Japan Journal of Research



Correspondence

Wenjie Cai, PhD

Department of Radiation Oncology, First Hospital of Quanzhou Affiliated to Fujian Medical University, Quanzhou, Fujian, People's Republic of China.

- · Received Date: 19 June 2025
- · Accepted Date: 28 June 2025
- Publication Date: 30 June 2025

Keywords

Head and neck cancer, progression-free survival, overall survival, surgical margin, adjuvant therapy

Copyright

© 2025 Authors. This is an open-access article distributed under the terms of the Creative Commons Attribution 4.0 International license.

Unveiling Survival Predictors in Postoperative Head and Neck Cancer: A Comprehensive Analysis

Wenjie Cai^{1*#}, lat-Weng Hong^{2#}, Chengfeng Cai³, Wanhua Chen⁴

- ¹Department of Radiation Oncology, First Hospital of Quanzhou Affiliated to Fujian Medical University, Quanzhou, Fujian, People's Republic of China
- ²School of Medicine, Sun Yat-sen University, Shenzhen, People's Republic of China
- ³First Clinical Medical College, Ningxia Medical University, Yinchuan, Ningxia, People's Republic of China
- ⁴Department of Clinical Laboratory, First Hospital of Quanzhou Affiliated to Fujian Medical University, Quanzhou, Fujian, People's Republic of China
- #First authors

Abstract

Background and Purpose: Head and neck malignancies remain a major global health burden, with poor survival outcomes despite advances in treatment. This study aims to identify key factors influencing progression-free survival (PFS) and overall survival (OS) in head and neck cancer patients, and to assess the impact of tumor characteristics, surgical margins, and postoperative therapies.

Materials and Methods: A retrospective analysis was conducted on 306 patients with head and neck tumors treated between 2017 and 2022. Demographic data, tumor classification, surgical margins, and postoperative treatments were collected. Survival data were analyzed using univariate and multivariate methods to identify factors influencing PFS and OS.

Results: Key determinants of survival identified include T and N categories, initial frozen section margins, postoperative recurrence, and adjuvant chemotherapy and radiotherapy. Patients with advanced T and N stages or initial positive frozen section margins exhibited significantly lower PFS and OS. Multivariate analysis further established postoperative chemotherapy as an independent factor negatively associated with PFS, potentially reflecting its application in advanced cases with poorer prognosis. Subgroup analysis revealed significant survival differences across tumor types, particularly between oral and salivary gland cancers.

Conclusion: These findings underscore the need for individualized treatment strategies and more precise intraoperative assessments to improve outcomes. Future prospective studies are necessary to corroborate these findings and support evidence-based clinical decision-making.

Introduction

Head and neck carcinoma represents a significant burden in oncology, characterized by its diverse anatomical locations and challenging management. Head and neck cancers constitute a diverse group of malignancies that arise from the epithelial lining of the upper aerodigestive tract. Among head and neck carcinoma, squamous cell carcinoma (SCC) is the predominant histological type, accounting for approximately 90% of cases worldwide [1]. This high prevalence is particularly concerning given the aggressive nature of SCC and its association with poor prognosis, especially in advanced stages of the disease [2]. The incidence of head and neck carcinoma has been rising, with factors such as tobacco use, alcohol consumption, and human papillomavirus (HPV) infection contributing to this trend [3,4].

Survival outcomes in head and neck carcinoma are influenced by several factors, including tumor stage at diagnosis, primary site involvement, and the presence of regional or distant metastases. Despite advancements in treatment modalities, including surgery, radiotherapy, and chemotherapy, the overall survival rates for patients with head and neck carcinoma remain unsatisfactory, with five-year survival rates hovering around 50% [3,5]. The heterogeneity of head and neck carcinoma, both in terms of molecular characteristics and clinical presentation, complicates treatment strategies and necessitates a more personalized approach to therapy [6].

Clinically, head and neck carcinoma can manifest in various anatomical sites, including the oral cavity, oropharynx, larynx, and hypopharynx, each presenting unique challenges in diagnosis and treatment. Pathologically, differentiation grade, extent of local invasion, and involvement of regional lymph nodes significantly impact prognosis and treatment decisions. Understanding the prognostic factors associated with head and neck carcinoma is paramount for several reasons. Firstly, it aids in risk stratification and personalized treatment planning, optimizing therapeutic efficacy while minimizing treatment-related morbidities. Secondly, prognostic markers provide insights into disease biology and may guide the

Citation: Cai W, Hong IW, Cai C, Chen W. Unveiling Survival Predictors in Postoperative Head and Neck Cancer: A Comprehensive Analysis. Japan J Res. 2025;6(7):129

development of novel targeted therapies aimed at improving outcomes for patients with advanced or recurrent disease. Lastly, by identifying high-risk patient subsets, clinicians can implement vigilant surveillance protocols to detect disease recurrence early, further enhancing long-term survival rates [7]

Head and neck carcinoma remains a complex entity influenced by a multitude of clinical, pathological, and molecular factors. By delineating the epidemiology, survival statistics, clinicalpathological correlates, and the importance of survival-related research, we aim to underscore the multifaceted nature of head and neck carcinoma and the ongoing efforts to improve patient outcomes.

