Nutritional Management in Laryngeal Cancer with Pharyngocutaneus Fistula Post Total Laryngectomy

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ABSTRACT: Laryngeal cancer with total laryngectomy can lead to the reduction of nutritional parameters. In regards to the high catabolism waste in cancer patients due to underlying diseases or surgery and were worsen by postoperative complications such as fistulas and wound healing problems, special attention to nutritional management is recommended. A 36 years-old male was consulted after a total laryngectomy two weeks before and had a tracheostomy inserted previously. He had received blended diet and nutrition formula through a naso gastric tube (NGT) and 24-hours food recall were 1390 kcal. He has history of alcohol abuse and smoking since 13 years ago. He ate eat grilled and salted fish almost every day. He was malnourished (BMI 18.25 kg/m^2). The following readings were obtained: hemoglobin 11.0 g/dL, albumin 2.6 g/dL, total protein 4.2 g/dL and total lymphocyte count (TLC) 390/μL. Diet were given slowly until total energy requirement achieved with target 2400 kcal and protein 1,5-2,0 gram/kg/day through NGT. Extract snake-head fish, multivitamin and zinc were given as food supplement. On the sixth day, we started to weane enteral nutrition by giving oral nutrition from liquid to semisolid diet. Pharyngocutaneus fistula was found on the 10th day of nutrition therapy, NGT was then inserted again. Fish oil and vitamin C were added as antiinflammatory to improve fistula wound healing. After the fifth week, we began to provide him oral intake. Patient was discharge with BMI 18.4 kg/m^2, hemoglobin 12.8 g/dL, albumin 4.2 g/dL, total protein 7.3 g/dL and TLC 1250/μL. We conclude that a adequate nutrient intake include food supplementation were recommended to improve wound healing and nutritional parameters.

Keywords: Laryngeal cancer, nutritional management, pharyngocutaneus fistula, total laryngectomy.

Introduction

Laryngeal cancer is the most common head and neck cancer with up to 95% being squamous cell carcinomas (SCC). An estimated of 12,360 adults in the USA would be diagnosed with laryngeal cancer in 2012 (9840 men and 2520 women) with 3650 deaths. In Australia, the risk of being diagnosed with laryngeal cancer by age 85 is 1 in 275 with 214 deaths reported in 2007 (Martin *et al.,* 2012). The male-to-female incidence ratio is about 4:1. In Indonesia, head and neck cancer is 5% of all malignancies and the incidence of laryngeal cancer about 1-2% (Ferryan, 2012). Major risk factors for SCC are tobacco, smoking and alcohol consumption. There are also occupational risk factors which include exposure to asbestos, chemicals and solvents (Martin *et al.,* 2012).

Treatment for laryngeal cancer is determined by the site and extent of the tumor. Over the last decade, treatment for early laryngeal cancer has shifted towards organ sparing management approaches using surgical options and/or radiotherapy. However, in advanced laryngeal

disease, primary total laryngectomy may be indicated particularly if other surgeries or concurrent chemotherapy/radiotherapy alone are not appropriate (Vilho, 2004). Total laryngectomy is a surgical procedure which involves the removal of larynx, along with the epiglottis, thyroid cartilage, a number of tracheal rings and the hyoid bone. There is no longer any connection between the upper airway and the trachea. The person permanently breathes through a stoma at the base of the neck. Patients who had suffered from laryngeal cancer and have undergone laryngectomy complain not only about physical disability and psychological changes, but also nutritional impairment (Vilho, 2004; Asthiani, 2010).

Nutrition in cancer is an important aspect in the overall approach to the cancer patient. Cancer is associated with the increased morbidity and mortality in the general population. One of the co-morbidities associated with cancer is malnourished and this is associated with a risk of complications, increased length of stay in hospital, and mortality. All of that increase cost of care and represent an important financial burden on the healthcare system. Therefore, it is important to understand how cancer affects the metabolism in order to prevent a decline in nutritional status which will affect the development of disease (Liu *et al.,* 2011).

