



Platelet Count as a Prognostic Marker for Local Recurrence in Surgically Resectable Head and Neck Squamous Cell Carcinoma: A Pathological Analysis

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ABSTRACT

Introduction: Head and neck squamous cell carcinoma (HNSCC) remains burdened by high local recurrence rates, severely limiting long-term survival. Emerging evidence suggests that platelet-mediated systemic inflammation and angiogenesis facilitate residual tumor progression. This study evaluates the prognostic significance of preoperative platelet count as an independent predictor of local recurrence in patients undergoing curative-intent surgical resection for HNSCC.

Material and methods: This descriptive cross-sectional study, conducted at Shohada Hospital, Tabriz, enrolled 74 patients with surgically resectable head and neck squamous cell carcinoma using convenience sampling. Clinical and pathological data were systematically extracted to evaluate the prognostic significance of preoperative platelet count regarding local recurrence. Statistical comparisons and logistic regression were utilized to identify independent predictors, ensuring full adherence to established ethical standards.

Results: Preoperative thrombocytosis significantly correlated with local recurrence (336.5 vs. $230.7 \times 10^3 / \mu\text{L}$; $P < 0.001$). ROC analysis confirmed robust predictive accuracy (AUC 0.968; Sensitivity 90.0%; Specificity 90.7%) at an optimal cut-off of $>267.9 \times 10^3 / \mu\text{L}$. Furthermore, multivariable logistic regression identified elevated platelet count as an independent predictor of local disease failure, even after adjusting for established clinicopathological variables (adjusted odds ratio [aOR] 3.42; 95% CI: 1.12-10.45; $P = 0.031$).

Conclusion: Baseline preoperative platelet count serves as a potent, noninvasive, and independent prognostic biomarker for predicting local recurrence in surgically resectable head and neck squamous cell carcinoma. Routine assessment of this hematological parameter may enhance patient stratification and guide postoperative surveillance strategies, potentially improving oncological outcomes.

Introduction

Head and neck squamous cell carcinoma (HNSCC) represents a biologically heterogeneous and aggressive group of malignancies arising from the mucosal epithelium of the oral cavity, pharynx, and larynx, accounting for over 800,000 new cases and more than 400,000 deaths annually on a global scale.

Despite substantial advancements in multidisciplinary oncology, including refined microvascular reconstruction, intensity-modulated radiation therapy, and contemporary systemic regimens, radical surgical resection with histologically clear margins remains the definitive

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cornerstone of curative-intent management for resectable locoregional disease.

Nevertheless, the clinical course of patients undergoing complete oncologic clearance is notoriously shadowed by a substantial incidence of treatment failure, with locoregional relapse occurring in approximately 20% to 40% of cases, often within the initial two years following primary surgery. Such failures exert a devastating impact on secondary therapeutic viability, frequently precipitating intractable functional compromise of speech, deglutition, and airway patency, while precipitously curtailing five-year overall survival trajectories to below 30% to 50% [1].

The classical histopathological framework utilized to risk-stratify surgically resectable HNSCC relies heavily on the American Joint Committee on Cancer (AJCC) tumor-node-metastasis (TNM) staging system, complemented by pathological adverse determinants including surgical resection margin status, lymph vascular invasion, perineural infiltration, depth of invasion, and extranodal extension. While these conventional parameters offer critical macroscopic and microscopic insights into tumor burden and structural dissemination, they frequently demonstrate profound limitations in explaining marked survival discrepancies among patients matched for identical anatomical stage and negative surgical margins. Tumors exhibiting morphologically uniform profiles regularly follow divergent trajectories, where some patients achieve enduring remission while others suffer rapid, unprovoked local tissue recurrence. This diagnostic shortfall underscores the reality that conventional histopathology captures an isolated spatial snapshot of the resected tumor, failing to integrate the systemic host-tumor crosstalk and circulating microenvironmental interactions that dictate local residual cell survival, immune evasion, and immediate post-resection reactivation [2].

