ARTICLE

Characterization Analysis of Loss of Appetite among Cancer patients and Development of a Monitoring Check Sheet Corresponding to Changes in Appetite

K. Watanabe[1], M. Tanaka[2,*], I. Shimada[2], K. Juman[2], K. Saga[2], K. Sakamoto[2], S. Morita[2], and M. Yamashita[2]

1 Department of Human Life Sciences, Educational Corporation Kochi Gakuen College, Kochi, Kochi 780-0955, Japan
2 Department of Nutrition, University of Kochi, Kochi, Kochi 781-8515, Japan

E-mail: m-tanaka@cc.u-kochi.ac.jp

In the present study, we investigated ways in which chemotherapy/radiation therapy is manifested in appetite changes among cancer patients, and how these changes are related to treatment. We also developed a monitoring check sheet to grasp changes in appetite. From August 2013 to April 2015, we investigated the relationship between chemotherapy/radiation therapy and changes in appetite among 126 neck, upper chest, and esophageal cancer patients who reported decreased appetite during hospitalization at Kochi Health Sciences Center. The analysis was conducted using nutritionists' records input into electronic medical charts. Among all cancer patients who were undergoing treatment, 48.7% showed changes in food shape/texture preference, and those who were undergoing chemotherapy/radiation therapy showed the most number of changes in palate and olfaction. In addition, when measuring correlations with treatment, the relationship between chemotherapy/radiation therapy and changed palate and/or olfaction was revealed. When investigating food shape, although only subtle changes were detected, we found that the patients with altered olfaction experienced more complex changes in their reported changes in food shape/texture and food preferences. From these results, to clarify factors that lead to a decreased appetite in individual cancer patients, we considered it necessary to develop a monitoring check sheet focused on changes in appetite. Our developed monitoring check sheet was based on appetite, palate, olfaction, food shape, temperature, change in taste, and treatment.

.

Introduction

Cancer patients who undergo radiotherapy and chemotherapy have side effects in the actual course of treatment and have a great influence during the patient's recuperation. The frequency of side effects of nausea and vomiting caused by the action of anticancer drugs ranges from about 70 to 80% of patients receiving cancer chemotherapy.1,2 In addition, it has been reported that there are many patients who complain of eating disorders in particular.3 Radiation therapy in head and neck cancer patients must include mouth and salivary glands in irradiation field. Therefore, many patients have adverse events of the sensory system such as dysgeusia, intraoral defect and oral mucosal damage.4,5 Therefore,it is necessary to provide nutrition management by meals for nutrition support corresponding to symptoms of cancer patients. Adverse effects of the organ sensory system associated with radiotherapy of oral cancer patients include texture, seasoning, temperature, odor, food shape as important food characteristics that affect appetite and the appetite of the patient is determined by comprehensively judging these food characteristics6). Furthermore, it has been it has been reported that the appetite of a patient is greatly affected by the blissfulness that continues after meals, the palatability that continues after meals, the palatability that is perceived as satisfaction.6 Common Terminology Criteria for Adverse Events (CTCAE) is generally usedas a method for evaluating adverse events of drugs such as anticancer drugs. Although CTCAE is suitable for classifying the severity of adverse events, it is difficult to assess appetite changes that affect dietary intake. The Kochi Medical Center dietitians arranged in wards promptly hear to the symptoms from patients whose eating intake has decreased as a daily work, and individual correspondence of meals based on the appetite change is done. These correspondences are described in detail in the electronic medical charts as a managed nutritionists' records. Consequently, a nutritionists' record is considered to be suitable for capture the change in appetite. In this study, we extracted keywords related to appetite changes from the nutritionists' records, and investigated ways in which chemotherapy/radiation therapy is manifested in appetite changes among cancer patients, and how these changes are related to treatment. We also developed a monitoring check sheet to grasp changes in appetite.

Materials and Methods

Subjects

The subjects were 126 neck, upper chest, and esophageal cancer patients admitted to the Kochi medical center from August 2013 to April 2015. This study was started with the approval of the Kochi Medical Center Clinical Research Review Board and University of Kochi Research Ethics Committee.

Survey components

Survey items were age, gender, Body mass index (BMI), radiation dose and presence or absence of chemotherapy/radiation therapy.

