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Original Article

# Perioperative symptom burden and its influencing factors in patients with oral cancer: A longitudinal study

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ABSTRACT

*Objective:* The aim of this study was to identify the symptom burden of perioperative oral cancer patients, its trajectory, and the factors influencing it.

*Methods:* A longitudinal, repeated measures design with consecutively identified sampling was used to recruit oral cancer patients scheduled for surgical treatment. Data collected included sociodemographic and clinical information, nutritional risk by the Nutritional Risk Screening 2002, and symptom burden by M. D. Anderson Symptom Inventory-Head and Neck Module (MDASI-HN) at preoperation, 7 days postsurgery, and 1 month postsurgery.

*Results:* Perioperative patients with oral cancer had multiple symptoms. Pain, difficulty swallowing/chewing, and mouth/throat sores (61.9%–76.1%) were the most prevalent symptoms before surgery. The symptom burden was the highest at 7 days after surgery, with the most prevalent symptoms, including difficulty swallowing/chewing, difficulty with voice/speech, and problems with mucus (87.8%–95.4%). At 1 month postsurgery, the 3 main symptoms were numbness or tingling, difficulty swallowing/chewing, and difficulty with voice/speech (all 87.8%). Treatment stage, job, comorbidity, cancer stage, adjuvant therapy, and Nutritional Risk Screening 2002 score were correlated with symptom burdens.

*Conclusions:* Our study illustrates that perioperative oral cancer patients have multiple symptoms and high symptom burdens, especially at 7 days postsurgery, with prominent symptoms and symptom burdens varying with the treatment stage.

## Introduction

The oral cavity is the most common subsite of head and neck mucosal malignancies, ranking 11th among the most common carcinoma around the world.[1] Approximately 405,000 new cases of oral cancer occur each year, and the incidence has shown an upward trend for the last decade.[1–3] Because of the heterogeneity in habits and customs, the incidence of oral cancer varies widely across countries and regions. For example, oral cancer accounts for approximately 5% of all malignancies in the United States, whereas in India, oral cancer accounts for 35% to 40%.[4] Squamous cell carcinoma is the most common histological subtype, and the standard treatment for oral cancer is primary tumor resection with or without radiochemotherapy.[2]

The oral cavity consists of lips, tongue, floor of mouth, buccal mucosa, upper and lower gums, retromolar trigone, and hard palate, all of which perform critical physiological functions in eating, chewing, tasting, phonation, respiration, and communication. Oral cancer patients experience multiple symptoms after surgery because of the damage to physiological structures. Chewing difficulties, decreased salivary function, and swallowing dysfunction are the most significant issues in oral cancer patients undergoing radical tumor resection and simultaneous reconstruction after neoadjuvant radiochemotherapy.[5] The literature showed that 10% of patients with oral cancer had moderate to severe dysphagia before treatment, and 27% had moderate to severe dysphagia 6 months after treatment, and their swallowing functions failed to reach the baseline level at 1-year posttreatment.[6]

The severity of symptoms in oral cancer patients is affected by a variety of factors. Hasegawa et al. reported that advanced tumor stage, bilateral neck dissection, and the resection of unilateral or bilateral suprahyoid muscles were associated with the severity of dysphagia in

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oral cancer patients.[7] A pilot study concluded that the speech and swallowing function of oral cavity cancer patients depended on many factors, including tumor size, tumor site, area of resection, method of reconstruction, and tongue's range of motion.[8] Weight loss and malnutrition were associated with many symptoms, such as swallowing, dry mouth, pain, and speech.[9] However, there are limited studies on the factors influencing the total symptom burden of patients.

The types, manifestations, and severity of symptoms in oral cancer patients change dynamically with different stages of treatment. Roba et al. reported that the quality of life and functional status of tongue cancer patients 1 month after surgery were worse than those before surgery and 3 months after surgery.[10] A systematic review noted that speech and swallowing functions showed a significant decline at the early postoperative (1 month) stage in tongue cancer patients.[11] There was also evidence that head and neck cancer patients receiving radiotherapy and chemotherapy suffered from the heaviest symptom burden in the treatment phase, whereas those treated with surgery experienced the heaviest symptom burden at 3–9 days postsurgery.[12,13] However, it remains unclear what the trend of symptoms is for patients undergoing oral cancer surgery. As shown by studies, enhanced recovery after surgery, with one of its main principles being to reduce stress, including symptom relief,[16] could significantly improve the clinical outcomes for head and neck cancer patients undergoing surgery.[14,15] Therefore, if the main symptoms and their severity in oral cancer patients undergoing surgery were clarified, health care providers could implement treatment protocols accordingly to promote rapid rehabilitation and improve clinical outcomes.

Hunan Province is located in South Central China, where residents are accustomed to betel nut chewing. In consequence, the incidence of oral cancer is much higher than the average level in China and is on the rise year by year.[17] Patients with oral cancer experience moderate to severe deterioration in quality of life due to the development of multiple symptoms, including xerostomia, dysphagia, and chewing difficulties.[18,19] Yet, the prominent trajectory of change in perioperative symptom burdens and the factors influencing symptoms in oral cancer patients have not been clearly identified. A better understanding of the characteristics and change trajectories of symptoms would facilitate more effective management of these symptoms.

