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Original Article

Perioperative symptom burden as an independent predictor of long-term functional and survival outcomes in oral squamous cell carcinoma patients undergoing free flap reconstruction: a retrospective cohort study

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Abstract: This study aimed to evaluate the prognostic significance of acute perioperative symptom burden as an independent predictor for long-term functional recovery and survival outcomes in patients with oral squamous cell carcinoma (OSCC) undergoing microvascular free flap reconstruction. A retrospective cohort of 355 OSCC patients treated between June 2022 and December 2024 at Henan Provincial People's Hospital was analyzed. All patients underwent primary tumor resection followed by immediate microvascular free flap reconstruction. Perioperative symptom burden was quantified using the validated MD Anderson Symptom Inventory-Head and Neck module (MDASI-HN). Based on the median core severity score on postoperative day 3 (POD 3) of 5.79, patients were stratified into low symptom burden (n=178) and high symptom burden (n=177) groups. Over a 12-month follow-up period, comprehensive assessments encompassed long-term speech function measured by the Speech Handicap Index (SHI) and Percent Consonants Correct (PCI), swallowing function evaluated via the MD Anderson Dysphagia Inventory (MDADI), quality of life assessed by the University of Washington Quality of Life questionnaire (UW-QOL) and the Functional Assessment of Cancer Therapy-Head and Neck (FACT-H&N), as well as survival outcomes. Multivariate linear regression, Cox proportional hazards models, and subgroup analyses were employed to ascertain the independent prognostic value of symptom burden. Findings revealed that elevated perioperative symptom burden was significantly associated with delayed and incomplete functional recovery. At 12 months, the high symptom burden cohort demonstrated markedly worse SHI scores (29.2 vs. 19.2, t=12.45, P<0.001), reduced PCI (84.4% vs. 94.4%, t=-15.32, P<0.001), and lower MDADI scores (84.0 vs. 94.0, t=-14.88, P<0.001). Multivariate analysis identified the area under the curve (AUC) of the perioperative MDASI severity trajectory as an independent predictor for 12-month SHI (B=2.83, 95% CI 1.52-4.14, P=0.001) and UW-QOL scores (B=-3.82, 95% CI -5.14 to -2.50, P=0.001). Furthermore, a high symptom burden was independently correlated with poorer overall survival (Log-rank P=0.019) and recurrence-free survival (Log-rank P=0.025); Cox regression confirmed high symptom burden as an independent risk factor for overall survival (HR=1.78, 95% CI 1.06-2.99, P=0.029). Subgroup analyses upheld the robustness of these associations across diverse clinical and demographic strata. In conclusion, acute perioperative symptom burden transcends being a mere transient reflection of surgical trauma, serving instead as a pivotal independent prognosticator of long-term functional outcomes, quality of life, and survival in OSCC patients undergoing free flap reconstruction. Early identification and proactive management of perioperative symptoms may constitute a novel therapeutic avenue to enhance both oncologic and functional prognoses.

Keywords: Oral squamous cell carcinoma, free flap reconstruction, perioperative period, symptom burden, prognosis, quality of life

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Introduction

Oral squamous cell carcinoma (OSCC) is among the most prevalent malignant tumors of the head and neck worldwide. According to GLOBOCAN 2022 data, lip and oral cancers impose a significant global health burden, with particularly high incidence and mortality rates in low- and middle-income countries [1]. For patients with locally advanced OSCC, radical surgical resection combined with immediate microvascular free flap reconstruction has become the standard therapeutic approach. However, this extensive surgical intervention results in substantial trauma, and patients frequently experience a multidimensional cluster of symptoms during the acute perioperative period, including severe pain, dysphagia, speech difficulties, fatigue, and anxiety or depression, collectively constituting a considerable "symptom burden" [2].

In recent years, the significance of patient-reported outcomes in the comprehensive management of cancer has garnered increasing attention. Emerging methodologies such as network analysis have uncovered intricate synergistic amplification effects among core perioperative symptoms in patients with head and neck cancer [3]. Systematic review studies indicate that the symptom burden experienced by cancer patients during the perioperative period is often of moderate to severe intensity and may evolve into chronic issues [4]. However, traditional prognostic research has predominantly focused on objective clinicopathological parameters, including TNM staging, resection margin status, and lymph node metastasis, while comparatively overlooking the potential prognostic value of patients' subjective symptom experiences [5].

Emerging evidence suggests that inadequately managed acute symptom burden can trigger perioperative immunosuppression by activating the hypothalamic-pituitary-adrenal axis and the sympathetic nervous system, thereby impairing the antitumor activity of natural killer cells and cytotoxic T lymphocytes [6]. Although previous studies have explored the application value of enhanced recovery after surgery in head and neck reconstruction [7] and the predictive role of baseline symptom scores for chemoradiotherapy toxicity [8], there remains a significant lack of large-scale longitudinal research investigating how the severity of acute symptoms independently influences long-term speech function [9], swallowing function, and overall survival [10].

Based on this, the present retrospective cohort study aims to systematically quantify the perioperative symptom burden in OSCC patients undergoing free flap reconstruction and comprehensively evaluate its independent impact on postoperative speech function, swallowing function, quality of life, and survival outcomes over a 12-month period [11, 12]. This will provide evidence-based support for individualized risk stratification and precise perioperative management.

Methods

Research subjects

In this single-center retrospective cohort study, clinical data were collected from patients diagnosed with primary OSCC who were hospitalized in the Henan Provincial People's Hospital between June 2022 and December 2024. All patients underwent radical tumor resection and immediate microvascular free flap reconstruction following evaluation by a multidisciplinary tumor board (MDT).

Inclusion criteria: (1) Age ≥18 years; (2) Diagnosis of primary OSCC confirmed by histopathology; (3) Undergoing radical tumor resection combined with simultaneous microvascular free flap reconstruction (e.g., fibular osteocutaneous flap, anterolateral thigh flap); (4) Possessing basic communication abilities preoperatively, capable of understanding and completing relevant questionnaires; (5) Provision of written informed consent.

Exclusion criteria were as follows: (1) A history of other malignant tumors in the head and neck region or concurrent treatment for other cancers; (2) Undergoing non-microsurgical reconstruction (such as local flaps or simple free skin grafts); (3) Presence of severe psychiatric disorders, cognitive impairments, or speech difficulties that precluded accurate reporting of symptom experiences; (4) Concurrent active systemic infection, severe dysfunction of the heart, liver, or kidneys, or autoimmune diseases; (5) Death within 30 days postoperatively or occurrence of severe complications preventing continued follow-up (e.g., extensive cerebral infarction, persistent coma), to ensure that all included patients had the opportunity to complete

comprehensive perioperative symptom assessments; (6) Significant missing core clinical data or questionnaire responses. This exclusion framework may have systematically omitted extreme cases with the highest symptom burden and worst outcomes, potentially leading to an underestimation of adverse prognoses in the high-burden group. To assess the impact of this selection bias, a sensitivity analysis was conducted.

The study protocol was reviewed and approved by the Ethics Committee of Henan Provincial People's Hospital, and all research procedures strictly adhered to the ethical principles outlined in the Declaration of Helsinki. Due to the retrospective design, the requirement for written informed consent was waived by the ethics committee.

Symptom burden assessment

The perioperative symptom burden of patients was quantified using the culturally validated Chinese version of the MD Anderson Symptom Inventory-Head and Neck (MDASI-HN) module [13]. This instrument demonstrates high reliability and validity in symptom assessment among head and neck cancer patients and has been extensively utilized in numerous international multicenter clinical trials [14]. Assessment time points were set at preoperative baseline, postoperative day 3 (POD 3), postoperative day 7 (POD 7), and at discharge or 4 weeks post-surgery, whichever occurred first.

The MDASI-HN utilizes a 0-10 Numerical Rating Scale (NRS), where 0 signifies "no symptom" or "no interference", and 10 represents "the most severe symptom imaginable" or "complete interference". This scale encompasses three primary dimensions: (1) Core symptom severity, consisting of 13 items such as pain, fatigue, nausea, and disturbed sleep; (2) Symptom interference with daily activities, including 6 items like general activity, mood, work, and interpersonal relationships; and (3) Head and neck-specific symptoms, comprising 9 items such as difficulty swallowing, chewing problems, speech clarity issues, and thick mucus.

Postoperative day 3 (POD 3) was selected as the primary time point because patients typically experience peak surgical trauma and have not fully recovered from anesthesia, making symptoms most pronounced at this time. Using the median MDASI core severity score (5.79 points) at POD 3 as the cut-off, patients were categorized into low- (<5.79) and high-burden (≥5.79) groups.

