

Intro

Colorectal cancer (CRC), the third most common cancer worldwide¹, develops in the tissues of the colon or rectum. The colon absorbs water and nutrients from foods, while converting leftover waste products into feces. The fecal matter is then stored in the rectum until elimination occurs². The primary treatment for CRC is the removal of tumors via surgery. Other treatments include radiation therapy, chemotherapy, immunotherapy, and targeted therapy. These treatments can be combined to produce better outcomes. Examples include radiation or chemotherapy before surgery to reduce tumor size or chemotherapy post-surgery to kill leftover cancer cells^{1,3}. Cancer treatments can have adverse effects on physiological and psychological measures. During treatment, feelings of isolation, fear, and sadness are common. Extreme fatigue, digestive issues, neuropathy, increased risk of infections, and cachexia are physiological side effects seen during treatment⁴⁻⁶. Epidemiology has provided evidence demonstrating the positive effects of exercise in various cancer types. Exercise is associated with positive changes in physiological measures and quality of life (QOL) in cancer patients. In preclinical studies, the most common outcome is a reduction in tumor growth rates, with decreases as high as 67%⁷.

Scientists have also inspected nutrition as a possible during treatment intervention for cancer patients. Nutrition interventions are of interest due to cancer's association with a dysregulated metabolism. For example, the Warburg effect is a process where, even in the presence of oxygen, tumor cells ferment glucose into lactic acid to form energy for proliferation. Due to these concepts, the oncology community has studied nutrition interventions that limit carbohydrates, limit calories, and/or limit raw foods, but evidence is limited⁸⁻⁹.

Exercise as a during treatment intervention needs further investigation, while nutritional interventions have been under examined. Most of the oncology research focuses on the more prevalent cancer types, like breast and lung cancer. Due to the challenges of complex research design and the limited availability of cancer patients for trials, studies often analyze mixed cancer populations. Currently, there is sparse research exploring the effects of during treatment exercise and nutritional diets on colorectal cancer outcomes.

The purpose of this perspective review is to explore the current literature examining the effects of during treatment exercise and nutritional interventions in CRC patients, specifically looking at patient outcomes. The aim of this review is to bring awareness to the gap in oncology research and during treatment interventions, while contributing to the foundation of a clinical exercise and nutrition prescription database.

Purpose

The purpose of this perspective review is to explore the current literature examining the effects of during treatment exercise and nutritional interventions in CRC patients, specifically looking at patient outcomes. Due to the challenges of complex research design and the limited availability of cancer patients for trials, studies often analyze mixed cancer populations. Currently, there is limited research examining solely CRC patient populations, and even less so when investigating patient outcomes influenced by during treatment exercise and nutritional diets. The aim of this review is to bring awareness to this gap in oncology research and intra-treatment interventions, while contributing to the foundation of a clinical exercise and nutrition prescription database.

Methods

77 pieces of literature were collected. 22 articles were selected from the collection because of their focus on CRC patient samples, patient outcomes, and interventions given during post-diagnosis, perioperative, and cancer therapies periods. These studies were considered recent research as all except one article was published within the last 10 years.

Results

Dependent variables included fatigue, cancer control, physical function, and QOL, as well as the safety and feasibility of the interventions. Cancer related fatigue is the most prevalent and research side effect of cancer and its treatments affecting 80% to 100% of cancer patients¹⁰. Physical function was

defined as physical strength, endurance, flexibility, and mobility. QOL consisted of physical and mental health and wellbeing.

The first pre-clinical exercise oncology study was conducted in 1944, with clinical populations reported in 1981. Studies focused solely on CRC patients did not emerge until the early 2000's¹¹. The earliest known study connecting nutrition and CRC was in 1980¹²⁻¹³. Because exercise and nutritional oncology is broad and research is fairly recent with CRC specific samples sparse, evidence recommending or not recommending these types of interventions is insufficient, especially for certain research outcomes. In the case of cancer related fatigue and physical function, aerobic and resistance exercise has been shown to be beneficial when done during CRC treatment⁸.

