pISSN 2460-9684, eISSN 2476-8863, Accredited number 36/E/KPT/2019
Volume 10, Number 2, December 2025
doi.org/10.21460/bikdw.v10i2.1250

Research

THE ASSOCIATION BETWEEN TUMOR INFILTRATING LYMPHOCYTES (TILS) LEVELS AND METASTATIC STATUS IN PATIENTS WITH HEAD AND NECK CANCER

Anton Sony Wibowo[1,2], Sulis Ernawati[1], Herfis Avindati[1]

[1]Universitas Gadjah Mada Academic Hospital, Indonesia
[2]Otorhinolaryngology-Head and Neck Surgery Department Faculty of Medicine Public Health and Nursing School of Medicine Universitas Gadjah Mada, Indonesia

Corresponding Author: antonsonywibowo@ugm.ac.id

Received: 23-11-2025 / Accepted: 05-02-2026

ABSTRACT

Background: Head and neck cancer (HNC) is a major public health issue, ranking as the seventh most prevalent cancer worldwide. The challenge is the early detection of the disease. Despite advances in imaging techniques, detecting early metastases remains problematic. Tumor-infiltrating lymphocytes (TILs) have been recognized as key players in the tumor microenvironment, influencing tumor growth and cancer spread across multiple tumor types. Their significance as a biomarker has been widely investigated.

Objectives: This study aimed to investigate the association between tumor-infiltrating lymphocytes (TILs) levels and metastatic status in patients with head and neck cancer.

Method: This was an observational analytic cross-sectional study of patients at Universitas Gadjah Mada Academic Hospitals and Dr. Sardjito General Hospital, Yogyakarta. The study was performed from Jun 2025 until December 2025 on patients who had been diagnosed with head and neck cancer based on histopathologic examination. Tumor-infiltrating lymphocytes (TILs) were assessed from diagnostic biopsy specimens obtained at initial presentation, before any treatment. Metastatic status was determined at the time of diagnosis based on clinical evaluation and imaging studies. TIL levels differences between metastatic and non-metastatic head and neck carcinoma cases were assessed using the Chi-square test. Odds ratios (OR) were calculated, and multivariate analysis was conducted. The cut-off point for TIL levels was established through receiver operating characteristic (ROC) curve analysis.

Result: Seventy-five head and neck cancer patients were involved in this study. The patients were divided into metastatic and non-metastatic groups. The study subjects comprised 32 patients without metastasis and 43 with metastasis. Based on the receiver operating characteristic curve, the cut-off points 12.5% with a sensitivity of 62.8% (0.628) and a specificity of 87.5% (0.875). There was a significant difference in TIL levels between the metastatic and non-metastatic groups based on a cut-off value of 12.5 ($p = 0.001$; OR: 11.8; 95% CI: 3.5–39.8).

Conclusion: There was a significant difference in TILs levels between metastatic and non-metastatic head and neck carcinoma. Higher TILs levels (≥12.5%) were significantly associated with non-metastatic head and neck carcinoma.

Keyword: head and neck cancer, metastasis, predictor, tumor-infiltrating lymphocytes (TILs)

INTRODUCTION

Head and neck cancer (HNC) is a major public health issue, ranking as the seventh most prevalent cancer worldwide, with an estimated 660,000 new cases and around 325,000 deaths each year.[1,2] Head and neck cancers (HNC), predominantly squamous cell carcinomas (HNSCC), pose a major global health challenge, with over 650,000 new cases and around 330,000 deaths reported each year.[3] These cancers develop in different regions of the upper aerodigestive tract, including the oral cavity, oropharynx, larynx, and nasopharynx.[4,5]

Diagnosing head and neck cancer (HNC) presents several challenges that can influence patient outcomes. A major difficulty is the early detection of the disease. The challenge is the early detection of the disease. Despite advances in imaging techniques, detecting early metastases remains problematic. Diagnostic methods still need an invasive procedure to detect metastasis. Neck dissection is needed to detect lymphatic spread patterns in various tumor types.[6]

Lymphocytes infiltrating tumors (TILs) have been recognized as key players in the tumor microenvironment, impacting tumor growth and cancer spread across multiple tumor types. Their significance as prognostic markers has

been widely investigated, with studies showing that elevated levels of TILs, especially CD8+ TILs, are associated with better patient prognoses and a lower likelihood of metastasis.[7] This indicates that TILs are involved not only in immune defense against tumors but also in shaping tumor dynamics, potentially restraining metastatic spread.