For symptom-specific interpretation, the MDASI-HN item profile was further organized into three clinically dominant perioperative symptom domains: a pain-surgical distress domain, a swallowing/oral-function domain, and a psychological distress domain. These domains were used to guide translational interpretation and targeted postoperative management, whereas the primary statistical exposure remained the validated MDASI core severity score and perioperative MDASI severity AUC.

Long-term outcome measures and follow-up

During outpatient follow-ups at 1, 3, 6, and 12 months postoperatively, patients' functional recovery and quality of life were systematically assessed by dedicated researchers who had undergone standardized training.

Speech Function Assessment: A combined approach utilizing both subjective and objective methods was employed. The subjective evaluation involved the Speech Handicap Index (SHI) questionnaire, which consists of 30 items with a total score range of 0 to 120, where higher scores indicate more severe psychosocial impairment related to speech. The objective assessment utilized the Percentage of Consonant Intelligibility (PCI) test. Recordings of patients reading a standardized word list were blindly rated by two experienced speech-language pathologists who were unaware of the patients' group assignments, and the percentage of correctly articulated consonants was calculated.

Swallowing Function Assessment: The MD Anderson Dysphagia Inventory (MDADI) was utilized for evaluation. This instrument comprises 20 items categorized into four domains: global, emotional, physical, and functional. After score transformation, the total score ranges from 20 to 100, with higher scores indicating better swallowing function and a lesser negative impact on quality of life.

Quality of Life (QOL) Assessment: The University of Washington Quality of Life questionnaire (UW-QOL) and the Functional Assessment of Cancer Therapy-Head and Neck scale (FACT-H&N) were utilized. The UW-QOL comprises 12 specific domains, including pain, appearance,

activity, and recreation, with each domain scored from 0 to 100. The FACT-H&N consists of five subscales: Physical Well-Being (PWB), Social/Family Well-Being (SWB), Emotional Well-Being (EWB), Functional Well-Being (FWB), and Head and Neck Cancer Subscale (HNCS), where higher scores correspond to better quality of life.

Perioperative complication assessment: All complications occurring within 30 days postoperatively were standardized and classified using the internationally recognized Clavien-Dindo grading system [15, 16]. Grades I-II were defined as mild complications, while grade ≥III was classified as severe complications, requiring surgical, endoscopic, or radiological intervention, or posing a life-threatening risk. Particular attention was given to flap-related complications (such as vascular crisis, partial or complete necrosis) and donor site complications (including wound infection, dehiscence, and sensory or motor abnormalities).

Survival Outcomes: The primary endpoints included Overall Survival (OS) and Recurrence-Free Survival (RFS). OS was defined as the time from the date of surgery to death from any cause; RFS was defined as the time from the date of surgery to the first occurrence of local regional recurrence, distant metastasis, or death from any cause. The follow-up cutoff date was December 31, 2025. Median follow-up time was estimated using the reverse Kaplan-Meier method.

Quality control and data review

To ensure the accuracy and reliability of the research data, this study implemented rigorous quality control measures throughout the entire process of data collection, entry, and analysis: (1) Establishment of Standard Operating Procedures (SOPs): A detailed clinical data dictionary and electronic case report forms (eCRFs) were developed to standardize the definitions of all variables, measurement units, and principles for handling missing data; (2) Personnel Training: All researchers involved in questionnaire administration, functional assessments, and data extraction underwent standardized training and passed consistency assessments prior to formal study commencement; (3) Double-Blind Assessment: Objective evaluations of speech and swallowing functions, as well as the grading of complications using the Clavien-Dindo classification, were independently conducted by two senior experts blinded to the patients' symptom grouping. In cases of disagreement, a third senior expert adjudicated; (4) Dual Data Entry and Logical Validation: A dual independent data entry system was employed with built-in logical validation rules (e.g., age range limits, maximum scale scores). Monthly random audits covering 10% of entries were conducted, revealing an entry discrepancy rate below 0.5%; (5) Verification of Outliers and Logical Inconsistencies: Extreme values exceeding physiological plausibility or data with logical contradictions were traced back to the original medical records for verification on a case-by-case basis; (6) Reproducibility of Statistical Analyses: All statistical datasets and code were independently re-run and cross-checked by a second statistician within the research team to ensure reproducibility of results [17, 18].

Statistical methods

Statistical analyses were performed using SPSS version 26.0 (IBM Corp., Armonk, NY, USA) and R software version 4.2.1. The normality of continuous variables was assessed using the Shapiro-Wilk test combined with histogram visualization. Normally distributed data were presented as mean ± standard deviation ($\bar{x} \pm s$), and comparisons between groups were conducted using independent samples t-tests. Non-normally distributed data were expressed as median and interquartile range [M (Q1, Q3)], with group comparisons performed by the Mann-Whitney U test. Categorical variables were summarized as counts and percentages [n (%)], and differences between groups were evaluated using the chi-square test or Fisher's exact test when the expected frequency was less than 5. For ordinal categorical variables, such as ASA classification, TNM staging, and histological grading, trend chi-square tests (Cochran-Armitage) or Mann-Whitney U tests were applied.

The perioperative MDASI severity area under the curve (AUC) was calculated using the trapezoidal method by integrating the core severity scores at four time points: preoperative, POD 3, POD 7, and discharge/4 weeks. This approach comprehensively reflects the cumulative symptom burden exposure during the perioperative period. Pearson or Spearman correlation analyses were performed to assess the relationship

between the AUC and various functional and quality-of-life (QOL) outcome measures at 12 months. Multivariable linear regression models were employed to identify independent predictors of 12-month SHI and UW-QOL scores, with unstandardized regression coefficients (B) and their 95% confidence intervals (CI) reported. Variables included in the multivariable models were those with P<0.10 in univariate analyses or those with established clinical relevance based on prior literature (e.g., age, TNM stage, defect size, adjuvant chemoradiotherapy), and multicollinearity was excluded by ensuring variance inflation factors (VIF) <5. Given individual differences in discharge timing (median hospital stays of 18 and 13 days in the two groups, respectively), to ensure comparability, day 28 postoperatively was set as the common endpoint. For patients discharged earlier, the discharge score was carried forward assuming linear decay to day 28. Furthermore, to eliminate the influence of varying calculation intervals, the final AUC values were normalized by dividing by the standardized time window of 28 days, converting them into mean daily symptom intensity, thus enabling comparability across patients with differing lengths of hospitalization. To address concerns that postoperative complications might confound the effect of symptom burden, severe postoperative complications (Clavien-Dindo grade ≥III) were additionally included as covariates in all multivariable regression models to evaluate whether the independent effect of symptom burden was attenuated by complications.

Survival analysis was conducted using the Kaplan-Meier method to generate survival curves, with intergroup survival rate comparisons performed via the Log-rank test. Univariate and multivariate Cox proportional hazards regression models were employed to identify independent risk factors affecting overall survival (OS) and recurrence-free survival (RFS), calculating hazard ratios (HR) and their corresponding 95% confidence intervals (CI). The proportional hazards assumption of the Cox model was verified using Schoenfeld residuals and log-minus-log survival plots [19]. To assess the robustness of the prognostic value of symptom burden, pre-specified subgroup analyses were conducted based on key clinical characteristics including age, sex, primary tumor site, TNM stage, and flap type, with results displayed in a forest plot. All statistical tests were two-sided, with a significance threshold set at P< 0.05. Considering the multiple outcome comparisons in this study, the Benjamini-Hochberg procedure was applied to control the false discovery rate (FDR) for primary endpoints, thereby minimizing the risk of type I errors due to multiple testing. Because no external validation cohort was available, all prediction-performance estimates, including partial R2 and C-index comparisons, were interpreted as internally derived and hypothesis-generating rather than as a fully validated clinical prediction model. Marginal *P* values in the multivariable models were therefore interpreted together with effect sizes and 95% confidence intervals to reduce overinterpretation of statistically borderline findings.

Results

Patient characteristics and study process

A total of 442 patients with oral squamous cell carcinoma (OSCC) scheduled for free flap reconstruction were initially screened, among whom 355 met the inclusion criteria and completed the study (**Figure 1**). The median follow-up duration was 24.5 months (range: 12.0-42.0 months). Based on the median score of the MDASI core symptom severity on postoperative day 3 (POD 3) (5.79 points), 178 patients were classified into the low symptom burden group, while 177 patients were classified into the high symptom burden group. To ensure comparability between the two groups, extensive baseline data were collected. As shown in **Table 1**, over 20 variables including demographic characteristics, lifestyle habits, comorbidities, preoperative nutritional status, tumor features, surgical details, and preoperative baseline symptoms were well balanced between the groups, with no statistically significant differences observed (all P>0.05). This suggests that the outcome differences observed between the two groups are unlikely to be attributed to systematic differences in baseline characteristics.

