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Original Article

Symptom distress and interference among cancer patients with osteoradionecrosis of jaw: A cross-sectional study

Dongye Yang^{a,*}, Feng Zhou^b, Xinyu Fu^a, Jinsong Hou^a, Liting Lin^a, Qiyu Huang^a, Chao Hsing Yeh^c^a Guanghua School of Stomatology, Hospital of Stomatology, Sun Yat-sen University, Guangdong Provincial Key Laboratory of Stomatology, Guangzhou, China^b Center for Adverse Drug Reaction Monitoring of Chengdu, Sichuan, China^c Johns Hopkins School of Nursing, Baltimore, USA

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ABSTRACT

Objective: Osteoradionecrosis of the jaws (ORNJ) is among the most serious oral complications of head and neck cancer treatment with radiation therapy. This study aimed to examine the level of symptom distress and interference of ORNJ in head and neck cancer patients in China.

Methods: A cross-sectional study was conducted to profile patient reported symptom severity. Ninety-five hospitalized ORNJ patients were recruited. Participants completed the MD Anderson Symptom Inventory–Head and Neck Module-Chinese version.

Results: The percentage of participants who reported that they experienced at least one type of symptom was 97.9%, and 85.2% patients reported interference. The 10 most severe symptoms were as follows: limited mouth opening, problem with teeth/gums, difficulty swallowing/chewing, dry mouth, oral malodor, difficulty with voice/speech, dental ulcer, tinnitus/ear obstruction, skin pain/burning/rash, and difficulty hearing. The problem of limited mouth opening was more severe in patients with longer time to onset of ORNJ after radiotherapy. The interference of patients positively correlated with core symptoms ($r = 0.612$), head and neck symptoms ($r = 0.709$), and ORNJ symptoms ($r = 0.440$) ($P < 0.01$). The longer time to the onset of ORNJ after radiotherapy was positively and significantly correlated with symptom distress ($r = 0.479$, $P < 0.001$), and mouth opening correlated negatively with symptom distress ($r = -0.298$, $P = 0.003$).

Conclusions: ORNJ patients suffered mainly from limited mouth opening and other maxillofacial symptoms. The problem of limited mouth opening was more severe in patients with longer time to onset of ORNJ after radiotherapy. ORNJ patients commonly had symptom distress, which influenced their quality of life.

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What is known?

- Osteoradionecrosis of the jaws (ORNJ) is one of the most serious oral complications of head and neck cancer treatment with radiation therapy.
- Patients who have ORNJ suffer from severe pain, orofacial fistulas, exposed necrotic bone, and pathological fractures.

- There are many reports on the diagnosis and treatment of ORNJ at home and abroad, but reports symptom distress and interference of ORNJ patients are lacking.

What is new?

- Symptom distress and interference of ORNJ patients begin to be concerned about, and ORNJ patients commonly have symptom distress, which is closely associated with the symptom interference.
- ORNJ patients suffer mainly from limited mouth opening and other maxillofacial symptoms, and that the problem of limited

* Corresponding author. No.56, Lingyuan West Road, Guangzhou, 510055, China.

E-mail address: yangdy@mail.sysu.edu.cn (D. Yang).

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mouth opening is more severe in patients with longer time to onset of ORNJ after radiotherapy.

- The longer time to the onset of ORNJ after radiotherapy is closely associated with more serious symptom distress.

1. Introduction

Head and neck cancer (HNC) is identified as the seventh most common cancer, and over 500,000 new cases of head and neck squamous cell carcinoma (HNSCC) are reported annually in the world [1,2]. Radiotherapy combined with surgery or chemotherapy has become an effective treatment for many malignancies at the head and neck area. While the prognosis has improved, it comes with a price. For example, one of the most severe adverse effects of radiotherapy is osteoradionecrosis of jaws (ORNJ) [3]. It was reported that 5%–15% of patients with HNC suffer from ORNJ [4–6]. ORNJ is defined as an area of exposed devitalized irradiated bone that fails to heal over a period of 3–6 months in the absence of local neoplastic disease [7,8]. ORNJ can also be characterized by bone tissue necrosis and failure of healing; ORNJ either stabilizes or gradually worsens and is notoriously difficult to manage [7–9].