The spatial distribution and functional state of TILs within the tumor microenvironment significantly influence their ability to suppress tumor growth and metastasis. For example, the presence of inhibitory receptors on TILs can alter their function, shifting them from fighting tumors to promoting tumor progression, thereby affecting metastatic potential. This dual behavior highlights the intricate nature of TILs interactions in the tumor microenvironment and their role in metastasis.[8] In head and neck cancers, TILs have been linked to the metastatic process, with research showing that increased TILs levels are associated with improved patient outcomes and a lower occurrence of metastasis.[9,10]

Based on the data presented, it can be inferred that TILs function both as prognostic indicators and as active contributors to the metastatic process across diverse cancers. The diagnostic value of TILs can help assess the likelihood of different stages and metastasis of head and neck carcinoma, enabling more optimal management of head and neck cancer. The goal of this study was to explore the cutoff point for TILs levels and the contribution of other variables to metastatic head and neck cancer.

MATERIALS AND METHODS

This was an observational, analytic cross-sectional study to determine differences in TILs levels between patients with metastatic and non-metastatic head and neck carcinoma. The study was started after receiving approval from the Medical and Health Research Ethics Committee (MHREC), Faculty of Medicine, Public Health, and Nursing, Universitas Gadjah Mada, Yogyakarta (Ref. KE/FK/0911/EC/2025).

The study was performed from Jun 2025 until December 2025 on patients who had been diagnosed with head and neck cancer based on histopathologic examination. TILs measurements were carried out by certified anatomical pathologists. For each sample included in the study, TILs were evaluated by counting lymphocytes in 10 high-power fields (HPF) at 100x magnification. Only the lymphocytes present within the viable tumor region were considered in this count.

TIL's level was one of the variables that affected metastatic and non-metastatic head and neck cancer. The target population in this study was patients with head and neck cancer whose diagnosis had been established through anatomical pathology examination. The sample consisted of head and neck squamous cell carcinoma patients who were at Dr. Sardjito General Hospital and Universitas Gadjah Mada Academic Hospital, Yogyakarta, during Jun 2025 until December 2025, who met the inclusion and exclusion criteria.

Population and samples

The research sample consisted of patients at Universitas Gadjah Mada Academic Hospitals and Dr. Sardjito General Hospital, Yogyakarta. The sample size was determined using the difference proportion formula, with α set at 5% and β at 20%.[11] The recommended sample size was 75. The sampling method used in this study was consecutive sampling, in which all patients who met the inclusion and exclusion criteria during the study period were consecutively enrolled until the required sample size was achieved.

The inclusion criteria were cases of nasopharyngeal carcinoma and other head and neck cancers treated at the Academic Hospital of Universitas Gadjah Mada, Dr. Sardjito General Hospital, that met the criteria: 1. Cases of nasopharyngeal carcinoma and other head and neck cancers diagnosed through nasopharyngeal tissue biopsy as the basis for diagnosis. 2. Cases of nasopharyngeal carcinoma and other head and neck cancers that have not yet undergone radiotherapy or chemotherapy. The Exclusion Criteria were cases of nasopharyngeal carcinoma accompanied by other malignancies, individuals unwilling to participate as research subjects, and patients with incomplete medical records.

Metastasis was identified through a comprehensive diagnostic workup, including chest X-rays, contrast-enhanced MSCT scans, bone surveys, and ultrasound imaging of the upper and lower abdomen. Metastatic status was determined according to the TNM classification (AJCC, 8th ed., 2017) by evaluating lymph node characteristics (N) and the presence of distant metastasis (M).

