Effects of nutritional intervention in head and neck cancer patients undergoing radiotherapy: A prospective randomized clinical trial

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Abstract. Head and neck malignant tumors have numerous locations of the disease. After patients receive radiotherapy, their nutritional status is very poor, thus the curative effect is unsatisfactory. The aims of the present study were to investigate and analyze the nutritional status of patients with head and neck cancer undergoing radiotherapy (RT) in order to provide positive nutrition intervention for assisting the radiotherapy effect. A total of 40 patients with head and neck cancer were selected using a method of subjective global assessment (SGA) to assess nutritional status, including calorie intake and energy expenditure. In a randomized, controlled study, 20 patients received intensive dietary counseling and nutritional therapy (G1) and 20 received regular dietary as controls (G0) preradiotherapy and postradiotherapy. The primary endpoint was calorie intake and energy expenditure. The secondary endpoint was SGA rating with nutritional therapy. At the end of RT, energy intake showed a net increase in G1 (1,691±301 kcal) compared with that in G0 (1,066±312 kcal) (P<0.05); energy expenditure increased in G1 (1,673±279 kcal) compared with G0 (1,490±298 kcal) (P<0.05). The prevalence of severe malnutrition following radiotherapy was significantly different between the two study groups (10 patients in G0 and 4 patients in G1; P<0.05). The number of the normal malnutrition patients postRT in G0 decreased from 4 to 2 and conversely, in G1 it increased from 3 to 6 (P<0.05). In conclusion, patients with head and neck cancer were most malnutritioned, which impacted on clinical outcome. Timely nutritional intervention can effectively prevent weight loss and muscle wasting. Additionally, it may improve quality of life by decreasing the frequency of severe malnutrition.

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Introduction

Head and neck cancer is the most common tumor type, the sixth leading cancer by incidence worldwide and the eighth by mortality, which radiation therapy is the preferred and effective treatment (1). However, due to the influence of the tumor and tumor treatment, patients with head and neck cancer are mostly becoming a malnutrition group. Malnutrition is caused by a lack of nutrient intake or nutritional metabolism of damage to the nutrition state of disorder. The predominant symptoms are progressive emaciation, weight loss or edema. When hypoalbuminemia are serious, they can cause multiple organ damage. The malnutrition incidence of patients depends on tumor location, type and disease stages. The malnutrition prevalence rate of head-neck cancer patients is as high as 74.2%. Patients with malnutrition have numerous effect factors, predominantly including the tumor caused by the body's metabolic abnormalities, antitumor treatment side effects and tumor diagnosis of psychological social factors.

Radiation therapy is used to cure or as palliative treatment for patients with head and neck cancer (2). Due to the toxic effects of radiation to the tumor cells and normal tissue cells, including blood cells, the hair follicle and cells on the surface of the digestive tract, are sensitive to radiation damage. During treatment, the patients also suffer from nausea and vomiting, anorexia, full bilge, diarrhea, mucositis, oral inflammation, pain and other symptoms, This symptoms influence the patient's interest in food, food preparation and feeding capacity. Therefore the patients lack of a sufficient nutrient intake, causing malnutrition (3). Ottery (4) believed that ~20% of the cancer patients did not succumb to the tumor itself, but the consequences of malnutrition. To better fit the antitumor treatment and improve the quality of life for the patients, in the past twenty years, the issue of 'tumor patient nutritional support' has been performed in numerous studies. The American society for parenteral enteral nutrition and the France cooperation organization based on the collecting previous evaluation research results put forward several opinions for the principles and methods on nutritional support. Clarifying nutritional assessment must

be performed for all patients, particularly cancer patients suffering from malnutrition during therapy. These important principles emphasized that the evaluation of nutritional status as a regular assessment must be performed as early as possible. Additionally, when patients require nutritional interventions, these must be initiated as early as possible. The nutrition intervention project implementation must become part of the whole treatment. This requires more staff to cooperate in the various fields, including doctors, nurses, dietitians and pharmacists. There should be close associations with the professional team in the lab and the management department (2).

Oral nutritional support includes food-based interventions, the use of snacks to supplement intake from meals and the use of oral nutritional supplements (5). When a stable disease or complete remission is achieved, the nutritional status can impact cancer recurrence. Dietary habits can also prevent certain cancer types in healthy individuals (6). The advantage in prostate cancer is less obvious (7). Suzuki *et al* (8) reviewed an in-depth description of cancer-related malnutrition pathophysiology. The well-being of the patient may largely be influenced by a good nutritional status (9). However, measuring quality of life remains controversial (10). It is not appropriate to focus on feeding without anticipating changes in physiological and psychosocial behavior (11). On the contrary, optimal nutrition in combination with systemic antiinflammatory treatment and erythropoietin improves the survival of underweight malignant patients (12,13). Additionally, the number of patients receiving intensive multimodality therapy is likely to increase (14).

