Radical Radiotherapy of Head and Neck Cancer

Sung Beom Ban, M.D., Chul Young Kim, M.D., Myung Sun Choi, M.D.
and Won Hyuck Suh, M.D.

Department of Radiation Therapy, College of Medicine, Korea University
Hae Wha Hospital

Sixty patients with head and neck carcinoma were studied retrospectively to assess the impact of treatment on survival and local control rate by stage in the Dept of Radiation Therapy, Korea University Hae Wha Hospital between March 1981 and March 1986.

Prior to definite radiotherapy, patients were evaluated by physical examination and radiologic studies including chest, laryngogram and CT scan and then these patients were grouped according to the American Joint Committee (AJC) staging system.

They were treated with RT alone or postoperative irradiation to the dose of 7,200 cGy/8 weeks and 6,000 cGy/7 weeks respectively.

The results were obtained and as follows;

1. Overall male to female sex ratio was 3.6:1. The peak age of patients with head and neck cancer was 6th decade.
2. In all patients treated by RT, the ratio of squamous cell carcinoma to non-squamous cell carcinoma was 3.5:1 (60/77 patients).
3. The incidence according to the anatomic site of primary tumor was 22 cases in the larynx, 12 cases in PNS, 7 cases in nasopharynx, 6 cases in oropharynx, and 3 cases in hypopharynx.
4. According to AJC staging system, 4 cases were Stage I, 7 in Stage II, 19 in Stage III and 27 in Stage IV.
5. The overall incidence of cervical lymph node metastases was 43% and subdigatric and submaxillary triangle lymph nodes were the most frequent site of metastases.
6. Local control was achieved in 48% of patients treated by radio-therapy.
7. The lung was the most common site for distant metastases, comprising 4 cases among 7 cases in which distant metastases occured.
8. The overall estimated 5-year survival rate was 43% in the head and neck cancer treated with radiotherapy by life-table analysis.

Key words: Radiotherapy, Head and Neck Cancer.

INTRODUCTION

Epidermoid carcinoma that arises in the mucosa of the upper respiratory tract located in the head and neck is generally caused by smoking and drinking and has a common clinical tendency to spread locally to the neck nodes before developing distant metastases.

Because of such a clinical or biological aspects of epidermoid carcinoma, radiation therapy, surgery or combination of these two methods has been used as an accepted treatment to cure carcinoma of the head and neck completely.

However, radiotherapy or surgery is either effec-

tive or ineffective. Especially in carcinoma of the head and neck, radiotherapy produces better results than surgery in the anatomical, functional and cosmetic aspects after the radiotherapy.

Recently, with the development of high energy radiotherapeutic equipment and planning system by computerized unit, head and neck cancer has been managed more effectively.

With such teletherapy unit, the tumor dose of 6,600-8,000 cGy in 7-8.5 weeks to primary site results in satisfactory local tumor control.[1)]

Particularly in case that the clinical staging is early like stage I, II, local tumor control is shown in 90% of patients treated with radiotherapy.

But if disease advances in larger area, reasonable local tumor control can not be made only by radiotherapy or surgery.

To improve the local tumor control rate in the advanced stage, surgery pre or postoperative irradiation or hyperfractionated RT[2)] and induction chemotherapy[3)] have been used recently and have shown marked local tumor control rate of 50-60%[2)] in light of 25-30%[4)] by RT only.

However, in spite of such an effort, it was reported that the tumor recurrence rate in the head and neck area was around 15-34%[1)] showed slight differences depending on the anatomical site, clinical stage or treatment methods of the primary site.

Therefore, the importance of the campaign for the early diagnosis and the prevention of the head and neck cancer is continuously emphasized as in other cancers.

So, we analysed and examined the results of the head and neck cancer patients treated by radical RT or postoperative RT through the follow up and prepared for the further management.

MATERIALS AND METHODS

1. Materials

Total 60 cases out of 77 patients with primary head and neck cancer treated at the Dept. of Radiation Oncology, Korea University, School of Medicine, Hae Wha Hospital during the periods from March 1981 to March 1986 were analysed.

