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RESEARCH

Core preoperative symptoms and patients' symptom experiences in oral cancer: a mixed-methods study

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Abstract

Aims Patients with oral cancer frequently experience a substantial symptom burden, especially during the preoperative phase, which is typically marked by increased anxiety, pain, and functional impairments. This study aimed to construct contemporaneous symptom networks and investigate symptom experiences of patients with preoperative oral cancer in China.

Methods This study employed a mixed-methods design that integrated a cross-sectional study with qualitative research. Data were collected from 527 patients with oral cancer at the Department of Head and Neck Oncology in a tertiary hospital between September 2023 and May 2024 in China. The MD Anderson Symptom Inventory for Head and Neck Cancer (MDASI-H&N) was used to assess the prevalence and severity of the cancer-related symptoms. Symptom networks were constructed using the networktools, qgraph, and Bootnet packages in R, with centrality indices calculated to identify core symptoms within the network. Qualitative data were analyzed using content analysis with NVivo software to extract themes, thereby providing a comprehensive understanding of patients' symptom experiences.

Results Distress (89.56%) and sadness (63.95%) were the most prevalent and severe symptoms, respectively. Two distinct symptom clusters emerged: the Emotional-Sleep Symptoms Cluster (Cluster 1) and Eating Disorder Symptoms Cluster (Cluster 2). Difficulty swallowing or chewing ($r_s = 0.87$, $r_b = 102$) and disturbed sleep ($r_s = 0.64$, $r_b = 77$) exhibited the highest centrality indices, indicating that these symptoms were more likely to co-occur with others within the network. Additionally, fatigue had the most significant negative impact on quality of life ($r = -0.16$).

Conclusion This study identified core symptoms through preoperative symptom network analysis and offered valuable insights into the lived experiences of patients with oral cancer regarding their symptoms. These findings serve as a foundation for personalized targeted treatment strategies designed to improve symptom management and enhance quality of life in oral cancer care.

Keywords Oral cancer · Symptom networks · Network analysis · Symptom management

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Introduction

Oral cancer, the most common form of head and neck cancer (HNC), poses a significant global health challenge, with a 5-year survival rate of less than 50%. This malignancy can originate in multiple regions of the oral cavity, including the tongue, gums, palate, floor of the mouth, and buccal mucosa [1, 2]. According to the International Agency for Research on Cancer (IARC), approximately 378,000 new cases of oral cancer were diagnosed worldwide in 2020, resulting in an estimated 178,000 deaths attributed to the disease in the same year [3]. Approximately 90% of oral cancers are classified as oral squamous cell carcinomas (OSCC). Data from the Global Cancer Observatory indicate a continuing increase in the global incidence of OSCC, with projections forecasting a 30% increase in the coming decades [3, 4].

Extensive evidence indicates that many cancer survivors experience a significant symptom burden due to both the disease and its treatments [5, 6]. The primary therapeutic strategy for oral cancer typically involves surgical intervention followed by adjuvant radiation therapy and/or chemotherapy [7]. Due to the anatomical complexity of the head and neck and its vital physiological and social functions, surgical treatment can result in structural changes and functional impairments. Patients may experience symptoms like pain, depression, difficulties with chewing and swallowing, speech impairment, sleep disturbances, and dry mouth [8, 9]. Radiotherapy and chemotherapy can further exacerbate symptoms, leading to inflammation, fatigue, and cognitive issues [10]. Importantly, the symptom burden is dynamic, varying in frequency and intensity over time, which complicates symptom management.

Comprehensive reviews indicate that cancer patients often endure multiple co-occurring symptoms, with depressive symptoms, pain, and fatigue being the most prevalent and debilitating [11, 12]. Given this complexity, analyzing symptom patterns through symptom clustering is essential to understand how these symptoms interact [13, 14]. A recent study in India identified two symptom-based subgroups among oral cancer patients, with 61% reporting severe difficulties in swallowing or chewing, along with dental issues [15]. Similarly, research in Taiwan on head and neck cancer patients identified two main symptom clusters: an HNC-specific cluster, which encompasses symptoms such as dry mouth, pain, lack of appetite, fatigue, and sleep disturbances and the gastrointestinal cluster, which includes symptoms such as nausea, vomiting, shortness of breath, and memory difficulties [16]. Despite these findings, there remains a significant knowledge gap in identifying core symptoms, particularly in the preoperative phase of oral cancer. Due to the gradual onset of the disease, many patients face a substantial symptom burden even before diagnosis [17]. Addressing preoperative core symptoms establishes a critical baseline for symptom assessment and enables healthcare professionals to provide targeted prehabilitation interventions. Prehabilitation, implemented between cancer diagnosis and the initiation of treatment, involves a comprehensive approach combining nutrition, exercise, and psychological strategies to optimize the ability to cope with treatment and post-treatment recovery [18]. Given the significant symptom burden and complex management of treatment-related toxicities in patients with head and neck cancer, prehabilitation is particularly relevant for this population, offering an opportunity to improve outcomes and better prepare patients for the challenges of treatment [19].

Traditional methods of symptom analysis often fail to capture the complexity and variability of patients' symptom experiences [20]. Network analysis (NA) offers a novel approach to model the interconnectedness of symptoms, allowing identification of core symptoms and potential intervention points [21, 22]. By constructing multidimensional symptom networks, NA provides critical metrics like centrality and density, helping healthcare providers understand the relationships between symptoms and develop targeted interventions. Symptom network analysis is gaining traction in various fields for identifying core symptoms [23]. For instance, fatigue has been recognized as a key driver of overall symptom burden, and depression is central in the symptom experience of head and neck cancer patients [24, 25]. Moreover, a study conducted in China involving older adults with cancer utilized network analysis to investigate core symptoms specific to this population, offering valuable insights for future targeted symptom management in older adults [26].

To address gaps in understanding symptom networks specifically in oral cancer, this study employed cross-sectional network analysis to construct a contemporaneous symptom network and identify core preoperative symptoms in a Chinese cohort. This study uniquely integrates qualitative research, providing deeper insights into the lived symptom experiences and personalized management needs of oral cancer patients, enriching the findings from the network analysis.

