A Comparision of Radiotherapy Alone with Induction Chemotherapy-Radiotherapy in Inoperable Head and Neck Cancer

In Kyu Park, M.D., Sang Mo Yun, M.D., Sang Bo Kim, M.D.
Samuel Ryu, M.D. and Jun Sik Park, M.D.*

*Department of Radiation Oncology, Department of Otolaryngology**
School of Medicine, Kyungpook National University, Taegu, Korea

In order to determine the value of induction chemotherapy (CT) for inoperable head and neck cancer, the authors conducted a retrospective study. Fifty-five patients were treated with CT and radiotherapy (RT) (CT+RT group). This group was compared with a group of 54 patients treated RT alone (RT alone group). The CT regimen used were CF (cis-platine + 5-FU), CVB (cyclophosphamide + vincristine + bleomycin), CAP (cyclophosphamide + adriamycin + prednisolone) or PVBM (cis-platine + vincristine + bleomycin + methotrexate). Toxicity from induction chemotherapy was minimal, and toxicity was limited primarily to nausea and vomiting, mucositis and myelosuppression.

The complete response (CR) rate to CT was 14.5% and the partial response (PR) rate was 47.3% for an overall major response rate of 61.8%. The major response rate at the completion of loco-regional therapy was 87.3% (48/55) with 32 CR (58.2%) and 16 PR (29.1%) for CT-RT group and 81.5% (44/55) with 27 CR (50.0%) and 17 PR (31.5%) for RT alone group ($p=0.57$).

Median follow-up of CT-RT group was 17 months and 11 months for RT alone group. Median survival was 36 months for CT-RT group and 24 months for RT alone group ($p=0.3$). The overall survival rate at 2 years, 3 years and 5 years, respectively was 60.9%, 48.6% and 42.5% for CT-RT group, and 54.9%, 49.9% and 49.9% for RT alone group ($p=0.33$).

Comparision between patients in both groups, stratified by overall stage, T and N stage, site, and pathology, all failed to show any significant difference in survival rates. We conclude that this retrospective study failed to demonstrate an advantage for induction chemotherapy in inoperable head and neck cancer.

Key Words: Head and Neck cancer, Induction chemotherapy, Radiotherapy

INTRODUCTION

The treatment of head and neck cancer is usually surgery and/or radiation therapy. This is especially true for the early lesions of head and neck, where a 70~90% cure rate can be expected[1,2]. However, the results of the standard therapy of patients with locally advanced lesions, particularly unresectable or inoperable, remains unsatisfactory[3,4]. Despite advances in surgery and radiation therapy techniques, those patients manifest a two-year disease-free survival of only 15~30%[4].

Attempts to improve tumor control rates utilizing radiation therapy under using hyperbaric oxygen, hyperfractionation and combined radiation therapy and definitive surgery have had limited impact on overall survival[4~8].

This unfavorable results, combined with the functional and cosmetic disabilities with treatment and/or local tumor recurrence, have led to the investigation of the addition of induction chemotherapy to combined modality program[9]. The concept of giving induction chemotherapy prior to definitive local therapy for locally advanced head and neck cancer is attractive for a number of theoretical reasons[4,10~12].; (1) improved tumor vascularity and better drug delivery, (2) optimal nutritional performans status, (3) destruction of rapidly growing malignant cells, (4) conversion of a primary unresectable lesion into a potentially resectable one, and (5) possible erradication of subclinical distant metastasis.

Many non-randomized studies of induction chemotherapy with radiation therapy showed improvement in response and survival compared with historical controls treated by radiation therapy alone in inoperable head and neck cancer[13~15].

However, several randomized studies indicated that although response rates were increased with addition of induction chemotherapy, there was no difference in survival when compared to radiation threrapy alone in inoperable head and neck cancers[13~15]. We report a non-randomized retrospective study to evaluate the role of induction chemotherapy before radiation therapy in the treatment of inoperable, previously untreated head and neck cancers.