Statistical analysis

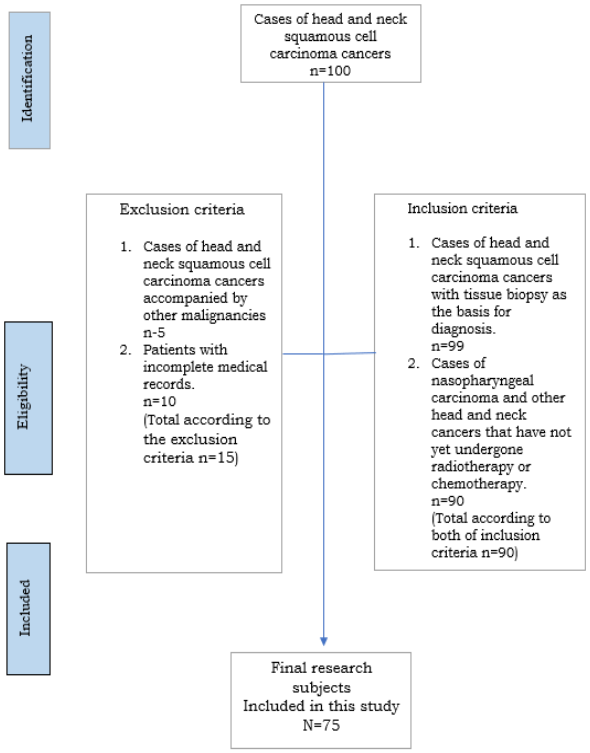

Figure 1. Participant flow diagram

TILs levels differences between metastatic and non-metastatic head and neck carcinoma cases were assessed using the Chi-square test. Odds ratios (OR) were calculated, and multivariate analysis was conducted. The cut-off point for TILs levels was established through receiver operating characteristic (ROC) curve analysis. A p-value of less than 0.05 was regarded as statistically significant.

Receiver operating characteristic (ROC) curve analysis was performed to evaluate the discriminatory ability of TILs levels in differentiating metastatic from non-metastatic head and neck carcinoma. The optimal cut-off value was determined using the Youden index, defined as the maximum value of (sensitivity + specificity − 1). The area under the curve (AUC) with its 95% confidence interval (CI) was calculated to assess overall diagnostic performance.

For logistic regression analysis, TILs levels were dichotomized using the ROC-derived cut-off value of 12.5% and coded as a binary variable. High TILs levels (≥12.5%) were used as the reference category, and low TILs levels (<12.5%) were considered the exposure group. Odds ratios were interpreted accordingly.

RESULTS AND DISCUSSION

The participants in this study were patients diagnosed with head and neck cancer through a histopathological examination conducted at Universitas Gadjah Mada Academic Hospitals and Dr. Sardjito General Hospital, Yogyakarta. Among them, 32 patients were identified as having non-metastatic head and neck carcinoma, while 43 were diagnosed with metastatic head and neck carcinoma.

Histopathological analysis of the following tissue biopsy was carried out at the Department of Anatomical Pathology, Faculty of Medicine, Public Health, and Nursing, Universitas Gadjah Mada/Dr. Sardjito General Hospital, Yogyakarta. The subjects' characteristics, including gender, age, and cancer type, are summarized in Table 1.

Table 1. Baseline characteristics of study participants according to metastatic status (n = 75)

		Non metastasis n (%)	Metastasis n (%)	Total n (%)	p
Sex	Male	28 (87.5)	31 (72.1)	59 (78.7)	0.107
	Female	4 (12.5)	12 (27.9)	16 (21.3)	
Age	15-24 Years old	1 (3.1)	2 (4.7)	3 (4.0)	0.277
	25-34 Years old	0 (0.0)	2 (4.7)	2 (2.7)	
	35-44 years old	5 (15.6)	5 (11.6)	10 (13.3)	
	45-54 years old	5 (15.6)	9 (20.9)	14 (18.7)	
	55-64 years old	9 (28.1)	18 (41,9)	27 (36.0)	
	> 65 year old	12 (37.5)	7 (16.3)	19 (25.3)	
Cancer	Nasopharyngeal cancer	13 (40.6)	29 (67.4)	42 (56.0)	0.042
	Laryngeal cancer	8 (25)	4 (9.3)	12 (16.0)	
	Sinonasal cancer	8 (25.0)	4 (9.3)	12 (16.0)	
	Oral cancer	1 (3.1)	5 (11.6)	6 (8.0)	
	Oropharyngeal cancer	0 (0.0)	1 (2.3)	1 (1.3)	
	Hypopharyngeal cancer	1 (3.1)	0 (0.0)	1 (1.3)	
	Other squamous cell head and neck cancer	1 (3.1)	0 (0.0)	1 (1.3)	