Therefore, we formulated our research hypothesis as follows: (1) patients with oral cancer in Hunan Province endure a heavy burden of symptoms; (2) the prominent perioperative symptoms will change over time; and (3) their symptoms may be affected by sociodemographic factors, disease conditions and treatments, and nutritional risk. In this study, we aim to (1) describe the main symptoms and their changing trends from preoperation to 7 days postsurgery and 1 month postsurgery and (2) identify the correlates of total symptom burdens among oral cancer patients.

## Methods

### *Study design and setting*

A longitudinal descriptive study design was used. From February to September 2020, we recruited participants from 3 Head & Neck Surgery Departments at a tertiary cancer hospital in Hunan Province, China.

### *Participants and procedures*

Eligible participants had been diagnosed with oral cancer by pathological examination. Inclusion criteria were patients who were (1) aged > 18 years; (2) scheduled for surgical treatment; (3) able to understand Chinese; and (4) willing to participate and provide informed consent. Patients were excluded if they had (1) other cancers and distant metastases; (2) recurrent head and neck cancer; (3) declined surgery; and (4) secondary surgery due to complications, such as vascular crisis of free flaps.

Evidence showed that the severity of symptoms in oral cancer patients was the greatest at approximately 3–9 days after operation as a result of surgical trauma.[12] The symptoms will be relieved after discharge as tissues are repaired and functions recover. Therefore, we chose 3 time points for symptom burden assessment, preoperation (Time #1), 7 days postsurgery (Time #2), and 1 month postsurgery (Time #3).

A research nurse who was responsible for presenting information regarding the research to eligible participants screened potential patients via electronic medical records. If the patients were willing to participate in the study, they would complete questionnaires at 3 periods.

### *Sociodemographic and clinical characteristics*

The sociodemographic information included gender, age, education, marital status, place of residence, job, income, medical insurance, and history of smoking, alcohol consumption, and betel nut chewing. Clinical information was extracted from electronic medical records, covering comorbidity, diabetes mellitus, cancer stages, tumor histology, treatment methods, and tracheotomy.

### *Nutritional risk*

Nutritional Risk Screening 2002 (NRS 2002), consisting of impaired nutritional status (based on weight loss, body mass index, and general condition or food intake) and disease severity, was used to assess the nutritional risk. Each predictor was scored between 0 and 3 points, with an extra point for patients aged $\geq$ 70 years.[20] A data collection form was used to obtain information about changes in body weight, food intake, and severity of disease. A total score exceeding 3 points was considered a "risk" of malnutrition. This scale has been recommended as a screening tool by the European Society of Parenteral and Enteral Nutrition.[21]

### *Symptom burden*

Symptom burden was measured using the M.D. Anderson Symptom Inventory-Head and Neck Module-Chinese version (MDASI-HN).[22] This instrument was developed by Rosenthal et al. at the University of Texas M.D. Anderson Cancer Center in 2007[23] to evaluate the symptom burden and its interference with daily life. MDASI-HN includes 3 subscales (13 core MDASI items are used to assess the severity of generic cancer-related symptoms, 9 head and neck cancerspecific items to rate the severity of head and neck cancerrelated symptoms, and 6 items to evaluate daily life distress). In this study, we used the 13 core items and 9 specific items. All symptoms were rated on an 11-point (0–10) scale to indicate the presence and severity of symptoms in the past 24 h, with 0 indicating "not present" and 10 indicating "as bad as you can imagine." In this study, the Cronbach's alpha coefficients of the 22-item instrument were between 0.739 and 0.927.

### *Data analysis*

Descriptive statistics were used to summarize sociodemographic and clinical characteristics as well as symptom scores. Frequencies and percentages were used to describe categorical variables. The Kolmogorov–Smirnov test was used to identify whether the data conformed to the normal distribution. Continuous variables were summarized in terms of means, standard deviation, and range for normal distribution. Nonnormally distributed variables were summarized in terms of quantile [M (Q1, Q3)]. Age was categorized into 3 groups for easier comparisons (< 40 y, 40–60 y, and > 60 y).

The $\chi^2$ test was used for the presence or absence of symptoms at the 3 time points. The symptom scores at the 3 time points were compared using the Wilcoxon rank-sum test. The alpha level of multiple comparisons was adjusted according to the following formula:

$$\alpha' = \frac{\alpha}{\frac{k(k-1)}{2} + 1}$$

to control the type I error. In this study, the $\alpha'$ was 0.0125.

To investigate the factors associated with the total symptom scores, a generalized estimating equation (GEE) model was applied to accommodate the correlated data of repeated measurements (Time #1, Time #2, and Time #3) in the same patient. The symptom scores served as a continuous dependent variable, whereas sociodemographic and clinical characteristics served as covariates.

A 2-tailed test with $P < 0.05$ was considered statistically significant. Internal consistency was estimated by calculating the Cronbach's alpha coefficient. Statistical analyses were performed using IBM SPSS Statistics for Windows (Version 25.0; IBM Corp).