Perioperative complications and symptom trajectories

The high symptom burden group exhibited significantly elevated scores across all MDASI

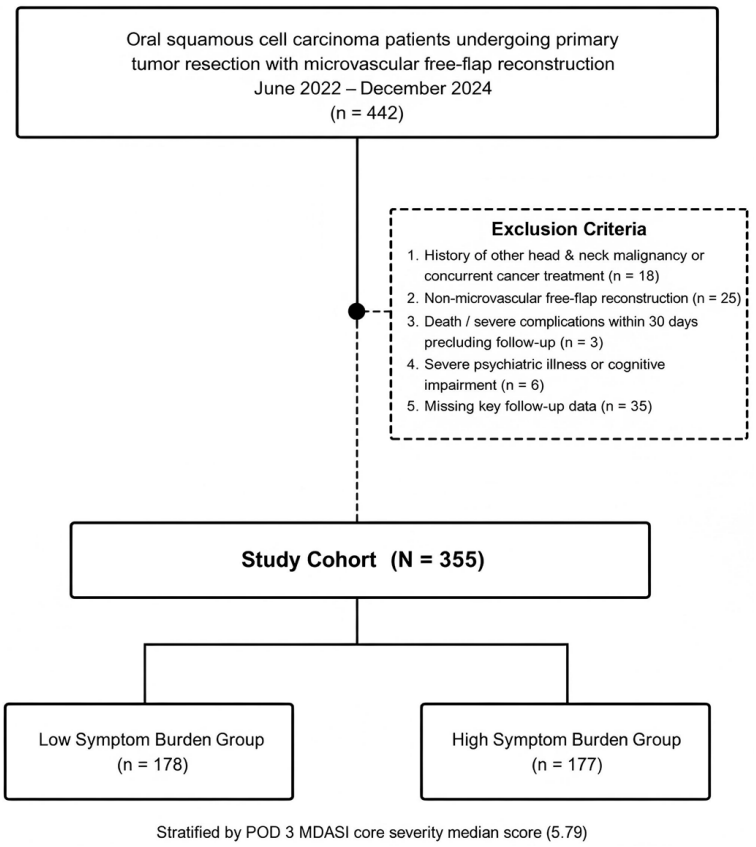

Figure 1. Flowchart of participant inclusion and follow-up analysis. Patient screening, eligibility assessment, exclusion criteria, final cohort allocation, and follow-up analysis. OSCC, oral squamous cell carcinoma; MDASI-HN, MD Anderson Symptom Inventory-Head and Neck module.

domains throughout the perioperative period (**Figure 2**). Core severity, symptom interference, and head and neck-specific symptoms peaked on POD 3 and remained significantly higher in the high burden group at discharge/4 weeks (all P<0.001). Moreover, the high burden group had a significantly greater incidence of severe complications (Clavien-Dindo grade ≥III) compared to the low burden group (20.3% vs. 5.6%, χ^2=17.152, P<0.001) (**Table 2**).

Long-term functional recovery and nutritional status

Longitudinal analysis revealed that a high perioperative symptom burden was significantly associated with delayed and incomplete functional recovery over the 12-month follow-up period (**Figure 3**). At 12 months, the high-burden group exhibited markedly poorer speech function, evidenced by higher SHI scores (29.2 vs. 19.2, t=12.45, P<0.001) and lower objective PCI values (84.4% vs. 94.4%, t=-15.32, P<0.001) [20]. Similarly, swallowing function, assessed by MDADI, was significantly impaired in the high-burden cohort (84.0 vs. 94.0, t=-14.88, P<0.001) [21]. This deterioration in swallowing function was also reflected in postoperative nutritional status differences, with the high-burden group experiencing a significantly prolonged duration to gastrostomy tube removal and lower serum albumin levels at 6 months postsurgery (**Table 3**) [22].

Quality of life outcomes

Quality of life assessed by the UW-QOL radar chart (**Figure 4**) revealed widespread deficits in multiple domains, including swallowing, chewing, speech, and mood, in the high symptom burden group at 6 and 12 months postoperatively. Detailed analysis of the FACT-H&N subscales (**Table 4**) further confirmed these findings, with the high burden group scoring significantly lower than the low burden group in physical well-being, functional well-being, and head and neck additional concerns [23, 24].

Correlation and multivariate analysis

The hexagonal density plot (**Figure 5**) shows a moderate but statistically significant correlation between the perioperative MDASI severity area under the curve (AUC) and all 12-month outcomes. A higher perioperative symptom burden was significantly associated with poorer SHI scores (r=0.452, moderate correlation), lower PCI scores (r=-0.483, moderate correlation), reduced MDADI scores (r=-0.391, moderate correlation), and decreased overall survival months (r=-0.286, weak to moderate correlation) (all P<0.001).

To validate the incremental predictive value of incorporating the AUC metric compared to a single time-point (POD 3) score, we further

Table 1. Comprehensive comparison of baseline demographic, clinicopathological characteristics, and surgical parameters between the two groups

Characteristics	Low burden group (n=178)	High burden group (n=177)	Statistic	*P* value
Age (years), mean ± SD	58.4 ± 10.2	59.1 ± 11.5	t=-0.610	0.542
Gender (Male/Female)	112/66	115/62	χ^2=0.162	0.687
Smoking history (Never/Former/Current)	65/45/68	60/48/69	Trend χ^2=0.412	0.814
Alcohol history (Never/Former/Current)	70/40/68	65/42/70	Trend χ^2=0.558	0.756
Charlson Comorbidity Index (CCI)	1.8 ± 1.2	1.9 ± 1.3	t=-0.743	0.458
ASA grade (I/II/III)	45/105/28	42/108/27	Trend χ^2=0.228	0.892
Preoperative KPS score	88.5 ± 8.2	87.9 ± 8.5	t=0.683	0.495
Preoperative BMI (kg/m^2)	23.5 ± 3.2	23.1 ± 3.4	t=1.116	0.265
Preoperative Albumin (g/L)	42.5 ± 4.1	41.8 ± 4.5	t=1.501	0.134
Preoperative Hemoglobin (g/L)	135.2 ± 14.5	133.8 ± 15.2	t=0.896	0.371
Preoperative MDASI core severity score	2.1 ± 1.5	2.3 ± 1.6	t=-1.217	0.224
Primary site (Tongue/Floor of mouth/Buccal/Other)	98/35/25/20	102/32/28/15	χ^2=1.498	0.682
TNM stage (I/II/III/IV)	25/50/65/38	22/46/68/41	Trend χ^2=0.815	0.845
Histological grade (Well/Moderate/Poor)	45/95/38	42/98/37	Trend χ^2=0.184	0.912
Perineural invasion (PNI) (Yes/No)	42/136	45/132	χ^2=0.098	0.754
Lymphovascular invasion (LVI) (Yes/No)	38/140	41/136	χ^2=0.165	0.685
Maximum defect size (>6 cm/≤6 cm)	82/96	88/89	χ^2=0.568	0.451
Flap type (Fibular/ALT)	65/113	70/107	χ^2=0.346	0.556
Neck dissection (Unilateral/Bilateral)	145/33	140/37	χ^2=0.398	0.528
Tracheotomy (Yes/No)	152/26	155/22	χ^2=0.253	0.615
Operative time (min), mean ± SD	485 ± 85	492 ± 92	t=-0.746	0.456
Intraoperative blood loss (mL), median [IQR]	350 [250-500]	380 [280-550]	U=14852.5	0.312
Postoperative adjuvant chemoradiotherapy (Yes/No)	105/73	112/65	χ^2=0.664	0.415

Note: Normally distributed continuous data are presented as mean ± standard deviation ($\bar{x}$ ± s), while skewed data are expressed as median (Q1, Q3). Between-group comparisons are conducted using t-tests or Mann-Whitney U tests, respectively. Categorical data are reported as n (%), with group differences analyzed via χ^2 tests or Fisher's exact test. Ordered categorical variables are assessed using the trend χ^2 test (Cochran-Armitage test).

