Radiotherapy of Squamous Cell Carcinoma of Maxillary Antrum

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One hundred-ten patients with squamous cell carcinoma of the maxillary antrum treated at the Department of Therapeutic Radiology, Seoul National Unviersity Hospital between February 1979 and September 1986 were retrospectively analyzed.

Of these, only 73 patients were eligible for analysis.

Forty-one patients were treated with combination of surgery and radiation therapy and 32 patients were treated with radiation therapy alone.

The majority of patients had advanced stage (including 47% T_4 tumor).

Overall 5 year survival rate was 40.4%. In the radiotherapy alone group, 5 year survival rate was 22.1%, and in the combined surgery and radiotherapy group, 5 year survival rate was 65.3%.

Of 31 patients who had failures, 22 patients (71.0%) had local failures, 6 patients (19.3%) had regional failures and 3 patients (9.7%) had distant metastasis.

Planned combined treatment with surgery followed by radiation therapy is an effective modality for carcinoma of the maxillary antrum.

Key Words: Squamous cell carcinoma, Maxillary antrum, Radiation therapy, 5 year survival rate

INTRODUCTION

Carcinomas of maxillary sinus are relatively rare neoplasms, and account for only 0.1~1.0% of all cancers. Squamous cell carcinoma is the most common type of maxillary malignancy.

Early cancer within the maxillary antrum, which would have a good prognosis, is rarely diagnosed since early symptoms are scarce. The patients are usually diagnosed at an advanced stage, which makes curative treatment extremely difficult.

In early cases, surgery can be a curative treatment. Locally advanced cases are usually managed by combination of surgery and radiotherapy. Five year survival rate has been reported to be in the range of 10% to 68% by surgery or radiotherapy, alone or in combination. Considerable controversy exists regarding the role of surgery, radiotherapy or combination of surgery and preoperative or postoperative radiotherapy in the management of carcinoma of the maxillary sinus. In recent reports, the advantage of preoperative or postoperative radiotherapy has been emphasized.

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In order to ascertain the relationship between the treatment modality and the results, 110 patients with carcinoma of maxillary sinus treated at the Department of Therapeutic Radiology, Seoul National University Hospital between 1979 and 1986 were studied.

MATERIALS AND METHODS

Between February 1979 and September 1986, 110 patients with the carcinoma of the maxillary antrum were treated with radiation therapy consisting external beam irradiation alone or in combination with surgery. Thirty-seven patients were excluded from this analysis: 21 patients who had other histology, 12 patients with incomplete treatment and 4 patients with recurrent or disseminated disease at presentation. Therefore, 73 patients were eligible for this study (Table 1).

All patients had a minimum follow-up of 2 years with 75% having at least 5 year follow-up. Follow-up range of survivors was from 36 months to 104 months. The mean age of patients was 50 years, ranging from 22 to 75 years. Fifty three patients were male and 20 patients were female with a ratio of 2.65 : 1 (Table 2).

All patients were retrospectively staged accord-

Table 1. Eligibility for Patient Group

Total Maxillary Ca Cases			110
Squamous cell ca		89	
Exclusion		16	
incomplete tx (dose < 40 Gy)	12		
recurrent cases	3		
palliation cases	1		
Eligible cases		73	
Other histology		21	

Table 2. Patient Characteristics
Feb. 1979 – Sep. 1986, SNUH

	No. of pts (%)
Age	
– 29	2 (2.7)
30 – 39	16 (21.9)
40 – 49	18 (24.7)
50 – 59	23 (31.5)
60 – 69	11 (15.1)
70 –	3 (4.1)
Sex	
Male	53 (72.6)
Female	20 (27.4)
T–Stage	
T2	8 (11.0)
T3	29 (39.7)
T4	36 (49.3)
N–Stage	
N0	56 (76.7)
N1	11 (15.1)
N2	3 (4.1)
N3	3 (4.1)

ing to the TNM classification proposed by AJC in 1978. The stage distribution was presented in Table 4. Thirty six patients (49%) had T4 disease and only 8 patients (11%) had T2 disease. Seventeen patients (23%) had cervical lymph node metastases at presentation, of whom, 1 patient had T2 disease, 8 patients had T3 disease and 8 patients had T4 disease.

Of 73 patients with carcinoma of the maxillary sinus, forty one patients were treated with definite radiation therapy and 32 patients with surgery and radiation (3 preoperatively and 29 postoperatively).