MATERIALS AND METHODS

Between March, 1985 and October, 1990, 109 patients with inoperable head and neck cancer were treated in our hospital. All patients were previously untreated, histologically proven cancer of head and neck region. All patients had measurable local disease without distant metastasis. Patients with multiple tumors or treated with a palliative intent were excluded. Criteria for inoperability were (1) technical unresectability, (2) physician selection based on lower surgical curability and/or high functional disability, (3) medical contra-indication to surgery and (4) undifferentiated histology. Patients were staged according to criteria recommended by the American Joint Committee for Cancer Staging[16].

Performans status was graded by the Eastern Cooperative Oncology Group (ECOG) scale from 0 to 4. Initial examination of each patient included history, physical examination, complete blood cell count (CBC), routine chemistry, chest x-ray, bone scan, CT scan of head and neck and panendoscopy. One hundred and nine patients divided into two groups were evaluated for this retrospective study. In CT+RT group, 55 patients were treated by induction chemotherapy followed by radiotherapy. This group was compared with RT Group of 54 patients treated by radiotherapy alone.

1. Treatment Methods

All the patients were treated either by chemotherapy and radiotherapy or by radiotherapy alone.

2. Chemotherapy

CT-RT group patients received one of four possible induction chemotherapy regimens from 1 to 4 cycles; (1) CVB (2) CF (3) CAP or (4) PVBM. Two main combination were applied. The 32 patients received CVB; cisplatin (80 mg/m^2) on day 1, Vincristine (1.4 mg/m^2) on day 2 and Bleomycin 10 mg from day 2 to day 3, and 21 patients received CF; cisplatin (100 mg/m^2) on day 1 and day 3 and 5-FU 1000 mg/m^2 infusion for 24 hours on day 2 and day 4. Cycles were repeated every 3 weeks for 2 to 4 cycles. Two patients who received CAP or PVBM were referred to radiation oncology department from community hospital for radiotherapy. CAP consisted of cyclophosphamide, adriamycin and prednisolone, and PVBM consisted of cisplatin, vincristine, bleomycin and methotrexate.

3. Radiotherapy

Radiotherapy was started 2 weeks after completion of induction chemotherapy. External radiotherapy alone was the most widely used treatment technique. Radiotherapy was also used in persistent disease after external radiotherapy. Radiotherapy portals included all known areas of gross disease with proper margins to encompass microscopic disease. Lower neck irradiated if involved or prophylactically when microscopic invasion was probable. All patients received 180~200 cGy/day, five times a week using 6MV X-ray with or without 8-10 MV electron. 6000~7500 cGy were delivered to the regions of the primary tumor bed and the involved neck disease, and 4500~5000 cGy were delivered to clinically uninvolved neck.

The response status of the patients was assessed at two points. Within two weeks of completing induction chemotherapy, CT+RT group patients were evaluated to determine chemotherapy response and at 4 weeks following radiotherapy another evaluation was undertaken to assess response. A complete response (CR) was defined as complete disappearance of all clinically detectable disease and partial response (PR) was defined as a greater than 50% reduction in the production of perpendicular diameters of all measurable disease.

No response (NR) was defined as a less than 50% reduction in the product of the perpendicular diameter of any measurable disease. All the patients have been followed up either by personal contact or by information from city-office.

The end points of this study were response and overall survival. Comparision of response and survival among the different patients group were evaluated by the Peto-Wilcoxon test in univariate analysis and Cox's regression proportional hazards model in multivariate analysis[17]. The survival curves were estimated by Kaplan-Meier method[17]. All these analysis were done with the EPILOG PLUS software package (EPICENTER SOFTWARE, Pasadena, CA, USA)[18]. Survival was measured in

month from the day of diagnosis. The results were considered significant when P value was ≤ 0.05.

RESULTS

1. Patients Characteristics

The patients characteristics are summarized in Table 1. The median age was 51 years in CT+RT group and 58 years in RT alone group. The majority patients (77%) were male. The performance status was similar in the both group. Most patients had a performance status of 0(86%) or 1(12%) and only two patients had a performance status of 2. Eighty-nine patients had squamous cell carcinoma, 14 patients had undifferentiated carcinoma, 4 patients had adenoid cystic carcinoma and 2 patients had mucoepidermoid carcinoma.

