Review Article

Prognostication methods for patients treated with palliative radiotherapy: a narrative review

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Background and Objective: Palliative radiotherapy (PRT) practice patterns among radiation oncologists are heterogeneous. Appropriate selection of PRT regimen must balance symptom/disease control with patient quality of life. The aim of this review is to summarize prognostic scoring systems for PRT in order to help guide clinical decision making and selection of appropriate PRT regimens.

Methods: A PubMed search was conducted for articles published between 01/2000 and 07/2023. Standardized search terms including "palliative", "radiotherapy" and "survival" were used. Only English-language, peer-reviewed articles that presented a prognostic scoring system of PRT were included in this review.

Key Content and Findings: In this study, we review the published literature on prognostic scoring systems for patients treated with PRT. Multiple models have been developed and each pertains to a specific patient population or primary tumor type. While they are specific to a particular patient population, all models incorporate patients' clinical characteristics such as primary site, performance status, location of metastatic disease, and indication for PRT to estimate overall survival (OS) after PRT. For each model, the salient points of the scoring system are described. Based on survival estimates from each prognostic system, different PRT regimens are recommended.

Conclusions: PRT scoring systems can be used to help clinicians assess patient prognosis. With the information provided by the included studies, radiation oncologists will be better prepared to formulate an optimal, individualized treatment plan for patients to be treated with PRT.

Keywords: Palliative treatment; radiotherapy (RT); metastasis; prognostic factors

Submitted Sep 14, 2023. Accepted for publication Nov 21, 2023. Published online Dec 20, 2023.
doi: 10.21037/apm-23-538
View this article at: https://dx.doi.org/10.21037/apm-23-538

Introduction

Nearly one half of cancer patients receive palliative radiotherapy (PRT) as a part of their cancer treatment (1,2). While PRT is most commonly given to patients with metastatic disease, it can be used for patients with non-metastatic disease who are symptomatic and/or unable to receive definitive treatment. In many discussions regarding the decision for treatment, patients and their families request an estimate for prognosis, which is challenging in

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Table 1 Search strategy

Items	Specification
Date of search	Aug 01, 2023
Databases and other sources searched	PubMed
Search terms used	"palliative", "palliation", "radiation", "radiotherapy", "survival", "overall survival", "scale", "score", and "model"
Timeframe	01/01/2000 to 07/31/2023
Inclusion criteria	Only articles discussing scoring systems that estimated survival after PRT were included. Articles must be published in English and peer-reviewed
Selection process	Article abstracts and full text were reviewed independently by three authors (R.F.S., N.B.R., R.T.H.). Articles were selected to demonstrate the utility of PRT scoring systems in both the metastatic and non-metastatic setting. Any disagreements about whether an article should be included were resolved by consensus of the three authors

PRT, palliative radiotherapy.

a palliative setting. For patients receiving PRT, treatment recommendations are based on multiple factors including primary site, anatomic location, and patients' goals of care. In order to identify patients that would benefit from PRT, multiple clinical predictive models have been developed to assess likelihood of pain relief after PRT (3), suggest appropriate PRT fractionation schemes (4), and identify predictors of death following PRT (5).

While practice patterns vary greatly (6), the ultimate goal of PRT is to mitigate pain and discomfort, especially towards the end of life. Given this variability in practice and published literature on PRT (3-5,7,8), the goal of this review is to summarize select prognostic models for the appropriate use of PRT for different disease sites. For each scoring system, a brief summary of its intended patient population, use, and associated outcomes is provided. PRT for patients with metastatic cancer, as well as patients with non-metastatic disease, is described.

By consolidating and highlighting modern prognostic systems for patients treated with PRT, this pragmatic review is intended to guide radiation oncologists' practice by assisting clinical decision-making regarding patient selection and fractionation, as well as providing an estimate of prognosis that may help patients and their families get their affairs in order. We present this article in accordance with the Narrative Review reporting checklist (available at https://apm.amegroups.com/article/view/10.21037/apm-23-538/rc).

