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Prognostic significance of telomerase activity in oral squamous cell carcinoma

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Background: Squamous cell carcinoma of oral cavity is one of the ten most frequent cancers in the world. Recently, research had indicated that telomerase activity (TA) may play a role in carcinogenesis. We examined the expression and clinical association of TA with oral squamous cell carcinoma in an area where betel chewing is prevalent, to provide a theoretical foundation for further clinical applications of molecular prognosis.

Methods: A PCR-based EIA method was used to measure TA in 148 paired (normal and cancerous) tissues from the oral cavity cancer patients. Clinical information was available for all patients. Kaplan-Meier method and Cox logistic regression model were used for prognostic analysis.

Results: TA was detected of low, medium and high level in 36.4%, 51.6% and 12% in cancerous tissues, and 95.9%, 4.1%, 0% in normal mucosa samples, respectively.

Telomerase was marginal associated with T stage (P = 0.053), N stage (P = 0.085), and strongly associated with lymph node extra-capsular spread (P = 0.018), and poor survival (P = 0.001). On multi-variant analysis, only overall stage (P = 0.024) and telomerase (P = 0.046) were significantly associated with overall survival.

Conclusion: Telomerase activity and N stage are independent prognostic factors for survival of oral cancer. Telomerase may be a potential molecular target for clinical use in prognostication and therapy of oral cancer.

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Cysteine proteinase inhibitor cystatin C (CC) in operable squamous cell carcinoma of the head and neck (SCCHN): expression pattern and relation to prognosis

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Background: To determine the role of cysteine proteinase inhibitor CC in the invasive behaviour of SCCHN and as a prognosticator in this particular type of cancer. Patients and methods: CC concentration was measured in cytosols of primary tumors and corresponding normal mucosa from 82 patients with operable SCCHN. Data available for each patient were age and sex, tumor site, stage (pT-, pN-, overall UICC TNM-stage), histopathological grade and extracapsular spread. CC concentration was determined using quantitative immunosorbent assay (ELISA, KRKA d.d., Novo mesto, Slovenia) and expressed in ng/mg tissue proteins.

Results: The median CC concentration was lower in tumors than in their normal counterparts (14.9 vs. 16.3; P=0.031). Considering normal mucosa measurements, the CC concentration was influenced by the site of sampling, being lower in non-laryngeal tissue samples (oral cavity, oro-, hypophyrynx) compared to those from the larynx (11.5 vs. 24.0; P=0.004). The tumor CC concentration correlated inversely with pN-stage (pN0 vs. pN+: 18.4 vs. 14.2; P=0.047), whereas a trend of lower CC concentrations was observed in the group with extracapsular tumor extension compared to that with no extracapsular spread (14.0 vs. 17.4; P=0.069). On univariate analysis, pN- and overall UICC TNM-stage, and extracapsular spread significantly influenced the disease-free survival (DFS) and disease-specific survival (DSS). When using a median CC concentration to divide the patient into low- and high-CC groups no difference in survival was observed. After optimization, using isotonic regression analysis, the CC cutoff concentration was the 68th percentile in the group. Five-year DFS and DSS rates were higher in a low-CC group giving in both cases the P-value of 0.013. On multivariate analysis, pN-stage was the most powerful predictor of DFS (HR 2.78, P=0,040) and DSS (HR 4.36, P=0.011), followed by CC concentration (DFS: HR 0.22, P=0.043; DSS: HR 0.25, P=0.061).

Conclusions: Our data indicate: 1. CC is implicated in the invasive behavior of SCCHN; 2. variations in regulation of cancer-related poteolytic pathways - the inherent characteristic of individual subsites inside the upper aerodigestive tract; 3. protective role of high CC concentrations as measured in tumor cytosols - the concept that has been proposed for other cysteine proteinase inhibitors by the survival results in breast and lung carcinoma as well as SCCHN.

