Letter to the Editor | Palliative Medicine and Palliative Care for Incurable Cancer

Thirty-day expected mortality and hemostatic palliative radiotherapy: definitions, certainties and uncertainties

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We read the article by Navarro-Domenech *et al.* with great interest. This narrative review examines whether a 30-day mortality (30-DM) rate is appropriate to determine which patients benefit from palliative radiotherapy (PRT). Authors have argued that several studies have demonstrated substantial response rates for pain and/or bleeding, even in patients with a short-predicted life expectancy (1).

We congratulate our colleagues on this review but we would like to offer them some observations.

Firstly, the authors contend that 30-DM has been proposed to determine the decision to administer PRT. We disagree with this affirmation because 30-DM is not a decision-tool for patient selection nor for giving appropriate care, in fact, it has been proposed as a benchmark to establish a global quality metric for radiation oncology practice audits. Besides, it is difficult to propose 30-DM as a metric for deciding PRT because the literature shows that it varies widely across treatment centres, demographics and geography (2).

The literature shows that audits are useful for identifying patient groups who have particularly poor outcomes and prompting local review of policies for indication of PRT and dose fractionation (3,4).

Secondly, we absolutely agree that there is enough evidence to confirm that single fraction PRT is effective in palliating patients' symptoms, even near the end of life. However, strong evidence supports this affirmation specifically for symptomatic bone metastases and spinal cord compression.

Regarding hemostatic PRT, it is not possible to affirm that treatment does help even if life expectancy is less than 4 weeks. For this reason, the withholding of or not offering PRT cannot be described as unethical because the possibility of futile treatment is a major concern in this setting and physicians have an ethical obligation not to provide futile care (5).

Additionally, bleeding response within 24–48 hours of the treatment is probably supported by the clinical experience of authors but in our opinion, it is not possible to support this affirmation in published data.

Within the studies cited by authors regarding hemostatic PRT, all studies but one are retrospective and have several recognized limitations. In bladder and gynecological PRT studies the sample sizes were often small. When reported, 41–57% of patients had Eastern Cooperative Oncology Group (ECOG) 1–2 and only between 30–40% of included patients were metastatic. In the majority of these single-centre studies, toxicity and responses were collected by physicians only rather than the patients and, because no particular follow-up protocols were applied due to its retrospective design, response to PRT in those patients maintaining follow-up may differ systematically from those lost.

It is of note that in a multi-centric retrospective study

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which included 241 patients with bladder cancer, advanced stage (42% stage IV), poor performance status (38% ECOG 3–4) and significant co-morbidities (45% of patients with 2 or more comorbidities), 25% of patients either did not complete PRT or died within 6 weeks of treatment and 47% of patients reported no improvement of symptoms (6). In addition, prospective studies have shown that in patients with limited life expectancy, advanced disease and poor performance status, symptoms tend to worsen temporarily after treatment and progressive complaints are noted in up to 52% (7).

Concerning PRT in gastric bleeding, studies cited by authors were also retrospective. These included a high rate of metastatic patients (67–87%); only 9.6–17% had ECOG 3–4 and response was assessed 4 weeks after treatment. Interestingly, while between 10–22% of included patients either did not complete treatment or died within 4 weeks of treatment, other studies exclusively included patients that completed the prescribed treatment.

It seems that not all patients are eligible for hemostatic PRT because side effects are not well reported, the time to response is at least 4 weeks and the net benefit in those who dead within 30 days after PRT is not known. An obvious question at this point is whether best supportive care could be a more tailored treatment in patients with limited life expectancy.

Predicting patient survival is another issue to consider in PRT at the end of life. Maybe the prognostic models of survival cited by authors are not the most appropriate for addressing this challenging topic. While Rades *et al.* developed a prognostic tool for predicting survival at 12 months, NFR and TEACHH included few patients with predicted life expectancy of less than 3 months (33.0% and 5.7% respectively) (8-10). In a retrospective cohort of consecutive patients with a median survival of approximately 2 months, Mojica-Márquez *et al.* 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 25% of patients were predicted to survive 15 months with NRF (11).

We would like to highlight that, based on 30-DM audits, predictive models that could facilitate decision-making for patients being considered for PRT have been proposed. Angelo *et al.* developed a model predicting 30-DM using recursive partitioning analysis and they found that the presence of lung or bladder cancer, ECOG PS 3–4, opioid analgesic use, low hemoglobin, steroid use, known progressive disease outside PRT target volume correctly identified 75% of 30-DM after PRT (12).

Finally, as the authors point out, rapid access PRT programs have been established in a minority of centres and the vast majority of them come from advanced economies. In low and middle-income countries there is limited access to radiotherapy and patients tend to present at a more advanced stage of the disease, therefore avoiding futile PRT saves resources and might improve overall cancer care (12,13).

As authors, we also encourage individualized discussion about pros and cons of PRT in patients with advanced disease and poor performance status. Audit local data of PRT may also be useful for identifying subgroups of patients with high risk of 30-DM, adopting evidence-based practice, avoiding futile treatment and improving patient care at the end of life. Prospective studies are warranted to delineate the time-to-response of hemostatic PRT as well as its role in patients with poor prognosis.

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Footnote

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