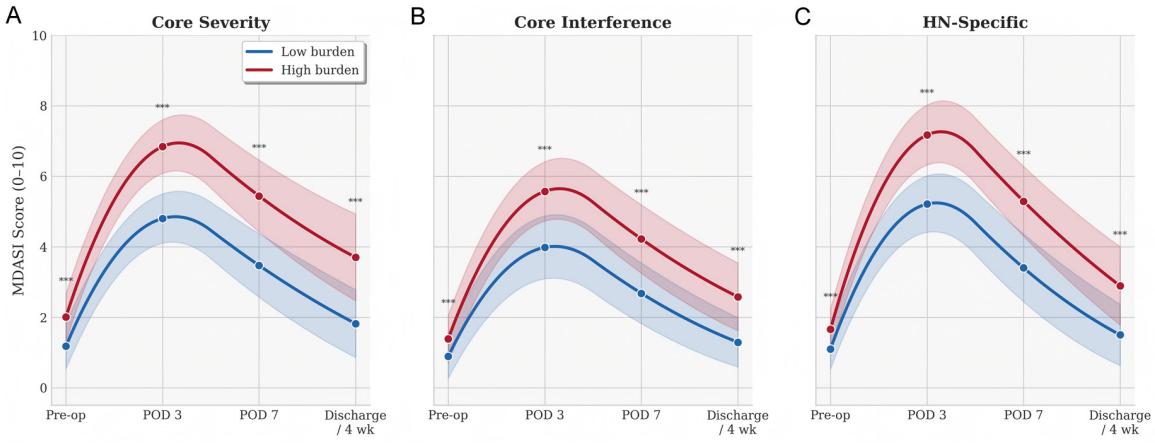

Figure 2. Perioperative trajectory of symptom burden assessed by MD Anderson symptom inventory-head and neck (MDASI-HN). A. Core severity. B. Core interference. C. Head and neck-specific symptoms. Values are shown across preoperative baseline, POD 3, POD 7, and discharge/4 weeks. Lines represent group trajectories and shaded areas represent variability around the estimates. POD, postoperative day. *P* values are reported to three decimal places where possible; values smaller than 0.001 are shown as P<0.001.

Table 2. Comparison of perioperative specific complication incidence rates (According to Clavien-Dindo Classification)

Complication Type	Low burden group (n=178)	High burden group (n=177)	Statistic	*P* value
Overall complication rate, n (%)	45 (25.3%)	78 (44.1%)	χ^2=13.824	<0.001
Mild complications (Grade I-II)	35 (19.7%)	42 (23.7%)	χ^2=0.859	0.354
Severe complications (Grade ≥III)	10 (5.6%)	36 (20.3%)	χ^2=17.152	<0.001
Flap crisis/partial necrosis	5 (2.8%)	14 (7.9%)	χ^2=4.598	0.032
Donor site infection/dehiscence	12 (6.7%)	25 (14.1%)	χ^2=5.327	0.021

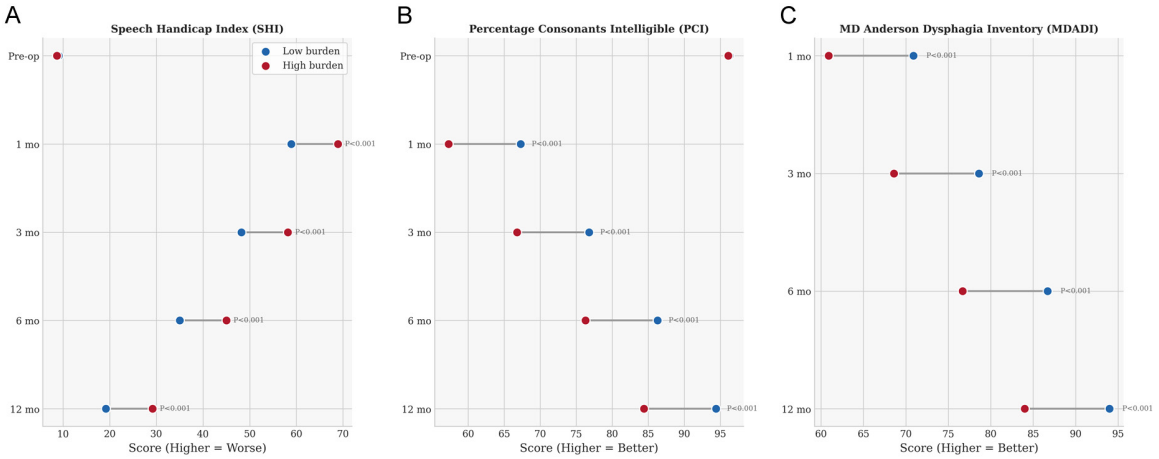

Figure 3. Longitudinal recovery of speech and swallowing functions within 12 months. A. Speech Handicap Index (SHI). B. Percentage of consonants correct (PCI). C. MD Anderson Dysphagia Inventory (MDADI). SHI, Speech Handicap Index; PCI, percentage of consonants correct; MDADI, MD Anderson Dysphagia Inventory. Higher SHI indicates worse speech-related impairment, whereas higher PCI and MDADI indicate better functional recovery. *P* values are reported to three decimal places where possible; values smaller than 0.001 are shown as P<0.001.

Table 3. Comparison of nutritional status and tube feeding dependence at various postoperative time points

Nutritional Indicator	Low burden group (n=178)	High burden group (n=177)	Statistic	*P* value
Gastric tube removal time (days), median [IQR]	14 [10-18]	22 [15-35]	U=8452.0	<0.001
Tube feeding dependence at 3 months post-op, n (%)	12 (6.7%)	35 (19.8%)	χ^2=13.158	<0.001
Albumin at 6 months post-op (g/L)	41.2 ± 3.5	38.5 ± 4.1	t=6.685	<0.001
BMI decrease >10% at 12 months post-op, n (%)	18 (10.1%)	42 (23.7%)	χ^2=11.782	<0.001

compared the predictive performance of the POD 3 core severity score and the perioperative MDASI severity AUC for 12-month primary outcomes (**Table 5**). The results demonstrated that the AUC explained a significantly greater variance in 12-month SHI (partial R^2=0.185) than the single POD 3 score (partial R^2=0.142; Steiger Z-test, P=0.012). Similarly, for predicting UW-QOL, the AUC's partial R^2 (0.168) outperformed that of POD 3 (partial R^2=0.125; P=0.008). Regarding survival prediction, the Cox model using AUC as a continuous variable yielded a C-index of 0.682 (95% CI: 0.635-0.729), which was significantly higher than the model using the POD 3 score as the predictor (C-index = 0.651, 95% CI: 0.604-0.698; likelihood ratio test P=0.031). These findings indicate that the perioperative AUC, by integrating symptom data across multiple time points, provides incremental predictive utility beyond a single POD 3 score, thereby confirming the necessity and rationality of introducing a cumu-

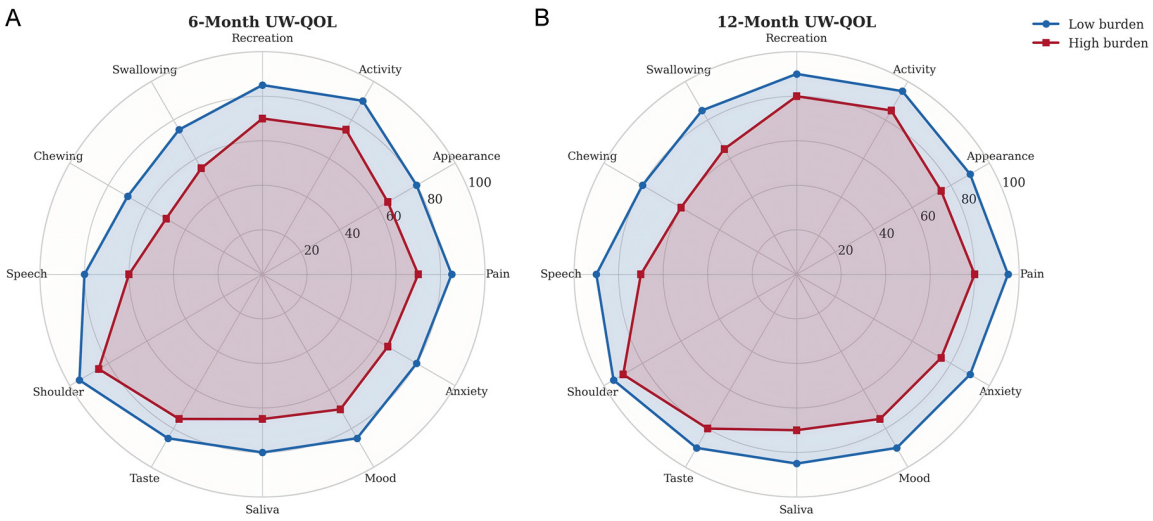

Figure 4. University of Washington Quality of Life (UW-QOL) domain scores at 6 and 12 months postoperatively. A. 6-month UW-QOL. B. 12-month UW-QOL. The radar plots compare domain-specific quality of life between low and high symptom burden groups at 6 and 12 months.