Nonetheless, certain exercise and nutritional interventions are being sought after for their potential to improve or at least maintain certain patient outcomes. We will discuss these interventions next.

Exercise

Fatigue

- Aerobic and Resistance Exercise (4;+)^{8,15-17,19}
- Sport and Leisure time Moderate and Vigorous Physical Activity (1;+)²⁰

Cancer Control

- Aerobic and Resistance Exercise (2;+)^{8,18}

Physical Function

- Aerobic and Resistance Exercise (5;+)^{8,14,16,18,19}

QOL

- Aerobic and Resistance Exercise (7;+)^{8,14-19}

Safety and Feasibility

- Aerobic and Resistance Exercise (4;+)^{8,15-16,19}

Nutrition

Fatigue

- Plant-based dietary pattern has a potential effect, with weight loss diets, and healthy diets having no effect⁸

Cancer Control

- Neutropenic diets not recommended to prevent infections during active treatment⁸
- Mediterranean diet significantly improved inflammatory markers (TNF- α , hs-CRP, IL-6)²¹
- Multidisciplinary Treatments can improve immune function, chemotherapy effects, prealbumin levels^{22,27}
- Peripheral Parenteral Nutrition improved postoperative outcomes²⁸
- Immune-enhancing feed decreased hospitalization duration and complications (infections)^{29,30}
- High protein conserved performance status (ADL)³³
- No significant effects from dietary interventions when compared to controls (high fiber, Vitamin D supplementation, simple sugar IV, total parental)^{25,26}
- Prebiotics produced significant positive effects on immunologic indices (IgG; IgM; transferrin)³⁴

Physical Function

- Mediterranean diet significantly increased body composition (weight, lean body mass, fat mass, and muscle strength) and physical performance²¹
- Increased protein intake suggests positive effects on muscle mass and physical function²³
- A multidisciplinary treatment conserved weight of patients²⁷
- A glutamine-enriched oligomeric diet and Perioperative Oral Nutrition improved functional status^{31,32}

QOL

- Plant-based diets, weight loss diets, and healthy diets showed no effect⁸
- Mediterranean diet significantly improved health status, QOL, and nutritional status²¹
- Multidisciplinary Treatments can enhance nutritional levels²²

- Foods rich in lactose and FODMAP (fermentable oligosaccharides, disaccharides, monosaccharides, and polyols) increased risk of diarrhea²⁴
- Glutamine-enriched oligomeric diet improved stool consistency and reduced number of stools. It reduced the risk of developing intestinal mucositis³¹
- Perioperative Oral Nutrition improved nutritional status, and reduced relative dose intensity, chemotherapy regime change, and chemotherapy delay³²
- High protein nutritional support improved nutritional status, with no effect on systemic therapy toxicity³³

Safety and Feasibility

- Multidisciplinary treatments and perioperative oral nutrition reduced adverse effects^{22,32}

Conclusion

Exercise and nutritional oncology are still developing, with the majority of research being conducted on mixed cancer patients. While specific exercise modalities and nutritional interventions are still being investigated for more conclusive outcomes, especially in specific cancer type populations like CRC, exercise and nutritional support are safe and feasible during treatment for CRC. Current research, regarding fatigue, cancer control, physical function, and QOL, suggest that aerobic and/or resistance exercise can improve these outcomes. For nutritional interventions, no one diet seems to do it all. Current research supports mediterranean, high protein, and immune enhancing diets in creating better outcomes in CRC patients. These interventions share the common focus of including a variety of nutrient rich foods instead of restricting foods such as low-carbohydrate, neutropenic, or fasting interventions. Multidisciplinary treatments showed to be an effective tool, most likely due to its focus on individualized patient care, on improving patient outcomes. As of now, aerobic and/or resistance training interventions have shown the benefit they have in CRC patients during treatment. Future research might consider investigating high intensity interval exercise for its aerobic, anaerobic, and hypertrophic properties. Emerging research suggests immune enhancing nutritional feeds and patient focused nutritional interventions are beneficial during treatment. Currently, there is insufficient evidence to recommend or not recommend restrictive or uniform nutrient rich diets.

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