

\* , † , ‡  
\* † ‡ \* †

60.8 Gy	73.8 Gy (cisplatin)	68.6 Gy (cisplatin)	1.75 Gy bleomycin	2.0 Gy vinblastin	5-FU	cisplatin
3	7	134	6	2	24	32
66%	43%	5	12	38%	19	59%
		75%	19	가	8	가
		8	2			6
		5	60%, 35.1%, 50%		5	
		(p=0.93).	가			(p<0.01).
		73.3%, 14.7%				
		(CR vs. PR, p<0.01).				
		가				가

가

가

가

1991 The Department of Veterans Affairs (VA) Laryngeal Cancer Study Group 332

가

pyriform sinus, hypopharyngeal

2

wall, postcricoid area

가 (p=0.9846),

가

2000 6 24

2000 11 6

Tel: 02)760-3177, Fax: 02)765-3317  
E-mail: wuhg@snu.ac.kr

가

3 :

7, 8)

29 ,

2 , 가 1 .  
Co-60 4 MV 6 MV 가  
1.75 2.0 Gy 5  
60.8 73.8 Gy ( 68.6 Gy)

45 Gy

1979 8 1

60 Gy . 26

1997 7 31

37.8 45.0 Gy (

46

42.9 Gy)

1992 AJCC III

IV

9)

9-12 MeV 9 18 Gy ( 16.5 Gy)

가

1 ,

가

29

cisplatin (100 mg/

2 ,

60 Gy

10 ,

m<sup>2</sup>, on Day 1) 5-FU (1,000 mg/m<sup>2</sup>, on Day 1 5)

24

1

32

가 cisplatin

bleomycin (15 mg/m<sup>2</sup>)

vinblastin (1 mg/m<sup>2</sup>)

가

(75%)

3

3

, 6

2 , 2

1

3

2

29 79 ( 57 )

가 2

29:3 (Table 1).

AJCC

III 가 4 ,

,

가

가 5 ,

IV 가 28

. T

N

Table 2

가 1

2 4

Table 1. Patient Characteristics

Characteristics	No.
Age (years)	
Range	29 79
Median	57
Sex	
Male	29
Female	3
Performance	
0 1	27
2 4	5
Stage	
III	4
IV	28
Primary site	
Pyriform sinus	29
Posterior pharyngeal wall	1
Postcricoid area	1
Not specified	1
Histology	
Squamous cell carcinoma	29
Undifferentiated carcinoma	2
Poorly differentiated adenocarcinoma	1

Table 2. T and N Stages (n=32)

	T1	T2	T3	T4	Total
N0	-	-	2	2	4
N1	-	1	1	2	4
N2a	-	1	2	3	6
N2b	-	1	5	3	9
N2c	-	-	1	3	4
N3	1	1	2	1	5
Total	1	4	13	14	32

가 2 2  
4 6  
7 134  
28  
(Kaplan-Meier method)  
Cox regression analysis  
log-rank test  
5 60%, 35.1%, 50%  
5  
( $p=0.93$ ).  
5  
가 0.69,  
5  
0.74  
2 5 65.6%, 43.0  
% , 35 . 2 5  
40.6%, 30.7% (Fig. 1).  
32  
가 24  
75% . 5 (16%) , 19 (59%)  
, 8 (25%)  
19 가 8  
8 2  
6

(Table 3).

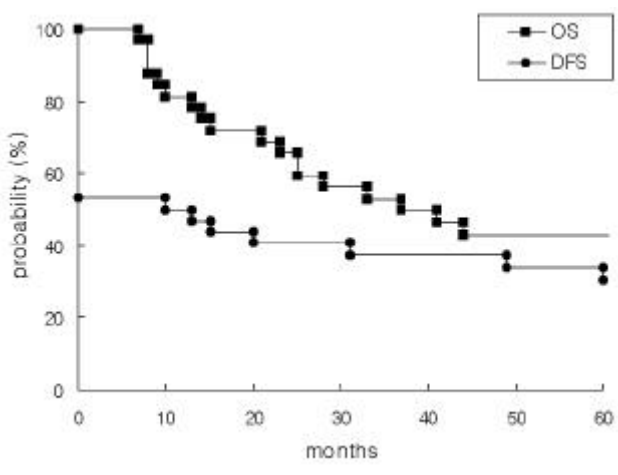


Fig. 1. Overall survival and disease-free survival curves. OS : overall survival, DFS : disease-free survival