**Table 1**
Baseline sociodemographic and clinical characteristics of all participants ($n = 197$).

| Variables | *n* | % |
|---|---|---|
| Gender | | |
| Male | 171 | 86.8 |
| Female | 26 | 13.2 |
| Age (years) | | |
| < 40 | 21 | 10.7 |
| 40–60 | 139 | 70.6 |
| > 60 | 37 | 18.8 |
| Education level | | |
| Elementary school graduation | 52 | 26.4 |
| Middle school graduation | 103 | 52.3 |
| High school graduation | 27 | 13.7 |
| College graduation or above | 15 | 7.6 |
| Marital status | | |
| Without spouse | 7 | 3.6 |
| With spouse | 190 | 96.4 |
| Place of residence | | |
| Rural area | 117 | 59.4 |
| Town | 36 | 18.3 |
| Urban area | 44 | 22.3 |
| Job | | |
| Farmer | 96 | 48.7 |
| Worker | 53 | 26.9 |
| Staff | 14 | 7.1 |
| Retired | 17 | 8.6 |
| Self-employed | 17 | 8.6 |
| Income per month (yuan) | | |
| < 3000 | 82 | 41.6 |
| 3000–5000 | 77 | 39.1 |
| > 5000 | 38 | 19.3 |
| Medical insurance | | |
| None | 12 | 6.1 |
| New Cooperative Medical System | 111 | 56.3 |
| Basic Medical Insurance for Urban Employees | 27 | 13.7 |
| Basic Medical Insurance for Urban Residents | 47 | 23.9 |
| Smoking | | |
| No | 56 | 28.4 |
| Yes | 141 | 71.6 |
| Alcohol consumption | | |
| No | 120 | 60.9 |
| Yes | 77 | 39.1 |
| Betel nut chewing | | |
| No | 92 | 46.7 |
| Yes | 105 | 53.3 |
| Comorbidity | | |
| No | 143 | 72.6 |
| Yes | 54 | 27.4 |
| Diabetes mellitus | | |
| No | 178 | 90.4 |
| Yes | 19 | 9.6 |
| Cancer stage at diagnosis | | |
| Early stage (Phase 0 and I) | 61 | 31.0 |
| Moderate stage (Phase II) | 34 | 17.3 |
| Moderate or advanced stage (Phase III) | 49 | 24.9 |
| Advanced stage (Phase IV) | 53 | 26.9 |
| Tumor histology | | |
| Squamous cell carcinoma | 167 | 84.8 |
| Others | 30 | 15.2 |
| Adjuvant treatment | | |
| No | 147 | 74.6 |
| Yes | 50 | 25.4 |
| Tracheotomy | | |
| No | 151 | 76.6 |
| Yes | 46 | 23.4 |

### *Ethical considerations*

The study protocol and consent form were reviewed and approved by the Medical Ethics Committee of the University of South China (Approval No. January 6, 2020) before data collection. Each potential participant was informed of the purpose of the study, what they would be required to do, issues of confidentiality and anonymity, voluntary participation, and the right to withdraw at any time without consequences.

## Results

### *Characteristics of study participants*

Of the 260 patients screened, 22 were excluded. Among the excluded samples, 19 had recurrent oral cancer, 3 received secondary surgery (secondary free flap reconstruction surgery), and 32 declined to participate. Of the remaining 206 patients, as 9 did not complete all 3 questionnaires, 197 were included in the final sample.

Participants' sociodemographic and clinical characteristics are presented in Tables 1 and 2. The mean age of the participants was 52.6 years (standard deviation, 10.2; range, 30–87), 86.8% were male, 47.7% were in an advanced stage at the time of diagnosis, 84.8% had squamous cell carcinoma, and most participants did not receive adjuvant treatment (74.6%) at the end of the study. Of the participants, 27.4% suffered from certain comorbidities, such as hypertension, 9.6% had diabetes mellitus, and 23.4% had a tracheotomy after operation. Weight, body mass index, and NRS scores at 3 time points are presented in Table 3.

### *Prevalence, severity, and change of symptoms*

Figure 1 shows the presence of all 22 symptoms. At Time #1, pain (76.1%) was the most common symptom, followed by difficulty swallowing/chewing (64.0%), and mouth/throat sores (61.9%). At Time #2, difficulty swallowing/chewing (95.4%) became the most prevalent symptom, followed by problem with voice/speech (94.4%) and problem with mucus (87.8%). At Time #3, the incidence of numbness or tingling, difficulty swallowing/chewing, and difficulty with voice/speech all stood at 87.3%, being the most common symptoms.

Table 4 shows the change trajectory of the incidence and severity of 22 symptoms at 3 time points. The incidence of fatigue, feeling drowsy, dry mouth, problem with mucus, difficulty swallowing/chewing, and difficulty with voice/speech was the greatest at Time #2 and decreased at Time #3 but was still higher than at Time #1. The incidence of disturbed sleep and feeling sad significantly increased at Time #2 but returned to preoperative levels at Time #3. Feelings of being distressed,

**Table 2**
Years and quantity of smoking, alcohol consumption, and betel nut chewing.

| Variables | Years [Mean (SD)] | Quantity per day [Mean (SD)] |
|---|---|---|
| Smoking ($n = 141$) (number of cigarette) | 18.22 (14.42) | 18.53 (24.93) |
| Alcohol consumption ($n = 77$) (mL) | 8.90 (13.22) | 76.42 (147.43) |
| Betel nut chewing ($n = 105$) (piece) | 6.25 (8.17) | 12.92 (19.31) |

**Table 3**
Changes and comparison of weight, BMI, and NRS score at 3 time points.

| Variables | Time #1 [Mean (SD)] | Time #2 [Mean (SD)] | Time #3 [Mean (SD)] |
|---|---|---|---|
| Weight (kg) | 65.32 (9.80) | 63.71 (9.51) | 63.06 (8.93) |
| BMI (kg/m$^2$) | 23.66 (3.13) | 23.06 (3.02) | 22.84 (2.93) |
| NRS | 1.93 (1.08) | 2.97 (0.97) | 1.68 (1.26) |

BMI, body mass index; NRS, Nutritional Risk Screening 2002.