Patients who have ORNJ suffer from severe pain, orofacial fistulas, exposed necrotic bone, and pathological fractures. The symptoms of ORNJ can negatively affect their quality of life [4,5]. Severe symptom distress may delay scheduled treatments, decrease the effectiveness of treatment protocols, and delay the rehabilitation process [10]. Alleviation of symptoms can greatly affect patients' quality of life [10]. To improve the symptom management of ORNJ patients, understanding the symptom distress and interference before development of effective interventions is crucial to reduce distressing symptoms and improve their quality of life [11]. To date, reports on symptom distress and interference of ORNJ patients at home and abroad are lacking. This study aimed to examine the level of symptom distress and interference of ORNJ in HNC patients in China.

2. Methods

2.1. Study design

This was a cross-sectional study that investigated the symptom distress and interference among Chinese patients with ORNJ.

2.2. Setting and sample

The inclusion criteria were as follows: (1) first diagnosis of ORNJ; (2) primary medical diagnosis was HNC; (3) received radiotherapy for HNC; (4) ≥ 18 years old; (5) able to read and understand Chinese; and (6) willing to cooperate in the study. Exclusion criteria were as follows: (1) mental illnesses or drug dependency; (2) local recurrence or distant metastasis; or (3) severe infection or other comorbidity.

2.3. Ethical consideration

This study obtained ethical approval from the institutional review board of a stomatological hospital (approval no. ERC-2014-32). Permission for the use of research instruments in the present study was obtained. All participants signed the consent form. All personal information was placed securely as highly confidential file according to the Institutional Review Board policies.

2.4. Measurements

2.4.1. Demographics record

The following data were collected from participants' charts: age, gender, primary disease, and ORNJ onset time.

2.4.2. Symptom distress and interference

The M. D. Anderson Symptom Inventory–Head and Neck Module (MDASI-HN) was a reliable and valid instrument to measure HNC symptom distress, as well as symptom interference in the major aspects of a patient's daily life [12]. The 28-item instrument consisted of three subscales, namely, 13 core MDASI items that rated the severity of general symptoms associated with generic cancer, 9 HNC-specific items that rated the severity of specific symptoms associated with HNC, and 6 interference items that assessed the influence of symptoms on daily activities. The core and HNC-specific symptoms were rated by using a 0–10 scale to indicate the presence and severity of the symptoms, with 0 indicating “not present” and 10 indicating “as bad as you can imagine.” The interference items were also measured on a 0–10 scale, with 0 indicating “did not interfere” and 10 indicating “interfered completely.” The cut point of the severity of symptoms on the MDASI-HN was categorized as mild (score 1–4), moderate (score 5–6), or severe (score 7–10) [12]. Patients were asked to rate each item according to severity in the previous 24 h. In this study, The Chinese version of the MDASI-HN was used, and 17 items were added to assess symptom distress for ORNJ patients [13]. The Cronbach's α reliability coefficients were 0.91, 0.95, 0.93, and 0.87 for the 13 core items, the 9 HNC-specific items, the 6 interference items, and the 17 supplementary items, respectively. The supplementary items had good content validity and were assessed by five oral and maxillofacial surgery experts.

2.4.3. Mouth opening

The mouth opening was the vertical distance between upper, middle, and lower incisors near the central incisal margin and was measured by a millimeter steel ruler [14]. According to Subjective Objective Management Analysis (SOMA) [15], mouth opening wider than 3 cm was regarded as normal, and limited mouth opening was divided into four grades, as follows: (1) Grade I: 2–3 cm, limitation of mouth opening; (2) Grade II: 1–2 cm, difficulty in eating dry food; (3) Grade III: 0.5–1 cm, difficulty eating of diet; and (4) Grade IV: < 0.5 cm, need nasal feeding. Grades III and IV were defined as severe trismus.

2.5. Data collection

Participants were recruited consecutively (from February 2015 to February 2017) from the inpatient unit of a stomatological hospital. The researchers explained the purpose and content of the research to potential participants. All participants signed the consent form and received a package of the study questionnaires on the first day of hospitalization. The questionnaires were collected immediately after completion. The entire procedure took about 20 min. Questionnaires were distributed to 100 participants; and 5 questionnaires were not completed. In total, 95 completed questionnaires were regarded as valid.

2.6. Statistical analysis

All statistical analysis procedures were performed on SPSS for Windows software (version 17.0; Chicago, IL, USA). The scores of symptom distress and interference were described with means and standard deviation, and the relationship was analyzed by using Pearson's correlation analysis. The differences in symptom distress

between gender and cancer diagnosis groups were compared by *t*-tests. The Spearman's correlation analysis was used to examine the correlation of symptom distress and age, the longer time to onset of ORNJ after radiotherapy and the mouth opening of ORNJ. A *P* value of less than 0.05 was considered statistically significant.