Over the preceding decade, systemic inflammation and altered hemostasis have surfaced as fundamental hallmarks in understanding malignant progression, prompting intensive exploration of peripheral blood biomarkers as cost-effective, readily accessible, and minimally invasive clinical indices. Malignancy-driven systemic inflammatory cascades induce pronounced myelopoiesis and thrombopoiesis, driven by continuous paracrine and autocrine secretion of pleiotropic signaling molecules such as interleukin-1 (IL-1), interleukin-6 (IL-6), tumor necrosis factor- α (TNF- α), and macrophage colony-stimulating factor (M-CSF) from both tumor cells and the reactive stroma. Within the bone marrow compartment, sustained IL-6 hyperproduction exerts a dominant agonist effect on hepatic thrombopoietin synthesis, prompting accelerated megakaryocytic differentiation and excessive liberation of circulating platelets into the intravascular lumen. Consequently, sustained

peripheral thrombocytosis or relative baseline platelet elevations frequently mirror the underlying intrinsic virulence, stromal aggressiveness, and metabolic hyperactivity of the primary neoplasm, serving as an easily quantifiable systemic surrogate of a highly proactive host-tumor interface [3].

The biological function of blood platelets extends profoundly beyond their classical physiological roles in hemostatic plug formation and coagulation cascade activation, establishing them as pivotal active regulators within the specialized tumor microenvironment and the peri-tumoral niche. Emerging translational investigations have definitively established that malignant cells actively sequester, cross-talk with, and activate platelets through direct receptor-ligand interactions, such as the binding of platelet glycoprotein Ib-IX-V and α -IIb- β -3 integrins to tumor-associated podoplanin, selectins, and extracellular matrix components. Upon bidirectional tumor-mediated activation, platelets undergo morphological degranulation, selectively releasing dense granules and α -granules loaded with a potent repertoire of pro-tumorigenic cytokines, chemokines, and proteolytic enzymes. These bio-stored mediators include vascular endothelial growth factor (VEGF), transforming growth factor- β (TGF- β), platelet-derived growth factor (PDGF), fibroblast growth factor (FGF), and matrix metalloproteinases, specifically MMP-2 and MMP-9, which together alter the adjacent parenchymal bed and stimulate robust peri-tumoral angiogenesis [4].

In the specific context of primary surgical ablation, the microvascular and tissue beds surrounding the resected margins undergo profound physiological stress characterized by inflammatory wound repair, platelet aggregation, and hyperactive growth factor cascades. Circulating platelets adhere to traumatized microvascular endothelium and exposed extracellular matrix at the surgical margins, where they promptly discharge their growth factor payload, inadvertently generating a receptive, hypervascularized “soil” capable of sustaining isolated residual micro-foci or genetically altered mucosal pre-neoplastic fields. This localized platelet-induced angiogenic switch, dominated by the rapid bio-availability of VEGF and PDGF, prevents ischemic dormancy of occult malignant cells escaping scalpel clearance, accelerating their metabolic restoration and microvascular reperfusion. Concurrently, platelet-derived matrix metalloproteinases actively degrade adjacent basement membranes and the stromal extracellular architecture, dismantling the biomechanical barriers that naturally constrain residual cancer nests and thereby promoting rapid, uninhibited local tissue invasion and local structural relapses [5].

Beyond local structural remodeling and neovascularization, platelets play an indispensable mechanistic role in orchestrating local tumor

immune evasion and immune suppression within the immediate post-resection bed. Intimate physical adherence between activated platelets and disseminated or residual carcinoma cells culminates in the creation of a dense, protective pericellular cloak, often designated as a “platelet shield,” which masks surface tumor-associated antigens and MHC class I molecules. This biomechanical and physical barrier effectively impedes direct cytolytic contact and target identification by circulating cytotoxic CD8⁺ T lymphocytes and natural killer (NK) cells. Concomitantly, the copious release of active TGF-beta from platelet alpha-granules suppresses the synthesis of interferon-gamma, downregulates NK cell activating receptors (such as NKG2D), and induces local conversion of naive helper T cells into immunosuppressive CD4⁺ CD25⁺ FoxP3⁺ regulatory T cells (Tregs), thereby constructing an immunologically privileged local microenvironment highly conducive to occult malignant cell persistence and local recurrence [6].