Values are presented as numbers (percentages). Percentages are calculated based on column totals. Fisher's exact test was used where appropriate.

There was no statistically significant difference in the sex distribution of the sample between the metastatic and non-metastatic groups (p = 0.107), as shown in TABLE 1. The highest age frequency was observed in the 55-64 years old age group, comprising 27 patients (36%) (TABLE 1). Fisher's exact test revealed no statistically significant difference in age between the metastatic and non-metastatic groups (p=0.277). The most common type of head and neck cancer is nasopharyngeal carcinoma, followed by laryngeal cancer and sinonasal cancer.

Head and neck cancers are a diverse group of malignancies arising from various anatomical sites in the head and neck region, including the oral cavity, pharynx, larynx, nasal cavity, and salivary glands. The most common type of head and neck cancer is head and neck squamous cell carcinoma (HNSCC), which accounts for over 90% of these cancers.[12]

The primary objective of this study was to assess the association between TIL levels and the metastatic status of head and neck carcinoma. High and low TIL levels were classified using a cut-off point for TIL levels determined through receiver operating characteristic (ROC) curve analysis (FIGURE 1). ROC curve analysis demonstrated an AUC of 0.793 (95% CI: 0.687–0.899; p = 0.001), indicating good discriminatory ability of TILs levels for metastatic status. The optimal cut-off value identified using the Youden index was 12.5%, yielding a sensitivity of 62.8% and a specificity of 87.5%. Based on this cut-off value, TIL levels were categorized as low (<12.5) and high (≥12.5).

Tumor-infiltrating lymphocytes (TILs) are essential for metastatic progression in head and neck cancer (HNC), especially head and neck squamous cell carcinoma (HNSCC). The presence and makeup of TILs within the tumor microenvironment (TME) can profoundly impact tumor behavior, immune evasion, and patient prognosis.

TILs, consisting of CD8+ cytotoxic T lymphocytes, are crucial for initiating a robust anti-tumor immune response. Their presence in the tumor has been linked to better survival outcomes in several cancers, including HNSCC.[13-15]

As shown in Table 2, there was a significant difference in TILs levels between the metastatic and non-metastatic groups based on a cut-off value of 12.5 (p = 0.001; OR: 11.8; 95% CI: 3.5–39.8). Head and neck cancer patients with TILs levels below 12.5 were 11.8 times more likely to develop metastases compared to those with TILs levels more than 12.5. Head and neck cancer patients with TIL levels below 12.5% were significantly more likely to be associated with metastatic disease compared to those with higher TIL levels.

Table 3 shows that a logistic regression analysis was performed to determine the contribution of variables to metastasis in head and neck cancer. Result of this study showed that TILs was significantly play a role in the metastasis of head and neck carcinoma, with p value of 0.001 (OR: 0.09; 95% CI: 0.02-0.29), while sex and age was not significantly play role (p = 0.215, OR: 0.40; 95%CI: 0.09 -1.69; p = 0.590, OR: 0.98; 95% CI: 0.95 -1.03).

Multivariate logistic regression analysis demonstrated that TIL levels remained independently associated with metastatic status after adjustment for age and sex. Using high TILs levels (≥12.5%) as the reference category, patients with low TILs levels (<12.5%) had significantly higher odds of metastasis (adjusted OR = 0.09; 95% CI: 0.02–0.29; p = 0.001), indicating a protective effect of higher TILs levels.

