

## Barriers to nausea management, end of life conversations, early palliative care interventions, and patient education

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This issue of *Annals of Palliative Medicine* starts off with a pair of editorials. In this first, Ahrari and colleagues from Sunnybrook Health Sciences Centre discuss anticipatory nausea, which is nausea occurring before a new cycle of chemotherapy begins (1). Molassiotis *et al.* (2) recently assessed the risk factors for the development of anticipatory nausea and its relationship to chemotherapy-induced nausea and vomiting (CINV). Those investigators demonstrated that while anticipatory nausea can be a conditioned response to previous poorly control CINV, it also appears to be bidirectional, with anticipatory nausea predicting CINV with the subsequent chemotherapy cycles. Fortunately, the frequency of anticipatory nausea has declined over time as medical management of CINV has improved. However, approximately one in 10 patients receiving chemotherapy still suffers from anticipatory nausea (3), with its associated detrimental effects on quality of life. Ahrari and colleagues call for more research to examine both chemotherapy-specific and patient-specific factors related to CINV and treatment strategies for both anticipatory nausea and CINV (1).

Karl Lorenz then discusses quality of end-of-life care for multicultural patients (4). Currently, there remain disparities in the provision of end of life care across different racial and cultural groups (5). While other barriers to optimal end of life conversations between providers and patients and their families have been reported on more extensively, including insurance status, medical costs, access to physicians, language diversity, family dynamics, and interpersonal communication (6), there are unique barriers surrounding religious and cultural preferences with distinct implications and potential solutions. Karl Lorenz calls for more investigation into these barriers and highlights a need

for novel, culturally sensitive ways of communicating with patients at the end of their life (4).

The first original investigation in the current issue of *Annals of Palliative Medicine* assesses palliative care unit utilization and outcomes for patients with lung cancer. Lung cancer remains the leading cause of death from cancer worldwide (7) and is associated with numerous symptoms associated with declines in quality of life, including pain, dyspnea, and cough, as well as anxiety and depression (8-10). Researchers from Medical University of Vienna evaluated 91 patients with lung cancer treated in their palliative care unit over a 3-year period, representing 20% of all patients admitted to the palliative care unit during that time period (11). Patients had a median Karnofsky performance status of only 50% at the time of admission, and they were most commonly admitted for deterioration of performance status, uncontrolled cancer-related pain, and dyspnea. Alarming, 75% of all patients died during their first admission. This report underscores the persistence of late referrals to palliative care. Early palliative care has been associated with clinically meaningful improvements in quality of life and less aggressive end of-life care, and it was the subject of a recent dedicated focused issue of *Annals of Palliative Medicine* (12,13). Specifically for lung cancer, early palliative care has also been shown to improve overall survival (14,15).

Chan and colleagues have previously found that the time of day in which whole brain radiation therapy for brain metastases was delivered may impact overall survival among elderly females (16). Now, they report on how the time of radiotherapy delivery impacts radiotherapy response for painful bone metastases. Females treated in the middle third of the day exhibited a significantly higher

response rate compared with those treated in the morning or late afternoon (17). While this work is interesting, future prospective radiation therapy studies and investigation of responses to chemotherapy according to chronotherapy are needed.

In a pilot study, Bushehri *et al.* assess the urinary cytokine and chemokine patterns in 10 patients prospectively enrolled with painful bone metastases treated with magnetic resonance-guided high intensity focused ultrasound (MRgHIFU) (18). MRgHIFU allows for focusing a beam of ultrasound energy into a small volume at a specific target site in the body that can result in therapeutic hyperthermia in the target field and tumor ablation (19). When assessing urine samples 3 days before and 2 days after MRgHIFU, 9 urinary cytokines were significantly reduced following MRgHIFU therapy. They also found differences in cytokine and chemokine patterns in these patients relative to historically controls of patients treated with palliative radiotherapy. At this time, it is unclear if decreases or differential expression of certain cytokines or chemokines correlates with pain response or tumor control, but this hypothesis-generating study can help to shape future studies assessing chemokines and cytokines in palliative care.