Table 4. Detailed Comparison of FACT-H&N Subscale Scores at 12 Months Postoperatively

FACT-H&N Subscale	Low burden group (n=178)	High burden group (n=177)	Statistic	*P* value
Physical Well-Being (PWB, 0-28)	24.5 ± 3.2	19.8 ± 4.5	t=11.352	<0.001
Social/Family Well-Being (SWB, 0-28)	22.1 ± 4.0	20.5 ± 4.8	t=3.415	0.001
Emotional Well-Being (EWB, 0-24)	19.5 ± 3.5	16.2 ± 4.1	t=8.165	<0.001
Functional Well-Being (FWB, 0-28)	21.8 ± 4.2	17.5 ± 5.0	t=8.782	<0.001
Head & Neck Additional Concerns (HNCS, 0-40)	32.5 ± 5.1	26.8 ± 6.5	t=9.215	<0.001

lative exposure metric. For clinical implementation, these findings support a preliminary two-step triage approach: POD 3 core severity score ≥5.79 identifies patients requiring immediate symptom-oriented assessment, whereas a persistently high perioperative MDASI severity AUC indicates the need for intensified rehabilitation, nutritional support, and closer oncologic follow-up.

Multivariate linear regression analysis (**Figure 6**) confirmed that perioperative MDASI severity AUC remained a robust independent predictor of 12-month SHI (B=2.83, 95% CI: 1.52-4.14, P=0.001) and UW-QOL (B=-3.82, 95% CI: -5.14 to -2.50, P=0.001) even after adjusting for critical clinical variables such as defect size, TNM staging, and concurrent chemoradiotherapy. This finding strongly supports the central premise of this study, namely that symptom burden serves as a prognostic indicator independent of traditional clinical parameters.

Furthermore, when severe complications (Clavien-Dindo grade ≥III) were additionally included as a covariate in the multivariable linear regression model, the independent predictive effect of the perioperative MDASI severity AUC on 12-month SHI was only slightly attenuated (B decreased from 2.83 to 2.61, 95% CI: 1.28-3.94, P=0.003). Its effect on UW-QOL similarly remained robust (B decreased from -3.82 to -3.55, 95% CI: -4.89 to -2.21, P=0.001). Severe complications themselves reached statistical significance within the model (for SHI: B=3.45, 95% CI: 1.12-5.78, P=0.004; for UW-QOL: B=-4.12, 95% CI: -6.55 to -1.69, P=0.001), but their inclusion only resulted in an approximately 7%-8% attenuation of the symptom burden AUC regression coefficients, which is well below the commonly used 10% change threshold for confounding. These findings suggest that the prognostic impact of perioperative symptom burden is independent of postoperative complications, with both potentially influencing long-term out-

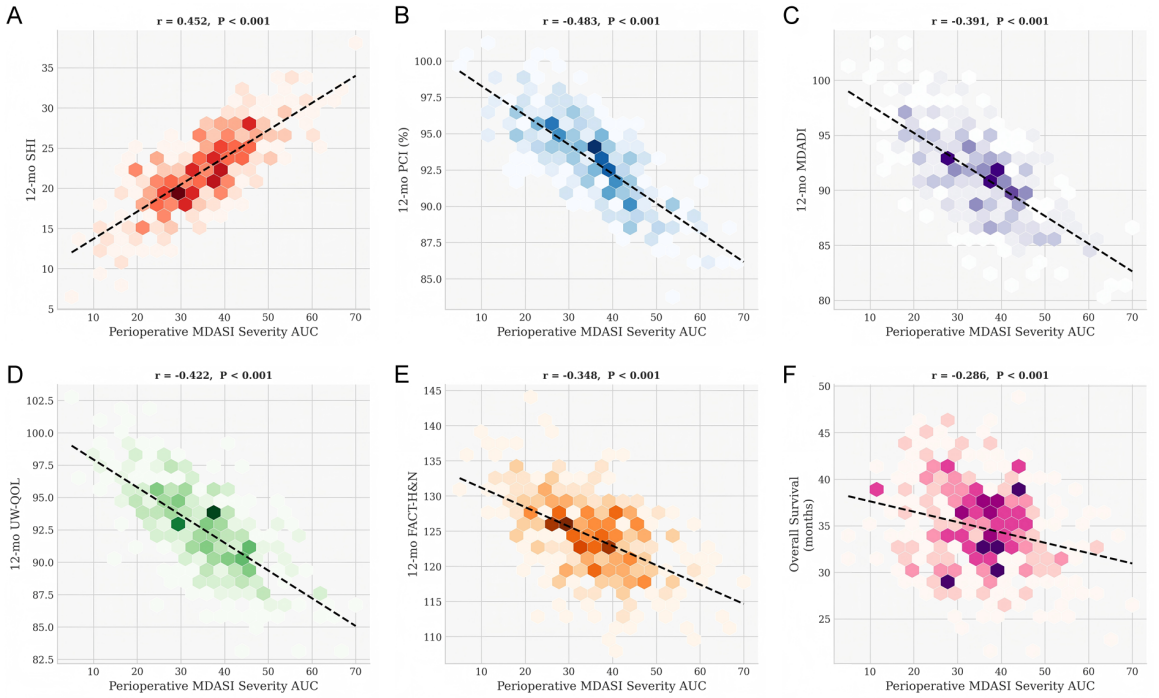

Figure 5. Hexagonal density plot of perioperative MD Anderson symptom inventory-head and neck (MDASI-HN) severity area under the curve (AUC) in relation to 12-month outcomes. A. 12-month SHI. B. 12-month PCI. C. 12-month MDADI. D. 12-month UW-QOL. E. 12-month FACT-H&N. F. Overall survival months. AUC, area under the curve; SHI, Speech Handicap Index; PCI, percentage of consonants correct; MDADI, MD Anderson Dysphagia Inventory; UW-QOL, University of Washington Quality of Life questionnaire; FACT-H&N, Functional Assessment of Cancer Therapy-Head and Neck. The x-axis represents perioperative MDASI-HN severity AUC, and the y-axis represents the corresponding 12-month outcome in each panel. Correlation coefficients (r) and *P* values are presented in each panel; *P* values are reported to three decimal places where possible, and values smaller than 0.001 are shown as P<0.001.

Table 5. Comparison of predictive performance for 12-month outcomes between POD 3 core severity scores and perioperative MDASI severity AUC

Outcome Measure	POD 3 Partial R^2/C-index	AUC Partial R^2/C-index	*P* value (Difference Test)
12-month SHI	0.142	0.185	0.012*
12-month UW-QOL	0.125	0.168	0.008**
12-month PCI	0.138	0.172	0.025*
12-month MDADI	0.112	0.148	0.018*
Overall Survival (C-index)	0.651	0.682	0.031*

Note: The partial R^2 values are derived from multivariable linear regression models adjusting for TNM stage, defect size, adjuvant chemoradiotherapy, perineural invasion (PNI), lymphovascular invasion (LVI), and severe complications; the C-index values are obtained from Cox proportional hazards models; P<0.05, P<0.01. *P<0.05 and **P<0.01 indicate statistically significant differences between the POD 3 model and the perioperative MDASI severity AUC model.

comes via distinct pathophysiological mechanisms.