Table 1. Patients Characteristics

Characteristics	CT+RT	RT alone
No. of patients	55	54
Age (in year)		
Median	51	58
Range	26–78	21–76
Sex		
Male	44	40
Female	11	14
Performance status (ECOG)		
0	47	47
1	7	6
2	1	1
Pathology		
Squamous	43	46
Undifferentiated	12	2
Mucoepidermoid	0	2
Adenoid Cystic	0	4
Primary Site		
Nasopharynx	23	8
Oral Cavity	5	16
Oropharynx	18	11
Hypopharynx	5	5
Paranasal sinus	4	14
Stage of disease		
I	0	4
II	3	8
III	7	19
IV	45	23

CT : Chemotherapy, RT : Radiotherapy

The site of the primary disease are also listed in Table 1. The site was the nasopharynx in 28.5%, oropharynx in 26.6%, oral cavity in 19.3%, paranasal sinus in 16.5% and hypopharynx in 9.1% of patients. Most patients had stage IV(62.4%) or stage III(23.9%). The patients distribution according to the TNM classification is listed in Table 2.

2. Response

The overall response to chemotherapy was evaluated within 2 weeks after the completion of chemotherapy, just prior to radiotherapy and response to radiotherapy was evaluated at 4 weeks after radiotherapy. Overall response rate to induction chemotherapy was analyzed in 55 patients. For the patients in the CT+RT group, the CR rate to induction chemotherapy was 14.5% and the PR rate was 47.3% for an overall major response rate of 61.8% (Table 3).

With the chemotherapy regimen associated CVB there was a 75% response rate and 47.2% with CF (Table 4). But, the difference was not statistically significant) $p=0.098$). The response rate to chemotherapy according to tumor variables was analyzed. Overall stage, tumor size, nodal status, primary site and pathology did not affect the response to chemotherapy in statistically significant manner.

The association between initial response to chemotherapy and subsequent response after radiotherapy is summarized in Table 5. Of the 26 patients partially responding to chemotherapy initially, 19 patients (73.1%) achieved CR. Of the 21 patients that failed to respond to initial chemotherapy, 6 patients (28.1%) achieved CR. This association was highly significant ($p=0.0098$). At the com-

Table 2. Patient Distribution by Tumor and Nodal Status

Nodal Status	Tumor Status				
	T1	T2	T3	T4	Tx
CT + RT					
N0	0	4	1	0	0
N1	1	1	1	1	0
N2	2	9	10	6	1
N3	0	10	2	2	1
RT alone					
N0	4	8	9	10	0
N1	2	4	5	2	0
N2	2	2	2	2	0
N3	0	1	1	0	0

Table 3. Response to Induction Chemotherapy

CR	8 (14.5%)	61.8%
PR	26 (47.3%)	
NR	21 (38.2%)	

CR : Complete Response
PR : Partial Response
NR : No Response

Table 4. Response to Induction Chemotherapy According to Regimens

	CR	PR	NR	p value
CVB	7	17	8	
CF	1	9	11	p=0.0982
Others	0	0	2	

Table 5. Correlation Between Response to Induction Chemotherapy and Subsequent Response to Radiotherapy

Initial Response to Chemotherapy		Response to Radiotherapy			
		CR	PR	NR	p value
PR	26	19 (73.1%)	5 (19.2%)	2 (7.7%)	p = 0.0098
NR	21	6 (28.1%)	11 (52.4%)	4 (19.0%)	

Table 6. Response After Radiotherapy According to Treatment Group

	CT + RT	RT alone	p value
CR	32 (58.2%)	27 (50.0%)	
PR	16 (29.1%)	17 (31.5%)	p=0.800
NR	7 (12.7%)	10 (18.5%)	