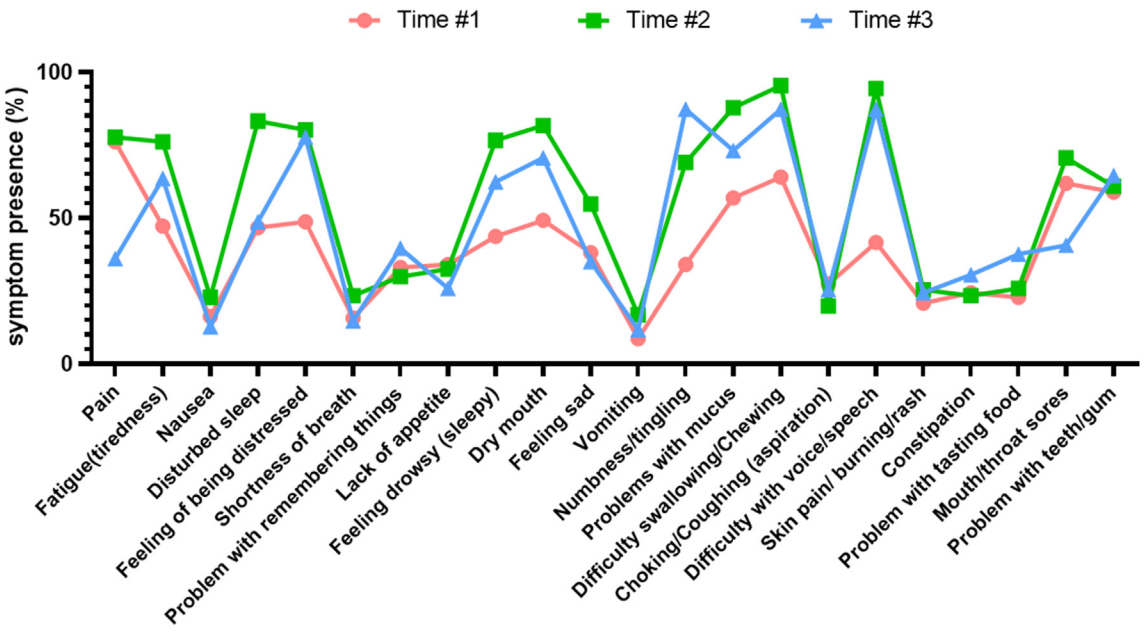


**Fig. 1.** Symptom presence ($n = 197$).

numbness/tingling, and problem with tasting food were more prevalent after surgery. The incidence of pain and mouth/throat sores significantly decreased at 1 month postsurgery.

Nonparametric estimation showed that the total symptom severity scores in terms of quartile [M (Q1, Q3)] were 20 (9, 40), 43 (31.5, 60), and 24 (16, 33.5) at Time #1, Time #2, and Time #3, respectively. At Time #2, fatigue, disturbed sleep, feelings of being distressed, feeling drowsy, dry mouth, feeling sad, vomiting, numbness/tingling, problem with mucus, difficulty swallowing/chewing, and difficulty with voice/speech were significantly more severe than at Time #1 ($P < 0.0125$). At Time #3, feelings of being distressed, dry mouth, numbness/tingling, problem with mucus, difficulty swallowing/chewing, difficulty with voice/speech, and problem with tasting food were significantly more severe than at Time #1; fatigue, nausea, disturbed sleep, feeling of being distressed, feeling drowsy, dry mouth, feeling sad, problem with mucus, difficulty swallowing/chewing, and difficulty with voice/speech were significantly less severe than at Time #2, whereas pain and mouth/throat sores were significantly less severe than at Time #1 and Time #2. Moreover, the total scores of MDASI-HN were significantly higher at Time #2 than at Time #1 and Time #3. At Time #3, the total scores of MDASI-HN decreased to the level of Time #1.

