

## p53

### Association of p53 Protein Expression with Clinical Outcome in Advanced Supraglottic Cancer

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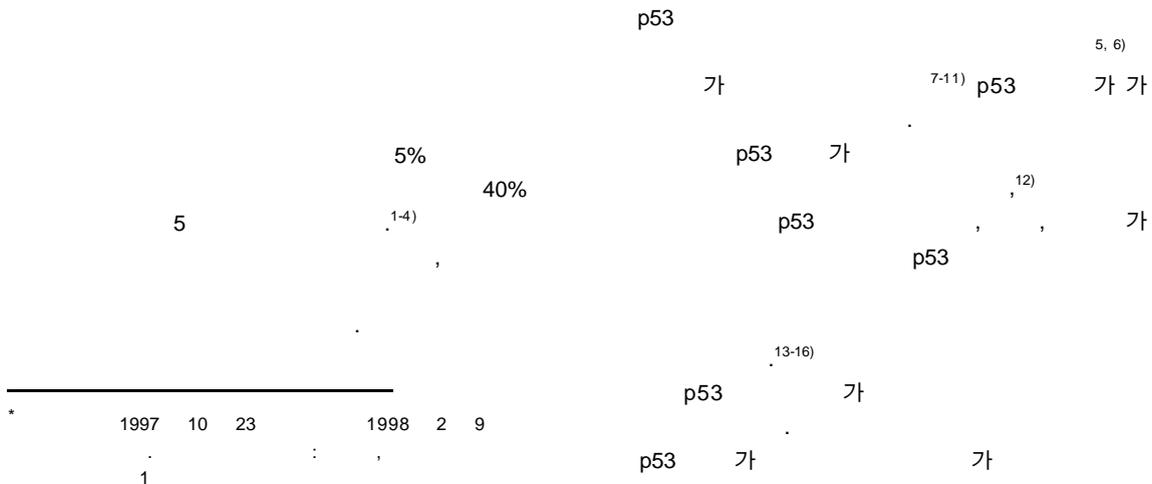
**Purpose** : To determine the incidence and prognostic effect of p53 expression in patients with advanced supraglottic cancer.

**Materials and Methods** : Twenty-one cases of total 48 advanced supraglottic cancer patients who received postoperative adjuvant radiation therapy were evaluated by immunohistochemical staining employing p53 monoclonal antibody.

**Result** : Three out of six stage patients and four out of fifteen stage patients showed p53 expression without statistically significant difference ( $p=0.608$ ). Five year survival rates are 93% in p53 negative, 86% in p53 positive patients and there was no significant difference ( $p=0.776$ ). p53 expression does not show statistically significant correlation with primary tumor status ( $p=0.877$ ), lymph node status ( $p=0.874$ ) and age ( $p=0.64$ ).

**Conclusion** : There was no statistically significant correlation between traditionally known risk factors and p53 expression.

**Key Words** : Supraglottic cancer, p53 expression, Prognostic factor



17) apoptosis wild-type p53 H<sub>2</sub>O<sub>2</sub> 5 PBS(Phosphate buffered saline) 2 0.05M TrisHCl 2.5% BSA(Bovine serum albumin) 5 blocking blocking agent (mouse antihuman p53 monoclonal Ab, NCL-p53-BP, Novocastra Lab. Ltd.)

18-20) p53 가 DNA 가 p53 1:100 30

21, 22) DNA 가 가 2

DNA 가

p53 peroxidase-antiperoxidase LSAB kit(Dako Co./USA) 2 (biotin conjugated-anti rabbit immunoglobulin antibody) 10 PBS avidin biotin enzyme reagent 10 PBS AEC chromogen solution 5 10

PBS 3-5

PBS crystal mount

1. 1985 1995 가

48 21 TNM Kaplan-Meier

p53 40 70 2 test

59 20 1 3

6 4 15 가 10 가 9 가 2

Vertical hemilaryngectomy 가 61 Stage 6 stage 가 70

( 4860cGy 6160cGy 16 Stage 6 Stage 15 2 15 29

154 57 16 16 32 16

2. p53 32 8 p53 1 81 stage

p53 5 stage

-70 24 가 100%, stage 가 87% (p=0.073). 5000cGy

20 60 xylene 20 3 21 14 p53 (66%) 7

20 xylene 10 100% 10 2 (33%) p53

90% 10 80%

10 2

Poppen 3%

가 (Fig. p value 0.877 0.874 가 .  
 1). p53 60 , 76 5 59 (p=0.365). p53  
 86%(p=0.776) p53 93%, 60 p53 (p=0.640).  
 (40 ) p53 (84  
 ) (Fig. 2).  
 Stage 6 3  
 (50%) stage 15 4  
 (27%)  
 (p=0.608)(Table 1). Stage 가 . 20  
 p53 가 (p=0.995). 가  
 46.3, 46.2 가 (p=0.995). 가  
 T stage N stage p53 23)