Survival analysis and healthcare resource utilization

Kaplan-Meier survival analysis (**Figure 7**) demonstrated that patients with a high symptom burden exhibited significantly poorer overall survival (Log-rank P=0.019) and recurrence-free survival (Log-rank P=0.025) compared to those in the low burden cohort. Cox proportional hazards regression analysis (**Table 6**) further confirmed that a high symptom burden is an independent risk factor for overall survival (OS). It is noteworthy that age, with a *P*-value of 0.085 in univariate analysis, was excluded from the multivariate model due to collinearity with other covariates and lack of statistical significance. In the preliminary model including only TNM stage, margin status, and extranodal extension (ENE), the hazard ratio (HR) for high symptom burden was 1.85 (95% CI: 1.12-3.05, P=0.016). In the final comprehensive model presented in **Table 6**, which additionally incorporated adjuvant chemoradiotherapy, perineural invasion (PNI), lymphovascular invasion

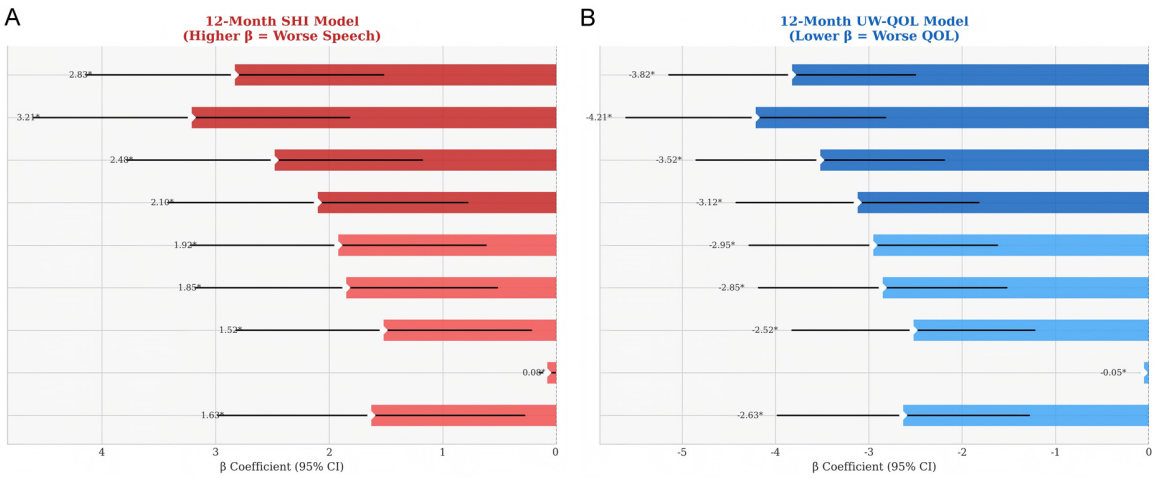

Figure 6. Butterfly forest plot of multivariate predictors for 12-month speech handicap index (SHI) and University of Washington quality of life (UW-QOL) outcomes. A. 12-month SHI model. B. 12-month UW-QOL model. Regression coefficients are shown with 95% confidence intervals. SHI, Speech Handicap Index; UW-QOL, University of Washington Quality of Life questionnaire; CI, confidence interval.

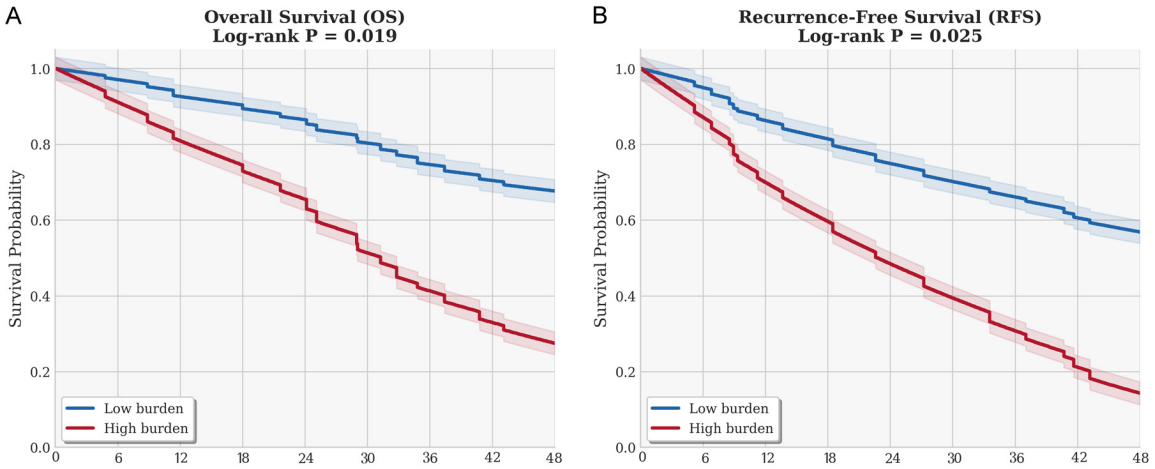

Figure 7. Kaplan-Meier survival curves. A. Overall survival (OS). B. Recurrence-free survival (RFS). OS, overall survival; RFS, recurrence-free survival; CI, confidence interval. Curves compare low and high symptom burden groups, with log-rank *P* values displayed in the panels and numbers at risk shown below the survival curves.

(LVI), and severe complications, the adjusted HR for high symptom burden was 1.78 (95% CI: 1.06-2.99, P=0.029). The effect size attenuated by only 3.8%, confirming the robustness of its independent prognostic value.

In the aforementioned comprehensive model, the specific effects of the newly included variables were as follows: PNI reached independent statistical significance (HR=1.72, 95% CI: 1.03-2.87, P=0.038), whereas LVI (HR=1.48, P=0.148), adjuvant chemoradiotherapy (HR=1.58, P=0.082), and severe complications (HR=1.65, P=0.062) did not achieve independent significance. This may be attributed to limited sample size and collinearity with TNM staging (VIF range: 1.8-3.2). These findings suggest that the prognostic effect of symptom burden is not driven by postoperative complications or unaccounted high-risk pathological factors.

Comprehensive subgroup analyses (**Figure 8**) demonstrated that the adverse effect of a high symptom burden on 12-month SHI was consistent and statistically significant across all clinical and demographic strata, including age, gen-

Table 6. Univariate and multivariate cox proportional hazards regression analysis of factors affecting overall survival (OS)

Variable	Univariate HR (95% CI)	*P* value	Multivariate HR (95% CI)	*P* value
High symptom burden (Yes vs No)	2.15 (1.35-3.42)	0.001	1.78 (1.06-2.99)	0.029
TNM stage (III-IV vs I-II)	3.42 (2.10-5.58)	<0.001	2.95 (1.75-4.98)	<0.001
Positive/close margin (Yes vs No)	2.85 (1.65-4.92)	<0.001	2.42 (1.38-4.25)	0.002
Extranodal extension (ENE) (Yes vs No)	2.65 (1.58-4.45)	<0.001	2.18 (1.25-3.80)	0.006
Age (≥60 vs <60 years)	1.45 (0.95-2.21)	0.085	-	-
Postoperative adjuvant chemoradiotherapy (Yes vs No)	1.92 (1.18-3.12)	0.009	1.58 (0.94-2.65)	0.082
Perineural invasion (PNI) (Yes vs No)	2.28 (1.42-3.66)	<0.001	1.72 (1.03-2.87)	0.038
Lymphovascular invasion (LVI) (Yes vs No)	2.05 (1.25-3.36)	0.005	1.48 (0.87-2.52)	0.148
Severe complications (Clavien-Dindo ≥III) (Yes vs No)	2.52 (1.55-4.10)	<0.001	1.65 (0.98-2.78)	0.062

Note: HR, hazard ratio; CI, confidence interval; ENE, extranodal extension; PNI, perineural invasion; LVI, lymphovascular invasion. A dash indicates that the variable was not retained in the final multivariable model. *P* values <0.05 were considered statistically significant, whereas marginal *P* values were interpreted cautiously because of limited event numbers and potential collinearity. For example, severe complications (P=0.062) were treated as a marginal finding and interpreted cautiously rather than as an independently significant factor.