**Table 4**
The incidence, severity and comparison of symptoms at 3 time points ($n = 197$).

| Symptom | Time #1 | | | Time #2 | | | Time #3 | | | *Z* | Significant |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | With symptom[a] | | Median (Q1, Q3) | With symptom[a] | | Median (Q1, Q3) | With symptom[a] | | Median (Q1, Q3) | | |
| | *n* | % | | *n* | % | | *n* | % | | | |
| Pain | 150 | 76.1 | 2 (1, 3) | 153 | 77.7 | 2 (1, 4) | 71 | 36.0*# | 0 (0, 2)*# | 89.913 | <0.001 |
| Fatigue (tiredness) | 93 | 47.2 | 0 (0, 2) | 150 | 76.1* | 2 (1, 3.5)* | 125 | 63.5*# | 1 (0, 2)# | 45.640 | <0.001 |
| Nausea | 32 | 16.2 | 0 (0, 0) | 45 | 22.8 | 0 (0, 0) | 25 | 12.7# | 0 (0, 0)# | 7.812 | 0.020 |
| Disturbed sleep | 92 | 46.7 | 0 (0, 3) | 164 | 83.2* | 4 (2, 6)* | 96 | 48.7# | 0 (0, 2)# | 111.590 | <0.001 |
| Feeling of being distressed | 96 | 48.7 | 0 (0, 2) | 158 | 80.2* | 2 (1, 3)* | 153 | 77.7* | 2 (1, 3)*# | 36.057 | <0.001 |
| Shortness of breath | 31 | 15.7 | 0 (0, 0) | 46 | 23.4 | 0 (0, 0) | 29 | 14.7# | 0 (0, 0) | 6.995 | 0.030 |
| Problem with remembering things | 65 | 33.0 | 0 (0,1.5) | 59 | 29.9 | 0 (0, 1) | 78 | 39.6# | 0 (0, 2) | 3.965 | 0.138 |
| Lack of appetite | 67 | 34.0 | 0 (0,1) | 64 | 32.5 | 0 (0, 1) | 51 | 25.9 | 0 (0, 1) | 3.599 | 0.165 |
| Feeling drowsy (sleepy) | 86 | 43.7 | 0 (0,2) | 151 | 76.6* | 3 (1, 4)* | 123 | 62.4*# | 1 (0, 2)# | 59.174 | <0.001 |
| Dry mouth | 97 | 49.2 | 0 (0, 2.5) | 161 | 81.7* | 4 (1, 5)* | 139 | 70.6*# | 1 (0, 3)*# | 76.159 | <0.001 |
| Feeling sad | 75 | 38.1 | 0 (0, 2) | 108 | 54.8* | 1 (0, 2)* | 69 | 35.0# | 0 (0, 1)# | 17.033 | <0.001 |
| Vomiting | 17 | 8.6 | 0 (0, 0) | 33 | 16.8* | 0 (0, 0)* | 23 | 11.7 | 0 (0, 0) | 6.606 | 0.037 |
| Numbness/tingling | 67 | 34.0 | 0 (0, 2) | 136 | 69.0* | 2 (0, 4)* | 172 | 87.3*# | 3 (1, 4)* | 111.5867 | <0.001 |
| Problems with mucus | 114 | 56.9 | 1 (0, 3) | 173 | 87.8* | 4 (2, 6)* | 144 | 73.1*# | 2 (0, 3)*# | 87.676 | <0.001 |
| Difficulty swallowing/chewing | 126 | 64.0 | 2 (0, 5) | 188 | 95.4* | 8 (5, 9)* | 172 | 87.3*# | 3 (2, 5)*# | 167.830 | <0.001 |
| Choking/coughing (aspiration) | 54 | 27.4 | 0 (0, 1) | 39 | 19.8 | 0 (0, 0) | 50 | 25.4 | 0 (0, 1) | 1.974 | 0.373 |
| Difficulty with voice/speech | 82 | 41.6 | 0 (0, 2) | 186 | 94.4* | 5 (3, 8)* | 172 | 87.3*# | 2 (1, 4)*# | 205.139 | <0.001 |
| Skin pain/burning/rash | 41 | 20.8 | 0 (0, 0) | 50 | 25.4 | 0 (0, 1) | 48 | 24.4 | 0 (0, 0) | 1.442 | 0.486 |
| Constipation | 48 | 24.4 | 0 (0, 0) | 46 | 23.4 | 0 (0, 0) | 60 | 30.5 | 0 (0, 1) | 2.166 | 0.339 |
| Problem with tasting food | 45 | 22.8 | 0 (0, 0) | 51 | 25.9 | 0 (0, 1) | 74 | 37.6*# | 0 (0, 2)* | 11.319 | 0.003 |
| Mouth/throat sores | 122 | 61.9 | 1 (0, 3) | 139 | 70.6 | 2 (0, 3) | 80 | 40.6*# | 0 (0, 1)*# | 51.938 | <0.001 |
| Problem with teeth/gum | 116 | 58.9 | 1 (0, 3.5) | 120 | 60.9 | 2 (0, 5) | 127 | 64.5 | 1 (0, 4) | 2.532 | 0.282 |
| MDASI [Median (Q1, Q3)] | 20 (9, 40) | | | 43 (31.5, 60.0)* | | | 24 (16, 33.5)# | | | 109.494 | <0.001 |

*$P < 0.05$ compared with Time #1.
#$P < 0.05$ compared with Time #2.
[a] The percentage of patients who reported any level (1–10) of the symptom surveyed.

*Correlates of total symptom burden*

Table 5 shows a GEE model of total symptom scores. After other factors were controlled in the multivariate GEE model, symptom scores at 7 days postsurgery were significantly higher than at preoperation ($P < 0.001$). Self-employed patients had higher scores than farmers ($P = 0.035$). Patients with comorbidity, later stage, and higher NRS scores had higher MDASI-HN scores ($P < 0.05$), and patients receiving adjuvant therapy had higher scores than did those not ($P = 0.037$).

## Discussion

This study demonstrated that perioperative oral cancer patients experience many symptoms, with the most prominent ones being pain, difficulty swallowing/chewing, difficulty with voice/speech, and problem with mucus. The main symptoms in preoperative patients with oral cancer were pain and difficulty swallowing/chewing, whereas in postoperative patients, difficulty swallowing/chewing, difficulty with voice/speech, and problem with mucus. As observed, the presence and severity