Table 7. Survival Probability by Treatment Group

Time (month)	CT + RT		RT alone		
	Risk	Proba-bility	Risk	Proba-bility	p value
0	55	1.0000	54	1.0000	1.0000
12	36	0.8323	28	0.7261	0.1115
24	19	0.6093	12	0.5490	0.3050
36	11	0.4862	7	0.4991	0.4602
48	5	0.4254	6	0.4991	0.2915
60	3	0.4254	3	0.4991	0.2915

pletion of radiotherapy, the CR rate was 58.2% and PR rate was 29.1% for the CT+RT group, and CR rate was 50.0% and PR rate was 31.5% for RT alone group (Table 6). The difference in response rate among the different patients group was not significant (p=0.8).

The major response rate at completion of radiotherapy was 87.3% for CT+RT group and 81.5% for RT alone group. There was no statistically significant difference (p=0.05). Chemotherapy was generally well tolerated. The toxicities were predominantly nausea and vomiting, mucositis and myelosuppression. There was two nephrotoxicities and two pulmonary toxicities. There was no drug-related death. Induction chemotherapy did not appear to increase the toxicity of radiotherapy compared to RT alone group.

3. Survival

Median survival was 36 months for CT+RT group and 24 months for RT alone group. The difference was not significant (p=0.3). There was no significant difference in the overall survival rates for the patients in the CT+RT group and RT alone group (p=0.33). The overall survival rates was 60.9% at 24 months, 48.6% at 36 months and 42.5% at 60 months for the CT+RT group, and 54.9%, 49.9% and 49.9% for the RT alone group, respectively (Table 7) (Fig. 1). We then tried to find out if there was a subgroup of patients whose overall survival was increased by chemotherapy.

For the this reason, we analyzed separately results obtained with two groups for all tumor variables. Comparision between patients in both groups, stratified by overall stage, T and N stage, primary site, and pathology, all failed to show any significant difference in survival rates. Only one group of patients with N3 appeared to benefit from chemotherapy in univariate analysis (p=0.043), but there was no significant difference in multivariate analysis (p=0.075) (Fig. 2). Comparison of overall survival rates for the patients whose tumor did not, showed no significant difference (p=0.342) (Fig. 3)

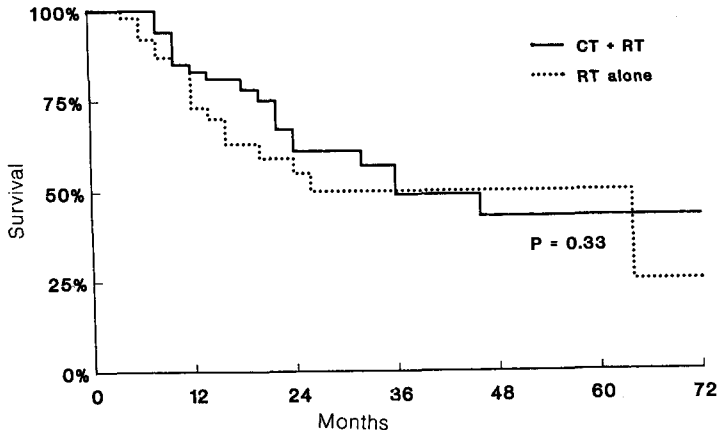

Fig. 1. Overall Survival in the two groups (CT-RT vs. RT alone).

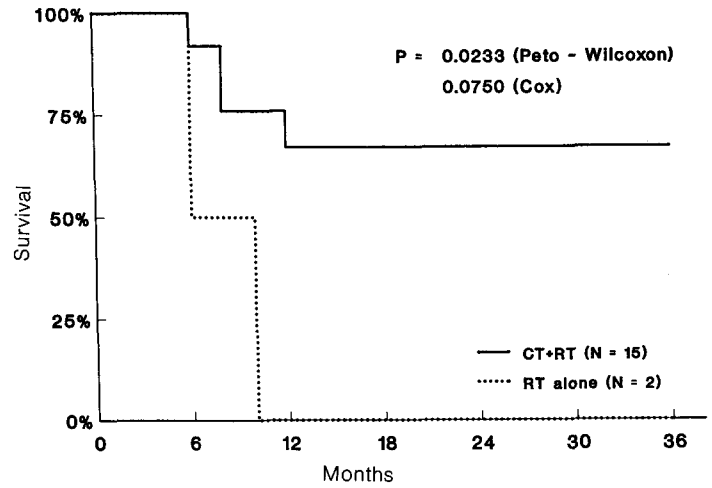

Fig. 2. Survival for N3 patients.