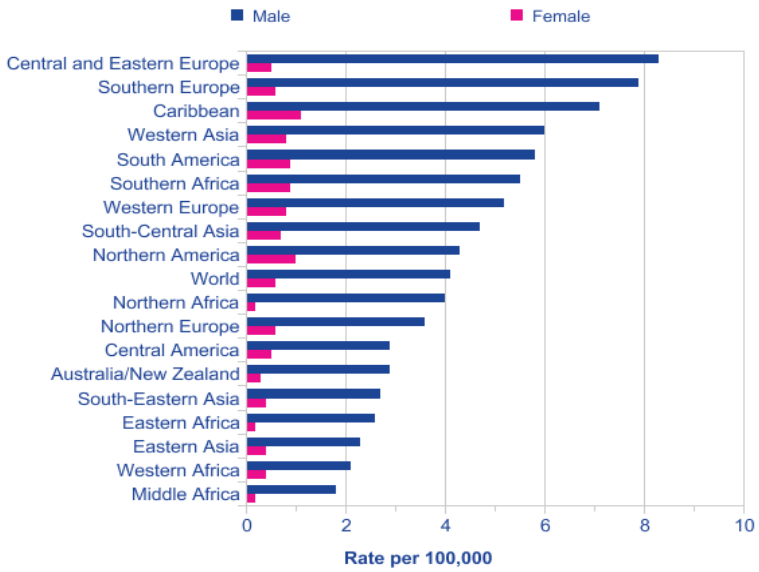

Figure 1: Laryngeal cancer (C32), World Regions, 2008 Estimates
Adopt from Cancer Research UK (available at: http://www.cancerresearchuk.org/cancer-info/cancerstats/types/larynx/incidence/uk-laryngeal-cancer-incidence-statistics).

Patients who have to undergo total laryngectomy for laryngeal cancer often experience malnutrition before surgery and this increases the risk of postoperative complications. It has been reported that about 40% of new patients diagnosed with laryngeal cancer are malnourished even before the initiation of the treatment protocol. Some related researches have found that several nutritional parameters such as body mass index (BMI), and total lymphocyte count in cancer patients are lower than normal subjects. Some researchers also suggest that weight loss is the best parameter for assessing nutritional status in patients with head and neck cancer surgery. All the parameters of nutritional status, including weight loss, weight variation, BMI, and several laboratory values such as albumin and lymphocytes worsened after surgery. In another study in the Netherlands, it was shown that the nutritional parameters of nutritional status were identified as aspects involved, such as malnutrition,

which varied between 20% and 67% in patients undergoing major surgery in head and neck cancers. Approximately 54% of head and neck cancer patients who had undergone surgery became malnourished (Asthiani *et al.,* 2010).

Adequate nutrition is a contributing factor in the success of therapy in cancer patients. Malnutrition during the postoperative period affects wound healing and increases risk of complications. Prioperative nutritional supplementation has been shown to be effective in improving clinical outcomes in multiple surgeries and reduce the incidence of postoperative complications and improve quality of life (Grant B, 2008; Liu *et al*., 2011).

Nutrition intervention in cancer patients can involve many strategies, including nutritional education and food supplementation. The goals of nutritional support in patients with cancer are numerous and include maintaining an acceptable weight and preventing or treating protein-calorie and micronutrient deficiencies, leading to better tolerance of treatment and its side effects, more rapid healing and recovery, reduced risk of infection during treatment, and enhanced overall survival (Jager-Wittenaar *et al.,* 2010; Buijs *et al*., 2010).

Case Report

The patient, a 36-years old male, was admitted to the hospital on 29 th November, 2011 with a known diagnosis of laryngeal cancer. The patient, who underwent a total laryngectomy on 1st December, had a tracheostomy inserted previously. He had no previous history of any other illnesses. He had received blended diet and nutrition formula through naso gastric tube (NGT) and 24-hours food recall were 1390 kcal. He has a history of alcohol abuse and smoking since 13 years ago. He ate grilled and salted fish almost every day due to his accupation as a sailorman and seldom took fruits and vegetables.

The patient was referred to the clinical nutrition department on 15th December 2011 for nutritional management. Upon physical examination, we found anemis in his conjungtiva and pitting edema on lower extremity. The patient's laboratory values for hemoglobin was 11.0 g/dL, albumin 2.6 g/dL, total protein 4.2 g/dL and total lymphocyte count (TLC) 390/µL. Body weight at the consulted time was 54 kg after correction for edema.

The assesment of nutritional status for the patient was stated as mild underweight based on the BMI of 18.25 kg/m2 according to WHO classification. His metabolic statuses were anemia normositic normokromic, hypoalbuminemia, hypoproteinemia and severe immune depletion. His gastrointestinal status was stated as functional.

