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Audit of 30-day mortality following palliative radiotherapy: are we able to improve patient care at the end of life?

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ABSTRACT

Background: Several measurements defining the expected 30-day mortality (30-DM) to use in audit of radiation oncology departments have been proposed. However, its external validity is limited because of the lack of data from non-English speaking countries. This study assessed 30-DM in patients treated with palliative radiotherapy (PRT) in a Chilean-reference radiotherapy centre and explored if there had been tailored treatment at the end of life.

Materials and methods: Retrospective data collection was carried out for all patients treated at our institution between 1st January 2018 and 31st December 2021. Individual factors were modelled first to check for univariate association with 30-DM, those variables with a significance level of < 0.05 were considered for the final multivariable model.

Results: 3,357 patients were included. The most common primary malignancies were breast (22%) and lung (16.1%). The most common treatment sites were bone (47.7%) and brain (12.2%). Overall, 30-DM was 14.7%, this rate was higher in patients treated for brain metastases (25.7%) and thoracic palliation (22.1%). 30-DM was associated with poor performance status ($p < 0.01$), lung and esophageal-gastric cancer ($p = 0.04$ and $p = 0.02$, respectively), metastases other than bone ($p < 0.01$), brain metastases ($p < 0.01$) and private health insurance ($p < 0.01$).

Conclusions: In patients treated for brain metastasis and thoracic palliation 30-DM was higher than suggested benchmarks. Moreover, in these groups long courses of PRT were often performed. Audit data should be useful for planning interventions that improve selection of patients and prompting review of policies for indication and fractionation schedules of PRT.

Key words: palliative radiotherapy; prognosis; audit; 30-day-mortality

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Introduction

In developed countries, between 40-50% of referrals to radiotherapy departments are sent for palliative treatment and 60%-80% of patients experience relief from a wide variety of symptoms [1, 2]. However, the time frame for symptomatic improvement is typically measured in weeks; therefore, patients undergoing palliative radiotherapy (PRT) at the end of life may not experience symptomatic benefit and may spend a significant proportion of their remaining life expectancy (LE) receiving treatment, particularly when fractionated schedules are used [3–5]. In patients with advanced cancer, the decision to fractionate treatment, with increased acute toxicity and treatment burden, is sometimes considered necessary to relieve symptoms with durable control, although the evidence base for this approach is limited [6, 7].

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Currently, an evidence-based quality measurement defining the expected 30-day mortality (30-DM) worldwide to use in audit of radiation oncology departments is lacking in the literature, although several metrics have been proposed [8–11]. The first measurement was proposed by the Royal College of Radiologists which established that, ideally, no more than 20% of patients should die within 30 days of receiving PRT. If the rate is higher than this, it would suggest that too many patients are being treated without surviving long enough to benefit but would be at risk of acute toxicity [8]. If this proves to be the case, PRT in the last 30 days of life could turn out to be a futile treatment. This means that in those patients with limited LE this therapy should not be performed because available data shows that it will not improve the patient's medical condition [12].

Published literature shows that practice patterns of PRT at the end of life vary widely across treatment centers, demographics, and geography and 30-DM ranges between 9 and 15% [9]. So far, all data published regarding this topic has been obtained in high-income countries but there is a lack of information from low- and middle-income countries where there is limited access to radiotherapy and patients tend to present at a more advanced stage of the disease [13]. A retrospective study to determine 30-DM in patients treated with PRT was conducted in a Chilean-reference radiotherapy center. The goal was to explore whether there had been appropriate patient selection and a tailored dose/fractionation treatment at the end of life.

Materials and and methods

Patients and data collection

Retrospective data collection was carried out for all patients receiving their first PRT course at our institution between 1st January 2018 and 31st December 2021. January 2018 was chosen as the starting point because electronic records were fully implemented at that time.

Exclusion criteria were: patients under the age of 18, non-melanomatous skin cancer and treatment with stereotactic body radiation therapy or radiosurgery. Demographic data, radiation dose/fractionation, and disease characteristics were collected from the medical records for each patient. The type of primary tumour was classified into eight groups according to the most frequent tumours: lung, breast, prostate, kidney, colorectal, gynecological, haematological and others. Episodes were identified when the treatment intent was registered as palliative by a radiation oncologist. Site of the treatment was allocated by bone, brain, thoracic, abdominal, pelvis, head & neck, and skin-soft tissue. For patients who were treated more than once, we took into account the last treatment to avoid data duplication.

