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Institutionen för Klinisk Vetenskap, Intervention och Teknik, Enheten för Öron-, Näs- och Halssjukdomar

Predictive and prognostic biomarkers in oral tongue squamous cell carcinoma

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ABSTRACT

Oral tongue squamous cell carcinoma (OTSCC) is an aggressive disease frequently associated with poor prognosis due to the high risk of regional failure and mortality rates have been practically unchanged in Sweden the last fifty years, despite advancements in both diagnostics and treatment.
Today we lack means to assess the biological aggressiveness of each individual tumor which varies largely. Treatment hinges on the International Union Against Cancer (UICC) TNM classification and comprises surgery with additional radio/chemotherapy in more advanced tumors.

This thesis focuses on molecular biomarker expression in OTSCC. Increased knowledge paves the way to a more individualized cancer treatment aiming for better outcome and less overtreatment and sequele.

The aim of this thesis was to investigate the predictive and prognostic value of quantitative DNA aberration, Ki-67, epidermal growth factor receptor (EGFR) and cyclooxygenase-2 (COX-2) in OTSCC. These biomarkers have all been found to influence carcinogenesis in head and neck cancer but little is known about their potential clinical role in OTSCC.
We also wanted to evaluate outcome after elective neck dissection compared with observation of the neck in T1N0 OTSCC patients.

A consecutive material consisting of biopsies taken from 78 OTSCC patients treated between the years 2000-2004 at Karolinska University Hospital in Stockholm Sweden were examined. Quantitative DNA aberration was analyzed using image cytometry. Immunohistochemistry (IHC) evaluating protein expression was performed on Ki-67, EGFR and COX-2. Furthermore EGFR gene copy number was investigated using fluorescence in situ hybridization (FISH).

Results of these studies show that a high proliferative activity (Ki-67 expression) is associated with locoregional recurrence in stage I OTSCC. EGFR and COX-2 was overexpressed by IHC and high EGFR gene copy number was seen in OTSCC. Improved disease free and overall survival was found for patients when elective neck dissection was added to the primary treatment of T1N0 OTSCC.

The high number of regional recurrence observed in patients with small tongue cancer with clinically negative necks resulted in a new treatment protocol. The head and neck group at Karolinska University Hospital has since 2006 included elective neck dissection to tumor resection in patients with T1N0 OTSCC.

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