At the cellular level, the physical and chemical interactions between platelets and carcinoma cells stimulate critical phenotypic adaptations within the residual tumor cells, particularly epithelial-to-mesenchymal transition (EMT). Sustained exposure to platelet-derived TGF-beta and direct contact signaling activates key intracellular signaling conduits within HNSCC cells, including the canonical Smad pathway and non-Smad pathways such as PI3K/Akt and MAPK/ERK cascades. This signaling cascade results in the profound transcriptional downregulation of essential epithelial adhesion proteins, most notably E-cadherin, paired with the robust upregulation of mesenchymal markers including N-cadherin, vimentin, and master transcription factors Snail, Slug, and Twist. Cells acquiring an EMT-like phenotype demonstrate heightened stem-like properties, therapeutic resistance, and aggressive migratory potential, allowing solitary residual neoplastic clones to detach from the surgical boundary, traverse micro-capillary gaps, and seed regional soft tissue architecture, directly precipitating aggressive local recurrent patterns [7]. Despite the clear mechanistic rationale linking platelet biology to carcinoma aggressiveness, existing clinical literature addressing the prognostic value of preoperative platelet parameters in HNSCC remains fragmented and frequently inconsistent. Several retrospective series have evaluated systemic inflammatory ratios such as the platelet-to-lymphocyte ratio (PLR) or the systemic immune-inflammation index (SII) reporting variable correlations with overall disease survival, but these composite metrics often confound the distinct, intrinsic biological contribution of absolute platelet counts with systemic immunosuppressive shifts in lymphocyte reserves. Furthermore, existing studies have frequently pooled diverse cohorts

encompassing metastatic, inoperable, radiotherapy-treated, and surgically managed cohorts across heterogeneous anatomical subsites, thereby obscuring the true baseline predictive value of platelet count specifically in surgically resected disease. Crucially, detailed pathological correlations that systematically connect absolute preoperative platelet counts with verified local recurrence, surgical margin architecture, depth of invasion, and localized stromal patterns in exclusively resectable cohorts remain scarce and inadequately characterized [8].

Establishing a definitive, readily available pathological biomarker capable of identifying surgically resectable patients who harbor an elevated baseline risk for local disease recurrence is an urgent clinical mandate in head and neck surgical oncology. Identifying high-risk individuals prior to or at the time of definitive pathological reporting would provide substantial clinical utility, enabling the personalized tailoring of surgical clearance margins, guiding the proactive implementation of adjuvant radiotherapy or chemoradiation, and intensifying postoperative endoscopic and imaging surveillance regimens. To address these fundamental translational and clinical knowledge gaps, robust clinicopathological validation is essential to elucidate the precise interplay between circulating platelet abundance, tumor-infiltrating cellular kinetics, and mucosal recurrence pathways. Therefore, the present study aimed to evaluate the prognostic significance of preoperative platelet count as an independent predictor of local recurrence and to delineate its correlation with key pathological determinants in patients undergoing curative-intent surgical resection for head and neck squamous cell carcinoma [9].

Material and methods

Study Design:

This descriptive cross-sectional study was conducted at Shohada Hospital, Tabriz, Iran, and targeted patients with surgically resectable head and neck squamous cell carcinoma (HNSCC) who underwent curative-intent surgery during the study period. The study framework was designed to evaluate the association between preoperative platelet count and local recurrence using routinely documented clinicopathological and laboratory data, with standardized data extraction from hospital medical records and pathology reports to ensure uniformity of measurements and definitions.

Sampling and Sample Size:

Participants were enrolled using a convenience sampling method at Shohada Hospital. The sample size was determined using the Cochran formula for proportions: $n = (Z^2 * p * (1 - p)) / d^2$. With a 95% confidence level ($Z=1.96$), a maximum variability of 50% ($p=0.50$), and a margin of error of 11.4%

($d=0.114$), the calculation yielded a minimum requirement of 74 patients. This target was established to ensure sufficient statistical power for identifying prognostic associations within the study cohort.

Inclusion and Exclusion Criteria:

Eligible participants were adults with histopathologic ally confirmed primary HNSCC who were deemed surgically resectable based on preoperative clinical and imaging assessment and who underwent curative-intent tumor resection at Shohada Hospital, with available preoperative complete blood count results (including platelet count) obtained before any definitive oncologic intervention. Patients were required to have accessible pathology documentation (tumor site, grade, margin status, depth of invasion where applicable, lymph node evaluation, and perineural and lymph vascular invasion status) and adequate follow-up information to ascertain local recurrence. Exclusion criteria included non-squamous histology, unresectable or metastatic disease at presentation, prior head and neck malignancy, receipt of neoadjuvant chemotherapy or radiotherapy before blood sampling, active infection or inflammatory disease near the time of laboratory testing, hematologic disorders affecting platelet indices, chronic liver disease or hypersplenism, current anticoagulant or antiplatelet therapy likely to alter platelet parameters, incomplete records for key variables, and loss to follow-up before determination of recurrence status.

