



Symptom clusters in patients with nasopharyngeal carcinoma during radiotherapy



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ABSTRACT

Purpose: Despite the improvement in radiotherapy (RT) technology, patients with nasopharyngeal carcinoma (NPC) still suffer from numerous distressing symptoms simultaneously during RT. The purpose of the study was to investigate the symptom clusters experienced by NPC patients during RT.

Methods: First-treated Chinese NPC patients ($n = 130$) undergoing late-period RT (from week 4 till the end) were recruited for this cross-sectional study. They completed a sociodemographic and clinical data questionnaire, the Chinese version of the M. D. Anderson Symptom Inventory - Head and Neck Module (MDASI-HN-C) and the Chinese version of the Functional Assessment of Cancer Therapy - Head and Neck Scale (FACT-H&N-C). Principal axis factor analysis with oblimin rotation, independent *t*-test, one-way analysis of variance (ANOVA) and Pearson product-moment correlation were used to analyze the data.

Results: Four symptom clusters were identified, and labelled general, gastrointestinal, nutrition impact and social interaction impact. Of these 4 types, the nutrition impact symptom cluster was the most severe. Statistically positive correlations were found between severity of all 4 symptom clusters and symptom interference, as well as weight loss. Statistically negative correlations were detected between the cluster severity and the QOL total score and 3 out of 5 subscale scores.

Conclusion: The four clusters identified reveal the symptom patterns experienced by NPC patients during RT. Future intervention studies on managing these symptom clusters are warranted, especially for the nutrition impact symptom cluster.

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1. Introduction

Nasopharyngeal carcinoma (NPC) is endemic in South-East Asia (Torre et al., 2015), with the highest rates observed in the Cantonese population of southern China (Chang and Adami, 2006; Jia et al., 2006). For this reason, NPC is called “Cantonese cancer” (Jia, 2008). Radiotherapy (RT) alone for early stage patients and combined chemoradiotherapy for locoregionally advanced cases of the

disease are the main treatments for NPC (Agulnik and Epstein, 2008; Xia et al., 2013). With RT techniques advanced and transformed from conventional 2-dimensional (2D) RT to 3-dimensional (3D) conformal or intensity-modulated RT (IMRT), the curative effect of treatment has increased and the 5-year overall survival rate of NPC patients can reach up to 70–80%. (Cao et al., 2011; Tsai et al., 2012).

However, significant disease- and treatment-related symptoms such as taste change, dry mouth, sticky saliva, sore throat, lack of appetite and difficulty in swallowing remain of major concern to NPC patients undergoing treatment (Chan et al., 2003; Han et al., 2010; Huang et al., 2000; Liu and Qin, 2011). During the widely practiced 6- to 7-week course of the RT regimen for treating NPC, it was found that most symptoms escalated at week 3 and continued

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to worsen throughout the RT course (Huang et al., 2000). Further, the severity and duration of symptoms increased when chemotherapy (CTX) was combined with RT (Agulnik and Epstein, 2008; Qiu et al., 2011; Sumitsawan et al., 2009), leading to treatment interruption, psychological distress, decreased functional status and poor quality of life (QOL) (Chen et al., 2000; Fang et al., 2002; Wu et al., 2007). Timely identification and management of these symptoms can yield better patient outcomes (Chan et al., 2014; Lenz and Pugh, 2013).

Further, instead of occurring in isolation, there is ample evidence that symptoms often occur in clusters, which may exacerbate the overall symptom experience (Cheng et al., 2009; Cleeland, 2007; Kwekkeboom et al., 2010). A symptom cluster has been defined as 2 or more related symptoms which occur together and form a stable group, relatively independent of other clusters (Kim et al., 2005). Because cancer patients seldom present with a single symptom, understanding and managing symptom clusters could be of considerable clinical significance. Further, there is evidence that symptom clusters can have synergistic effects on important patient outcomes, including functional status (Dodd et al., 2010; Oh et al., 2012), QOL (Dodd et al., 2010; So et al., 2009; Wang and Fu, 2014), emotional status (Breen et al., 2009) and even survival (Aktas et al., 2012; Jiménez et al., 2011). Managing a symptom cluster as a whole could therefore be more efficient and effective than managing single symptoms (Chan et al., 2011, 2013; Kwekkeboom et al., 2010). However, there seems to be no information on symptom clusters in NPC patients during RT. Studies to examine symptom clusters in NPC patients are needed, which is the first step to be taken before testing any interventions to manage them.

The current study was guided by the updated Theory of Unpleasant Symptoms (TOUS) (Lenz et al., 1997), which consists of 3 main reciprocal elements: symptoms, influencing factors and functional performance. Symptoms form the central concept. In this study, we investigate symptom clusters experienced by NPC patients. In respect of influencing factors, we focus on patients' sociodemographic and clinical characteristics. Functional performance is the consequence of the symptom experience. In the current study, symptom interference with daily living is the outcome of particular interest. QOL is also examined because it was considered as another important outcome of symptom experience by the TOUS developers (Lenz and Pugh, 2013).

