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Review Article

Exercise Treatment for Cancer-Related Pain

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Abstract

Background: Cancer-related pain should be a target of active palliative care. **Methods**: The aim of this narrative review was to provide an comprehensive overview regarding assessment and treatment of cancer-related pain by exercise treatment and its derivative cognitive behavioral therapy. **Results**: Range-of-motion training and stretching are useful in alleviating pain and improving shoulder joint mobility in the axillary web syndrome occurring after axillary lymph node dissection for breast cancer. Strength training reduces trapezius paralysis caused by head and neck cancer surgery. Exercise treatment alleviates pain and improves functional independence after bone surgery for spinal metastases. Furthermore, it alleviates pain and improves physical function and activities of daily living (ADLs) in patients undergoing chemotherapy and radiotherapy. Adjuvant exercise treatment can mitigate adverse effects and increase the tolerated chemotherapy dose. Psychotherapy (cognitive behavioral therapy comprising patient education and exercise treatment) for cancer-related pain management achieves improvement in both pain and ADLs. Behavioral therapy aims to improve the level of ADL by constantly planning goal settings and maintaining motivation for exercise habits. Cognitive rehabilitation using the virtual reality system to treat cancer-related pain and exercise regimens utilizing peer networks, where patients support each other in virtual reality spaces are promising. **Conclusion**: Exercise treatment is useful in ameliorating pain associated with cancer surgery, bone metastasis, and cancer chemotherapy and radiotherapy. Public health education on the efficacy of exercise in reducing cancer risk and countering the side effects of cancer treatment can motivate patients to undergo exercise treatment.

Keywords: Cancer-related pain; Exercise treatment; Cognitive behavioral therapy; Virtual reality; Peer support.

Key points

• Pain is an important factor in patients with cancer, since it affects the QOL and ADLs, and plays an important in their life prognosis.

• Exercise treatment, including strength training, aerobics, stretching, and range-of-motion training, is effective in ameliorating pain associated with cancer surgery, bone metastasis, cancer chemotherapy, and radiotherapy.

• Psychotherapy called as cognitive behavioral therapy, grounded in patient education, positive reinforcement, repeated exercises and constantly goal settings for achieving improvements in ADLs, is also beneficial in the management of several types of cancer-related pain.

• Public health education on the efficacy of exercise in reducing cancer risk and countering the side effects of cancer treatment can act as robust motivators for exercise treatment.

From the term "cancer pain" toward the term "cancer-related pain"

Approximately 70–90% of patients with advanced or terminal cancer experience pain, and nearly 20% complain of pain that requires analgesics from the time of the initial manifestation of cancer. Furthermore, 45–60% of patients undergoing cancer treatment who are expected to live for a year experience pain related to cancer treatment (chemotherapy-induced neuropathy, hormone therapy-induced joint pain, prolonged pain after cancer surgery, etc.), and 30–40% of cancer survivors continue to experience pain even after their cancer becomes inactive. Therefore, in addition to cancer pain experienced by patients with advanced cancer, there is a gradual recognition that pain from the initial onset of cancer to cancer treatment-related pain should also be a target of active palliative care. Cancer-related pain has been defined in the 11th edition of the International Classification of Diseases (a system established globally by the World Health Organization, which was revised from the 10th to the 11th edition for the first time in 2018 after approximately 30 years) [1]. When considering the problem of pain in patients with cancer, we should consider not only pain caused by the cancer itself but also that associated with cancer treatment. This term, cancer treatment-related pain, also encompasses pain experienced by cancer survivors.

Assessment of the activities of daily living and quality of life based on cancer-related pain

The evaluation of cancer-related pain is not restricted to merely the severity of pain itself but also extends to the fundamental activities of daily living (ADL), which refers to physical independence that is hampered by the presence of pain. Generally, evaluation of fundamental ADL is essentially based on at least 5 items (mobility, dressing, eating, sleeping, lying comfortably). The ADL assessments can also be used to select analgesics and set goals for dose adjustment with the patient's input. For example, a medical professionalal might explain a patient who feel a negative reaction opioid analgesics "I understand that it is hard to sleep at night, so I would like you to try using a small dose of opioid analgesics to help you get a good night's sleep." or "If you were able to sleep better, would you like to increase the dose of opioid analgesics so that you can move from your bedroom to the lounge?" Comprehensive assessment of the severity of pain facilitates evaluation of the balance between the patient's needs and satisfaction. Since pain has been introduced as the fifth vital sign, only numerical rating scales and visual analog scales of pain severity have been considered in the same manner as other vital signs like as blood pressure and heart rate. However, in real-world clinical practice, it is more effective to evaluate pain severity based on ADLs through dialogue and observation with the patient than to periodically evaluate pain values. Evaluating whether the patient's performance of ADLs is appropriate based on the intensity of pain and their physical condition is also essential. While it is natural that pain has a deleterious effect on the ADL and quality of life (QOL), a disparity sometimes exists between the severity of pain reported by patients and their actual level of ADL performance. Medical professionalals should assess comprehensive severity of pain and ADL and then prescribe appropriate doses of analgesics. In the event of disparity between pain severity and the physical condition, ADL, and QOL, the patient's psychological factors (emotional distress and also lack of self-confidence in one's own body which is called as self-efficacy) can have a negative impact on the patient's well-being (Figure 1) [2].

