

Pain and quality of life in palliative care

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This issue of *Annals of Palliative Medicine* features several articles addressing pain, from defining pain severity cut points, to quantifying and reducing pain acquired after bone marrow biopsy, to treating neuropathic pain, to using reirradiation for recurrent pain from bone metastases.

Several pain-rating scales have been validated and are in widespread clinical use (1,2). Currently, several studies have employed a numeric rating scale to assess pain severity or to group patients into pain categories within a single patient population (3,4). However, recent review articles across patient populations and current recommendations for the optimal pain cut points for mild, moderate, and severe pain are lacking. In this issue of *Annals of Palliative Medicine*, Woo *et al.* provide a thorough and thought-provoking review of cut points for mild, moderate, and severe pain for both cancer and non-cancer patients (5). This is a high-impact publication that can help clinicians assess for changes in the functional status of their patients and better develop and evaluate treatment options to improve the pain of their patients. Given the broad scope of the review, this report has clear implications for patients suffering from pain from a plethora of causes, from osteoarthritis to lower back pain to diabetic neuropathy to cancer-related pain.

Pain is one of the most common symptoms experienced by patients with cancer and a common cause for depression, sense of hopelessness and fear, and decline in quality of life (6-8). Neuropathic bone pain is just one of a number of types of pain that can result from bone metastasis, which is reviewed in detail along with optimal treatment approaches in this issue of *Annals of Palliative Medicine* by Roos (9). Despite improvements in the understanding of the different causes and types of pain experiences by patients with cancer, implementation of clinical guidelines recommending systemic pain assessments, and high pain response rates

that are achievable with analgesics and other medical interventions, many patients with cancer continue to receive inadequate medical management of their pain (10-12). This is particularly true in the approximately half of all advanced cancer patients who develop bone metastases (13).

Palliative radiation therapy is a commonly utilized modality for treating pain from cancer, and particularly from bone metastasis, and it is effective in achieving a pain response in the majority of patients (14). However, not all patients have a pain response to radiation therapy, and a significant portion that do have a pain response that is not durable, allowing for pain to recur. This is a byproduct of the improvements in systemic therapy and supportive care, which have allowed patients with metastatic disease to live longer, and often to outlive the duration of benefit from an initial short-course course of palliative radiotherapy (15).

The utilization of and need for palliative reirradiation has received increasing attention and is highlighted in the current issue's Palliative Radiotherapy Column. Chiu and colleagues address optimal management of painful bone metastasis previously treated with palliative radiotherapy in an evidence-based review (16). Reirradiation can be considered after lack of pain relief following an initial course of radiotherapy, after a partial but unsatisfying pain response to an initial course of radiotherapy, or after pain recurrence following a complete or partial pain response to an initial course of radiotherapy. Reirradiation has been shown to be effective at controlling cancer-related pain, and it may be most optimally used in patients who achieve an initial pain response to a first course of palliative radiotherapy (17,18). In this setting, the majority of patients can achieve a pain response to reirradiation based on a recent systemic review report (19).

Despite the potential benefits of reirradiation in

improving pain and quality of life for patients with advanced malignancies, the optimal dose and fractionation for reirradiation remains undefined. The first randomized controlled trial comparing different schedules of reirradiation to palliative painful bone metastases, which was undertaken by the National Cancer Institute of Canada (NCIC) Clinical Trials Group (CTG) Symptom Control (SC20), was published in 2014 (20). This 850-patient international study compared 8 Gy in a single fraction to 20 Gy in multiple fractions for patients with bone metastases requiring analgesics for pain following a prior course of palliative radiotherapy. The study found no significant difference in overall pain response to treatment for intention-to-treat (28% for single fraction *vs.* 32% for multiple fractions, $P=0.21$) or per-protocol analysis (45% *vs.* 51%, $P=0.17$), whereas acute toxicities of lack of appetite (56% *vs.* 66%, $P=0.011$) and diarrhea (23% *vs.* 31%, $P=0.018$) were less common with the single-fraction regimen. While tradeoffs in efficacy and toxicity need to be considered, this study established 8 Gy in a single fraction to be non-inferior than multiple fraction reirradiation regimens for patients with painful bone metastases requiring a repeat course of radiation therapy.

