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Title: Epidermal growth factor receptor and related biomarkers evaluated by immunohistochemistry in patients with resected non-small cell lung cancer

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Body: Purpose: It has been demonstrated that mutated EGFR and angiogenic biomarkers have relationship with clinical outcome in patients with non small cell lung cancer (NSCLC). The usefulness of mutation specific antibodies evaluated by IHC still remains to be determined. We evaluated if EGFR and angiogenic markers are related to prognosis and survival in a population of Brazilian patients with resected NSCLC. Methods: We used IHC to quantify EGFR, c-erb B2, VEGF, CD31, CD44 and Inhibitor of DNA binding proteins (Ids) 1-3 in tumor tissues from 92 patients with lung squamous cell carcinoma (SCC) or adenocarcinoma (Adeno). The impact of these markers was tested on patients' survival until death. Results: We observed increased amount of EGFR, c-erb B2, CD31, VEGF, CD44 and Id1-3 in the tumor tissue. Adeno showed higher expression of EGFR, c-erb B2, VEGF and CD44 than SCC. Tumors in N2 stage presented higher CD44 expression in the tumor stroma. Positive correlation was observed between tumor EGFR and c-erb B2 (R=0.40; p<0.001), as well as between tumor EGFR and CD31 (R=0.26; p=0.01). EGFR expression was indirectly associated to Id1 (R=-0.24; p=0.03). The following variables had impact on long term patients' survival: N stage, EGFR, CD44, VEGF, Id2 and CD31. For SCC, the Cox model showed lower risk of death for N0 stage, EGFR < 7.33, VEGF < 24.73% and CD44 < 25.28%. Conclusion: Abnormal expression of proteins related to tumor growth, progression and invasion can be demonstrated by IHC, mainly if we use mutation specific antibodies, supporting the idea that IHC may be promising in detecting biomarkers with impact on NSCLC patients' survival.