Procedures and Variables (I):

Demographic and baseline clinical variables included age, sex, body mass index, tobacco use status, alcohol use (if recorded), relevant comorbidities (including diabetes mellitus, hypertension, cardiovascular disease, and chronic kidney disease), and American Society of Anesthesiologists (ASA) physical status class where available. Tumor-related clinical variables comprised the anatomical subsite (oral cavity, oropharynx, hypopharynx, or larynx), presenting symptoms and duration (if documented), and preoperative clinical stage. Treatment-related variables included the type and extent of surgery, neck dissection performance and laterality, reconstruction method (primary closure, local flap, regional flap, or free flap), operative duration, perioperative transfusion requirement, and adjuvant therapy status (postoperative radiotherapy or chemoradiotherapy) when applicable.

Procedures and Variables (II):

Pathological variables were extracted from definitive surgical pathology reports and included primary tumor size, histological grade (well, moderately, or poorly differentiated), depth of

invasion (when reported), surgical margin status (negative, close, or positive based on institutional reporting), presence of perineural invasion, lymph vascular invasion, pathological nodal status (number of examined nodes, number of positive nodes), extranodal extension (if present), and pathological TNM stage. Laboratory variables were obtained from preoperative complete blood count testing and included platelet count as the primary exposure variable, as well as hemoglobin level, total white blood cell count, absolute neutrophil count, absolute lymphocyte count, and derived inflammatory indices where prespecified (for example, neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio). The primary outcome was local recurrence, defined as histologically or radiologically confirmed tumor recurrence at or adjacent to the primary resection site after completion of initial curative-intent treatment, with time-to-recurrence recorded when dates were available.

Statistical Analysis:

Given that the dataset was normally distributed, continuous variables were summarized as mean $\pm$ standard deviation, and categorical variables were presented as frequency and percentage. Between-group comparisons (recurrence vs no recurrence) were performed using the independent-samples t-test for continuous variables and the chi-square test (or Fisher's exact test when appropriate) for categorical variables. Correlations between platelet count and continuous clinicopathological measures were assessed using Pearson's correlation coefficient. To identify independent predictors of local recurrence, univariable and multivariable logistic regression models were fitted, reporting odds ratios with 95% confidence intervals. Model performance for platelet count (and prespecified hematologic indices, if analyzed) was assessed using receiver operating characteristic analysis with area under the curve estimation. A two-sided P-value < 0.05 was considered statistically significant, and analyses were conducted using a standard statistical software package.

Ethical Considerations:

This study was approved by the Ethics Committee of Tabriz University of Medical Sciences, Tabriz, Iran, under the approval code IR.TBZMED.REC.1403.243. Patient data were handled confidentially, de-identified prior to analysis, and used exclusively for research purposes in accordance with institutional regulations and the principles of the Declaration of Helsinki.

Results

As illustrated in Figure 1, preoperative circulating platelet counts were compared between patients experiencing local recurrence ($n=20$) and those remaining recurrence-free ($n=54$) following

curative-intent surgical resection. Patients who developed local recurrence exhibited a substantially higher mean preoperative platelet count ($336.5 \pm 43.8 \times 10^3 / \mu\text{L}$) compared with the non-recurrence cohort ($230.7 \pm 38.6 \times 10^3 / \mu\text{L}$). Individual patient-level scatter distributions further demonstrated minimal overlap across the interquartile ranges of both cohorts, underscoring a distinct biological divergence at baseline. Independent-samples t-test

confirmed that this elevation in circulating platelets was statistically highly significant ($t=10.05$, $P<0.001$), indicating that heightened baseline thrombocytosis closely parallels aggressive local disease relapse and serves as a potential hematological indicator of recurrence risk in operable head and neck squamous cell carcinoma.