Vital status and date of death were confirmed with the national death registry.

This study was approved by the institutional review board.

Statistical methods

Baseline characteristics were stratified by 30-DM after PRT. 30-DM was calculated from the date of the last treatment fraction to the date of death. The association between the 30-DM and various demographic and clinical factors was assessed with the logistic regression model. Individual factors were modelled first to check for univariate association with 30-DM. Variables with a significant level of < 0.05 from the univariate analyses were considered for the final multivariable model. Multivariable logistic regression was performed to identify the factors associated with 30-DM. Point estimates from the multivariable model are reported as odds ratios (ORs) with the corresponding 95% confidence interval (CI) for each OR. All statistical analyses were conducted using R statistical software package (www.r-project.org).

Results

Patients' characteristics

3357 patients were included in this study. The median age was 64 years [interquartile range (IQR) 55–73years]. The median survival time from final PRT course to death was 7.9 months (IQR 1.9–10 months).

The most common primary malignancies were breast (22%, 740/3357), lung (16.1%, 541/3357), prostate (10.3%, 347/3357) and colorectal (9%, 302/3357). Haematological malignances represented 8.1% (273/3357).

The most common treatment sites were bone (47.7%), brain (12.2%), pelvic (10.9%) and thoracic (9.3%). These results are summarized in Table 1.

Table 1. Baseline patient characteristics stratified by receipt of end-of-life radiation therapy

	Overall n = 3357 (%)	≤ 30 days n = 493 (%)	> 30 days n = 2864 (%)	p-value
Age				
≤ 65 years	1830 (54.5)	260 (53)	1570 (55)	0.40
> 65 years	1527 (45.5)	233 (47)	1294 (45)	
Gender				
Female	1772 (52.8)	230 (47)	1542 (54)	0.03
Male	1585 (47.2)	263 (53)	1322 (46)	
Health insurance				
Public	1695 (50.5)	260 (53)	1435 (50)	0.01
Private	1125 (33.5)	140 (28)	985 (34)	
Others	537 (16)	93 (19)	444 (16)	
Primary tumor				
Lung	541 (16.1)	130 (26)	411 (14)	< 0.001
Haematologic	273 (8.2)	33 (6.7)	240 (8.4)	
Breast	740 (22)	67 (14)	673 (23)	
Prostate	347 (10.3)	28 (5.7)	319 (11)	
Renal	185 (5.5)	27 (5.5)	158 (5.5)	
Colo-rectal	302 (9)	44 (8.9)	258 (9)	
Cervix-uterine	141 (4.2)	16 (3.2)	125 (4.4)	
Esophageal-gastric	144 (4.3)	28 (5.7)	116 (4.1)	
Other	684 (20.4)	120 (24)	564 (20)	
ECOG				
0–2	2878 (85.7)	349 (71)	2529 (88)	< 0.001
3–4	479 (14.3)	144 (29)	335 (12)	
Treatment site				
Head & neck	147 (4.3)	22 (4.5)	125 (4.4)	< 0.001
Brain	408 (12.2)	105 (21)	303 (11)	
Bone	1600 (47.7)	187 (38)	1413 (49)	
Intra-abdominal	204 (6.1)	30 (6.1)	174 (6.1)	
Intra-pelvic	367 (10.9)	38 (7.7)	329 (11)	
Intra-thoracic	312 (9.3)	69 (14)	243 (8.5)	
Skin & soft tissues	319 (9.4)	42 (8.5)	277 (9.7)	
Fractions				
1	1301 (38.8)	198 (40)	1103 (39)	0.04
2–5	1225 (36.5)	157 (32)	1068 (37)	
≥ 5	831 (24.7)	138 (28)	693 (24)	
Metastases other than bone				
No	1238 (36.9)	117 (24)	1121 (39)	< 0.001
Yes	2119 (63.1)	376 (76)	1743 (61)	

ECOG — Eastern Cooperative Oncology Group

A significative variation in the use of different fractionation schedules was observed throughout the studied period (Supplementary File — Tab. S1)

Overall, 2.6% of patients did not complete their PRT because clinical deterioration.