(stage III vs. IV)  
Table 4  
가 가  
Ridit (relative to an indentified distribution)  
Mantel-Haenszel Chi-square (Ridit scores) 7.419  
probability 0.006  
가

5 60%, 35.1%, 50%  
5  
( $p=0.93$ ).  
5  
가 0.69,  
5  
0.74  
p-value  
p-value

Table 3. Response to Each Treatment in Induction Chemotherapy and Radiotherapy

CRx <sup>+</sup> Response	RT <sup>+</sup> Response	
	CR	PR
CR <sup>+</sup> ( 5)	5	0
PR <sup>§</sup> (19)	8	11
NR ( 8)	2	6
Total (32)	15	17

<sup>+</sup> Chemotherapy, <sup>†</sup> Radiotherapy, <sup>‡</sup> Complete response, <sup>§</sup> Partial response, No response

Table 4. Tumor Stages vs. Response to Neoadjuvant Chemotherapy

Response to Chemotherapy	Stage III	Stage IV
CR <sup>+</sup>	3	2
PR <sup>†</sup>	1	18
NR <sup>‡</sup>	0	8

<sup>+</sup> Complete response, <sup>†</sup> Partial response, <sup>‡</sup> No response

Table 5. Overall Survival According to Response to Each Treatment

CTx <sup>+</sup> Response	Survival	RT <sup>+</sup> Response	Survival
CR <sup>+</sup>	60.0%	CR	73.3%
PR <sup>§</sup>	35.1%	PR	14.7%
NR	50.5%		( $p=0.0001$ )
	( $p=0.93$ )		

<sup>+</sup> Chemotherapy, <sup>†</sup> Radiotherapy, <sup>‡</sup> Complete response, <sup>§</sup> Partial response, No response

Table 6. Failure Patterns According to Response to Treatment

Response to CTx/ RT	LR*	DM†	LR+DM
CR/ CR (5)	2	0	0
PR/ CR (8)	4	0	0
NR/ CR (2)	0	0	0
PR/ PR (11)	-	2	0
NR/ PR (6)	-	0	0

\* loco-regional failure, † distant metastasis

Table 7. Chemotherapy-Related Toxicity (WHO criteria)

	Grade 1	Grade 2	Grade 3
Hematologic			
WBC	9	3	0
Platelet	2	1	1
Hemoglobin	6	2	0
Nausea/ Vomiting	8	5	1
Diarrhea	2	1	0
Heart†	0	1	0
Lung†	0	0	1

† Palpitation, † Respiratory failure

Table 8. Prognostic Factors for Overall Survival

Prognostic factors	Univariate analysis	Multivariate analysis
Age	0.96	
Performance	0.21	0.45
Stage	0.77	0.99
T stage	0.99	
N stage	0.01	0.99
No. of chemotherapy cycle	0.87	
Chemotherapy response	0.93	0.39
Radiotherapy response	0.0001	0.007

2

Table 8

(CR vs. PR,  $p < 0.01$ ) (65 vs. >65), (ECOG 0-1 vs. 2-4), (III vs. IV), (1 vs. 2, 3),

(0, 1 vs. 2, 3) log-rank test ( $p=0.01$ )

가 Cox regression analysis ( $p=0.99$ ).

(AJCC I-II)

<sup>10-13</sup>

(AJCC III-IV)

5 73.3%, 14.7% ( $p < 0.01$ , Table 5).  
 , 15 6 (40%) 가  
 , 3 , 2 가 6  
 , 1 가 6 4 , 2  
 . 가 17  
 2 가  
 32 6% (2/32) (Table 6). 50 80% ,<sup>14-16</sup> 20 30%  
<sup>17-20</sup>  
 가 1 ,  
 가 1 ,  
 가 2 . 32 ,  
 12 (38%) 5 ,<sup>21-24</sup> 가  
 88 ,  
 가 ,  
 가 (Table 7).<sup>25-28</sup>

Cisplatin Cisplatin  
 Cisplatin 5-FU  
 가  
 가

가 , 가 가 .