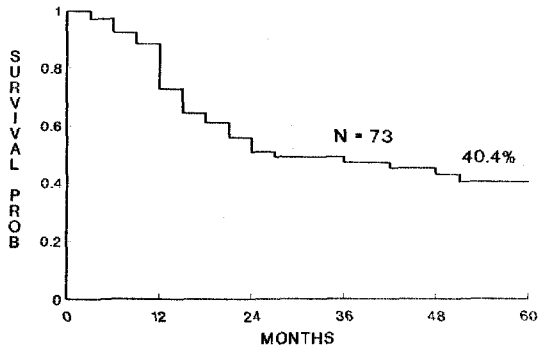

Fig. 1. Overall survival.

Exentration of orbit was performed if orbit was involved.

All patients were treated with cobalt 60 teletherapy or 6 MV X-ray. The treatment portals included only the primary tumor and in 17 patients, the regional lymph nodes were also irradiated. Generally two field (anterior and lateral wedge) or three field technique (anterior, right and left lateral wedge) was used to deliver relatively uniform dose to the maxillary sinus, nasal cavity and ethmoid or sphenoid sinus. The tumor doses for 41 patients who were treated with radiation therapy alone ranged from 4550 cGy in 26 fractions to 7580 cGy in 42 fractions to the primary lesion, and majority of them received 7000 cGy in 7 to 8 weeks. Thirty two patients treated with either postoperative (29 cases) or preoperative (3 cases) radiation therapy, received 5000 cGy in 28 fractions to 7000 cGy in 39 fractions (the majority of them received 6000 cGy).

Neck node was not treated unless clinically positive. The common sites of lymph node metastasis at presentation were submandibular lymph node and subdigastric lymph node.

The treatment results were analyzed in relation to clinical findings. Analysis of statistical significance was performed using log rank chi-square test and life table method was used to calculate the survival rate.

RESULTS

For the 73 patients, the 5 year survival rate was 40.4% (Fig. 1). The radiation therapy alone group included patients with inoperable advanced disease (T4 32/41, 78%) and its treatment results were inferior to those treated by combined therapies. Five of 41 patients were alive more than 4 years in radiation alone group but 15 of 32 patients were

alive after 4 years in the combined group. The 5 year survival rates for radiation therapy alone and combined therapies were 22.1% and 65.3%, respectively (Fig. 2, Table 3, Table 6). The 5 year survival rates by T-stage were 57.1%, 56.3% and 26.7% for T2, T3 and T4, respectively (Fig. 3). Statistical significance was found according to T stage. The 5 year survival rates for node negative and node positive patients were 40.9% and 36.8%, respectively. No significant relationship between N-stages and survival was probably due to small number of patients with positive neck nodes. Table 9 shows histological subtype has no significant impact on survival rate.

Of 31 patients who had relapsed, twenty two patients (71.0%) had local failure, 6 patients (19.3%) did regional failure and 3 patients (9.7%) did distant failure. Initial failure sites of radiation alone patients were as follows; persistence or recurrence at primary site in 19 patients (82.6%), neck node failure in 2 patients (8.7%) and distant metastasis in 2 patients (8.7%). Initial failure sites of combined therapy group were as follows; failure at primary site in 3 patients (37.5%), neck node failure in 4 patients (50.0%) and distant metastasis in 1 patient (12.5%) (Table 5).

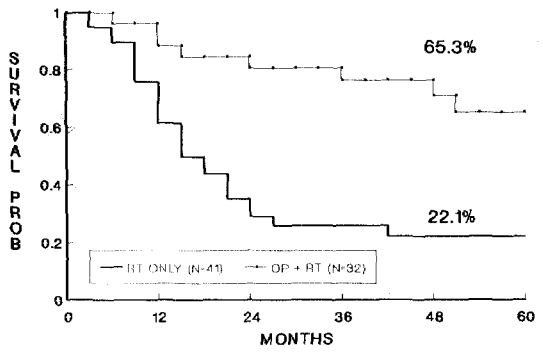

Fig. 2. Survival by Tx modality.

