Exercise Prescription for People With Metastatic Cancer of the Skeleton

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ABSTRACT

Exercise is increasingly accepted as a therapy in the management of cancer, and is now described as a medicine, giving rise to a new discipline in clinical practice and research termed *exercise oncology*. Exercise medicine has been evaluated in clinical trials and implemented in patient care at all phases of disease and treatment trajectory. Advanced disease involving bone metastases presents considerable challenges in terms of patient assessment and exercise prescription. Over the past decade research evidence has accumulated attesting to the safety and efficacy of appropriately designed exercise medicine interventions. Combined with a need for well-developed guidelines, an expert consensus has been developed. Through a rigorous process the overarching recommendation was that exercise professionals should work with the patient and their health care team to balance the risk of adverse events due to participation in exercise therapy against the risk of more rapid patient decline through not exercising, as well as the potential loss of health benefits that could be realized through exercise. This is the basic tenet of health care and withholding or not offering a therapy that is likely to provide greater benefit than the potential risk it may cause for fear of that risk is untenable.

Keywords: fracture, bone, lesion, therapy

Exercise is increasingly accepted as a therapy in the management of cancer, and is now described as a medicine, giving rise to a new discipline in clinical practice and research termed *exercise oncology* (1). Application of exercise medicine in the oncology setting spans all phases from initial diagnosis through to end-of-life (2). As a neoadjuvant (precursor to primary treatment) therapy, exercise is prescribed to increase fitness, build physical and psychological resilience, reduce inflammation, enhance immune function, and improve body composition in preparation for surgery or commencement of chemotherapy or radiotherapy (1). For patients undergoing their main cancer treatment of chemotherapy, radiation therapy, immunotherapy, or hormone therapy, exercise is prescribed as an adjuvant to alleviate possible treatment side effects and toxicities as well as potentially enhance treatment effectiveness (1). After cancer treatment, exercise is an important rehabilitation therapy to facilitate patient recovery from disease and treatments while also reducing the risk of cancer recurrence and development of other chronic diseases (1).

While the benefits of exercise medicine for a range of cancer types and treatments is undisputed, patients with advanced disease, including those with cancer that has metastasized to their skeleton, have been less likely to receive exercise guidance. This is primarily because of concerns from both the clinician and patient about safety, especially the risk of skeletal complications (3). There has also been some speculation that patients under such a high disease load who have received, or are currently receiving, extensive systemic and radiation therapies may lack the physiological capacity to adapt to the exercise training loads and thereby improve fitness and health (3). Such caution on

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behalf of medical and allied health professionals has resulted in these patients reducing their exercise and physical activity participation, or even consciously avoiding any physical exertion. Certainly, exercise medicine has been underused or completely omitted from supportive care of these patients. The result can only be further decline in fitness and health, physical capacity, and quality of life, ultimately reducing the capacity of the patient to participate in activities of daily living, tolerate treatment regimens, and for their immune system to slow cancer progression.

Subsequently, over the past 5 to 10 years, several research trials have been conducted to evaluate the safety and efficacy of exercise medicine specifically prescribed for patients with bone metastatic disease (3,4). This work, combined with a strong demand for guidance from exercise and oncology associations, and medical and allied health professionals, has resulted in formation of the International Bone Metastases Exercise Working Group (IBMEWG). The clinical question that the group addressed was, "What are the best practice recommendations for exercise programming for people with bone metastases?" with an expert consensus published in 2022 (5).

The IBMEWG undertook a series of sequential steps to inform the recommendations: (a) modified Delphi survey, (b) systematic review (6), (c) cross-sectional survey to physicians and nurse practitioners (7), (d) in-person meeting of IBMEWG to review evidence from steps a through c to draft recommendations, and (e) stakeholder engagement to refine and conclude the recommendations. The overarching outcome was that exercise professionals should work with the patient and their health care team to balance the risk of adverse events due to participation in exercise therapy against the risk of more rapid patient decline through not exercising as well as the potential loss of health benefits that could be realized through exercise. This is the basic tenet of health care and withholding or not offering a therapy that is likely to provide greater benefit than the potential risk it may cause for fear of that risk is untenable.