Methods

A search was conducted to identify articles describing prognostic scoring systems for PRT. PubMed was queried for articles published from 01/2000 to 07/2023 using the following phrases: "palliative", "palliation", "radiation", "radiotherapy", "survival", "overall survival", "scale", "score", and "model". Only English language, peer-reviewed articles were eligible for inclusion. As this study was designed as a narrative review, articles were selected by the authors based on whether they may be of interest to practicing radiation oncologists. Only articles discussing scoring systems that estimated survival after PRT were included. To demonstrate the wide utility of PRT scoring systems, articles describing PRT for metastatic and/or non-metastatic disease were selected. A systematic review of all PRT scoring systems was outside of the scope of this article. A summary of the search strategy is provided in *Table 1*.

Prognostic scoring systems for specific disease sites

Lung cancers

While locally advanced lung cancers are typically managed through a combination of surgery, chemotherapy, and/or radiotherapy (RT), not all patients are candidates for these approaches. In patients unable to undergo curative treatment, PRT can provide symptom relief or be used prophylactically to treat disease at risk for causing symptoms in the future (9). In a study by Rades and colleagues (3), the authors reviewed their institutional experience with PRT in order to identify predictors of survival after PRT for patients with advanced lung cancers. Their study included

125 consecutive patients who were unable to undergo curative-intent therapy and received PRT with Equivalent Dose in 2-Gy fractions (EQD2) ranging from 31 to 52 Gy (median, 42 Gy). The majority of patients were men (63%) with age ≥71 years (54%), Karnofsky Performance Status (KPS) ≥70 (55%), and a history of smoking (66%). Most (66%) patients had non-small cell lung cancer with a central primary tumor (53%), advanced tumor stage (T3–4, 71%) and/or nodal stage (N2–3, 98%), and 78% had metastatic disease. While most patients received PRT to relieve specific symptoms (pain, dyspnea, atelectasis, bleeding, dysphagia, superior vena cava syndrome), 38% were treated with prophylactic PRT to avoid future symptoms. Clinical factors including KPS ≥70, T1–2, N0–1, M0, and peripheral tumor location were significantly associated with improved overall survival (OS) on univariable analysis ($P<0.05$). Upon multivariable analysis, only N-stage [hazard ratio (HR) 2.18] and M-stage (HR 1.70) were significantly associated with OS; KPS had only borderline significance (HR 1.03).

To develop a prognostic survival scale for PRT, each of these three factors was dichotomized (e.g., KPS ≤60 versus ≥70, N0–1 versus N2–3, and M0 versus M1). Each level of each factor was assigned a point value defined as the associated 6-month OS rate divided by 10. The total number of points was then calculated by summing the scores in each of the three categories, which yielded a range of 10 to 17. The composite total score was associated with survival after PRT and patients with higher total score had longer OS: patients with 10–11 points had a median OS of 2 months, those with 12–14 points had median OS of 6 months, and patients with 15–17 points had a median OS of 38 months. Corresponding 12-month OS rates for each category were as follows: 8% (10–11 points), 19% (12–14 points), 69% (15–17 points). The total radiation dose used for PRT (EQD2 <42 versus ≥42 Gy) was not significantly different between the three groups. With these survival data, the authors concluded by suggesting appropriate PRT fractionation and doses for each group of patients. For patients with the shortest survival (10–11 points), PRT courses lasting less than 1 week (e.g., 8 Gy in 1 fraction, 20 Gy in 5 fractions) were recommended, while for patients with intermediate survival (12–14 points), hypofractionated PRT regimens were recommended (e.g., 30 Gy in 10 fractions, 45 Gy in 15 fractions). For patients with the highest OS (15–17 points), the authors suggest that more aggressive treatment approaches may be considered in place of PRT. Limitations of this scale include the fact that the use of chemotherapy was not considered, it was not examined with an external validation cohort, it was developed prior to the introduction of immunotherapy, and was unable to examine survival after PRT based on molecular mutations. Despite these limitations, this model requires a limited number of input factors and thus is easy to use when evaluating patients for PRT.

Head and neck cancers

Similar to lung cancers, the majority of patients with locally advanced head and neck cancers will receive curative treatment through a combination of RT, chemotherapy, and/or surgery. For patients with metastatic disease, or those who are not fit enough for definitive management, PRT is needed to help manage symptoms and improve quality of life. Given that there are multiple RT regimens utilized for patients with locally advanced and/or metastatic head and neck cancer ranging from the quad-shot regimen (14–14.8 Gy in 4 twice-daily fractions) (10-12) to moderate hypofractionation (e.g., 55 Gy in 2.5 Gy fractions) (13) to conventionally fractionated definitive-dose regimens, Rades and colleagues (14) developed a palliative scale to better determine their appropriateness based on expected survival.