30-DM

Overall, four hundred and ninety-three patients (14.7%) died within 30 days of PRT, this rate was variable during the studied period (2018: 15.4%; 2019: 16.9%; 2020 15.6%; 2021 11.2%). Almost 30% of these patients had a poor performance status [Eastern Cooperative Oncology Group (ECOG) 3 or 4]. The median survival was 16 days in this group (IQR 9–23) and 14.6% patients did not complete the prescribed treatment because of clinical deterioration.

30-DM rates was higher than suggested benchmarks in patients treated with whole brain radiotherapy (WBRT) for brain metastases (25.7%) and in those treated for thoracic palliation (22.1%) (Tab. 1). In both groups lung cancer was the most frequent primary (38% and 64%, respectively). 59.4% of patients who received WBRT were treated with 30 Gy in 10 fractions, whereas 52.1% of those who received thoracic PRT were treated with multiple fraction schedules.

In univariate analysis female gender, presenting with lung cancer or esophageal-gastric cancer, poor performance status, metastasis other than bone, treatment with single dose and received palliation for brain were significantly associated with 30-DM (Supplementary File — Tab. S2).

In multivariate logistic regression, 30-DM was associated with poor performance status ($p < 0.01$), lung and esophageal-gastric cancer ($p = 0.04$ and $p = 0.02$, respectively), metastases other than bone ($p < 0.01$), brain metastases ($p < 0.01$) and private health insurance ($p < 0.01$) (Tab. 2).

Table 2. Multivariate analysis investigating potential risk factors of expected 30-day mortality (30-DM)

	OR	95% CI	p-value
ECOG			
0–2	–	0.27–0.45	< 0.01
3–4	0.35		
Health Insurance			
Public	–		
Private	0.65	0.51–0.83	< 0.01
Other	0.94	0.70–1.25	0.67
Metastases other than bone			
No	–	1.44–2.41	< 0.01
Yes	1.86		
Fractions			
> 5	–		
2–4	1.87	1.26–2.82	< 0.01
1	1.47	1.00–2.19	0.05
Primary tumor			
Cervix-Uterine	–		
Prostate	0.99	0.48–2.14	0.98
Breast	0.84	0.43–1.70	0.60
Haematologic	1.60	0.78–3.41	0.21
Colorectal	1.80	0.93–3.64	0.09
Esophageal-gastric	2.50	1.16–5.57	0.02
Renal	1.55	0.73–3.37	0.20
Others	1.97	1.07–3.87	0.04
Lung	2.03	1.07–4.07	0.04
Treatment site			
Head & neck	–		
Pelvic	0.61	0.33–1.16	0.12
Bone	0.92	0.55–1.60	0.24
Abdominal	0.67	0.34–1.32	0.24
Skin-soft tissues	1.08	0.60–2.0	0.79
Thoracic	1.24	0.70–2.27	0.47
Brain	2.13	1.15–4.09	0.02

ECOG — Eastern Cooperative Oncology Group; OR — odds ratio; CI — confidence interval

Discussion

Estimating life expectancy in patients with advanced cancer is a critical issue and objective criteria for reducing futile treatment is of critical importance [14].

The Royal College of Radiologists agreed that, ideally, no more than 20% of patients should die within 30 days of receiving PRT; Spencer et al. reported 12.3% in a population-based study, Park et al. reported a 30-DM between 9-15% and a recent meta-analysis report that a 30-DM rate of 16% can be used as a benchmark to establish a global quality metric for radiation oncology practice audits [8–11]. However, the lack of data from non-English speaking countries limits its external validity [11].

We found a 30-DM of 14.7% which is similar to previously reported results and adjusted to the aforementioned recommendations, therefore it could be assumed that in our centre the overall selection of patients for PRT was adequate.