Materials and methods

Study subjects

This study included a cohort of 306 patients with head and neck malignancies who underwent primary tumor resection and neck lymphadenectomy at the Departments of Stomatology and Otorhinolaryngology, Quanzhou First Hospital Affiliated to Fujian Medical University, between January 2017 and December 2022. Inclusion criteria encompassed patients with a pathological diagnosis of head and neck malignancy postsurgery. Subjects with a history of malignancy in other systemic regions and cases without follow-up data are excluded. Disease staging was classified according to the 8th edition of the UICC TNM stage system. Various clinicopathological factors were recorded based on medical documentation, including gender, age, tumor subsite (oral cavity, oropharynx, larynx, hypopharynx, and others), pathological T (pT) category, pathological N (pN) category, tumor differentiation, and prognosis (survived, cancerrelated death, or death from other causes).

Ethical approval for this study was granted by the Ethics Committee of Quanzhou First Hospital Affiliated to Fujian Medical University (Approval No.: 2024K177).

Statistical analysis

Statistical analyses were performed using SPSS version 27.0.

- 1. Descriptive Analysis: Non-parametric Mann-Whitney U tests were employed for data analysis, with categorical data presented as percentages. Independent sample t-tests or χ² tests were utilized to compare event outcome incidences. Given the non-normal distribution of variables, Spearman rank correlation analysis was used to examine inter-variable relationships.
- 2. Survival Analysis: Overall survival (OS) and progression-free survival (PFS) rates were analyzed using the Kaplan-Meier method, with group comparisons conducted through log-rank tests. Univariate and multivariate analyses were performed using the Cox proportional hazards model to assess the relationship between clinical variables and prognosis. A p-value of <0.05 was considered statistically significant.

Results

Patient characteristics

A total of 312 patients were initially enrolled, of whom 6 (1.92%) with concurrent esophageal carcinoma were excluded, resulting in a final cohort of 306 patients, comprising 231 males (75.5%) and 75 females (24.5%), with a median age of 61 years (95% CI: 28.68–84.00 years). Tumor types included oral cavity cancer (122 cases, 39.9%), laryngeal cancer (82 cases, 26.8%), salivary gland tumors (37 cases, 12.1%), hypopharyngeal

Table 1. Clinical characteristics of patients with head and neck tumors.

| Variable | N = 306 | | | | | |
|-----------------------------------|---------------------------|--|--|--|--|--|
| Age | 61.00 [53.00, 68.00] | | | | | |
| PFS | 927.50 [482.25, 1,598.00] | | | | | |
| OS | 948.50 [567.75, 1,522.25] | | | | | |
| Sex | | | | | | |
| Male | 231 (75.49%) | | | | | |
| Female | 75 (24.51%) | | | | | |
| Recurrence situation | (=) | | | | | |
| No recurrence | 249 (81.37%) | | | | | |
| Recurrence | 57 (18.63%) | | | | | |
| Tumor types | T ((- 0.102 / -) | | | | | |
| Oral cavity | 122 (39.87%) | | | | | |
| Throat | 82 (26.80%) | | | | | |
| Hypopharynx | 23 (7.52%) | | | | | |
| Salivary glands | 37 (12.09%) | | | | | |
| Oropharynx | 10 (3.27%) | | | | | |
| Other | 32 (10.46%) | | | | | |
| Differentiation level | 32 (10.4070) | | | | | |
| 1 grade | 27 (8.82%) | | | | | |
| 2grade | 160 (52.29%) | | | | | |
| 3grade | 119 (38.89%) | | | | | |
| Radiotherapy status | 117 (36.6970) | | | | | |
| No Radiotherapy | 245 (80.07%) | | | | | |
| Radiotherapy | 61 (19.93%) | | | | | |
| T categories | 01 (17.7370) | | | | | |
| T1 | 108 (35.29%) | | | | | |
| T2 | 109 (35.62%) | | | | | |
| T3 | 30 (9.80%) | | | | | |
| T3 | 59 (19.28%) | | | | | |
| N categories | 39 (19.28%) | | | | | |
| | 242 (70 000/) | | | | | |
| N0 | 242 (79.08%) | | | | | |
| N1 | 21 (6.86%) | | | | | |
| N2 | 35 (11.44%) | | | | | |
| N3 | 8 (2.61%) | | | | | |
| Pathological margins | 206 (67 220) | | | | | |
| Negative | 206 (67.32%) | | | | | |
| Positive | 100 (32.68%) | | | | | |
| Margins in the initial frozen sec | | | | | | |
| Negative | 155 (50.65%) | | | | | |
| Positive | 75 (24.51%) | | | | | |
| No frozen section margin | 76 (24.84%) | | | | | |
| Chemotherapy | T - | | | | | |
| No | 276 (90.20%) | | | | | |
| Yes | 30 (9.80%) | | | | | |

cancer (23 cases, 7.5%), oropharyngeal cancer (10 cases, 3.3%), and other malignancies (32 cases, 10.5%). Tumor differentiation grades were as follows: well-differentiated (27 cases, 8.8%), moderately differentiated (160 cases, 52.3%), and poorly differentiated (119 cases, 38.9%). Postoperative radiotherapy was administered to 61 patients (19.9%) and chemotherapy to 30 patients (9.8%). T category included T1 (108 cases, 35.3%), T2 (109 cases, 35.6%), T3 (30 cases, 9.8%), and T4 (59 cases, 19.3%). N category was including N0 (242 cases, 79.1%), N1 (21 cases, 6.9%), N2 (35 cases, 11.4%), and N3 (8 cases, 2.6%). Initial frozen section margins were negative in 155 patients (50.7%) and positive in 75 patients (24.5%), with 76 patients (24.8%) not undergoing frozen section analysis. Pathological margins were negative in 226 patients (73.9%) and positive in 80 patients (26.1%). The median follow-up duration was 948.5 days (95% CI: 240.38-2462.87 days). During follow-up, 57 patients (18.6%) experienced recurrence or metastasis, with a median time to recurrence of 927.5 days (95% CI: 125.08-2386.28 days). At the end of follow-up, 257 patients (84.0%) were alive, while 48 (16.0%) had died (see Table 1).