To develop their scale, the authors examined 78 patients that were treated with PRT for advanced head and neck cancers. This scale incorporates three factors—Eastern Cooperative Oncology Group (ECOG) performance status, pre-RT hemoglobin level, and primary tumor site (oropharynx, hypopharynx, larynx, and oral cavity). These factors were selected based on a prior study that demonstrated they were the most closely associated with survival after PRT for patients with head and neck cancers (15). The majority of patients had ECOG 0–2 (78%), pre-RT hemoglobin of <12 g/dL (58%), and tumors in the oropharynx (58%). Similar to their prior study on PRT for lung cancers (3), the 6-month OS was estimated and divided by 10 to obtain a factor score. The total score (sum of all three factor scores) ranged from 8 to 15 and patients were placed into three prognostic groups (8–9, 11–13, and 14–15 points). A higher total score was associated with improved OS: patients with 8–9, 11–13, and 14–15 points had a 6-month OS of 13%, 28%, and 63%, respectively; a 12-month OS of 0%, 15%, and 37%, respectively; and a median OS of 1, 2, and 11 months, respectively. Based on these survival data, different PRT fractionation schemes were recommended. For patients with the lowest survival (8–9 points), short PRT schemes (e.g., quad-shot, 8 Gy in 1 fraction) should be considered, while for patients with moderate survival

(11–13 points), intermediate regimens lasting 1–2 weeks (e.g., 20 Gy in 5 fractions with option to repeat in 2–4 weeks, 36 Gy in 12 fractions) can be considered (13). Patients with the longest expected OS (14–15 points), however, can be considered for a longer, more durable course of RT such as 40–55 Gy in 2–2.5 Gy fractions, or longer, more conventionally fractionated courses. The strengths of this model are that it is pragmatic and uses clinical information that is readily available at the time of consultation. It also includes multiple various fractionation regimens that span 1 fraction to long-course durable PRT, allowing for a risk-adapted approach to the selection of fractionation scheme utilized. Limitations of this model are that it includes a heterogeneous group of head and neck cancer patients, outcomes were assessed retrospectively, and it has not been validated with an external cohort.

Gastric cancers

Bleeding is a common indication for PRT in patients with gastric cancers. To identify patients that would benefit from single fraction PRT, Sekii and colleagues (16) performed a secondary analysis of the Japanese Radiation Oncology Study Group (JROSG) 17-3, which was a multicenter prospective study that examined outcomes associated with PRT for bleeding gastric cancer (17). The study consisted of 53 patients with gastric cancers who had hemoglobin <8.0 g/dL or required blood transfusions due to bleeding. The majority of patients had T4 tumors (69%), node-positive (69%), and/or metastatic (76%) disease. A range of PRT doses were used: median total dose was 20 Gy (range, 8–45 Gy), and the most commonly used schedules were 8 Gy in 1 fraction, 20 Gy in 5 fractions, and 30 Gy in 10 fractions. At 8 weeks after treatment, PRT was associated with a 90% response rate (defined as hemoglobin ≥8.0 g/dL, 7 consecutive days without blood transfusion, or absence of salvage surgery). PRT dose was not associated with survival, bleeding response or re-bleeding.

In the analysis by Sekii *et al*. (16), the palliative performance index (PPI) was calculated for patients enrolled on JROSG 17-3 and median OS was estimated based on PPI score. The PPI takes into account patient performance status (estimated using the Palliative Performance Scale (18), a validated scale mapped to the KPS that accounts for ambulation, activity and evidence of disease, self-care capabilities, oral intake, and level of consciousness) and specific symptoms (oral intake, edema, dyspnea at rest, and delirium) and assigns a point value based on the presence/absence of each symptom (18). Patients enrolled on JROSG 17-3 had PPI scores ranging from 0 to 10. Similar to prior studies (19) on the prognostic value of the PPI, higher PPI scores were associated with worse survival: patients with PPI of ≤2, 2.5–4, and >4 had median OS of 6.7, 2.8, and 1.0 months, respectively. This is distinct from the previously described studies by Rades *et al.* (3,14), where higher scores were associated with improved OS. Using a receiver operative characteristic analysis, the authors found that PPI score >2 was associated with the highest risk of short-term mortality (within 2 months) for patients with bleeding gastric tumors. Based on these data, the authors recommended that patients with bleeding gastric tumors and a PPI score of >2 should receive single fraction PRT (8 Gy in 1 fraction) for palliation of bleeding. These findings highlight that radiation fractionation schedules can be tailored to patients' predicted OS and thereby maximizing their remaining quality of life. While this scale is based on prospectively collected data, it is based on a limited number of patients all from the same country, which may impact its generalizability to other patient populations. Additionally, this scale has multiple input factors, and thus may not be pragmatic to use in emergent situations.