and also survival between patients achieving CR to CTX and patients achieving PR to CTX was not significantly different (p=0.6124) (Fig. 4). There was significant difference in the survival rates of patients treated with CVB regimen compared to patients treated with CF regimen for CT+RT group (p=0.016) (Fig. 5).

DISCUSSION

In patients with unresectable and/or inoperable head and neck cancers, radiotherapy is being used as the standard treatment. It was reported that the rate of loco-regional control obtained by radiotherapy was the most important factor that determined the overall survival of these patients[19]. In spite of the initial good loco-regional control with radiotherapy, local recurrence and/or distant metastasis are still major problems in the majority of these patients.

Therefore, the achievement of a complete remission and long-term disease free survival are the greatest therapeutic challenge in oncology. During last decade, induction CT has been used before radiotherapy and the concept of combining CT and radiotherapy is attractive in treatment of unresectable and/or inoperable head and neck cancers[13~15].

The major objective of the retrospective study was to evaluate the efficiency of induction chemotherapy on response and survival of patients with unresectabvle and/or inoperable head and neck

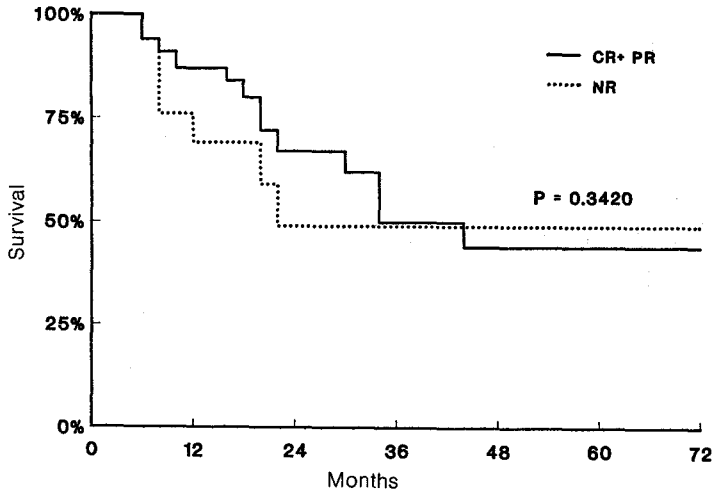

Fig. 3. Survival in patients with CR and PR after induction chemotherapy compared with NR.

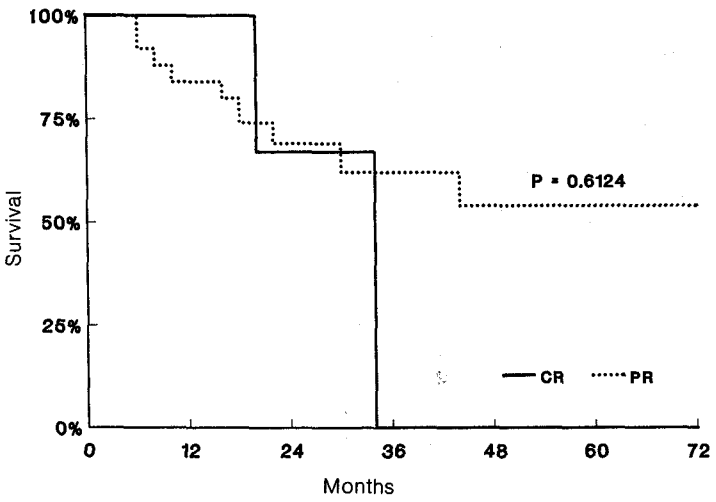

Fig. 4. Survival in patients with CR after induction chemotherapy compared with PR.

cancers. The objective response rate to induction chemotherapy for CT+RT group is 61.8% with 14.5% of patients achieving CR.