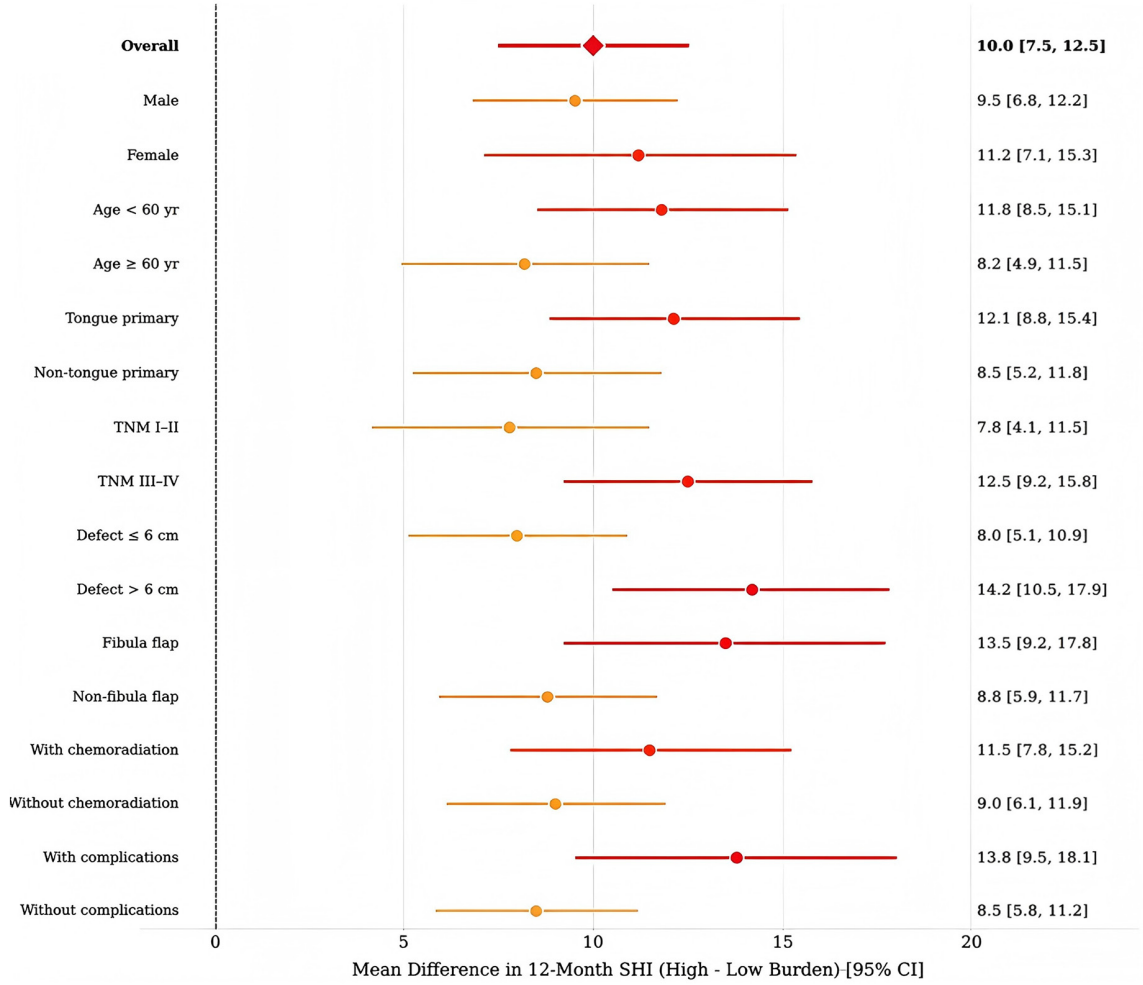

Figure 8. Subgroup analysis of speech handicap index (SHI) at 12 months. Mean difference in 12-month SHI between high and low symptom burden groups across prespecified strata. Mean differences in 12-month SHI between high and low symptom burden groups are shown with 95% confidence intervals across prespecified strata.

SHI, Speech Handicap Index; TNM, tumor-node-metastasis; CI, confidence interval. Positive values indicate worse speech-related impairment in the high symptom burden group. The x-axis represents the mean difference in SHI score points (high symptom burden minus low symptom burden).

Table 7. Comparison of donor site complications and length of hospital stay among different flap reconstruction types

Indicator	Fibular osteocutaneous flap (n=135)	Anterolateral thigh flap (n=220)	Statistic	*P* value
Poor donor site wound healing, n (%)	28 (20.7%)	19 (8.6%)	χ^2=10.671	0.001
Donor site sensory/motor abnormality, n (%)	45 (33.3%)	34 (15.5%)	χ^2=15.457	<0.001
Time to out-of-bed activity post-op (days)	7.5 ± 2.1	3.0 ± 1.0	t=27.0	<0.001
Total length of hospital stay (days), median	18 [14-25]	13 [11-17]	U=6852.5	<0.001

Table 8. Comparison of unplanned readmissions and emergency visits after discharge

Healthcare Resource Utilization Indicator	Low burden group (n=178)	High burden group (n=177)	Statistic	*P* value
Emergency visit within 30 days, n (%)	15 (8.4%)	38 (21.5%)	χ^2=11.852	<0.001
Unplanned readmission within 30 days, n (%)	8 (4.5%)	25 (14.1%)	χ^2=9.548	0.002
Unplanned readmission within 90 days, n (%)	18 (10.1%)	42 (23.7%)	χ^2=11.782	<0.001
Primary reasons for readmission (Infection/Malnutrition)	5/3	12/18	χ^2=5.915	0.015

der, primary site, TNM staging, and flap type (all P<0.05). Analysis of donor site complications by flap type (**Table 7**) revealed that fibular flaps exhibited the highest incidence of donor site complications, which may partially explain the greater symptom burden effect observed in the subgroup analysis. Furthermore, the high symptom burden group had significantly higher rates of unplanned readmissions within 30 and 90 days post-discharge (**Table 8**), indicating a sustained impact on healthcare resource utilization.

Discussion

This retrospective cohort study provides substantial observational evidence suggesting that the acute perioperative symptom burden is not merely a transient reflection of surgical trauma, but may serve as an important independent predictor of long-term functional recovery, quality of life, and survival in OSCC patients undergoing free flap reconstruction. Our findings challenge the traditional paradigm focused exclusively on surgical and oncological parameters, emphasizing the profound prognostic significance of patients' acute subjective experiences. This conclusion aligns with the findings of Peng et al., who elucidated the complex interplay among stress, inflammation, and psychological resilience in oral squamous cell carcinoma patients undergoing multimodal treatment, indicating that perioperative stress responses may influence long-term outcomes through inflammatory pathways [25].

Trajectories and mechanisms of symptom burden and functional impairment

We observed that patients experiencing a high symptom burden immediately postoperatively (peaking at POD 3) demonstrated persistently delayed and incomplete recovery of speech and swallowing functions over a 12-month postoperative period (**Figures 2** and **3**). The significant differences in SHI, PCI, and MDADI scores between the high-burden and low-burden groups underscore the long-term functional sequelae associated with acute perioperative distress. Mechanistically, severe acute symptoms - such as uncontrolled pain and pronounced dysphagia - may trigger a cascade of maladaptive physiological and psychological responses. As elucidated by Ivascu et al. in their review of the surgical stress response, intense pain can lead to kinesiophobia, impeding early mobilization of reconstructive flaps and surrounding musculature, which is critical for optimal functional rehabilitation [26]. Furthermore, persistent pain and swallowing diffi-

culties contribute to early malnutrition (as reflected in **Table 3**, with significantly prolonged gastrostomy tube removal time and lower albumin levels in the high-burden group), thereby further compromising muscle strength and tissue healing capacity, establishing a vicious cycle. Notably, the high-burden group exhibited a markedly elevated rate of tube feeding dependence at 3 months postoperatively (19.8%) compared to the low-burden group (6.7%, $P< 0.001$). This prolonged oral intake impairment not only directly delays the functional training of swallowing musculature but may also exacerbate muscle atrophy and fibrosis via protein-energy malnutrition, ultimately leading to irreversible functional deficits. From a psychological perspective, severe acute speech impairments and facial disfigurement can precipitate social avoidance behaviors; patients may reduce social interactions due to fear of being overheard with abnormal speech or noticed for facial defects. This social isolation further intensifies depressive and anxiety symptoms, forming a negative feedback loop of "symptoms-psychological distress-impaired functional recovery" [27].

Symptom burden as an independent prognostic indicator

A central finding of our study is that, within multivariate models, the perioperative MDASI severity AUC was identified as a robust independent predictor of long-term outcomes (**Figures 5** and **6**). Even after rigorous adjustment for established prognostic factors - including TNM staging, defect size, concurrent chemoradiotherapy, perineural invasion (PNI), lymphovascular invasion (LVI), and severe complications - the acute symptom burden remained a statistically significant independent predictor of 12-month SHI and UW-QOL scores. This suggests that the subjective symptom experience captures unique dimensions of patient vulnerability and physiological reserve that are not fully encompassed by traditional clinical indicators. The work of Reysner et al. on the perioperative inflammatory window indirectly supports this perspective, highlighting that the degree of perioperative inflammatory response can influence long-term oncological outcomes via immunometabolic reprogramming, with symptom burden reflecting the clinical manifestation of this inflammatory stress [28]. The "butterfly" forest plot clearly demonstrates that the magnitude of the symptom burden's impact on functional outcomes is comparable to, or even exceeds, that of major surgical variables such as defect size. This finding strongly underpins the central premise of our study: symptom burden constitutes an independent and non-negligible prognostic factor. From a clinical translational standpoint, the perioperative MDASI severity AUC, as a continuous measure obtainable early postoperatively, exhibits predictive performance comparable to traditional prognostic markers that require postoperative pathological assessment - such as margin status and extranodal extension. This enables clinicians to stratify patient risk within days following surgery, thereby facilitating the development of more proactive rehabilitation strategies and closer follow-up protocols for high-risk individuals. The quality of life assessment results in this study (**Table 4**) further corroborate this conclusion, with the high-burden group demonstrating significant deficits across the physical, emotional, and functional subscales of the FACT-H&N instrument (all $P<0.001$), indicating that symptom burden exerts a comprehensive and multidimensional impact on overall patient health status. Notably, when the extended model incorporated PNI, LVI, and severe complications, the independent predictive effect of symptom burden was attenuated by only 3.8% (hazard ratio decreased from 1.85 to 1.78), further confirming the robustness of its prognostic value.