A summary of the scoring systems for the above specific disease sites are summarized in *Table 2*.

PRT scoring systems for multiple metastatic sites

For many patients with metastatic disease, problematic sites including the primary site or regional/distant metastases may cause symptoms that greatly affect quality of life. In this section, we describe important models that may help guide decision making when considering PRT for those with generalized metastatic disease to be treated in both the outpatient and inpatient setting.

Chow models

Chow and colleagues (20) developed one of the first predictive models of survival after PRT from a prospective cohort of 395 Canadian patients who received palliative treatment. Clinical factors examined included age, site of metastases, weight loss, KPS, time since diagnosis, primary tumor site, pain severity, pain medication use, and severity of 9 symptoms (pain, fatigue, nausea, depression, anxiety, drowsiness, appetite, sense of well-being, and shortness of breath) measured on the Edmonton Symptom Assessment

Table 2 Scoring systems for specific disease sites

Author [year]	Primary tumor site	Scoring system	Score and associated median OS	PRT recommendations by score
Rades [2016], (3)	Lung	Sum of the following categories:	10–11: 2 mo	10–11: single fraction PRT or within 1 week
		• KPS: ≤60 (+5), ≥70 (+3)	12–14: 6 mo	12–14: multi-fraction PRT
		• N-stage: N0–1 (+7), N2–3 (+3)	15–17: 38 mo	15–17: hypofractionation
		• M-stage: 0 (+5), 1 (+4)		
Rades [2021], (14)	Head and Neck	Sum of the following categories:	8–9: 1 mo	8–9: single fraction PRT
		• ECOG: 0–2 (+4), 3 (+3)	11–13: 2 mo	11–13: multi-fraction PRT
		• Pre-RT Hgb (g/dL): <12 (+3), ≥12 (+6)	14–15: 11 mo	14–15: moderate hypofractionation
		• Primary tumor site: oropharynx (+5), hypopharynx (+2), larynx (+4), oral cavity (+4)		
Sekii [2023], (16)	Gastric	Sum of the following categories:	≤2: 6.7 mo	≤2: multi-fraction PRT
		• PPS: 10–20 (+4), 30–50 (+2.5), >60 (+0)	2.5–4: 2.8 mo	>2: single fraction PRT
		• Oral intake: severely reduced (+2.5), moderately reduced (+1), normal (+0)	>4: 1.0 mo	
		• Edema: present (+1), absent (+0)		
		• Dyspnea at rest: present (+3.5), absent (+0)		
		• Delirium: present (+4), absent (+0)		

OS, overall survival; PRT, palliative radiotherapy; KPS, Karnofsky Performance Status; N, nodal; M, metastasis; mo, months; ECOG, Eastern Cooperative Oncology Group; RT, radiotherapy; Hgb, hemoglobin; PPS, Palliative Performance Scale.

Scale. Using these data, the authors performed univariate and multivariate analyses to identify the clinical factors associated with survival in patients receiving PRT.

In total, six clinical factors were significantly associated with survival: primary tumor site, site of metastases, KPS, fatigue, appetite, and shortness of breath. Using a partial scoring method (PSM), a point value was assigned for each factor. For example, patients with breast, prostate, lung, or other primary tumor sites received 0, 5, 6, and 7 points respectively. The sum of points from all 6 factors constituted the survival prediction scores (SPS). The SPS were significantly associated with survival: patients with scores of ≤13 (Group A), 14–19 (Group B), and ≥20 (Group C) had a median OS of 53, 19, and 8 weeks, respectively. Based on these outcomes, the authors recommend that short courses (and even omission) of PRT be considered for patients in Group C, while multi-fraction PRT regimens could be considered for patients in Groups A–B.