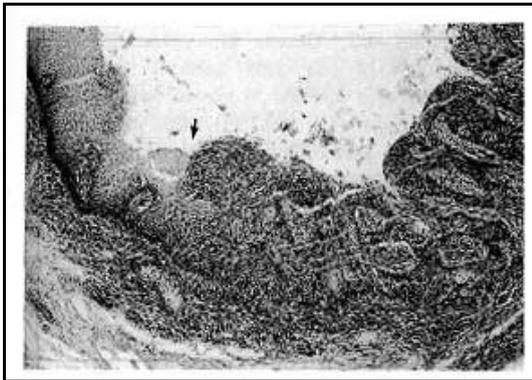


Fig. 1. Immunohistochemical staining for p53 in supraglottic cancer. p53 staining shows marked differences between neoplastic tissue and normal epithelium (arrow) (x 200).

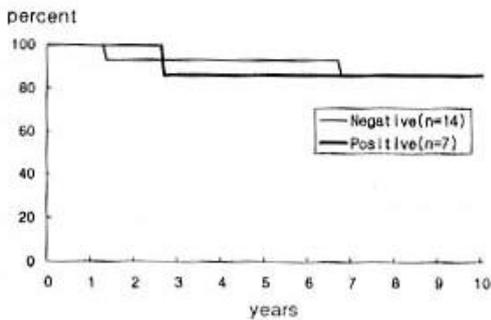


Fig. 2. p53 expression and survival. There was no statistically significant difference between p53 negative and positive groups (p=0.776).

p53 p53  
 24) p53

Table 1. p53 Expression and Clinical Parameters

	p53		p value
	( - )	( + )	
Stage	3	3	0.608
	11	4	
T stage			
1-2	6	4	0.877
3-4	8	3	
N stage			
0-1	5	3	0.874
2-3	9	4	
No. of LNs			
0-3	12	4	0.365
> 4	2	3	
Age			
< 59	7	5	0.64
> 60	7	2	

Brennan <sup>29)</sup> p53

25-28) p53

50% (positive margin) p53

p53 가 , p53

33-100% p53 가 , 11, 30-33) , 가 가

21 가 p53 , p53

8, 34) , p53

21 가 , p53

P53 , T , N , 가 p53

1. **Jacobs C.** The internist in the management of head and neck cancer. *Ann Intern Med* 1990; 113(10):771-778
2. **Boring CC, Squires TS, Tong T, et al.** Cancer statistics, 1994. *CA Cancer J Clin* 1994; 44(1):7-26
3. **Vokes EE, Weichselbaum RR, Lippman SM, et al.** Head and neck cancer. *N Engl J Med* 1993; 328(3):184-194
4. **Pinborg JJ.** Control of oral cancer in developing countries. *Bull WHO* 1984; 62:817-839
5. **Hollstein M, Sidransky D, Vogelstein B, et al.** p53 mutations in human cancers. *Science* 1991; 253(5015):49-53
6. **Levine AJ, Momand J, Finlay CA, et al.** The p53 tumour suppressor gene. *Nature* 1991; 351(6326):453-456
7. **Brachman DG, Graves D, Vokes E, et al.** Occurrence of p53 gene deletions and human papilloma virus infection in human head and neck cancer. *Cancer Res* 1992; 52(17):4832-4836
8. **Field JK, Spandidos DA, Malliri A, et al.** Elevated P53 expression correlates with a history of heavy smoking in squamous cell carcinoma of the head and neck. *Br J Cancer* 1991; 64(3):573-577
9. **Field JK, Pavelic ZP, Spandidos DA, et al.** The role of the p53 tumor suppressor gene in squamous cell carcinoma of the head and neck. *Arch Otolaryngol Head Neck Surg* 1993; 119(10): 1118-1122
10. **Somers KD, Merrick MA, Lopez ME, et al.** Frequent p53 mutations in head and neck cancer. *Cancer Res* 1992; 52(21):5997-6000
11. **Watling DL, Gown AM, Coltrera MD.** Overexpression of p53 in head and neck cancer. *Head Neck* 1992; 14(6):437-444
12. **Dolcetti R, Doglioni C, Maestro R, et al.** p53 over-expression is an early event in the development of human squamous-cell carcinoma of the larynx: genetic and prognostic implications. *Int J Cancer* 1992; 52(2):178-182
13. **Levine AJ, Momand J, Finlay CA.** The p53 tumour suppressor gene. *Nature* 1991; 351(6326):453-456
14. **Lane DP.** p53, guardian of the genome. *Nature* 1992; 358(6381):15-16
15. **Sidransky D, Mikkelsen T, Schwechheimer K, et al.** Clonal expansion of p53 mutant cells is associated with brain tumour progression. *Nature* 1992; 355(636)