The total enegy expenditure (TEE) that we planned for this patient was based on Harris-Bennedict calculations, using the ideal body weight of 64.8 kg and added with physical activity and stress factor of 1.2 and 1.3, respectively. From the calculation, the value of TEE was 2400 kcal/day, which were made up with protein: 1.5 – 2.0 gram/kg body weight/day = 97-129.5 gram/day (16% - 21.5 %); carbohydrate: 50 % (300 gram/day), and fat: 28.5%-34% (76-90.5 gram/day). Diet were given starting from 1800 kcal through naso-gastric tube (NGT) with blended diet 3x300 kcal /day, high protein nutrition formula 3 size/day, and juice 100 ml/day. The amount of these nutrients will gradually increased based on patient's condition and tolerance until TEE achieved. Fluid requirement for the patient was 2400 ml/day. Supplementation was also given with extract snake-head fish 6 capsules/day, multivitamin injection 1 vial/day and zink 20 mg/day. Food intake was monitored every day and his nutritional statuses such as body weight and mid upper arm circumference were

measured every week. Laboratory examination was also carried out. Nutrition counselling was also given to the patient and his families.

The patient received enteral nutrition through NGT between 16 December and 20 th December. On the sixth day, we started to weane enteral nutrition by giving him oral nutrition from liquid to semisolid diet. However, pharyngocutaneus fistula was developed on the 10th day of nutrition therapy (**Figure 2**); NGT was inserted for enteral nutrition. Therefore, 2 gram fish oil /day and 500 mg vitamin C /day were given as anti-inflammatory agents to improve fistula wound healing.

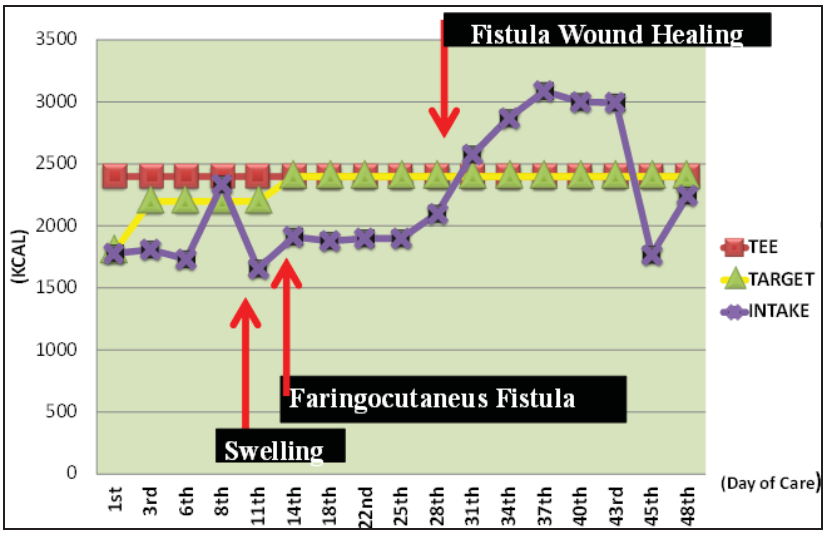

Figure 2: Monitoring of Daily Calorie Intake

After the fifth week, we began to provide him with oral intake. Patient was discharge after two months of hospitalization with BMI 18.4 kg/m^2, hemoglobin 12.8 g/dL, albumin 4.2 g/dL, total protein 7.3 g/dL and TLC 1250/µL, **Figure 3**.