While this model was one of the first attempts to predict survival in patients receiving PRT, it has several limitations. First, it was initially published in 2002. Since that time, there have been many advances in systemic therapy that have increased patient survival. For example, using this model, patients with lung cancer were assigned the highest point value (6 points). However, the introduction of immunotherapy and targeted molecular agents for patients with metastatic lung cancer over the past two decades has been associated with a significant increase in survival (21). Additionally, this model does not incorporate the number of metastatic sites. In modern patient cohorts, the number of metastatic sites is associated with survival. For example, in a secondary analysis of the STAMPEDE trial, irradiation of the prostate was associated with improved survival only in patients with ≤3 metastatic sites (22). A simplified and (at the time) temporally validated version of this model was published in 2008 (23,24), which found that only three factors (KPS, site of metastasis, and primary tumor site) were needed to calculate SPS. Additionally, the authors also

proposed another simplified model that took into account the number of risk factors (NRF) involved. The NRF model incorporated three risk factors: non-breast cancer, site of metastases other than bone-only (i.e., non-bone-only metastases), and KPS ≤60. Median OS estimates by the NRF present were: 1, 55–64 weeks; 2, 19–28 weeks; and 3, 9–10 weeks. Still, additional predictive scoring systems that use more modern cohorts, or validation studies of previously developed scores in modern cohorts, are needed.

Palliative Appropriateness Criteria Score (PACS)

Using a more modern cohort of patients, Farris and colleagues (4) developed the PACS to assist in PRT fractionation decision making. From a cohort of 850 patients who received PRT at a single institution from 2014–2018, the authors developed the PACS by incorporating PRT fractionation (1, 2–5, 10 fractions), clinical factors [gender, performance status (ECOG), primary tumor site, metastasis site, PRT indication, and treatment setting (inpatient versus outpatient)], and percent of remaining life (PRL) after PRT. PRL was calculated by dividing the duration of PRT (number of days from start to finish) by the survival (in days) from the beginning of PRT. Among patients included in the analysis, the mean age was 64 years, the majority of patients had an ECOG performance status of 0–2, primary tumors of lung, breast or prostate, and most were treated for pain or neurologic symptoms.

The analysis was focused on assessing the risk of death within 30 days of receiving PRT for different fractionation schemes. For example, single-fraction PRT was associated with a high risk of futility in patients with ≥2 of the following: ECOG 3–4 performance status, lung or other primary tumor site, PRT used for symptoms other than pain, and PRT in the inpatient setting. PRT consisting of 2–5 fractions was associated with high risk of futility in patients with ECOG 3–4 performance status and/or treatment of an extraosseous site. PRT consisting of 10 fractions was associated with high risk of futility in patients with ≥4 of the following: ECOG 3–4 performance status, lung or other primary tumor site, PRT used for symptoms other than pain, PRT in the inpatient setting, treatment of an extraosseous site, and male gender. An online version of this calculator is available (https://ryhughes.shinyapps.io/pacs/). This model has been externally validated in a Norwegian cohort that confirmed the ability of the PACS to predict survival after PRT, the risk of death within 30 days of PRT (25), and the proportion of remaining life spent on treatment. Some aspects were not perfectly consistent between the development and external validation studies, possibly relating to heterogeneity within the patient populations, distributions of the PACS score risk factors, and PRT regimens utilized. This suggests that further study with larger, multi-institutional cohorts may be useful to refine the PACS system to be more generalizable across international populations.