Hammad *et al.* next report on the efficacy of different palliative therapies for hepatocellular carcinoma (20). In their National Cancer Database (NCDB) analysis, which is a retrospective database capturing approximately 70% of all patients treated for cancer in the United States (21), 3,267 unresectable patients were identified, of which 827 (25.3%) received palliative radiotherapy. Interestingly, palliative radiation therapy on multivariate analysis was found to be a positive predictor of overall survival, including for patients specifically with stage IV disease. While such a retrospective analysis is not able to definitively address the topic and future prospective work is needed, the findings by Hammad and colleagues suggest that in addition to palliative radiotherapy being able to improve quality of life and control local disease for advanced cancer patients, it may also be able to extend survival.

Another assessment of the NCDB reported on in this issue was performed by Schreiber *et al.* (22). They analyzed 3,871 patients with prostate cancer and bony metastases treated with either short course (8 Gy  $\times$  1, 4 Gy  $\times$  5) or longer course (3 Gy  $\times$  10, 2.5 Gy  $\times$  14 – 15, 2 Gy  $\times$  20 – 30) palliative radiation therapy. Short course treatment was given in fewer than 10% of patients and was delivered more commonly at academic centers, for patients living at increasing distances from treatment centers, when

delivered to the ribs, and during more recent treatment years. Multivariable analysis suggested that longer courses of radiation therapy were associated with improved overall survival, but this benefit was not seen on landmark analysis limiting the survival analysis to men surviving at least 18 months. While multiple prior reports in this journal and other journals have assessed the relative benefits of short versus longer course radiation therapy (23,24), this study across a large number of patients is a valuable addition to the literature, and it does demonstrate that the utilization of shorter courses of 1 and 5 fraction radiotherapy regimens is increasing.

The Palliative Radiotherapy Column in this issue of *Annals of Palliative Medicine* features two additional articles. First, Marta and Saad discovered that health-related quality of life parameters have only been investigated in approximately one-fifth of phase III trials of radiotherapy in head and neck cancers over the past two decades, with few significant differences in parameters seen between study arms (25). Then, Barnes and colleagues performed a review on the collaboration between primary care physicians and radiation oncologists (26). A prior report demonstrated that primary care providers have identified limited communication with oncologists as a major concern in caring for cancer patients (27). However, communication from primary care providers to oncologists is critical to ensure that patients and their families are managed most optimally during the active part of their cancer treatment. Additionally, with the dramatic rise in the number of cancer survivors over the past few decades (28,29), in patients with a good cancer-specific prognosis, survivorship care is increasingly being recognized as pivotal to overall care of patients. A large portion of survivorship care is performed by primary care providers, and communication from oncologists to primary care providers is critical for survivorship care. For patients with terminal malignancies, primary care providers often provide symptomatic management and palliative care for patients, further requiring communication between providers to ensure optimal patient care (26).

Also in this issue, Lam and colleagues perform a review assessing the use of multimedia interventions for patient and caregiver education (PCE) on pain management. While the number of high quality studies on this topic is still limited, their analysis suggests that the use of multimedia in pain management education for patients and caregivers has greater benefit compared with standard education (30). The need for patient education is increasingly solicited

and critical, including information designed to best target specific patient groups (31). The work by Lam *et al.* may foster future large-scale studies that evaluate the usability and user-friendliness of these tools in clinical practice.

This issue of *Annals of Palliative Medicine* is concluded with an Ethics Column editorial, a case report, and a news report. Blair Henry writes a provocative editorial on the ethical and legal implications for feeding at the end of life (32). Then, So *et al.* describe a patient with superior mesenteric artery (SMA) syndrome who presented with symptoms of upper intestinal obstruction (33). Finally, Wei and colleagues report on the proceedings of the Third Annual Meeting of the Society for Palliative Radiation Oncology (SPRO) (34), a society dedicated to promoting and advancing the practice of evidence-based palliative radiation therapy through research, education, and advocacy (35).

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### Footnote

*Conflicts of Interest:* The author has no conflicts of interest to declare.

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