The purpose of the study was to identify symptom clusters experienced by NPC patients undergoing RT, with or without CTX, and to examine the relationships between symptom clusters and patients' sociodemographic and clinical characteristics, as well as key patient outcomes, including symptom interference and QOL.

2. Methods

2.1. Patient recruitment

In this cross-sectional study, patients were recruited consecutively from the NPC department of Sun Yat-sen University Cancer Center (SYSUCC). The inclusion criteria were: (1) first-treated Chinese NPC patients; (2) currently in the late period (from week 4 till the end) of RT because symptoms are obvious then; (3) 18 years old or above; and (4) able to understand either Mandarin or Cantonese. Patients with other serious diseases, including diagnosed psychiatric morbidity and other types of cancer, were excluded. Ethical approval was obtained from the Survey and Behavioural Research Ethics Committee (SBREC) of the Chinese University of Hong Kong before data collection began. All participants signed consent forms.

2.2. Treatment regimen

In SYSUCC, IMRT is currently the mainstay RT modality for NPC. The primary gross tumor volume (GTVnx) and the involved lymph nodes (GTVnd) include all known gross disease as determined by imaging, clinical and endoscopic findings. The clinical target volume-1 (CTV-1) is defined as the high-risk region that includes GTV plus a 5- to 10-mm margin. It also includes the entire nasopharyngeal mucosa plus 5-mm submucosal volume. The CTV-2 is designed for potentially involved regions, which include CTV-1 plus a 5- to 10-mm margin. High-risk nodal regions are also included. Generally, the prescribed RT doses for GTVnx, GTVnd, CTV-1 and CTV-2 are 68–70 Gy, 60–70 Gy, 60–64 Gy and 54–58 Gy respectively, in 30–32 fractions. In SYSUCC, RT is delivered at 1 fraction per day, 5 days per week, and lasts for 6–7 weeks.

For patients with locoregionally advanced NPC, concurrent CTX with or without neoadjuvant CTX is adopted. The typical regimen for neoadjuvant CTX uses a combination of cisplatin (80–100 mg/m², d1) and 5-fluorouracil (total dose: 4000 mg/m², d1–5) administered intravenously every 3 weeks in 2 cycles before RT starts. While for concurrent CTX the regimen delivers cisplatin (80–100 mg/m², d1) alone at the same time as RT every 3 weeks in 2 or 3 cycles.

2.3. Study instruments

The instruments consisted of a sociodemographic and clinical data questionnaire, a weighing scale, the Chinese version of the M. D. Anderson Symptom Inventory - Head and Neck Module (MDASI-HN-C), and the Chinese version of the Functional Assessment of Cancer Therapy - Head and Neck Scale (FACT-H&N-C) (version 4).

The sociodemographic and clinical data questionnaire was designed to collect information on gender, age, place of residence, educational level, marital status, occupational status, monthly household income, body weight before RT, co-morbidities, stage of disease, type of RT, number of times of RT, and whether being treated with CTX. The data were collected by participants' self-reporting and review of medical records.

Patients' current body weight was measured by a weighing scale. The weighing scale has an electronic screen and the body weight can be displayed on it directly. The unit for body weight is kilogram with one digit after the decimal point. Patients were required to weigh themselves twice to assure the accuracy of reading. Weight loss was calculated by subtracting current body weight from the body weight before RT.

The MDASI-HN-C was used to examine symptom clusters among NPC patients. The 28-item MDASI-HN is a validated head and neck cancer (HNC) specific instrument (Rosenthal et al., 2007) with 3 subscales: 13 core MDASI items that assess the severity of generic cancer related symptoms, 9 HNC-specific items that rate the severity of symptoms associated with HNC, and 6 interference items that evaluate the influence of symptoms on daily living activities. All symptoms are rated on a 0–10 scale to indicate the presence and severity of the symptoms in the last 24 h, with 0 indicating "not present" and 10 "as bad as you can imagine". The interference items are also measured on a 0–10 scale, with 0 indicating "did not interfere" and 10 "interfered completely". In this study, the Cronbach's α coefficients were 0.91, 0.85 and 0.88 for the 13 core MDASI items, the 9 HNC-specific items, and the 6 interference items, respectively.

The 39-item FACT-H&N (version 4) is a validated HNC-specific QOL instrument (List et al., 1996; Ringash et al., 2008) consisting of 5 subscales that measure patients' physical well-being (7 items), social/family well-being (7 items), emotional well-being (6 items), functional well-being (7 items) and HNC-specific QOL issues (12

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