Variation of 30-DM during the studied period, from 15.4% (2018) to 11.2% (2021), could be ex-

plained by the increasing use of single dose PRT from March 2020 due to the global COVID-19 pandemic that arrived in Chile at that time. How the pandemic affected 30-DM in radiation oncology departments in low- and middle-income countries is not known but in Norway, Nieder et al. found that at their centre, the previously reported rate of 30-DM did not change, despite rapid adoption of modified PRT regimens [15]. Extended PRT has been associated with a greater likelihood of 30-DM mortality and this is probably the difference between the study by Nieder et al. and our findings because in that study 60% of patients received 10 or more fractions while at our institution PRT ≥ 5 fractions was used in only 25% of patients.

In line with previously published studies, in multivariate analysis we found that 30-DM was higher in patients with lung cancer, metastases other than bone and brain PRT [9–11]. We found that esophageal-gastric cancer was also a risk factor with regards to that outcome. Although we have included esophageal and gastric cancer in the same group for analysis, our results are consistent with epidemiological data in Chile where gastric cancer is the primary cause of cancer deaths [16].

In the present study, private health insurance patients have had a higher risk to be treated with PRT within their last 30 days of life. A study conducted using the Surveillance, Epidemiology, and End Results (SEER) — Medicare linked database obtained similar results [17]. A higher expected 30-DM rate for patients treated with PRT in the United States (US) compared to elsewhere has been reported possibly as a consequence of the unique and complex collection of private and publicly based health insurance funds used to pay for health care utilization [11]. As in the US, the Chilean health system involves the co-existence of public and private health insurance schemes. Access to these schemes depends on patient´s income. Consequently, a disparity in the use of cancer treatments, including PRT at the end of life, may well depend on patient's health insurance coverage — or lack of it.

However, this finding could also be in relation with a wider distribution and better quality of palliative care services at the end of life in the public health system, which may privilege the best supportive care approach in seriously ill patients [18].

Additionally, we also found that in our practice 30-DM of those patients treated with WBRT and thoracic PRT exceeded the proposed rates of 12–20%. Moreover, in these groups long courses of PRT were often performed.

WBRT may offer some clinical benefit and remains the standard of care for those patients who do not qualify for surgery or radiosurgery. Studies have confirmed the equivalence of various dose fractionation schemes without statistically significant differences in overall survival or symptoms control [19].

In an observational prospective study of patients receiving 20 Gray/5 fractions WBRT, Bezjack et al. found that many patients may not benefit from even short duration radiation schedules. In fact, at follow-up 1 month after WBRT, only 19% of patients either showed an improvement or resolution of their presenting neurological symptoms [4]. In addition, QUARTZ trial found no evidence of a difference in overall quality of life, or dexamethasone use between non-small cell lung cancer patients who received optimal supportive care (OSC) including dexamethasone plus 20 Gray/5 fractions WBRT or OSC alone.[20] At our centre, 22% of patients treated with WBRT had an ECOG 3–4 and the most common schedule was 30 Gy in 10 fractions.

The indication of PRT in patients with brain metastases, poor prognoses and short survival is questionable and they may be best treated with OSC mainly because their prevailing cause of 30-DM is the extracranial tumour progression [21, 22].

Reducing the use of end-of-life radiotherapy in patients with brain metastasis should be a very desirable goal. Developing networks between doctors involved in palliative care, in this case by integrating palliative care expertise to address the complex needs of patients with newly diagnosed brain metastases, may decrease WBRT at the end of life [23].

Regarding thoracic PRT, a noteworthy finding is that more than half of patients who died within 30 days after treatment were treated with 4 or more fractions, almost 40% of them had ECOG 3 or 4. These results are similar to the findings of Koshy et al. because approximately half of all patients with metastatic lung cancer received a higher number of fractions than recommended [24]. Some authors have argued that the primary factors that

influence PRT dose fractionation schemes should be performance status (PS) and comorbidities. However, Radiation Oncologists should be aware that available evidence shows that higher doses and more fractionated regimens of PRT increase acute toxicity, do not provide better or more durable palliation and their use in prolonging survival is not supported by strong evidence [7, 25].