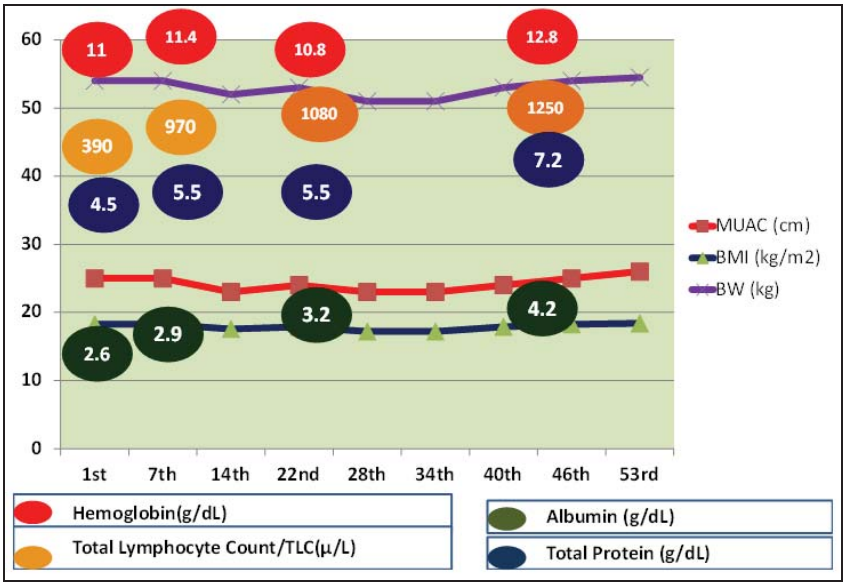

Figure 3: Antropometric and Laboratory Monitoring

Discussion

Patients was referred to the clinical nutrition by the Ear, Nose and Throat specialist to get nutritional management with medical diagnosis post laryngectomy total et causa laryngeal cancer and malnutrition status. Total laryngectomy was done two weeks ago. He had a tracheostomy inserted previously for breathing and naso gastric tube (NGT) for enteral nutrition line since the surgery and had received blended diet and nutrition formula through NGT since the third day of surgery. There were about 63% of total energy expenditure with protein 0.95 g/kg /day. No heavy complaints except the patient sometimes feel pain in the postoperative wound.

Upon physical examination we found anemis of conjunctiva which is accompanied by a decrease in Hb laboratory result at 11 g/ dL. The results for MCV, MCH, and MCHC were normal so it can be said that the patient had normochromic normocytic anemia (red blood cells with normal size and colour). This type of anemia is common in patients with malignancy. Anemia in patients with surgical wound can cause delay in wound healing and could lead to complications such as fistula formation in patients post total laryngectomy. Collagen deposition and wound healing is limited by perfusion and tissue oxygen tension. It is therefore important to maintain the hemoglobin level at a normal level to maintain peripheral tissue perfusion that can supply oxygen to the wound healing process (Jonsson *et al.,* 1991). For this patient, we treat the anemia symptom with ensured intake of macronutrient and micronutrient.

Ascites was found characterised by shifting dullness and pitting edema of the pretibial and dorsal pedis. Laboratory results showed hypoalbuminemia and hypoproteinemia. This is due to the process of malignancy (cancer cachexia) as the protein reserves are used. Low albumin level might increase morbidity and mortality. This is because albumin is important to maintain colloid osmotic pressure, the binding and transport of drugs, especially and some nutrients, as an antiplatelet and antithrombotic, effector of vascular permeability, and a powerful antioxidant that binds to free radicals (ROS) (Don and Kaysen, 2004; Bernardi *et al.,* 2012). Our corrections to hypoproteinemia and hypoalbuminemia were with a high protein intake of between 1.5 to 2 g/kg/day and snake-head fish extract 6 capsules per day. One capsule of snake-fish extract weighs 750 mg, containing 70% protein and 21% albumin (Taslim *et al.,* 2005).

Systemic proinflammatory processes are activated in majority of tumour-bearing patients. Resulting metabolic derangements include insulin resistance, increased lipolysis and higher than normal or increased lipid oxidation with loss of body fat, increased protein turnover with loss of muscle mass and an increase in production of acute phase proteins. Systemic inflammatory reaction that develops in many of the cancer cases is an important cause of loss of appetite (anorexia) and weight. The syndrome of decreased appetite, weight loss, metabolic alterations and inflammatory state is referred to as cachexia, cancer cachexia or cancer anorexia–cachexia syndrome (CACS), **Figure 4**. These cytokine-induced metabolic alterations appear to prevent cachectic patients from regaining body cell mass (BCM) during nutritional support. They are also associated with a reduced life expectancy that is not relieved by exogenous nutrients alone. Attempts to modulate these changes by other means should be integrated into the management of cancer patients. Nutritional assessment of cancer patients should be performed frequently. Nutritional intervention should be initiated as early as possible when deficits are detected (Oncology Nutrition Dietetic Practice Group, 2006; Kumar, 2012; Sauer and Voss, 2012).

