

Abstract

The aim of this thesis is the comparison of immunohistochemical and molecular biological methods for the detection of human papillomavirus (HPV) in tumour tissue and their subsequent use in the study of HPV role in the etiopathogenesis of malignant tumors of sinonasal region.

Several methods for the purpose of HPV detection were applied: in situ hybridization, immunohistochemical detection of expression of p16INK4a protein, classic polymerase chain reaction combined with two different enzyme immunoassay detection methods, and reverse hybridization, followed by polymerase chain reaction with real time reverse transcription.

All methods (p16 DNA in situ hybridization, RNA in situ hybridization, quantitative polymerase chain reaction with reverse transcription - RT-qPCR mRNA) used for the detection of HPV performed very well when compared, showing concordance with statistical significance $p < 0,0001$. Detection of p16 vs. DNA polymerase chain reaction (PCR) had correlation coefficient $p = 0.004$ in the whole group, and $p = 0.002$ in the subgroup of squamous cell carcinoma (SCC). Correlation coefficient between detection of p16 and overall HPV status was 0,659 for entire set and 0,864 for set of SCC, indicating significant linear dependence.

Immunohistochemical detection of p16 in combination with the detection of mRNA by RT-qPCR can be used with advantage for HPV testing. These methods provide information about HPV type, transcription activity and HPV interaction with cell cycle.

The above-mentioned methods demonstrated that 24.7% (18/73) of carcinomas in sinonasal region showed HPV association regardless of their histological subtype. The group of SCC showed association with HPV infection in 35.7% (17/49).

According to the clinical part of our study, median survival of the subgroup diagnosed with SCC differed depending on HPV status of the carcinomas: when evaluated by p16 expression, the cohort with p16-positive SCC showed median survival 71 months compared to 27 months in the group with p16- negative SCC. Similarly the HPV- positivity evaluation showed prolonged median survival in patient with HPV-positive SCC (30 months) compared to those with HPV-negative SCC (14 months).