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Assessment of DUSP1 Expression Levels in Tumor and Surgical Margin Samples of Laryngeal Squamous Cell Carcinoma

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ABSTRACT

Introduction: Laryngeal squamous cell carcinoma remains a major clinical challenge, and conventional margin assessment may overlook molecular alterations associated with residual disease and field cancerization. DUSP1, a regulator of MAPK signaling, may contribute to tumor behavior. This study aimed to assess DUSP1 expression levels in tumor and surgical margin samples of LSCC.

Material and methods: This descriptive cross-sectional study was conducted in 2024 at Tabriz University of Medical Sciences on 50 patients with laryngeal squamous cell carcinoma, selected through convenience sampling based on the Cochran formula for single-group studies. DUSP1 expression was measured in paired tumor and surgical margin samples, alongside demographic, clinical, and pathological variables, including age, sex, smoking status, tumor site, grade, TNM stage, lymph node involvement, and margin status.

Results: In this study of 50 patients with laryngeal squamous cell carcinoma, mean DUSP1 expression was significantly higher in tumor tissue than in paired surgical margins (2.73 ± 0.68 vs. 1.41 ± 0.37; P=0.001). Tumoral DUSP1 expression was also greater in smokers, poorly differentiated tumors, advanced-stage disease, node-positive cases, and positive surgical margins, indicating a consistent association between elevated DUSP1 levels and more aggressive clinicopathological characteristics.

Conclusion: DUSP1 was significantly overexpressed in LSCC tumor tissue compared with surgical margins and was associated with adverse clinicopathological features. These findings suggest that DUSP1 may serve as a promising molecular indicator of tumor aggressiveness and local disease extension.

Introduction

Laryngeal squamous cell carcinoma (LSCC) is one of the major malignancies of the head and neck region and remains a clinically challenging disease because of its impact on airway protection, speech, swallowing, and quality of life. Despite advances in surgery, radiotherapy, chemotherapy, and organ-preservation protocols, survival outcomes have improved only modestly in many patient groups, particularly in those diagnosed at advanced stages. This clinical burden highlights the need for molecular markers that can improve biological understanding, risk stratification, and postoperative decision-making in LSCC [1].

The development of LSCC is a multistep process driven by long-term exposure to carcinogenic

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factors, most notably tobacco smoking and alcohol consumption, along with additional influences such as environmental exposures, chronic inflammation, and genetic susceptibility. These factors promote progressive molecular alterations within the laryngeal epithelium, leading to dysplasia, invasive carcinoma, and, in some cases, local recurrence or metastatic spread. Understanding the molecular events that distinguish tumor tissue from histologically adjacent or surgical margin tissue may provide valuable insight into early field changes and residual disease risk [2].

Surgical margin assessment is a critical component of LSCC management, as margin status is strongly associated with local control, recurrence, and the need for adjuvant therapy. Although conventional histopathological examination remains the standard method for evaluating margins, it may not fully detect molecular abnormalities in apparently tumor-free tissue. The concept of field cancerization suggests that genetically or epigenetically altered mucosa may extend beyond the visible tumor boundary, creating a biologically at-risk field even when margins appear negative under routine microscopy [3].

In this context, molecular evaluation of tumor and surgical margin samples has gained increasing attention. Biomarkers that reflect cellular stress, proliferation, apoptosis, invasion, or treatment response may help characterize the biological behavior of LSCC more accurately than morphology alone. Comparing gene expression profiles between tumor tissue and matched margin samples can identify molecular changes associated with tumorigenesis and may reveal whether margin tissue carries early alterations that are not apparent by standard pathological assessment [4].

Dual-specificity phosphatase 1, commonly known as DUSP1 or MKP-1, is an inducible nuclear phosphatase that regulates mitogen-activated protein kinase signaling by dephosphorylating threonine and tyrosine residues on activated MAPKs. Through this function, DUSP1 modulates key signaling pathways involving ERK, JNK, and p38 MAPKs, which participate in cellular proliferation, differentiation, apoptosis, inflammation, and stress responses. Because MAPK signaling frequently altered in cancer, dysregulation of DUSP1 may have important consequences for tumor biology [5].