Univariate survival analysis

Univariate factors associated with PFS included T category (P = 0.044) (Figure 1), N category (P = 0.037) (Figure 2), and postoperative chemotherapy (P < 0.001) (Figure 3). Factors

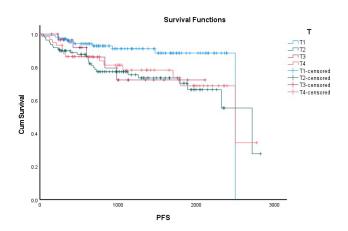


Figure 1. The PFS across different T categories.

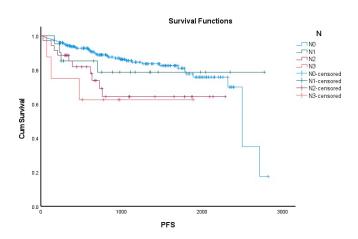


Figure 2. The PFS across different N categories.

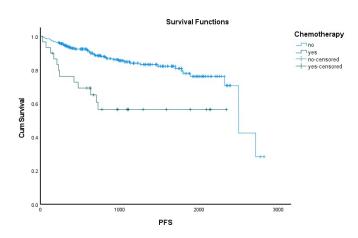


Figure 3. PFS of patients with and without chemotherapy.

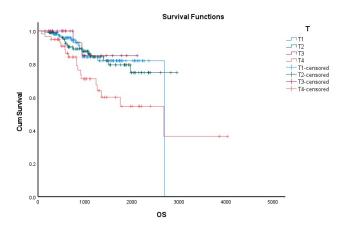


Figure 4. OS of patients with different T categories.

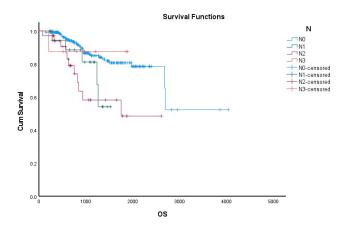


Figure 5. OS of patients with different N categories.

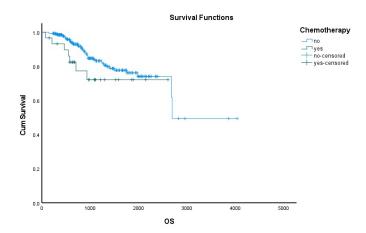


Figure 6. OS of patients with and without chemotherapy.

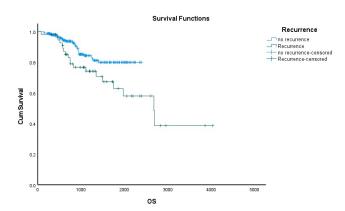


Figure 7. OS of patients with different recurrence statuses.

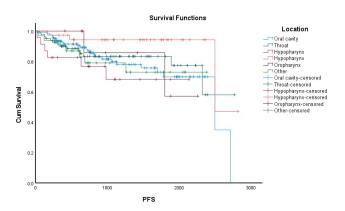
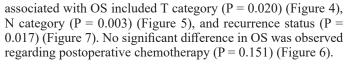


Figure 8. PFS of patients with different tumor types.



Significant differences in PFS were noted between oral cavity cancer and salivary gland tumors (P = 0.022), hypopharyngeal cancer and salivary gland tumors (P = 0.015), and other tumors and salivary gland tumors (P = 0.041) (Figure 8; Table 2).

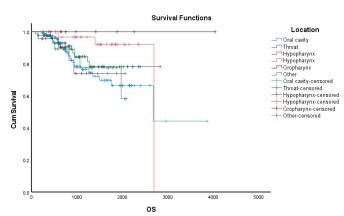


Figure 9. OS of patients with different tumor types.

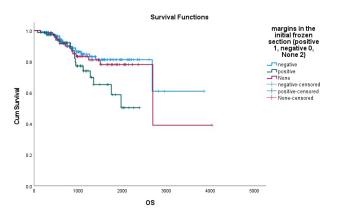


Figure 10. OS of patients with different margins in the initial frozen section.

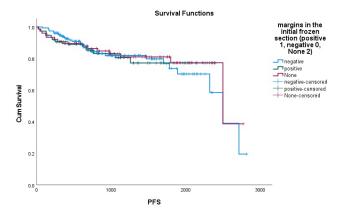


Figure 11. PFS of patients with different margins in the initial frozen section

Significant differences in OS were also observed between oral cavity cancer and salivary gland tumors (P = 0.028) and between other tumors and salivary gland tumors (P = 0.040) (Figure 9; Table 3). A significant difference in OS was found between patients with positive versus negative initial frozen section margins (P = 0.041) (Figure 10; Table 4), while the difference in PFS between these groups was not statistically significant (P = 0.977) (Figure 11; Table 5).