Posting from a nutritionists' records

We extracted from the subject nutritionists' records of 126 patients with neck, upper chest, and esophageal cancer from the subjective data on dietary characteristics as shown in Table 1 and found the followings: 1. Palate change, 2. Olfactory change, 3. Food shape change, 4. Temperature change, 5. Taste change were observed was defined as changes in appetite.

Statistical analysis

Data were expressed as the mean ± SD. All statistical analysis was performed using IBM SPSS Statistics software version 21.0 (IBM Japan, Tokyo, Japan). The two matched groups were compared using the non-paired Student's t-test, or the $\chi 2$ test for comparisons of proportions. Data were considered to be significantly different with p-values of less than 0.05.

Results and Discussion

Basic attribute

The subjects had an average age of 68.2±9.9 years, 643 nutritionists' records with contents related to dietary changes. Of the 643 cases, 430 men and 213 women, BMI was 21.3±3.1. The treatment was 313 cases with radiation therapy, 327 cases without radiation therapy, and radiation dose was 62.4±15.6 Gy and 416 cases with chemotherapy and 227 cases with chemotherapy. Appetite changes were 27 cases with palate change, 616 cases without taste change, 40 cases with olfactory change, 603 cases without olfactory change, 296 cases with food shape change, 312 cases without change in food shape, 11 cases with temperature change, 632 cases without temperature change, 54 cases with taste change, 578 cases without taste change, 144 cases with anorexia, 1 cases without anorexia (Table 2). The primary disease rate of neck, upper chest, and esophageal cancer patient was 155 cases (24%) of esophagus cancer, 73 cases (11%) of tongue cancer, 70 cases (11%) of piriform recess cancer, 56 cases (9%) of hypopharyngeal cancer, 54 cases (8%) of glottis carcinoma, 35 cases (5%) of metastatic brain tumor, 34 cases (5%) of cervical lymph node metastasis, 28 cases (4%) of carcinoma of mandible, 22 cases (3%) of head (frontal region side), 22 cases (3%) of carcinoma of maxilla, 17 cases (3%) of nasal cavity cancer, 16 cases (2%) of oropharyngeal cancer, 14 cases (2%) of upper pharynx cancer, 11 cases (2%) of thyroid cancer, 6 cases (1%) of carcinoma of buccal mucosa, 4 cases (1%) of oral cancer, 26 cases (4%) of others (Fig. 1).

Comparison of radiation dose with or without chemotherapy

A comparison of radiation dose with or without chemotherapy is shown in Fig. 2. The radiation dose of patients undergoing chemotherapy (64.3±15.2 Gy) was significantly higher than those who did not (55.3±15.4 Gy).

Comparison of treatment and appetite changes

Appetite changes in neck, upper chest, and esophageal cancer patients in the therapeutic situation are shown in Table 3A. A significant association was found between chemotherapy/radiation therapy and palate, olfactory sensation, palate change and olfactory change were numerous in patients with both radiotherapy and chemotherapy (Table 3B). Furthermore, chemotherapy and radiation therapy were divided into groups and appetite changes were examined (Table 4A).As a result, significant associations were found between radiotherapy and appetite changes, and palate changes and olfactory changes were more frequent in radiation therapy patients (Table 4B). On the other hand, there was no significant difference between chemotherapy and appetite changes (Table 4). Many patients have decreased appetite for some reasons during cancer treatment, about 50% of patients have a change in food shape. Patients undergoing chemo-radiation therapy have been found to cause palate and olfactory changes. A comprehensive survey on the relationship between chemotherapy/radiation therapy and appetite changes that are factors causing a decrease in loss of appetite are compounded. It was also reavealed that changes in palate and olfactory have occurred in particular by radiotherapy.

Relationship between appetite changes

The relationship between appetite changes in neck, upper chest, and esophageal cancer patients is shown in Table 5A. A significant association was found between palate change and olfactory change, food shape change, and patients with palate change had more olfactory changes and many people without food shape change (Table 5B). Olfactory, food shape and taste changes were observed a significant association, patients with olfactory change had more changes in food shape change and taste change (Table 5C). A significant association was found between change in food shape and taste change, and patients with food shape change had less preference change (Table 5D). The association between appetite changes is that a

patient with taste change has an olfactory change appearing at the same time but the change in food shape is small, and the patients with altered olfaction experienced more complex changes in their reported changes in food shape/texture and food preferences.