DUSP1 has described as a context-dependent regulator in cancer, with evidence supporting both tumor-promoting and tumor-suppressive functions depending on tumor type, cellular context, and microenvironmental conditions. In some malignancies, increased DUSP1 expression may protect cancer cells from apoptosis and contribute to resistance against chemotherapy or radiotherapy by attenuating stress-activated MAPK signaling. In other settings, reduced DUSP1 activity may facilitate uncontrolled MAPK activation and enhance malignant transformation, indicating the complexity of its biological role [6].

The relevance of DUSP1 in squamous cell carcinomas is particularly important because these tumors often arise in chronically exposed epithelial fields and influenced by inflammatory and stress-related signaling networks. MAPK pathway activation can support epithelial cell survival, invasion, angiogenesis, and immune interactions, all of which contribute to tumor progression. Since DUSP1 acts as a negative feedback regulator of MAPK activity, altered DUSP1 expression may reflect adaptive responses of tumor cells to oncogenic stress, hypoxia, oxidative injury, or therapeutic pressure [7].

In head and neck squamous cell carcinoma, molecular heterogeneity is a major obstacle to accurate prognosis and treatment selection. Tumors with similar anatomical stage and histological grade may show different clinical outcomes, suggesting that conventional clinicopathological parameters are insufficient to capture the full biological diversity of the disease. Therefore, investigation of genes such as DUSP1 in site-specific cancers like LSCC may help clarify molecular differences that influence local aggressiveness, recurrence potential, and response to treatment [8].

Evaluation of DUSP1 expression in tumor samples can provide information about the intracellular signaling state of LSCC cells. Increased expression may indicate activation of compensatory mechanisms that limit excessive MAPK signaling while simultaneously promoting tumor cell survival under stressful conditions. Conversely, decreased expression may suggest loss of regulatory control over MAPK-driven proliferation or inflammatory signaling. These possibilities make DUSP1 a biologically plausible candidate for investigation in laryngeal tumor tissues [9].

The assessment of DUSP1 expression in surgical margin samples is equally significant. Margin tissue represents the interface between the tumor and surrounding mucosa and may contain molecular alterations related to field cancerization, premalignant transformation, or residual microscopic disease. If DUSP1 expression differs between tumor and margin samples, or if altered expression is detectable in histologically negative margins, this may provide evidence of molecular involvement beyond the visible tumor mass and may have implications for recurrence risk assessment [10].

A comparative analysis of DUSP1 expression between tumor and surgical margin tissues may also help determine whether this gene is primarily

associated with established malignant transformation or with broader epithelial field changes. Higher expression in tumor tissue compared with margin tissue may suggest a role in tumor progression or survival, whereas similar expression patterns in both compartments may indicate early molecular alteration across the affected mucosal field. Such findings could support refined molecular classification of LSCC tissue compartments [11].

From a translational perspective, identifying reliable expression differences in DUSP1 may contribute to the development of biomarker panels for LSCC. Single biomarkers rarely capture the complexity of tumor behavior; however, genes involved in major signaling pathways can provide useful components of broader molecular signatures. If DUSP1 expression correlates with clinicopathological variables such as tumor stage, grade, lymph node involvement, margin status, or recurrence, it may offer additional prognostic or predictive value [12].

DUSP1 is also of interest in relation to treatment response. Radiotherapy and chemotherapy induce cellular stress and activate MAPK-related pathways, including JNK and p38, which are involved in apoptosis and DNA damage responses. By deactivating these kinases, DUSP1 may reduce treatment-induced cell death and contribute to therapeutic resistance in some tumor models. Therefore, determining its expression pattern in LSCC may help generate hypotheses about sensitivity or resistance to standard therapeutic modalities [13].

Despite increasing interest in molecular markers in head and neck cancers, data specifically focused on DUSP1 expression in LSCC and matched surgical margin tissues remain limited. Anatomical and biological differences among head and neck subsites mean that findings from oral cavity, oropharyngeal, or hypopharyngeal tumors may not be directly applicable to laryngeal cancer. Site-specific investigation is therefore necessary to define the relevance of DUSP1 within the distinct clinical and biological context of LSCC [14].