Table 3. Overall 5-Yr Survival Rate (%)

	RT only (N=41)	OP + RT (N=32)	Total (N=73)
T2	0.0	66.7	57.1
T3	17.3	69.8	56.3
T4	24.0	50.0	26.7
LN (+)	28.6	66.7	36.8
LN (−)	19.8	65.0	40.9
Total	22.1	65.3	40.4

Table 4. .Therapeutic Modality

	RT only (N=41)	OP + RT (N=32)	Total (N=73)
T2	1 (2.4%)	7 (21.9%)	8 (11.0%)
T3	8 (19.5%)	21 (65.6%)	29 (39.7%)
T4	32 (78.1%)	4 (12.5%)	36 (49.3%)
LN (+)	11 (26.8%)	6 (18.8%)	17 (23.3%)
LN (−)	30 (73.2%)	26 (81.2%)	56 (76.7%)

DISCUSSIONS

The results of this study showed that combined treatment with surgery and radiation therapy was an effective treatment modality for carcinoma of the maxillary sinus. The 5 year survival rate was 22.1% in radiation alone group and 65.3% in combined surgery and radiation therapy group. These results were similar to those reported in the literature. The survival rate in the reported series ranged from 15%~44% in radiation therapy alone[1~3, 5,7,9~11,13,14] and 35~50% in combined surgery and radiation therapy[2,4,7~9,13~17].

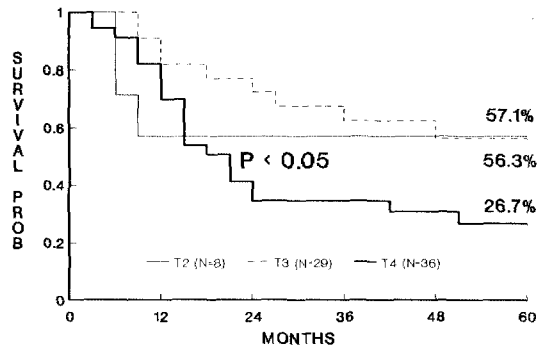

Fig. 3. Survival by T-stage.

Table 5. Distribution of Initial Failure Sites

	Radiation alone	OP + RT	Total
Primary site	19 (82.6%)	3 (37.5%)	22 (71.0%)
Neck nodes	2 (8.7%)	4 (50.0%)	6 (19.3%)
Distant metastasis	2 (8.7%)	1 (12.5%)	3 (9.7%)

Table 6. Treatment Result According to T–Category

Author	No. of success/No. of patients				End point
	T1	T2	T3	T4	
Hu	–	2/4*	22/31	3/14	5 Yr Survival
Sato	# /1	12/13	30/41	# /2	Local Control
Goepfert	–	–	4/7*	5/11	2 Yr RFS
Ireland	11/39	2/9	3/31	0/2	5 Yr Survival
Pearlman	1/1	1/2	3/8	4/8	Local Control
Bush	–	1/1*	7/14*	2/12	Local Control
Cheng	1/2*	5/11*	8/24*	0/2*	3 Yr RFS
Lee	5/7*	14/17*	13/27*	15/45	Local Control
Weymuller	–	–	14/23	8/24	Local Control
Korzeniowski	–	7/8	7/18	6/31	5 Yr Survival
Kondo, 1984	–	2/3	28/55	7/27	Local Control
Kondo, 1986	–	1/3	16/25	9/24	Local Control

RFS : relapse free survival * : without N+ patients # : not stated

Table 7. Incidence of Neck Node

Authors	No. of cases	Neck nodes (+)
Datani	31	11 (35.5%)
Birkhead	24	3 (12.5%)
Cheng	66	11 (16.7%)
Dalley	121	25 (21.0%)
Kurohara	224	48 (21.4%)
Shidnia	88	23 (26.1%)
Our Series	73	17 (23.3%)

Table 8. Survival by RT Dose

Dose (cGy)	No. of pts	5YSR (%)
RT alone		
< 6000	7	34.6
6000 – 6999	9	52.6
7000 ≤	25	11.7
OP + RT		
< 6000	12	68.2
6000 ≤	20	63.0

Table 9. 5Yr Survival Rate by Histologic Grade

	Histologic Grade			
	W/D	M/D	P/D	unknown
RT	10 (22.2%)	9 (37.0%)	7 (28.6%)	15 (9.6% (*))
OP + RT	14 (66.7%)	9 (56.7%)	5 (66.7%)	4 (**)
Total	24 (47.6%)	18 (43.8%)	12 (43.6%)	19 (21.4%)

(*) 4 year survival rate
(**) Among 4 patients, 3 patients were lost to follow-up and 1 patient showed long-term survival