Methods

Study design and setting

This study employed a mixed-methods design, combining a cross-sectional quantitative approach with qualitative analysis, following an explanatory sequential mixed-methods design. The design involved initially conducting the quantitative phase to explore preoperative symptom experiences in patients with oral cancer, followed by qualitative interviews to gain a deeper understanding of these experiences. The study adhered to the GRAMMS checklist [27] and STROCSS 2021 guidelines [28] to ensure rigorous and transparent reporting. Participants were recruited through convenience sampling from the Department of Head and Neck Oncology in a tertiary hospital in China between July 2023 and May 2024.

Participants

Inclusion and exclusion criteria

The inclusion criteria for this study were as follows: (1) a confirmed diagnosis of oral cancer without any concomitant malignancies; (2) scheduled for surgical intervention; (3) age 18 years or older; (4) free from psychiatric or severe psychological disorders, with the ability to communicate effectively; and (5) provision of informed consent. The exclusion criteria were as follows: (1) presence of other serious physical illnesses, (2) having undergone radiotherapy or chemotherapy prior to surgery, and (3) participation in other ongoing clinical trials or related treatments.

Sample size calculation

Using the pairwise Markov random field (PMRF) method [29], the required sample size was calculated using the formula: sample size = threshold parameter (N) × pairwise association parameter $[N(N-1)/2]$ + threshold parameter (N). In this study, the threshold parameter, which represents network nodes, was set to $N=24$. Substituting this value into the formula yields the required sample size of 300. To account for a potential invalid response rate of 15%, the final estimated sample size was adjusted to 353.

Data collection

Data collection commenced on the second day following admission and was carried out by trained healthcare professionals who were well-versed in the study protocols. Eligible participants were approached at their bedside to obtain consent and to collect data, ensuring that the process remained efficient and centered on the patient.

To investigate preoperative symptom experiences among patients with oral cancer, semi-structured interviews were conducted using an interview guide developed by the research team. This guide emphasizes key aspects of patients' symptom experiences, offering a structured yet flexible framework for data collection. Among the participants in the questionnaire survey, only those who reported at least two symptoms on the MD Anderson Symptom Inventory for Head and Neck Cancer (MDASI-H&N) were selected for interviews. To ensure a comprehensive representation of symptom experiences, careful attention was given to the demographic diversity of the sample, including factors such as gender, age, education, occupation, and lesion distribution. A minimum of seven patients was targeted for interviews, with data collection continuing until saturation was reached—defined as the point at which no new information emerged from the interviewees. The interviews were conducted in a secure, private, and comfortable environment to ensure confidentiality and participant comfort. Prior to each session, the participants received a comprehensive explanation of the study's purpose and significance, and informed consent was obtained. The interviews were audio-recorded, and the interviewer meticulously documented non-verbal cues, including facial expressions and body language. Each session lasted approximately 15 to 30 min, and all interviews were transcribed verbatim within 24 h and securely archived.

Measures

Sociodemographic and clinical data

Sociodemographic and clinical information was gathered using a self-administered questionnaire completed by the participants. The collected demographic variables included age, sex, educational attainment, occupation, marital status, place of residence, income, and method of healthcare payment. Clinical information included body mass index (BMI), presence of comorbid chronic conditions, TNM stage, tumor location, and surgical procedures.

MDASI-H&N

The MD Anderson Symptom Inventory for Head and Neck Cancer (MDASI-H&N) was selected for its effectiveness in assessing symptom burden, which was the central focus of this study. Developed by Rosenthal et al. at the M.D. Anderson Cancer Center, this self-report instrument was specifically designed for patients with head and neck cancer [30]. Cronbach's alpha ranging from 0.72 to 0.92 demonstrates strong internal consistency [31]. The MDASI-H&N effectively captures both general and disease-specific symptoms, making it an ideal tool for evaluating the wide range of physical and psychological challenges faced by this patient population. The questionnaire consists of two sections. The first section evaluates the severity of symptoms experienced over the past 24 h using 22 items. Thirteen core items addressed symptoms that are common among most cancer patients, such as pain, fatigue, and nausea, which aligns with the study's objective of assessing the overall preoperative symptom burden. The remaining nine items focus on symptoms specific to head and neck cancer, including difficulties with swallowing and speech, thereby providing a comprehensive understanding of the patient's experience. Each symptom is rated on a scale from 0 to 10, with 0 indicating "not present" and 10 representing "the worst imaginable severity."

To comprehensively capture preoperative symptoms in patients with oral cancer, additional symptoms, including shoulder discomfort and limitation of mouth opening, were incorporated based on evidence from literature reviews and clinical practice [15]. These additions enhance the instrument's ability to provide a more complete representation of symptom burden.

SSRS

Chinese scholars developed the Social Support Rating Scale (SSRS) to evaluate the level of social support [32]. This instrument consists of 10 items distributed across three dimensions: objective support (3 items: 2, 6, and 7), subjective support (4 items: 1, 3, 4, and 5), and support utilization (3 items: 8, 9, and 10). Each item is rated on a 4-point Likert scale, with higher scores indicating greater levels of social support. The cumulative score reflects the overall level of social support, which was categorized into three tiers: low (≤ 22), moderate (23–44), and high (≥ 45).

University of Washington Quality of Life Questionnaire (UW-QOL)

Quality of life was assessed using the University of Washington Quality of Life Questionnaire (UW-QOL), specifically designed for individuals with oral cancer. This instrument evaluates the symptoms experienced by participants over the previous 7 days [33], providing a comprehensive view of their health-related quality of life. The UW-QOL consists of two primary domains: physical function, which includes aspects such as chewing, swallowing, speech, taste, saliva, and appearance, and social-emotional function, which encompasses factors such as anxiety, mood, pain, activity, recreation, and shoulder function [34]. Lower UW-QOL scores indicate a greater negative impact on quality of life.

Data analysis

Statistical analyses were performed using SPSS version 27.0 and R version 4.2.1. As the continuous data displayed a skewed distribution, the demographic characteristics and symptom severity were summarized using frequencies, percentages, medians, and interquartile ranges (IQR). In this study, a P value of less than 0.05 was considered statistically significant. Semi-structured interview transcripts were coded and analyzed using directed content analysis.

