Nutrition/Exercise in Upper Gastrointestinal Cancers

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Malnutrition and muscle wasting are associated with impaired physical functioning and quality of life in oncology patients. Patients diagnosed with upper gastrointestinal (GI) cancers are considered at high risk of malnutrition and impaired function. Due to continuous improvement in upper GI cancer survival rates, there has been an increased focus on multimodal interventions aimed at minimizing the adverse effects of cancer treatments and enhancing survivors' quality of life.

Keywords: cancer; gastrointestinal; nutrition; exercise; rehabilitation; multidisciplinary; body composition

1. Introduction

Upper GI cancers, namely esophageal cancer, gastric cancer, hepatobiliary cancers, and pancreatic cancer, were reported to affect 3.12 million individuals (17.3% of the global cancer incidence) in 2018 [1]. Adding to this, upper GI cancers were responsible for 2.6 million deaths worldwide in 2018. The treatment for upper GI cancer includes surgery, chemotherapy, and radiotherapy. Although advances in these cancer treatments, and early cancer diagnosis, has led to higher survival rates, the treatments are accompanied by adverse effects on patients' nutritional status and physical function [2][3][4][5][6].

Cachexia and muscle loss are one of the main complications in cancer patients that hinder cancer treatment and survival [3]. Muscle wasting is accompanied by reduced physical function, fatigue, chemotherapy toxicity, lower quality of life, and a higher rate of postoperative complications [7][8][9][10]. Due to the tumor location and the unique influences of curative surgery on a patient's dietary intake, patients with upper GI cancer are at a greater risk of malnutrition and its related complications [11][12][13]. As the survival rates for upper GI cancer continue to improve, the long-term nutritional and physical status of upper GI cancer survivors requires further attention. There is a need to offer effective care plans to prevent muscle wasting and optimize nutritional and functional status in upper GI cancer patients, which subsequently would improve treatment outcomes and enhance survivors' quality of life.

Multimodal interventions consisting of nutrition and exercise prescription have been reported to favorably change health-related outcomes in cancer patients, such as fatigue, quality of life, and functional capacity $\frac{[14][15]}{15}$. These multimodal interventions may play an even more significant role in older cancer patients who are at a further increased risk of suboptimal nutritional and functional status $\frac{[16]}{15}$.

As both nutrition and exercise have positive effects on muscle loss, combining nutrition and exercise may further improve muscle protein synthesis and increase muscle mass [17]. It should be mentioned that the impact of combined nutritional care with physical exercise specifically on body composition is not clear yet [18][19][20][21][22][23]. Thus, the present systematic review of combined nutritional and exercise interventions in upper GI cancer patients aimed to determine whether these interventions are an effective approach for preserving muscle mass. In addition, these care programs need to be evaluated to define optimal intervention design and optimal timepoint for delivery within the cancer trajectory, i.e., prehabilitation or rehabilitation. Moreover, patients' acceptance and adherence to these programs need to be reviewed, as the effectiveness and acceptance of nutritional and exercises interventions may be different in patients with upper GI cancer compared to other cancer types, owing to the impact of surgery on food intake and postoperative complications, such as food intolerance and malabsorption.

2. Nutrition Interventions Combined with Exercise in Upper Gastrointestinal Cancers

Nutritional interventions were mainly individual consults alone or along with prescribing oral nutritional supplements to ensure energy and protein requirements were met. It is noteworthy that the rationale behind prescribing nutritional supplements or support (PN) was not explained in the Ausania et al. and Minnella et al. studies. This is important as a

lack of details regarding the delivered intervention may complicate interpretation of the reported results in these studies [15][24]. Exercise training included supervised and/or home-based walking and/or resistance training. Although there is growing interest in multidisciplinary care plans for cancer patients, acknowledging the potential beneficial effects of these interventions on patients' quality of life, a limited number of studies have examined the effectiveness of these interventions in upper GI cancers to date [25][26][27].

Interventions incorporating nutrition and exercise appear to be safe and acceptable in patients diagnosed with upper GI cancer, with a higher rate of compliance with supervised interventions [22][28]. However, only three studies reported compliance with the intervention, of which a single study reported adherence to nutrition consult sessions [15][22][28]. O'Neil et al. did not report adherence to dietetic consult and education sessions and Minnella et al. reported overall compliance with prehab intervention rather than specifying adherence to exercise and nutrition components separately [15][22]. A lack of sufficient data regarding the adherence rate in some of the reviewed studies makes it difficult to understand whether non-significant findings were due to the ineffectiveness of the interventions or lack of compliance with the intervention.

Regarding physical functioning, the promising effects of combined nutritional interventions with physical training on functional and cardiorespiratory outcomes have been reported in several studies [29][30]. This improvement in physical performance is important as higher physical performance and functioning has been associated with improved quality of life, treatment response, and prognosis in cancer patients in several studies [31][32][33]. Although, further high-quality studies are needed to confirm the positive effects of multidisciplinary interventions on physical functioning due to the poor quality of the included studies.

The present study showed that changes in body composition following multimodal interventions in upper GI cancer patients have been understudied and the limited available evidence showed mixed results. As mentioned previously, muscle wasting is associated with impaired quality of life and reduced survival following cancer treatments [34]. However, the optimal care that can effectively counteract cancer-associated cachexia has not been defined yet [34]. Cachexia and muscle wasting have received much attention in the scientific literature in recent years, but there remains limited evidence regarding the effectiveness of combined nutritional and exercise interventions in improving impaired body composition [16] [35]. It is acknowledged that meeting patients' protein and energy requirements is crucial to maintain muscle mass during cancer treatment and recovery, and exercise interventions may be effective in preventing and reversing muscle wasting [36][37][38]. It is worthy of note that, although four of the included studies assessed dietary intake at some time point of the study, none of them reported dietary intake data [15][22][24][28]. This could be considered as one of the factors that resulted in a high risk of bias in the reviewed studies as lack of dietary intake data makes it difficult to examine whether nutritional adequacy had been achieved by these interventions. Dietary intake assessment is crucial to ensure whether adequate protein and energy intake has been supported during multidisciplinary interventions. This is even more important in UGI cancer survivors as they experience severe reductions in their dietary intake and impaired food tolerance following surgeries [111].

The increased survival rate of patients diagnosed with cancer is accompanied by an acknowledgement of the need to ensure good quality of life. Cancer can negatively impact the quality of life and improved HRQOL may be associated with lower mortality and recurrence [39]. Assessing changes in HRQOL during and beyond cancer, and following interventions can assist researchers to have a better understanding of the effects of treatment on patients' physical, mental, and emotional status [40].

The limited studies that examined the effectiveness of prehabilitation versus rehabilitation in cancer reported inconsistent results from observing no significant differences in functional walking capacity to better responses to prehabilitation compared with rehabilitation [41][42]. Therefore, the optimal timepoint for providing multidisciplinary care programs is yet to be known and requires further studies.

3. Conclusions

Limited evidence is available on the effectiveness of multimodal interventions, with a core component of nutrition and exercise, in improving outcomes in upper GI cancer patients. Although studies showed an improvement in physical function and exercise capacity, the evidence regarding positive changes in muscle mass and quality of life was scarce and conflicting. In conclusion, due to the poor quality of limited available evidence, further high-quality studies are warranted to examine the effectiveness of multidisciplinary care programs in improving outcomes in upper GI cancers with a focus on improving the body composition and quality of life in these patients. Considering a core outcome set for measuring the clinical effectiveness of multidisciplinary supportive care programs may improve the consistency and quality of future investigations [43]. Moreover, it may facilitate more meaningful comparison across studies and support evidence synthesis.

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