Still controversy remains as to whether radiation therapy should be given preoperatively or postoperatively. Recently two reports gave support to preoperative radiotherapy. Hu reported on 50 patients with the carcinoma of maxillary sinus treated with combination of surgery and radiation therapy. The 5 year survival rate was 61% in preoperative radiotherapy group and 29% in postoperative radiotherapy group[8]. Cheng reported a 3 year survival rate of 58% in preoperative group and 36% in postoperative radiotherapy group[13]. However, a high portion of patients in these studies was treated

with low doses, i.e., below 40 Gy and patients in the postoperative group had a high proportion of advanced stage. In our study, we could not make a conclusion because of small number of patients, i. e., 3 patients in preoperative group and 29 patients in postoperative group.

In spite of high proportion of patients with advanced disease, i.e., 49% had T4 tumors, the incidence of neck node metastasis (23%) on presentation was similar to other reports (Table 7).

Batani reported that initial cervical node metastasis does not influence prognosis[3] but Robin and others reported that initial cervical node metastasis influences prognosis adversely[18].

In our study, 5 year survival rates for node negative and node positive patients were 40.7% and 36.8%, respectively. The relationship between node status and survival was not statistically significant. Elective irradiation of neck nodes remains controversial. Fletcher recommended elective irradiation in T_3 and T_4 patients[24], on the other hand, pezner could not find any subgroup of patients with high risk of developing nodal metastasis[25]. We feel that elective irradiation of clinically negative lymph node appears to be of little benefit.

The doses required for the sterilization of the carcinoma of the maxillary sinus was not well established. In our study, 5 year survival rate was 52.6% in doses of 6000 cGy to 7000 cGy as compared to 34.6% with doses less than 6000 cGy in radiation alone group. In excess of 7000 cGy, 5 year survival rate was 11.7%. Majority of these patients had far locally advanced disease so that survival rate was low (Table 8). Based on our data, more than 7000 cGy was needed for tumor control in radiation alone group. In combined radiotherapy and surgery group, the survival rate was not correlated with doses (Table 8). We currently treat the patients with the carcinoma of maxillary sinus with a dose of 6000 cGy in 30 fractions.

Considering the survival curve of our study, majority of failure occurred within two years from the base of follow-up (Fig. 1). Hu Yu et al. reported 19 local failure, 2 nodal failure and 1 distant failure among 22 failure cases[8]. Shibuya et al. reported 27 local failure, 15 nodal failure, 14 distant failure among 39 failure cases[9]. Korzeniowski et al. reported 28 local failure, 10 nodal failure, 7 distant failure among 38 failure cases[15]. Other studies also showed that local failure was dominant pattern of failure[2~4,9,10,16,17,19~23]. Lee et al. reported, in combined treatment group, initial sites of tumor recurrence were primary site in 38.4% (10/26)., neck nodes 46.2% (12/26), and distant metastasis 15. 4% (4/26). They also reported in radiation alone group, primary site 79.3% (23/29), neck node 6.9% (2/29) and distant metastasis 13.8% (4/29)[16]. All these results are similar to those of our study (Table 5).

In our study, of 32 patients who had combined treatment, 17 cases received total maxillectomy with or without eyeball exenteration and 15 cases received hemimaxillectomy or partial maxillectomy. Five year survival rates for each group were 67.4% and 62.9%, respectively. There was no significant difference between two groups. Of 17 total maxillectomy cases, 8 cases received eyeball exenteration (5 year survival rate; 85.7%) and 9 cases received maxillectomy only (5 year survival rate: 50.0%). Som reported that orbital exenteration influenced prognosis adversely[6]. Ketcham et al. and Weymuller et al. reported that orbital exenteration influence prognosis somewhat favourably, but they concluded that orbit had to be preserved when there is no gross involvement of the orbital periosteum by tumor[26,27]. Our results show that planned combined treatment with surgery followed by radiation therapy in an effective modality for carcinoma of the maxillary antrum.

