

**ABSTRACT****Correlations between The Expression of Protein Cyclooxygenase-2 (COX-2), Microvascular Density with The Differentiation Grading in Squamous Cell Carcinoma of the Uterine Cervix**

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**Background** : The importance of carcinoma of the uterine cervix as a cause of morbidity and mortality around the world, particularly in developing countries, has already been emphasized. The most common carcinoma of the uterine cervix is squamous cell carcinoma (75%). Carcinoma of the uterine cervix progresses through a multistage process of carcinogenesis. Numerous studies have emphasized the importance of cyclooxygenase-2 (COX-2) activity during carcinogenesis and overexpressed in any kind of malignancies. The degree of tumor angiogenesis quantified as the number of microvessels in a unit area, microvessel density (MVD) is associated with the risk of metastasis, recurrence, and proliferative activity in various tumors.

**Objective** : The purpose of this study was to investigate the expression of protein COX-2, microvascular density and their correlation with the differentiation grading in squamous cell carcinoma of the uterine cervix.

**Methods** : The following samples were analyzed: 45 paraffin tissue blocks from patients with squamous cell carcinomas of the uterine cervix, including 15 samples of keratinizing squamous cell carcinomas, 15 samples of large cell non keratinizing squamous cell carcinomas and 15 samples of small cell non keratinizing squamous cell carcinomas. Immunohistochemical analysis was performed with a rabbit monoclonal antibody against human COX-2 and a rabbit polyclonal antibody against human factor VIII. Then, the correlations between expression of protein COX-2, microvascular density with the differentiation grading in squamous cell carcinoma of the uterine cervix were analyzed.

**Results** : Expression of COX-2 was positive in 37,8% of squamous cell carcinoma of the uterine cervix, but there was no a significant correlation between COX-2 with the differentiation grading ( $p = 0,422$ ). MVD was significantly correlated with the differentiation grading ( $p = 0,001$ ;  $r=0,741$ ).

**Conclusions** : Overexpression of protein COX-2 was found in both keratinizing squamous cell carcinoma and non keratinizing squamous cell carcinoma, but small cell non keratinizing squamous cell carcinomas showed infrequent and low expression. These results suggested that increased COX-2 expression might play an important role in carcinogenesis of squamous cell carcinoma. The microvascular density showed a positive correlation with the differentiation grading and recognized as an independent prognostic indicator of patients with cervical squamous cell carcinoma.

**Keywords**: Cyclooxygenase (COX-2); Microvascular density; Differentiation grading; Squamous cell carcinoma