In this article, we present a narrative review on the management of cancer-related pain, with a focus on exercise treatment.

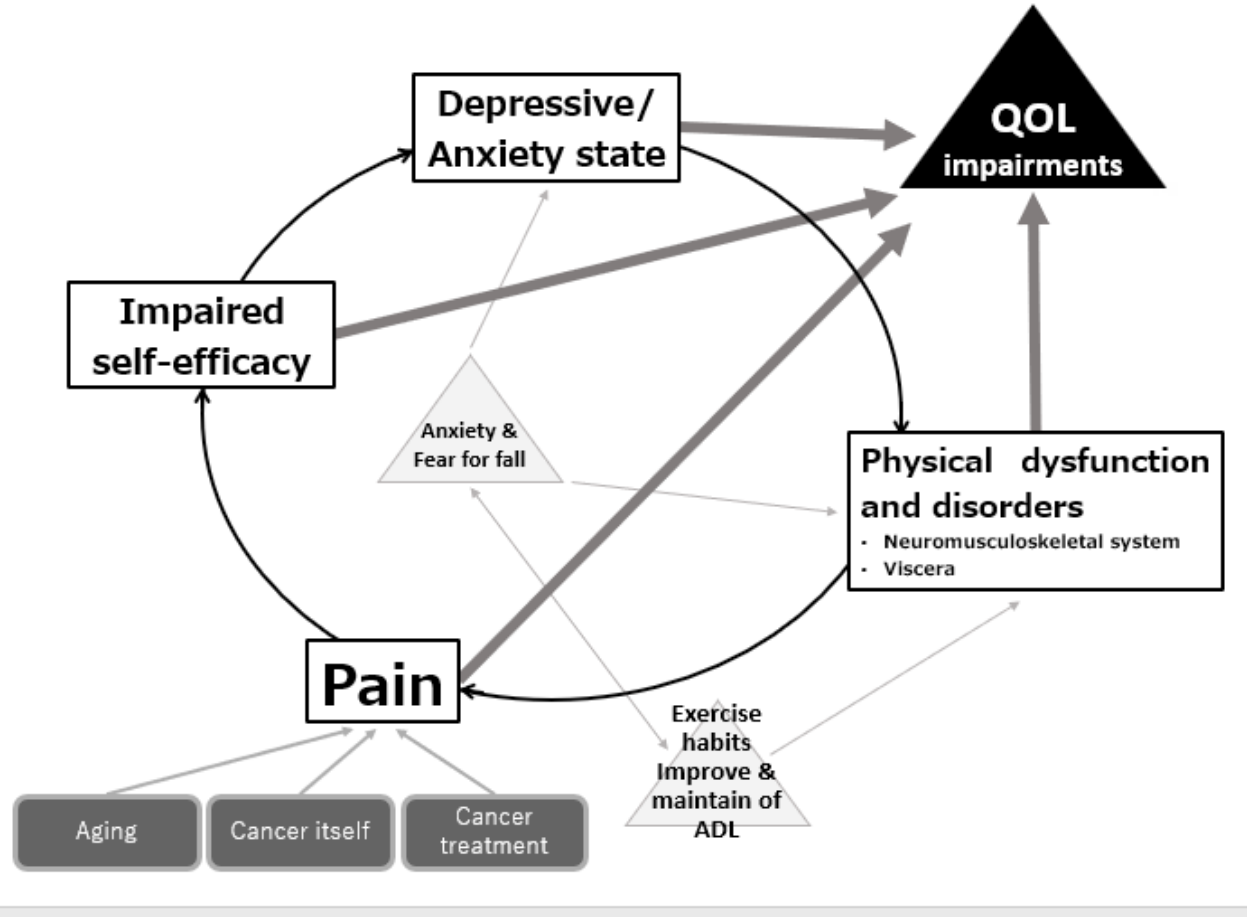

Figure 1: Vicious cycle model of pain modified and quoted from a previous study [2].