Though PS is generally a useful and valid tool for predicting survival, it is subject to a series of factors that limit its accuracy and should not be used alone but in conjunction with other prognostic factors [26]. In fact, physicians tend to rate patients as healthier for the ECOG PS and have a 40% accuracy in predicting patient survival as a consequence [27, 28].

A reliable assessment of PS for deciding PRT is not trivial because many of the symptoms reported by patients with PS 3–4 tend to worsen temporarily after treatment and those with short survival may not experience a net benefit during the few weeks before death [29].

The TEACHH and Chow models have been proposed to estimate LE in patients evaluated for PRT and help physicians in their clinical decision-making. Both were developed using patient cohorts seen at academic centres, with relatively long predicted LE, in fact few patients with predicted LE less than 3 months were included (33.0% and 5.7%, respectively) [30, 31]. Mojica-Márquez et al. retrospectively analyzed a cohort of consecutive patients with a median survival of approximately 2 months and found that nearly 80% of patients were classified into prognostic groups with predicted survivals of at least 5 months per the TEACHH model, and nearly a quarter of patients were predicted to survive 15 months by the Chow model. Thus, these models may not accurately predict prognosis in patients with LE of less than 3 months [32].

Angelo et al. developed and validated a predictive model that would allow a reduction of PRT utilization during the final 30 days of life in patients with incurable cancer. This model included six parameters (lung or bladder cancer, ECOG performance status of 3–4, low haemoglobin, opioid analgesic use, steroid use, known progressive disease outside PRT volume), which correctly identified 75% of PRT courses administered during the final 30 days of life [14].

Because these models have limited accuracy, particularly for predicting whether patients will die within the next 30 days, some authors have discouraged the routine use of the 30-DM as the only metric to decide whether to offer PRT, particularly in painful bone metastases, spinal cord compression and hemostatic treatments. For these indications,

several trials have demonstrated substantial response rates by four weeks and sometimes within the first two weeks after PRT [33].

However, as in other studies, audit 30-DM may be useful for planning interventions that improve selection of patients and prompting review of policies for indication and fractionation schedules of PRT, especially when resources are limited [22, 34].

In Chile, there is a well described unequal distribution of radiotherapy facilities throughout the country because cancer resources are highly concentrated in the capital city, Santiago de Chile [35]. In fact, 72% of palliative care physicians do not have access to radiotherapy at the same hospital and 30% have to refer patients to another city [36]. These limitations stress the need for saving resources, from both patients and providers because avoiding futile PRT may contribute to improving overall cancer care. Moreover, for patients with advanced disease and poor prognosis large distances between radiotherapy centres, the associated financial burden (accommodation and travel costs) and associated radiation side effects could result in an undesirable but avoidable toxicity [14]. Adopting evidence-based practice, supported by several large palliative trials, and formal education in PRT may be a key issue for avoiding futile treatment as well as long courses of PRT in patients with limited life expectancy and improving patient care at the end of life as a consequence.

As with other similar studies, our study has an inherent bias due to its retrospective design, which limited, for example, a collection of variables with demonstrated impact on 30-DM as blood cells count, dyspnea, cachexia, opioid and steroid use, known progressive disease outside PRT volume and others. Additionally, this study reflects the clinical practice of a single centre and only those patients who started the treatment were included in the analysis. Patients who had been scheduled for PRT but died before it started were excluded.

Nevertheless, we think this data is relevant because clinically relevant groups with high risk for

30-DM were identified after more than 3,000 patients treated in a radiotherapy reference-centre in Chile had been analysed.

To the best of our knowledge, our study is the first contribution from Latin America to address this issue. Audit data have made it possible to carry out interventions that have resulted in an increased utilization of evidence-based practice, reduction of costs and improved patient convenience [34]. As a result, we hope our findings will be a necessary step for improving care of patients who require PRT at our institution as well as throughout our country. Likewise, it could be a starting point for analysing quality of care when PRT is utilized at other institutions from low- and middle-income countries.

Conflicts of interest

The authors declare that there is no conflict of interest.

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Research ethics and respondent consent

The study was approved on 8th June 2021 by the Institutional Review Board (Servicio de Salud Metropolitano Oriente).

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