These response rate are comparable to those reported by others[13~15]. However, other reports were higher than that reported by here[20]. Possible explanation for this discrepancy include difference in regimens used or difference in extent of disease in treated patients. The initial response to induction chemotherapy predicted the subsequent response to radiotherapy. Other studies noted this association[21].

The patients achieving a PR with CT had a 73% CR after radiotherapy. Conversely, in the group with less than a PR to CT, 28% achieved CR to subsequent radiotherapy. These results indicates that initial objective response to CT benefit from subsequent radiotherapy. Our results suggest that the use of chemotherapy prior to radiotherapy dose not improve the final response rate compared to that seen in radiotherapy alone group. CT+RT group was associated with a 58.2% complete response rate compared to a 50% complete response rate in patients treated with radiotherapy alone. This results of our study do not show that induction chemotherapy improve the final

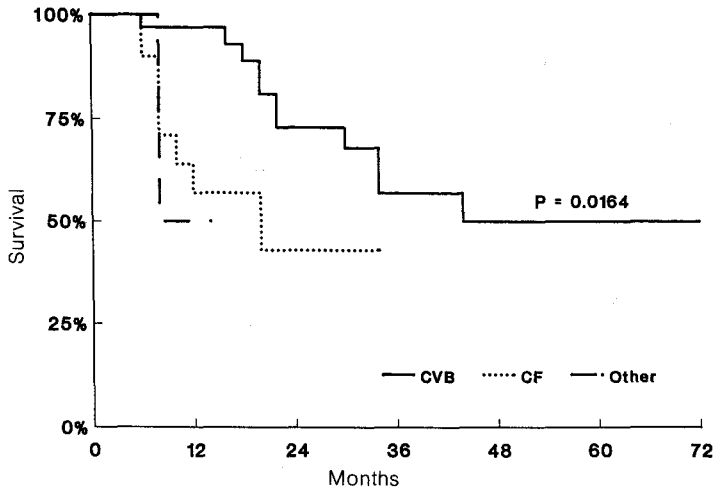

Fig. 5. Survival of patients in the CT-RT group according to induction chemotherapy regimens.

response rate after radiotherapy.

These data are different from those other studies or in controlled trials[13~15]. Although increase in median survival has been described in other studies for CT+RT group compared with radiotherapy alone group, our results do not show improvement in median survival. Median was 36 months for CT+RT group and 24 months for RT alone group in our study. Our results showed no significant difference in overall survival between CT+RT and RT alone group.

Although single arm studies have reported an improvement in survival compared to historical control, none of the randomized studies with induction chemotherapy showed significant difference in overall survival, and rather some showed poorer survival in induction chemotherapy group[13~15]. Thus our and other's results suggest that the use of chemotherapy prior to radiotherapy dose not improve survival.

Some investigators have demonstrated that patients who respond to induction chemotherapy survive longer than non-responder[11,14,22]. The Wayne State group reported that responder to initial chemotherapy had better survival rate than nonresponder[22]. Others have cautioned that this difference may not result from chemotherapy response, but rather had better survival than non-responder, but when they corrected difference in survival based on disease stage and site, the difference between responder and non-responder disappeared.

They concluded that response to CT is not an independent factor which influence disease outcome. Therefore, our and other's data suggest that it is still questionable whether induction chemotherapy simply identifies a better prognosis group or actually achieves a therapeutic effect. Although some found a relationship between overall survival and tumor variables including overall stage, T and N stage, primary site and pathology, in most studies, tumor parameters did not find to be prognostic factors for survival[11,24].

Our data showed that survival was not dependent on tumor parameters. Only patients with N3 lymph node treated by chemotherapy and radiotherapy had a statistically better overall survival than patients receiving RT alone in univariate analysis, but these was not significantly better in overall survival in multivariate analysis.