Involuntary weight loss for head and neck cancer of >5% in 1 month, or >1-2% per week is a reliable indicator of malnourishment, which has been associated with hospitalization and treatment interruptions (14-17). The present study performed a prospective, randomized controlled trial in patients with head and neck cancer referred for RT, which was designed to investigate whether dietary counseling or oral nutrition supplements preRT and postRT affected nutritional status. Furthermore, the impact of nutritional intervention may have predefined outcomes, (nutritional status, calorie intake and energy expenditure) during treatment.

Materials and methods

Patients. The present study selected 40 patients with head and neck cancer who underwent radiotherapy in 323 Hospital of Chinese People's Liberation Army (Xi'an, China). Between March 2010 and March 2014, all patients with head and neck cancer who were referred for RT were considered eligible, regardless of whether the proposed RT was primary, adjuvant to surgery, combined with chemotherapy or administered with palliative intent. The present study was approved by the Human Research Ethics Committees of 323 Hospital of Chinese People's Liberation Army (no. PLA3232031). Informed consent was obtained from all patients. There were 25 male and 15 female patients, ranging between 19- and 76-years-old old (mean 59.8±17.3 years; Table I). Eligibility criteria included the following: Range age of 19-76-years-old, definite diagnosis of head and neck cancer and undergoing radiation therapy, and normal cognition and cooperation. Exclusion criteria were critical illness, kidney function failure, renal disease and/or diabetes mellitus. The patients stratified by cancer stage (18) were randomly assigned into two groups, classified as group G0 and G1. A copy of the randomization sequence was maintained separately from the study personnel. Randomization envelopes were opened prior to the first patient appointment by an individual in a blinded manner (19).

Nutritional assessment. The present study used subjective comprehensive nutritional status/subjective global assessment (SGA) to evaluate patients undergoing radiation therapy (20). A confirmed nutritional assessment tool included the patient's medical history (weight change, changes in diet, the last two weeks of the digestive tract symptoms and functional capacity) and physical examination (loss of body fat tissue, muscle, ankle and sacrum edema, and ascites). Clinicians provided a comprehensive overall impression, via the collection of history and physical examination, to determine the patients' nutritional status. This was categorized into three degrees: Normal (Class A), moderate (Class B) and severe (Class C) malnutrition. SGA was originally designed for the evaluation of the nutrition status of gastrointestinal surgery patients; however, this has been widely used as a nutritional assessment ideal method and has been successfully applied to a variety of different patient groups to assess nutritional status (21). It assists with predicting complications of different groups of patients, including tumor patients (22). SGA was expected to predict malnutrition, which the sensitivity was 82% and the specificity was 72%. It was better compared with other self-test methods. SGA coincidence rate were as high as 80% with traditional evaluation methods. The present study furthered the results of the survey using statistics and analysis.

Study design. All patients were randomly treated with either intensive dietary counseling (nutrition intervention) compared with regular dietary (control), preRT and postRT in 20 patients receiving nutrition therapy (G1) and 20 controls (G0). The primary endpoint was calorie intake and energy expenditure following nutritional therapy. Secondary endpoints declined in the SGA rating with nutritional therapy.

Statistical analysis. The data were analyzed using the SPSS software (version 19.0; IBM SPSS, Chicago, IL, USA). Categorical data were analyzed by one-way analysis of variance and measurement data using Fisher's exact probability method. $P<0.05$ was considered to indicate a statistically significant difference.

Results

Comparison of patient characteristics. A total of 40 patients (25 male; 15 female) were involved in the present study. Patient characteristics are shown in Table I. Patient distribution among groups after randomization was as follows: G0 (n=20), patients received routine care, feeding and nutritionally individualized dietary counseling based on regular foods; G1 (n=20) patients were provided nutritional support and nutritionally individualized dietary counseling based on regular foods. The patient age range was 19-76-years-old (mean age, 59.8±17.3 years). The control group had an average age of 58.3±17.2 years and the nutritional intervention group had an average age of 60.8±16.9 years. The two groups of patients

Table I. Patient characteristics and treatment details.

Characteritic	No. of patients in G0 (n=20)	No. of patients in G1 (n=20)	P-value
Gender			>0.05
Male	13	12	
Female	7	8	
Average age, years	58.3±17.2	60.8±16.9	>0.05
Rang age, years			>0.05
19-36	3	4	
37-60	12	9	
60-76	5	7	
TNM stage			>0.05
T2	4	5	
T3	5	5	
T4	11	10	
Child-pugh			>0.05
A	3	4	
B	6	6	
C	11	10	
Tumor site			>0.05
Nasopharyngeal	3	4	
The throat and swallow	2	1	
Salivary gland	3	3	
Oral	4	2	
The thyroid gland	4	5	
Neck soft tissue	4	5	

TNM, tumor node metastasis.

Table II. Patient energy intake and energy expenditure as measured by indirect calorimetry.

