

cyclooxygenase-2

cyclooxygenase- 2

2001 6



	1
I.	3
II.	6
1.	6
2.	6
3.	6
4.	7
III.	9
1.	9
2. COX-2	10
3. COX-2	12
VI.	16
V.	20
	21
	28

1.	T 1,	3	
	cyclooxygenase-2		
		11
2.	T 1,	3	
	cyclooxygenase-2		
	Kaplan - Meyer	 15

1.	T 1,	3	
	cyclooxygenase-2		
	,	,	,
		 13
2.	T 1,	3	
	cyclooxygenase-2		
		 14

cyclooxygenase-2

cyclooxygenase-2(COX-2) 가

가 가 ,

가

T 1, 3(T 1G3) COX-2

가 .

1991 1 1998 12

T 1G3

Bacillus Calmette- Guerin(BCG)

1 37

COX-2

, , ,

. 5%

. 66 (34- 80), 36:1,

27(12- 67) . 16 (43.2%) 1

, 7 (18.9%) .

37 16 (43.2%) COX-2 .

5 10% 5 (13.5%), 10 20%

8 (21.6%), 20% 3 (8.1%) . 2

COX-2 50.0% 68.6%

37.5% 71.4%

(p=0.039). , COX-2

. 2 COX-2

81.3% 90.5% 68.7% 90.5%

.

T 1G3 43%

COX-2가 . COX-2

, COX-2

COX-2

가 가 가 .

: , cyclooxygenase-2, ,

cyclooxygenase-2

< >

I.

Cyclooxygenase(COX) arachidonate prostaglandin
thromboxane prostaglandin H2
prostaglandin
, , , integrity

가

^{1,2}

(nonsteroidal anti-inflammatory drug: NSAID)가

NSAID 가

^{3,4}

가

(familial polyposis)

가

⁵⁻⁹

NSAID가

COX

COX isoform

COX- 1,

isoform COX-2

^{10,11} COX- 1

COX- 2

가
 COX-2 NSAID가
 COX-1 COX-2 가 12-14
 COX-2 가
 가
 가
 90%
 가
 70 75%
 Bacillus
 Calmette- Guerin (BCG)
 1 10 15%
 3 , T 1G3
 10% 가 50%
 15 T 1G3
 T 1 , 16,17
 p53,^{18,19} pRb^{20,21} T 1G3
 COX-2 가
 COX-2

COX-2

BCG

가

COX-2

가

가

,

가

가

COX-2가

22-24

T 1G3

,

COX-2

T 1G3

가

가

COX-2

가

II.

1.

1991 1 1998 12

TNM

WHO grading system

T 1, 3

BCG

6

1

2.

3.

Vectastain ABC Elite kit (Vector Laboratories
Inc., Burlingame, CA, USA)

4 μ m

, xylene

graded alcohol rehydration . 5
 0.3%
 30 phosphate buffered
 saline(PBS) . 5%
 normal goat serum 20 1% bovine serum
 albumin 1% 가 Tris-buffered saline(50mmol/L
 Tris, pH 7.5, 300mmol/L NaCl) 1:200 goat polyclonal
 anti COX-2 (Santa Cruz Biotechnology, Santa Cruz, CA, USA)
 2 . PBS 3
 biotinylated rabbit anti-goat antibody() 30
 . PBS 3 avidin-biotin horseradish
 peroxidase reagent 30 PBS
 3,3'-diaminobenzidine tetrahydrochloride H₂O₂ 3
 hematoxylin
 . buffer
 permount

4.

1000

COX-2

. COX-2

5% , 5% 10% , 10% 20% , 20%

5% .²² COX-2

Windows SPSS

²-test Fisher's exact test ,

Kruskal-Wallis test

Kaplan-Meyer

log-rank test .

p<0.05 가 .

III.

1.

