trend of the score, in addition to the initial absolute score, may be important for predicting survival [26]. This reflects the dynamic nature of the prognostication, and clinicians may need repeated estimations to gain insight into the disease trajectory.

Palliative Prognostic Score

The Palliative Prognostic Score ranges from 0 to 17.5. It classifies patients into three risk groups (scores of 0–5.5, 5.6–11.0, and 11.1–17.5 correspond to 30-day survival probabilities of >70, 30–70, and <30%, respectively) based on six variables, including dyspnea, anorexia, Karnofsky performance status, clinician prediction of survival, total leukocyte count, and percentage of lymphocytes [13]. Of note, clinician prediction of survival has the highest weighting in the scoring system. Recent studies have found that both the total score and the component of clinician prediction in the Palliative Prognostic Score showed good predictive performance among patients with advanced cancer in the palliative care setting [17,18,23,27,28] and those who were referred for palliative radiotherapy [16].

Palliative Prognostic Index

The Palliative Prognostic Index was developed by incorporating five clinical items, including the Palliative Performance Scale, oral intake, edema, dyspnea at rest, and delirium [14]. The score was found to be helpful in predicting survival among patients with solid or hematological cancers. One advantage of using this scoring system is that it does not require blood testing or imaging. Interestingly, an abbreviated form of the Palliative Prognostic Index that simplifies the diagnosis of delirium was found to be predictive for patients with advanced cancer in a home hospice setting in South Korea [29]. Studies in Asian countries generally show good and comparable prognostic accuracy between the Palliative Prognostic Index and other

systems or clinical prediction in predicting short-term survival in acute or palliative ward settings across various cancer types [19,23,28–34].

Glasgow Prognostic Score

The Glasgow Prognostic Score considers only a readily available inflammatory parameter [C-reactive protein (CRP)] and a nutritional marker (serum albumin level) to predict survival in various kinds of cancer types [35]. In contrast to the above prognostic models, this score seems to be more appropriate for patients who have a life expectancy in terms of months because this score was derived from a cohort of advanced lung cancer patients who were receiving platinum-based chemotherapy [36]. The scores are between 0 and 2 : 0 points for CRP less than or equal to 10 mg/l and albumin greater than or equal to 35 g/l, one point for either CRP greater than 10 mg/l or albumin less than 35 g/l and two points for CRP greater than 10 mg/l and albumin less than 35 g/l [36]. However, hypoalbuminemia without elevated CRP was rare, and hypoalbuminemia itself was not found to be associated with lower overall survival in cancer patients [35]. The Glasgow Prognostic Score was subsequently modified so that patients with an elevated CRP (>10 mg/l) and hypoalbuminemia (<35 g/l) were allocated a score of 2, whereas a score of 1 was assigned when either one of these blood biochemical abnormalities was present [37]. A higher score is associated with a poorer prognosis. From our literature review, few studies in the past 2 years have examined the performance of these scores in the advanced cancer setting. Limited data still show that the scores could classify different types of cancer patients into distinct prognostic groups in a variety of clinical settings, including acute [38] and palliative care settings [30,39].

Other and novel prognostic scores

Over the years, new prognostic scoring systems have been devised and/or validated (Table 2) [16,18,23,24,28,40–62]. These models often incorporate additional symptoms or laboratory values, which may be independent prognostic factors, to enhance the predictive power of the existing scoring systems. A detailed description of every score is out of scope for this short review. The readers can refer to individual articles to understand their features and get familiar with them before considering applying them to their own patients. Every instrument has its strengths and weaknesses; however, it is challenging to compare them systematically due to different study populations, cancer types and stages, and definitions of survival time.

Table 2. Summary of other prognostic scoring system for advanced cancer patients in the past 2 years

