



Managing persistent pain and numbness in cancer survivorship

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The January issue of *Annals of Palliative Medicine* featured 14 Original Articles, 3 Editorial Commentary, several Case Reports, and 10 Editorials. One of those Editorials and the article it comments on will be highlighted in this Message From the Editor-in-Chief.

With improved screening and earlier detection of cancer, advances in the primary treatment modalities for cancer that include surgery, systemic therapy and radiation therapy, and the aging of the population, there are more cancer survivors alive today than ever before (1). With this growing population of cancer survivors, defined as patients diagnosed with cancer who completed active cancer treatment, are clinically stable and have no evidence of recurrent or progressive disease, cancer survivorship care is increasingly important (2) and is driving an increasing value to patient reported outcomes and the developing survivorship care plans (3,4).

Two of the more common and distressing symptoms among cancer survivors are pain and numbness. These symptoms can lead to patient anxiety and depression, limit activities of daily living, and affect quality of life (5-8). Patients with active cancer can experience pain directly from their underlying malignancy, whereas survivors can continue to experience pain from their cancer-directed therapies for weeks, months, years or even indefinitely after their cancer treatment (9,10). While narcotics can help alleviate treatment-induced pain, many patients do not use analgesics due to concerns of addiction, cost, or their healthcare providers not recommending the agents (11), they are less commonly prescribed following the completion of cancer therapy (12), and their use has become more controversial in the setting of the ongoing opioid crisis (13). Additionally, chemotherapy-induced peripheral neuropathy can be a debilitating long-term sequela of therapy in cancer survivors and has very few effective treatment options (14,15).

Abe and colleagues from The University of Tokyo Hospital and National Cancer Center, Tokyo reported the first-ever systematic review and meta-analysis on the efficacy of treatments for pain and numbness in cancer survivors in the December 2022 issues of *Annals of Palliative Medicine* (12). They assessed 36 randomized controlled trials that evaluated any type of treatment for pain or numbness among 2,870 cancer survivors. Their meta-analysis across 35 studies pertaining to pain concluded that physical exercise, acupuncture, and alternative medicine could significantly reduce pain, whereas a pain benefit was not seen with nonopioid pharmacotherapy, education, or cognitive behavioral therapy. Furthermore, studies assessing the benefits of opioid therapy and interventional therapy on pain were lacking. Fewer studies (n=5) in their meta-analysis assessed numbness, with no benefit demonstrated for acupuncture, and the effectiveness of opioid therapy, nonopioid pharmacotherapy, interventional therapy, education or cognitive behavioral therapy, physical exercise, and alternative medicine were not able to be determined.

It should be noted that the analysis by Abe *et al.* had some limitations in generalizability, as the assessed studies were restricted to adult patients and to studies reporting on patients with predominantly early-stage disease. In addition, many of the included trials were specific to breast cancer survivors. This overrepresentation of breast cancer, however, is in part reflective of the growing survivorship in the breast cancer community. Recent estimates report that over 4,000,000 women with a history of breast cancer are alive in the United States, over four times more survivors than the next closest cancer type among women (uterine corpus with 891,560 survivors) (16).

Dev and Bruera provide a comprehensive editorial about this systemic review and meta-analysis. Themselves internationally recognized experts in palliative care and

cancer-related pain, Dev and Bruera comment on the striking lack of data critically evaluating the benefits of opioids to treat persistent pain in cancer survivors. They note the cautious recommendation by the American Society of Clinical Oncology for using opioids in patients who fail conservative management (17).

Their editorial also focuses on chemotherapy-induced peripheral neuropathy, the most common neurological complication of cancer treatment. As no pharmacological agent has been proven to be effective in preventing chemotherapy-induced peripheral neuropathy, and only a single agent (duloxetine) has evidence supporting its use to help control pain associated with chemotherapy-induced peripheral neuropathy (14,15), Dev and Bruera discuss non-pharmacological approaches to managing this treatment sequela, including the evidence supporting aerobic and resistance exercises and the evidence not supporting acupuncture and yoga. Dev and Bruera call for more research in non-pharmacological interventions in cancer survivors, as these interventions generally have a better safety profile than opioids. They also employ healthcare providers to be vigilant in conduct a thorough clinical and physical examination to determine an optimal treatment approach when pain persists or increases and to personalize care to include non-pharmacological interventions, nonopioid pharmacotherapy, and/or opioids, as needed.

We are fortunate to see continued year-over-year improvements in cancer survival rates, but clinicians and the palliative medicine community must be as committed to helping cancer survivors as they are in caring for patients with active malignancies. Additional advances in cancer care are needed to further improve cancer survival rates while also preserving patient quality of life during cancer therapy and minimizing long-term treatment morbidities, including pain and numbness, in survivors.

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Footnote

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