

## Physical Exercise in Patients with Cancer Cachexia

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### Introduction

#### Cachexia

Cancer cachexia results from numerous complex factors, involving a decline in muscle mass and physical function that occurs with cachexia [1,2]. Thus, it is a combination of anorexia and wasting syndrome due to cachexia [3]. Cancer cachexia is a complex disorder characterized by progressive weight loss with catabolism of adipose tissue and skeletal muscle, affecting approximately 50%–80% of cancer patients, leading to substantial weight loss, primarily due to the loss of skeletal muscle and body fat [4,5]. Although cachexia is defined as the loss of muscle, fat may also be lost [6]. Cancer patients often experience muscle wasting and appetite loss as well as anorexia and fatigue. In addition, they find it difficult to perform regular daily activities [7,8]. This difficulty may also be due to cancer cachexia. These patients have a poor overall quality of life and shorter survival time [9,10]. There are different stages of cancer cachexia that are defined by differences in food intake, weight loss, and ability to function. Proposed three stages of cancer cachexia: pre-cachexia, cachexia, and refractory cachexia.

#### Pre-cachexia

Pre-cachexia starts with the metabolic change with substantial involuntary weight loss ( $\leq 5\%$ ).

#### Cachexia

In this phase, patients have  $>5\%$  loss of body weight or  $<20 \text{ kg/m}^2$  loss of body mass index and an ongoing weight loss of  $>2\%$ .

#### Refractory cachexia

In this phase, patients are not responsive to anticancer treatment. They are characterized by low performance status and have an expected survival time of less than 3 months.

#### Physical Exercise

Physical exercise can improve the fitness or health of patients with cancer cachexia [11]. Physical exercises have an important role in sustaining and building muscle mass; it is thus beneficial to people with cancer cachexia or those at risk of cancer cachexia. It is also effective in improving physical activity levels in cancer survivors [12]. A systematic review has identified benefits including improvement in physical activity levels, aerobic fitness, muscular strength, functional quality of life, anxiety and self-esteem in cancer survivors [13]. Aerobic and resistance exercises or a combination of both, have been found to improve upper and lower body strength compared with usual care [14]. Physical exercise helps maintain or slow the loss of physical function [15]. Aerobic exercise training for skeletal muscles improves wasting in both cardiac and cancer cachexia [16]. Physical exercise may promote a disruption in the cycle of events leading to cachexia advancement and in turn may promote enhanced functionality, thus improving the quality of life of cancer patients [17]. Physical exercise has been suggested to counteract the effect of exercise training in cancer cachexia [18]. Furthermore, physical exercise is associated with reduced levels of C-reactive protein in cancer patients [19]. It has been proposed as a complementary treatment in cancer patients and represents a function-

preserving, anti-inflammatory, and metabolism-modulating strategy that has a low cost [20]. It may reverse protein degradation, while increasing protein synthesis and lean body mass, thus counteracting the wasting seen in cachexia [21]. As described above, physical exercise may benefit patients with cancer cachexia. Research investigating physical activity/exercise in cancer patients undergoing treatment has demonstrated an improvement in physical performance, fatigue and functional quality of life. However, there is insufficient evidence to determine the effectiveness of physical exercise in cancer cachexia patients. Future studies on the effect of physical exercise on patients with cancer cachexia during each phase need to be conducted. Additionally, the intensity and duration of physical exercise can be changed to suit the needs of the patients in each stage; patients in pre-cachexia phase may be able to perform aggressive physical exercise; however, such exercises might not be suitable for patients in the refractory cachexia phase.

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