Accordingly, assessment of DUSP1 expression levels in tumor and surgical margin samples of laryngeal squamous cell carcinoma may provide meaningful insight into the molecular alterations associated with malignant transformation, field effects, and local disease behavior. By comparing expression patterns between these paired tissue compartments, such a study may improve understanding of DUSP1-related signaling in LSCC and support future research into its potential utility as a diagnostic, prognostic, or therapeutic biomarker.

Material and methods

Study Design:

This descriptive cross-sectional study conducted at Tabriz University of Medical Sciences, Tabriz, Iran, during 2024. The study designed to evaluate DUSP1 expression in paired tumor and surgical margin samples obtained from patients with laryngeal squamous cell carcinoma who underwent surgical treatment at affiliated teaching hospitals. All clinical, pathological, and molecular data collected within the defined study period and analyzed to describe the expression profile of DUSP1 in the selected specimens.

Sampling

The sample size was determined using the Cochran formula for estimating a proportion in a single-group descriptive cross-sectional study: $n = Z^2p(1-p)/d^2$. Assuming a 95% confidence level ($Z = 1.96$), a conservative estimated proportion of 0.50, and a precision of 0.14, the calculated sample size was approximately 49 cases, which was rounded up to 50 patients. Sampling performed using a convenience sampling method, and eligible patients recruited consecutively until the target sample size reached.

Inclusion/Exclusion Criteria

Eligible participants were patients with a definitive histopathological diagnosis of laryngeal squamous cell carcinoma who underwent surgical resection during the study period, had available paired tumor and surgical margin tissue samples of adequate quality for molecular analysis, and provided informed consent for participation. Patients were excluded if they had received neoadjuvant chemotherapy or radiotherapy before surgery, had recurrent laryngeal carcinoma, had a history of other head and neck malignancies, had inadequate or necrotic tissue samples, had incomplete clinical or pathological records, or if RNA quality was insufficient for DUSP1 expression analysis.

Procedure

Fresh tumor tissue and corresponding surgical margin tissue collected immediately after surgical resection by the operating team in coordination with the pathology department. Tissue samples confirmed by a pathologist, and representative specimens preserved under appropriate conditions for molecular analysis. DUSP1 expression measured after surgery and before the initiation of any adjuvant treatment in order to avoid treatment-related alterations in gene expression. Total RNA extracted from each specimen, complementary DNA synthesized, and DUSP1 expression quantified using real-time quantitative polymerase chain reaction (RT-qPCR). Relative gene expression

calculated using an internal housekeeping gene and the comparative Ct method.

In addition to DUSP1 expression levels in tumor and margin tissues, relevant demographic, clinical, and pathological variables were recorded for each patient. These variables included age, sex, smoking status, alcohol consumption history when available, tumor subsite within the larynx, tumor size, histopathological grade, TNM stage, lymph node involvement, presence of lymph vascular invasion, perineural invasion, and pathological margin status. The paired assessment of tumor and margin samples allowed direct comparison of DUSP1 expression between the two tissue compartments and evaluation of its relationship with clinicopathological characteristics.

Data Analysis

Because the data were normally distributed, parametric statistical methods were used for analysis. Quantitative variables were reported as mean ± standard deviation, and categorical variables were presented as frequency and percentage. The paired t-test was used to compare DUSP1 expression levels between tumor and surgical margin samples. The independent t-test and one-way analysis of variance (ANOVA) were applied to compare mean expression values across binary and multi-category clinicopathological variables, respectively. Pearson correlation analysis was used to assess associations between continuous variables. Categorical data were compared using the chi-square test or Fisher's exact test where appropriate. Statistical analysis was performed using SPSS software, and a p-value of less than 0.05 was considered statistically significant.

Ethical Considerations

This study was approved by the Ethics Committee of Tabriz University of Medical Sciences under the ethics code IR.TBZMED.REC.1403.458. Written informed consent was obtained from all participants before enrollment. Patient information was kept confidential throughout the study, and all samples and records were coded to protect participant identity. The study was conducted in accordance with the ethical principles of the Declaration of Helsinki.