Symptom clustering

Symptoms with an incidence rate of 20% or higher were grouped using factor analysis in SPSS by employing the principal component method to extract factors. The Kaiser–Meyer–Olkin (KMO) test (KMO value > 0.5) and Bartlett's test of sphericity ($p < 0.01$) were conducted to evaluate the suitability of the data for factor analysis. Factors were selected based on an eigenvalue ≥ 1 and symptom loading ≥ 0.4. If a symptom exhibited a loading ≥ 0.4 across multiple factors, it was assigned to the factor with the highest loading. Each factor was required to include at least two symptoms. The occurrence of symptom clusters was subsequently analyzed as the dependent variable in binary logistic regression models to identify potential influencing factors. Correlation analyses were performed between symptom cluster scores and quality of life to explore their associations.

Concurrent symptom network construction

Symptom network analysis and visualization were performed using network tools and qgraph packages in R version 4.2.1. The EBICglasso function was utilized for network estimation, and the spring layout was employed for visualization. In the network, nodes represented symptoms and were color-coded to distinguish between symptom clusters and stand-alone symptoms. Edges connecting the nodes indicated correlations, with green edges signifying positive correlations and red edges denoting negative correlations; the thickness of the edges corresponded to the strength of the correlations. Quality of life was integrated into the concurrent symptom network to evaluate the impact of individual symptoms on overall quality of life.

Centrality and stability

To identify the core symptoms within the network, centrality analysis was conducted using the qgraph package, focusing on three centrality indices: strength, closeness, and betweenness. Strength centrality quantifies the total weight of edges connected to each node, reflecting both the degree of connectivity and influence of a symptom within the network [35]. As the most significant and reliable indicator, strength centrality served as the primary measure for identifying core symptoms. Closeness centrality, calculated as the inverse of the shortest path length from a symptom node to all other nodes, indicates the central position of a symptom within the network [12]. Betweenness centrality, which quantifies the frequency of the shortest paths between any two nodes that pass through a specific symptom, highlights the bridging role of symptoms within the network [26]. Bridge strength was also analyzed to identify bridge symptoms. The network accuracy and stability were evaluated using the Bootnet package. Nonparametric bootstrapping (nBoots = 1000) was applied to generate 95% bootstrap confidence intervals for edge weights, whereas case resampling (nBoots = 1500) was used to compute the stability coefficients for node influence. A stability coefficient > 0.25 was considered acceptable.

Thematic extraction from interview data

Content analysis was conducted using the NVivo 14 software. The research questions and objectives were carefully clarified before the interview transcripts were imported into the system. The transcripts were reviewed multiple times to identify key information and emerging themes. During the coding phase, categories were dynamically developed, and relevant segments were openly coded to extract core concepts. Finally, the findings were interpreted in alignment with the research objectives to ensure comprehensive understanding of the data.

Ethical considerations

The study adhered to the guidelines established in the 1995 Helsinki Declaration (revised in Edinburgh, 2000) and was approved by the Ethics Committee of West China Hospital of Stomatology, Sichuan University (Grant No. WCHSIRB-CT-2022–105). Permission to access the participants' electronic medical records was also obtained from the hospital. Informed consent was obtained from all the participants prior to data collection. To ensure confidentiality, data privacy measures were rigorously implemented, including anonymization of all collected data to safeguard participants' identities.

Results

Characteristics of the participants

The demographic and clinical characteristics of the participants are summarized in Table 1. A total of 527 oral cancer patients met the inclusion criteria. The predominant age group was 60–79 years, representing 46.87% of the cohort ($n = 247$). The majority of the participants were male ($n = 335$, 63.57%) and married ($n = 464$, 87.86%). The tongue was the most common tumor site, accounting for 27.51% of the cases ($n = 145$). The mean quality of life (QoL) score was 89, with an interquartile range (IQR) of 47–100.

Symptom incidence and symptom cluster extraction

The symptoms experienced by the participants, along with their respective severities, are summarized in Table 2. Distress was the most frequently reported symptom, affecting 89.56% of the cohort ($n = 472$), followed by sadness ($n = 337$, 63.95%), pain ($n = 291$, 55.22%), and sleep disturbance ($n = 244$, 46.30%). An exploratory factor analysis identified two distinct symptom clusters. Cluster 1, labeled the Emotional-Sleep Symptoms Cluster, included sadness (S11), distress (S5), and sleep disturbance (S4). Cluster 2,

Table 1 Participant characteristics ($N = 527$)

Variables	Category	*N* (%) or Median (IQR)
Age	≤ 39	59 (11.20%)
	40–59	211 (40.04%)
	60–79	247 (46.87%)
	≥ 80	10 (1.90%)
Gender	Male	335 (63.57%)
	Female	192 (36.43%)
Education attainment	Primary or below	178 (33.78%)
	Junior high	169 (32.07%)
	High school or vocational	73 (13.85%)
	College or above	107 (20.3%)
Occupation	Farmer	117 (22.20%)
	Worker	31 (5.88%)
	Civil servant	20 (3.80%)
	Professional technician	24 (4.55%)
	Retired	169 (32.07%)
	Other	166 (31.50%)
Marital status	Unmarried	21 (3.98%)
	Married	463 (87.86%)
	Divorced/widowed	43 (8.16%)
Tumor location	Gum	91 (17.27%)
	Tongue	145 (27.51%)
	Cheek	106 (20.11%)
	Hard and soft palate	29 (5.50%)
	Floor of mouth	80 (15.18%)
	Other	76 (14.42%)
Number of chronic diseases	0	294 (55.79%)
	1	181 (34.35%)
	≥ 2	52 (9.87%)
SSRS		43 (39–47)
Average QOL entry score		89 (47–100)

M mean, *SD* standard deviation, *IQR* interquartile range termed the eating disorder symptoms cluster, comprises symptoms such as difficulty in swallowing or chewing (S15) and problems with teeth or gums (S22).

Associated factors with the overall symptom severity

Table 3 summarizes the logistic regression analysis of factors associated with symptom severity across the two symptom clusters. In cluster 1 (emotional-sleep symptoms cluster), gender was significantly linked to symptom severity, with female participants reporting higher severity than males (OR = 1.824, $p = 0.004$). Marital status also showed an influence, with married individuals reporting lower symptom severity than unmarried participants (OR = 0.284, $p = 0.042$). In cluster 2 (eating disorder symptoms cluster), educational attainment emerged as a significant factor, with participants holding high school or vocational education reporting lower symptom severity (OR = 0.294, $p = 0.026$). Tumor location was also identified as a relevant factor, with tumors located on the tongue (OR = 0.041, $p < 0.001$) and other sites (OR = 0.104, $p = 0.001$) associated with reduced symptom severity.