Of these, 3 cases were unknown primary metastatic head and neck cancer. One patient in this group was on RT schedule but was dropped due to patient refusal.

So, total 56 cases of primary head and neck carcinoma were studied retrospectively (Table 1).

Table 1. Pathologic Types of Head and Neck Cancer

Registry of head and neck cancer (1981-1986)	77 cases/1155 (6.6%)
Pathologic types:	
Squamous cell carcinoma	60
Lymphoma	11
Malignant midline reticulosis	2
Adenocarcinoma	1
Mucoepidermoid carcinoma	2
Adenocystic carcinoma	1
Total	77

The sex ratio of these patients was 3.6:1 (M:F =47:13) and the age distribution demonstrated the highest incidence in the 51-60 age group, and 33.2% (19 cases) of total patients occurring in this age group (Fig. 1).

According to type of therapy and clinical staging of the 56 patients, radical radiation therapy was employed in 42 (75%) and combined surgical and RT was used in 14 (25%) patients (Table 2).

Table 2. Treatment Modality according to Clinical Staging

	Stage				
	I	II	III	IV	Total
RT alone	3	4	9	26	42
Postoperative RT	1	3	8	2	14

By the analysis of pathologic type, sixty out of seventy-seven (78%) were squamous cell carcinoma, and 11 cases were non-Hodgkin's lymphoma.

The overall incidence of head and neck cancer during this study period at our Dept. was 6.6% (Table 1).

2. Pretreatment Evaluation and Determination of Clinical Staging

The pretreatment evaluation of patients with carcinoma of the head and neck includes thorough history and physical examination; hematologic, urine, blood chemistry tests and radiologic studies of chest, pharynx, mandible and maxilla when clinically indicated. Computerized axial tomogram (CAT scan) is used in cases where the

standard radiologic procedures have limitation, particularly in nasopharynx, paranasal sinuses and hypopharynx.

Indirect laryngoscopy gives a better panorama of the laryngeal lesion and more information regarding vocal cord mobility than direct laryngoscopy under general anesthesia.

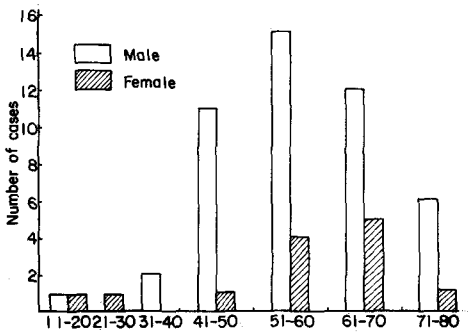


Fig. 1. Age and sex distribution of head and neck cancer.

Table 3. The AJC Neck Staging

N0	No clinically positive node
N1	Single clinically positive homolateral node 3cm or less in diameter
N2	Single clinically positive homolateral node more than 3cm but not more than 6cm in diameter or multiple clinically positive homolateral nodes, none more than 6cm in diameter
	N2a: Single clinically positive homolateral node more than 3cm but Inot more than 6cm
	N2b: Multiple clinically positive homolateral nodes none more than 6cm
N3	Massive homolateral node(s), bilateral nodes, or contralateral node(s)
	N3a: Clinically positive homolateral node(s), one more than 6cm
	N3b: Bilateral clinically positive nodes
	N3c: Contralateral clinically positive Node(s)

Direct laryngoscopy, however, allows examinations of areas invisible to the mirror such as the ventricle, subglottic space, apex of the pyriform sinus and postcricoid pharynx.

In addition, laryngogram shows general appearance of laryngeal lesion and extent of invasion.

By thorough search for metastatic lymph nodes in the neck, we determined neck node staging as AJC staging system (Table 3) with special reference to size, location and the presence of adhesion to underlying structures.

3. Radiotherapy Technique

All patients were treated by external beam radiation therapy with Co-60 teletherapy unit.

