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Original Article

Prognostic significance of SUVmax and recurrence site on 18F-FDG PET/CT for overall survival prediction in recurrent hypopharyngeal cancer

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Abstract: Background: Recurrent hypopharyngeal carcinoma is associated with poor prognosis, yet the prognostic utility of maximum standardized uptake value (SUVmax) from 18F-FDG PET/CT and its relation to recurrence site remain insufficiently characterized. Objective: This study aimed to evaluate the association of SUVmax and recurrence site with overall survival (OS) in patients with recurrent hypopharyngeal carcinoma. Methods: We retrospectively analyzed 69 patients with biopsy-confirmed recurrent hypopharyngeal carcinoma without distant metastasis treated at Viet Nam National Cancer Hospital between 2019 and 2024. PET/CT scans performed at recurrence diagnosis were used to measure SUVmax at the primary tumor and/or metastatic lymph nodes. Patients were classified by recurrence site: primary tumor only (Tumor-only), lymph nodes only (Node-only), or both (Tumor + Node). OS was assessed using Kaplan-Meier estimates and Cox proportional hazards regression, adjusted for age, ECOG, time to recurrence and type of treatment. Results: Mean SUVmax was 12.3 ± 6.3. Patients with SUVmax > 12 had a median OS of 11.45 months (95% CI: 7.1-37.1) vs. 13.06 months (95% CI: 6.7-37.4) for SUVmax ≤ 12 (P < 0.01). Tumor + Node recurrence had a median OS of 11.2 months (95% CI: 6.8-37.4) vs. 13.6 months (95% CI: 6.7-34.5) for Tumor-only/Node-only (P = 0.009). In multivariate Cox regression, SUVmax > 12 (HR = 2.69, 95% CI: 1.37-5.30, P = 0.004), Tumor + Node recurrence (HR = 2.96, 95% CI: 1.45-6.06, P = 0.003), Non-surgery treatment (HR = 2.98, 95% CI: 1.23-7.23, P = 0.016) and ECOG PS ≥ 2 (HR = 2.22, 95% CI: 1.12-4.41, P = 0.023) independently predicted reduced OS. Conclusion: Elevated SUVmax and combined tumor-nodal recurrence on PET/CT are significant predictors of reduced OS, supporting their role in prognostic stratification for recurrent hypopharyngeal carcinoma.

Keywords: Recurrent hypopharyngeal carcinoma, 18F-FDG PET/CT, SUVmax, recurrence site, overall survival

Introduction

Hypopharyngeal carcinoma, a highly aggressive subtype of head and neck squamous cell carcinoma (HNSCC), is characterized by frequent recurrence and dismal prognosis. Despite multimodal therapy - surgery, radiotherapy, and chemotherapy - locoregional or distant recurrence occurs in up to 50% of patients within two years of initial treatment [1]. The hypopharynx's anatomical complexity, coupled with post-therapeutic tissue changes, hinders early detection, contributing to 5-year survival rates below 20% [2]. Timely identification and robust prognostic assessment of recurrence are critical to tailor salvage interventions and improve patient outcomes.

Integrated 18F-fluorodeoxyglucose (FDG) positron emission tomography with computed tomography (PET/CT) has transformed HNSCC management by enhancing the detection of metabolically active recurrence. With sensitivity and specificity exceeding 90%, it surpasses conventional modalities like CT or MRI in detecting recurrent lesions [3, 4]. Beyond its diagnostic role, PET/CT provides the maximum standardized uptake value (SUVmax), a quantitative measure of glucose metabolism that reflects tumor aggressiveness. Numerous studies have demonstrated that in head and neck squamous cell carcinoma (HNSCC), high SUVmax values on 18F-FDG PET/CT are consistently associated with poor prognosis [5, 6]. However, the prognostic significance of SUVmax in recurrent hypopharyngeal carcinoma remains underexplored, with most studies focusing on primary disease or heterogeneous HNSCC cohorts, overlooking the distinct biology of recurrence shaped by prior therapy.

The hypopharynx's tendency for submucosal spread and frequent nodal metastasis complicates recurrence prognosis. Emerging data suggest that in recurrent HNSCC, higher SUVmax correlates with shorter progression-free survival (PFS) and OS [3, 7], yet hypopharynx-specific evidence is limited. Moreover, the site of recurrence - whether at the primary tumor (Tumor-only), regional lymph nodes (Node-only), or both (Tumor + Node) - may further influence survival due to differences in disease extent and therapeutic challenges. Combined tumor and nodal recurrence likely reflect advanced progression, potentially amplifying the prognostic impact of SUVmax. This interplay between metabolic activity and recurrence pattern remains poorly defined in hypopharyngeal carcinoma, despite its relevance to treatment decisions, where

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options are often limited to aggressive salvage therapy or palliation.