Overall network

Density of symptom networks

Figure 1A illustrates the symptom network ($n = 527$), characterized by a network density of 0.170. Of the 253 possible edges, 43 were connected, with the majority demonstrating positive correlations. The strongest partial correlation in the network was observed between disturbed sleep and drowsiness ($r = 0.32$) followed by a moderately strong correlation between drowsiness and fatigue ($r = 0.27$). In cluster 2, the most prominent correlation was identified between distress and sadness ($r = 0.31$)

Concurrent symptom network and QoL

Figure 2 presents the symptom network analysis incorporating quality of life (QoL), highlighting the varying degrees of influence individual symptoms exert on QoL. Fatigue (S2) emerged as the symptom with the most significant negative impact on QoL ($r = -0.16$), demonstrating that greater fatigue severity correlates with poorer QoL. Similarly, three symptoms from cluster 1 (disturbed sleep (S4), distress (S5), and sadness (S11)) were consistently

Table 2 Severity and prevalence of the experienced symptoms ($N = 527$)

Item	Experienced symptoms	Prevalence n (%)	Mean ± SD/median(IQR)	Range
s1	Pain	291 (55.22%)	3.28 ± 1.75	0–10
s2	Fatigue	88 (16.70%)	2.50 ± 1.17	0–6
s3	Nausea	4 (0.76%)	2.50 (2–3)	0–3
s4	Disturbed sleep	244 (46.30%)	4.05 ± 1.97	0–10
s5	Distress	472 (89.56%)	3.68 ± 1.74	0–8
s6	Shortness of breath	11 (2.09%)	2.00 (1.00–3.00)	0–5
s7	Difficulty remembering	42 (7.97%)	2.00 (1.00–2.00)	0–5
s8	Lack of appetite	84 (15.94%)	2.00 (2.00–3.00))	0–7
s9	Drowsiness	76 (14.42%)	2.50 ± 1.22	0–6
s10	dry mouth	52 (9.87%)	3.00 (2.00–4.00)	0–9
s11	Sadness	337 (63.95%)	2.85 ± 1.59	0–8
s12	Vomiting	4 (0.76%)	2.50 (1.50–4.00)	0–5
s13	Numbness/tingling	59 (11.2%)	2.80 ± 1.48	0–7
s14	Mucus in the mouth or throat	100 (18.98%)	2.00 (1.00–3.00)	0–8
s15	Difficulty swallowing or chewing	188 (35.67%)	4.13 ± 1.99	0–10
s16	Choking or coughing	7 (1.33%)	5.00 (1.00–8.00)	0–10
S17	Difficulty with voice or speech	71 (13.47%)	3.00 (2.00–4.00)	0–10
s18	Skin pain, burning, or rash	16 (3.04%)	2.38 ± 0.81	0–4
s19	Constipation	12 (2.28%)	2.00 (1.00–2.50)	0–4
s20	Problems with tasting food	19 (3.61%)	3.00 (2.00–4.00)	0–9
s21	Mouth or throat sores	14 (2.66%)	2.00 (1.00–3.00)	0–5
s22	Problems with teeth or gums	216 (40.99%)	3.46 ± 1.67	0–9
s23	Shoulder Discomfort	0 (0%)	3.00 (2.00–5.00)	0–10
s24	limitation of mouth opening	47 (8.92%)	3.28 ± 1.75	0–10

Table 3 Linear regression model of overall symptom severity ($n = 527$)

Variable	Cluster 1 Emotional-sleep symptoms cluster		Cluster 2 Eating disorder symptoms cluster	
	OR (95% CI)	p value	OR (95% CI)	p value
Gender	1.824 (1.208, 2.755)	**0.004**	0.783 (0.423, 1.449)	0.436
Education				
Junior High	0.732 (0.433, 1.239)	0.245	0.93 (0.467, 1.852)	0.835
High School or Vocational	0.526 (0.259, 1.068)	0.075	0.294 (0.1, 0.867)	**0.026**
College or Above	0.573 (0.288, 1.141)	0.113	0.525 (0.195, 1.417)	0.203
Marital Status				
Married	0.284 (0.084, 0.957)	**0.042**	0.583 (0.042, 8.067)	0.688
Divorced/widowed	0.335 (0.085, 1.318)	0.117	1.833 (0.123, 27.209)	0.660
Tumor location				
Tongue	1.128 (0.602, 2.113)	0.706	0.041 (0.011, 0.148)	**< 0.001**
Cheek	1.343 (0.706, 2.555)	0.369	0.649 (0.324, 1.301)	0.223
Hard and soft palate	0.515 (0.162, 1.633)	0.260	0.146 (0.029, 0.722)	**0.018**
Floor of mouth	1.118 (0.545, 2.294)	0.760	0.805 (0.377, 1.72)	0.576
Other	1.630 (0.802, 3.312)	0.177	0.104 (0.028, 0.385)	**0.001**
Number of chronic diseases				
1	1.08 (0.694, 1.680)	0.733	1.094 (0.6, 1.997)	0.769
≥ 2	0.714 (0.332, 1.534)	0.388	1.228 (0.515, 2.929)	0.642
SS	1.020 (0.981, 1.061)	0.319	1.008 (0.956, 1.063)	0.757
Age group				
40–59	1.208 (0.559, 2.608)	0.631	7.361 (0.706, 76.757)	0.095
60–79	1.209 (0.516, 2.834)	0.663	9.597 (0.888, 103.712)	0.063
≥ 80	0.872 (0.139, 5.472)	0.884	6.865 (0.271, 174.196)	0.243
Constant	0.253 (-)	0.297	0.406 (-)	0.669

Cluster 1 (emotional-sleep symptoms cluster): Distress (S11), Sadness (S5), Insomnia (S4); Cluster 2 (eating disorder symptoms cluster): Swallowing Difficulties (S15), Dental Issues (S22)