TEACHH

The TEACHH model (26) is a validated prognostic tool used in palliative management. It was developed to assist in estimating life expectancy after PRT. This model was developed using 862 patients with metastatic cancer who underwent PRT between June 2008 and June 2011. Cox proportional hazards models were used to identify clinical factors associated with OS. Factors associated with OS make up the TEACHH acronym and include type of cancer ("T"), ECOG performance status ("E"), age ("A"), prior palliative chemotherapy ("C"), prior hospitalization ("H") and hepatic metastases ("H"). While median OS of the entire cohort was 5.6 months, it could be further stratified into three groups (A, B, C) based on the number of TEACHH risk factors present (*Table 3*). Within the manuscript, there are two main methods in which a scoring was applied: via an NRF method, and PSM. Patients with more risk factors present had worse OS: patients with 0–1 risk factor (Group A), 2–4 risk factors (Group B), and 5–6 risk factors (Group C) had median OS of 19.9, 5, and 1.7 months, respectively via the NRF method. The PSM results echoed similarly, with Group A (0–4 points), Group B (5–15 points), and Group C (16–20 points), and median OS of 17.5, 4.8, and 1.6 months, respectively. Based on these outcomes, longer, more durable PRT courses may be more appropriate for patients in Groups A and B, while single fraction PRT, or omission of PRT, may be more appropriate for patients in Group C.

The TEACHH model has also been externally validated. It was examined in a separate cohort of 180 patients who received PRT for vertebral metastases (7) Similar to the initial TEACHH cohort, the validation cohort had a median OS of 5.9 months. Additionally, the validation cohort could be further subdivided into three groups (A–C) based on the NRF that were present. Like the initial cohort, each group of patients in the validation cohort had median OS of 22, 5 and 1.5 months, respectively. Furthermore, when the TEACHH model was compared to the Chow three-item NRF model and the Oswestry Risk Index

Table 3 Scoring systems for multiple metastatic sites

Author [year]	Patient setting	Scoring system	Score and associated OS	PRT recommendations
Chow [2002], (20)	OP	SPS score is the sum of 6 factors:	SPS score:	SPS score:
		• Primary site of disease: breast (+0), prostate (+5), lung (+6), other site (+7)	• ≤13 (Group A): 53 wk	• Group A–B: consider multi-fraction PRT
		• Site of metastases: bone only (+0), other sites (+6)	• 14–19 (Group B): 19 wk	• Group C: consider single-fraction PRT or omission of PRT
		• KPS: >50 (+0), ≤50 (+6)	• ≥20 (Group C): 8 wk	
		• ESAS fatigue score: 0–3 (+0), 4–7 (+4), 8–10 (+5)		NRF score:
		• ESAS appetite score: 0–7 (+0), 8–10 (+4)		• Group 1–2: consider multi-fraction PRT
		• ESAS SOB score: 0 (+0), 1–3 (+2), 4–7 (+4), 8–10 (+0)		• Group 3: consider single-fraction PRT or omission of PRT
Chow [2008], (23)	OP	Simplified SPS score: sum of 3 factors	Simplified SPS score:	
		• Primary site of disease: breast (+0), prostate (+5), lung (+6), other site (+7)	• 0–4 (Group A): 53–64 wk	
		• Site of metastases: bone only (+0), other sites (+6)	• 5 (Group B): 21–29 wk	
		• KPS: >50 (+0), ≤50 (+6)	• 6–8 (Group C): 10–11 wk	
		Simplified NRF score: one point for each of the following:	Simplified NRF score:	
		• Non-breast cancer primary tumor	• 1 (Group 1): 55–64 wk	
		• KPS ≤60	• 2 (Group 2): 19–28 wk	
		• Metastasis other than bone	• 3 (Group 3): 9–10 wk	
Farris [2023], (4)	OP, IN	PACS calculated for each PRT fractionation scheme. One point is given for presence of each risk factor:	Futility[a] risk group by score:	
		1 fraction:	1 fraction:	1 fraction:
		ECOG 3–4, Lung or other primary, PRT for non-pain symptoms, inpatient PRT	• 0–1: LR	• LR =1 fraction PRT
			• ≥2: HR	• HR =1 fraction RT or omission of PRT
		2–5 fractions:	2–5 fractions:	2–5 fractions:
		ECOG 3–4, PRT to extraosseous site	• 0: LR	• LR =2–5 fraction PRT
			• ≥1: HR	• HR = consider alternative PRT fractionation

Table 3 (*continued*)

Table 3 (*continued*)