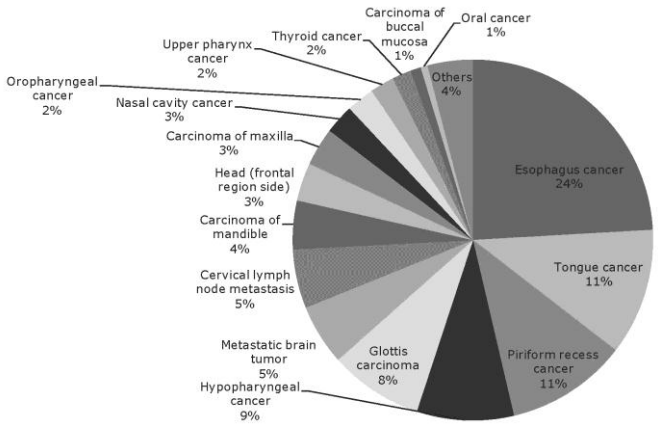

Fig. **1.** The primary disease rate of neck, upper chest, and esophageal cancer patient

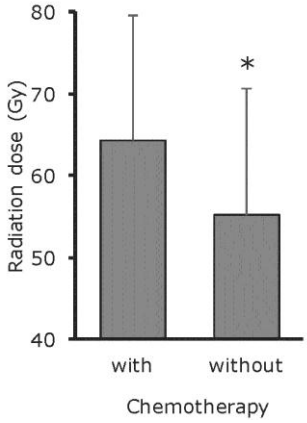

Fig. **2.** Comparison of radiation dose with or without chemotherapy; Data are presented as the mean±SD. The two matched groups were compared using the non-paired Student's t-test. *p＜0.05

Table 1. Difinition of appetite changes

Dietary characteristics	Symptoms
Palate	No matter what he/she eat, it does not taste. He/She feel the strong taste. Whatever he/she eat, it will taste metallic.
Olfactory	The smell became hard to feel. It became sensitive to smell. He/She got to feel an unpleasant smell.
Food shape	Hard foods can not be eaten. He/she started to like good foods over the throat. It became difficult to chew. It became difficult to swallow.
Temperature	Warm foods got hard to eat. Cold foods became easier to eat.
Taste	He/She hated the greasy foods. He/She hated the smell of strong foods. He/She began to like clear foods with a strong taste. He/She began to like fresh foods.

Table 2. Basic attribute

Subjects	126
Number of cases	643
Age (years)	68.2±9.9
Sex (man/woman)	430/213
BMI	21.3±3.1
Radiation therapy (with/without)	313/327
Radiation dose (Gy)	62.4±15.6
Chemotherapy (with/without)	416/227
Palate change (with/without)	27/616
Olfactory change (with/without)	40/603
Change in food shape (with/without)	296/312
Temperature change (with/without)	11/632
Taste change (with/without)	54/578
Anorexia (with/without)	144/1

Table 3. Comparison of treatment and appetite changes; Results were indicated that trends of appetite changes in patients with neck, upper chest, and esophageal cancer depending on treatment situations (A), and as a result of statistical analysis, the treatment situation in which a significant difference was recognized and the appetite change and olfactory change (B). Comparisons of proportions were compared using the χ^2 test. *$p<0.05$

A

	Chemotherapy/radiation therapy
Palate change	p=0.022*
Olfactory change	p=0.037*
Change in food shape	p=0.224
Temperature change	p=0.117
Taste change	p=0.604
Anorexia	p=0.298

B

	Chemotherapy/radiation therapy			
	None	Chemotherapy only	Radiation therapy only	Both
Palate change				
With	3 (1.9%)	3 (1.8%)	5 (7.8%)	16 (6.4%)
Without	157 (98.1%)	164 (98.2%)	59 (92.2%)	233 (93.6%)
Olfactory change				
With	4 (2.5%)	8 (4.8%)	5 (7.8%)	23 (9.2%)
Without	156 (97.5%)	159 (95.2%)	59 (92.2%)	226 (90.8%)

Patients who are undergoing treatment for chemotherapy/radiation therapy in cancer suffer from changes in palate, smell, food shape, taste and cooking temperature etc. with respect to meal intake due to adverse events such as surgery, radiation, anticancer drug treatment. These appetite changes greatly affect the dietary intake and quality of life (QOL), which may lead to worsening of nutritional status and lead to treatment interruption. Therefore, in order not to worsen the nutritional condition, it is necessary to grasp the change in the appetite of patients receiving cancer therapy.