Results

The demographic and clinicopathological profile of the 50 patients enrolled in this study is summarized in Table 1. The study cohort had a mean age of 59.36 ± 10.42 years, with a predominant male distribution accounting for 86.0% of the cases. Regarding risk factors, 62.0% of the participants were active smokers. Anatomically, the majority of tumors were located in the glottis (54.0%), followed by the supraglottic (36.0%). Histopathological analysis revealed that 48.0% of the tumors were moderately differentiated, while nearly 58.0% of the patients presented with advanced-stage disease (Stage III/IV) at the time of diagnosis. Furthermore, lymph node involvement was observed in 34.0% of the cases, and histologically positive surgical margins were identified in 16.0% of the specimens, providing a comprehensive baseline for the subsequent molecular analysis of DUSP1 expression across different clinical subgroups (Table 1).

Table 1. Demographic and clinicopathological characteristics of the study population (n=50).

Characteristic	Category	Frequency (n)	Percentage (%)
Age (years)	Mean ± SD	59.36 ± 10.42	—
Sex	Male	43	86.0
	Female	7	14.0
Smoking Status	Smoker	31	62.0
	Non-smoker	19	38.0
Tumor Subsite	Glottic	27	54.0
	Supraglottic	18	36.0
	Subglottic	5	10.0
Histological Grade	Well-differentiated (G1)	14	28.0
-	Moderately differentiated (G2)	24	48.0
	Poorly differentiated (G3)	12	24.0
TNM Stage	Early (Stage I/II)	21	42.0
	Advanced (Stage III/IV)	29	58.0
Lymph Node Status	N0 (Negative)	33	66.0
	N+ (Positive)	17	34.0
Surgical Margin Status	Negative	42	84.0
	Positive	8	16.0

As shown in Table 2, DUSP1 expression was markedly higher in tumor tissue than in paired surgical margin tissue, supporting a significant differential expression pattern between the two compartments. Higher tumor DUSP1 expression was also observed in smokers, patients with poorly differentiated tumors, advanced TNM stage, lymph node involvement, and positive surgical margins. Although margin tissues showed lower overall expression than tumor samples, a gradual increase was still evident in clinically more aggressive subgroups. These findings suggest that elevated DUSP1 expression is associated not only with malignant tissue itself but also with unfavorable clinicopathological features in laryngeal squamous cell carcinoma, as detailed in Table 2.

Table 2. Comparison of DUSP1 expression levels in tumor and surgical margin tissues and their associations with clinicopathological variables

Variable	Category	Mean DUSP1 Expression in Tumor Tissue ± SD	Mean DUSP1 Expression in Surgical Margin Tissue ± SD	P-value
Tissue type	Tumor	2.73 ± 0.68	1.41 ± 0.37	0.001
Sex	Male	2.79 ± 0.66	1.43 ± 0.35	0.284
-	Female	2.38 ± 0.71	1.29 ± 0.41	0.317
Smoking status	Smoker	2.91 ± 0.62	1.47 ± 0.34	0.041
	Non-smoker	2.44 ± 0.69	1.32 ± 0.39	0.058
Histological grade	Well differentiated	2.36 ± 0.49	1.28 ± 0.26	0.083
-	Moderately differentiated	2.74 ± 0.57	1.39 ± 0.31	0.027
-	Poorly differentiated	3.12 ± 0.73	1.59 ± 0.44	0.012
TNM stage	Stage I/II	2.31 ± 0.51	1.26 ± 0.29	0.009
	Stage III/IV	3.04 ± 0.63	1.53 ± 0.38	0.002
Lymph node status	N0	2.49 ± 0.58	1.33 ± 0.30	0.018
	N+	3.07 ± 0.65	1.56 ± 0.41	0.006
Surgical margin status	Negative	2.61 ± 0.60	1.36 ± 0.32	0.014
	Positive	3.21 ± 0.74	1.69 ± 0.46	0.004

As illustrated in Figure 1, there is a significant discrepancy in DUSP1 expression between the two tissue compartments. The paired dot plot demonstrates that DUSP1 expression levels were consistently elevated in tumor samples compared to the matched surgical margin tissues obtained from the same patients. This significant upregulation ($P<0.001$) in malignant tissue suggests that DUSP1 is differentially expressed in laryngeal squamous cell carcinoma and may play a role in the molecular pathogenesis of the tumor compared to the surrounding histologically normal or reactive mucosa.