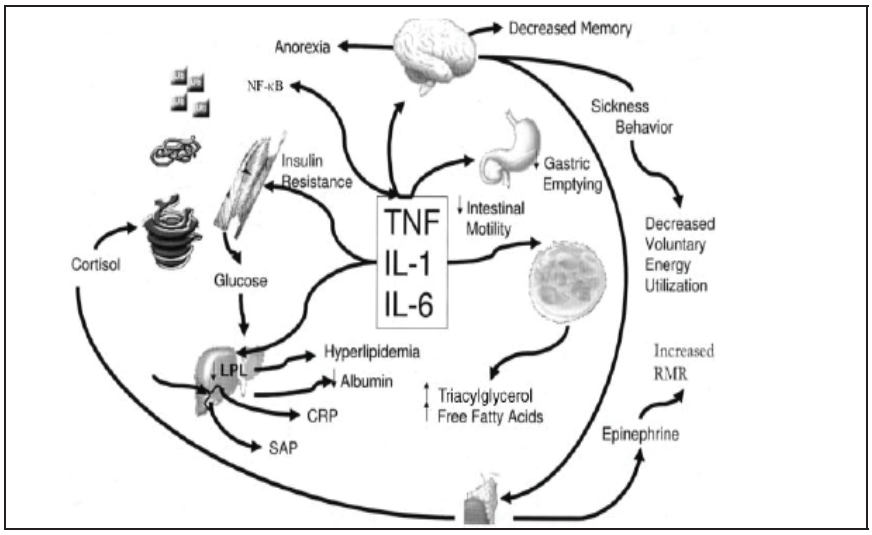

Figure 4: The pathophysiologic role of cytokines in the production of cachexia. (TNF, tumor necrosis factor; IL-1, interleukin 1; IL-6, interleukin 6; RMR, resting metabolic rate; LPL, lipoprotein lipase; CRP, C-reactive protein; SAP, serum amyloid protein).(Adopt from Morley. J.E, Thomas. D.R, Wilson. M.G.(2006). Cachexia: pathophysiology and clinical relevance. Am J Clin Nutr. 83:735– 43)

Three major mechanisms that have impact on the nutritional status in patients with cancer are reduced ability to efficiently process nutrients as a result of impaired glucose, lipid, and protein metabolism; increased energy requirements, secondary to tumor growth, infection/fever, inflammatory status, surgery, and cancer treatments; and decreased food intake, resulting from side effects such as nausea, vomiting, constipation, diarrhea, and anorexia. Many studies have demonstrated that maintaining a good nutritional status through nutrition intervention can help individuals with cancer. Cancer patients undergo treatment often need extra calories and nutrients, especially protein. Resting energy expenditure (REE) is often increased and thus making it difficult to gain or maintain weight. Adequate calorie and protein intake is vital for maintaining and improving nutritional status (Buijs *et al*., 2010; Kumar, 2012).

Nitrogen balance is an index of whether physiological protein requirements are being met. Many patients with cancer are in negative nitrogen balance, a catabolic state in the body involving muscle degradation resulting in excess nitrogen excretion, in contrast to nitrogen consumption. Provision of additional dietary protein is essential to supply nitrogen for maintenance of nitrogen balance and to prevent muscle breakdown (Buijs *et al*., 2010). Recomendation for optimal target protein supply in cancer patients based on the European Society for Clinical Nutrition and Metabolism (ESPEN) guidelines was 1,2-2 g/kgBW/d (Sauer and Voss, 2012).

The patient received enteral nutrition through NGT for five days. On the sixth day we started to weane enteral nutrition by giving oral nutrition from liquid to semisolid diet. Swelling around operative wound was found on the 10^{th} day nutrition therapy and pharyngocutaneus fistula developed one week later with leakage of saliva and food material from an opening

wound on the neck. NGT was inserted again on the 10th day to maintain adequate nutrient intake and to prevent the worsening of wound.

Numerous contributing factors have been implicated in fistula formation. Preoperative radiotherapy especially of high doses, short interval between radiotherapy and operation, prior tracheotomy, tumor localization and size, advanced tumor stage, tumor differentiation, presence of positive tumor margins, extensive surgery, type of pharyngeal closure, concurrent radical neck dissection, suture material, low serum albumin (<3.5 g/dL), low level of serum proteins (<6.5 g/dL), poor preoperative nutritional and medical status such as uncontrolled diabetes, liver diseases, low postoperative hemoglobin level, gastroesophageal reflux, alcohol consumption, fever in the immediate postoperative period, significant postoperative vomiting, technical errors and early oral feeding have been implicated as potential risk factors contributing to fistula formation (Landera, 2008; Sharifian, 2008).

