

Summary

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The impact of fish oil on clinical parameters and quality of life in patients with cancer

Introduction

The occurrence and burden of cancer is progressively increasing, and its treatment has many side effects. Patients with cancer often experience weight loss and cachexia, both of which are associated with a worse clinical outcome and quality of life. Conventional nutritional interventions appear to be ineffective on functional outcomes in patients with cancer. Because of the immune-modulating effects of n-3 fatty acids from fish oil, we were interested to investigate effects of supplementation of fish oil on the outcomes in two patient populations who encounter many complications during their treatment trajectory: patients with non-small-cell lung carcinoma (NSCLC) undergoing concurrent chemoradiotherapy, and those with Graft-versus-Host disease (GVHD) after allogeneic hematopoietic stem cell transplantation. Complementary studies explored the presence and prognostic value of weight loss and cachexia at diagnosis of lung cancer, as well as the nutritional issues and nutritional support strategies in patients with GVHD.

Presence and prognostic value of weight loss and cachexia in patients with cancer

In **Chapter 3**, we studied the presence of precachexia and cachexia in patients at diagnosis of stage III non-small-cell lung carcinoma (NSCLC), by using two consensus-based frameworks: a cancer-specific and a general framework. The cancer-specific framework found precachexia in 23% and cachexia in 18% of the patients; the general framework found cachexia in 28% of patients. Cachexia, not precachexia, appeared to be associated with a reduced quality of life and shorter survival.

Chapter 7 shows that weight loss during chemoradiotherapy was associated with a shorter progression-free and overall survival in patients with stage III NSCLC undergoing concurrent chemoradiotherapy followed by surgery. In particular patients with a BMI > 25 kg/m² who experienced more than 5% weight loss during chemoradiotherapy had a significantly shorter survival. This study raises the awareness for the risk of malnutrition and sarcopenia in cancer patients with overweight or obesity.

A literature review (**Chapter 8**) demonstrated that GVHD of the digestive tract is often associated with malnutrition, protein losing enteropathy, magnesium derangements, and

deficiencies of zinc, vitamin B₁₂ and vitamin D. Limited evidence exists on derangements of resting energy expenditure, bone mineral density and pancreatic function. A few studies suggest beneficial effects of n-3 PUFAs and pancreatic enzyme replacement therapy. This chapter concluded with evidence-based nutritional recommendations for patients following allogeneic hematopoietic stem cell transplantations and patients with GVHD.

The impact of fish oil in clinical parameters

A systematic review (**Chapter 2**) investigated the effects of n-3 PUFAs supplementation on clinical outcomes, and showed that there is some evidence for the beneficial effects on body weight and quality of life of oral or enteral supplementation in patients with cancer. Parenteral supplementation of n-3 PUFAs reduced the length of hospital or ICU stay after surgical oncology, and enteral supplementation improved the clinical outcome in critical care patients.

This literature review also investigated the incorporation of n-3 PUFAs into phospholipids of plasma and blood cells, as well as the subsequent washout after cessation of supplementation of n-3 fatty acids. The incorporation of n-3 PUFAs in plasma and blood cells was slower with enteral supplementation (4–7 d) than with parenteral supplementation (1–3 d). No studies on the washout of n-3 fatty acids from plasma and blood cells in cancer patients were retrieved; in patients undergoing surgery and critical care, washout after parenteral supplementation of n-3 fatty acids was 5–7 d.

An updated evidence analysis, carried out in collaboration with Australian experts (**Chapter 6**), showed that oral or enteral supplementation of n-3 fatty acids appears to be safe and may have positive effects on quality of life and physical activity in patients with cancer. However, the effects on body weight, fat free mass and performance status were inconclusive.

Chapter 4 and 5 demonstrated that a 5-week intervention of oral nutritional supplements containing (n-3) polyunsaturated fatty acids beneficially affects the nutritional status, quality of life, performance status and physical activity of patients with stage III non-small cell lung cancer during multimodality treatment.

In patients with chronic GVHD of the digestive tract, intermittent fish oil infusions resulted in incorporation of EPA in plasma and white blood cells. However, due to the increase in serum triglycerides, the intermittent fish oil infusions were not feasible in this patient population (Chapter 9).

Chapter 10 summarizes and discusses the main findings of this thesis. Furthermore, methodological issues related to the studies are explored, relevance and implications for

clinical practice are discussed and recommendations for future research are made.

Conclusion

In conclusion, weight loss, (pre)cachexia and muscle wasting are prevalent in patients with stage III NSCLC as well as in patients with GVHD-DT, and are associated with a reduced quality of life and shorter survival. Supplementation of fish oil during combined modality treatment improves nutritional status, quality of life, performance status and physical activity in patients with stage III NSCLC. Furthermore, intermittent fish oil infusions in patients with GVHD-DT alter the fatty acid composition of plasma and blood cells, but can be complicated by a reversible increase in serum triglycerides.

Chemoradiotherapy and allogeneic HSCT have become a part of the usual cancer care and will be applied more and more. Consequently, the number of patients who experience nutritional issues, severe complications and GVHD will increase. The findings of this thesis can be used to improve the condition and quality of life around chemoradiotherapy and allogeneic HSCT. Future research needs to focus on the refinement and validation of (pre)cachexia definitions, as well as on nutritional support strategies for GVHD and multimodal treatments for (pre)cachexia.