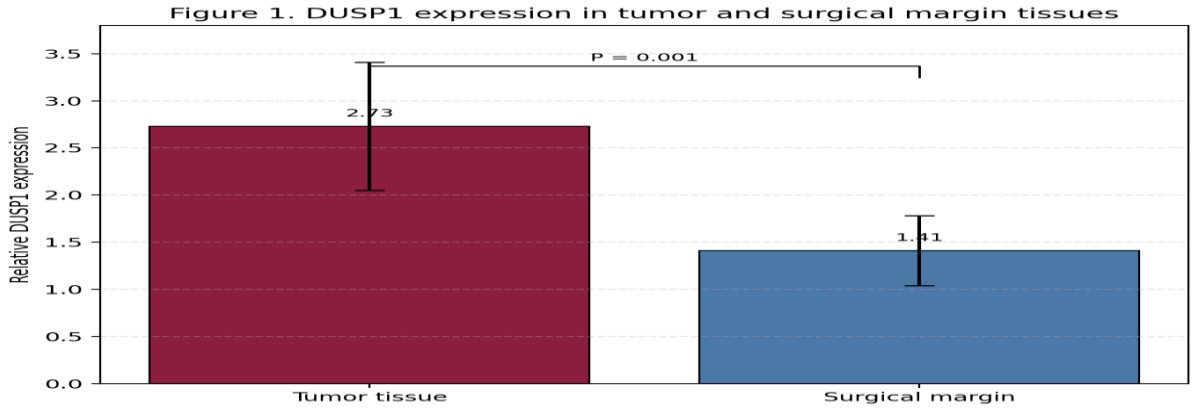

Figure 1. Comparison of DUSP1 relative expression levels in tumor tissues versus matched surgical margin samples.

As shown in Figure 2, DUSP1 expression in tumor tissue was higher in patients with advanced-stage disease than in those with early-stage disease. The plot indicates a clear upward trend in expression with increasing clinical severity, suggesting that DUSP1 may be associated with tumor progression in laryngeal squamous cell carcinoma. This pattern supports the possibility that DUSP1 could serve as a molecular marker related to disease aggressiveness and staging, as illustrated in Figure 2.

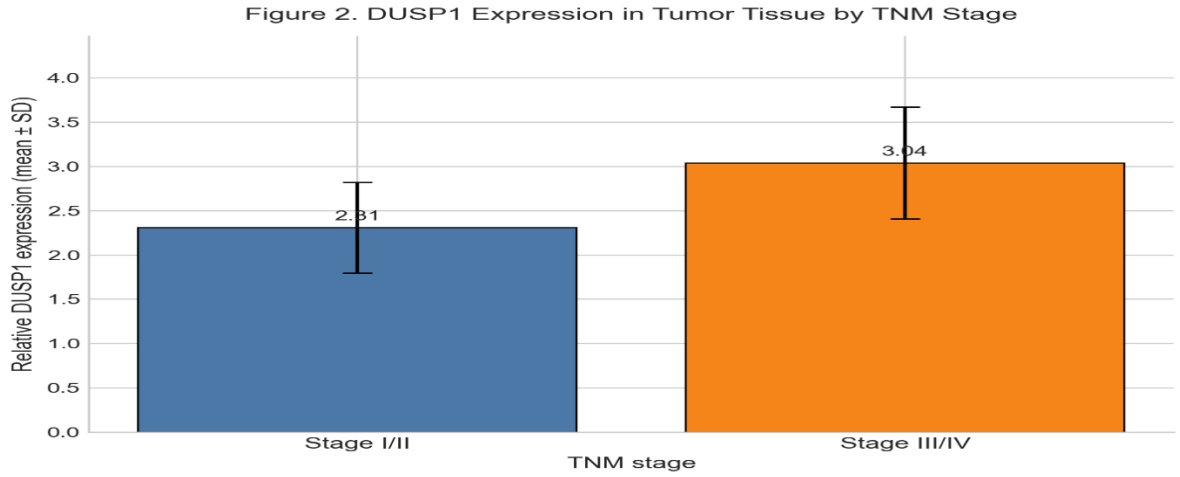

Figure 2. DUSP1 relative expression in tumor tissue according to TNM stage.

