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Head and Neck Cancer Salvage Surgery: External Validation of Disease-Specific Survival Predictors

Yabing Han*

Department of Head and Neck Surgery, Peking University, China

Abstract

For patients with recurrent head and neck cancer, salvage surgery is an essential option that might potentially increase survival time and enhance quality of life. Salvage surgery efficacy, however, varies greatly, and it is still very difficult to find accurate survival indicators unique to head and neck cancer. With a cohort of patients receiving salvage surgery for head and neck cancer, the objective of this study is to externally evaluate survival predictions. We evaluated the prognostic significance of demographic, clinical, and pathological characteristics using a large dataset. According to our research, a number of clinical and pathological characteristics, including as the location of the tumor, the surgical margins, and the involvement of lymph nodes, are important indicators of prognosis for this group of patients. The study emphasizes the need of customized treatment planning and the requirement for ongoing research to refine survival prediction models.

Keywords: Salvage surgery; Head and neck cancer; Survival predictors; External validation; Tumor location

Introduction

Head and neck cancer represents a heterogeneous group of malignancies that originate in the squamous cells lining the mucosal surfaces of the head and neck region, including the oral cavity, pharynx, and larynx. Despite advances in treatment modalities, including surgery, radiation, and chemotherapy, a significant proportion of patients experience disease recurrence [1]. Salvage surgery, defined as surgical resection performed after the failure of initial curative treatment, remains a cornerstone in the management of recurrent head and neck cancer. However, the success of salvage surgery is highly variable, and predicting which patients will benefit from this intervention remains a critical challenge. Several studies have proposed survival predictors for patients undergoing salvage surgery for head and neck cancer. These predictors include demographic factors (e.g., age, gender), clinical variables (e.g., tumor stage, prior treatments), and pathological characteristics (e.g., surgical margins, lymph node involvement). However, these predictors have often been derived from single-institution studies with limited external validation. The lack of robust, externally validated survival predictors hinders the ability to tailor salvage surgery to individual patients, potentially leading to suboptimal outcomes. This study aims to externally validate survival predictors specific to head and neck cancer in a multicenter cohort of patients undergoing salvage surgery [2]. By analyzing a comprehensive dataset, we seek to identify reliable prognostic factors that can inform clinical decision-making and improve patient outcomes. A growing body of literature has focused on identifying survival predictors for patients undergoing salvage surgery for head and neck cancer. These predictors include demographic factors such as age and gender, clinical variables such as tumor stage at initial diagnosis and the time interval to recurrence, and pathological characteristics such as surgical margins, lymph node involvement, and perineural invasion. However, many of these predictors have been derived from retrospective single-center studies with limited external validation. The generalizability of these findings to broader patient populations remains uncertain, and there is a pressing need for externally validated prediction models to guide clinical decision-making [3].

This study aims to address this gap by conducting an external validation of survival predictors in a multicenter cohort of patients undergoing salvage surgery for head and neck cancer. By analyzing a comprehensive dataset from multiple institutions, we seek to evaluate the prognostic value of previously identified predictors and determine their applicability to diverse patient populations. Additionally, we aim to identify new prognostic factors that may be specific to this patient cohort and to assess the overall accuracy and discriminatory ability of existing prediction models. The ultimate goal of this research is to enhance the ability of clinicians to stratify patients based on their risk profiles, thereby optimizing the selection of candidates for salvage surgery and improving overall survival outcomes. By providing robust, externally validated survival predictors, this study has the potential to contribute to more personalized and effective management strategies for patients with recurrent head and neck cancer [4].

Methods

Study design and population

This retrospective cohort study included patients with recurrent head and neck cancer who underwent salvage surgery between 2015 and 2020 at three tertiary care centers. Patients were included if they had histologically confirmed squamous cell carcinoma and had previously received curative-intent treatment (surgery, radiation, and/or chemotherapy). Patients with distant metastases at the time of recurrence or those who received palliative surgery were excluded from the analysis [5].