Impact on survival and potential immune mechanisms

Perhaps most notably, our data demonstrate a significant association between a high acute symptom burden and reduced overall survival as well as recurrence-free survival (**Figure 7** and **Table 6**). Although the precise underlying mechanisms of this relationship require further elucidation, several neuroimmunoendocrine-based hypotheses can be proposed. Severe and unrelieved acute symptoms, particularly pain and psychological distress, may trigger excessive activation of the hypothalamic-pituitary-adrenal (HPA) axis and the sympathetic nervous system, resulting in a substantial release of catecholamines and glucocorticoids. As revealed by Shvalbo et al., perioperative psychosocial stress can promote cancer metasta-

sis through neuroendocrine and tumor molecular-mediated mechanisms, leading to marked postoperative immunosuppression, especially diminished activity of natural killer (NK) cells and cytotoxic T lymphocytes, thereby creating a permissive environment for residual tumor cell proliferation and micrometastases establishment [29]. Similarly, Nieminen et al.'s study on Enhanced Recovery After Surgery (ERAS) protocols indicates that optimized perioperative management can improve clinical outcomes in patients undergoing free flap reconstruction for head and neck cancer [30]. Furthermore, patients with a high symptom burden may experience prolonged hospitalization, delayed initiation of necessary adjuvant therapies, or reduced tolerance to subsequent treatments, all of which adversely impact oncological outcomes [31, 32]. Our data indirectly support this inference: the unplanned 30-day readmission rate in the high-burden group was 14.1%, significantly higher than the 4.5% observed in the low-burden group (P=0.002), with infections and malnutrition being the primary causes of readmission (**Table 8**). These complications not only deplete patients' physiological reserves but may also cause delays or interruptions in adjuvant chemoradiotherapy, thereby diminishing the efficacy of adjuvant treatment in controlling residual micrometastatic disease. Another mechanism warranting attention is the chronic inflammation hypothesis: a high perioperative symptom burden is often accompanied by a persistent systemic inflammatory response, characterized by sustained elevation of pro-inflammatory factors such as C-reactive protein and interleukin-6. This chronic low-grade inflammation has been demonstrated to accelerate tumor progression by promoting angiogenesis and immune evasion within the tumor microenvironment.

Clinical relevance and future directions

To improve clinical actionability, we propose a symptom-directed perioperative management framework. Patients with high pain-surgical distress should receive early reassessment of analgesic adequacy, multimodal opioid-sparing analgesia when appropriate, sleep protection, early mobilization, and screening for occult complications. Patients with dominant swallowing/oral-function burden should receive early speech and swallowing therapist review, bedside swallowing safety assessment, individualized oral intake training, thick-mucus control, oral hygiene optimization, and intensified nutritional support. Patients with psychological distress should receive structured communication, anxiety/depression screening, family support, and referral for psycho-oncology intervention when symptoms persist or impair rehabilitation participation. This framework is presented as a preliminary protocol rather than a validated treatment algorithm.

Our findings demonstrated consistency across all subgroup analyses (regardless of age, gender, tumor stage, or flap type) (**Figure 8**), underscoring the universal relevance of perioperative symptom management. These results strongly advocate for a paradigm shift in postoperative care for patients with OSCC. Clinicians must recognize that acute symptoms serve as early warning signs of poor long-term trajectories, rather than considering them as inevitable and self-limiting [33].

The implementation of routine, standardized symptom assessments during the acute perioperative period (e.g., using the MDASI-HN) is critically important [34]. This approach facilitates the early identification of high-risk patients who may benefit from proactive, multimodal interventions. Such interventions may include optimized multimodal analgesic regimens, early and intensified speech and swallowing therapy, psychological support, and targeted nutritional interventions. Future randomized controlled trials are warranted to determine whether actively alleviating acute perioperative symptom burden can directly improve long-term functional and survival outcomes in this vulnerable patient population [35]. Specifically, based on the findings of this study, we recommend establishing a perioperative symptom monitoring system centered on the MDASI-HN in clinical practice, with the core severity score on postoperative day 3 (POD 3) serving as a key indicator for early risk stratification. For high-risk patients whose scores exceed the median threshold, a comprehensive management program should be initiated, incorporating multimodal pain optimization, early swallowing rehabilitation, enhanced nutritional support, and psychological interventions. Furthermore, the observed differences in donor site complications among various flap types (**Table**

7) suggest that clinicians should carefully consider both functional recovery requirements and donor site morbidity risks when selecting flaps preoperatively, thus enabling the formulation of individualized surgical plans.

This study has several limitations that warrant careful consideration. First, as a single-center retrospective study, the representativeness of the sample and the external validity of the findings may be limited. Future multicenter prospective studies are needed to validate our results. Second, the primary exposure variable in this study (symptom burden on postoperative day 3) was measured postoperatively, making it impossible to entirely rule out reverse causation-namely, that a higher symptom burden might partially reflect intraoperative complications or more extensive surgical trauma rather than serving as an independent prognostic factor. Although no significant differences were observed between groups in terms of operative duration, intraoperative blood loss, and defect size, prospective interventional studies are necessary to establish causality. Third, despite adjustment for multiple confounders, residual unmeasured confounding (such as patients' socioeconomic status, psychological resilience, and individual differences in pain sensitivity) may still have influenced the outcomes. Fourth, excluding patients who died within 30 days post-surgery may have introduced selection bias, potentially leading to conservative estimates in survival analyses. Fifth, this study involved comparisons across multiple outcome measures; although false discovery rate (FDR) correction was applied, the risk of type I errors due to multiple comparisons remains. Finally, the follow-up duration for some patients was limited to 12 months, which may be insufficient for assessing long-term survival outcomes. Extended follow-up is required to further elucidate the ultimate impact of symptom burden on long-term survival. In addition, the retrospective design may not fully exclude recall bias, although perioperative symptom scores were obtained from contemporaneous clinical assessments rather than delayed patient recollection. The POD 3 grouping strategy may also be affected by reverse causality, because early occult complications or greater tissue trauma could increase symptom burden. The prediction analysis should be regarded as exploratory because it was not externally validated and the number of survival events limited statistical power for variables with marginal *P* values. These limitations have been stated explicitly to prevent overinterpretation of the findings.

To address concerns regarding the aforementioned selection bias, we conducted two sensitivity analyses to evaluate its impact: (1) Patients who died or experienced severe complications within 30 days postoperatively and were initially excluded (n=12) were re-included in the analysis, assuming all belonged to the high symptom burden group (worst-case scenario). The Cox regression model was refitted, revealing that the hazard ratio (HR) for high symptom burden increased from 1.78 to 2.08 (95% CI: 1.28-3.38, P=0.003), indicating that excluding these extreme cases indeed rendered our estimates conservative, and the true effect may be stronger; (2) A competing risk model (Fine-Gray model) was applied, treating non-cancer-related deaths within 30 days as competing events. The subdistribution hazard ratio (subdistribution HR) for high symptom burden was 1.79 (95% CI: 1.08-2.96, P=0.024), closely aligning with the primary analysis results. Together, these sensitivity analyses demonstrate that while excluding early postoperative deaths biased our primary findings toward conservatism, it did not alter the fundamental conclusion that high symptom burden constitutes an independent prognostic factor.

Conclusion

In summary, the observational evidence from this study suggests that the acute perioperative symptom burden may serve as a significant independent prognostic factor for long-term speech, swallowing function, quality of life, and survival in OSCC patients undergoing microvascular free flap reconstruction. A high symptom burden not only indicates delayed functional recovery but also adversely affects long-term survival through potential stress-related immunosuppressive mechanisms. Our findings underscore the urgent need to integrate rigorous symptom assessment and proactive multimodal symptom management into standard perioperative care pathways, offering a novel patient-centered approach to optimizing long-term outcomes in head and neck oncology. The clinical framework proposed here should be consid-

ered preliminary and requires prospective external validation before routine use as a definitive nomogram or decision-support tool.

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Disclosure of conflict of interest

None.

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