Addressing this gap, our study investigates the prognostic utility of PET/CT-derived SUVmax and recurrence site in recurrent hypopharyngeal carcinoma. We hypothesize that elevated SUVmax, alongside recurrence involving both tumor and nodal sites, predicts poorer OS in a cohort of 69 patients with biopsy-confirmed recurrence. By focusing on this understudied population and integrating recurrence site with SUVmax, we aim to extend PET/CT's role beyond detection, establishing its value in risk stratification and personalized management of this lethal disease.

Patients and methods

Patients

This retrospective cohort study evaluated 69 consecutive patients with locoregional recurrent hypopharyngeal carcinoma treated at Viet Nam National Cancer Hospital between January 2019 and December 2024. Eligible patients had histologically confirmed recurrence following primary treatment (surgery, non-surgery or palliative care) for hypopharyngeal squamous cell carcinoma. Inclusion criteria required an 18F-FDG PET/CT scan performed within 1 month of recurrence diagnosis, with measurable SUVmax at the recurrence site(s). Patients were excluded if they had incomplete PET/CT data, second primary malignancies, distant metastasis.

Methods

Data collection: A total of 91 patients were initially included in the study. However, 9 patients were excluded due to the presence of distant metastases, 5 patients were excluded due to unconfirmed pathology and 8 patients were excluded due to loss of follow-up or insufficient data. Ultimately, clinical data were collected from 69 patients with biopsy-confirmed locoregional recurrent hypopharyngeal carcinoma who were treated at the Vietnam National Cancer Hospital between January 2019 and December 2024. The recorded variables included age, sex, Eastern Cooperative Oncology Group (ECOG) performance status, time to recurrence, maximum standardized uptake value (SUVmax) from PET/CT scans, location of recurrence as identified on PET/CT and other imaging modalities and survival outcomes.

PET/CT scans were performed using a standardized protocol. Patients fasted for ≥ 6 hours, with serum glucose levels maintained at 3.9-6.5 mmol/L before intravenous injection of 148-296 MBq of 18F-FDG. After a 40-60-minute rest period in a designated room, imaging was acquired from head to mid-thigh. CT parameters included 140 kV, 2.5 mA, a 16 × 16 matrix, and 4-mm slice thickness. PET data were analyzed using PETVCAR software (GE Healthcare), calculating the maximum standardized uptake value (SUVmax) at recurrence sites. SUVmax ≥ 2.5 was considered positive for malignancy at the primary tumor and/or metastatic lymph nodes. Recurrence was classified based on PET/CT findings as Tumor-only (primary site), Node-only (regional lymph nodes), or Tumor + Node (both primary site and nodes). SUVmax was determined by a board-certified nuclear medicine physician blinded to clinical outcomes, using manually delineated regions of interest (ROIs) around the primary tumor and, if present, the largest metastatic lymph node. Additional treatments following recurrence were also documented.

Statistical analysis

Patient characteristics and SUVmax were summarized using medians with interquartile ranges (IQR) for continuous variables and frequencies with percentages for categorical variables. The Mann-Whitney U test compared SUVmax between survivors and non-survivors, with non-normal distribution confirmed by the Shapiro-Wilk test.

Survival was analyzed using the Kaplan-Meier method, with log-rank tests comparing OS across SUVmax tertiles (or an optimal cutoff from receiver operating characteristic [ROC] curve analysis) and recurrence sites (Tumor-only, Node-only, Tumor + Node). The optimal SUVmax cutoff of 12 was determined by ROC curve analysis, demonstrating good discriminatory ability with an AUC of 0.829 (95% CI: 0.728-0.931, $P < 0.001$), a sensitivity of 66.7%, and a specificity of 81.5% (Youden Index: 0.482). Given the absence of a significant difference in OS between Tumor-only and Node-only recurrence groups (log-rank $P = 0.508$), these two groups were combined into a single reference group for Kaplan-Meier and Cox regression analyses. Multivariate Cox proportional hazards regression assessed the prognostic value of SUVmax and recurrence site, adjusting for age, ECOG, time to recurrence, following treatment, reporting hazard ratios (HRs) and 95% confidence intervals (CIs). Subgroup analysis explored differences in SUVmax by recurrence site. Missing data (< 5%) were excluded, with sensitivity analyses verifying their impact. Statistical significance was set at $P < 0.05$ (two-tailed). Analyses were performed using SPSS version 22.