First authors	Methods of prognostic prediction	Titles
Zaorsky NG	METSSS model	Survival after palliative radiation therapy for cancer: the METSSS model
Miyagi T	Combination of routine blood test values	Prognostic model for patients with advanced cancer using a combination of routine blood test values
Turrillas P	NECPAL prognostic factors	NECPAL prognostic tool: a palliative medicine retrospective cohort study
Stone P	Feliu prognostic nomogram	Prognostic tools or clinical predictions: which are better in palliative care?
Rades D	New tool (performance, Hb level, tumor site)	A new survival score for patients scheduled for palliative irradiation of locally advanced carcinoma of the head and neck
Hiratsuka Y	Objective prognostic score	Comparison of Objective Prognostic Score and Palliative Prognostic Score Performance in Inpatients with Advanced Cancer in Japan and Korea
Momokita M	Prognostic nutritional index (PNI)	Prognostic Nutritional Index in patients with end-stage oral cancer
Koyama N	Patient reported (EORTC PAL)+blood markers	The Role Of EORTC QLQ-C15-PAL Scores and inflammatory biomarkers in predicting survival in terminally ill patients with cancer
Lund JL	geriatric assessment model	Life expectancy in older adults with advanced cancer: evaluation of a geriatric assessment-based prognostic model
Nieder C	LabBM (which is based on objective lab tests)	The LabBM Score is an excellent survival prediction tool in patients undergoing palliative radiotherapy
Goh ZNL	Shock index	Shock index is a validated prediction tool for the short-term survival of advanced cancer patients presenting to the emergency department
Nieder C	METSSS model	Independent external validation of the METSSS model predicting survival after palliative radiotherapy
Lee SH	Prognosis in palliative care study (PiPS) and objective prognostic score (OPS)	Prognosis Palliative Care Study, Palliative Prognostic Index, Palliative Prognostic Score, and Objective Prognostic Score In Advanced Cancer: A Prospective Comparison
Ieda S	CRP/albumin, PNI, fibrosis-4 index, alb-bili score (ALBI)	Identification of remaining life expectancy less than two weeks by C-reactive protein/albumin ratio, Prognostic Nutritional Index, Fibrosis-4 Index, And Albumin-Bilirubin Score in Terminal Cancer Patients
Maltoni M	Survival prediction score, TEACHH	Prognostication in Palliative Radiotherapy-Propart: Accuracy of Prognostic Scores
Ueshima J	Cachexia Staging Score	Cachexia Staging Score Predicts Survival in Patients With Cancer Who Receive Palliative Care
Oyama K	Prognostic nutritional index	Predicting Short-Term Life Expectancy of Patients With End-Stage Gastric Cancer Using Onodera's Prognostic Nutritional Index
Ikari T	One-day surprise question	Is the 1-day surprise question a useful screening tool for predicting prognosis in patients with advanced cancer? a multicenter prospective observational study
Feng C	Neutrophil-albumin ratio and patient generated subjective global assessment (PG-SGA)	A prognostic model using the neutrophil-albumin ratio and PG-SGA to predict overall survival in advanced palliative lung cancer
Howdon D	Self-care dimension of EQ-5D	Replacing performance status with a simple patient-reported outcome in palliative radiotherapy prognostic modeling
Onishi K	Laboratory prognostic score for gynecologic malignancy (G-LPS)	Laboratory prognostic score for predicting 14-day mortality in terminally ill patients with gynecologic malignancy
Stone PC	Prognosis in palliative care study models	The prognosis in palliative care study II (Pips2): a prospective observational validation study of a prognostic tool with an embedded qualitative evaluation
Feng Y	Liver chemistry score	Incorporation of liver chemistry score in predicting survival of liver-involved advanced gastric cancer patients who received palliative chemotherapy
Kuijper SC	Source beyond first-line model	SOURCE beyond first-line: a survival prediction model for patients with metastatic esophagogastric adenocarcinoma after failure of first-line palliative systemic therapy
De Giglio A	LIPI score, 'palliative prognostic score without clinical prediction of survival' (PaPwCPS)	The palliative prognostic (Pap) score without clinical evaluation predicts early mortality among advanced NSCLC patients treated with immunotherapy
Nagai H	Laboratory prognostic score for GI malignancy (GI-LPS)	Development and internal validation of laboratory prognostic score to predict 14-day mortality in terminally ill patients with gastrointestinal malignancy

Table 2. (continued)

First authors	Methods of prognostic prediction	Titles
Tanaka M	Prognostic score for respiratory malignancy (R-LPS)	Prognostic laboratory score to predict 14-day mortality in terminally ill patients with respiratory malignancy
Mori N	SARC-F	High SARC-F Score predicts poor survival of patients with cancer receiving palliative care

KNOWLEDGE GAP

Despite the availability of multiple prognostic scores, clinicians have not been adopting them routinely in clinical practice, and many clinicians are still relying on their clinical judgement alone. Several reasons may contribute to this. First, the accuracy of many of these models has been validated in another independent cohort; however, clinicians may feel that they cannot adequately account for individual patient variability. Second, multiple models are applicable to a particular patient group. It can be confusing as to which one should be used for which patient, and it is often difficult to interpret if these scores applied to the same patient show different prognoses. Finally, information provided by prognostic models can be confusing to patients and their families, for example, what does it mean to have a 90% chance of survival in 30 days?

CONCLUSION

According to recent publications, the commonly used prognostic scores for advanced cancer patients generally show good prognostic accuracy. No single score demonstrated superior survival prediction over another or over clinical prediction. These scores have the advantages of being more objective and having less inter-rater variability than clinical prediction alone. Additionally, clinicians can use them as a second opinion before making a clinical decision. However, clinicians should be mindful of the additional burden on patients approaching the end-of-life period when employing many of these scales, as laboratory tests are often required. Judicious use of the prognostic scores is needed, especially when the clinical decision or advanced care plan is formulated based on the predicted survival.

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Conflicts of interest

There are no conflicts of interest.

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- of outstanding interest

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