

**Prognostic utility of angiogenesis and hypoxia effectors in patients with operable squamous cell cancer of the larynx.**

[Pentheroudakis G](#), [Nicolaou I](#), [Kotoula V](#), [Fountzilias E](#), [Markou K](#), [Eleftheraki AG](#), [Fragkoulidi A](#), [Karasmanis I](#), [Tsigka A](#), [Angouridakis N](#), [Vlachtsis K](#), [Nikolaou A](#), [Pavlidis N](#), [Fountzilias G](#).

**Source**

Department of Medical Oncology, Ioannina University Hospital, Ioannina, Greece.  
gpenther@otenet.gr

**Abstract**

Angiogenesis is active in localised laryngeal squamous cell carcinoma. We assessed relative messenger RNA (mRNA) and immunohistochemical (IHC) expression of Vascular Endothelial Growth Factors (VEGF) A, B, C, their receptors VEGFR1, 2, 3, Neuropilins 1, 2 (NRP1, 2) and Hypoxia-Inducible Factor 1A (HIF1A) in paraffin-embedded localised laryngeal carcinomas. In 289 patients with T3-4 (77.8%), node-negative (84.1%) tumours of the larynx, high VEGFA and VEGFR1 mRNA correlated with advanced T stage, while low VEGFB and VEGFC mRNA with alcohol abuse and supraglottic primary, respectively ( $p < 0.05$ ). Age  $< 55$  was associated with high IHC expression of VEGFA, C and poor tumour differentiation with high IHC VEGFA. At a median follow-up of 74.5 months, patients with VEGFR1-high tumours had significantly poorer disease-free survival (Hazard Ratio [HR] 1.93,  $p = 0.008$ ) and shorter overall survival (OS, HR 1.71,  $p = 0.041$ ). An association with dismal OS was seen for high VEGFR3 tumoural mRNA expression (HR 1.76,  $p = 0.02$ ). IHC expression of VEGF family proteins in the tumour was not prognostic and had poor concordance with mRNA expression ( $\kappa < 0.1$ ,  $p = \text{NS}$ ). In multivariate analysis, node-positive status, non-supraglottic localization, high VEGFR1 mRNA and high IHC VEGFA expression were significantly associated with relapse, while node-positive status, high VEGFR1 and VEGFC mRNA expression in the tumour with risk of death. In laryngeal cancer, upregulated mRNA expression of VEGFR1 and VEGFC is associated with poor patient outcome.