OR odd ratio, *CI* confidence interval

The bolded values in the table indicate statistically significant results ($p < 0.05$)

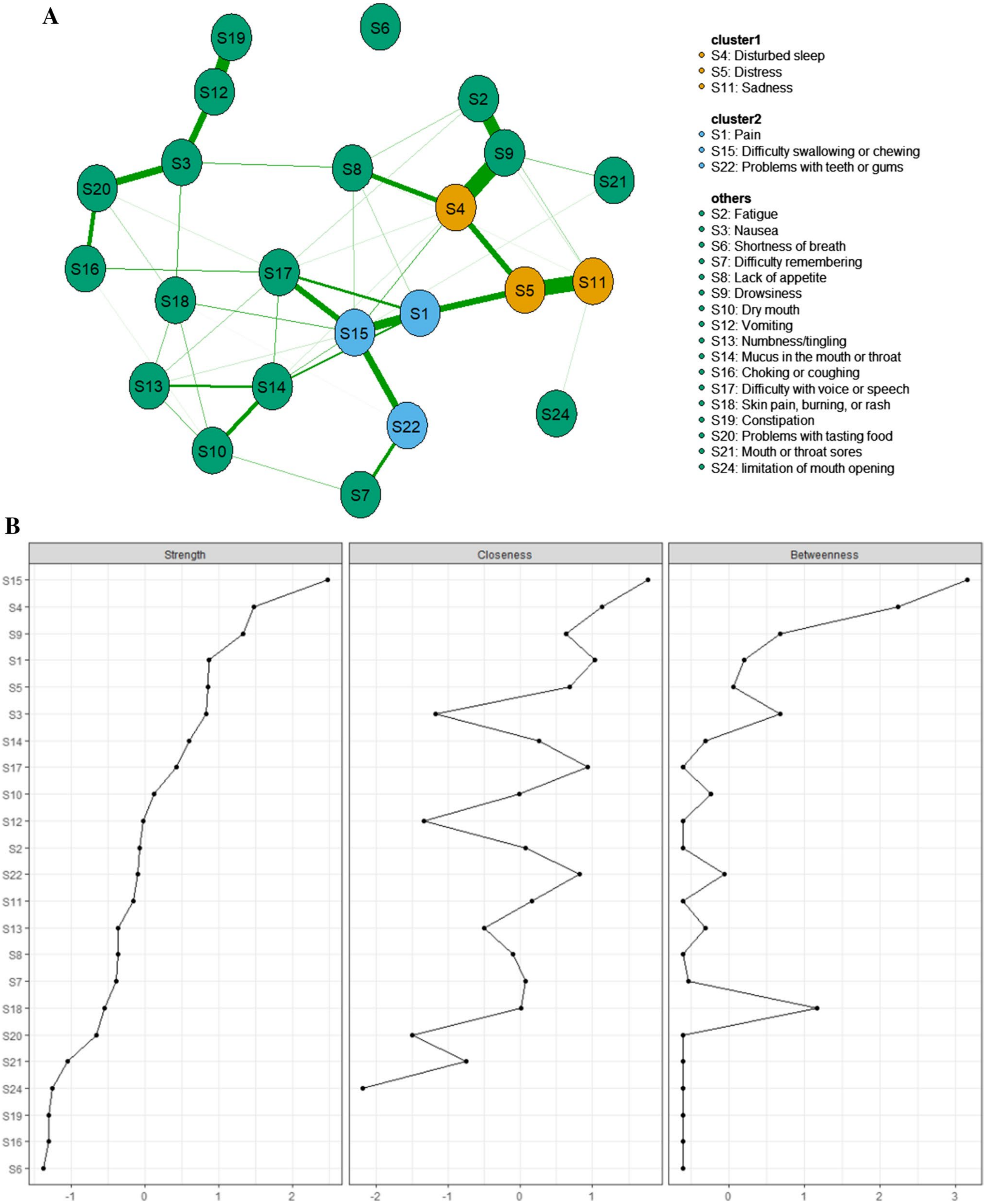
negatively correlated with QoL ($r = -0.07, -0.10$, and -0.10, respectively). Pain (S1) from cluster 2 also showed a negative association with QoL ($r = -0.12$). Conversely, difficulty swallowing or chewing (S15) was negatively correlated with QoL ($r = -0.10$), indicating that increased severity of swallowing or chewing difficulties leads to further QoL deterioration.

Centrality, accuracy, and stability

Figure 1B presents the centrality measures of strength, betweenness, and closeness for the 24 symptoms examined. Centrality analysis revealed difficulty swallowing or chewing ($r_s = 0.87$, $r_b = 102$), disturbed sleep ($r_s = 0.64$, $r_b = 77$), and drowsiness ($r_s = 0.61$, $r_b = 35$) exhibited the highest strength and betweenness values. This indicates that difficulty swallowing or chewing occupies a central position in the symptom network, frequently co-occurring with other symptoms, and playing a critical role in the overall symptom dynamics of oral cancer. Figure 3A displays the results of the bootstrap analysis for edge weights, which demonstrate narrow bootstrapped confidence intervals (CIs), reflecting a high degree of accuracy in the network estimation. Additionally, Fig. 3B presents the stability coefficients for betweenness, bridge strength, and strength, with values of 0.049, 0.516, and 0.438, respectively, suggesting that the strength centrality results were stable.