Table 2. Comparison of PFS Across Different Tumor Types

| | Oral cavity | | Thr | oat | Нурор | Hypopharynx | | Hypopharynx | | Oropharynx | | Other | |
|-------------|----------------|-------|----------------|-------|----------------|-------------|----------------|-------------|----------------|------------|----------------|-------|--|
| Tumor types | Chi- Square | Sig. | Chi- Square | Sig. | Chi- Square | Sig. | Chi- Square | Sig. | Chi- Square | Sig. | Chi- Square | Sig. | |
| Oral cavity | | | 1.163 | 0.281 | 0.000 | 1.000 | 4.802 | 0.028 | 2.596 | 0.107 | 0.031 | 0.860 | |
| Throat | 1.163 | 0.281 | | | 0.382 | 0.537 | 1.898 | 0.168 | 1.496 | 0.221 | 0.298 | 0.585 | |
| Hypopharynx | 0.000 | 1.000 | 0.382 | 0.537 | | | 3.659 | 0.056 | 1.889 | 0.169 | 0.026 | 0.872 | |
| Hypopharynx | 4.802 | 0.028 | 1.898 | 0.168 | 3.659 | 0.056 | | | 1.412 | 0.235 | 4.214 | 0.040 | |
| Oropharynx | 2.596 | 0.107 | 1.496 | 0.221 | 1.889 | 0.169 | 1.412 | 0.235 | | | 2.099 | 0.147 | |
| Other | 0.031 | 0.860 | 0.298 | 0.585 | 0.026 | 0.872 | 4.214 | 0.040 | 2.099 | 0.147 | | | |

Table 3. Comparison of OS Across Different Tumor Types.

| Oral cavity | | Thi | Throat Hypop | | oharynx Hypopharynx | | harynx | Oropharynx | | Other | | |
|-------------|----------------|-------|----------------|-------|---------------------|-------|----------------|------------|----------------|-------|----------------|-------|
| Tumor types | Chi- Square | Sig. | Chi- Square | Sig. | Chi- Square | Sig. | Chi- Square | Sig. | Chi- Square | Sig. | Chi- Square | Sig. |
| Oral cavity | | | 0.199 | 0.656 | 1.336 | 0.248 | 5.222 | 0.022 | 0.006 | 0.936 | 0.131 | 0.860 |
| Throat | 0.199 | 0.656 | | | 1.597 | 0.206 | 2.705 | 0.1 | 0.015 | 0.903 | 0.269 | 0.585 |
| Hypopharynx | 1.336 | 0.248 | 1.597 | 0.206 | | | 5.889 | 0.015 | 0.474 | 0.491 | 0.318 | 0.872 |
| Hypopharynx | 5.222 | 0.022 | 2.705 | 0.1 | 5.889 | 0.015 | | | 1.882 | 0.17 | 4.174 | 0.040 |
| Oropharynx | 0.006 | 0.936 | 0.015 | 0.903 | 0.474 | 0.491 | 1.882 | 0.17 | | | 0.081 | 0.147 |
| Other | 0.131 | 0.717 | 0.269 | 0.604 | 0.318 | 0.573 | 4.174 | 0.041 | 0.081 | 0.776 | | |

Table 4. Comparison of OS among patients with different margins in the initial frozen section

| margins in the initial | Negativ | e | Pos | itive | None | | |
|------------------------|------------|-------|------------|-------|------------|-------|--|
| frozen section | Chi-Square | Sig. | Chi-Square | Sig. | Chi-Square | Sig. | |
| Negative | | | 4.195 | 0.041 | 0.254 | 0.614 | |
| Positive | 4.195 | 0.041 | | | 2.416 | 0.120 | |
| None | 0.254 | 0.614 | 2.416 | 0.120 | | | |

Table 5. Comparison of PFS among patients with different margins in the initial frozen section.

| margins in the initial | Negativ | e | Pos | itive | None | | |
|------------------------|------------|-------|------------|-------|------------|-------|--|
| frozen section | Chi-Square | Sig. | Chi-Square | Sig. | Chi-Square | Sig. | |
| Negative | | | 0.001 | 0.977 | 0.264 | 0.607 | |
| Positive | 0.001 | 0.977 | | | 0.044 | 0.834 | |
| None | 0.264 | 0.607 | 0.044 | 0.834 | | | |

Multivariate survival analysis

A multivariate analysis for PFS and OS was conducted by taking into accounts gender, age, tumor site, tumor differentiation, T category, N category, initial frozen section margin status, final pathological margin status, postoperative radiotherapy, postoperative chemotherapy, and recurrence status. Our data revealed that postoperative chemotherapy was the sole independent factor associated with PFS (P=0.026). Age (P=0.03), N category (P=0.029), and postoperative

radiotherapy (P = 0.004) were independently associated with OS (see Table 6).

To further elucidate the T and N classifications of patients undergoing postoperative chemotherapy, an exploratory analysis was conducted. It was observed that the proportion of T1, N0 and Pathological margins negative patients was significantly higher in the non-chemotherapy group (P = 0.020, P < 0.001 and 0.030 respectively) (see Table 7).

