Prognostic significances of Cox-2, Cyclin D1 and P21 expression in colorectal cancer patients

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Introduction
Colorectal cancer (CRC) is the 3rd commonest cancer and the 4th most frequent cause of cancer related death worldwide.

It is important to detect novel prognostic markers for CRC patients to detect recent targeted therapy and to improve patients’ survival.
* Cyclooxygenase-2 (COX-2) is an enzyme that is upregulated in response to inflammation and carcinogenesis.

* Cyclin D1 is an oncogene which regulates cell cycle progression.

* Cyclin D1 is blocked by cyclin D1-dependent kinase (CDK) inhibitors, such as p27 and p21.
Many studies have evaluated Cox-2, cyclin D1 & p21 expression as prognostic factors for survival of patients with CRC.

However, the results of the studies are conflicting.
AIM of the work
* To evaluate immunohistochemical expression of COX-2 in colon cancer patients correlating its expression with the cell cycle markers cyclin D1, and p21.

* To analyze the relationship between their expression, clinicopathological criteria and the prognosis of patients.
MATERIAL & METHOD
* Expressions of Cox-2, Cyclin D1 and P21 were evaluated using immunohistochemistry in 60 patients of colon cancer, that were followed up for 3 years.

* The relationship between their level of expressions and prognosis of patients was analyzed.
RESULTS
Cox-2 & Cyclin-D expression in the studied cases:

* The expression of Cox-2 & Cyclin-D in CRC was positively associated with higher grade and advanced stage of the tumor, presence of L.N spread, peritoneal dissemination (p<0.001), and distant metastases (p=0.012) & (p=0.009) respectively.
P-21 expression in the studied cases

* The expression of P21 in CC was significantly correlated with lower grade & early stage of the tumor, absence of L.N, distant metastases (p<0.001), bilaterality and ascites.
Follow up and clinical results

* Low Cox-2 & Cyclin D1 and high P21 expression were associated with;

* Optimal surgical eradication of the tumor.

* Increased 3-year overall survival (OS) rate.

* Low incidence of recurrence after therapy (P < 0.001).
Fig 1 immunohistochemical expression of Cox-2 in colorectal carcinoma (CRC). A; High expression in the cytoplasm of poorly differentiated CRC x400, B; High expression in the cytoplasm of moderately differentiated CRC x400, C; low expression in the cytoplasm of well differentiated CRC x400, D; negative expression in the cytoplasm of well differentiated CRC x400.
Fig 2 Immunohistochemical expression of Cyclin D1 in colorectal carcinoma (CRC)

A; High expression in the nucleus of poorly differentiated CRC x400, B; High expression in the nucleus of moderately differentiated CRC x400, C; low expression in the nucleus of well differentiated CRC x400.
Fig 3 immunohistochemical expression of P21 in colorectal carcinoma (CRC)

A; High expression in the nucleus of well differentiated CRC x400,
B; High expression in the nucleus of moderately differentiated CRC x400,
C; low expression in the nucleus of poorly differentiated CRC x400.
Summery & conclusion
High levels of expression of Cox-2 & Cyclin D1 in poorly differentiated and advanced stage CRC suggests that they play a role in tumor initiation & progression.

Cox-2 & Cyclin D1 are markers of poor prognosis in CRC patients.

P21 is a marker of good prognosis in CRC patients.
These results clarified the roles of inflammation and disturbances in cell cycle control in progression and poor prognosis of CRC patients.
Recommendations
We recommend that a large scale study on large number of patients with CRC to prove our results and detect the value of IHC in prediction of CRC patients prognosis and response to therapy.
Thank you

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