

## COX-2

### The Clinical Significance of Cyclooxygenase 2 Expression in Colorectal Cancer

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**Purpose:** Epidemiologic studies have indicated that the use of nonsteroidal anti-inflammatory drugs, which inhibit cyclooxygenase activity, reduce the risk of colorectal cancer. In addition, several studies have demonstrated the increased expression of cyclooxygenase-2 (COX-2) in human colorectal cancer tissues. However, the role of COX-2 in colorectal cancer has not been fully established. The aim of this study was to clarify the clinicopathologic significance of COX-2 expression in human colorectal cancer.

**Methods:** We performed immunohistochemical staining for COX-2 expression in 124 human colorectal cancer specimens. COX-2 expression was then compared with clinicopathologic factors and survival outcomes.

**Results:** COX-2 was expressed in the cytoplasm of the cancer cells. COX-2 expression was noted in 86.3% of the cancer patients and significantly correlated with the histologic type. The depth of invasion, tumor size, lymph node metastasis and stage were not correlated with COX-2 expression. Multivariate analysis for the factors associated with survival showed that serum CEA, size, depth and lymph node involvement correlated with survival, but COX-2 expression had no correlation.

**Conclusion:** These data suggest that COX-2 expression in primary lesion of colorectal cancer may not be a useful

marker for evaluating prognosis. However, further studies are necessary for identification of the roles in colorectal carcinogenesis. (J Korean Surg Soc 2003;64:39-43)

**Key Words:** Cyclooxygenase-2 (COX-2), Colorectal cancer, Immunohistochemistry  
 : COX-2,

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4  
 가 가 가  
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 Aspirin (non-steroidal anti-inflammatory drug, NSAID)  
 가 (1-5) NSAID가 chemical carcinogen  
 , (1) , 가  
 sulindac NSAID  
 가 (2,3)  
 NSAID  
 (4,5)  
 NSAID cyclooxygenase (COX)  
 arachidonic acid PGH2 (prostaglandins, prostacyclin, thromboxane prostanoid )  
 (6) 가 COX  
 (COX-1, COX-2)가 (7) COX-1  
 , COX-  
 2 mitogen

(8,9) COX-2 (up-regulator)  
 apoptosis (10,11) COX-2가  
 metalloproteinase (MMP) (12) , (13) matrix  
 (14)

COX-2  
 COX-2 가



1.

1994 1997  
 124 가 가 63± 10  
 가 75 , 50  
 AJCC (American Joint Committee on Cancer) TNM  
 I 19 , II 49 , III 41 , IV 15

2.

4 µm coating slide xylene  
 , 70%  
 10 peroxidase  
 (Fig. 1). microwave  
 30  
 COX-2 (Cayman chemical, Ann Arbor, MI, USA, 1:1,000) avidin-biotin complex-immunoperoxidase  
 1 PBS  
 (universal biotinylated secondary immunoglobulin antibody)  
 . Streptavidin, 3,3-diaminobenzidine tetrahydrochloride Harris

3.

SPSS version 10.0  
 Chi-square  
 IV 15 Kaplan-Meier , Cox  
 . P 0.05



COX-2 (crypt cell)  
 COX-2  
 (Fig. 1).  
 124 COX-2 107  
 (86.3%)가 ,

55/62 (88.7%), 52/62 (83.9%)  
 , CEA  
 (P=0.593). COX-2  
 (P=0.902) 가 (P=0.001).  
 4/9 (44.4%)  
 T1, T2 (95.0%)가 T3, T4 (84.6%)

75.0%  
 (P=0.227).  
 S 가  
 . TNM

(P=0.123, P=0.196)(Table 1). COX-2  
 5 80.9%, 68.8%  
 (P=0.1299)(Fig. 2).  
 Cox  
 , ,  
 COX-2 , ,

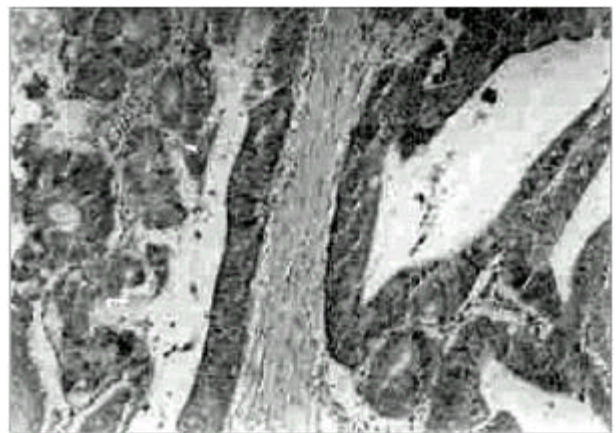


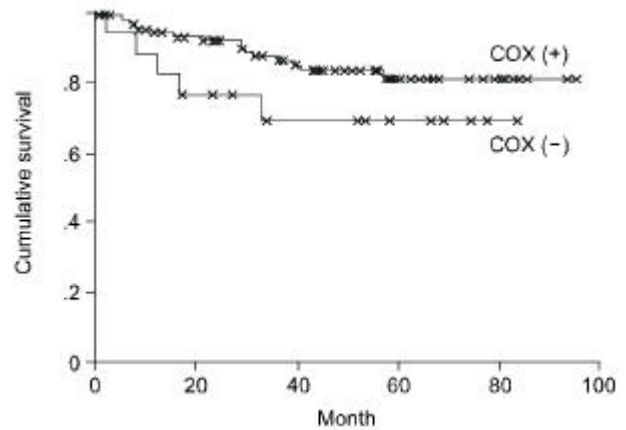
Fig. 1. Immunohistochemical staining of COX-2 in a representative section of colorectal carcinoma (× 100). COX-2 expression is observed in the cytoplasm and in the nuclear envelope of the tumor cells, and some stromal cells are stained.