37 . 66
(34-80), 36:1 .
가 가 6 BCG
2 6 , 2 3 ,
1
27(12-67) 16
(43.2%) 1 , 6 . 1
BCG
T0
41 가
7 (18.9%)

2. COX-2

COX-2

가

가

가

5% - 20%

heterogeneous

가

. Anti COX-2

buffer

(1).

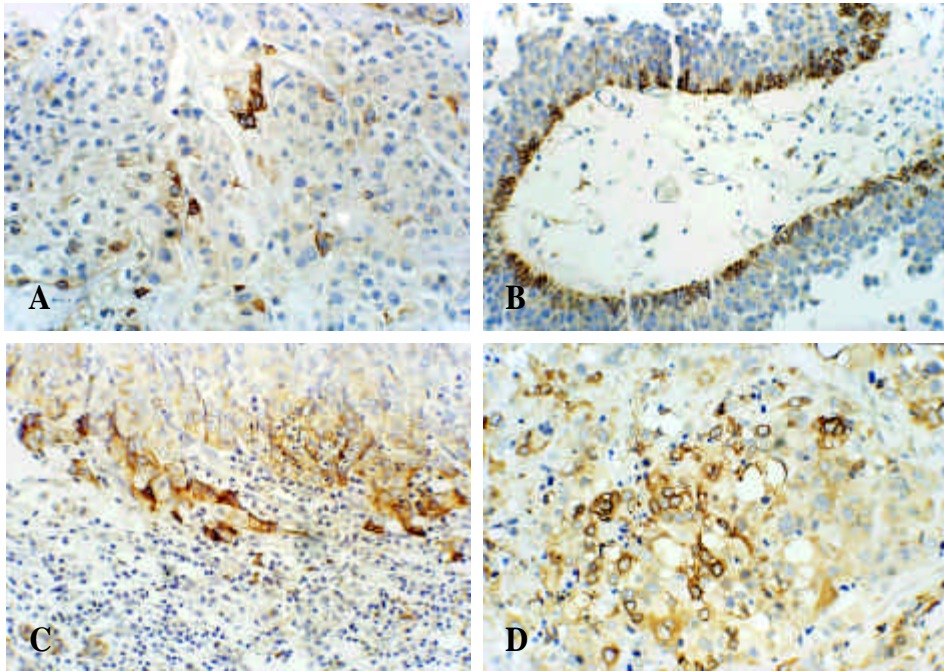
5%

37 16 (43.2%) COX-2 21 (56.8%)

5

10% 5 (13.5%), 10 20% 8 (21.6%), 20% 3

(8.1%)



1. T1, T3, T4 cyclooxygenase-2
 . A: 5-10%
 . cyclooxygenase-2
 . B, C: 10-20%
 가
 (B), 가
 (C). D: 20%
 가
 (× 250).

3. COX - 2

COX-2 ,
,
(1).
COX-2 5% , 5%
10% , 10% 20% , 20% 4
(2).
Kaplan-Meyer 2
COX-2 50.0% 68.6% (2)
2 81.3% 90.5% .

1.	T 1,	3	cyclooxygenase- 2		p
			COX- 2 ²		
	35	19	16		
1	14	8	6		p=0.782 ³
2	21	11	10		
	36	20	16		
	22	12	10		p=0.878 ³
	14	8	6		
	37	21	16		
	21	15	6		p=0.039 ³
	16	6	10		
	37	21	16		
	30	19	11		p=0.202 ⁴
	7	2	5		
	37	21	16		