The review by Chiu *et al.* fills a current knowledge gap following the recent publications of NCIC CTG SC20 and other primary reports on reirradiation, and it outlines the optimal reirradiation dose fractionation in the treatment of painful bone metastases (16). The authors also discuss novel bone biomarkers as a potential means for predicting patients who will and will not respond to reirradiation.

In the second article on this important topic in the current issue of *Annals of Palliative Medicine*, Tsang *et al.* author an interesting debate on the current best practices for the retreatment of uncomplicated bone metastases (21). Single-fraction reirradiation offers optimal patient convenience and a more mild acute toxicity profile, whereas multi-fraction reirradiation, most commonly delivered in 5 to 10 fractions, is commonly believed to provide superior and/or more durable pain control. The debate format is quite lively and interesting, and the article is complete with commentary to summarize the relevant issues, pros, and cons of single- and multi-fraction reirradiation. Ultimately, as in the setting of an initial course of palliative radiotherapy (22), the choice of dose and fractionation for reirradiation should be individualized to provide personalized care to patients that offers the greatest chance of pain response and durable pain control while maximizing quality of life and convenience of treatment with as few side effects as

possible.

Bone marrow biopsy and aspiration are commonly employed diagnostic tools for a variety of benign and malignant hematologic disorders. Although the procedure has exceptionally low rates of major complications, the majority of patients do experience pain of variable duration, and up to half of all patients report severe or unbearable pain following bone marrow biopsy (23). Currently, the most common pain mitigation strategy used clinically is local anesthetics, which has only modest effects at reducing sensations and minimizing pain at the biopsy site (24). In this issue of *Annals of Palliative Medicine*, Zahid discusses other methods in use that can reduce pain during bone marrow biopsy and focuses on other pharmacological agents, including sedatives, opioids, and inhalation anesthetics, as well as non-pharmacologic methods, including cognitive behavioral therapy, hypnosis, and music therapy (25).

In the Surgical Palliative Care Column, Rodriguez *et al.* report on a novel assessment of the utilization of palliative care consultation service by surgical services (26). Despite the significant increase in hospital-based palliative care services over the past decade, there currently are little data on how palliative care consultation services are utilized by surgical services. In a single tertiary care center in the United States, the authors found that 15% of all palliative care consultations were requested by surgical services and 85% by medical services, and important differences in patients and reasons for consultation were identified between medical-based and surgical-based palliative care consultations. Despite the work of the American College of Surgeons Committee on Surgical Palliative Care to improve the knowledge and integration of palliative care among surgeons (27), this study reinforces other recent findings that referrals to palliative care by surgeons remain underutilized (28). The Surgical Palliative Care Column also features a novel original report assessing the ability of using the American College of Surgeons' National Surgical Quality Improvement Program (ACS-NSQIP) as a surgical quality-measurement tool for advanced cancer patients (29).

This issue of *Annals of Palliative Medicine* also features innovative reports on symptomatic control for brain metastasis and voice-related quality of life after total laryngectomy. Following the recently reported interim analysis of the Medical Research Council's Quality of Life after Treatment for Brain Metastases (QUARTZ) trial (30) and the 2015 randomized phase III report of combining stereotactic radiosurgery with whole brain radiation

therapy (31), Tsao reports on a systematic review summarizing management options for patients with brain metastases. She discusses medical management with steroids and anti-epileptics, systemic therapy and molecular targeted therapy, whole brain radiation therapy, stereotactic radiosurgery, and surgical resection for patients with both single and multiple brain metastases, and she focuses on symptom management, quality of life, and neurological function in addition to detailing survival and brain control outcomes (32). Agarwal and colleagues assess voice-related quality of life after total laryngectomy using patient-reported outcomes for a large patient population in India (33). Their findings that patients with lower socioeconomic status had better voice preservation and quality of life may offer interesting insights into the important of social support on yet another aspect of quality of life for patients with advanced diseases.

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Footnote

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