**Table 1.** Correlation between COX-2 expression and clinicopathological features

Variable	COX-2 expression		P
	(-)	(+)	
Gender	M	12 (1.2%) 62 (83.8%)	0.324
	F	5 (10.0%) 45 (90.0%)	
Age	< 60	7 (12.7%) 48 (87.3%)	0.776
	≥ 60	10 (14.5%) 59 (85.5%)	
Location	Colon	7 (11.3%) 55 (88.7%)	0.433
	Rectosigmoid	10 (16.1%) 52 (83.9%)	
S-CEA (ng/ml)	< 10.0	7 (14.6%) 41 (85.4%)	0.593
	≥ 10.0	8 (11.3%) 63 (88.7%)	
Size (cm)	< 5	9 (15.5%) 49 (84.5%)	0.607
	≥ 5	8 (12.3%) 57 (87.7%)	
Gross	Polypoid	2 (10.0%) 18 (90.0%)	0.902
	Ulcerofungate	9 (13.8%) 56 (86.2%)	
	Ulceroinfiltrate	5 (13.5%) 32 (86.5%)	
Micro	Well	8 (100.0%)	0.001
	Moderate	11 (10.8%) 91 (89.2%)	
	Poor	1 (20.0%) 4 (80.0%)	
	Mucinous	5 (55.6%) 4 (44.4%)	
Depth	pT1, T2	1 (5%) 19 (95.0%)	0.196
	pT3, T4	16 (15.4%) 88 (84.6%)	
LN involvement	(-)	5 (11.6%) 38 (88.4%)	0.623
	(+)	12 (14.8%) 69 (85.2%)	
Venous invasion	(-)	5 (11.6%) 38 (88.4%)	0.227
	(+)	5 (25.0%) 15 (75.0%)	
	(++)	7 (11.5%) 54 (88.5%)	
DNA ploidy	Diploid	5 (15.6%) 27 (84.4%)	0.747
	Aneuploid	6 (13.0%) 40 (87.0%)	
S-phase fraction	< 15	5 (16.1%) 26 (83.9%)	0.525
	≥ 15	5 (11.1%) 40 (88.9%)	
Stage	1	1 (5.3%) 18 (94.7%)	0.123
	2	7 (14.3%) 42 (85.7%)	
	3	4 (9.8%) 37 (90.2%)	
	4	5 (33.3%) 10 (66.7%)	
	0	11 (11.3%) 86 (88.7%)	
	1	6 (23.1%) 20 (76.9%)	0.196

LN = lymph node a.

(Table 2).



**Fig. 2.** Kaplan-Meier disease-free survival curves of patients with and without COX-2 expression. A statistically difference was not observed between the two groups (P=0.1299).

(16) . NSAID 가 . NSAID  
 NSAID가  
 (1, 16)  
 가 COX-2  
 COX-2  
 (11)  
 1990 NSAID  
 40 50% (4, 17-19)  
 slulindac 가  
 (2, 3, 20, 21)  
 NSAID COX 가  
 . COX-2가 80%  
 COX-2  
 COX-2 . 43  
 Fujita (22) COX-2가  
 가 . Yang (23) 가  
 prostanoid가 가  
 . Sheehan (24) COX-2  
 가 ,  
 가 ,  
 COX-2  
 가  
 COX-2 (P=0.001).  
 COX-2

가 1998 가  
 55,000 (15) 가

**Table 2.** Cox proportional hazards model for risk factors associated with survival. Values in parenthesis are 95% confidence intervals

Factor	B	Standard error	P	Odds ration
Serum CEA (< 10 vs. ≥ 10)	0.176	0.087	0.043	1.192 (1.006 1.413)
Size (<5 vs. ≥5)	-0.346	0.170	0.042	0.708 (0.507 0.988)
Microscopic Finding	0.499	0.514	0.332	1.647 (0.602 4.507)
Depth (pT1, 2 vs pT3, 4)	1.957	0.911	0.032	7.078 (1.188 42.166)
LN involvement (negative vs. positive)	2.315	1.007	0.022	10.127 (1.406 72.950)
Venous invasion (negative vs. positive)	0.053	1.185	0.083	7.794 (0.764 79.543)
DNA ploidy (diploid vs. aneuploid)	-0.979	0.654	0.134	0.376 (0.104 1.353)
S-phase fraction (< 15% vs. ≥ 15%)	-0.105	0.690	0.879	0.900 (0.233 3.483)
COX-2 expression (negative vs. positive)	2.553	1.497	0.088	12.851 (0.684 241.467)

LN = lymph node.

Shattuck-Brandt (25) COX-2가 TNM COX-2가 (vas-cular endothelial growth factor, VEGF), apoptosis 가

I 가 COX-2 가 . Tsujii collagenase level Elder (26) COX-2 NS-398 apoptosis가 COX-2 가

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