3. Results

3.1. Demographic characteristics

Among 95 participants, 65 were male, and 30 were female. The cancer diagnosis was consistent with nasopharyngeal carcinoma (NPC) ($n = 75$, 79.0%) and oral and maxillofacial malignancy ($n = 20$, 21.0%), including tongue carcinoma ($n = 1$), gingival carcinoma ($n = 2$), palatal carcinoma ($n = 2$), buccal mucosa carcinoma ($n = 1$), maxillary sinus carcinoma ($n = 1$), and oropharyngeal cancer ($n = 1$). The mean age of the participants was 54.00 ± 11.04 years (range: 29–80).

The median onset time of ORNJ was 6.0 years (range: 0.5–20.0). Among participants with NPC, 60.0% developed ORNJ after 3–10 years since radiotherapy; 70.0% of participants with other oral and maxillofacial malignancies developed ORNJ within the first 3 years after they received radiotherapy.

3.2. Symptom distress and interference of ORNJ participants

The mean scores of symptom distress and interference of ORNJ participants were 4(1.95, 5.36) and 2.67(1.00, 5.67), respectively. In terms of the prevalence of the symptom distress, 97.9% of participants reported that they suffered from at least one type of symptoms, 57.9% at mild level, 30.5% at moderate level, and 9.5% at severe level, whereas 85.2% of participants reported interference. The 10 most severe symptoms were one core symptom (Dry mouth), four HNC-specific symptoms (Problem with teeth/gums, difficulty in swallowing/chewing, difficulty with voice/speech and skin pain/burning/rash), and five ORNJ symptoms (Limited mouth opening, oral malodor, dental ulcer, tinnitus/ear obstruction and difficulty hearing)(Table 1). Among the symptoms experienced by the participants, limited mouth opening had the highest level of severity, and symptom distress had the greatest influence on ORNJ participants' mood. Limited mouth opening had 84.2% incidence, and among patients who experienced this, 48.4% reported severely limited mouth opening.

3.3. Relationship between symptom distress and interference of ORNJ participants

The study presented the relationships among core symptoms, HNC-specific symptoms, ORNJ symptoms and interference, which indicated that the interference of patients positively correlated with core symptoms ($r = 0.612$), head and neck symptoms ($r = 0.709$), and ORNJ symptoms ($r = 0.440$) ($P < 0.01$). The associations between symptom distress and general activity and walking were not statistically significant ($r_{\text{general activity}} = 0.182$, $P = 0.078$; $r_{\text{walking}} = 0.172$, $P = 0.095$) (Table 2).

3.4. Relationships between symptom distress and sociodemographic and clinical characteristics of ORNJ participants

The associations between symptom distress and age and gender were not statistically significant. However, the longer time to onset of ORNJ after radiotherapy was positively and significantly correlated with more serious symptom distress ($r = 0.479$, $P < 0.001$). Limited mouth opening was the most severe symptom of ORNJ participants. The mean dimension of the mouth opening

was 1.2(0.5, 3.0) cm, which was classified as "Grade 2," which means the participant had "difficulty eating dry food." Limited mouth opening correlated negatively with symptom distress ($r = -0.298$, $P = 0.003$).

Furthermore, the mean score of symptom distress in participants with NPC was 4.01 ± 1.71 , which was higher than that with oral and maxillofacial malignancy (3.08 ± 2.05) ($t = -2.086$, $P = 0.040$).

4. Discussion

This is a study to investigate symptom distress and interference of ORNJ among patients with ORNJ in China. Clarifying symptom distress is the first step to the development of effective strategies to manage symptoms for ORNJ patients.

4.1. Symptom distress and interference of most patients were at mild level

The mean score of symptom distress was 4(1.95,5.36), and the mean score of symptom interference was 2.67(1.00,5.67), both were higher than the results of Han Yuan [13] and Lai et al. [11]. Han Yuan et al. [13] reported that NPC patients typically had symptom distress during and after radiotherapy, as follows: 86.7% were mild and 13.3% were moderate to severe. In this study, the incidence of symptom distress was 97.9%; 57.9% of participants had mild symptom distress, whereas 40.0% had moderate to severe. The incidence of interference symptoms was 85.3%; 52.6% of the participants had mild interference symptoms, whereas 32.6% had moderate to severe. ORNJ patients commonly experienced symptom distress. Symptom distress and interference were at mild level for most patients.