**Table 5**
Multivariable estimates of the MDASI-HN total score from GEE modeling ($n = 197$).

| Variables | $\beta$ | SE | 95% CI | | Wald $\chi^2$ | Significant |
|---|---|---|---|---|---|---|
| | | | Lower bound | Upper bound | | |
| Time point | | | | | | |
| Time #1 | Reference | – | – | – | – | – |
| Time #2 | 17.850 | 2.574 | 12.806 | 22.895 | 48.103 | <0.001 |
| Time #3 | 2.654 | 1.858 | −0.987 | 6.295 | 2.041 | 0.153 |
| Gender | | | | | | |
| Male | Reference | – | – | – | – | – |
| Female | 0.722 | 5.549 | −10.154 | 111.598 | 0.017 | 0.897 |
| Age (years) | | | | | | |
| < 40 | Reference | – | – | – | – | – |
| 40–60 | 0.567 | 4.137 | −7.541 | 8.675 | 0.019 | 0.891 |
| > 60 | −3.233 | 5.753 | −14.510 | 8.043 | 0.316 | 0.574 |
| Education level | | | | | | |
| Elementary school graduation | Reference | – | – | – | – | – |
| Middle school graduation | 1.629 | 3.105 | −4.457 | 7.716 | 0.275 | 0.600 |
| High school graduation | 4.748 | 3.634 | −2.374 | 11.871 | 1.707 | 0.191 |
| College graduation or above | −1.220 | 7.182 | −15.295 | 12.856 | 0.029 | 0.865 |
| Marital status | | | | | | |
| Without spouse | Reference | – | – | – | – | – |
| With spouse | 11.340 | 9.008 | −6.315 | 28.994 | 1.585 | 0.208 |
| Place of residence | | | | | | |
| Rural area | Reference | – | – | – | – | – |
| Town | −1.593 | 4.687 | −10.780 | 7.593 | 0.116 | 0.734 |
| Urban area | −1.564 | 3.666 | −8.749 | 5.621 | 0.182 | 0.670 |
| Job | | | | | | |
| Farmer | Reference | – | – | – | – | – |
| Worker | 5.288 | 3.538 | −1.647 | 12.223 | 2.234 | 0.135 |
| Staff | −2.206 | 6.269 | −14.493 | 10.080 | 0.124 | 0.725 |
| Retired | −4.749 | 4.903 | −14.359 | 4.861 | 0.938 | 0.333 |
| Self-employed | 11.344 | 5.375 | 0.810 | 21.878 | 4.455 | 0.035 |
| Income per month (yuan) | | | | | | |
| < 3000 | Reference | – | – | – | – | – |
| 3000–5000 | 1.534 | 2.815 | −3.983 | 7.051 | 0.297 | 0.586 |
| > 5000 | 2.607 | 3.649 | −4.545 | 9.759 | 0.510 | 0.475 |
| Medical insurance | | | | | | |
| None | Reference | – | – | – | – | – |
| New Cooperative Medical System | −12.156 | 8.558 | −28.929 | 4.618 | 2.018 | 0.155 |
| Basic Medical Insurance for Urban Employees | −7.293 | 9.470 | −25.853 | 11.267 | 0.593 | 0.441 |
| Basic Medical Insurance for Urban Residents | −10.565 | 8.675 | −27.567 | 6.437 | 1.483 | 0.223 |
| Smoking | | | | | | |
| No | Reference | – | – | – | – | – |
| Yes | −6.467 | 4.760 | −15.796 | 2.862 | 1.846 | 0.174 |
| Alcohol consumption | | | | | | |
| No | Reference | – | – | – | – | – |
| Yes | −1.779 | 4.272 | −10.151 | 6.593 | 1.173 | 0.677 |
| Betel nut chewing | | | | | | |
| No | Reference | – | – | – | – | – |
| Yes | 5.168 | 4.288 | −3.236 | 13.572 | 1.453 | 0.228 |
| Comorbidity | | | | | | |
| No | Reference | – | – | – | – | – |
| Yes | 12.125 | 3.669 | 4.935 | 19.315 | 10.924 | 0.001 |
| Diabetes mellitus | | | | | | |
| No | Reference | – | – | – | – | – |
| Yes | 6.081 | 4.971 | −3.663 | 15.825 | 1.496 | 0.221 |
| Cancer stage at diagnosis | | | | | | |
| Early stage (Phase 0 and I) | Reference | – | – | – | – | – |
| Moderate stage (Phase II) | 6.718 | 3.217 | 0.413 | 13.024 | 4.361 | 0.037 |
| Moderate or advanced stage (Phase III) | 7.680 | 3.529 | 0.764 | 14.597 | 4.737 | 0.030 |
| Advanced stage (Phase IV) | 13.871 | 3.338 | 7.328 | 20.415 | 17.266 | <0.001 |

(*continued on next page*)

**Table 5** (*continued*)

| Variables | $\beta$ | SE | 95% CI | | Wald $\chi^2$ | Significant |
|---|---|---|---|---|---|---|
| | | | Lower bound | Upper bound | | |
| Tumor histology | | | | | | |
| Squamous carcinoma | Reference | – | – | – | – | – |
| Others | −3.471 | 3.455 | −10.242 | 3.300 | 1.010 | 0.315 |
| Adjuvant treatment | | | | | | |
| No | Reference | – | – | – | – | – |
| Yes | 6.790 | 3.259 | 0.402 | 13.178 | 4.340 | 0.037 |
| Tracheotomy | | | | | | |
| No | Reference | – | – | – | – | – |
| Yes | 1.443 | 3.201 | −4.831 | 7.716 | 0.203 | 0.652 |
| Smoking history (years) | 0.139 | 0.143 | −0.141 | 0.419 | 0.946 | 0.331 |
| Numbers of cigarettes smoked per day | 0.013 | 0.028 | −0.042 | 0.068 | 0.226 | 0.635 |
| Alcohol consumption history (years) | −0.215 | 0.159 | −0.527 | 0.097 | 1.821 | 0.177 |
| Amount of alcohol consumed per day (mL) | 0.020 | 0.013 | −0.006 | 0.045 | 2.350 | 0.125 |
| Betel nut chewing history (years) | −0.014 | 0.220 | −0.446 | 0.418 | 0.004 | 0.949 |
| Pieces of betel nuts chewed per day | −0.105 | 0.095 | −0.290 | 0.081 | 1.219 | 0.270 |
| BMI | −0.664 | 0.516 | −1.675 | 0.346 | 1.660 | 0.198 |
| NRS score | 3.679 | 1.039 | 1.642 | 5.716 | 12.529 | <0.001 |