Radiation fields would cover the primary tumor, surrounding actual or potential areas of involvement and the neck nodes to supraclavicular area even though they were clinically negative at the time of presentation.

As a single daily treatment, a daily tumor dose of 180 cGy was employed for 5 days a week.

Spinal cord was excluded at tumor dose of 4,000 cGy and field was reduced to primary tumor at 5,000 cGy. Additional reductions were usually made at 6,000 cGy and 7,000 cGy. Total tumor dose was determined by the anatomic structures of primary tumor, clinical staging and type of treatment modalities. Generally, in case that radiation therapy alone was employed, total tumor dose of 6,600-7,000 cGy/7-8 weeks was irradiated. Whereas, in case of postoperative RT, 5,000 cGy/5.5 weeks was irradiated to operative area and then cone-down to the residue area according to operative findings to dose of 6,000 cGy/7 weeks. When the neck node was not palpated clinically, surface dose of 5,000 cGy per 5 weeks was delivered. However, clinically positive nodes were irradiated to a dose of 6,000-7,000 cGy with small boost fields.

4. Follow-up

Follow-up of patients after treatment was performed 1 month later, and then we recommended CT scan for comparing with pre-treatment CT scan and evaluated the local tumor control and neck node control.

Thereafter, we recommended the follow-up every 2 month for a year, and every 3 month for next year.

RESULTS

1. Anatomic Location of Primary Head and Neck Cancer

The incidences according to the anatomic location of primary tumor were 22 cases in the larynx and 12 in the paranasal sinus. In the oral cavity and oropharynx, there were 6 cases. 7 cases were originated in the nasopharynx and 3 cases in the hypopharynx (Table 4).

Table 4. Anatomic Site of Head and Neck Cancer Patients

	RT alone	Postop. RT	Total (%)
Nasopharynx	7	0	7 (12.5)
PNS	10	2	12 (21.4)
Oral Cavity	5	1	6 (10.7)
Oropharynx	6	0	6 (10.7)
Larynx	12	10	22 (39.2)
Hypopharynx	3	0	3 (5.3)
Total	42	14	56

2. Neck Node Involvement by AJC Staging System

Neck node involvement in head and neck cancer patients was analysed as AJC staging system (Table 3), by the physical examination at the time of presentation and CT scan employed (Table 5).

Frequency of neck node involvement increased as the T-stage of tumor advances and showed more than 50% in T2 and T3 lesions at presentation.

However, neck node involvement in T4 lesion was 29% and this may be explained that 7 of 11 cases of T4 lesion in this study were paranasal sinus primary which did not show neck node involvement frequently.

Of total 57 cases, 24 cases (43%) showed neck node involvement, and the ipsilateral subdigastric node was the most common site. 5 cases also showed contralateral neck node involvement (Fig. 2).

Table 5. Clinical Staging of Head and Neck Cancer

Stage	N0	N1	N2	N3	Total with nodes (%)
T 1	4	0	0	0	0/4 (0%)
T 2	7	3	3	2	8/15 (53%)
T 3	11	5	4	3	12/23 (52%)
T 4	11	1	2	1	4/15 (29%)
Total	33	9	9	6	24/57 (43%)

3. Results of Radiotherapy for Head and Neck Cancer

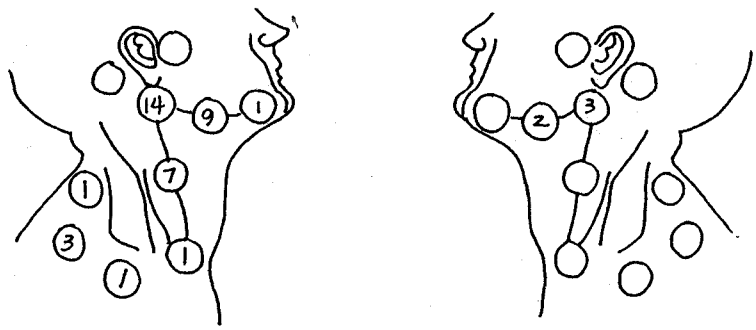
1) Local Tumor Control Rate

Local tumor control rate was 100% in T1 lesion (4/4), however, decreased gradually as T and N stage advanced. In T4 lesions, overall local tumor control rate was 33% but there was no one whose tumor showed local tumor control in T4 N1-3 stage (Table 6).