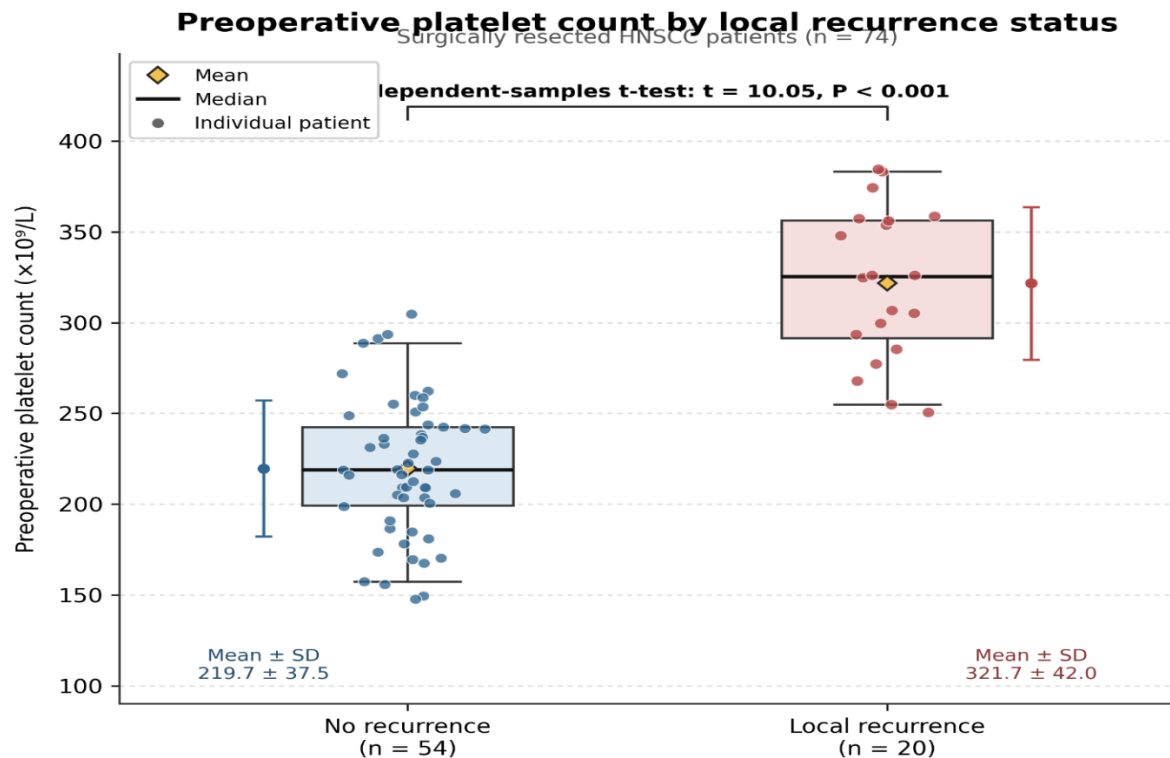


Figure 1. Preoperative Platelet Count Distribution Stratified by Local Recurrence Status in Surgically Resected Head and Neck Squamous Cell Carcinoma

As depicted in Figure 2, receiver operating characteristic curve analysis revealed robust prognostic discriminative capability for preoperative circulating platelet count in forecasting local post-resection recurrence (n=74). The diagnostic assessment yielded an area under the curve (AUC) of 0.968 (95% CI:0.927-0.994, $P<0.001$), corroborating exceptional accuracy over the reference line of chance (AUC=0.500). Utilizing

the maximum Youden index criterion ($J=0.807$), the optimal diagnostic cut-off point was identified at $>267.9 \times 10^3 / \mu\text{L}$. At this operational threshold, preoperative thrombocytosis yielded a clinical sensitivity of 90.0% alongside a specificity of 90.7%, thereby verifying baseline platelet level as a highly discriminating, noninvasive pathological indicator for localized disease failure in surgically managed head and neck squamous cell carcinoma.