Theme extraction from interviews

We identified five major themes from the semi-structured interviews (Fig. 4): (1) the psychological impact resulting from physiological symptoms, (2) fear of surgery and its associated uncertainties, (3) information needs and inadequate support, (4) the diversity and limitations of coping mechanisms, and (5) challenges of diagnostic delays and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S15
S13
S14
S22
S24
S10
S7
cluster1
S4: Disturbed sleep
S5: Distress
S11: Sadness
cluster2
S1: Pain
S15: Difficulty swallowing or chewing
S22: Problems with teeth or gums
others
S2: Fatigue
S3: Nausea
S6: Shortness of breath
S7: Difficulty remembering
S8: Lack of appetite
S9: Drowsiness
S10: Dry mouth
S12: Vomiting
S13: Numbness/tingling
S14: Mucus in the mouth or throat
S16: Choking or coughing
S17: Difficulty with voice or speech
S18: Skin pain, burning, or rash
S19: Constipation
S20: Problems with tasting food
S21: Mouth or throat sores
S24: limitation of mouth opening
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◂**Fig. 1** Symptom networks and centrality measures ($n=527$). **A** Symptom network of 24 symptoms. Symptom network analysis of 24 symptoms, categorized into two primary clusters and additional symptoms. Cluster 1 (emotional-sleep symptoms cluster) includes S4 (disturbed sleep), S5 (distress), and S11 (sadness). Cluster 2 (eating disorder symptoms cluster) consists of S1 (pain), S15 (difficulty swallowing or chewing), and S22 (problems with teeth or gums). **B** Strength, closeness, and betweenness of 24 symptoms with z-scores standardization. The plots display strength, closeness, and betweenness centrality measures. Difficulty swallowing or chewing (S15) exhibits the highest strength and betweenness centrality

misdiagnoses. For further details, please refer to the supplementary material.

Discussion

To our knowledge, this is the first study to examine the multidimensional symptom network of preoperative oral cancer patients, while integrating qualitative insights to capture their lived symptom experiences. The construction of a contemporaneous symptom network allows for the identification of core symptoms within the network structure, providing actionable insights to guide healthcare providers in developing targeted interventions for improved symptom management and patient outcomes. Our analysis revealed that distress and sadness were the most severe symptoms reported by the patients with oral cancer. Simultaneously, difficulty swallowing or chewing was identified as the core symptom with the highest impact strength, reflecting its central role in the symptom network. Through symptom clustering analysis, we identified two primary symptom groups: cluster 1, the emotional-sleep symptoms cluster, encompassing distress, sadness, and insomnia, and cluster 2, the eating disorder symptoms cluster, characterized by difficulties with swallowing and dental issues. Additionally, fatigue emerged as the symptom exerting the most significant negative impact on the quality of life among patients with oral cancer.

In this study, difficulty swallowing or chewing exhibited the highest centrality measure, underscoring its critical role in the overall symptom burden. These symptoms should be prioritized as clinical targets for intervention because of their substantial impact on patients' health outcomes. This finding aligns with those of previous studies that reported high prevalence rates of dysphagia and masticatory difficulties in patients with oral cancer [8, 36]. The elevated prevalence of symptoms may be attributed to factors such as increased salivary secretion, impaired swallowing reflexes, and intense tumor-induced pain. Another factor contributing to the severity of swallowing and chewing difficulties

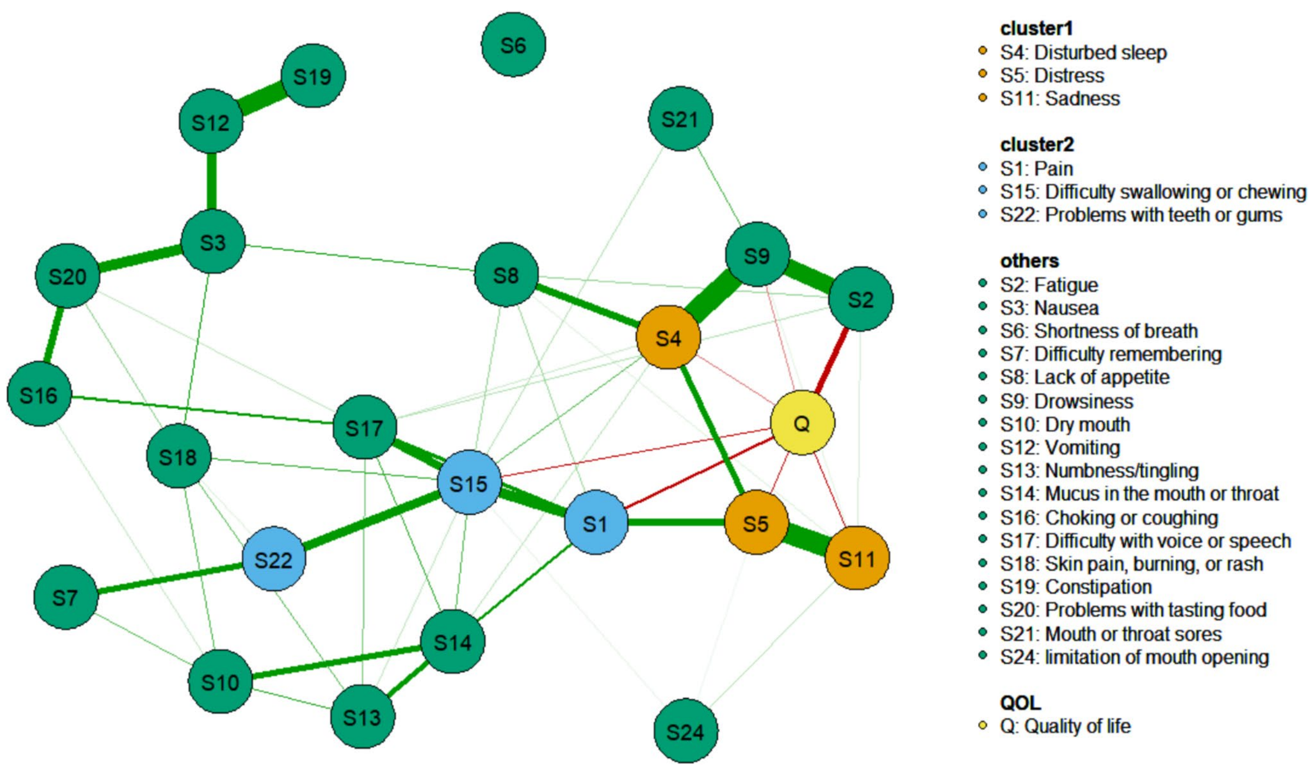

Fig. 2 Symptom network analysis with quality of life. The network depicts relationships among 24 symptoms and their correlations with QoL. Nodes represent symptoms grouped into cluster 1 (emotional-sleep: S4, S5, S11) and cluster 2 (eating disorder: S1, S15, S22), with other symptoms unclustered. Edges indicate correlation strength, with thicker edges representing stronger associations