4.2. Symptoms interfered with patients' daily lives

Correlation analysis showed that symptom distress was positively correlated with symptom interference. It meant that higher symptom interference scores were reported for patients with more severe symptoms. The results were the same as those in other studies [13,16]. The reasons were the stress reaction of patients to disease and hospitalization, and their negative mood, which was due to sequelae of radiotherapy and disease development. Symptoms interfered with patients' lives in the aspects of fun, work, and relationships. The possible causes of interference include troubles of pronunciation or speaking, hearing loss, or oral malodor. Symptoms may cause communication barriers and may affect interpersonal relationships and work. Problems with teeth or gums, difficulty chewing/swallowing, dry mouth, and other oral health problems may affect patients' food consumption, thereby affecting their daily life. The associations between symptom distress and general activity and walking were not statistically significant, possibly because ORNJ patients were mainly affected by oral and maxillofacial symptoms.

4.3. Limited mouth opening was the most severe symptom for ORNJ patients

Different cancers have different symptom distress. Han Yuan et al. [13] reported that the main symptoms in NPC patients included taste alteration, throat pain, dry mouth, oropharyngeal mucus, chewing, or swallowing difficulties. Lai et al. [11] reported that the symptoms in Taiwanese NPC patients within 3 years of receiving radiation therapy (RT) commonly included dry mouth, oral ulcers, pain, fatigue and weakness, anorexia, and change in flavor perception. Rosenthal et al. [16] reported that severe

Table 1
Order of symptom distress and interference of ORNJ participants ($n = 95$).

Item	$M (P_{25}, P_{75})$	Range
Symptom distress(core and HNC items)	4.00 (1.95, 5.36)	0–7
Core		
Dry mouth	5.00 (2.00, 8.00)	0–10
Pain	4.00 (1.00, 6.00)	0–9
Difficult remembering	4.00 (1.00, 6.00)	0–10
Distress	4.00 (1.00, 7.00)	0–10
Fatigue	4.00 (2.00, 5.00)	0–8
HNC		
Problem with teeth/gums	7.00 (4.00, 9.00)	0–10
Difficulty swallowing/chewing	5.00 (4.00, 9.00)	0–10
Difficulty with voice/speech	5.00 (2.00, 7.00)	0–10
Skin pain/burning/rash	5.00 (2.00, 7.00)	0–10
Problem tasting food	5.00 (0, 7.00)	0–10
ORNJ		
Limited mouth opening	7.00 (5.00, 10.00)	0–10
Oral malodor	5.00 (3.00, 7.00)	0–10
Dental ulcer	5.00 (2.00, 8.00)	0–10
Tinnitus/ear obstruction	5.00 (2.00, 7.00)	0–10
Difficulty hearing	5.00 (0, 7.00)	0–10
Symptom interference	2.67 (1.00, 5.67)	0–8
Mood	3.00 (2.00, 6.00)	0–10
Enjoyment of life	4.00 (0, 6.00)	0–10
Work	3.00 (0, 6.00)	0–8
Relations with other people	2.00 (0, 5.00)	0–10
General activity	2.00 (0, 5.00)	0–9
Walking	2.00 (0, 5.00)	0–10

Note:HNC = head and neck cancer; ORNJ = osteoradionecrosis of jaws.

Table 2
Relationship between symptom distress and interference of ORNJ participants ($n = 95$).

Interference of ORNJ	Symptom interference	Mood	Enjoyment of life	Work	Relations with other people	General activity	Walking
r	0.664*	0.608*	0.473*	0.541*	0.554*	0.182	0.172

Note: $P < 0.01$.