In addition to pain, physical function, disability, confidence in one's own body (self-efficacy), and feelings of distress (depressed mood) form a vicious cycle that results in deterioration in the quality of life. Therefore, a comprehensive evaluation of these factors is important.

Exercise treatment for pain in cancer patients has been evidently shown the usefulness for ameliorating (1) pain after cancer surgery, (2) pain associated with bone metastasis, and (3) pain associated with cancer chemotherapy and radiation therapy.

1) Usefulness of exercise treatment on pain after cancer surgery

Cervical lymph node dissection for head and neck cancer can lead to accessory nerve palsy, not only when the accessory nerve is removed (radical neck dissection) but also when the accessory nerve is preserved or reconstructed, resulting in trapezius muscle paralysis. As the trapezius muscle stabilizes the scapula and moves the shoulder joint, pain in the shoulder joint or muscle pain, commonly referred to as stiff shoulder, may occur after head and neck cancer surgery. Strengthening the muscles is important for preventing pain and movement disorders in the shoulder girdle, as muscle strength training is more effective in reducing pain and improving upper limb function than standard shoulder joint range of motion training [3]. Furthermore, approximately 70% of patients develop subcutaneous cord-like tissue extending from the axilla to the inside of the upper arm after axillary lymph node dissection for breast cancer, resulting in a condition called as the axillary web syndrome. This condition is thought to be caused by postoperative soft tissue adhesions, scar tissue formation, and thrombus formation in the lymphatic vessels, and it can cause severe pain and limit the range of motion of the shoulder joint. While many patients recover spontaneously, the condition may be prolonged or have late onset in some cases. In such cases, a study has reported that range-of-motion training and stretching of the shoulder joint as well as stereoarthrolysis surgery on the shoulder joint are usefull in alleviating pain and improving movement of the shoulder joint [4].

2) Usefulness of exercise treatment on pain associated with bone metastasis

Pain associated with bone metastasis from any cancer origins is an indicator of fracture risk and is responsible for deterioration in the ADLs [5]. Bone fixation surgery is sometimes performed in patients with bone metastases for pain relief and to prevent and treat fractures and paralysis; however, the risk of fracture should be appropriately assessed, and then exercise treatment can be applied for patients with bone metastases. Notably, exercise treatment has accumulated evidence to alleviate pain, improve ADL, and increase patient satisfaction [6-8].

3) Usefulness of exercise treatment on pain associated with cancer chemotherapy and radiation therapy

Exercise treatment is useful in improving pain, motor function, and ADL in patients undergoing cancer chemotherapy and radiation therapy [9-11]. Pain in the distal extremities due to chemotherapy-induced peripheral neuropathy and pain at the radiation sites are classified as localized pain. Full-body exercises such as aerobics and muscle strength training have been shown to be useful for localized pain. This positive effect has been attributed to the activation of the central nervous system and effects on the immune system by whole-body exercise rather than the local effects on the peripheral tissues of the musculoskeletal system [12]. Furthermore, adjuvant exercise treatment during chemotherapy can mitigate the adverse effects of chemotherapy and increase the tolerated dose of cancer chemotherapeutic drugs. Moreover, exercise treatment may be useful in the treatment of cancer itself [13].

Pain management for patients with cancer: Cognitive behavioral therapy

In addition to exercise treatment (rehabilitation), adjuvant psychological therapy, also known as cognitive behavioral therapy, is useful for treating pain in patients with cancer. The initial treatment goals when implementing cognitive behavioral therapy for cancer patients comprise two perspectives based on the vicious cycle model of pain (Figure 1): (A) alleviation of pain intensity and (B) improvement in ADLs. If amelioration of cancer pain in the advanced or terminal stages is achieved, the ADLs automatically improve, as does the QOL in most cases. However, in the case of chronic pain including cancer treatment-related pain and non-cancer-related pain of cancer patients and survivors both of who are in the stage between cancer diagnosis and supportive care, these two treatment goals do not necessarily function together to achieve a synergistic effect. It is necessary to treat both aspects owing to the mutual interaction between them [14]. Cognitive behavioral therapy is a general term for combined cognitive therapy and behavioral therapy, wherein the former constitutes patient education and the latter is achieved with exercise treatment. When implementing cognitive behavioral therapy especially for patients who believe that the cause of pain is only due to tissue damage, medical professionals set a goal for synergistically improving ADLs and pain. Medical professionals help patients understand and educate that this therapy is necessary not only for pain alleviation but also recovery of their meaningful daily lives. This type of patient education has been shown to be also important for pain management in the terminal stages of cancer and in home medical care [15].

