



# Pain in cancer survivors: a challenge for the next decade

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Abe *et al.* recently published (1) article on the effectiveness of pain treatments in cancer survivors is an essential contribution for renewing oncologic patients care.

Indeed, during the last decades, these patients are increasing in number because of a significant rise in cancer incidence in developed countries (2), but also due to a huge improvement in cancer diagnostic and also in treatments efficacy. At the same time, cancer pain remains a symptom often uncontrolled in these specific oncologic patients and unfortunately often under diagnosed (3,4). In addition, the efficacy of the various analgesic treatments proposed is inconstant, sometimes unsuitable and infrequently evaluated as the Hiroaki article highlights (1).

First, cancer treatment benefited from remarkable therapeutic developments over the last decades, leading to significantly improve the patients' prognosis. This amazing evolution is first due to advances in the diagnosis and the monitoring of cancer progression with new imaging such as positron emission tomography (PET)-scan and magnetic resonance imaging (MRI) allowing earlier and more suitable therapies (5). Treatments have also been the subject of huge improvements as well as surgical treatments including early micro-invasive treatments, but also, radiosurgery treatments including tomotherapy (Cyberknife) (6) or interventional radiology using radiofrequency and cryotherapy (5). Moreover, at advanced stages of the disease, large debulking procedures associated with hyperthermic intra peritoneal chemotherapy also improve overall survival (7).

Furthermore, the development of anti-cancer drugs is significant. Targeted therapies such as anti-angiogenic treatments, immunotherapies considerably improve

patients' overall survival. Tomorrow, chimeric antigen receptor (CAR)-T therapy will probably be the next step for solid tumors (8). Thus, for metastatic kidney tumors, the 5-year survival rate increased from 30% to 91% between 2000 and 2018. Globally, in the United States, 15.5 millions cancer survivors were alive in 2016, and that number is expected to increase to nearly 20 millions by 2026 (9).

However, in this context, the cancer survivors 'quality of life is often affected by pain. Unfortunately, despite of encouraging progress in the treatment of cancer pain, a third of cancer pain remains undertreated. Global incidence is not available, but Gartner in 2009 in a large survey in Denmark found 47% of patients suffering after breast cancer surgery (10). Pain is also provoked by radiotherapy and chemotherapy. Chemotherapy induced peripheral neuropathy (CIPN) commonly occurs in 30–40% of patients (11). These types of pain are often neuropathic in nature requiring a specific approach for treatment. Finally, aromatase inhibitors (AIs) commonly used throughout five to ten years after initial treatment for women with hormone receptor positive breast cancer often provoke myalgia and arthralgia with a huge impact on patients' quality of life (12).

The number of these patients is steadily increasing. In two successive literature reviews, van den Beuken-van Everdingen observed a significant increase in pain incidence after treatment of 30% to 39% between the studies published before 2004 and those published between 2005 and 2014 (13). In a recent survey including a total of 505 head and neck cancer (HNC) survivors with a median follow up of 3 years from cancer diagnosis 45% reported pain but

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only 14.5%, reported use of prescribed pain medication (14).

Moreover, impact on patients' quality of life is major issue. Another study found that chronic pain was the main negative predictor of HRQoL and was associated with decreased functionality (15). In a recent online survey conducted to evaluate cancer related neuropathic pain incidence and impact, for 1/3 of patients the diagnosis of neuropathic pain was not established before the survey despite of reporting painful symptoms to a health care provider (HCP) (16).

Thus, the management of these patients requires a radical change in paradigm to improve patients' quality of life. Improving screening and monitoring for cancer pain is the first step to achieve this change. The training of caregivers and the development of specific consultations are major steps to improve pain management in cancer survivors.

Given to the diversity of clinical situations, the therapeutic approaches are obviously very extensive. However, as the recent article by Abe *et al.* underlines, this support is not currently evaluated and poorly protocolized (1). This meta-analysis suggests that physical exercise, acupuncture, and alternative medicine may reduce pain in cancer survivors, with a very small to moderate amount of evidence.

Therefore, to facilitate evaluation of these treatments, is mandatory. For example, for post therapeutic cancer neuropathic pain, drug treatments are often poorly accepted by patients due to a high rate of adverse effects. Moreover, the efficiency is low with a number needed to treat (NNT), often high. So, the recent WHO guideline (17) does not recommend Anticonvulsants and Antidepressants for cancer pain management. On the other side, topical treatments such as capsaicin and botulinum toxin are substantial alternatives (18) but little evaluated and therefore cannot so far be recommended.

Another area of improvement is specific therapeutic approaches, such as intrathecal analgesia, which is efficient to improve patients suffering intractable pain. Currently, on one hand, Intrathecal Drug delivery is widely recommended, but the impact on patients' quality of life is poorly evaluated and indications are usually considered only in the limited context of failure of systemic treatments and/or intolerable medication side effects. On the other hand, the survival of such patients is also extended and an earlier use should improve the patients' quality of life and overall survival so an evaluation is mandatory.

Finally, we need to change the paradigm for the pain management of such patients. First, specific training of

healthcare providers for pain diagnostic and new treatments options for cancer survivors are mandatory. In addition, developing specific management approaches for these patients is necessary. Moreover, research needs to be enlarged to better assess the effectiveness on pain relief and the impact of these therapeutic options on patients' quality of life. Then, thanks to published data, guidelines should be updated.

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