Table 6. Local Control Rate by TNM System

Stage	N0	N1-3	Total
T 1	4/4 (100%)		4/4 (100%)
T 2	3/7 (43%)	3/7 (43%)	6/14 (43%)
T 3	6/10 (60%)	6/13 (46%)	12/23 (52%)
T 4	5/11 (45%)	0/4 (0%)	5/15 (33%)
Total	18/32 (56%)	9/24 (37%)	27/56 (48%)

*1 patient was excluded due to refusal of treatment.



Ipsilateral						Contralateral	
N0	N1	N2A	N2B	N3A	N3B	N3C	N1-N3/Total
33	9	3	6	1	4	1	24/57 (43%)

Fig. 2. Nodal distribution of head and neck cancer on admission.

Overall five-year survival in head and neck cancer was 43% ± 7% and NED survival was 30% ± 8%. (Fig. 3)

And the 5-year survival rate according to clinical staging of head and neck cancer was 100% in stage I, 48% in stage II, 29% in stage III, and 46% in stage IV (Table 7).

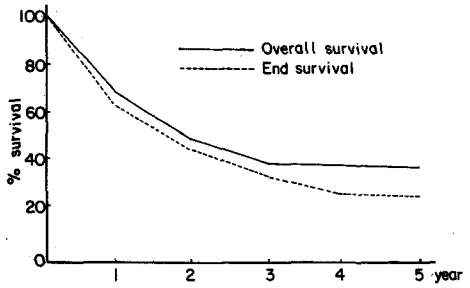


Fig. 3. Estimated 5-year survivals in head and neck cancer according to AJC staging.

Table 7. 5-year Survival Rate according to AJC Staging

Stage	Number of cases	5-Year survival
I	4	100%
II	7	48%
III	17	29%
IV	28	46%
Total	56	43%

2) Failure Pattern after Radiotherapy

Treatment failure after radiotherapy was analysed according to the clinical staging of head and neck cancer (Table 8).

50% of total patient was failed due to locoregional recurrence and so were 19 cases (33%) in primary alone, 2 cases (6%) in neck nodes alone, 7 cases (13%) in both primary and neck nodes. 7 cases developed distant metastases and of them lung was the most common site (4/7, 57%), next bone and brain. 1 patient with laryngeal cancer showed complete local tumor control but died due to hepatoma rupture.

DISCUSSION

The American Cancer Society has estimated that 27,500 new cases of buccal cavity and pharyngeal cancer, and 11,100 new cases of laryngeal cancer occur in the United States in 1984; the corresponding numbers of death were estimated to be 9,350 and 3,750 respectively.[7]

Seel et al.[8] reported that oral and oropharyngeal cancer constitute 3.9% of all malignancies in his 20-year experience in Korea.

And due to increased tendency of smoking and alcohol consumption, active studies for the effective management of head and neck cancer patients must be continued.

Even though, eiology of head and neck cancer is not still known, epidemiologic studies demonstrated that the risk of oral cavity and laryngeal (i.e., both glottis and supraglottis) cancer was increased among cigarette smoker.

By Kahn et al.,[9] when compared with nonsmokers, a prospective study of United States Veterans who smoked two packs of cigarette or more per day and continued for more than 40 years indicated that the relative risk of dying of head and neck cancer was increased almost 12-32 fold.

Schottenfeld[10] reported that alcohol and tobacco act synergistically, and are the salient co-factors responsible for at least 75% of upper aero-digestive tract cancer deaths.

