



ORIGINAL ARTICLE

## Correlation between vascular endothelial growth factor expression and presence of lymph node metastasis in advanced squamous cell carcinoma of the larynx<sup>☆,☆☆</sup>



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### KEYWORDS

Squamous cell carcinoma of larynx;  
VEGF;  
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Cervical lymphatic metastases

### Abstract

**Introduction:** Squamous cell carcinoma is the most common neoplasm of the larynx, and its evolution depends on tumor staging. Vascular endothelial growth factor is a marker of angiogenesis, and its expression may be related to increased tumor aggressiveness, as evidenced by the presence of cervical lymphatic metastases.

**Objectives:** To evaluate the expression of the vascular endothelial growth factor marker in non-glottic advanced squamous cell carcinoma of the larynx (T3/T4) and correlate it with the presence of cervical lymph node metastases.

**Methods:** Retrospective clinical study and immunohistochemical analysis of vascular endothelial growth factor through the German scale of immunoreactivity in products of non-glottic squamous cell carcinomas.

**Results:** This study analyzed 15 cases of advanced non-glottic laryngeal tumors (T3/T4), four of which exhibited cervical lymphatic metastases. There was no correlation between vascular endothelial growth factor expression and the presence of cervical metastases.

**Conclusion:** Although vascular endothelial growth factor was expressed in a few cases, there was no correlation with the spread of cervical lymph metastases.

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**PALAVRAS-CHAVE**

Carcinoma epidermoide de laringe; VEGF; Imunohistoquímica; Metástase

## Correlação entre expressão do fator de crescimento endotelial e presença de metástase linfática nos carcinomas epidermóides avançados de laringe

**Resumo**

**Introdução:** O carcinoma de células escamosas é a neoplasia mais frequente da laringe e seu prognóstico depende do estadiamento. A progressão da doença está relacionada a fatores intrínsecos celulares do câncer, não conhecidos. O VEGF (vascular endothelial growth factor) é um marcador de angiogênese e sua expressão pode estar relacionada a uma maior agressividade tumoral, evidenciada pela presença de metástases linfáticas cervicais.

**Objetivos:** Avaliar a expressão do marcador VEGF em carcinoma de células escamosas da laringe avançados (T3/T4), não glóticos e correlacionar quanto à presença de metástases linfáticas cervicais.

**Método:** Estudo clínico retrospectivo de análise imunohistoquímica do VEGF através da escala Germânica de imunorreatividade em produtos de carcinomas epidermóides não glóticos.

**Resultados:** Analisados 15 casos de tumores avançados de laringe (T3/T4) não glóticos, sendo sete com presença de metástases linfáticas cervicais. Não houve correlação entre a expressão do VEGF e a presença de metástases cervicais.

**Conclusão:** O VEGF foi pouco expressado nos casos estudados e não foi observada sua correlação com a disseminação de metástase linfática cervical.

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**Introduction**

Angiogenesis is characterized by the formation of new capillary blood vessels that originate from a pre-existing vasculature. This process is essential to provide nutrients, oxygen, and growth factors that support cell function and survival. Therefore, it is associated with tumor growth and metastasis.<sup>1,2</sup>

A complex interaction between endothelial cells, extracellular protein matrix, and soluble factors in plasma occurs in angiogenesis. Endothelial cells leave their quiescent state when stimulated by VEGF (vascular endothelial growth factor) and initiate the following steps: dissolution of the basal membrane; migration and proliferation of endothelial cells; capillary tube formation; and maturation and survival of newly formed vessels. This ensures the required blood supply for neoplastic evolution.<sup>1,2</sup>

Squamous cell carcinoma is the most common neoplasm of the larynx and its prognosis depends on the size of the lesion, the level of local invasion, cervical lymphatic spread, and presence of distant metastases.<sup>1,3</sup>

Histologically, squamous cell carcinoma of the larynx and hypopharynx are similar to that of other regions and are classified into different degrees of differentiation by the neoplastic proliferation of squamous cells and the nature of tumor infiltration. Depending on the degree of keratinization and cellular atypia, they are classified as well, moderately, or poorly differentiated.<sup>3</sup>

Lymphatic drainage of the glottic region is scarce; this decreases the metastatic potential of tumors that develop in this region. The supraglottic and subglottic regions have rich lymphatic drainage, with the supraglottic region draining mainly into the upper jugulocarotid chain lymph nodes and to a lesser degree into the middle jugulocarotid chain lymph

nodes whereas the subglottic region tends to drain ipsilaterally to the middle and lower jugulocarotid lymph nodes, that may drain to the anterosuperior mediastinal chain.<sup>3</sup> For this reason, we decided to exclude glottal tumors from the study.

The literature discussing treatment of these tumors has increased and studies of new chemotherapeutic agents and targeted therapies have gained prominence. Examples of this include the promising results reported for cetuximab, a monoclonal antibody that blocks endothelial growth factor receptor (EGFR) used for the treatment of head and neck cancer, and bevacizumab and other recombinant anti-VEGF monoclonal antibodies.<sup>4,5</sup>

These antibodies bind to VEGF isoforms with high affinity and prevent the cytokine from binding with the endothelial cell receptor and triggering the angiogenesis process. The use of angiogenesis-inhibiting monoclonal antibodies for the treatment of colorectal, kidney, and lung cancer has already been approved by the FDA. For the treatment of larynx/head and neck cancer, they are still being assessed.<sup>4,5</sup>

Considering that VEGF plays an important role in tumor angiogenesis and that this factor is associated with tumor formation, progression, and metastasis, its expression could be related to increased tumor aggressiveness evidenced by cervical metastatic spread.<sup>2</sup>

The present study aimed to evaluate the expression of VEGF marker in advanced, non-glottic squamous cell carcinoma of the larynx (T3/T4) and correlate it with the presence or absence of cervical lymph node metastasis.

**Methods**

This was a retrospective clinical study, conducted in a sample obtained by a cross-section design in a historical

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