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Impact of nutritional parameter variations during definitive chemoradiotherapy in locally advanced oesophageal cancer

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ABSTRACT

Background: Undernutrition is frequently observed in patients with a locally advanced oesophageal carcinoma. However, variations of nutritional parameters during chemoradiotherapy have not been thoroughly investigated.
Aim: To evaluate the characteristics and the impact of nutritional variations during treatment.
Methods: Weight loss, body mass index (BMI), serum albumin level and daily food intake at baseline and during treatment (T1 = week 1; T2 = week 5 or 8; T3 = week 11) were retrospectively analyzed in 101 patients with oesophageal carcinoma.
Results: Significant variations occurred during chemoradiotherapy with a decrease in serum albumin level ($p < 0.001$), body mass index ($p < 0.001$) and weight ($p < 0.001$). Response rate to treatment was significantly lower in patients with undernutrition at T1 ($p = 0.05$), from T1 to T2 ($p = 0.01$) and from T1 to T3 ($p = 0.04$). Median overall survival was 25 months in patients with persistent undernutrition from T1 to T2 vs 42 months in wellnourished patients from T1 to T2 and those malnourished only at T1 or T2 ($p = 0.05$). In responders, patients presenting with a lower weight or a lower food intake from T1 to T3 had worse survival (33 vs 59 months, $p < 0.001$ and 29 vs 61 months, $p = 0.001$, respectively).
Conclusion: Significant variations of nutritional parameters occurred during chemoradiotherapy with a worse impact on response and survival.

1. Introduction

Oesophageal cancer is the sixth leading cause of cancer death worldwide with an incidence of 30,000 per year in European countries [1,2]. In approximately one half of cases, patients present with a locally advanced oesophageal carcinoma (LAOC), which is defined by tumours with perioesophageal tissue or contiguous structure invasion, and/or lymph node metastasis [2,3]. Two randomized trials including mainly squamous cell LAOC reported similar survival between oesophagectomy and chemoradiotherapy alone, particularly in patients who underwent a complete clinical response (CCR) to this treatment [3,4].

Undernutrition is associated with a poorer outcome, reduced objective response and worse quality of life in patients with cancer [5–7]. Until now, there has been no consensual diagnostic test for undernutrition in cancer patients, but the parameters frequently included are body mass index (BMI), recent weight loss and food intake evaluation for the screening [8]. At first referral, it has been reported that undernutrition in cancer patients ranged from 31% to 87%, with the highest frequencies observed in malignancies of the aerodigestive tract [5,9]. In oesophageal cancer, approximately two thirds of patients were malnourished at the first presentation, irrespective of the disease stage [5,10–12]. Anorexia and dysphagia are the two main factors leading to undernutrition in patients with oesophageal carcinoma. Food intake is basically decreased owing to mechanical oesophageal obstruction of the tumour whereas metabolic changes mediated through increased pro-inflammatory cytokine activity also play a key role in anorexia and weight loss [13,14]. To date, the characteristics and impact of nutritional parameter variations during chemoradiotherapy have been inadequately investigated in patients treated for an LOAC. In the field of supportive measures development for CRT, this knowledge should be of interest in order to define the most appropriate nutritional intervention before and during treatment.