Our results are comparable to most other studies[11,24]. In conclusion, survival data from non-randomized trials has tempted some investigators to state that survival may be improved by the use of induction chemotherapy. However, data from randomized trials has failed to demonstrate an advantage for induction chemotherapy. Therefore, at present time, induction chemotherapy should not be routinely proposed for patients with head and neck cancers. It is necessary to perform randomized trials to evaluate new chemotherapy regimens and sequence, and we have to await results before concluding that there is any benefit from chemotherapy for patients with head and neck cancers.

ACKNOWLEDGEMENT

The authors thank B.Y. Chun, M.D., department of preventive medicine, school of medicine, Kyunpook national university for statistical analysis.

REFERENCES

1. **Gilbert EH, Goffinet DR, Bagshow MA:** Carcinoma of the tongue and floor of the mouth. Cancer 35: 1517-1524, 1975
2. **Giri PGS, Taylor SA:** Concurrent chemotherapy and radiation therapy in advanced head and neck cancer. Am J Clin Oncol 10:417-421, 1987
3. **Kun LE, Tooth RJ, Holoye PY, et al:** A randomized study of adjuvant chemotherapy for cancer of the aerodigestive tract. Int J Radiat Oncol Biol Phys 12:173-178, 1986
4. **Glick JH, Marcial V, Richter M, et al:** The adjuvant treatment of inoperable stage III and IV epidermoid carcinoma of the head and neck with platinum and bleomycin infusion prior to definitive radiotherapy. Cancer 46:1919-1924, 1980
5. **Wildermuth O, Warner GA, Marty R:** Clinical hyperbaric radiotherapy after five years. Radiology 93: 1149-1154, 1969
6. **Cox JD, Byhardt RW, Komaki R:** Reduced fractionation and the potential of hypoxic cell sensitizers in irradiation of malignant epithelial tumors. Int J Radiat Oncol Biol Phys 6:37-40, 1980
7. **Fletcher GH, Jessee RH:** The place of irradiation in the management of the primary lesion in head and neck cancers. Cancer 39:862-867, 1977
8. **Snow JB Jr, Kramer S, Marcial VA, et al:** Evaluation of randomized preoperative and postoperative radiation therapy for supraglottic carcinoma. Ann Otol Rhinol Laryngol 87:686-691, 1978
9. **Final Report of the Head and Neck Contracts Program:** Adjuvant chemotherapy for advanced head and neck squamous carcinoma. Cancer 60:301 -311, 1987
10. **Mead GM, Jacobs C:** The role of chemotherapy in the treatment of head and neck cancers. Am J Med 73:582-595, 1982
11. **Jacobs C, Goffinet DR, Goffinet L, et al:** Chemotherapy as a substitute for surgery in the treatment of advanced resectable head and neck cancers. Cancer 60:1178-1183, 1987
12. **Hong KI, Bromer RH, Amato DA, et al:** Patterns of relapse in locally advanced head and neck cancer patients who achieved complete remission after combined modality therapy. Cancer 56:1242-1245, 1985
13. **Tannok IF:** Combined modality treatment with radiotherapy and chemotherapy. Radiother Oncol 16:83-101, 1989
14. **Chang TM:** Induction chemotherapy for advanced head and neck cancers. Head Neck Surg 10:150 -159, 1988
15. **Jacobs CD:** Head and neck squamous cancers. Curr Probl Cancer pp54-58, 1990
16. **American Joint Committee on Cancer:** Manual for staging for cancer. JB Lippincott 1988
17. **Lee ET:** Statistical methods for survival data analysis. Lifetime Learning Publications. 1980, pp122 -156
18. **EPILOG PLUS Statistical Analysis System:** Statistic package for epidemiology and clinical trials. Epicenter Software
19. **Fazekos JT, Sommer C, Krammer S:** Tumor regression and other prognostic factors in advanced head and neck cancers. Int J Radiat Oncol Biol Phys 9:957-959, 1983
20. **Glick JH, Taylor SG:** Integration of chemotherapy into a combind modality treatment plan for head and neck cancers. Int J Radiat Oncol Biol Phys 7: 229-242, 1981
21. **Enseley JF, Jacobs JR, Weaver A, et al:** Correlation between response to cisplatinum-combination chemotherapy and subsequent radiotherapy in previously untreated patients with advanced squamous cell cancers of the head and neck. Cancer 54:811-814, 1984
22. **Weaver A, Fleming S, Enseley J, et al:** Superior clinical response and survival rates with initial bolus of cisplatin and 120 hour infusion of 5-fluorouracil before definite therapy for locally advanced head and neck cancers. Am J Surg 148: 525-529, 1984
23. **Taylor SG, Applebaum E, Showel JL, et al:** A randomized trial of adjuvant chemotherapy in head and neck cancer. J Clin Oncol 3:672-679, 1985
24. **Calais G, Garand G, Beutter P, et al:** Oropharynx carcinoma: Irradiation alone versus induction chemotherapy plus irradiation-5 year results. Br J Radiol 63:340-345, 1990