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Hemoglobin as a factor influencing the outcome in inoperable oropharyngeal carcinoma treated by concomitant radiochemotherapy

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Background: To analyze the prognostic significance of hemoglobin (Hb) concentration of patients with inoperable carcinoma of the oropharynx.

Patients and Methods: Seventy patients with inoperable carcinoma of the oropharynx were prospectively treated by concomitant regimen of conventional radiotherapy and chemotherapy with Mitomycin C and Bleomycin. The prognostic value of Hb concentration before and at the end of the therapy (Hb-S, Hb-E), the difference between both (Hb), and the average Hb concentration (Hb-Av) were analyzed.

Results: The median Hb concentration was falling from 139 to 122 g/L ($P<0.0001$) during the first three weeks of the therapy; after that, it reached a plateau. The median follow-up of the patients alive was 5.7 years (range 4-10.5 years). Longer disease-free survival (DFS) and disease-specific survival (DSS) correlated with higher values of Hb-S ($P=0.0005$, $P=0.008$) and Hb-E ($P=0.02$, $P=0.02$), while the Hb-Av was predictive for DFS only ($P=0.004$). The most significant difference between low- and high-Hb groups was calculated at cut-off concentrations of 122 (Hb-S), 116 (Hb-E), and 120 (Hb-Av) g/L. Only Hb-S was tested in multivariate model where its independent value for predicting both, DFS ($P=0.002$; RR 3.6) and DSS ($P=0.01$; RR 2.9), was confirmed.

Conclusions: In our patients, Hb-S was proved to be an independent prognostic factor in predicting DFS and DSS. We believe that the concentration of Hb=120 g/L should be maintained during radiotherapy course.

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Prognostic value of 99Tc-methoxyisobutilisonitrile (MIBI), Ki-67 and p53 in head and neck carcinoma treated with chemo-radiotherapy (CT-RT). Preliminary results.

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Background: The prognostic value of MIBI was studied in various tumours with non-conclusive results. Ki-67 and p53 showed prognostic relevance in a number of tumours including head and neck. This study correlates the results of 99Tc-MIBI-SPECT with Ki-67 and p53 to assess the prognostic value after CT-RT for head and neck carcinoma.

Material and Methods: We enrolled 27 patients (pts), 19 M and 8 F, stage II-IV head and neck carcinoma, aged 17-79 (median 56), PS 80-100. Tumour sites were: 9 oropharynx, 2 oral cavity, 4 hypopharynx, and 12 nasopharynx. Treatment included 3 cycles of carboplatin 75 mg/m2 and 5-fluorouracil 1000 mg/m2, days 1-4 and concomitant RT to total dose of 70 Gy, 2 Gy/fx. SPECT with 99Tc-MIBI was performed prior and 45-60 days after CT-RT. SPECT images were obtained 10' after administration of 740 MBq of 99Tc-MIBI with double-head gamma camera with high resolution and parallel hole collimator. Positive MIBI was scored 0-3. Ki-67 and p53 were assessed by immunohistochemical staining on paraffin-embedded material, and percentage of positive cells was evaluated.

Results: Pre-treatment MIBI was highly positive in 12/27 pts (score 2-3) and slightly positive or negative (score 0-1) in 15. Ki-67 and p53 were studied in 16 pts: Ki-67 positive cells were =50% in 8, p53-positive nuclei were observed in =15% in 11. Correlation by Spearman regression test was found between pre-treatment positive MIBI and low p53 expression (p=0.018) and not between MIBI and Ki-67. To date, 18 pts have completed CT-RT and received the second MIBI assessment: 15/18 pts obtained complete remission (CR) and 3/18 partial or no response. After 9-36 months follow-up (median 22), 5/18 pts recurred locally. No correlation was found between pre-CT-RT MIBI, Ki-67 or p53 and CR. Seven of the 13 cases with MIBI positive at the first assessment turned negative or reduced the uptake after CT-RT. This change was correlated with CR after CT-RT