

Assessment of hypoxia associated markers in oesophagogastric cancer

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Introduction: There is a need to increase understanding of oesophagogastric cancer biology and develop methods for determining prognosis. Hypoxia is implicated in the aetiology and prognosis of a number of cancers but has not been studied in oesophagogastric cancer.

Methods: HIF-1 α and HIF-2 α were examined using immunohistochemistry in 177 surgically-treated gastric and gastro-oesophageal junction cancers. Hypoxia-associated markers (HIF-1 α , HIF-2 α , VEGF, Epo, Epo-R, Glut-1) were studied in oesophageal and gastric carcinogenesis sequences. The Barrett's model consisted of 15 columnar-lined metaplasia, 20 intestinal metaplasia, 17 dysplasia and 20 adenocarcinoma samples. The Correa model of gastric adenocarcinoma development comprised 20 normal gastric mucosa, 20 *H. pylori* infected gastritis, 12 dysplasia, 20 intestinal adenocarcinoma and 20 diffuse adenocarcinoma samples.

Results: HIF-1 α and HIF-2 α were expressed in 53% (2% >30% staining) and 63% (44% >30% staining) of tumours, respectively. HIF-1 α expression at the invasive tumour edge was associated with a median patient survival of 18 mths versus 33 mths for negative tumours ($p=0.019$). High HIF-2 α was an adverse prognostic factor ($p=0.015$). Neither protein provided independent prognostic information in multivariate analysis. The expression of all the markers studied increased significantly from normal tissue to invasive malignancy in both carcinogenesis models. HIF-2 α was expressed late in the Barrett's sequence, and was only seen in dysplasia and cancer samples.

Conclusions: The high expression of HIF-2 α and its late expression in the carcinogenesis models suggest it is worth further study as a therapeutic target and as a marker of disease progression in patients with Barrett's dysplasia.