Discussion

The present study was conducted to evaluate the molecular landscape of laryngeal squamous cell carcinoma (LSCC) by assessing the expression levels of DUSP1 in tumor tissues and corresponding surgical margins. Beyond its role in phosphatase activity, the investigation aimed to explore how DUSP1 dysregulation might reflect the chronic inflammatory microenvironment and cellular stress responses inherent in laryngeal oncogenesis. By comparing malignant specimens with histologically normal margins, we sought to determine if DUSP1 could serve as a biological indicator of disease severity and field cancerization, particularly in the context of the persistent inflammatory signaling that drives squamous cell malignancies [15].

The primary findings of this investigation revealed a significant upregulation of DUSP1 in LSCC tumor tissues compared to matched surgical margin samples. Furthermore, elevated DUSP1 expression was strongly associated with adverse clinicopathological features, including advanced TNM stage, poorly differentiated histological grade, positive lymph node status, and positive surgical margins. We also observed that smokers exhibited higher DUSP1 levels, suggesting a potential link between environmental irritants and the induction of this phosphatase. These results collectively indicate that DUSP1 expression increases in parallel with tumor aggressiveness and may be involved in the adaptive survival mechanisms of cancer cells [16].

The observed upregulation of DUSP1 in tumor tissues is likely an adaptive response to the intense mitogen-activated protein kinase (MAPK) signaling that characterizes LSCC. DUSP1 serves as a critical negative feedback regulator of the ERK, JNK, and p38 pathways, which are frequently overactivated due to oncogenic mutations or autocrine growth factor signaling. In the stressful tumor microenvironment, cancer cells may overexpress DUSP1 to fine-tune MAPK activity, preventing excessive signaling that could lead to senescence or apoptosis while simultaneously promoting survival and chemoresistance. This compensatory mechanism allows malignant cells to thrive under conditions of hypoxia and oxidative stress common in laryngeal tumors [17].

The correlation between DUSP1 expression and advanced TNM stages (Stage III/IV) suggests that this phosphatase play a supportive role in tumor progression and expansion. As tumors grow and invade deeper tissues, the requirement for robust stress-management signaling increases. The significant rise in DUSP1 levels in more advanced stages may reflect an enhanced ability of late-stage tumor cells to evade stress-induced cell death and manage the metabolic demands of a rapidly proliferating mass. This suggests that DUSP1 levels could potentially mirror the evolutionary trajectory of the tumor toward a more resilient and aggressive phenotype [18].

Our findings regarding lymph node involvement further support the association between DUSP1 and metastatic potential. Patients with N+ status displayed significantly higher DUSP1 levels compared to those with N0 status, which may be

attributed to the role of DUSP1 in modulating the epithelial-to-mesenchymal transition (EMT) and cellular motility. By dampening the JNK-mediated apoptotic signals that usually occur when cells detach from the primary tumor, DUSP1 might facilitate the survival of circulating tumor cells and their subsequent colonization of regional lymph nodes. This molecular shielding effect is a hallmark of aggressive squamous cell carcinomas [19].

The significant association between DUSP1 expression and histological grade indicates that as cells lose their differentiation and become more primitive (G3), DUSP1 levels rise. This could be due to the fact that poorly differentiated tumors often exhibit higher rates of genomic instability and constant activation of stress pathways. In these highly proliferative and disorganized tissues, DUSP1 likely acts as a vital regulator that prevents "signaling overload," thereby maintaining the viability of the most aggressive cell clones. This trend highlights the potential of DUSP1 as a molecular surrogate for the degree of cellular anaplasia in the larynx [20].

A noteworthy observation in this study was the significantly higher expression of DUSP1 in smokers compared to non-smokers. Tobacco smoke is a potent inducer of chronic inflammation and oxidative DNA damage in the laryngeal mucosa. The chemical constituents of cigarette smoke activate stress-activated protein kinases, which in turn trigger the rapid induction of DUSP1 as part of the cellular defense mechanism. In the long term, this chronic induction may lead to a permanent shift in the phosphatase landscape of the epithelium, potentially creating a "pro-survival" field that is more susceptible to malignant transformation [21].