Pharyngocutaneus fistula found on the 32th day post total laryngectomy could be due to lack of some nutritional parameters such as patient who were already malnourished before surgery, had low level of albumin (2.6 g / dL), low total protein level (4.5 g / dL), and low postoperative hemoglobin level at 11 g / dL. Slow oral nutrition may also be a contributing factor to pharyngocutaneus fistula. Soylu et al., (1997) stated that early oral nutrition in 24-48 hours after surgery did not cause significant additional stress to the suture line. Under normal conditions, saliva is swallowed constantly at a rate of 1500 mL/24 hours. Saliva is potentially and mechanically as harmful as other swallowed liquids or soft foods. The concept of early oral feeding after laryngectomy stemmed from the realization that most laryngectomy patients begin to swallow their saliva in 24 to 48 hours after surgery. Furthermore, some authors thought that the NGT itself is probably more irritating to the suture line than swallowing. The time of oral feeding may have little to do with the development of fistula and the motion of the NG tube was probably more irritating than oral feeding three times a day. With both methods, patients swallow their saliva which never lets the pharynx rest totally. Oral feeding does not give significant additional stress to the suture line which may cause fistula formation. It is also clear that the carrying of an NG tube for approximately two weeks is uncomfortable and a major stress factor for the patient in addition to having its own complications. It has been shown that it can also be an ascending path to infect the wound (Sharifian et al., 2008).

The location of tumor in supraglotic areas influences fistula formation. Locations of supraglotic laryng includes epiglottic (including the surface of the tongue and larynx), aryepiglotic fold, aritenoid and false vocal cords. Squamous cell carcinoma in the supraglotic laryng accounted for 35% of laryngeal cancer, where 50% of these patients showed metastasis to servical lymphs (Beenken *et al.,* 2006).

Nutritional intervention in cancer patients must be supplemented with electrolytes, trace elements and vitamins (Areuds *et al*., 2006). Due to the elevated oxidative stress and increased levels of antioxidants in cancer patients, inclusion of increased doses of antioxidant vitamins might be suggested (Sauer and Voss, 2012). Patients are given a multivitamin supplementation injection 1 vial per day containing vitamin A, B, C and E. Zinc supplementation 20 mg / day is also added.

Six capsule of snake-headfish extract per day is also provided. In addition to protein and albumin, these capsules also contain several essential amino acids such as arginine and glutamine which play a role in wound healing and improved the immune status, as well as containing some essential minerals for the body such as zinc and selenium (Isenring *et al*.,

2007). Glutamate in extract snake-head fish improves flavor and palatability. Six capsules of pujimin per day contain 34.8 mg of glutamate. L-glutamic acid has a beneficial action of intestinal function by stimulating the l-glutamate receptors associated with the vagus nerve. In addition, dietary l-glutamate is an important energy substrate for enteric tissue. Glutamate is also important in the digestion of proteins and accelerates the gastric emptying (Yamamoto *et al.,* 2009; Zai *et al.,* 2009). Fish oil containing omega-3 is added when pharyngocutaneus fistula is formed. Omega-3 fatty acids are antagonist competitors of omega-6 arachidonic acid precursors that are converted into less active pro-inflammatory mediators. Omega-3 fatty acids have also been shown to increase appetite and body weight in cancer patients (Mac Kay and Miller, 2003; Arends *et al.,* 2006).

Nutrition education is an important part of nutrition interventions. Therefore, nutrition education is constantly given to patient and his family about the importance of balanced nutrition in order to achieve good quality of life.

The recommendations for this patient include the following:

1. Maintain BMI in range of 18.5–25 kg/m2.
2. Engage in regular physical activity
3. Consumption of alcoholic beverages is not recommended: if consumed, do not exceed 2 units/d (1 unit is equivalent to approximately 10 g of alcohol and is provided by one glass of beer, wine or spirits)
4. Chinese-style salted fish should only be eaten moderately. Overall consumption of salt-preserved foods and salt should be moderate
5. Have a diet which includes at least 400 g/d of total fruit and vegetables
6. Meat: those who are not vegetarian are advised to moderately consume of preserved meat (e.g. sausages, salami, bacon, ham etc.) and red meat (e.g. beef, pork, lamb).
7. Do not consume foods or drinks when they are at a very hot (scalding hot) temperature (Key *et al.,* 2004).

Conclusion

Poor nutritional status and malnutrition are common in patients with laryngeal cancer. These nutritional challenges significantly increase morbidity and mortality in these patients, and severe cases can lead to cancer cachexia. Nutritional management, including food supplementation, improves outcomes in cancer patients, nutritional parameters, wound healing, and quality of life. A multidisciplinary approach among all healthcare professionals involved in cancer care is necessary to identify at-risk patients early in the process and provide them with the appropriate and effective nutritional interventions.

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