

Cyclin D1, EGFR, and Akt/mTOR pathway. Potential prognostic markers in localized laryngeal squamous cell carcinoma.

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Source

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Abstract

INTRODUCTION:

EGFR (epidermal growth factor receptor), cyclin D1 and Akt/mTOR pathways are active in head and neck cancer. The aim of this study was to explore biomarker expression, their correlations with clinicopathological parameters and their prognostic utility in a cohort of patients with localized squamous laryngeal carcinoma.

PATIENTS AND METHODS:

We assessed relative messenger RNA expression of EGFR, Akt1, 2, and 3, mTOR and CCND1, copy number variants of the EGFR and CCND1 genes and immunohistochemical protein expression of EGFR, p-Akt308, p-Akt473, pmTOR, PTEN, p53 and cyclin D1 in paraffin-embedded tissue samples of localized laryngeal carcinomas.

RESULTS:

In 289 patients with T3-4 (77.8%), node-negative (84.1%) tumors of the larynx, high EGFR and CCND1 mRNA correlated with no or ex-smoking, ($p = 0.003$ and $p = 0.029$, respectively), while low Akt3 mRNA correlated with alcohol abuse, N0 stage, total laryngectomy, and absence of neck dissection. At a median follow-up of 74.5 months, high mTOR mRNA expression was marginally associated with shorter disease-free survival (hazard ratio [HR] = 1.54; $p = 0.093$) and high Akt3 mRNA with shorter overall survival (HR = 1.49; $p = 0.0786$), in univariate analysis. In multivariate analysis, node-positive status, subglottic-transglottic location, surgery other than total laryngectomy and mTOR/CCND1 mRNA interaction with a hazard ratio of 2.16 (p value for interaction: 0.0010) were independent predictors of relapse, while node-positive status and subglottic-transglottic location were associated with higher risk for death.

CONCLUSION:

In localized laryngeal cancer, clinicopathological parameters and an interaction of high mTOR and CCND1 mRNA expression were found to be associated with poor patient outcome.