Table 6. Multivariate and Univariate Analyses of Factors Associated with OS and PFS.

| | | P | FS | | os | | | | | |
|---------------------------------------|-------------|---------|-------------|---------|--------------|---------|-------------|---------|--|--|
| Variable | Multiv | variate | Univariate | | Multivariate | | Univariate | | | |
| | Statistical | p-value | Statistical | p-value | Statistical | p-value | Statistical | p-value | | |
| Age | 2.16 | 0.142 | | | 4.733 | 0.03 | | | | |
| Sex | 0.445 | 0.504 | 1.16 | 0.281 | 0.001 | 0.978 | 0.505 | 0.477 | | |
| Different tumor types | 0.004 | 0.947 | 7.174 | 0.208 | 0.458 | 0.498 | 7.791 | 0.168 | | |
| Differentiation level | 0.206 | 0.65 | 0.65 | 0.722 | 2.897 | 0.089 | 2.852 | 0.240 | | |
| Radiotherapy status | 0.479 | 0.489 | 0.294 | 0.588 | 8.122 | 0.004 | 3.303 | 0.069 | | |
| T | 1.882 | 0.17 | 8.104 | 0.044 | 2.755 | 0.097 | 9.844 | 0.020 | | |
| N | 0.848 | 0.357 | 8.507 | 0.037 | 4.779 | 0.029 | 14.076 | 0.003 | | |
| Pathological margins | 0.402 | 0.526 | 0.644 | 0.422 | 3.345 | 0.067 | 2.535 | 0.111 | | |
| Margins in the initial frozen section | 0.780 | 0.377 | 0.241 | 0.886 | 0.980 | 0.322 | 4.523 | 0.104 | | |
| Chemotherapy | 4.948 | 0.026 | 13.241 | < 0.001 | 0.677 | 0.411 | 2.060 | 0.151 | | |
| Recurrence situation | | | | | 3.020 | 0.082 | 5.661 | 0.017 | | |

Table 7. The distribution of TN categories Pathological margins between patients with and without chemotherapy.

| | | Chemotherapy | y, yes=1, no=0 | P Value |
|----------------------|----------|--------------|----------------|---------|
| | | no | yes | rvalue |
| | T1 | 105 (34.3%) | 3 (1%) | |
| | T2 | 94 (30.7%) | 15 (4.9%) | |
| T category | Т3 | 25 (8.2%) | 5 (1.6%) | 0.020 |
| | T4 | 52 (17%) | 7 (2.3%) | |
| | Total | 276 (90.2%) | 30 (9.8%) | |
| | N0 | 232 (75.8%) | 10 (3.3%) | |
| | N1 | 18 (5.9%) | 3 (1%) | |
| N category | N2 | 24 (7.8%) | 11 (3.6%) | < 0.001 |
| | N3 | 2 (0.7%) | 6 (2%) | |
| | Total | 276 (90.2%) | 30 (9.8%) | |
| | negative | 209 (68.3%) | 17 (5.6%) | |
| Pathological margins | positive | 67 (21.9%) | 13 (4.2%) | 0.030 |
| | Total | 276(90.2) | 30(9.8%) | |

Discussion

Head and neck malignancies ranked as the most prevalent cancer worldwide and have high mortality rates, accounting for over 15,000 deaths annually in the United States alone [8]. Despite advances in treatment modalities, including surgical resection chemotherapy and radiotherapy, the five-year survival rate remains below 50% [8]. This retrospective study of 306 head and neck cancer patients examines key factors influencing progression-free survival (PFS) and overall survival (OS), focusing on the impact of recurrence, postoperative chemotherapy, and radiotherapy on survival outcomes. The findings indicate that tumor T category, N category, initial frozen section margins, recurrence status, postoperative chemotherapy, and radiotherapy are significantly associated with PFS or OS.

In this study, T and N categories emerged as principal univariate factors affecting both PFS and OS. As tumor stage (T category, P=0.044) and nodal stage (N category, P=0.037)

advanced, PFS significantly declined. Patients with T1 tumors exhibited a more favorable PFS compared to those with T2 and T4 tumors, while patients classified as N0 had significantly better PFS outcomes than those with N2 or N3 category. The extent of local tumor invasion and nodal metastasis has a profound impact on both PFS and OS. Research by Mao et al. underscores that primary tumor volume and metastatic nodal volume are pivotal in determining the effectiveness of radiotherapy [9]. Additionally, the number and characteristics of cervical lymph nodes are established risk factors influencing survival in patients with cutaneous squamous cell carcinoma of the head and neck [10]. Lymph node involvement is closely linked to prognosis in head and neck cancers, especially in early-stage oral cancer, where nodal status markedly affects survival outcomes [11]. These findings underscore the necessity of understanding the patterns of local tumor spread and lymphatic metastasis to tailor individualized treatment strategies.

Furthermore, postoperative chemotherapy significantly impacted PFS (P < 0.001),with patients undergoing chemotherapy showing shortened PFS. Notably, the proportion of T1, N0 and Pathological margins negative patients was significantly higher in the non-chemotherapy group. Studies by Moratin et al. revealed a strong correlation between positive margins (presence of tumor cells at the resection margin) and increased recurrence rates, as well as diminished survival outcomes [12-14]. Positive margins often indicate incomplete tumor resection, potentially leading to local recurrence and poorer OS. For instance, in laryngeal and pharyngeal cancers, patients with positive margins exhibit markedly lower diseasefree survival and disease-specific survival [13]. Moreover, in squamous cell carcinoma of the head and neck, positive margins are associated with poorer outcomes, particularly in cases with low differentiation and deeper invasion [14,15]. Consequently, achieving negative surgical margins (absence of tumor cells at the resection margin) is essential to improving patient prognosis. Researchers advocate for more precise intraoperative margin assessment techniques to enhance the likelihood of negative margins and reduce recurrence risk [16-18]. For example, real-time evaluation of surgical margins using novel imaging and machine learning methods can guide surgeons in making more accurate intraoperative decisions [18,19]. In summary, the presence of positive margins may portend a worse prognosis in head and neck cancer patients, underscoring the need for meticulous surgical technique to achieve negative margins, thereby improving survival rates and quality of life [20-22].