Ethical considerations

This retrospective study complied with the Declaration of Helsinki and was approved by the Viet Nam National Cancer Hospital Ethics Committee. As data were retrieved from existing medical records and de-identified for analysis, the requirement for informed consent was waived by the ethics committee. Patient confidentiality was maintained throughout the study.

Results

This study included 69 patients with recurrent hypopharyngeal carcinoma treated at Viet Nam National Cancer

Table 1. Baseline characteristics (n = 69)

Characteristic	Value
Age (years), mean ± SD (range)	60.7 ± 8.2 (46-78)
ECOG Performance Status, n (%)	
< 2	46 (66.7%)
≥ 2	23 (33.3%)
Time to Recurrence (months), mean (range)	20.01 (6.4-88.8)
Time to Recurrence, n (%)	
≤ 12 months	42 (60.9%)
> 12 months	27 (39.1%)
Recurrence Site, n (%)	
Tumor-only	27 (39.1%)
Node-only	14 (20.3%)
Tumor + Node	28 (40.6%)
Treatment of recurrent disease, n (%)	
Surgery	22 (31.9%)
Non-Surgery	47 (68.1%)
Radiation therapy	9 (13.0%)
Chemotherapy	12 (17.4%)
CCRT	11 (15.9%)
Palliative care	15 (21.8%)
SUVmax, mean ± SD (range)	12.3 ± 6.3 (3.1-31.5)
Median Follow-up (months)	16.93

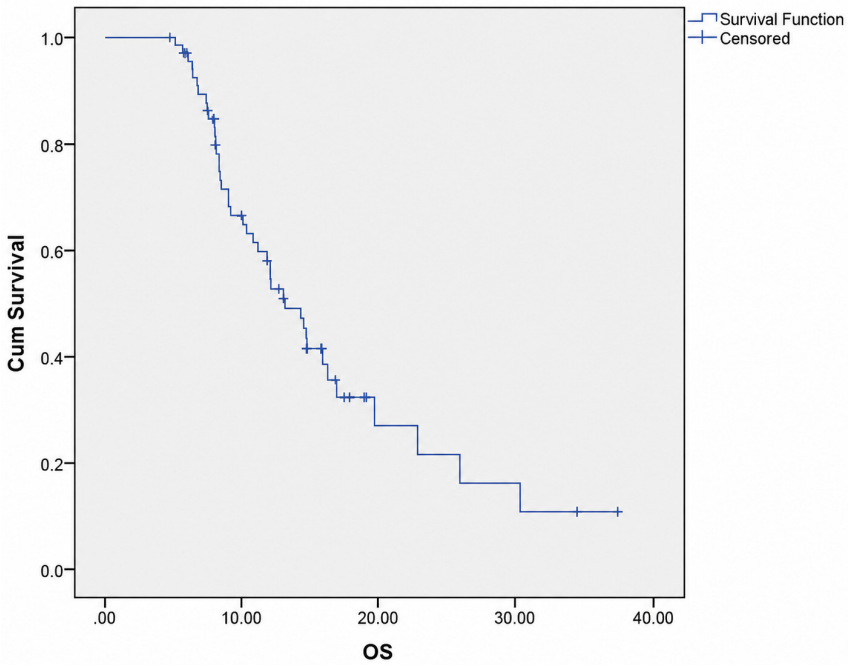

Figure 1. Overall survival of the study population.

Hospital (2019-2024). Baseline characteristics are in **Table 1**. Mean age was 60.7 ± 8.2 years, with 66.7% having ECOG PS < 2. Recurrence occurred at a mean of 20.01 months, with 40.6% Tumor + Node, 59.4% Tumor-only/Node-only. Treatment was surgical at 31.9% and non-surgical at 68.1%. Mean SUVmax was 12.3 ± 6.3; median follow-up was 16.93 months.