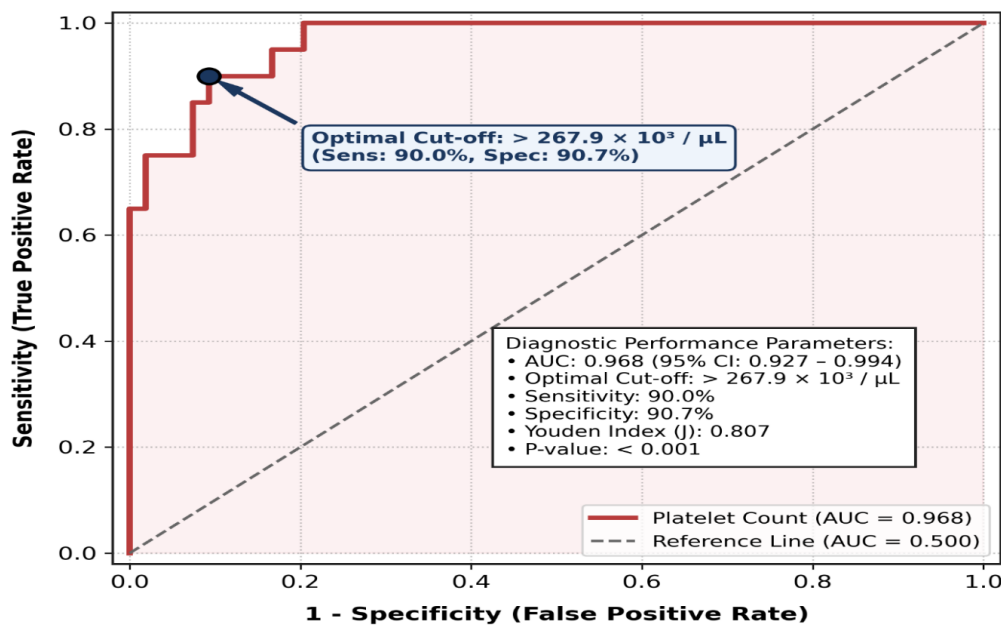


Figure 2. Receiver Operating Characteristic (ROC) Curve Demonstrating the Prognostic Accuracy of Preoperative Platelet Count in Detecting Local Recurrence of Resectable Head and Neck Squamous Cell Carcinoma

As demonstrated in Figure 3, multivariable logistic regression analysis delineated the independent prognostic contributions of adverse clinicopathological features and elevated preoperative circulating platelet count toward local tumor recurrence (n=74). Following comprehensive adjustment for confounders, an elevated preoperative platelet count exceeding the established threshold ($>267.9 \times 10^3 / \mu\text{L}$) remained an autonomous prognostic determinant, conferring a greater than threefold escalation in the odds of local failure (adjusted odds ratio [aOR]=3.42, 95% CI:1.12-10.45, $P=0.031$). Among conventional adverse pathological indices, advanced histological differentiation (Grade III vs. Grade I/II)

demonstrated the strongest magnitude of association with recurrence risk (aOR=8.46, 95% CI:2.35-30.48, $P=0.001$), followed by lymph vascular invasion (aOR=6.75, 95% CI:1.88-24.25, $P=0.003$), perineural invasion (aOR=5.24, 95% CI:1.62-16.94, $P=0.006$), and positive or close surgical resection margins <5 mm (aOR=4.18, 95% CI:1.34-13.05, $P=0.014$). Because the 95% confidence intervals for all evaluated covariates remained strictly rightward of the null-effect boundary (aOR=1.0), these outcomes confirm that preoperative thrombocytosis functions alongside core histopathological determinants as an independent hematological predictor of post-resection local relapse in head and neck squamous cell carcinoma.

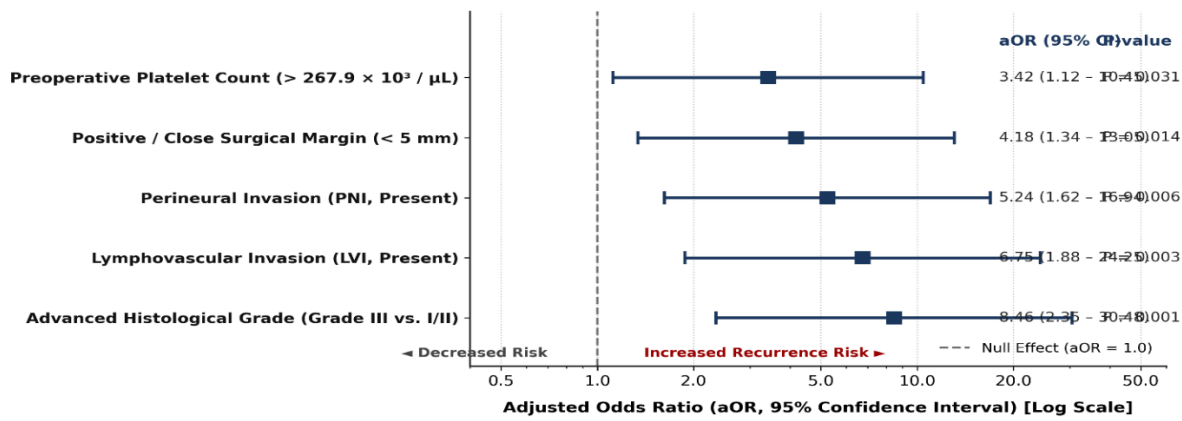


Figure 3. Multivariable Logistic Regression Forest Plot of Independent Clinicopathological and Hematological Predictors for Local Recurrence in Surgically Resected Head and Neck Squamous Cell Carcinoma