Furthermore, in behavioral therapy (exercise treatment), which is grounded in patient psycho-education, the initial goal is to improve the level of ADLs appropriate to the general physical condition of patients at the start of treatment. Specifically, the goal is to repeat exercises (such as walking and gymnastics) and recovering ADLs that can be performed with the actual physical function. As these goals are getting achieved, new behavioral contents corresponding to the ADLs would be added to the treatment goals. It is important to constantly plan achievable goals for the patients' adherence of this type of treatment and gradually increase the physically exercise load. Medical professionals appropriately educate and help understandings that they successfully become to recover and reacquire physical function, and then medical professionals can promote that patients notice their improved self-efficacy. Such self-affirmation helps maintain patients' motivation for exercise by themselves.

When implementing exercise treatment and cognitive behavioral therapy, medical professionals should be conscious of one important trap. In some cases of cancer-related pain arising from any anatomical and/or physiological changes, where the cause of pain is obvious from medical professionals' views, misconceptions by the patient's faith of pain might be overlooked over a prolonged period. In this misconceptions, patients and also medical professionals usually focus only the sensory experience of pain and pay less attention to the affective experience of pain which is always existing independent to the sensory experience and explainable pain origins. This misconceptions directs to and turns the vicious cycle (Figure 1) round and round, and consequently the patients' faith of pain becomes much worse and their behaviors in daily living also further restricted. In combination with or independent to pharmacotherapies, cognitive behavioral therapy should be applied to treat chronic pain that clearly arises from a physical disorder such as cancer-related pain, as well as non-specific nociplastic pain disorders like as chronic low back pain, whiplash injury pain and fibromyalgia which psychotherapy is traditionally considered to be useful.

Pain management for patients with cancer: Cognitive rehabilitation using virtual reality

We are currently developing a cognitive rehabilitation treatment

using the virtual reality (VR) system to treat pain in patients with cancer. Phantom limb pain, that occurs after limb amputation for malignant tumors in bone and soft tissue or nerve/neural plexus transection for neurogenic tumors, is a typical example of persistent pain in cancer survivors. Phantom limb pain has been traditionally considered refractory to pharmacotherapy [16]. We performed the VR-based cognitive rehabilitation for phantom limb pain: a three-dimensional infrared camera acquires joint information from the healthy upper limb; by reversing this information horizontally, an image of the limb affected by the neurological disorder is projected onto the VR space (Figure 2). Simultaneously performing the symmetrical movements with both the healthy limb in real space and the affected limb-image in the VR space, the patient feel as if he/she is moving the affected limb voluntarily, leading to improvement in phantom limb pain [17].

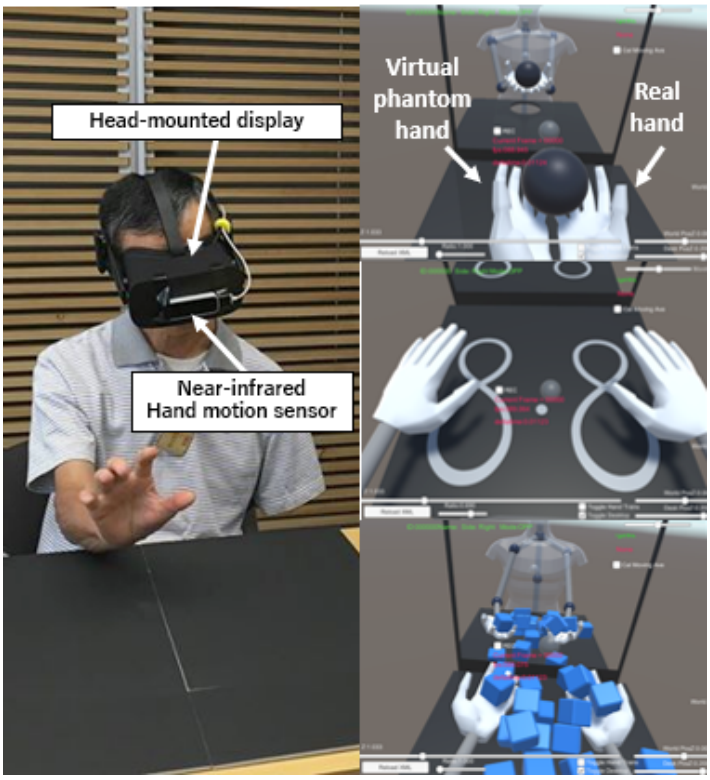

Figure 2: Video and scene of neurorehabilitation treatment using virtual reality (VR) modified and obtained from a previous study [17].