Median OS was 12.23 months (95% CI: 10.71-15.76, **Figure 1**). ROC curve analysis identified an optimal SUVmax cutoff of 12 for predicting overall survival, yielding an AUC of 0.829 (95% CI: 0.728-0.931, P < 0.001), with a sensitivity of 66.7% and a specificity of 81.5%. Kaplan-Meier analysis showed SUVmax ≤ 12 had a median OS of 13.06 months vs. 11.45 months for SUVmax > 12 (P < 0.01, **Figure 2A**). Patients who underwent surgery demonstrated a significantly longer median OS compared to those who did not (median OS: 16.4 months vs. 11.2 months, log-rank P = 0.022, **Figure 2B**). Patients with Tumor-only or Node-only recurrence had a significantly longer median OS compared to those with Tumor + Node recurrence (13.6 months vs. 11.2 months, log-rank P = 0.009, **Figure 2C**). SUVmax was higher in non-survivors (mean rank: 43.9) vs. survivors (mean rank: 21.2) (P < 0.01, **Figure 3**).

Univariate Cox regression (**Table 2**) identified ECOG PS ≥ 2 (HR = 2.31, P = 0.011), non-surgical treatment (HR = 2.5, P = 0.027), Tumor + Node recurrence (HR = 2.26, P = 0.011), and SUVmax > 12 (HR = 3.07, P = 0.001) as predictors of worse OS. Multivariate analysis (**Table 3**) confirmed SUVmax > 12 (HR = 2.69, P = 0.004), Tumor + Node recurrence (HR = 2.96, P = 0.003), ECOG PS ≥ 2 (HR = 2.22, P = 0.023), and non-surgical treatment (HR = 2.98, P = 0.016) as independent predictors.

Discussion

Vietnam is an endemic region for hypopharyngeal cancer. According to GLOBOCAN 2022, hypopharyngeal cancer ranks 16th in incidence, with over 2,300 new cases annually. Despite multimodal treatment approaches, the recurrence rate within the first two years exceeds 50% [1]. In our study, the median overall survival after recurrence detection was only 12.23 months. This finding is consistent with previous studies, highlighting the poor prognosis of recurrent hypopharyngeal cancer [8, 9].

This study demonstrates that in recurrent hypopharyngeal carcinoma, SUVmax > 12 and recurrence involving both the primary tumor and regional lymph nodes (Tumor + Node) are independent prognostic factors for

