

Summary

Introduction

Of all cancer patients, patients with head and neck cancer (HNC) are at the highest risk for malnutrition. One of the main symptoms of malnutrition is unintentional weight loss. Therefore, malnutrition is mostly defined as unintentional weight loss of more than 5% in one month or more than 10% in six months. In spite of the available knowledge on malnutrition in HNC patients, the detailed consequences and risk factors for weight loss during (chemo)radiotherapy ((C)RT) are not completely clear. For optimised nutritional therapy it is of importance to gain insight into the aspects related to the decline in nutritional status.

The general aim of this thesis was to investigate the causes, consequences and treatment options of a decline in nutritional status during (C)RT in patients with HNC and to develop a practical tool for early identification of the malnourished patients in need of nutritional support.

Prevalence and causes of malnutrition

Critical weight loss was prevalent in half of the patients with HNC during (C)RT (chapter 2, 3, 6). Weight loss, in the absence of malabsorption, is the result of a decreased energy intake and/or an increased energy expenditure. Several studies have found that patients with HNC have low energy intake during therapy.

In chapter 4, we investigated the role of an increased energy expenditure (hypermetabolism) before and during RT. In 71 HNC patients resting energy expenditure (REE) was measured longitudinal by indirect calorimetry before, during and after RT. Forty healthy control subjects were one-to-one matched to 40 patients by gender, age and fat free mass (FFM) index to compare REE. REE was not significantly different between patients and controls, neither in absolute values (1568 ± 247 vs. 1619 ± 244 kcal/d; $p=0.29$), nor after weight-adjustment or FFM-adjustment. Moreover, REE was independent of tumour stage, CRP, and prior tumour surgery. REE (kcal/d) decreased during RT and 3 months thereafter by 9% from pre-RT ($p<0.01$).

Consequences of malnutrition

In the treatment of HNC, survival and quality of life are main outcome parameters. In two studies (chapter 2 and 3) we investigated the association between weight loss during (C)RT and deterioration in quality of life (QOL) and disease-specific survival in HNC patients. We hereby adjusted for important socio-demographic and tumour

related characteristics.

In 533 patients the association between weight loss and change in QOL was analysed. Weight loss during (C)RT was significantly associated to deterioration of global QOL, physical functioning, social functioning, and with the subdomains social eating and social contact. After additional adjustment for disease specific symptoms and tube feeding, weight loss (>10%) remained significantly associated with global QOL, social eating, and social contact ($P < 0.05$).

To study the association with survival, weight change was collected in 1340 newly diagnosed patients with HNC during (adjuvant) (C)RT with curative intent. Five-year overall and disease specific survival rates for patients with critical weight loss during RT were 62% and 82%, compared with 70% and 89% for patients without critical weight loss ($p = 0.01$; $p = 0.001$). After adjustment, critical weight loss during RT remained significantly associated with a worse disease specific survival (HR 1.7; 95% CI 1.2–2.4; $p = 0.004$).

Treatment of malnutrition

To study the treatment options for malnutrition in patients with HNC receiving (C)RT, a systematic review was performed examining the effect of nutritional interventions on nutritional status, quality of life and mortality (chapter 7). The study was carried out according to the methods of The Cochrane Collaboration.

Of 1,141 titles identified, 12 study reports were finally included in the systematic review. Four studies examined the effects of individualized dietary counselling by a dietitian, and showed significant benefits on nutritional status and QOL compared to no counselling or general nutritional advice by a nurse ($p < 0.05$).

Early identification of malnutrition

Patients with early stage laryngeal cancer are thought to have a low incidence of malnutrition, but critical weight loss is observed in a subgroup of these patients during RT. We investigated risk factors for critical weight loss during RT in early stage laryngeal cancer patients in order to identify the patients at risk of malnutrition (chapter 5).

Of patients with T1/T2 laryngeal cancer, who received primary RT between 1999 and 2007 ($n = 238$), an extensive set of baseline characteristics was recorded, including patient, diagnostic and therapeutic characteristics, quality of life and nutrition related symptoms.

In the multivariate analysis, both RT on the neck nodes (HR 4.16, 95% CI 2.62–6.60) and dry mouth (HR 1.72, 95% CI 1.14–2.60) remained predictive for critical weight loss.

Nevertheless, RT on the neck nodes alone resulted in the best predictive model for malnutrition scores.

In a mixed HNC group, more diagnostic and therapeutic variation is expected than in the specific patient group of early stage laryngeal cancer. In a cohort study (n=910) we therefore investigated predictive factors for critical weight loss during (C)RT in the total group of patients with HNC (chapter 6). Predictive factors were RT on the lymph nodes, higher RT dose on the primary tumour, receiving 3D-RT instead of IMRT, and younger age. A decision tree was developed to select the patients at high risk of critical weight loss.

General conclusions

Malnutrition during (adjuvant) (C)RT is a serious problem in patients with HNC. Half of the patients suffer from critical weight loss during (C)RT. Low food intake rather than hypermetabolism is the main determinant for weight loss in HNC. Weight loss during (C)RT has a significant impact on the social eating, social contact, QOL and 5 year disease specific survival in HNC patients. Patients with critical weight loss during (C)RT have a 70% higher risk of dying due to cancer than patients without critical weight loss. Individualized dietary counselling has shown to have beneficial effects on nutritional status and QoL.

To predict critical weight loss during (C)RT, a practical decision tree was developed, including the risk factors RT to the neck, higher RT dose, 3D-RT, and age. In patients with early stage laryngeal cancer, RT on the neck nodes is the best predictor of malnutrition during RT. Our decision model might help to identify HNC patients in need of early monitoring and more intensive dietary counselling during (C)RT. Intensive dietary counselling might contribute to prevention and tailored management of malnutrition in patients with head and neck cancer, in order to reduce disease-burden and improve quality of life.