BMI, body mass index; GEE, Generalized estimating equation; MDASI-HN, M.D. Anderson Symptom Inventory-Head and Neck Module-Chinese version; NRS, Nutritional Risk Screening 2002.

of multiple symptoms changed over time, with the symptom burden being the heaviest about 7 days postsurgery. Job category, comorbidity, cancer stage, adjuvant therapy, and NRS score were all associated with symptom burdens.

In terms of symptom severity, the total symptom burdens were significantly increased at 7 days postsurgery, whereas at 1 month postsurgery, the symptom burdens decreased to a similar level as before surgery. This trend was also verified by Hu et al.,[12] which may be because of the acute postoperative stress reaction of patients 7 days after the operation, leading to some symptoms with no time to subside. Although most symptoms improved gradually over time, as mentioned previously, if the symptoms in the acute phase were well managed, patients could quickly recover and obtain a better anticancer therapy outcome.

According to the study, the most common and severe symptom in perioperative oral cancer patients was difficulty swallowing/chewing. The tumor itself and the discomfort it caused, such as pain, could impair swallowing and chewing function before surgery. Damage to the natural structure of the oral cavity could lead to the decline in normal physiological function, which inevitably causes chewing and swallowing dysfunction after radical surgery for oral cancer. Hutcheson et al. reported that the swallowing function of postoperative oropharyngeal cancer patients was significantly worse than that of patients who just started radiotherapy, but the results were reversed at the end of radiotherapy.[24] The swallowing and chewing function of patients with oral cancer was better at 1 month after operation than that at 7 days after operation, but it was still worse than before operation. This implies that the swallowing function of surgical patients declines sharply after operation but slowly recovers over time. A survey of long-term oropharyngeal cancer survivors (treatment completed 1 year ago or longer) showed that 16% of patients had moderate to severe dysphagia, which was a predictive factor for quality of life.[25] This suggests that swallowing problems are a long-term complication faced by patients with oral cancer. Several studies have verified that dysphagia has a significant impact on quality of life, social life, nutritional status, and emotion.[7,26–28] There is evidence that prophylactic swallowing therapy (swallowing training initiated before treatment) could improve swallowing function and quality of life in head and neck cancer patients.[29,30] This may be related to the prophylactic swallowing therapy that focuses on structural movements in the oral propulsive phase and pharyngeal phase, which can effectively maintain tongue and pharyngeal muscle tone and facilitate compensating for possible functional deficits. Therefore, nurses should coordinate prerehabilitation activities with multidisciplinary teams to help patients start functional exercise as soon as possible to restore their swallowing and chewing functions to the greatest extent.

Another major symptom that patients faced before surgery was pain, but the incidence and severity of pain decreased significantly at 1 month postsurgery, consistent with the findings of Sjamsudin et al.[31] In one study, the prevalence of pain among oral cancer patients without any therapeutic intervention was 67.5%, similar to that of preoperative patients in this study.[32] One month after operation, the presence of pain decreased to 36%, implying that surgery might serve as an effective method to relieve pain in patients with oral cancer. Before operation, compression or rupture of the tumor could stimulate the abundant nerves in the oral and maxillofacial region, causing severe pain. At 1 month postsurgery, with the removal of tumor, the factors causing the pain were mitigated, and so did the pain. It is worth noting that the pain was still a distressing symptom 7 days after operation, and its occurrence in oral cancer patients was positively correlated with the presence of tumor in the tongue and negatively correlated with TNM stage I.[32] TNM classification is the most commonly used cancer staging system according to tumor, nodes, and metastasis. Many studies have shown that optimizing the management of postoperative pain could reduce postsurgical complications, distress, duration of stay, and the risk of developing chronic pain.[33,34] Therefore, it is necessary to give patients active and reasonable analgesia in the perioperative period.

After radical oral cancer surgery, some important speech organs are removed, leaving patients with difficulty speaking. At 7 days and 1 month postsurgery, the percentage of patients with vocal difficulties was 94.4% and 87.3%, respectively, implying that speech rehabilitation is one of the main rehabilitation priorities after surgery. Balaguer et al. reported that surgery had a major impact on the deterioration of speech intelligibility in oral or oropharyngeal cancer.[35] Speech is an inevitable part of social interaction and is highly correlated with quality of life. However, even 1 month postsurgery, the presence and severity of difficulty with voice/speech remained more serious than before surgery. Balbinot et al. reported that speech therapy had a positive impact on swallowing quality of life in tongue cancer patients.[36] In assessing speech disorders, semispontaneous speech based on a picture description proved to be a better clinical measure than reading.[37] In the early rehabilitation phase, high-frequency speech therapy involving adaptation and compensation for new functional status after surgery could significantly improve objective speech intelligibility in oral cancer patients.[38] Nevertheless, research on the assessment and intervention of speech dysfunction is very limited, and voice/speech rehabilitation for patients with oral cancer remains a rehabilitation problem that needs further exploration.