Table 4. Comparison of chemotherapy or radiation therapy and appetite changes; Results were indicated that trends of the appetite change and olfactory change in patients with neck, upper chest, and esophageal cancer depending on chemotherapy or radiation therapy (A), and as a result of statistical analysis, the radiotherapy in which a significant difference was recognized and the appetite change and olfactory change (B). Comparisons of proportions were compared using the χ^2 test. *$p<0.001$

A

	Chemotherapy	Radiation therapy
Palate change	p=0.342	p=0.002*
Olfactory change	p=0.054	p=0.004*

B

	Radiation therapy	
	With	Without
	Number of cases (%)	Number of cases (%)
Palate change		
With	21 (77.8%)	6 (22.2%)
Without	292 (47.6%)	321 (52.4%)
Olfactory change		
With	28 (70.0%)	12 (30.0%)
Without	285 (47.5%)	315 (52.5%)

In the present study, we investigated ways in which chemotherapy/radiation therapy is manifested in appetite changes among cancer patients, and how these changes are related to treatment. We also developed a monitoring check sheet to grasp changes in appetite. It was revealed that during cancer treatment, many patients have decreased appetite for some reason, causing appetite changes that leads to anorexia, about 50% of patients have change in food shape, and palate and olfactory changes have been occurring in patients undergoing chemotherapy/radiation therapy.

Texture, seasoning, temperature, order and food form are important as food characteristics affecting appetite of oral cancer patients with adverse reactions. The appetite of the patient is determined by comprehensively judging these food characteristics. Additionally, it has been reported that the appetite of a patients is greatly influenced by the feeling of happiness that continues after a meal, the palatability that is caught as satisfaction6). Sako have reported that perception llike seasoning, smell and temperature is the characteristic that first affects appetite and then searches perception of texture and food form7). On the other hand, Nishinari et al., have reported that the texture greatly affects the taste depending on the content of intake8). In other words, it is a good guess to think that the superiority of food characteristics affecting taste will vary depending on the variety of foods and cooking contents. We thought that it was necessary to investigate the relationship between appetite changes and treatment in more detail and extracted the appetite changes from nutritionists' records and classified it into palate, olfaction, food shape, taste and temperature were classified. As a result, patients treated with cancer who undergo both radiation and chemotherapy were found to be complexly appearing as changes in appetite that causes palate and olfactory changes, which is a factor in the reduction in appetite. Especially, it became clear that radiation therapy affects palate and olfactory changes.

Table 5. Relationship between appetite changes; Results were indicated that trends of the relationship between appetite changes in patients with neck, upper chest, and esophageal cancer (A), and as a result of statistical analysis, a significant difference was palate change and olfactory change or change in food shape (B), olfactory change and change in food shape or taste change (C). change in food shape and taste change (D). Comparisons of proportions were compared using the χ^2 test. *$p<0.05$, **$p<0.001$

A

	Palate change	Olfactory change	Change in food shape	Temperature change	Taste change	Anorexia
Palate change		p=0.004**	p=0.032*	p=0.621	p=0.192	p=0.979
Olfactory change			p=0.027*	p=0.491	p=0.045*	p=0.924
Change in food shape				p=0.303	p=0.003**	p=0.815
Temperature change					—	p=0.993
Taste change						p=0.875
Anorexia						

B

	Palate change	
	With	Without
	Number of cases (%)	Number of cases (%)
Olfactory change		
With	6 (15.0%)	34 (85.0%)
Without	21 (3.5%)	582 (96.5%)
Change in food shape		
With	6 (2.0%)	290 (98.0%)
Without	16 (5.1%)	296 (94.9%)