For OS, T category (P=0.020), N category (P=0.003), and recurrence status (P=0.017) were significant univariate factors. Patients with T1 and T2 tumors demonstrated better OS outcomes compared to those with T4 tumors, aligning with existing research on the prognostic impact of tumor staging [9]. No category patients had significantly better OS than those with N2, with nodal metastasis in advanced N-stage patients contributing to poorer prognosis [10]. Recurrence substantially shortened survival, underscoring its negative impact on OS. In this study, OS in recurrent patients was significantly lower than in non-recurrent patients (P=0.017), consistent with findings in the literature [23]. Local recurrence in head and neck cancers often signals aggressive tumor biology or incomplete resection, contributing to a higher likelihood of recurrence and reduced OS. This association between surgical margin status and local recurrence is well-documented; for example, in aggressive vulvar Paget's disease, positive surgical margins correlate with increased local recurrence [24]. Furthermore, even when histologically tumor-free, 10-30% of patients still experience local recurrence, possibly due to microscopic residual disease or undetected precancerous lesions [25]. Thus, completeness of resection and margin status are critical in head and neck cancer management, highlighting the importance of a multidisciplinary approach to reduce recurrence and improve outcomes [23]. This study underscores the significant difference in overall survival (OS) between patients with positive and negative margins in the initial frozen section analysis. This finding suggests that patients with initial positive frozen section margins may benefit from intensified postoperative anti-tumor treatments, such as radiotherapy or chemotherapy, to improve their survival

Multivariate analysis identified postoperative chemotherapy as an independent factor affecting PFS. After adjusting for gender, age, tumor site, differentiation grade, T category, N category, and margin status, postoperative chemotherapy remained the only significant factor associated with reduced PFS (P=0.026). This finding is in agreement with the existing literature on certain head and neck cancers, where chemotherapy is often administered to more advanced-stage patients, thus representing an adverse prognostic factor for PFS [26].

Regarding OS, age (P=0.03), N category (P=0.029), and postoperative radiotherapy (P=0.004) were identified as independent factors. Elderly patients demonstrated poorer outcomes, with studies indicating a higher risk of postoperative complications and lower survival rates among older individuals undergoing surgical treatment [27]. Older patients also exhibit significantly reduced overall survival compared to younger patients, likely due to comorbidities, tumor characteristics, and surgery types [27]. In the postoperative recovery period, elderly patients may experience higher 90-day mortality rates and lower five-year survival rates [27]. Therefore, when treating elderly patients with head and neck cancer, it is crucial to consider their immunological status and overall health to enhance therapeutic strategies and improve survival [28]. The significance of N category further reinforces the adverse impact of nodal metastasis on prognosis. Postoperative radiotherapy was associated with improved OS in head and neck cancer patients, primarily by reducing local recurrence and metastasis. This is aligns with numerous studies demonstrating the survival benefits of postoperative radiotherapy. For instance, patients receiving postoperative radiotherapy exhibit significantly better disease-specific survival and recurrence-free survival over five years compared to those treated with surgery alone [29]. Additionally, postoperative radiotherapy has proven effective in controlling neck recurrence, further enhancing survival outcomes [30]. In some cases, even early-stage tumors with unilateral nodal metastasis show favorable long-term tumor control with postoperative radiotherapy [29]. Thus, postoperative radiotherapy is regarded as an essential therapeutic strategy in the treatment of head and neck cancer.

Significant differences in PFS and OS were observed among various tumor types in this study, particularly between oral cancer, hypopharyngeal cancer, and other tumors compared to salivary gland tumors. First of all, both PFS and OS differed significantly between oral cancer and salivary gland tumors (PFS: P=0.022; OS: P=0.028). The more aggressive nature of oral cancer may account for the accelerated risk of recurrence and progression, resulting in shorter survival. Although salivary gland tumors typically exhibit slower growth and lower recurrence rates, their malignancy and prognosis are influenced by several factors. For instance, adenoid cystic carcinoma (ACC), a common salivary gland tumor, despite its slow growth, has high recurrence rates and poor survival outcomes [31]. ACC prognosis is closely associated with the tumor's molecular characteristics and immune microenvironment [32]. Additionally, tumor grading, staging, and histological type significantly impact survival rates in salivary gland tumors [33]. In certain cases, high-grade transformation or dedifferentiation can lead to more aggressive behavior, adversely affecting survival [34]. Consequently, while salivary gland tumors are generally indolent, their malignant potential and recurrence risk warrant attention. Thus, salivary gland tumor patients tend to exhibit better PFS and OS outcomes.

Secondly, the PFS difference between hypopharyngeal cancer and salivary gland tumors was statistically significant (P=0.015). This disparity may stem from the fact that hypopharyngeal cancers are often diagnosed at advanced stages, with larger

tumor sizes and higher recurrence and metastasis risks. Previous studies have highlighted the anatomical challenges of hypopharyngeal cancer, which is near vital structures, complicating surgical resection and leading to high recurrence rates that adversely impact PFS [35-37]. Hypopharyngeal cancers are usually locally advanced at diagnosis, with a high incidence of submucosal infiltration and lymphatic metastasis, limiting surgical effectiveness [38,39]. Postoperative complications, such as anastomotic leaks and reflux, may further exacerbate the condition and impact the quality of life [38,40]. Early diagnosis and improved therapeutic strategies are crucial to enhancing survival and quality of life in hypopharyngeal cancer patients [41,42].