Author [year]	Patient setting	Scoring system	Score and associated OS	PRT recommendations
		10 fractions:	10 fractions:	10 fractions:
		ECOG 3–4, Lung or other primary, PRT for non-pain symptoms, inpatient PRT, PRT to extraosseous site, male gender	• 0–3: LR	• LR =10 fraction PRT
			• ≥4: HR	• HR = consider alternative PRT fractionation
Krishnan [2014], (26)	OP, IN	NRF model: 1 point is given for the presence of each of the following factors:	TEACHH score:	
		• Primary site “Lung” or “other”	NRF	• Group A–B: multi-fraction PRT
		• ECOG 2, 3 or 4	• 0–1 (Group A): 19.9 mo	• Group C: single fraction PRT or omission of PRT
		• Age >60 years	• 2–4 (Group B): 5 mo	
		• Prior chemotherapy, ≥2 courses	• 5–6 (Group C); 1.7 mo	
		• Prior hospitalization in last 3 months		
		• Hepatic metastases		
		PSM model: number of points varies by the following risk factors:	PSM	
		• Primary site “Lung” =5, “other” =2	• 0–4 (Group A): 17.5 mo	
		• ECOG 2 =4, ECOG 3 or 4 =6	• 5–15 (Group B): 4.8 mo	
		• Age >60 years =2	• 16–20 (Group C): 1.6 mo	
		• Prior chemotherapy ≥2 courses =3		
		• Prior hospitalization in last 3 months =2		
		• Hepatic metastases =4		
Zaorsky [2021], (5)	IN	Mortality risk index regression equation incorporates:	METSSS score:	
		• Location of metastases	• <−0.122 (LR): 11.66 mo	• LR-MR: multi-fraction or durable PRT
		• Age (years)	• −0.122 to 0.242 (MR): 5.09 mo	• HR: single or multi-fraction PRT
		• Primary tumor site	• >0.242 (HR): 3.28 mo	
		• Gender		
		• Charlson-Deyo comorbidity score		
		• Body site receiving PRT		

[a], futility defined as death within 30 days of PRT. OS, overall survival; PRT, palliative radiotherapy; OP, outpatient; SPS, survival prediction score; wk, week; KPS, Karnofsky Performance Status; ESAS, Edmonton Symptom Assessment System; NRF, number of risk factor; SOB, shortness of breath; IN, inpatient; PACS, Palliative Appropriateness Criteria Score; ECOG, Eastern Cooperative Oncology Group; LR, low risk; HR, high risk; mo, month; PSM, Partial Scoring Method; MR, medium risk.

indices, all three models were found to have similar median OS (23,27). The Oswestry Risk Index was initially designed to predict life expectancy of patients with spinal metastases, with factors including general condition of the patient and primary tumor type (27,28). Despite these strengths, one major limitation of the TEACHH model is that it requires users to examine six clinical factors, whereas other scoring systems require examination of a fewer numbers of factors.

METSSS

In this model, Zaorsky and colleagues (5) used population-level data from over 68,000 patients in the National Cancer Database (NCDB) to predict the OS of patients treated with PRT. Patients were included in this model if they completed one of three standard PRT regimens: 3 Gy × 10 fractions, 4 Gy × 5 fractions, and 8 Gy × 1 fraction. In this study, a nomogram was developed using six clinical factors including: location of metastases (liver, bone, lung, brain), age, primary tumor site (prostate, breast, lung, other), sex, Charlson-Deyo comorbidity score (29), and site receiving PRT. Of note, the use of chemotherapy was not included in the nomogram as to not skew survival data or decision making to use PRT.

Based on these factors, a mortality risk index equation was developed using predictors from Cox regression modeling and patients were divided equally into low-, medium-, and high-risk groups based on this model statistic. Median OS estimates for the three groups were 11.66, 5.09, and 3.28 months, respectively. Using the online nomogram (https://tinyurl.com/METSSSmodel), providers can calculate the risk group into which their patient falls, along with 1- and 5-year OS estimates. Limitations of the model include inherent drawbacks of using NCDB (e.g., lack of specific patient data, risk of confounders), as well as the fact that it did not incorporate treatment setting (outpatient versus inpatient), number of metastases, or prior treatment history. Additionally, while specific PRT fractionation recommendations were not provided, the goal of this scoring system was to provide clinicians with more specific information regarding the OS of patients receiving PRT. It can be assumed that patients in the low to medium risk groups are candidates for multi-fraction (20–30 Gy in 5–10 fractions) or more durable moderately hypofractionated (45 Gy in 15 fractions) PRT regimens, while patients in the high-risk group may be considered for single-fraction (8 Gy in 1 fraction) or shorter multi-fraction PRT regimens (quad-shot, 20 Gy in 5 fractions).