However, there is mounting seroepidemiologic and experimental evidence to support the hypothesis that the Epstein-Barr virus (EBV) is an etiologic factor in nasopharyngeal cancer.[11] Such serologic evidences are; 1) Antibodies against

Table 8. Treatment Failure Pattern After Radiotherapy

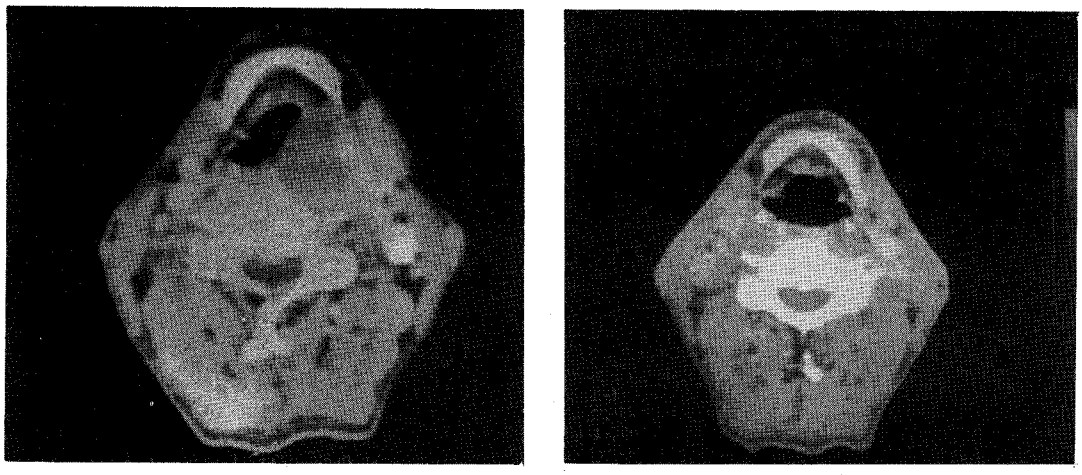
T-Stage	No.	Site of failure				
		Primary	Neck	P plus N	Distant	Intercurrent D
T1	4					
T2	14	4		4	1	1
T3	23	7	2		4	
T4	15	8		3	2	
Total	56	19	2	7	7	1

EBV components have been significantly increased in patient's serum. 2) The regular presence of EBV DNA in epithelial elements of nasopharynx cancer.

In addition, ingestion of foods containing vitamin-A and C tend to protect against epithelial tumors in head and neck.[12]

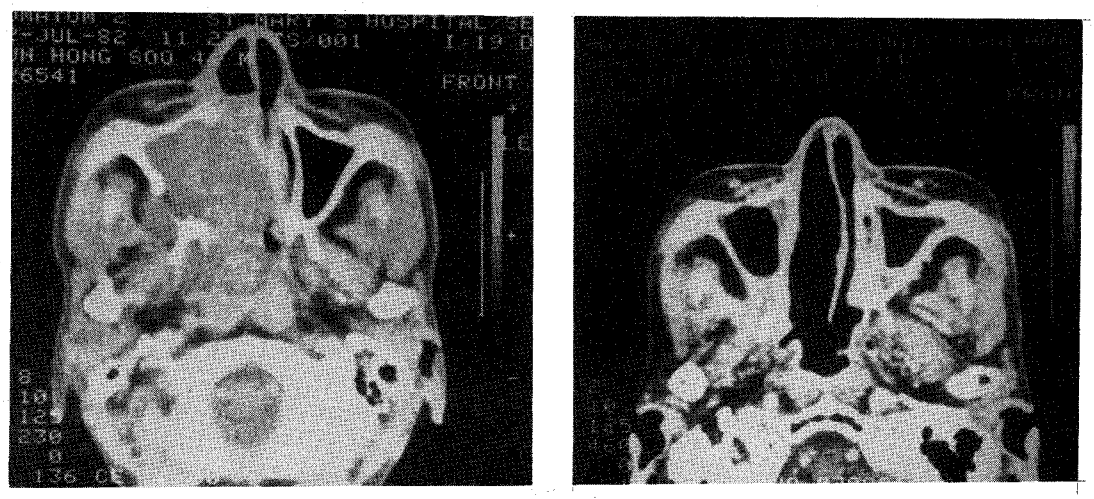
In the determination of clinical staging of head and neck cancer, CT scan is currently employed to evaluate the extent of primary tumor more objectively, in addition to physical examination and routine laboratory examinations at the time of presentation. Especially, in cases of submucosal tumor and tumor in areas which are difficult to palpate, such as the high oropharynx and nasopharynx, CT scan will give more important information than physical examination.[13), 14)]