Additionally, the PFS and OS differences between other tumor types and salivary gland tumors were statistically significant (PFS: P=0.041; OS: P=0.040), likely reflecting variations in tumor pathology, differentiation, and biological behavior. The survival disparities across tumor types underscore the necessity of tailoring individualized follow-up and treatment protocols to improve prognosis.

This study has several limitations, including single-center data, a relatively small sample size, limited follow-up duration, and potential selection bias inherent in the retrospective design. Future large-scale prospective studies are needed to validate these findings and enhance clinical applicability.

Conclusion

In summary, this study identifies several critical factors influencing progression-free survival (PFS) and overall survival (OS) in patients with head and neck malignancies, emphasizing the roles of tumor TN category, initial frozen section margins, and postoperative therapies. Our findings reveal that advanced T and N categories, as well as initial positive frozen section margins, are strongly associated with poorer survival outcomes, underscoring the need for precise intraoperative margin assessment. Postoperative chemotherapy and radiotherapy were also shown to significantly affect survival, albeit with varying impacts on PFS and OS. Distinct tumor types, notably oral and hypopharyngeal cancers, exhibited significant survival disparities when compared to salivary gland tumors, reflecting variations in their biological behavior and prognosis. These differences suggest a necessity for tumor-specific strategies in both treatment planning and long-term management.

While our study provides valuable insights, limitations such as the single-center, retrospective design, relatively short follow-up duration, and small sample size may hinder the generalizability of our findings. Future large-scale, prospective studies are warranted to validate these results and facilitate the development of evidence-based clinical practices aimed at enhancing survival and quality of life in patients with head and neck malignancies.

Funding Information

This work was supported by the Natural Science Foundation of Fujian Province (2023J011787) and the Quanzhou Science and Technology Program Project (2025QZC02DW).

References

- Song L, Liu J, Shang Y, et al. Enhanced MRI radiomics based model for predicting recurrence or metastasis of nasopharyngeal cancer (NC) undergoing concurrent chemoradiotherapy: a retrospective study. Cancer Control. 2024;31:10732748241250208.
- 2. Caruntu A, Yang SF, Acero J. New insights for an advanced

- understanding of the molecular mechanisms in oral squamous cell carcinoma. Int J Mol Sci. 2024;25(13):6964.
- Tarle M, Lukšić I. Pathogenesis and therapy of oral carcinogenesis. Int J Mol Sci. 2024;25(12):6343.
- 4. Saba NF, Pamulapati S, Patel B, et al. Novel immunotherapeutic approaches to treating HPV-related head and neck cancer. Cancers. 2023;15(7):1959.
- Shi M, Huang J, Sun Y. Neoadjuvant immunotherapy for head and neck squamous cell carcinoma: expecting its application in temporal bone squamous cell carcinoma. Curr Med Sci. 2023;43(2):213-222.
- Riva G, Pecorari G. Multimodality and sequential therapy in locally advanced head and neck cancer: a preface to the special issue. Cancers. 2021;13(11):2609.
- Wei J, Deng H, Wu L, et al. Lymphoepithelial carcinoma of the head and neck: a SEER analysis of prognostic factors for survival. J Int Med Res. 2023;51(1):03000605221148895.
- Strandberg S, Basurto-Sil D, Leh A, et al. Abstract 2456 for a few dollars more: treatment of metastatic head and neck cancers with dimerized CXCL12. J Biol Chem. 2024;300(3).
- Mao W, Zhang T, Li L, et al. Role of primary tumor volume and metastatic lymph node volume in response to curative effect of definitive radiotherapy for locally advanced head and neck cancer. Eur J Med Res. 2024;29(1):98.
- Grammatica A, Tomasoni M, Fior M, et al. Regional disease in head and neck cutaneous squamous cell carcinoma: the role of primary tumor characteristics and number of nodal metastases. Eur Arch Otorhinolaryngol. 2022;279(3):1573-1584.
- 11. Cheng CY, Sun FJ, Liu CJ. The influence of cervical lymph node number of neck dissection on the prognosis of the early oral cancer patients. J Dent Sci. 2020;15(4):519-525.
- Moratin J, Horn D, Oehme M, et al. Variation of resection margins in oral cancer in dependence of tumor stage and subsite—a retrospective cohort study. Clin Oral Investig. 2024;28(6):327.
- Bernard SE, van Lanschot CGF, Sewnaik A, et al. Clinical relevance of resection margins in patients with total laryngectomy or laryngopharyngectomy. Cancers. 2024;16(11):2038.
- 14. Abouhashem NS, Elwan A, Elaidy NF. Outcome of patients with head and neck squamous cell carcinoma can be predicted by expression of eIF4E and osteopontin in free surgical margins. Appl Immunohistochem Mol Morphol. 2022;30(5):e40-e49.
- Feng Y, Wei W, Guo S, et al. Associated risk factor analysis and the prognostic impact of positive resection margins after endoscopic resection in early esophageal squamous cell carcinoma. Exp Ther Med. 2022;24(1):1-7.
- de Kleijn BJ, Heldens GTN, Herruer JM, et al. Intraoperative imaging techniques to improve surgical resection margins of oropharyngeal squamous cell cancer: a comprehensive review of current literature. Cancers. 2023;15(3):896.
- 17. Young K, Ma E, Kejriwal S, et al. Intraoperative in vivo imaging modalities in head and neck cancer surgical margin delineation: a systematic review. Cancers. 2022;14(14):3416.
- Wang C, Hodge S, Ravi D, et al. Rapid and quantitative intraoperative pathology-assisted surgery by paired-agent imagingderived confidence map. Mol Imaging Biol. 2023;25(1):190-202.
- 19. Pertzborn D, Nguyen HN, Hüttmann K, et al. Intraoperative assessment of tumor margins in tissue sections with hyperspectral imaging and machine learning. Cancers. 2022;15(1):213.
- Slater NN, Farsi S, Rogers AL, et al. Reirradiation in head and neck squamous cell carcinoma; prognostic indicators, oncologic and functional outcomes. Am J Otolaryngol. 2024;45(6):104482.
- Chen Y, Zhong NN, Cao LM, et al. Surgical margins in head and neck squamous cell carcinoma: a narrative review. Int J Surg. 2024;110(6):3680-3700.