3):846-847

16. **Lane DP** **Cancer**. A death in the life of p53 *Nature*. 1993; 362(6423):786-787
17. **Brachman DG, Beckett M, Graves D, et al.** p53 mutation does not correlate with radiosensitivity in 24 head and neck cancer cell lines. *Cancer Res* 1993; 53(16):3667-3669
18. **Clark AR, Purdie CA, Harrison DJ, et al.** Thymocyte apoptosis by P53-dependent and independent pathways. *Nature* 1993; 362:849-852
19. **Chiarugi V, Magnelli L, Cinelli M, et al.** Dominant oncogenes, tumor suppressors, and radiosensitivity. *Cell Mol Biol Res* 1995; 41(3):161-166
20. **Lowe SW, Schmitt EM, Smith SW, et al.** p53 is required for radiation-induced apoptosis in mouse thymocytes. *Nature* 1993; 362(6423):847-849
21. **Kastan MB, Onyekwere O, Sidransky D, et al.** Participation of p53 protein in the cellular response to DNA damage. *Cancer Res* 1991; 51:6304-6311
22. **Kastan MB, Zhan Q, el-Deiry WS, et al.** A mammalian cell cycle checkpoint pathway utilizing p53 and GADD45 is defective in ataxia-telangiectasia. *Cell* 1992; 71(4):587-597
23. **Haffty BG, Son YH, Sasaki CT, et al.** Mitomycin C as an adjunct to postoperative radiation therapy in squamous cell carcinoma of the head and neck: results from two randomized clinical trials. *Int J Radiat Oncol Biol Phys* 1993; 27(2):241-250
24. **Hall PA, Lane DP.** p53 in tumour pathology: can we trust immunohistochemistry?-Revisited!. *J Pathol* 1994; 172(1):1-4
25. **Allred DC, Clark GM, Elledge R, et al.** Association of p53 protein expression with tumor cell proliferation rate and clinical outcome in node-negative breast cancer. *J Natl Cancer Inst* 1993; 85(3): 200-206
26. **Harris CC, Hollstein M.** Clinical implications of the p53 tumor-suppressor gene *N Engl J Med* 1993; 329(18):1318-1327
27. **Iwaya K, Tsuda H, Hiraide H, et al.** Nuclear p53 immunoreaction associated with poor prognosis of breast cancer. *Jpn J Cancer Res* 1991; 82(7):835-840
28. **Marchetti A, Buttitta F, Merlo G, et al.** p53 alterations in non-small cell lung cancers correlate with metastatic involvement of hilar and mediastinal lymph nodes. *Cancer Res* 1993; 53(12):2846-2851
29. **Brennan JA, Mao L, Hruban RH, et al.** Molecular assessment of histopathological staging in squamous-cell carcinoma of the head and neck. *N Engl J Med* 1995; 332(7):429-435.
30. **Brachman DG, Graves D, Vokes E, et al.** Occurrence of p53 gene deletions and human papilloma virus infection in human head and neck cancer. *Cancer Res* 1992; 52(17):4832-4836
31. **Boyle JO, Hakim J, Koch W, et al.** The incidence of p53 mutations increases with progression of head and neck cancer. *Cancer Res* 1993; 53(19):4477-4480
32. **Pavelic ZP, Gluckman JL, Gapany M, et al.** Improved immunohistochemical detection of p53 protein in paraffin-embedded tissues reveals elevated levels in most head and neck and lung carcinomas : correlation with clinicopathological parameters. *Anticancer Res* 1992; 12(5):1389-1394
33. **Somers KD, Merrick MA, Lopez ME, et al.** Frequent p53 mutations in head and neck cancer. *Cancer Res* 1992; 52(21):5997-6000
34. **Field JK, Spandidos DA, Stell PM.** Overexpression of p53 gene in head-and-neck cancer, linked with heavy smoking and drinking. *Lancet* 1992; 339(8791):502-503

= =

p53

: p53 가

21

antihuman monoclonal p53 antibody

: 3 6 3 가 4 15 4

( $p=0.608$ ). p53

5 93% 86%

( $p=0.776$ ). p53

( $p=0.64$ ), T stage( $p=0.877$ ), N stage( $p=0.874$ )

: p53

p53