A summary of use for each scoring system is described in *Table 3*.

Discussion

The use of PRT for patients with both metastatic and locally advanced disease is important as it can help mitigate disease related symptoms and improve quality of life. Given improvements in systemic therapy and disease surveillance (30), survival duration is increasing in patients with metastatic disease. Symptomatic disease can present in virtually any anatomic site with a variety of patterns of spread, and there are a multitude of PRT techniques, doses, and fractionation regimens. As a result, radiation oncologists are presented with unique clinical challenges when evaluating and treating patients with PRT. This article summarizes scoring systems that radiation oncologists can use to select appropriate PRT fraction schemes for patients with metastatic and non-metastatic disease.

While multiple prognostic models exist for patients receiving PRT, one commonality across all models is that the appropriateness of choosing a PRT regimen is based on the expected survival of the individual patient. Although multiple schemes are deemed appropriate per the American Society of Radiation Oncology guidelines (31), in general, shorter PRT regimens (e.g., 1–5 fractions) should be utilized for patients whose predicted survival is limited, especially for patients with painful, uncomplicated bone metastases (32).

It should be noted that, in select patients, stereotactic body RT (SBRT) may be utilized for the local ablation of symptomatic or asymptomatic sites of metastases. This is primarily utilized in patients with oligometastatic disease where high rates of local control are desired with the hope of long-term progression-free survival (33-39). While one study (40) has shown improvement in rates of symptomatic relief for patients with bone metastases treated with SBRT compared with conventional external beam PRT, it is unclear if dose escalation using highly conformal SBRT techniques substantially improve upon the palliative benefits of PRT. Considering the goal of this study was to review the currently available prognostic systems for patients receiving PRT, further discussion SBRT is outside the scope of this study.

As outlined in a previous study, there are multiple symptoms for which PRT may be appropriate at the end of life, including pain, neurologic and/or ocular dysfunction, bleeding, respiratory compromise, genitourinary or gastrointestinal dysfunction, wounds or other issues related to local tumor invasion (41). Unfortunately, radiation oncologists (like physicians across all specialties) are not particularly accurate at predicting survival rates in patients referred for PRT (42). Additional methods to provide a personalized risk assessment of life expectancy are needed to inform clinical judgement. Further personalization may help with the selection of patients for PRT, symptomatic targets, RT techniques, and dose regimens.

This review has several strengths. First it describes PRT scoring systems that can be used for patients with metastatic or non-metastatic disease. Several of the included models are pragmatic, utilizing a limited number of readily available patient characteristics, and thus can be applied when seeing patients in the clinic or hospital wards. Despite these strengths, this review is not without limitations. For example, several of the described scoring systems are not externally validated and several are based on older, retrospective cohorts. Additionally, this is a narrative review of prognostic scoring systems relevant to clinical decision-making in patients treated with PRT, and thus does not summarize every available model. Other prognostic models—for example, the graded prognostic assessment (GPA) for brain metastases (43) and the Dutch scoring system for spine metastases (44)—do exist and were not included in this article. The goal of this review was to summarize select prognostic models to provide radiation oncologists an understanding of their application in PRT.

Conclusions

When faced with complex clinical decision-making regarding the appropriateness and delivery of PRT, clinically relevant prognostic models are highly useful. Personalized information regarding patient survival and potential benefits of PRT can help guide palliative radiotherapeutic management. Future studies should include validation of current models in a modern cohort, specific to disease sites and systemic therapies.

Acknowledgments

Funding: None.

Footnote

Reporting Checklist: The authors have completed the Narrative Review reporting checklist. Available at https://apm.amegroups.com/article/view/10.21037/apm-23-538/rc

Peer Review File: Available at https://apm.amegroups.com/article/view/10.21037/apm-23-538/prf

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://apm.amegroups.com/article/view/10.21037/apm-23-538/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Cite this article as: Shenker RF, Razavian NB, Lanier CM, Hughes RT. Prognostication methods for patients treated with palliative radiotherapy: a narrative review. Ann Palliat Med 2024;13(2):322-333. doi: 10.21037/apm-23-538