CT scan findings have shown to alter treatment



A B

Fig. 4. Supraglottic cancer (Left).
A: Prior to radiotherapy
B: Follow-up CT scan after 6,600 cGy/7 weeks.
The tumor mass of left supraglottic area disappeared completely.



A B

Fig. 5. Maxillary antrum cancer (Right).
A: Prior to radiotherapy, Stage IV
B: Follow-up CT scan after 3 years of RT

planning in up to 35% of patients as a result of changes in primary tumor extent and nodal involvement.[15] Besides, CT scan can be used effectively to evaluate local tumor control after treatment.

In our study, we also could evaluate treatment response in patients with head and neck cancer after radiotherapy (Fig. 4-A, B 5-A, B 6-A, B). The risk of lymph node metastases may be predicted by the differentiation of the tumor, by the size of the primary lesion, and by the availability of capillary lymphatics.

The overall neck node involvement of head and neck cancer was 40-60%,[16] and in our series showed similar results (43%). The neck node involvement increased as the T-stage advanced. Particularly, the incidence of neck node involvement is high in nasopharynx cancer.[17]

Surgery and Radiation therapy are the only curative treatment for carcinoma arising in head and neck. For most early-stage head and neck squamous cell carcinoma that can be cured by an operation, irradiation shows comparable cure rates. The decision then rests on such factors as functional and cosmetic result, general state of the patient's health, and preference of the patient and family.

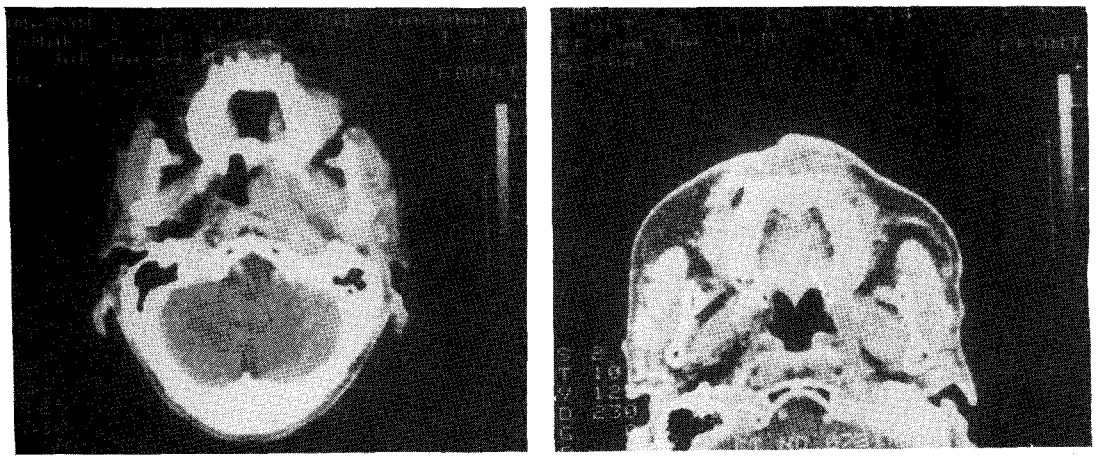
Patients with early-stage lesion (T1, N0-1, T2 N0-1) usually have a favorable prognosis when managed by either surgery or radiation therapy. So combined treatment should be avoided because it only increases the morbidity with little or no benefit. A few failures are often salvaged by a second procedure. Whereas, patients with moderately advanced lesions may benefit from combined therapy such as pre or postoperative irradiation, induction chemotherapy.