국문초록 =

수술 불가능한 두경부 종양에서 방사선 단독요법과 유도 화학요법 및 방사선 병용요법의 비교

경북대학교 의과대학 치료 방사선과학교실, 이비인후과학교실

박인규 · 윤상모 · 김상보 · 류삼열 · 박준식

수술 불가능한 두경부 종양에서 유도 화학요법의 효과를 알아보기 위해, 저자들은 후향성 조사를 실시하였다. 55명의 환자가 유도 화학요법 및 방사선 병용요법으로 치료를 받았으며, 이 환자군은 방사선 단독요법으로 치료받은 54명의 환자와 비교되었다. 치료에 이용된 화학요법은 CF (cis-platine + 5-FU), CVB (cyclophosphamide + vincristine, bleomycin), CAP (cyclophosphamide + adriamycine + prednisolone) 혹은 PVBM (cis-platine + vincristine + bleomycine + methotrexate)이었다. 유도화학요법의 독성은 미미했고, 주로 오심 및 구토, 점막 염증 그리고 골수 억제였다.

화학요법에 대한 주관해율은 61.8%였고, 이중 완전관해율은 14.5% 그리고 부분관해율은 47.3%로 나타났다. 유도 화학요법 및 방사선 병용요법에 있어서, 국소 치료이후 주관해율은 87.3% (48/55), 이중 완전관해율은 58.2% (32/55) 그리고 부분관해율은 29.1% (16/55) 였다. 방사선 단독요법으로 치료한 군에서는 주관해율 81.5% (44/55), 완전관해율 50% (27/55) 그리고 부분관해율 31.5% (17/55) 로 나타났다 ($p=0.57$). 중앙 추적기간은 유도 화학요법 및 방사선 병용요법으로 치료한 군에서는 17개월, 방사선 단독요법으로 치료한 군에서는 11개월 이었다. 중앙 생존기간은 유도 화학요법 및 방사선 병용요법으로 치료한 군에서는 36개월, 방사선 단독요법으로 치료한 군에서는 24개월 이었다 ($p=0.3$).

2년, 3년, 그리고 5년 생존율은 유도 화학요법 및 방사선 병용요법으로 치료한 군에서는 각각 60.9%, 48.6%, 42.5%로 나타났고, 방사선 단독요법으로 치료한 군에서는 54.9%, 49.9%, 49.9%로 나타났다 ($p=0.33$). 방사선 단독군과 유도 화학요법 및 방사선 병용요법 군에서 전체 종양의 병기, 원발 종양 및 임파절의 병기, 원발 병소의 위치, 그리고 조직학적 소견에 대하여 비교하여 보았으나, 모든 경우에 있어 생존율에 유의한 차이를 보이지 않았다. 따라서, 저자들은 이 후향성 조사에서 수술 불가능한 두경부 종양에 있어서 유도 화학요법의 이점을 발견하지 못했다.