Table 2. Association between TILs levels and metastatic status in head and neck cancer

	Non metastasis n (%)	Metastasis n (%)	Total n (%)	p	OR (95% CI)
TILs < 12.5	28 (87.5)	16 (37.2)	44 (58.7)	0.001	11.8 (3.5-39.8)
TILs >/= 12.5	4 (12.5)	27 (62.8)	31 (41.3)		

Chi-square test was used for comparison. The reference category for odds ratio calculation was TILs ≥12.5%.

Table 3. Logistic regression analysis: Contribution of independent variables

	β	p	OR	95 % C.I
Sex	-0.906	0.215	0.40	0.09-1.69
Age	-0,011	0.590	0.98	0.95-1.03
Tils	-2.449	0.001	0.09	0.02-0.29

The reference category for TILs in the logistic regression model was TILs ≥12.5%.

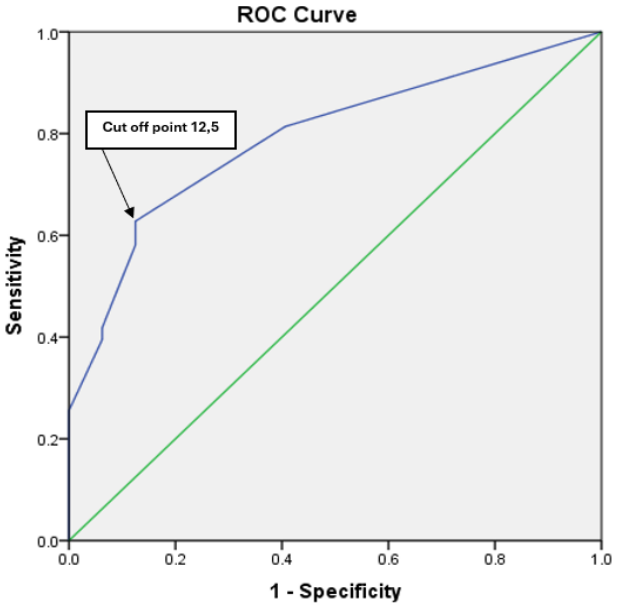

FIGURE 1. Receiver operating characteristic (ROC) curve of TILs levels for discriminating metastatic status in head and neck cancer. The area under the curve (AUC) was 0.793 (95% CI: 0.687–0.899; p = 0.001). The optimal cut-off value of 12.5% was determined using the Youden index.

Tumor-infiltrating lymphocytes (TILs) are a critical component of the immune response within the tumor microenvironment (TME), significantly influencing cancer progression and treatment outcomes. In particular, CD8+ T cells among TILs are frequently associated with better prognoses across several cancers, including breast, lung, and head and neck cancers. Their presence reflects an active immune defense against tumor cells and has been recognized as a key biomarker for predicting treatment efficacyof treatment.[16,17]

In this study, TILs levels demonstrated good discriminatory ability for metastatic status, with an AUC of 0.793. The identified cut-off value of 12.5% was associated with moderate sensitivity (62.8%) and high specificity (87.5%). This pattern suggests that higher TIL levels are more effective in correctly identifying patients without metastasis than in detecting all metastatic cases. Clinically, this implies that TILs assessment may be particularly useful for excluding metastatic disease, rather than serving as a stand-alone screening tool.

Head and neck cancer (HNC), especially head and neck squamous cell carcinoma (HNSCC), poses a major global health concern as the sixth most prevalent cancer worldwide. Its development and progression are driven by complex interactions among environmental, genetic, and immunological factors.[18,19]

The tumor microenvironment (TME) in HNSCC plays a vital role in understanding the disease's biology and response to therapy. It comprises tumor cells, stromal cells, and diverse immune cells, collectively forming a distinctive immunological landscape.[9,20] Recent studies have highlighted the importance of tumor-infiltrating

lymphocytes (TILs) in HNSCC, as their presence is associated with better prognosis.[21]

Metastasis in head and neck cancer, especially in head and neck squamous cell carcinoma (HNSCC), is a multifaceted process shaped by several biological mechanisms, such as epithelial-mesenchymal transition (EMT), immune evasion, and the tumor microenvironment (TME). Disruption of developmental pathways linked to EMT, such as Notch signaling, has been associated with the progression and metastasis of HNSCC, frequently correlating with poorer survival outcomes.[22]

Tumor-infiltrating lymphocytes (TILs) are essential for metastatic progression in head and neck cancer (HNC), especially head and neck squamous cell carcinoma (HNSCC). The presence and makeup of TILs within the tumor microenvironment (TME) can profoundly affect tumor behavior, immune evasion, and patient prognosis.