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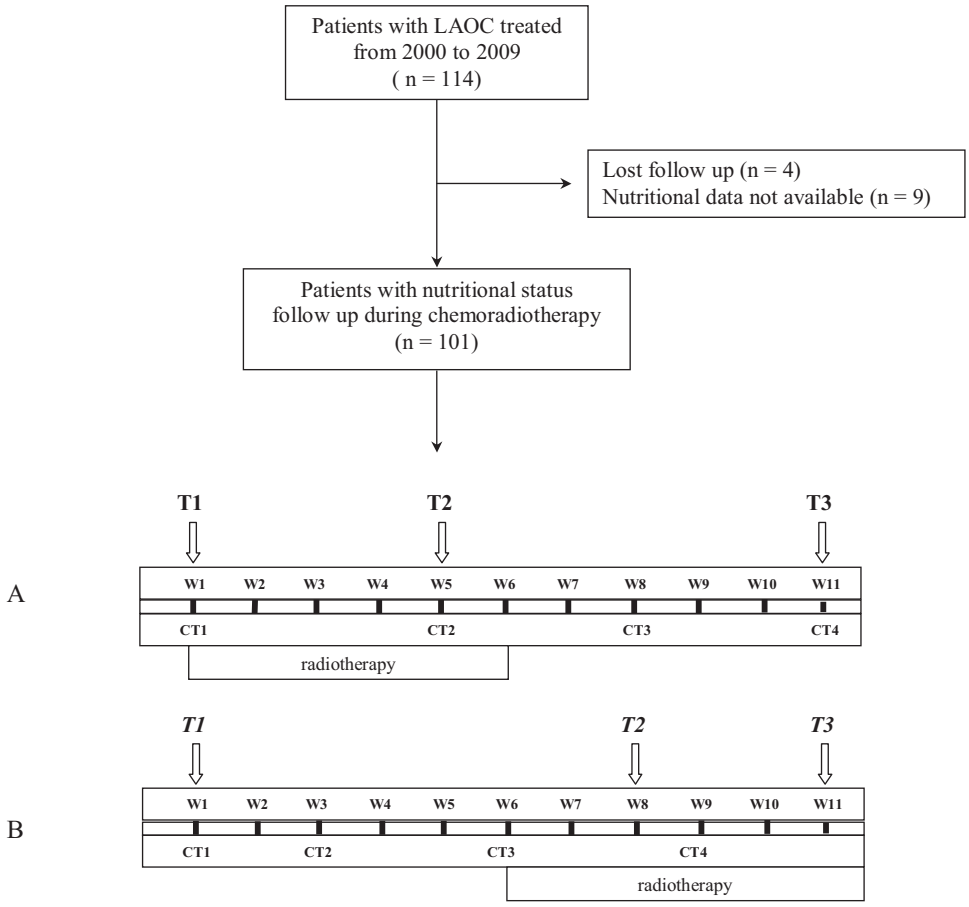

Fig. 1. Study schedule. Chemoradiotherapy according to Herskovic et al. (A), Michel al. and Lledo et al. (B). Body weight loss (%), body mass index (kg/m^2), serum albumin level (g/L) and food intake were evaluated at T1 (baseline), T2 (week 5 or 8) and T3 (week 11). LAOC, locally advanced oesophageal cancer; W, week; CT, chemotherapy

The aim of the present study was to evaluate the characteristics and the impact of nutritional parameter variations during a definitive chemoradiotherapy regimen in patients with locally advanced oesophageal cancer.

2. Patients and methods

2.1. Study population

All patients diagnosed from January 2000 to December 2009 and treated with a chemoradiotherapy regimen using a cisplatin or oxaliplatin based-chemotherapy were retrospectively included [15–17]. Baseline characteristics, including tumour stage, were collected [18]. Patients were considered to have a complete clinical response to treatment when no residual tumour was identified at endoscopy combined with negative biopsies and when no metastatic disease occurrence was observed on computed tomography (CT). PET imaging was not performed for all patients. This evaluation was performed 8 weeks after CRT completion.

2.2. Nutritional assessment during chemoradiotherapy

Nutritional parameters were collected at baseline (T1) and during the chemoradiotherapy sequence (Fig. 1: T2 = week 5 or 8 and T3 = week 11). These three time periods were not defined a priori and the analysis was basically performed in the first week (T1), in the last week of the whole treatment sequence (T3) and during radiotherapy (T2). Undernutrition was defined by a weight loss $\geq$ 10% (>5% at T2 and T3) and/or body mass index (BMI with weight [kg]/height [m^2]) < 18 kg/m^2 and/or serum albumin level $\leq$ 35 g/L. The percentage of weight loss at T1 was calculated according to pre-morbid weight. The weight loss at T2 and T3 was calculated on the one hand according to weight at T1 and T2 respectively, and on the other hand according to the premorbid body weight. All patients received dietary counselling by a senior dietician with calculation of daily food intake (kcal/day) at T1, T2 and T3. The nutritional support was not codified and was proposed at first evaluation according to nutritional parameters and grade of dysphagia according to Atkinson's dysphagia score [19].

2.3. Follow-up and statistical analysis

Nutritional parameters (weight loss, BMI, serum albumin level, daily food intake) and their variations between T1, T2 and T3 were analyzed. Response to chemoradiotherapy and survival were also analyzed according to clinical and nutritional parameters at T1, T2, T3 and according to their variations during the treatment sequence. Follow-up was performed until death or until October 2010, which was considered the cut-off date for the analysis. Chi-squared test, Fisher's exact test and Mann–Whitney test were used to compare non-continuous and continuous data, as appropriate. Survival curves were determined using the Kaplan–Meier method and compared using the Log-rank test. Univariate analysis of prognostic factors of overall survival included clinical data (sex, age, WHO performance status, dysphagia score, tumour location and length, tumour stage, histology and response to treatment), nutritional parameters and status at T1, T2 and T3, as well as their variations during the CRT sequence. Prognostic factors of survival were