symptom distress among patients with radiotherapy included problems with tasting food, saliva production, chewing, and swallowing. Wenli Xiao et al. [17] reported that the five most severe symptoms of NPC patients undergoing late-period RT included problem with tasting food, saliva production, dry mouth, difficulty swallowing/chewing, and lack of appetite. In this study, the 10 most severe symptoms were limited mouth opening, problem with teeth/gums, difficulty swallowing/chewing, dry mouth, oral malodor, difficulty with voice/speech, dental ulcer, tinnitus/ear obstruction, skin pain/burning/rash, and difficulty in hearing. Limited mouth opening was the most severe symptom. Furthermore, the top five symptom distress items were at moderate levels. The results are not completely in accordance with other studies possibly because of differences in subjects and research times after radiotherapy. Han Yuan et al. [13] and Lai et al. [11] targeted nasopharyngeal carcinoma patients during and after radiotherapy, whereas Rosenthal et al. [16] targeted HNC patients before radiotherapy or after chemoradiotherapy within 6 weeks. In this study, the majority of the participants were patients with NPC. Furthermore, Lai et al. [11] used a general symptom distress scale for HNC patients, which may have caused the differences in results.

Weber [18] indicated that radiotherapy is a major cause of limited mouth opening and other oral complications in patients with ORNJ. The incidence of limited mouth opening was influenced by multiple factors, as follows: radiotherapy dosage, age, radiation-induced fibrosis, dry mouth, and radiation stomatitis [19]. After radiotherapy, the incisor teeth spacing of patients reduced within 1–2 years, and progressing time after radiotherapy, the incidence of limited mouth opening increased and stabilized in 2–3 years; however, the severity of limited mouth opening increased [20]. Bhrany et al. [19] showed that 50.0% of patients had limitation of temporomandibular joint (TMJ) and masticatory muscles activity

after radiotherapy. Chen Ming et al. [21] showed that limited mouth opening was the most common complication after radiotherapy of NPC. The incidence rate was 58.5%, and the incidence of severe trismus was 7.1%. Severe trismus may cause malnutrition or cachexia, which can seriously affect patients' health and quality of life [22].

In this study, limited mouth opening was the most severe symptom and was very conspicuous among the ORNJ patients. The incidence of limited mouth opening was 84.2%, of which 48.4% was severe. The relationship between mouth opening and the longer time to onset of ORNJ after radiotherapy was statistically significant. Mouth opening of ORNJ patients showed a decreasing trend with progressing time after radiotherapy.

4.4. Characteristics of ORNJ patients in different primary diseases

Johnson [23] reported that ≥ 12 months and 24–60 months were high-risk periods of onset of ORNJ. Thorn et al. [24] found that 74.0% of patients developed ORNJ within the first 3 years. In this study, 60.0% of participants with NPC developed ORNJ after 3–10 years since radiotherapy. In 70.0% of participants with other oral and maxillofacial malignancies, ORNJ occurred within the first 3 years. In most case, ORNJ occurred earlier in participants with oral and maxillofacial malignancy than those with NPC after radiotherapy.

Furthermore, ORNJ patients diagnosed with NPC had more severe symptoms. Symptom distress was more severe in patients with the longer time to onset of ORNJ after radiotherapy. Given the finding that patients with NPC developed ORNJ with longer time to onset of ORNJ after radiotherapy, patients may suffer symptom distress for a longer duration than patients with other HNCs.

5. Limitations of this study

The major limitation of this study is the single-center design and the small sample size, which may negatively impact the generalizability of the findings to other study settings and populations. Furthermore, the study had a cross-sectional design. Thus it did not reveal the changing patterns of symptoms of ORNJ patients. The use of self-developed questionnaire was another limitation of this study.

6. Conclusions

ORNJ patients suffered mainly from limited mouth opening and other maxillofacial symptoms. The problem of limited mouth opening was more severe in patients with the longer time to onset of ORNJ after radiotherapy. Thus, routine screening of the level of limited mouth opening among HNC patients undergoing radiotherapy is needed. This study confirmed that ORNJ patients commonly have symptom distress, which can influence their quality of life. Oncology nurses should be aware of the complications of radiotherapy and recognize the distressing symptoms experienced by ORNJ patients. Healthcare providers should regularly evaluate symptom distress, including limited mouth opening and maxillofacial symptoms among ORNJ patients who underwent radiotherapy. Future research is required to address the symptom management strategies, such as symptom interventions, especially mouth opening training for patients after radiotherapy, as well as social support and cognitive therapy. Interventions should be developed to enhance the management of symptoms, including limited mouth opening and maxillofacial symptoms for ORNJ patients after radiotherapy, to improve their quality of life [24]. Next, we study the effect of interventions, such as singing practice, on the prevention and treatment of symptom distress of irradiated patients with HNC.

Conflicts of interest

There is no conflict of interest to declare.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ijnss.2019.05.006>.

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