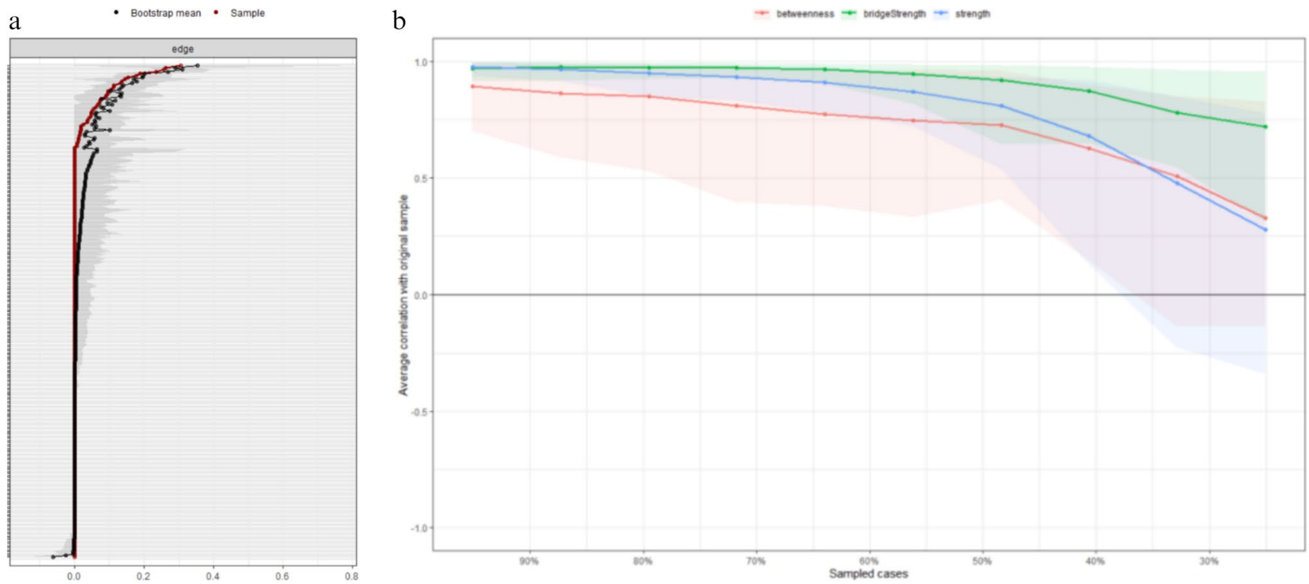

Fig. 3 Accuracy and stability of the symptom networks. **A** Bootstrap analysis results of the edge weight. Narrow confidence intervals around the edge weights indicate a high degree of network estimation accuracy. **B** Correlation stability coefficient for betweenness, closeness, and strength. Stability coefficients above 0.25 demonstrate acceptable reliability for centrality estimates

may be treatment delays and diagnostic inaccuracies. Such delays are often attributed to patients' limited health awareness, leading to neglect of early symptoms and postponement of specialized care. Additionally, misdiagnoses in primary care settings may result from limited experience or specialized knowledge of oral cancer among healthcare providers. Accordingly, enhancing the surveillance of swallowing and chewing functions at the time of diagnosis and hospital admission is crucial for optimizing early intervention, ensuring comprehensive symptom management, and promoting health awareness to support the early recognition of symptoms.

Our findings indicate that distress and sadness were the most severe symptoms reported by oral cancer patients, in contrast to previous studies on older adults with cancer, in which fatigue and disturbed sleep were identified as the most severe symptoms, with sadness ranking fifth [26]. This discrepancy may be influenced by the unique physiological and psychological challenges associated with oral cancer treatment, which involves surgical intervention in the head and neck region, affecting essential functions such as breathing, speech, and appearance, and often leading to dietary changes and taste alterations. These challenges significantly impact patients' emotional well-being and social interactions [37]. The interviews further underscored that inadequate informational support exacerbates psychological distress, with participants reporting unmet informational needs and heightened anxiety due to a lack of clarity regarding their treatment journey [38]. As one participant shared "The doctor offered no treatment or intervention during the waiting period for hospitalization, leaving me with no clarity or understanding of the situation." In clinical practice, early psychological interventions and comprehensive informational support can alleviate emotional distress, improve quality of life, and empower patients. Evidence suggests psychosocial and physical interventions like mindfulness, aerobic exercise, and Tai Chi effectively manage psychological symptoms [39, 40]. Nursing-led counseling and digital health tools also provide substantial benefits in addressing informational gaps and enhancing engagement during the diagnosis and treatment phases.

Logistic regression analysis reveals that female and married patients in cluster 1 reported more severe symptoms. Female patients may exhibit heightened sensitivity to appearance changes, with symptoms intensifying due to facial swelling, excessive salivation, and tumor-associated odors. Disturbed sleep warrants attention, as inadequate sleep triggers metabolic and neuroendocrine changes, especially affecting the hypothalamic–pituitary–adrenal (HPA) axis in women, which may subsequently lead to emotional disturbances [41]. This bidirectional relationship indicates that sleep disruptions and emotional distress mutually reinforce and perpetuate a cycle that intensifies the overall symptom burden in this patient population. Additionally, we observed that married patients reported lower symptom severity, which may be attributed to China's rich traditional culture. Rooted in Confucian philosophy, family is regarded as a primary source of psychological and emotional support, serving as a crucial component of an individual's social support network. Therefore, integrating family-centered approaches into