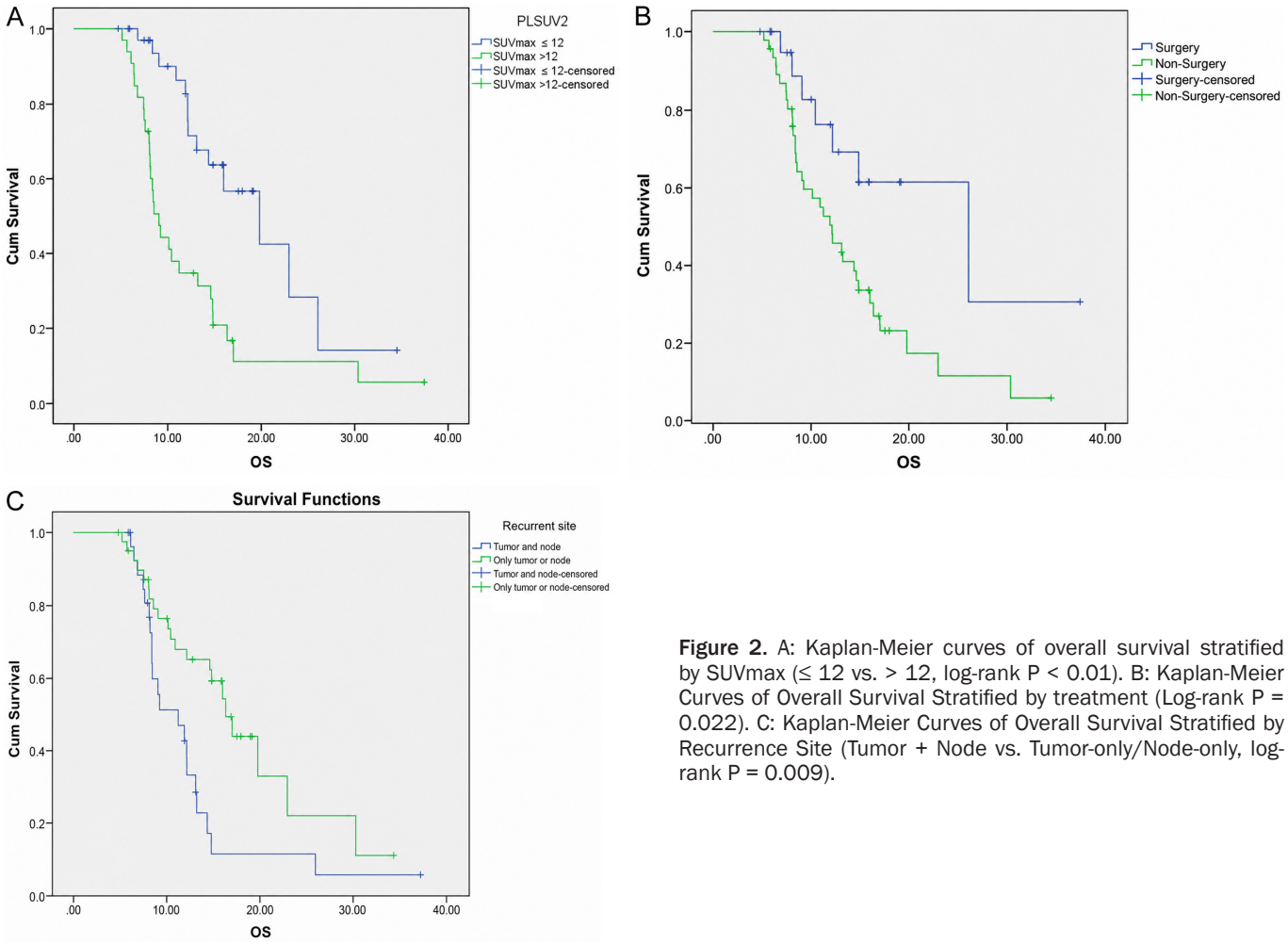

Figure 2. A: Kaplan-Meier curves of overall survival stratified by SUVmax (≤ 12 vs. > 12, log-rank P < 0.01). B: Kaplan-Meier Curves of Overall Survival Stratified by treatment (Log-rank P = 0.022). C: Kaplan-Meier Curves of Overall Survival Stratified by Recurrence Site (Tumor + Node vs. Tumor-only/Node-only, log-rank P = 0.009).

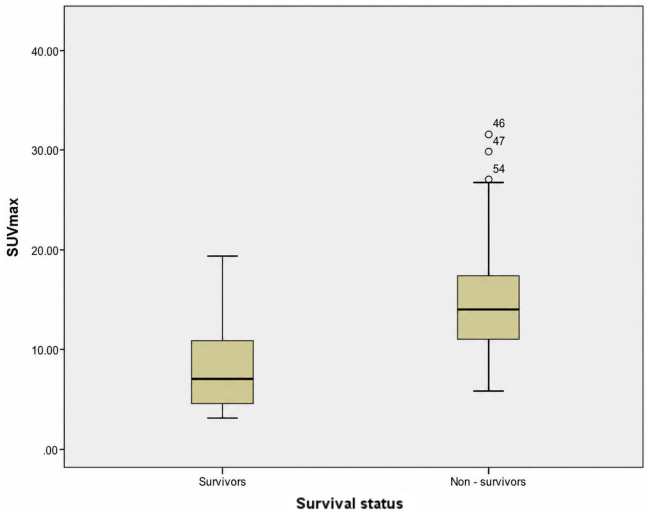

Figure 3. Boxplot of SUVmax distribution in survivors versus non-survivors (Mann-Whitney U, P < 0.01).

reduced overall survival (OS), with hazard ratios of 2.69 (P = 0.004) and 2.96 (P = 0.003), respectively. Additionally, ECOG performance status (PS) ≥ 2 and non-surgical treatment were associated with poorer OS. These findings not only reinforce but also extend prior research on the prognostic role of 18F-FDG PET/CT in head and neck cancer, particularly in the context of recurrence.

Table 2. Univariate cox regression analysis of factors associated with overall survival (OS)

Variable	OS	
	HR (95% CI)	*p* value
Age ≥ 60 years	1.06 (0.57-1.95)	0.863
ECOG PS ≥ 2	2.31 (1.21-4.39)	0.011
Time to recurrence ≤ 12 months	1.37 (0.70-2.68)	0.362
Non-surgery treatment	2.5 (1.11-5.62)	0.027
Tumor + Node recurrence	2.26 (1.21-4.21)	0.011
SUVmax > 12	3.07 (1.61-5.87)	0.001

The prognostic significance of SUVmax in primary head and neck cancer is well-established. For instance, Suzuki et al. reported that in primary hypopharyngeal carcinoma, SUVmax ≥ 13 was associated with reduced OS [5]. Our study builds on this foundation by identifying a slightly lower threshold (SUVmax > 12) in the context of recurrence, which may be attributable to alterations in tumor biology following initial treatment. It is conceivable that prior therapy induces changes in tumor metabolism - potentially through mechanisms such as dedifferentia-