TILs, consisting of CD8+ cytotoxic T lymphocytes, are crucial for initiating a robust anti-tumor immune response. Their presence in the tumor has been linked to better survival outcomes in several cancers, including HNSCC.[13-15]

The epithelial-mesenchymal transition (EMT) process plays a key role in the metastatic progression of HNSCC. EMT enables cancer cells to acquire invasive characteristics, facilitating their detachment from the primary tumor and their spread to distant sites. The regulation of EMT is intricate and can be affected by the immune environment, including TILs. For instance, TILs can release cytokines that either enhance or suppress EMT, thereby influencing the metastatic capability of tumor cells.[22,23]

Our findings are consistent with previous reports demonstrating an inverse relationship between TILs levels and metastatic risk. Tamari et al. reported that low TILs density was associated with increased lymph node metastasis in colorectal cancer, with effect sizes comparable to those observed in the present study. Similarly, studies in head and neck squamous cell carcinoma have shown that increased TILs infiltration is associated with improved survival and reduced metastatic spread. Although direct comparisons of cut-off values are limited due to methodological heterogeneity, the magnitude of the association observed in this study (unadjusted OR 11.8; adjusted OR 0.09) supports the biological relevance of TILs in metastatic progression.

Recent research has emphasized the prognostic importance of specific TIL subsets in HNSCC. For example, the ratio of different TILs populations, such as CD8+ T cells and Tregs, has been identified as a significant prognostic factor in advanced hypopharyngeal squamous cell carcinoma (Wang et al., 2020). This indicates that both the presence of TILs and their relative proportions can offer valuable insights into the tumor's metastatic behavior and the patient's overall prognosis.[24]

Besides tumor-infiltrating lymphocytes (TILs), several other factors play a significant role in the metastasis of head and neck cancer (HNC), especially head and neck squamous cell carcinoma (HNSCC). One important factor is the expression of microRNAs.[25] HNCEpithelial-mesenchymal transition (EMT) is another key factor in metastasis. EMT is a biological mechanism that allows epithelial cells to adopt mesenchymal characteristics, thereby increasing their migratory and invasive potential.[26]

TILs are a crucial component of the tumor immune landscape, serving as both prognostic and predictive biomarkers across different cancer types. Their presence is associated with better survival rates and improved responses to immunotherapy, highlighting the importance of incorporating TILs evaluation into clinical practice for personalized cancer treatment. In the case of head and neck cancer, TILs play a significant role in the metastatic process, affecting tumor progression and patient outcomes.

From a clinical perspective, the use of a TILs cut-off value may provide additional information during routine histopathological evaluation. In settings where advanced imaging or invasive nodal assessment is limited, TILs quantification could serve as an adjunctive marker to identify patients at lower risk of metastasis. However, given the moderate sensitivity observed, TILs assessment should not replace standard diagnostic procedures but may assist in risk stratification and individualized patient management.

This was a hospital-based study using consecutive sampling, which may introduce selection bias, as the study population may not fully represent all patients with head and neck cancer. Third, observation bias may have occurred in the assessment of TILs, as quantification was based on histopathological evaluation, which may be subject to inter-observer variability despite being performed by certified anatomical pathologists. Although standardized evaluation procedures were applied, some degree of measurement variability cannot be excluded.

Because of the cross-sectional nature of this study, temporal relationships between TILs levels and the development of metastasis could not be established. Longitudinal studies are required to confirm the predictive value of TILs for metastatic progression. Due to the limited sample size within individual subsites, subsite-stratified analysis or adjustment for tumor subsite in the multivariate model was not feasible. Future studies with larger, subsite-specific populations are warranted to elucidate further the role of TILs across different head and neck cancer subsites.