C

	Olfactory change	
	With	Without
	Number of cases (%)	Number of cases (%)
Change in food shape		
With	5 (1.7%)	291 (98.3%)
Without	0 (0.0%)	312 (100.0%)
Taste change		
With	7 (13.0%)	47 (87.0%)
Without	33 (5.7%)	545 (94.3%)

D

	Change in food shape	
	With	Without
	Number of cases (%)	Number of cases (%)
Taste change		
With	14 (29.2%)	34 (70.8%)
Without	278 (50.6%)	271 (49.4%)

Although the mechanism of olfactive disorder associated with radiotherapy has not been clarified, it has also been reported that palate disorder occurs due to olfactive disorder9）. In cancer patients, palate change triggers lower appetite and nutritional condition deteriorates10), so it is considered that the effect of palate change as a side effect symptom is great for the decrease in appetite during chemotherapy. Loss of appetite in radiotherapy in neck, upper chest, and esophageal cancer patients may lead to a decrease in nutritional indicators such as serum

total protein, serum albumin, BMI and others11-13）. Chemotherapy shows that nausea and vomiting, fever and anxiety in cancer patients affect the decrease in dietary intake and it has been reported that patients who have strongly episode of gastrointestinal symptoms such as nausea, stomatitis and the like, have not reached the basal metabolic rate reference value in terms of protein intake and ingested energy14-15). Palate disorders according to side effects of radiation therapy are often caused by damage of the salivary glands due to irradiation of the oral cavity, pharynx and neck16). Three adverse events, palate disorder, intraoral desiccation and oral mucositis, exacerbate symptoms with cumulative irradiation dose and have a great influence on the appetite of cancer patients15).

In the effect on radiation dose, radiation dose of chemotherapy patients was significantly higher than those without patients. Ogama et al., reported that when the cumulative irradiation dose reaches more than 50 Gy, it affects the appetite of oral cancer patients, and texture, seasoning and smell have a characteristic of affecting the decrease in appetite17. In this study, since 89.5% were greater than or equal to 50 Gy, similar results were observed.

The association between appetite changes was that more frequent in patients with palate change and less change in food shape. In addition, significant differences were observed between olfactory change and food shape change, taste change, and patients with olfactory changes were found to have many changes in food shape and taste. Since sensory disorders other than palate are considered to be involved with a large part of taste function of the patient during and after the treatment18）, it is presumed that there is also an influence on the form. Moreover, factors that affect taste include aging, sex, smoking and drinking etc19）. In general, the age at which taste disorder tends to occur is after 50-60 years old20), which is consistent with the age of the subjects of this study. In other words, it is necessary to take into consideration not only the effects of chemotherapy/radiation therapy but also factors such as age, sex, lifestyle, etc. as the cause of taste change.

There are differences between the health professional and the patient in judgment of symptoms, and variations in response to the patient occur, as a problem in the current clinical practice. Thus, we suppose that evaluating objectively by scoring symptoms of side effects of patients leads to prevention of serious side effects caused by radiation and chemotherapy. For cancer patients, the proper diet is very important in terms of maintaining and improving feeling of well-being and quality of life. In cases of patients who cannot eat sufficiently, it is important to adjust the form and content of meals to compensate for the necessary nutritional content. In addition to direct symptoms caused by cancer, ingenuity that can alleviate various symptoms such as fatigue feeling, taste disorder, decreased appetite, etc. is required. In order to clarify factors that lead to a decrease in the appetite of individual cancer patients, we developed a monitoring check sheet corresponding to changes in appetite. In the future, using this monitoring check sheet, it is necessary to consider to be able to predict the timing of provision of meals for nutrition support such as “Bocchiri Meal” 24) before the patient’s QOL decreases.

In conclusion, we demonstrated that the relationship between treatment and dietary change and importance of grasping appetite changes in addition to treatment situation in cancer patients. From these results, to clarify factors that lead to a decreased appetite in individual cancer patients, we considered it necessary to develop a monitoring check sheet focused on changes in appetite. Our developed monitoring check sheet was based on appetite, palate, olfaction, food shape, temperature, change in taste, and treatment.

Conflict of Interest

All the authors declare that they have no conflict of interest.

References

1 Morran, C. Smith, D. C.Anderson, D.C. et al.,(1979). Incidence of nausea and vomiting with cytotoxic chemotherapy: a prospective randomizer trial of antiemetics. BMJ 1: 1323-1324.