However, the most difficult decision is whether or not to offer a curative attempt to patients with advanced lesions but no metastases. There are anecdotal cases in which patients with advanced stage IV disease have been cured only by radiotherapy. But the cure rate for some advanced lesions may be estimated 1-2% at best. So, if the patient is in relatively good condition, especially if in a young age group, then a curative approach needs to be considered.

Treatment failure was correlated generally with clinical staging of disease at presentation. In our cases, there was no failure in T1N0 cases (0/4) but with advanced cases, we experienced loco-regional failure and uncommonly distant failures.

Loco-regional tumor recurrence rate in head and neck cancer range from 35-50%[18] depends on initial site, stage and type of therapy employed. Our study shows similar result of loco-regional tumor recurrence (50%). Distant metastases occurs mostly to the lung and comprise 52% of all cases. In our study, 7 cases showed distant metastases and of them, 4 cases (57%) showed distant metastases to the lung.

According to primary site of tumor, nasopharynx and hypopharynx tumor tends to show high incidence of distant metastases. By Lindberg et al [19]



A B

Fig. 6. Nasopharyngeal cancer (Left).
A: Prior to radiotherapy
B: Follow-up CT scan after completion of radiotherapy (5 months)

overall distant metastases rate was 10.9% in his study, which was comparable to our study result (12.5%). Therefore, loco-regional failure still remains the most important type of failure after definite treatment. The result of this failure pattern leads us to multimodality approach which has been used and has shown therapeutic response in 50% of stage III, IV head and neck cancer.

Loco-regional recurrence after this multimodal approach dropped to 14%.[6] C.C. Wang et al.[2] used hyperfractionated radiotherapy in stage III, IV and reported 2-year recurrence-free survival rate of 63-86%.

CONCLUSIONS

Through the periods from March 1981 to March 1986, 56 cases of head and neck cancer were treated at Dept. of Radiation Oncology, Korea University, Hae Wha Hospital.

We obtained following results by retrospective analysis:

1. 80.7% of all patients studied were Stage III, IV disease by AJC staging system.
2. Estimated 5-year survival rate by life-table method was 43 ± 7% and the survival rate according to the clinical stage is 100% in stage I, 48% in stage II, 29% in stage III, and 46% in stage IV.
3. Loco-regional tumor control failure is still the most common treatment failure which comprise 52% in our study.
4. In T1 or T2 lesion should be treated initially with radical radiotherapy and surgery should be reserved for the possible treatment failure to salvage. However, in T3 or T4 lesions multimodal approach (induction chemotherapy, hyperfractionated radiotherapy, pre or postoperative radiotherapy) should be attempted to improve loco-regional tumor control.

