ANALIZA KUANTITATIVE E IMAZHEVE DHE BIOLOGJIA MOLEKULARE E KARCINOMËS ME QELIZA SKUAMOZE TË EZOFAGUT, ME REFERENCË PROGRESIONIN NEOPLAZIK DHE IMPLIKIMIN E VIRUSIT TË PAPILLOMËS HUMANE (HPV)

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Summary

QUANTITATIVE IMAGE ANALYSIS AND MOLECULAR BIOLOGY OF OESOPHAGEAL SQUAMOUS CELL CARCINOMA, WITH SPECIAL REFERENCE TO TUMOUR PROGRESSION AND HUMAN PAPILLOMAVIRUS (HPV) INVOLVEMENT

Despite much research effort, the major prognostic factor of ESCC remains the pathological stage of the disease as defined by the TNM classification, whereas tumour grading is of limited value in this respect, mainly due to its low reproducibility. A better means for disease prognostic--ation based on improved understanding of the pathogenetic mechanisms is urgently required.

Materials and methods: The material of the present study was derived from a series of 1876 oesophageal surgical specimens taken from a total of 700 patients, who underwent oesophageal resection for an invasive ESCC in Anyang Tumour Hospital, Henan Province of China. Among the cohort of 700 cases of ESCC, previously subjected to extensive testing for Human Papillomavirus (HPV) involvement and expression of p53 gene. All cases are analysed by histopathology and by in situ hybridisation (ISH) and PCR, immunohistochemestry, and a group of 272 patients was randomly selected for analysis of the primary tumour, adjacent mucosa and regional lymph nodes, in the quantitative image analysis. All these cases were subjected to extensive univariate and multivariate analysis to disclose independent predictors of progressive disease.

Results: For the analysis, the ESCCs were graded into three degrees: well, moderately and poorly differentiated. For morphological evidence of HPV – suggested lesions have been use the criteria described previously by Syrjänen. HPV-DNA was detected in 201 cases (33,5%) of the analysed cases, from which 133 cases by ISH and in 68 cases by PCR. Using the quantitative image analyses, the diploid ESCC was detected in 19,1% of ESCC, and aneuploide ESCC was detected in 80,9% of cases. In univariate analysis, lymph node status (considered as the surrogate marker of progressive disease) was significantly ($p<0.01$) predicted by the following nuclear parameters: nuclear area, Go-G1 ratio, HPV-DNA status, integrated optical density, mean optical density and cells S-phase. In multi-variate analysis, 6 variables remained as independent predictors of disease progression ($p<0.05$), the three most significant ones being nuclear perimeter, nuclear roundness and equivalent diameter ($p<0.01$).

Conclusion: A series of quantitatively measured nuclear parameters seem to bear a close correlation with ESCC differentiation and progression in univariate analysis and some of these variables proved to be significant independent predictors of disease progression in multivariate modelling as well. These data clearly advocate the use of quantitative image analysis in searching for additional prognostic factors of ESCC. Study in the immunohistochemestry, and in the molecular biology, have confermed HPV involvement in the morphopathogenesis of KQSE.