¹ 37 2 , 1

² T 1, 3 COX- 2
가 5% , 5%

³ ²-test

⁴ Fisher's exact test

COX-2: cyclooxygenase-2

2. T 1, 3 cyclooxygenase-2

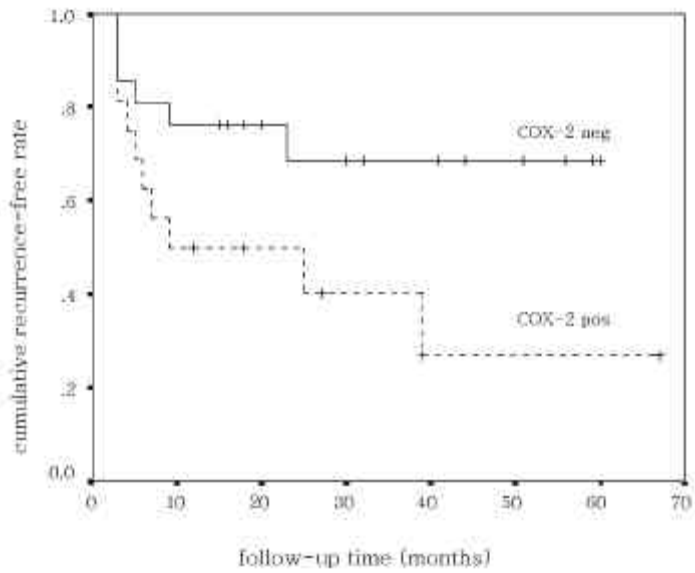
*

	COX-2 ¹			
	<5%	5- 10%	10- 20%	20%
21	15	3	2	1
16	6	2	6	2
37	21	5	8	3

¹ T 1, 3 COX-2
 COX-2 5% , 5%
 10% , 10% 20% , 20%

* p>0.05(Kruskal- Wallis test)

COX- 2: cyclooxygenase- 2



2. T1, 3 cyclooxygenase-2
Kaplan-Meier .
cyclooxygenase-2 가
5% , 5%
. 27(12-67) 2
cyclooxygenase-2 50.0% 68.6% .
log-rank test
(p<0.05).

IV.

가 가

1 10 15%

· , , ,

· ,

BCG

· T 1G3

BCG

가

BCG

·^{25,26}

가

p53

·

가

T 1G3 p53

가

·^{18,19,27,28}

p53

· cut-off

·²⁹

가

p53

value

가

TIG3
 COX-2
 가
 2
 COX-2
 , 가
 COX-2
 COX-2
 가
 COX-2
 Tomozawa³⁰ 63
 COX-2
 COX-2
 가
 COX-2 가 extracellular matrix protein
 가 COX-2 angiogenesis
³¹ COX-2가
 prostaglandin³²
 angiogenesis³¹ COX-2
^{33,34} 가 가
 COX-2

가 .