Table 3. Multivariate cox regression analysis of factors associated with overall survival (OS)

Variable	OS	
	HR (95% CI)	*p* value
Age ≥ 60 years	1.09 (0.58-2.04)	0.785
ECOG PS ≥ 2	2.22 (1.12-4.41)	0.023
Time to recurrence ≤ 12 months	1.05 (0.51-2.12)	0.89
Non-surgery treatment	2.98 (1.23-7.23)	0.016
Tumor + Node recurrence	2.96 (1.45-6.06)	0.003
SUVmax > 12	2.69 (1.37-5.30)	0.004

tion or clonal selection of more aggressive phenotypes - thereby modifying the metabolic profile of recurrent lesions relative to their primary counterparts. Our findings are consistent with those of Kim et al., who showed that elevated SUVmax on post-treatment PET/CT was associated with shorter progression-free survival and OS in recurrent head and neck squamous cell carcinoma [3]. To our knowledge, studies examining PET/CT parameters specifically in recurrent hypopharyngeal carcinoma are few, and our data add to this limited body of literature.

Recurrence site emerged as an important prognostic factor in our cohort. Patients with simultaneous Tumor + Node recurrence had significantly shorter OS than those with Tumor-only or Node-only recurrence (11.2 vs. 13.6 months, P = 0.009), suggesting that concurrent nodal involvement reflects a higher disease burden and more challenging treatment scenario compared to isolated recurrence. Matoba et al. found that in recurrent or metastatic head and neck cancer, higher tumor burden, particularly with multiple sites of involvement, was associated with poorer outcomes in patients receiving immunotherapy [7]. Our findings confirm this association in hypopharyngeal carcinoma and suggest that the interplay between SUVmax and recurrence site may serve as a combined prognostic marker, where elevated SUVmax exacerbates the adverse impact of nodal recurrence.

Multivariate analysis further identified ECOG PS ≥ 2 (HR = 2.22, P = 0.023) and non-surgical treatment (HR = 2.98, P = 0.016) as independent predictors of reduced OS. The role of performance status in cancer prognosis, including head and neck cancer, is well-documented [2]. The association of non-surgical treatment with poorer OS may reflect selection bias, as patients with more advanced or inoperable disease often receive radiotherapy or chemotherapy. Nonetheless, this highlights the importance of salvage surgery in improving outcomes for eligible patients.

Clinically, these findings suggest that SUVmax and recurrence site on PET/CT can be integrated into prognostic models to refine risk stratification and guide personalized treatment strategies. For instance, patients with SUVmax > 12 and both Tumor and Node recurrence may have poor prognosis, where aggressive local therapies such as salvage surgery and re-irradiation might provide limited benefit, and systemic or palliative approaches should be considered. Conversely, patients with lower SUVmax and isolated recurrence may be suitable candidates for more intensive curative interventions, including salvage surgery and adjuvant therapy. The prognostic value of PET/CT, beyond its diagnostic utility, reinforces its superiority over conventional imaging in assessing recurrence and optimizing therapeutic decision-making in hypopharyngeal carcinoma.

However, our study has several limitations. First, the retrospective design and modest sample size (n = 69) may limit the generalizability of the findings. Second, this study relied solely on SUVmax as the PET/CT-derived metabolic parameter. Volumetric parameters such as Metabolic Tumor Volume (MTV) and Total Lesion Glycolysis (TLG), which may provide additional prognostic information, were not available for analysis. As the PET/CT data were acquired and processed using PETVCAR software in routine clinical practice, these volumetric metrics were not systematically calculated or stored at the time of data acquisition, precluding their inclusion in the current analysis. Future prospective studies with standardized PET/CT protocols should incorporate these parameters to provide a more comprehensive metabolic assessment [6]. Additionally, comorbidities were not adjusted due to incomplete data, although their impact may be minimal given that cancer progression is the primary driver of mortality. Lifestyle factors such as heavy tobacco and alcohol consumption were not systematically documented and could not be adjusted for in our analyses. These factors may partly underlie the poor performance status observed in our cohort (ECOG PS ≥ 2, HR = 2.22) and should be prospectively collected in future studies. Future prospective studies with larger cohorts and incorporation of advanced PET metrics are needed to validate and refine these findings.

Conclusion

SUVmax > 12 and Tumor + Node recurrence on 18F-FDG PET/CT are robust predictors of reduced OS in recurrent hypopharyngeal carcinoma, offering a practical framework for risk stratification and treatment planning.

Disclosure of conflict of interest

None.

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