From the work undertaken by the IBMEWG, 5 key recommendations were developed to provide a more favorable balance between the perceived risks of skeletal complications and the potential benefits for the patient. The recommendations are provided in the Box, which have been jointly endorsed by CSEP (Canadian Society for Exercise Physiology) and ESSA (Exercise & Sport Science Australia), among other cancer and exercise organizations or associations worldwide.

It should be noted, the IBMEWG had to be rather cautious in developing their consensus because of the scarcity of research and large clinical trials assessing the feasibility, safety, and effectiveness of targeted exercise in people with bone metastases. A further limitation is that it is currently not possible to predict the risk of skeletal complications in these patients and for less studied groups such as the elderly or those with less common cancers. Accordingly, the intent of these recommendations, at this stage, was to provide health care providers and exercise professionals with an initial guiding framework that will evolve over time with newly curated evidence.

INTERNATIONAL BONE METASTASES EXERCISE WORKING GROUP BEST PRACTICE RECOMMENDATIONS FOR EXERCISE PRESCRIPTION FOR PEOPLE WITH BONE METASTASES.[a]

1. Before exercise testing or training, perform a risk assessment to inform the likelihood of a skeletal complication from exercise.
2. Consultation with the medical team is strongly encouraged to obtain key medical information and establish bidirectional communication.
3. Exercise professionals best suited for this population are physical therapists and clinical exercise physiologists (or equivalent) who have additional cancer exercise training.
4. Professional judgement should be used to consider if exercise testing is necessary.
5. Exercise prescription should follow the standard exercise recommendations as outlined by the International Exercise Guidelines for Cancer Survivors, with greater emphasis on postural alignment, controlled movement, proper technique, and consideration of the bone lesion location and presentation.

[a]Adapted from Campbell et al. (5)

Recommendation 1 is about understanding the likelihood of a skeletal complication resulting from exercise or, more specifically, what type, format, and dosage of exercise is appropriate to minimize the risk of complications. Practically, this involves reading and understanding the radiological report from the bone scans of the patient so that the type, size, and location of the metastatic lesions are known and considered when planning exercise. All patients with bone metastases will be able to do some form of exercise including both resistance and aerobic modes, but the prescription must be tailored to the individual. In 2011 the concept of a modular multimodal exercise program (M3EP) was proposed for cancer patients with bone metastases by which resistance and aerobic exercises were selected or excluded based on avoiding direct loading of the sites of the metastatic lesions (Table) (8).

The M3EP approach proved highly successful with a series of trials subsequently demonstrating safety, tolerance, acceptance, and efficacy (3,9). Subsequently, it has been proposed that highly controlled mechanical loading of metastatic lesions of the skeleton may actually suppress progression of the tumor (10,11) through exercises that are predominantly isometric or with very gradual application of force (12). The additional benefit is strengthening of the muscles in the region provides greater support and protection, as well as maintenance function, while seeking to preserve bone mass of the disease-affected site and neighboring skeletal tissue.

TABLE. Modular multi-modal physical exercise program (M3EP) for patients with bone metastases.[a]

Metastases site	Exercise mode					
	Resistance			*Aerobic*		*Flexibility*
	Upper	Trunk	Lower	WB	NWB	Static
Pelvis	√	√	√**		√	√
Axial Skeleton (lumbar)	√		√		√	√***
Axial Skeleton (thoracic/ribs)	√*		√	√	√	√***
Proximal Femur	√	√	√**		√	√
All regions	√*		√**		√	√***

√ = Target exercise region; * = exclusion of shoulder flexion/extension/abduction/adduction - inclusion of elbow flexion/extension; ** = exclusion of hip extension/flexion - inclusion of knee extension/flexion; *WB* weight bearing (e.g. walking); *NWB* non-weight bearing (e.g. cycling); *** = exclusion of spine/flexion/extension/rotation.