29, 30) . 가 가

AJCC III 가 4 , IV 가 28 , 가 가

IV 가

16% (5/32) , 가 가

5 가 60%, 35.1% 가 가 .<sup>37)</sup> 가

8 2 .

5 5

50% 가 , ,

가 가

가

가

1980 methotrexate,

<sup>31-35)</sup> 5-FU, bleomycin, cisplatin, carboplatin 가 가

가 가

가

가 가

Cisplatin/5-FU

가

1. **The Department of Veterans Affairs Laryngeal Cancer Study Group.** Induction chemotherapy plus radiation compared with surgery plus radiation in patients with advanced laryngeal cancer. *N Engl J Med* 1991;324:1685-1690
2. **Zelesky MJ, Kraus DH, Pfister DG et al.** Combined chemotherapy and radiotherapy versus surgery and post-operative radiotherapy for advanced hypopharyngeal cancer. *Head and Neck* 1996;18:405-411
3. **Salvajoli JV, Morioka H, Trippe N, Kowalski LP.** A randomized trial of neoadjuvant vs concomitant chemotherapy vs radiotherapy alone in the treatment of stage IV head and neck squamous cell carcinoma. *Eur Arch Otorhinolaryngol* 1992;249:211-215
4. **Dimery IW, Hong WK.** Overview of combined modality therapies for head and neck cancer. *J NCI* 1993;85:95-111
5. **Forastiere AA.** Randomized trials of induction chemotherapy: A critical review. *Hemtol Oncol Clin North Amer* 1991;5:725-736
6. **Lefebvre JL, Chevalier D, Lubinski B, Kirkpatrick A, Collette L, Sahnoud T.** Larynx preservation in pyriform sinus cancer: preliminary results of a European Organization for Research and Treatment of Cancer phase III trial *J NCI* 1996;88:890-899
7. **Shirinian MD, Weber RS, Lippman SM et al.** Laryngeal preservation by induction chemotherapy plus radiotherapy in locally advanced head and neck cancer: the MDAnderson cancer center experience. *Head and Neck* 1994;16:39-44
8. **Kraus DH, Pfister DG, Harrison LB et al.** Larynx pre-