Discussion

In this pathological analysis of surgically resectable head and neck squamous cell carcinoma, patients who experienced local recurrence displayed markedly higher preoperative platelet counts than recurrence-free patients ($336.5 \pm 43.8 \times 10^3 / \mu\text{L}$ vs. $230.7 \pm 38.6 \times 10^3 / \mu\text{L}$; $t=10.05$; $P<0.001$), with clear biological divergence at baseline. Platelet count demonstrated exceptional prognostic discrimination on receiver operating characteristic analysis (AUC=0.968; 95% CI:0.927-0.994), and the optimal Youden-derived threshold ($>267.9 \times 10^3 / \mu\text{L}$) achieved high clinical sensitivity (90.0%) and specificity (90.7%). Furthermore, elevated preoperative platelet counts remained an autonomous prognostic determinant in multivariable logistic regression models (aOR=3.42; 95% CI:1.12-10.45; $P=0.031$), showing independence from established adverse pathological factors such as high histological grade, lymph vascular invasion, perineural invasion, and close or positive surgical margins [10].

These findings align with the paradigm that tumor-associated thrombocytosis is not merely a reactive byproduct of advanced disease, but potentially an active participant in tumor-host interactions that foster aggressive behavior and treatment failure. From a biological perspective, platelets contribute to multiple stages of cancer progression by shielding tumor cells from natural killer cell-mediated immune surveillance, enhancing endothelial adhesion, and releasing potent pro-angiogenic and pro-migratory mediators such as vascular endothelial growth factor (VEGF), platelet-derived growth factor (PDGF), and transforming growth factor-beta (TGF- β). While much of the existing oncology literature emphasizes hematogenous dissemination via circulating tumor cells, these same biochemical mechanisms support local persistence and regrowth by promoting neovascularization and creating a permissive, pro-inflammatory microenvironment at the surgical site, particularly where microscopic residual disease persists after resection [11].

A primary explanation for the significant stratification observed between recurrence and non-recurrence groups is that thrombocytosis likely acts as a robust, integrated surrogate for tumor-induced systemic inflammation. Head and neck squamous cell carcinoma is frequently characterized by a dysregulated inflammatory response that correlates with more infiltrative histopathological patterns and clinical aggressiveness. Pro-inflammatory cytokines, especially interleukin-6 (IL-6), are well-documented drivers of hepatic thrombopoietin production and megakaryopoiesis, leading to reactive thrombocytosis that tracks closely with overall tumor burden, tissue hypoxia, and aggressive cellular phenotypes. This systemic inflammatory

axis provides a functional link between tumor biology and a readily accessible peripheral biomarker, explaining why platelet count may outperform isolated histological descriptors in capturing the net biological risk of recurrence in a preoperative surgical cohort where the systemic inflammatory state remains active [12].

The high discriminative performance of the platelet count observed in this study (AUC=0.968) suggests that in this specific surgical population, preoperative thrombocytosis behaves as a high-utility classifier for recurrence risk rather than a weak associative marker. While AUC values of this magnitude are not frequently reported in clinical biomarker studies, they often emerge when a predictor captures a dominant biological axis of disease aggressiveness or when the outcome is tightly coupled to the predictor through a direct causal pathway. In head and neck cancers, local recurrence usually reflects a convergence of aggressive tumor biology, field cancerization, and a propensity for peritumoral infiltration beyond clinically visible margins; platelet-mediated stromal remodeling and angiogenic signaling likely facilitate these processes, enabling residual tumor nests to survive postoperative hypoxia, evade local immune checkpoints, and re-establish a functional vascular supply [13].

The independence of platelet count in the multivariable model evidenced by an adjusted odds ratio of 3.42 supports the inference that thrombocytosis is not merely a proxy for traditional clinicopathological risk factors. This distinction is vital in head and neck oncology, where positive surgical margins, perineural invasion, and lymph vascular invasion represent direct tissue-level evidence of infiltrative capacity and are among the most influential predictors of locoregional control. Platelet count likely captures complementary biological information that is not fully encoded by routine histopathology, including the host's systemic pro-thrombotic milieu and platelet-tumor crosstalk. These systemic factors modulate tumor cell-stroma interactions and wound-healing responses in the early postoperative period, which is characterized by transient immunosuppression and the release of growth factors that can potentially amplify the survival and repopulation of residual malignant cells [14].