2 Jenns, K.: Importance of nausea. (1994). Cancer Nurs 16: 488-493.

3 Kanda, K. Iida, M. Kano, T. (1999). National survey of hospital meals for cancer patients. Annals of Gunma University School of Health Sciences (In Japanese). 20: 13-20.

4 Unsal, D. Mentes, B. Akmansu, M. et al.,(2006). Evaluation of Nutritional status in cancer patients receiving radiotherapy: a prospective study. Am J of Clin Oncol 29: 183-188.

5 Bansal, M. Mohanti, B.K. Shah, N. et al.,(2004) Radiation rerated morbidities and their impact on quality of life in head and neck cancer patients receiving radical radiotherapy. Qual Life Res. 13: 481-488.

6 Ogama, N. Ogama, N. Katayama, T.(2010). A reviw of the literature of sense organsystem adverse effect and food characteristics according to radiation therapy for oral cancer patients. Journal of Japanese Society of Human Caring Research (In Japanese). 10: 9-16.

7 Sako, N.(2006) Physiological basis of oral somatosensory and chemical senses. Journal of Japan Association on Odor Environment (In Japanese). 37: 417-423, 2006

8 Nishinari,K. Ogoshi,H. Koyam,K.(2005) SyokkanSouzou Handbook. Tokyo. Science Forum, Print, 2005, Pp.25-94.

9 Hahn, R. Kruskemper.G.(2007) The impact of radiotherapy on quality of life a survey of 1411 patients with oral cancer. Mund Kiefer Gesichtschir 11: 96-106.

10 Holmes, S. (1993) Food avoidance in patients undergoing cancer chemotherapy. Support Care Cancer 1: 326-330.

11 Tamura, S.Okada, K. Miki, H.(2009) Zoukibetsunimanabugannochishiki・chiryou・Eiyouryouhou Touchoubu gan.. Nutrition Care 2.Pp 360-365.

12 Nugent, B. Lewis, S. O’Sullivan, J.M.(2010) Enteral feeding methods for nutritional management in patients with head and neck cancers being treated with radiotherapy and/ or chemotherapy. Cochrane Database Syst Rev 17: 36-44.

13 Munshi, A. Pandey, B. Durga, T. et al.,(2003) Weight loss during radiotherapy for head and neck malignancies: what factors impact it? Nutr Cancer 47: 136-140.

14 Tonosaki, A. Kazuma, K. Ishiguro, Y.(1993) A study of changes in the Nutritionalstatus of patients receiving cancer chemotherapy. Japan Journal of Nursing Science (In Japanese). 13: 12-19.
15 Kanda, K. Iida, M. Ishida, K.(1998) The influence of cancer chemotherapy on the food intake in patients with hematological malignancies. Annals of Gunma University School of Health Sciences (In Japanese). 19: 51-57.
16 Ruo Redda M.S. Allis, S.(2006) Radiotherapyinduced taste impairment. Cancer Treat Rev 32: 541-547.
17 Ogama, N. Katayama, T. Ogama, N.(2011)Touchoubugankanja ni okeruhousyasenchiryounitomonau yuugaijishouto shokujisessyunikansurukentou. Journal of Japanese Society of Human Caring Research (In Japanese). 2: 1-10.
18 Nakazato, M. Endo, S. Tomita, H. et al., (1995) Influence of aging on electrogustometric threshold. Journal of Otolaryngology of Japan (In Japanese). 98: 1140-1153.
19 Ito, M. Okazaki, M. (1994) Roshihouniyorushokuenmikakuikichinioyobosuyouin. The Jornal of Kagawa Nutrition University (In Japanese). 25: 41-47.
20 Ikeda, M. (2006) Mikakuijou-Sonokijotochiryou-. MB ENT 70：1-7,
21 Watanabe, K. Numata, S. Shimada, I. et al.,(2016) Impact of meals for nutritional support in patients with cancer. Journal of the Japanese Association of Rural Medicine (In Japanese). 65: 758-765.
22 Hosoi, T.（2014） "Intake of Protein and Vitamins Effective at Preventing or Improving Sarcopenia" The Japanese Journal of Clinical Nutrition, Vol. 124，No. 3