- servation with combined chemotherapy and radiation therapy in advanced hypopharynx cancer. *Otolaryngol Head Neck Surg* 1994;111:31-37
9. **Hypopharynx.** In: **Beahrs, O, Henson, D., Hutter, R., Kennedy, B., eds.** American Joint Committee on Cancer Manual for staging of cancer. Philadelphia: J.B. Lippincott. 1993. P.31-36
  10. **Barkley HT Jr, Fletcher GH, Jesse RH Lindberg RD.** Management of cervical lymph node metastases in squamous cell carcinoma of the tonsillar fossa, base of tongue, supraglottic larynx and hypopharynx. *Am J Surg* 1972;124:462-467
  11. **Fletcher GH, Jesse RH.** The place of irradiation in the management of the primary lesion in head and neck cancer. *Cancer* 1977;39:862-867
  12. **Million R, Cassisi N.** Radical irradiation for carcinoma of the pyriform sinus. *Laryngoscope* 1981;91:439-450
  13. **Mendenhall W, Parsons J, Devine J.** Squamous cell carcinoma of the pyriform sinus treated with surgery and/or radiotherapy. *Head and Neck* 1987;10:88-92
  14. **Suen JY, Newman RK, Hannahs K, Fisher J.** Evaluation of the effectiveness of postoperative radiation therapy for the control of local disease. *Am J Surg* 1980;140:577-579
  15. **Jaram B, Strong EW, Shah J et al.** Postoperative radiation therapy in Stages III and IV epidermoid carcinoma of the head and neck. *Am J Surg* 1980;149:580-584
  16. **Wawro NN, Babcock A, Ellison L.** Cancer of the tongue: Experience at the Hartford Hospital from 1931 to 1963. *Am J Surg* 1970;110:455-461
  17. **Meoz-Mendez RT, Fletcher GH, Guillaumondegui OM, Peters LJ.** Analysis of the results of irradiation in the treatment of squamous cell carcinomas of the pharyngeal walls. *Int J Radiat Oncol Biol Phys* 1978;4:579-585
  18. **Byers RM, Krueger WWO, Sacton J.** Use of surgery and postoperative radiation in the treatment of advanced squamous cell carcinoma of the pyriform sinus. *Am J Surg* 1979;138:597-599
  19. **Mesic JV, Fletcher GH, Goepfert H.** Megavoltage irradiation of epithelial tumors of the nasopharynx. *Int J Radiat Oncol Biol Phys* 1981;7:447-453
  20. **Kalnins IK, Leonad AG, Sako K, Razack MS, Shedd DP.** Correlation between prognosis and degree of lymph node involvement in carcinoma of the oral cavity. *Am J Surg* 1977;134:450-454
  21. **Weaver A, Fleming S, Ensley J, Kish JA, Jacobs J, Kinzie J, Crissman J, Al-Sarraf M.** Superior complete clinical response and survival rates with initial bolus cisplatin and 120 hour 5-FU infusion before definitive therapy in patients with locally advanced head and neck cancer. *Am J Surg* 1984;148:525-530
  22. **Al-Sarraf M, Drelichman A, Peppard S et al.** Adjuvant cis-platinum and 5-fluorouracil 96 hour infusion in previously untreated epidermoid cancers of the head and neck. *Proc Am Soc Clin Oncol* 1981;22:428
  23. **Kish J, Drelichman A, Jacobs J et al.** Clinical trial of cisplatin and 5-fluorouracil infusion as initial treatment for advanced squamous cell carcinoma of the head and neck. *Cancer Treat Rep* 1982;66:471-474
  24. **Weaver A, Fleming S, Kish J, Vandenberg H, Jacob J, Crissman J, Al-Sarraf M.** Cisplatin and 5-Fluorouracil as induction therapy for advanced head and neck cancer. *Am J Surg* 1982;144:445-448
  25. **Al-Kourainy K, Kish J, Ensley J et al.** Achievement of superior survival for histologically negative versus histologically positive clinically complete responders to cisplatin combination chemotherapy in patients with locally advanced head and neck cancer. *Cancer* 1987;59:233-238
  26. **Jacobs JR, Pajak TF, Kinzie J et al.** Induction chemotherapy in advanced head and neck cancer. *Arch Otolaryngol Head Neck Surg* 1987;113:193-197
  27. **Mercier RJ, Neal D, Mattox DE, Gates GA, Pomeroy TC, Von Hoff DD.** Cisplatin and 5-fluorouracil chemotherapy in advanced or recurrent squamous cell carcinoma of the head and neck. *Cancer* 1987;60:2609-2612
  28. **Kies M, Kraut M, Gordon L et al.** Improved survival and pretreatment characteristics of complete responders to combination chemotherapy in advanced head and neck cancer (Abstr). *Proc Am Soc Clin Oncol* 1983;2:626
  29. **Taylor SG IV, Applebaum E, Showel JL et al.** A randomized neoadjuvant chemotherapy in head and neck cancer. *J Clin Oncol* 1985;3:672-679
  30. **Schuller DE, Metch B, Stein DW, Mattox D, McCracken JD.** Preoperative chemotherapy in advanced head and neck cancer. Final report of the Southwest Oncology Group. *Laryngoscope* 1988;98:1205-1211
  31. **Petrovich Z, Block J, Kuisk H, Mackintosh R, Casciato D, Rose L, Barton R.** A randomized comparison of radiotherapy with a radiotherapy-chemotherapy combination in stage IV carcinoma of the head and neck. *Cancer* 1981;47:259-2264
  32. **Stell PM, Dalby JE, Strickland P, Fraser JG, Bradley PJ, Flood LM.** Sequential chemotherapy and radiotherapy in advanced head and neck cancer. *Clin Radiol* 1983;34:463-67
  33. **Shetty P, Mehta A, Shinde S et al.** Controlled study in squamous cell carcinoma of base of the tongue using conventional radiation, radiation with single drug and radiation with multiple drug chemotherapy. *Proc Am Soc Clin Oncol* 1985;4:152
  34. **Jaulerry C, Rodriguez J, Braun F et al.** Induction chemotherapy in advanced head and neck tumors: results of two randomized trials. *Int J Radiat Oncol Biol Phys* 1992;23:83-89
  35. **Merlano M, Rosso R, Benasso M et al.** Alternating chemotherapy and radiotherapy vs. radiotherapy in advanced inoperable SCCHN: A cooperative randomized trial. *Proc Am Soc Clin Oncol* 1991;10:198
  36. **Harari PM.** Why has induction chemotherapy for advanced