[A] Video of a patient undergoing VR treatment. [B-D] Images of phantom limbs existing in the VR space. The patient experience phantom pain in the left upper limb and move the VR phantom limb in the VR space by moving the right upper limb. The left and right upper limbs always perform symmetrically coordinated movements in VR space.Pain management for cancer patients: Exercise treatment.

Aside from this cognitive rehabilitation, we are working to establish exercise habits of cancer patients through their peer support, where cancer patients support each other in the VR spaces. Through such VR-based cancer peer support program, we have successfully worked to alleviate their pain, increase their times of weekly exercises and increase adherence to cancer treatments (Figure 3) [18].

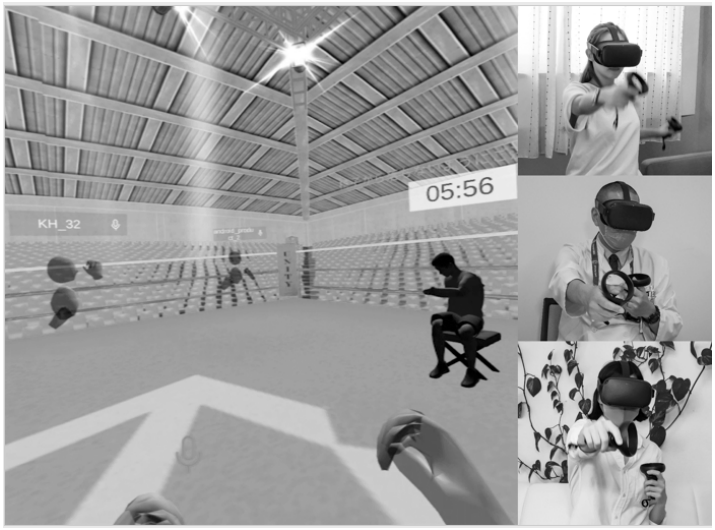

Figure 3: Scene of use of virtual reality (VR) cancer peer support obtained from a previous study [18].

In addition to an individual's own avatar, patients can see the avatars of other patients in the VR space. The participants perform fitness exercises (boxercise) presented by a VR instructor, and their movements are rendered in real time as avatar movements using a hand controller. Using the microphone, speaker, and hand controller of the head-mounted display, it is possible to have conversations using gestures. In a trial of VR cancer peer support conducted in this study, doctors regularly participate in the VR space as facilitators while doing fitness exercises with patients, and the patients talk about their worries and anxieties about cancer treatment and eating habits.

Conclusion: Significance of pain management for patients with cancer

Cancer-related pain severity is an independent factor that determines the prognosis of cancer patients [19]. Pain, a complication of cancer treatment (such as chemotherapy-induced neuropathy and radiation dermatitis), can sometimes interfere ideal cancer treatment regimens. Active palliative care interventions (including exercise treatment in addition to pharmacotherapy) have also been reported to improve life prognosis of cancer patients [20].

As cancer treatment periods become longer and the number of cancer survivors increases, aging cancer patients and survivors face the adverse effects of cancer itself in addition to age-related muscle loss. Muscle loss becomes more pronounced owing to the adverse effects of tissue damage associated with treatment (mainly chemotherapy) [21]. Loss of muscle mass is associated with exacerbation of the side effects of cancer chemotherapy and worsening of life prognosis in patients with cancer [22]. Exercise treatment is the most important preventive treatment against muscle loss, and studies have shown that patients with cancer who maintain muscle mass experience less fatigue due to chemotherapy and maintain a high QOL. Appropriate exercise habits (> 150 min of brisk walking per week) can reduce the risk of developing various cancers [23]. Patient education on reducing the risk of cancer development through exercise treatment and countering the side effects of cancer treatment will motivate patients to undergo this treatment modality.

Declaration of interest: Masahiko Sumitani reports equipments and softwares were provided by Kadinche corporation as a collaborative research project. Other authors declare no conflicts of interest.

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