CONCLUSION

There is a significant difference in TIL levels between metastatic and non-metastatic head and neck carcinoma. Higher TILs levels (≥12.5%) were significantly associated with non-metastatic head and neck carcinoma. Although causality cannot be inferred due to the cross-sectional design, TILs assessment may serve as a useful adjunct biomarker for risk prediction in clinical practice.

ETHICAL APPROVAL

Ethics committee approval from the Medical and Health Research Ethics Committee (MHREC) at the Faculty of Medicine, Public Health, and Nursing, Universitas Gadjah Mada, No KE/FK/0911/EC/2025

ACKNOWLEDGEMENTS

The author would like to express special thanks to the Universitas Gadjah Mada Academic Hospital, as the funding institution for this research program; the funding entities do not participate in the formulation or development of this study. We appreciate the valuable contributions of the support system and environment for this research.

REFERENCES

1. Gormley M, Creaney G, Schache A, Ingarfield K, Conway DI. Reviewing the Epidemiology of Head and Neck Cancer: Definitions, Trends and Risk Factors. BDJ. 2022;233(9):780-6.
2. Mohsin SF. Vaccine a Promising Immunotherapy Option for Head and Neck Cancer Patients. Pakistan Journal of Medical Sciences. 2024;40(7).
3. Oualla K, Castelo Branco L, Nouiyakh L, Amaadour L, Benbrahim Z, Arifi S, et al. Therapeutic Approaches With Immune Checkpoint Inhibitors in Head and Neck Cancers and the Role of PD-L1 as a Biomarker. Cancer Control. 2021;28:10732748211004878.
4. Huang C, Liu J, Liu H. Identification of the immune cell infiltration landscape in head and neck squamous cell carcinoma (HNSC) for the exploration of immunotherapy and prognosis. Genetics Research. 2022;2022:e2.
5. Wu Q, Shao T, Huang G, Zheng Z, Jiang Y, Zeng W, et al. FDCSP Is an Immune-Associated Prognostic Biomarker in HPV-Positive Head and Neck Squamous Carcinoma. Biomolecules. 2022;12(10):1458.
6. Behanova E, Pedan H, Hanzel P, Hajtman A, Calkovský V. Distribution of Metastases in Ent Area – Comparison of Theory and Practice. Acta Medica Martiniana. 2021;21(2):54-60.
7. Tamari H, Kitadai Y, Takigawa H, Yuge R, Urabe Y, Shimamoto F, et al. Investigating the Role of Tumor-Infiltrating Lymphocytes as Predictors of Lymph Node Metastasis in Deep Submucosal Invasive Colorectal Cancer: A Retrospective Cross-Sectional Study. Cancers. 2023;15(21):5238.
8. Virgilio AD, Veneroni MV, Costantino A, Festa BM, Fiamengo B, Sebastiani D, et al. Tumor-Infiltrating Lymphocytes and Tumor-Associated Macrophages as Potential Predictors of Lymph Node Metastases in Major Salivary Gland Cancers. Frontiers in Medicine. 2023;10.
9. Căruntu A, Moraru L, Surcel M, Munteanu A, Tănase C, Constantin C, et al. Assessment of Immune Cell Populations in Tumor Tissue and Peripheral Blood Samples From Head and Neck Squamous Cell Carcinoma Patients. Analytical Cellular Pathology. 2021;2021:1-7.
10. Intarawichian P, Sangpaibool S, Prajumwongs P, Sa-Ngiamwibool P, Sangkhamanon S, Kunprom W, et al. Prognostic Significance of Tumor-Infiltrating Lymphocytes in Predicting Outcome of Distal Cholangiocarcinoma in Thailand. Frontiers in Oncology. 2022;12.