head and neck cancer become a United States community standard of practice? J Clin Oncol 1997;15:2050-2055

37. Koch WM, Lee DJ, Eisele DW et al. Chemoradiotherapy for organ preservation in oral and pharyngeal carcinoma. Arch Otolaryngol Head Neck Surg 1995;121:974-980

---

**Abstract**

---

**Noadjuvant Chemotherapy and Radiotherapy in Locally Advanced Hypopharyngeal Cancer**

Suzy Kim, M.D.<sup>\*</sup>, Hong-Gyun Wu, M.D.<sup>\*†</sup>, Dae-Seog Heo, M.D.<sup>†</sup> and Charn Il Park, M.D.<sup>\*‡</sup>

<sup>\*</sup>Department of Therapeutic Radiology, <sup>†</sup>Internal Medicine, Seoul National University College of Medicine

<sup>‡</sup>Institute of Radiation Medicine, Medical Research Center, Seoul National University Seoul, Korea

**Purpose:** To see the relationship between the response to chemotherapy and the final outcome of neoadjuvant chemotherapy and radiotherapy in patients with locally advanced hypopharyngeal cancer.

**Methods and Materials:** A retrospective analysis was done for thirty-two patients with locally advanced hypopharyngeal cancer treated in the Seoul National University Hospital with neoadjuvant chemotherapy and radiotherapy from August 1979 to July 1997. The patients were treated with Co-60 teletherapy unit or 4MV or 6MV photon beam produced by linear accelerator. Daily fractionation was 1.75 to 2 Gy, delivered five times a week. Total dose ranged from 60.8 Gy to 73.8 Gy. Twenty-nine patients received continuous infusion of cisplatin and 5-FU. Other patients were treated with cisplatin combined with bleomycin or vinblastin. Twenty-four (75%) patients received all three prescribed cycles of chemotherapy delivered three weeks apart. Six patients received two cycles, and two patients received only one cycle.

**Results:** The overall 2-year and 5-year survival rates are 65.6% and 43.0%, respectively. 5-year local control rate is 34%. Organ preservation for more than five years is achieved in 12 patients (38%). After neoadjuvant chemotherapy, 24 patients achieved more than partial remission (PR); the response rate was 75% (24/32). Five patients had complete remission (CR), 19 patients PR, and 8 patients no response (NR). Among the 19 patients who had PR to chemotherapy, 8 patients achieved CR after radiotherapy. Among the 8 non-responders to chemotherapy, 2 patients achieved CR, and 6 patients achieved PR after radiotherapy. There was no non-responder after radiotherapy. The overall survival rates were 60% for CR to chemotherapy group, 35.1% for PR to chemotherapy group, and 50% for NR to chemotherapy group, respectively ( $p=0.93$ ). There were significant difference in five-year overall survival rates between the patients with CR and PR after neoadjuvant chemotherapy and radiotherapy (73.3% vs. 14.7%,  $p<0.01$ ). The prognostic factor affecting overall survival was the response to overall treatment (CR vs. PR,  $p<0.01$ ).

**Conclusion:** In this study, there were only five patients who achieved CR after neoadjuvant chemotherapy. Therefore the difference of overall survival rates between CR and PR to chemotherapy group was not statistically significant. Only the response to chemo-radiotherapy was the most important prognostic factor. There needs to be more effort to improve CR rate of neoadjuvant chemotherapy and consideration for future use of concurrent chemoradiotherapy.

---

**Key Words:** Hypopharyngeal cancer, Radiation therapy, Neoadjuvant chemotherapy