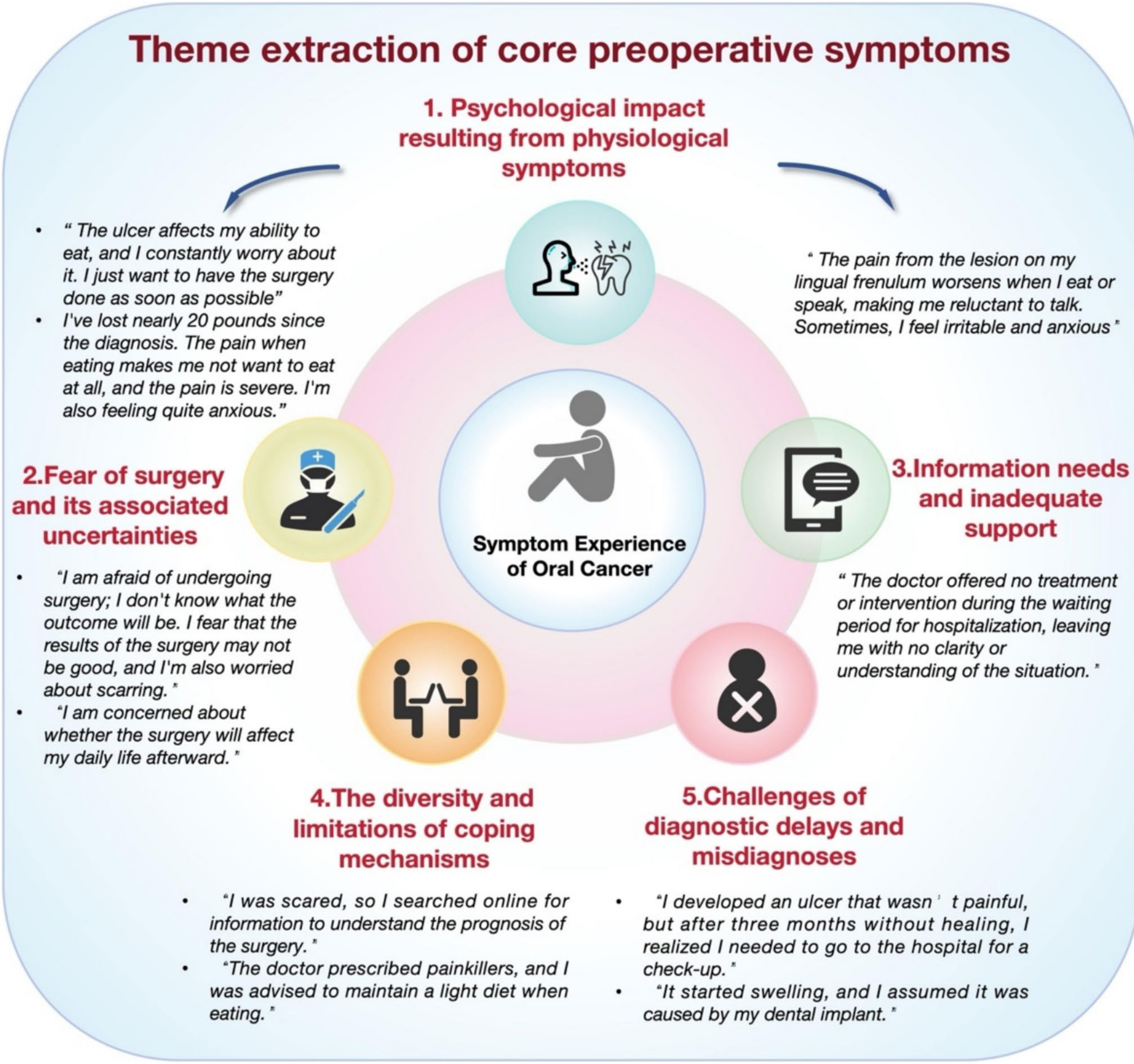

Fig. 4 Theme extraction of core preoperative symptoms. This figure illustrates the five major themes identified from semi-structured interviews with oral cancer patients regarding their preoperative symptom experiences

clinical interventions may enhance psychological resilience and reduce the symptom burden in this population.

Our study found that fatigue had the most significant negative impact on the quality of life. Prior network analyses identified fatigue as a central symptom in cancer patient populations, indicating its pervasive impact [12, 24]. Cancer-related fatigue affects all aspects of quality of life and may serve as a prognostic indicator for reduced survival, often affecting patients even before treatment initiation. Pre-treatment fatigue can increase physical and psychological vulnerability, potentially compromising patients' readiness for treatment and health outcomes. Cancer-related fatigue is influenced by a complex interplay of demographic, medical, psychosocial, behavioral, and biological factors, with studies indicating that approximately 25–33% of long-term cancer survivors experience persistent fatigue for up to a decade following diagnosis [42]. Despite its prevalence, fatigue remains underreported and insufficiently addressed, underscoring the need for early assessment and tailored interventions. Evidence suggests exercise and mind–body interventions, including aerobic and resistance training, acupuncture, mindfulness, and yoga, effectively alleviate fatigue throughout the cancer care trajectory [43]. The American College of Sports

Medicine (ACSM) recommends individualized exercise programs for cancer patients adjusted for exercise tolerance and specific diagnoses [44].

This study had several limitations. First, while the institution's large patient base provides a robust sample, the reliance on convenience sampling and the restriction to a single-center setting may limit the generalizability of the findings to broader populations. Additionally, while this study focused on a Chinese population, cultural factors can strongly influence swallowing and eating behaviors, which may influence the cross-cultural generalizability of the findings. Consequently, future research should account for cultural variations in symptom experiences to better assess the applicability of these results to diverse populations. Furthermore, the study's reliance on self-reported measures for assessing symptoms and quality of life introduces potential bias. Self-reporting is inherently susceptible to recall inaccuracies and subjective interpretations of symptom severity, which may affect data reliability. Additionally, the cross-sectional design offers only a snapshot of time and does not account for temporal changes in symptom presentation. To enhance the robustness and applicability of future studies, adopting a longitudinal design and incorporating a multicenter approach could provide deeper insights into symptom trajectories and improve generalizability across diverse populations.

Conclusion

Our study provides novel insights into the symptom networks of oral cancer in China by identifying core symptoms and capturing patients' real symptom experiences. The findings indicated that distress and sadness were the most severe symptoms, while difficulty in swallowing or chewing emerged as the core symptoms. Moreover, fatigue was identified as the symptom most closely associated with a negative impact on quality of life. This network analysis provides a foundation for developing targeted symptom management strategies and personalized interventions for oral cancer care. Future research should focus on constructing dynamic symptom networks to elucidate the mechanisms underlying symptom interactions and temporal trends.

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Author contribution YZ: Data curation, Formal analysis, Methodology, Writing-original draft. JYY: Data curation, Software, Supervision. TTL: Formal analysis, Software. LXK: Data curation, Supervision. XQB: Conceptualization, Funding acquisition, Supervision.

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Data availability The data supporting the findings of this study are available from the corresponding author upon reasonable request.

Declarations

Conflict of interest The authors declare no competing interests.

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