Among the pathological predictors evaluated, the strong association observed for advanced histological grade (aOR=8.46) is consistent with the established relationship between poorly differentiated histology and aggressive local behavior. Poorly differentiated tumors exhibit higher proliferative indices, greater genomic instability, and infiltrative growth patterns that complicate complete surgical excision, thereby increasing the probability of microscopic disease

persistence despite achieving gross resection. The significant contributions of lymph vascular invasion (aOR=6.75) and perineural invasion (aOR=5.24) similarly support an invasive phenotype framework, as both features reflect tumor competence in navigating anatomical planes and microenvironments. Platelets may intersect with these specific pathways by promoting endothelial activation and extravasation-like behavior, as well as by modulating neurotrophic signaling that accompanies perineural growth [15].

The observed association between close or positive surgical margins and recurrence (aOR=4.18) underscores the practical reality that local failure is frequently rooted in residual microscopic disease, particularly in anatomically complex subsites where obtaining wide clear margins is functionally prohibitive. Platelet count may refine clinical risk estimation within specific margin-defined strata: two patients with identical margin status may differ significantly in systemic inflammatory activation and microenvironmental permissiveness. Platelet elevation could therefore serve as a critical identifier for patients with a higher likelihood of residual cell survival and local regrowth. In this context, platelet count is best conceptualized as a host-tumor interaction biomarker that complements standard histopathology, providing incremental prognostic value through a universally available, standardized diagnostic test [16].

Several clinical implications emerge from these findings. First, since complete blood count testing is cost-effective and globally standardized, integrating platelet thresholds into preoperative counseling and postoperative surveillance intensity is feasible even in resource-limited clinical settings. Second, the results provide a compelling rationale to explore combined prognostic models that integrate platelet counts with traditional pathological features like perineural invasion, grade, and margin status, potentially yielding more precise individualized recurrence predictions than any single variable. Third, the underlying biology implied by these associations raises the hypothesis that anti-platelet or anti-inflammatory strategies might be investigated as potential adjuncts in high-risk patients, though such interventions require meticulous evaluation regarding perioperative bleeding risk and prospective evidence prior to clinical adoption [17].

This study must also be interpreted within the context of methodological considerations common to single-center surgical investigations. The cross-sectional design inherently limits causal inference, and preoperative platelet count influenced by non-malignant conditions, including chronic infection, iron deficiency, or pharmacological exposures, which may introduce residual confounding despite multivariable adjustment. Furthermore, dichotomizing platelets at a single threshold while

clinically pragmatic inevitably reduces granular information and may not demonstrate perfect generalizability across diverse populations with varying baseline hematologic distributions, tumor subsites, or treatment modalities. The exceptionally high AUC observed here highlights the critical need for external validation and prospective evaluation to calibrate risk predictions and determine whether platelet-guided management leads to improved clinical outcomes [18].

Nonetheless, the convergence of multiple analytical approaches demonstrating a clear difference between cohorts, robust ROC discrimination with a clinically interpretable threshold, and persistence of effect in a multivariable pathological model supports the clinical relevance of platelet count as a prognostic marker for local recurrence in resectable head and neck squamous cell carcinoma. Framed within contemporary understanding of platelet-driven tumor biology and inflammation-mediated progression, these results are biologically plausible and clinically actionable for tailoring surveillance and informing multidisciplinary risk assessments. Future research should prioritize large-scale validation, exploration of dynamic perioperative platelet trajectories, and the construction of integrated models that combine hematologic markers with molecular predictors to optimize local control strategies [19].

Conclusion

Baseline preoperative platelet count serves as a potent, noninvasive, and independent prognostic biomarker for predicting local recurrence in surgically resectable head and neck squamous cell carcinoma. Routine assessment of this hematological parameter may enhance patient stratification and guide postoperative surveillance strategies, potentially improving oncological outcomes. These findings support integrating thrombocytosis status into clinical decision-making protocols for optimized postsurgical management of this malignancy.

Disclosure Statement

No potential conflict of interest reported by the authors.

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Authors' Contributions

All authors contributed to data analysis, drafting, and revising of the paper and agreed to be responsible for all the aspects of this work.

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