REFERENCES

1. **Victor A. Marciac, Thomas F. Pajak:** Radiation Therapy Alone or in Combination with Surgery in Head and Neck Cancer. Cancer 55: 2259-2265, 1985
2. **Wang C.C., Peter H. Blitzer, et. al.:** Twice-a-day Radiation Therapy for Cancer of Head and Neck. Cancer 55:2100-2104, 1985
3. **Kim B.S.:** Induction Chemotherapy in Head and Neck cancer. Korean Journal of Head and Neck Oncology 1-1: 75-79, 1985
4. **Elias EG, Chretien PB, et. al:** Chemotherapy prior to local therapy in advanced squamous cell carcinoma of the head and neck, Preliminary assessment of an intensive drug regimen. Cancer 43: 1025-1031, 1979
5. **Kish JA, Weaver A, et. al:** Cisplatin and 5-FU in patients with recurrent and disseminated epidermoid carcinoma of the head and neck. Cancer 53: 1819-1824, 1984
6. **Ralph R.W, John R.C, et al.:** Combined modality treatment of head and neck cancer with Cisplatin, Bleomycin, Methotrexate-Leucovorin Chemotherapy. Cancer 55: 2149-2155, 1985
7. **American Cancer Society:** Cancer Facts and Figure, 1984
8. **Seel DJ:** Oral and oropharyngeal cancer 20-year experience in Korea. Korean Journal of Head and Neck Oncology 1-1: 7-13, 1985.
9. **Kahn HA:** The dorn study of smoking and mortality among US Veterans Report on 8.5 years of observation. J Natl Cancer Inst 19: 1-125, 1966
10. **Schottenfeld D:** Alcohol as a co-factor in the etiology of Cancer. Cancer 43: 1962-1966, 1979
11. **De The G, Zeng Y:** Epstein-Barr Virus and Nasopharyngeal Cancer. Head and Neck Cancer New York: 43-51, 1983
12. **Graham S, Mettlin C, Marshall J, et al:** Dietary factors in the epidemiology of cancer of the larynx. Am J Epidemiol 113: 675-680, 1981
13. **Mancuso AA, Hanafee WN:** Elusive head and neck tumors beneath intact mucosa. Laryngoscope 93: 133-139, 1983
14. **Harnsberger HR, Mancuso AA, et al:** The upper aerodigestive tract and neck CT evaluation of recurrent tumors. Radiology 149: 503-509, 1983
15. **Gatenby RA, Mulhern CB, et al:** Comparison of clinical and CT staging in patients with head and neck tumors. RSNA 1983
16. **Mendenhall WM, Million RR, et al:** Elective neck irradiation in squamous cell carcinoma of the head and neck. Head and Neck Surgery 3: 15-20, 1980
17. **Lindberg R:** Distribution of cervical lymph node metastases from squamous cell carcinoma of the upper respiratory and digestive tracts. Cancer 29: 1146-1149, 1972
18. **Marcial VA, Amato DA, et al:** Patterns of failure after Treatment for cancer of upper respiratory and digestive tracts. Cancer Treat Symp 2: 33-40, 1983
19. **Merino OR, Lindberg RD, et al:** An analysis of distant metastases from squamous cell carcinoma of the upper respiratory and digestive tract. Cancer 40: 145-151, 1977

국문초록=

두경부 종양의 방사선 치료 성적

고려대학교 의과대학 방사선과학교실

반성범 · 김철영 · 최명선 · 서원혁

1981년 3월부터 1986년 3월까지 고려대학교 의료원 혜화병원 치료방사선과에서 60명의 두경부 환자를 대상으로 방사선치료후의 임상적인 병기에 따른 생존율 및 국소종양 억제율을 후향적으로 재조사하였다.

근치적 방사선 치료전에, 이학적 검사와 방사선학적 검사로 흉부X-선, 후두촬영 및 콤퓨터 단층촬영등을 시행하였고 AJC의 임상병기에 따라 분류하였다.

치료는 방사선 치료 단독시, 7,200 cGy를 8주에, 그리고 수술후 방사선 치료시는 6,000 cGy를 7주에 각각 분할조사하였다.

이에 저자들은 다음과 같은 결과를 얻었다.

1) 남녀의 성비는 3.6 : 1이었고 50대의 연령군에서 가장 높은 빈도를 보였다.

2) 방사선 치료를 받은 환자에서, 병리조직학적으로 편평상피암이 비 편평상피암에 비해 3.5배의 높은 빈도를 보였다.

3) 원발병소의 해부학적 위치는 후두가 22예, 부비동이 12예, 비인후강이 7예, 구강인두가 6예, 하인두가 3예였다.

4) AJC의 병기에 따라 분류하면 Ⅰ기가 4예, Ⅱ기가 7예, Ⅲ기가 19예, 그리고 Ⅳ기가 27예였다.

5) 경부임파절로의 국소전이는 전체적으로 43%였고 subdigastric과 submaxillary 임파절이 가장 많은 것으로 나타났다.

6) 방사선 치료후 국소종양의 억제는 치료 환자의 48%에서 관찰되었다.

7) 원격전이는 7예에서 관찰되었는데 그중 4예에서 폐로의 원격전이를 보였다.

8) Life-table 방식에 의한 5년 생존율은 43%로 나타났다.