Data collection

Demographic, clinical, and pathological data were extracted from electronic medical records. Variables collected included age, gender,

*Corresponding author: Yabing Han, Department of Head and Neck Surgery, Peking University, China, E-mail: han7899@yahoo.com

smoking and alcohol use history, tumor location, tumor stage at initial diagnosis, prior treatments, and time to recurrence, tumor size, surgical margins, lymph node involvement, and postoperative complications. Survival data were obtained from follow-up records, with the primary endpoint being overall survival (OS) from the date of salvage surgery [6].

Statistical analysis

Descriptive statistics were used to summarize the patient population. Kaplan-Meier survival curves were generated to estimate OS, and log-rank tests were used to compare survival between groups. Cox proportional hazards models were employed to assess the impact of demographic, clinical, and pathological variables on OS. Variables with a p-value <0.05 in univariate analysis were included in multivariate analysis. Hazard ratios (HRs) and 95% confidence intervals (CIs) were calculated to quantify the strength of associations [7].

External validation was conducted by comparing the predictive performance of previously published survival predictors with those identified in our cohort. Calibration plots and concordance indices (C-indices) were used to assess the accuracy and discriminatory ability of the prediction models.

Results

Patient characteristics

The study included 250 patients who met the inclusion criteria. The median age at the time of salvage surgery was 62 years (range 35-85), with a male predominance (70%). The majority of tumors were located in the oral cavity (45%), followed by the larynx (30%) and pharynx (25%). Most patients had advanced-stage disease at initial diagnosis (Stage III or IV), and the median time to recurrence was 18 months (range 6-48 months).

Survival analysis

The median OS for the entire cohort was 24 months (95% CI: 20-28 months). Univariate analysis identified tumor location, surgical margins, and lymph node involvement as significant predictors of OS. Specifically, tumors located in the larynx were associated with poorer survival compared to those in the oral cavity (HR: 1.45, 95% CI: 1.10-1.91, p=0.01). Positive surgical margins were associated with a nearly two-fold increase in the risk of death (HR: 1.95, 95% CI: 1.40-2.70, p<0.001). Lymph node involvement at the time of salvage surgery was also a strong predictor of poor OS (HR: 1.75, 95% CI: 1.30-2.35, p<0.001).

Multivariate analysis confirmed the independent prognostic value of tumor location, surgical margins, and lymph node involvement. The final model demonstrated good discriminatory ability, with a C-index of 0.72.

External validation

The predictive performance of previously published survival predictors was assessed in our cohort. Calibration plots indicated that the models had moderate calibration, with some overestimation of survival probabilities in high-risk patients. The C-indices of the external models ranged from 0.65 to 0.70, indicating moderate discriminatory ability. Our internally derived model outperformed the external models, suggesting the need for population-specific survival predictors.

Discussion

Salvage surgery remains a pivotal intervention for patients with recurrent head and neck cancer, yet predicting survival outcomes in this population is fraught with challenges. Our study provides important insights into the survival predictors specific to patients undergoing salvage surgery and underscores the importance of external validation in diverse patient populations. The findings highlight the prognostic significance of tumor location, surgical margins, and lymph node involvement. Tumors located in the larynx and those with positive surgical margins or lymph node involvement were associated with significantly worse survival outcomes. These predictors can be used to inform clinical decision-making, guiding patient selection for salvage surgery and optimizing surgical planning. The external validation component of our study revealed moderate calibration and discriminatory ability of existing survival prediction models, emphasizing the need for ongoing research to refine these models. The superior performance of our internally derived model suggests that population-specific factors may influence survival outcomes and should be considered when developing prediction tools [8-12].

Conclusion

This study validates key survival predictors in patients undergoing salvage surgery for head and neck cancer, providing valuable insights for clinical practice. Tumor location, surgical margins, and lymph node involvement emerged as significant prognostic factors, and their assessment should be integrated into treatment planning. The moderate performance of existing prediction models highlights the importance of external validation and the need for continued refinement of survival predictors to enhance patient outcomes in this challenging clinical context.

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