The concept of field cancerization is further supported by our results showing that even in surgical margin tissues, DUSP1 levels showed a gradual increase in patients with more aggressive primary tumors. Although the margins were histologically negative, the elevation of DUSP1 in these areas suggests that molecular alterations precede morphological changes. This indicates that the inflammatory and oncogenic "field" extends beyond the visible tumor mass, and DUSP1 may serve as a sensitive marker for detecting sub-microscopic biological changes in the perilaryngeal mucosa that could predispose patients to local recurrence [22].

The higher expression found in positive surgical margins compared to negative margins reinforces the clinical utility of DUSP1 as a marker for residual disease risk. If the surgical resection does not clear the molecularly altered field, the remaining tissue characterized by high DUSP1 expression may harbor the necessary signaling machinery to initiate a recurrence. This suggests that DUSP1 could eventually complement standard histopathology in defining truly "clean" margins, providing a more refined assessment of the adequacy of surgical resection in LSCC patients [23].

From an inflammatory perspective, DUSP1 is a major regulator of the innate immune response and pro-inflammatory cytokine production. Its overexpression in LSCC might contribute to an immunosuppressive tumor microenvironment by deactivating MAPKs required for effective anti-tumor immune responses. By dampening the inflammatory signaling that would normally alert the immune system to the presence of malignant cells, DUSP1 may allow the tumor to "hide" and grow unchecked. This link between phosphatase activity and immune evasion is an emerging area of interest in head and neck oncology [24].

Comparison with other studies on squamous cell carcinomas reveals a complex role for DUSP1, as some reports suggest its downregulation in early stages but upregulation in advanced, treatment-resistant cases. Our data aligns with the latter, suggesting that in the specific context of the larynx, DUSP1 primarily functions as a pro-survival factor that correlates with worse outcomes. These discrepancies between studies may stem from different anatomical subsites or variations in the local inflammatory milieu, emphasizing the need for site-specific molecular investigations such as the current study [25].

The biochemical rationale for targeting DUSP1 in LSCC lies in its ability to confer resistance to standard therapies like radiotherapy. Radiation therapy works by inducing catastrophic oxidative stress and JNK/p38-mediated apoptosis; however, high levels of DUSP1 can counteract these effects by rapidly dephosphorylating these "death kinases." Consequently, the elevated DUSP1 levels we observed in aggressive LSCC cases may explain, at least in part, why advanced tumors often show a poor response to conventional organ-preservation protocols involving irradiation [26].

Despite the clear trends observed, this study is not without limitations, including its cross-sectional design and the relatively modest sample size of 50 patients. While we identified significant associations with clinicopathological variables, longitudinal follow-up data would be required to definitively establish the prognostic value of DUSP1 regarding overall survival and disease-free survival. Future studies should focus on the mechanistic pathways through which DUSP1 interacts with other components of the tumor microenvironment, such as infiltrating immune cells and fibroblasts [27].

In conclusion, our study demonstrates that DUSP1 is significantly overexpressed in laryngeal squamous cell carcinoma and is closely associated with markers of disease progression and

aggressiveness. The consistent upregulation in tumors compared to margins, and its higher levels in advanced stages and node-positive cases, suggest that DUSP1 plays a pivotal role in the survival and stress-adaptation of laryngeal cancer cells. Its association with smoking and surgical margin status further underscores its potential as a biologically relevant biomarker in the management of LSCC [28].

Ultimately, these findings provide a foundation for further research into DUSP1 as a therapeutic target or a prognostic marker. By better understanding the molecular crosstalk between inflammation, stress signaling, and phosphatase activity, clinicians may be able to develop more personalized treatment strategies for patients with laryngeal cancer. Continued exploration of the DUSP1-MAPK axis will be essential to translate these molecular observations into improved clinical outcomes and more effective management of this challenging malignancy [29].

Conclusion

The present findings demonstrate that DUSP1 expression is markedly increased in tumor tissues relative to paired surgical margin samples in laryngeal squamous cell carcinoma, with higher levels observed in clinically aggressive subgroups, including smokers, poorly differentiated tumors, advanced-stage disease, lymph node-positive patients, and cases with positive surgical margins. Collectively, these results support a potential role for DUSP1 in LSCC progression and highlight its possible value as a biomarker for tumor behavior and margin-related molecular alterations.

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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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