Energy	Control group (G0)	Nutrition intervention group (G1)
Intake (kcal)	1,066±312	1,691±301
Expenditure (kcal)	1,490±298	1,673±279

Table III. SGA rating between the preradiotherapy and postradiotherapy.

		Malnutrition		
Group	Time	Normal	Moderate	Severe
G0 (n=20)	PreRT	4	9	7
	PostRT	2	8	10
G1 (n=20)	PreRT	3	9	8
	PostRT	6	10	4
P-value[a]		<0.05	<0.05	<0.01
P-value[b]		<0.05	<0.05	<0.001

The data are expressed as the number of patients. [a]significance of statistical differences between intragroups, with regards to the nutritional status change between preRT and postRT; [b]significance of statistical differences between intergroups, with regards to the nutritional status change of post RT between G0 and G1. RT, radiotherapy; G0, control group; G1, intervention group.

were comparable; however, no significant difference was observed (P>0.05).

Nutritional intake. At the end of RT, compared with the control group, energy intake revealed a net increase in G1 (1,691±301 kcal) compared with G0 (1,066±312 kcal; P<0.05); energy expenditure increased in G1 (1,673±279 kcal) compared with G0 (1,490±298 kcal; P<0.05). Energy intake in the control group was less than energy consumption, thus it caused weight loss and severe malnutrition; however, in the nutrition intervention group, energy intake was more than energy expenditure, so patients absorbed nutrition well and were in a good nutritional state (Table II).

Nutritional status. The prevalence of severe malnutrition after radiotherapy was significantly different between the two study groups (10 patients in G0 and 4 patients in G1; P<0.05). The number of patients who had further nutritional deterioration, preRT and postRT between G0 and G1 is shown in Table III. In G1, provided with nutrition intervention, patients with normal malnutrition increased and severe malnutrition decreased. It improved their nutritional status. The number of the normal malnutrition patients postRT in G0 decreased from 4 to 2 and conversely, in G0 it increased from 3 to 6. The SGA rating was better compared with the control group and the differences were statistically significant (P<0.05).

Discussion

Head and neck malignant tumors can occur in numerous locations. The most common malignant tumor types are thyroid cancer, nasopharyngeal carcinoma (NPC) and salivary gland tumors (1). The most common cancer types were the oral cavity cancer, including the tongue, buccal mucosa, gums, mouth floor, hard palate and the soft palate, and tonsil, laryngeal cancer, malignant lymphoma, neck metastatic carcinoma of unknown primary tumor (1). The incidence of head and neck malignant cancer are different in different countries, regions, nationalities, races and times (2). Men are more prone to morbidity than women and the highest risk is 40-60-years-old. After 60 years the morbidity gradually declines. A total of 82.4% patients were male in this group, 60.0% of patients were 37-60-years-old, the average age was 59 and the overall morbidity was similar to a basic situation. Radiation therapy is used to cure or as palliative treatment for head and neck tumors. Due to the radiation, the tumor cells and normal tissue cells have toxic effects; all rapidly dividing cells, including blood cells, hair follicle and cells on the surface of the digestive tract, are sensitive to radiation damage (23). Oral mucosal surface is very sensitive to RT. After RT, throat ulcers, difficulty swallowing, dry mouth, loss of appetite, lack of sense

of taste and other symptoms will occur in patients with head and neck cancer. The radiation reaction is also prone to cause damage of the salivary glands, reduce salivation, saliva become viscous, and the patient can have chewing and swallowing difficulties. Radiation damage may improve over months and some may never return to the level prior to treatment (24). During the course of treatment, patients also appear nausea and vomiting, anorexic, with full bilge, diarrhea, catarrh, stomatitis, pain and other symptoms (25). The patient's interest in food and food preparation, and the ability to eat are influenced, which reduces the nutrient intake, resulting in malnutrition.

The present study showed that the nutritional status of the patients gradually declined during treatment. The symptoms may be caused during RT, and radiation adverse effects in patients are gradually strengthened and clinical symptoms appeared. When the SGA method was used to assess the patient's nutritional status, it assisted medical personnel to accurately evaluate and compare the nutritional state of patients to find the deterioration of nutritional status, so the necessary support measures as administered as early as possible (26). During RT, while in the care of the patients with head and neck cancer, we gave early nursing nutrition intervention, it can make the patients better cooperate to complete radiotherapy treatment and make the radiation effect achieve the best state.

Based on a review of the available literature, patients with head and neck cancer undergoing RT required nutrition intervention at regular intervals during treatment (14). Regular dietary counseling during treatment has also been recommended, as it has been associated with less weight loss during treatment (27). McQuellon *et al* (28) used megestrol acetate during treatment to stimulate appetite and may be of some benefit in certain circumstances.

In conclusion, the nutritional status of head and neck cancer patients during RT gradually declined and patients with good nutritional status gradually reduced. When providing nutritional intervention to the patients, the good nutritional status increased and the severe nutritional status decreased. Therefore, early intervention can improve curative effect for patients undergoing RT.

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