- Tzelnick S, Soroka HP, Tasnim N, et al. The impact of surgical resection margins on outcomes for adults with head and neck osteosarcomas: a Canadian sarcoma research and clinical collaboration (CanSaRCC) study. Oral Oncol. 2023;145:106495.
- Umino R, Nara S, Mizui T, et al. Impact of surgical margin status on survival and recurrence after pancreaticoduodenectomy for distal cholangiocarcinoma: is microscopic residual tumor (R1) associated with higher rates of local recurrence? Ann Surg Oncol. 2024:1-12.
- 24. Matsuo K, Nishio S, Matsuzaki S, et al. Surgical margin status and recurrence pattern in invasive vulvar Paget's disease: a Japanese Gynecologic Oncology Group study. Gynecol Oncol. 2021;160(3):748-754.
- 25. Pierik AS, Leemans CR, Brakenhoff RH. Resection margins in head and neck cancer surgery: an update of residual disease and field cancerization. Cancers. 2021;13(11):2635.
- Ullah A, Ahmed A, Lee KT, et al. Salivary gland adenoid cystic carcinoma in the US population: importance of grade, site of metastases, and adjuvant radiation for survival. Am J Otolaryngol. 2024;45(3):104266.
- Sobhi S, Wormald R, Hollitt S, et al. Survival and prognosis of surgical head and neck cancer patients aged 80 years and older. Laryngoscope Investig Otolaryngol. 2023;8(3):659-666.
- 28. de Bree R, van Beers MA, Schaeffers AWMA. Sarcopenia and its impact in head and neck cancer treatment. Curr Opin Otolaryngol Head Neck Surg. 2022;30(2):87-93.
- 29. Tsai CJ, Kuo YH, Wu HC, et al. Adjuvant radiotherapy significantly increases neck control and survival in early oral cancer patients with solitary nodal involvement: a national cancer registry database analysis. Cancers. 2021;13(15):3742.
- Weiss BG, Anczykowski MZ, Flach S, et al. Benefit of postoperative radiotherapy for early tumors with single ipsilateral lymph node metastasis. Laryngoscope. 2020;130(10):E530-E538.
- 31. Romani C, Lorini L, Bozzola A, et al. Functional profiles of curatively treated adenoid cystic carcinoma unveil prognostic features and potentially targetable pathways. Sci Rep. 2023;13(1):1809.
- 32. Linxweiler M, Kuo F, Katabi N, et al. The immune

- microenvironment and neoantigen landscape of aggressive salivary gland carcinomas differ by subtype. Clin Cancer Res. 2020;26(12):2859-2870.
- 33. Israel Y, Rachmiel A, Gourevich K, et al. Survival probabilities related to histology, grade and stage in patients with salivary gland tumors. Anticancer Res. 2019;39(2):641-647.
- Skalova A, Leivo I, Hellquist H, et al. High-grade transformation/ dedifferentiation in salivary gland carcinomas: occurrence across subtypes and clinical significance. Adv Anat Pathol. 2021;28(3):107-118.
- 35. Chiesa-Estomba CM, Mayo-Yanez M, Guntinas-Lichius O, et al. Radiomics in hypopharyngeal cancer management: a state-of-the-art review. Biomedicines. 2023;11(3):805.
- Shin J, Lee J, Hwang N, et al. Tumor dimension-dependent microscopic extensions of hypopharyngeal cancer: therapeutic implications for larynx-preserving hypopharyngectomy. J Surg Oncol. 2021;123(4):872-880.
- Suzuki S, Toyoma S, Kawasaki Y, et al. CD147 promotes invasion and MMP-9 expression through MEK signaling and predicts poor prognosis in hypopharyngeal squamous cell carcinoma. Adv Clin Exp Med. 2021;30(1):41-48.
- 38. Dai Z, He Q, Pan B, et al. Postoperative complication assessments of different reconstruction procedures after total pharyngolaryngoesophagectomy: tubular gastric pull-up versus whole gastric pull-up. Am Surg. 2018;84(12):1927-1931.
- 39. Tomioka T, Beppu T, Fujii T, et al. Surgical management around the paratracheal area of hypopharyngeal cancer. Jpn J Clin Oncol. 2019;49(5):452-457.
- 40. Huber GF. Opportunities and limits in salvage surgery in persistent or recurrent head and neck squamous cell carcinoma. Cancers. 2021;13(10):2457.
- 41. Zhang Y, Zhang Y, Peng L, et al. Research progress on the predicting factors and coping strategies for postoperative recurrence of esophageal cancer. Cells. 2022;12(1):114.
- 42. Dorobisz K, Włodarska-Polinska I, Pazdro-Zastawny K, et al. The impact of the patient's condition, diagnostic procedures and treatment on the survival of carcinoma of unknown primary site patients. Cancer Manag Res. 2019:6603-6614.