BCG

, BCG

field effect

³⁵ COX-2

COX-2

field effect

. Mohammed ²²

COX-2

80%

53%

field effect

COX-2

가

가

. Okajima

³⁶ BBN

initiation

COX-2

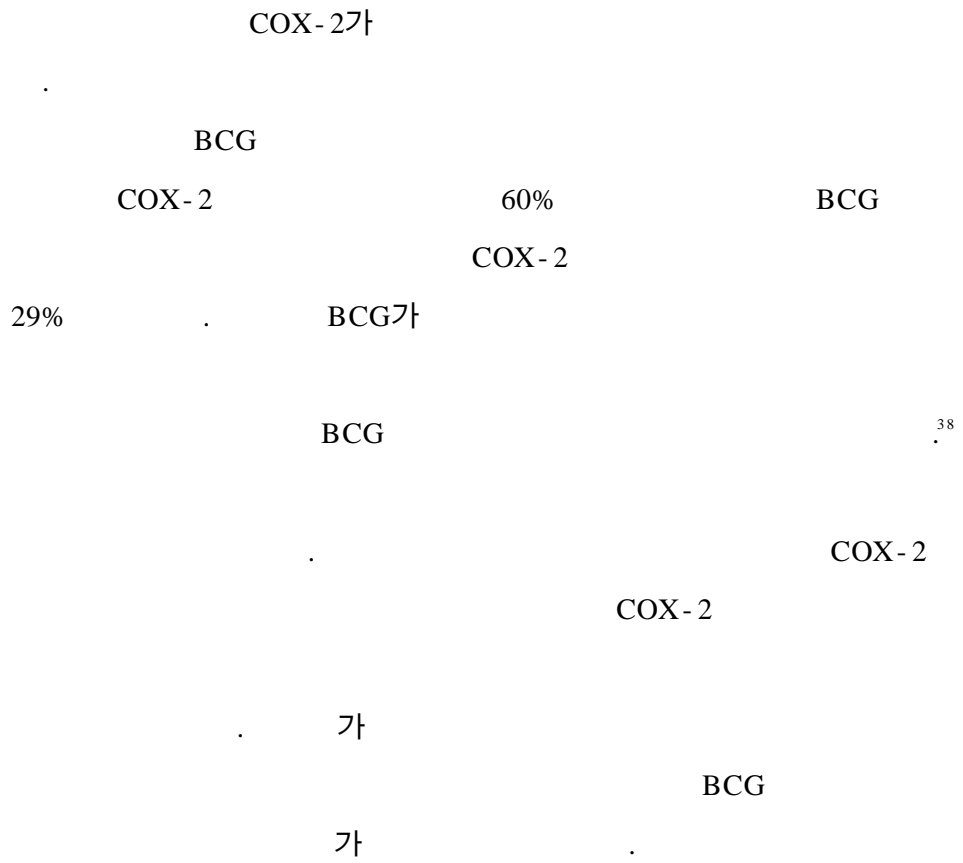
nimesulide

promotion

BBN

가 COX-2가 가

³⁷



V.

T 1G3

43% COX-2가

COX-2

가

가

COX-2

가

, COX-2

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Abstract

The expression of cyclooxygenase-2 and prognosis of superficial bladder cancer

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Recent reports suggest that the expression of cyclooxygenase-2(COX-2) is increased in bladder cancer. However, no study has yet specifically addressed whether the expression of COX-2 has prognostic significance in stage T1, grade 3(T1G3) superficial bladder cancer, the most unfavorable subgroup in terms of recurrence and progression of disease.

Thirty-seven consecutive patients with initial T1G3 transitional cell carcinoma(TCCa), who had complete transurethral resection of their tumor followed by 6 weeks of intravesical instillation of Bacillus Calmette-Guerin(BCG), and with at least 1 year follow-up, were enrolled in the study. Paraffin-embedded cancer tissues were immunohistochemically stained for COX-2 and possible correlation with clinicopathologic features such as shape and multiplicity of tumor, recurrence and progression was sought.

The median age was 66(34-80) years, the male-to-female ratio was 36:1, and the median follow-up period was 27(12-67)months. Sixteen(43.2%) patients experienced recurrence and 7(18.9%) patients had progression defined as muscle invasion or distant metastasis. Of 37, 16(43.2%) stained positive for COX-2 defined as 5% of positively stained cells. Cumulative 2-years recurrence-free rates for COX-2 positive and negative groups were 50.0% and 68.6%, respectively. Overall recurrence-free rates were 37.5% and 71.4%, respectively and was significantly lower in the positive group($p=0.039$). Cumulative 2-years progression-free rates for COX-2 positive and negative groups were 81.3% and 90.5%, respectively, and overall progression-free rates were 68.7% and 90.5%, respectively ($p>0.05$). The shape and multiplicity of tumors were not significantly different between the two groups.

In a pathologically homogeneous group of T1G3 TCCa of the bladder, 43% of cases expressed COX-2, and its expression correlated with recurrence. Thus, COX-2 positive superficial bladder cancer patients may need to be followed more vigorously. Further studies on implication of COX-2 in the mechanism of recurrence and possible application of COX-2 inhibitor in the prevention of recurrence of superficial bladder cancer are needed.

Key Words: bladder cancer, cyclooxygenase-2, recurrence, immunohistochemistry