11. Pourhoseingholi MA, Vahedi M, Rahimzadeh M. Sample size calculation in medical studies. Gastroenterol Hepatol Bed Bench. 2013;6(1):14-7.
12. Shen Z, Wang L, Dong Y. The Expression Profile and Clinical Application Value of Hsa_circ_0016148 in Head and Neck Squamous Cell Carcinoma. Journal of Clinical Laboratory Analysis. 2021;35(11).
13. Almangush A, Jouhi L, Atula T, Haglund C, Mäkitie A, Hagström J, et al. Tumour-Infiltrating Lymphocytes in Oropharyngeal Cancer: A Validation Study According to the Criteria of the International Immuno-Oncology Biomarker Working Group. British Journal of Cancer. 2022;126(11):1589-94.
14. Căruntu A, Moraru L, Lupu M, Vasilescu F, Dumitrescu M, Cioplea M, et al. Prognostic Potential of Tumor-Infiltrating Immune Cells in Resectable Oral Squamous Cell Carcinoma. Cancers. 2021;13(9):2268.
15. Hori Y, Kubota A, Yokose T, Furukawa M, Matsushita T, Katsumata N. Prognostic Role of Tumor-Infiltrating Lymphocytes and Tumor Budding in Early Oral Tongue Carcinoma. The Laryngoscope. 2021;131(11):2512-8.
16. Suwalska A, Zientek L, Polańska J, Marczyk M. Quantifying Spatial Heterogeneity of Tumor-Infiltrating Lymphocytes to Predict Survival of Individual Cancer Patients. Journal of Personalized Medicine. 2022;12(7):1113.
17. Fanale D, Dimino A, Pedone E, Brando C, Corsini LR, Filorizzo C, et al. Prognostic and Predictive Role of Tumor-Infiltrating Lymphocytes (TILs) in Ovarian Cancer. Cancers. 2022;14(18):4344.
18. Shao B, Zheng Y, Sun B, Zhang X. Molecular Evolutionary Landscape of the Immune Microenvironment of Head and Neck Cancer. Biomolecules. 2023;13(7):1120.
19. Mito I, Takahashi H, Kawabata-Iwakawa R, Ida S, Tada H, Chikamatsu K. Comprehensive Analysis of Immune Cell Enrichment in the Tumor Microenvironment of Head and Neck Squamous Cell Carcinoma. Scientific Reports. 2021;11(1).
20. Yu J, Sun X, Zhao Y, Chang Z, Zhou B. Development and Validation of an Individualized Immune Prognostic Signature in HNSCC. 2022.
21. Polesel J, Menegaldo A, Tirelli G, Giacomarra V, Guerrieri R, Baboci L, et al. Prognostic Significance of PD-L1 Expression in Patients With Primary Oropharyngeal Squamous Cell Carcinoma: A Meta-Analysis. Frontiers in Oncology. 2021;11.
22. Nagy Á, Munkácsy G, Győrffy B. Pancancer Survival Analysis of Cancer Hallmark Genes. Scientific Reports. 2021;11(1).
23. Wondergem NE, Nauta I, Muijlwijk T, Leemans CR, Ven Rvd. The Immune Microenvironment in Head and Neck Squamous Cell Carcinoma: On Subsets and Subsites. Current Oncology Reports. 2020;22(8).
24. Wang J, Tian S, Sun J, Zhang J, Lin L, Hu C. The Presence of Tumour-Infiltrating Lymphocytes (TILs) and the Ratios Between Different Subsets Serve as Prognostic Factors in Advanced Hypopharyngeal Squamous Cell Carcinoma. BMC Cancer. 2020;20(1).
25. Agarwal A, Kansal V, Farooqi H, Prasad R, Singh VK. Inhibition of miR-214 Expression by Small Molecules Alleviates Head and Neck Cancer Metastasis by Targeting ALCAM/TFAP2 Signaling. 2023.
26. Yun M, Choi AJ, Woo SR, Noh JK, Sung JY, Lee J, et al. Inhibition of Carbonyl Reductase 1 Enhances Metastasis of Head and Neck Squamous Cell Carcinoma Through Β-Catenin-Mediated Epithelial-Mesenchymal Transition. Journal of Cancer. 2020;11(3):533-41.