[a]Adapted from Galvão et al. (8)

Recommendation 2 emphasizes the importance of effective communication between the exercise professional and the patient's medical team (cancer specialists and primary care). While this should be routine in any multidisciplinary care environment it is particularly crucial for patients with advanced disease. Communication with the medical team facilitates access to the requisite imaging (e.g., bone scans, CT scans, MRI) required to accurately locate the sites of bone metastases and their stability. In addition, the health of patients with advanced disease can change rapidly, and often it is the exercise professional, who is closely and routinely monitoring the patient at each session, that recognizes changes in pain, function, fatigue, or other health indications that can be effectively communicated back to the medical team in a timely manner for clinical consideration or medical management.

Recommendation 3 is that the health and fitness assessment and tailored exercise prescription should be developed by a clinical exercise physiologist or physical therapist who have additional training and direct experience in exercise oncology, preferably including bone metastases. This is because these patients have very complex health issues and quite small variations to the exercise prescription have the potential to greatly increase risk of skeletal complications. Preferably, the patient should be monitored in their exercise sessions by the same allied health professional, although a fitness professional with additional training and experience working with people with cancer may deliver the exercise program, should this be permissible within their scope of practice. This may differ worldwide depending on the various local contexts and regulatory frameworks of a given region or country.

Recommendation 4 purports that careful consideration be given as to whether the risk outweighs the benefit of performing any assessments of strength, cardiorespiratory fitness, and physical function. Testing is normally conducted to provide a baseline for the exercise prescription, monitoring of the patient's progression or regression, and to provide feedback and motivation to the patient. However, getting the patient to perform some level of tolerable exercise is the higher priority, and certain tests may need to be omitted if they risk skeletal complication.

Recommendation 5 is to follow the international guidelines for exercise assessment and prescription for cancer survivors but with modification as necessary to accommodate the health issues, capacity, and, in particular, location and presentation of bone metastases of the individual patient. The M3EP approach (8) provides a strategy for exercise prescription modification, and this can be combined with some of the more recent recommendations around controlled loading (10–12). Exercise programs for all individuals should emphasize postural alignment, controlled movement, and proper technique, which is of paramount importance when working with a patient with bone metastases.

While this work by the IMBEWG represents an important initial guiding framework based on current research evidence and clinical experience, there are opportunities for future research to continue to develop this subcomponent of exercise oncology, including:

a. validation of current skeletal stability tools when used to underpin exercise testing and training programs for people with bone metastases;
b. higher fidelity exercise programs to optimize clinical effectiveness of exercise, inclusive of producing larger randomized controlled trials;
c. further development of targeted exercise for people with unstable or painful lesions;
d. greater exploration of minimum effective dose, dose-response relationships, and optimal dosage for various types and volumes of bone metastatic disease; and
e. implementation science investigation of exercise for people with bone metastases to overcome the barriers and promote facilitators of exercise education, referral, uptake, and adherence between clinicians, patients, and healthcare systems more broadly and worldwide.

These are just some of the pressing needs that we believe research can focus on, moving forward.

CONCLUSION

The *Exercise Recommendation for People with Bone Metastases: Expert Consensus for Health Care Providers and Exercise Professionals* (5) provides clear guidance for the assessment, exercise prescription, and exercise monitoring of patients with bone metastases and should be rapidly translated into best practice exercise oncology globally. People with bone metastases should be supported as much as possible to engage in some form of regular exercise and to minimize sedentary behavior as the key strategies to preserve physical function and maintain quality of life. Even those with advanced disease, undergoing difficult treatments, and with extensive metastatic lesions are able to perform some level of resistance and aerobic exercise; it is simply a matter of tailoring the prescription to the individual to control risk while maximizing health benefit.

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