Dry mouth and mucus problems were also common symptoms very distressing for patients with oral cancer. The incidence and severity of

dry mouth and mucus problems increased greatly after operation, as the salivary glands were removed and open mouth breathing was used. Moreover, a survey of long-term survivors of oropharyngeal cancer found that 39% and 22% of participants rated dry mouth and mucus problems as moderate/severe (MDASI-HN item score $\geq$ 5), respectively, despite having completed all treatment more than a year earlier.[39] The literature suggested that dry mouth and mucus problems were not only the acute but also late oral morbidities in oral cancer patients. Previous studies have confirmed that saliva substitutes were one of the most effective methods to alleviate dry mouth in cancer patients who had undergone radiotherapy.[40,41] Further research is needed to determine whether the saliva substitute is effective in postoperative oral cancer.

This study also showed that self-employed patients had a higher symptom burden than farmers. In general, self-employed patients may lack a stable source of income. After the illness, most of them were unable to proceed with their work and made little economic contributions to their families, leading to more self-reported symptoms. The patients with comorbidity had higher symptom burdens in the perioperative period, which was also confirmed by the literature.[13] It is well understood that comorbidities, such as hypertension, are often accompanied by some symptoms that result in a higher symptom burden due to the disease itself and medication. As expected, symptom burdens were more severe in patients with later-stage cancer. The later the disease stage and the larger the scope of surgical resection was, the greater the damage to the physiological structures of head and neck would be. Meanwhile, patients with later-stage cancer usually receive a combination treatment of surgical procedures, radiotherapy, and chemotherapy, whereas patients in the early stages might receive only surgical interventions. Radiochemotherapy increased the symptom burden of surgical patients because of its negative impacts. Similar results were also found by Mott et al., where pain, xerostomia, and dysphagia all increased with combined radiochemotherapy.[42] Both radiotherapy and chemotherapy are toxic and can damage the normal oral physiological structure and function of the oral cavity, increasing the symptom burdens. Patients with higher NRS scores exhibited more serious symptoms. Many symptoms such as dysphagia and pain were directly related to nutrition, and higher NRS scores indicated a greater risk of malnutrition. There is evidence that nutrition was significantly associated with symptoms in oral cancer patients.[9]

### *Strengths and limitations*

This study updates our knowledge about symptom patterns in perioperative oral cancer patients. The prospective design enables us to survey perioperative symptoms over time and identify the predictors of symptom burdens in patients with oral cancer. Moreover, the analysis of influencing factors by the GEE model allows for the elimination of confounding factors. However, several limitations need to be acknowledged in this study. First, convenience sampling was adopted in a single institution of only one province in South Central China. The limitations in representative sampling might restrict the generalization of the findings to other areas in China. Second, the patients were followed up for only 1 month after operation, and the medium- and long-term symptom burdens of oral cancer patients remained unclear. In future studies, the observation period for the symptom burden in oral cancer patients can be extended to 3 months, 6 months, or even 1 year after operation to provide a basis for health care providers to manage oral cancer symptoms.

### *Implications for practice*

The perioperative symptoms of patients with oral cancer changed dynamically, with the heaviest symptom burdens around 7 days after operation, which is consistent with previous studies.[12,13] Health care providers should pay attention to the prominent symptoms at each stage, especially about 7 days postsurgery, and provide care to alleviate the symptoms of oral cancer patients and promote their recovery. Swallowing, chewing, speech, and saliva problems are the most significant concerns in oral cancer patients after radical surgery. On the one hand, prophylactic swallowing and speech therapy implemented by a nurse-based multidisciplinary team (swallowing therapists, speech therapists, nutritional therapy practitioners, etc.) could be used to enhance the recovery of swallowing and speech function. On the other hand, problems with mucus could be improved with the aid of innovative interventions and useful medical products. As shown in this study, employment type, comorbidity, clinical stage, adjuvant therapy, and NRS score are all associated with symptom burdens. Therefore, nurses should conduct a detailed assessment at the time of patient admission and pay more attention to those who are self-employed or have comorbidities, advanced stage of cancer, multimodal therapy, and nutritional risk.

## Conclusions

Patients with oral cancer suffer from multiple symptoms and great symptom burdens in the perioperative period. Pain, difficulty swallowing/chewing, problems with voice/speech, and problems with mucus were the prominent symptoms for patients with oral cancer undergoing surgery. The presence and severity of symptoms, such as dry mouth, problems with mucus, difficulty swallowing/chewing, and difficulty with voice/speech, increased significantly at 7 days postsurgery and then improved slightly at 1 month postsurgery but were still more serious than before surgery. Patients' pain was significantly relieved at 1 month after operation. These findings may provide a reference for patients with oral cancer when choosing treatment options. According to this study, patients bore a heavier symptom burden 7 days postsurgery, hindering the process of postoperative rehabilitation. In addition, patients with self-employment, comorbidity, later-stage cancer, adjuvant therapy, and higher nutritional risk were associated with more serious symptom burdens. Our study demonstrates the importance and urgency of symptom management in patients undergoing oral cancer surgery. Future research should focus on developing targeted interventions for the prevalent symptoms to promote patient rehabilitation and improve prognosis.

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## Authors' contributions

M.O., H.C., and X.X conceived and designed the analysis. M.O., G.W., Y.Y., and H.C. collected the data. G.W. and Y.Y. contributed data or analysis tools. M.O., Y.Y., and X.X. performed the analysis. M.O. and X.X. wrote the article.

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## Declaration of competing interest

None declared.

## Ethics statements

This study was approved by the Medical Ethics Committee of the University of South China (Approval No. January 6, 2020).

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