REFERENCES

1. **Spratt JS, Mercado P:** Therapy and staging in advanced cancer of maxillary antrum. Am J Surg 110:502-510, 1965
2. **Jesse RH:** Preoperative versus postoperative radiation in the treatment of squamous carcinoma of the paranasal sinuses. Am J Surg 110:552-556, 1965
3. **Bataini JP, Ennuyer A:** Advanced carcinoma of the maxillary antrum treated by cobalt teletherapy and electron beam irradiation. British J of Radiology 44:590-598, 1971
4. **Badib AO, Kurohara SS, Webster JH, et al:** Treatment of cancer of the paranasal sinuses. Cancer 25:533-537, 1969
5. **Kurohara SS, Webster JH, Ellis F, et al:** Role of radiation therapy and of surgery in the management of localized epidermoid carcinoma of the maxillary sinus. Am J Roentgenol 114:35-42, 1972
6. **Som ML:** Surgical management of carcinoma of the maxilla. Arch Otolarynogolgy 99:270-273, 1974
7. **Ahmad K, Cordoba RB, Fayos JV:** Squamous cell carcinoma of the maxillary sinus. Arch Otolaryngology 107:48-50, 1981
8. **Hu YH, Tu GY, Qi YQ, et al:** Comparison of pre- and postoperative radiation in the combined treatment of carcinoma of maxillary sinus. Int J Radiat

Oncol Biol Phys 8:1045-1047, 1982
9. **Shibuya H, Horiuchi JI, Suzuki S, et al:** Maxillary sinus carcinoma: Result of radiation therapy. Int J Radiat Oncol Biol Phys 10:1021-1026, 1984
10. **Frich Jr JC:** Treatment of advanced squmous carcinoma of the maxillary sinus by irradiation. Int J Radiat Oncol Biol Phys 8:1453-1459, 1982
11. **Amendola BE, Eisert D, Harza TA, et al:** Carcinoma of maxillary antrum: Surgery or radiation therapy. Int J Radiat Oncol Biol Phys 7:743-746, 1981
12. **Frazell EL, Lewis JS:** Cancer of the nasal cavity and accessory sinuses. Cancer 16:1293-1301, 1963
13. **Cheng VST, Wang CC:** Carcinomas of the paranasal sinuses. Cancer 40:3038-3041, 1977
14. **Bush SE, Bagshaw MA:** Carcinomas of the paranasal sinuses. Cancer 50:154-158, 1982
15. **Korzenski S, Reinfuss M, Skolyszewski J, et al:** The evaluation of radiotherapy after incomplete surgery in patients with carcinoma of the maxillary sinus. Int J Radiat Oncol Biol Phys 11:505-509, 1985
16. **Lee F, Ogura JH:** Maxillary sinus carcinoma. Laryngoscope 91:133-139, 1981
17. **Beale FK, Molony TJ:** The role of radiotherapy in benign and malignant disease of the maxillary antrum. Otolaryng Clinics of N Am 9:269-289, 1976
18. **Robin PE, Powell DJ:** Regional node involvement and distant metastasis in carcinoma of the nasal cavity and paranasal sinuses. J Laryngol Otol 94: 301-309, 1980
19. **Kondo M, Inuyama Y, Ando Y, et al:** Patterns of relapse of squamous cell carcinoma of the maxillary sinus. Cancer 53:2206-2210, 1984
20. **Kondo M, Ogawa K, Inuyama Y:** Prognostic factors influencing relapse of squamous cell carcinoma of the Maxillary Antrum. Cancer 55:190-196, 1985
21. **Sato Y, Morits M, Takahashi H, et al:** Combined surgery, radiotherapy, and regional chemotherapy in carcinoma of the paranasal sinuses. Cancer 25: 571-575, 1970
22. **Shibuya H, Takagi M, Horiuch J, et al:** Clinicopathological study of maxillary sinus carcinoma. Int J Radiat Oncol Biol Phys 11:1709-1712, 1985
23. **O'brien PH, Carson R, Steubner Jr EW, et al:** Distant metastasis in epidermoid cell carcinoma of the head and neck. Cancer 27:304-307, 1971
24. **Fletcher GH:** Elective irradiation of subclinical disease in cancers of the head and neck. Cancer 29:1450-1454, 1972
25. **Pezner RD, Moss WT, Tong D, et al:** Cervical lymph node metastases in patients with squamous cell carcinoma of the maxillary antrum: The role of elective irradiation of the clinically negative neck. Int J Radiat Oncol Biol Phys 5:1977-1986, 1979
26. **Weymuller Jr EA, Reardon EJ, Nash D:** A comparison of treatment modalities in carcinoma of the maxillary antrum. Arch Otolaryngol 106:625-629, 1980
27. **Ketcham AS, Chretien PB, Van Buren JS, et al:** The ethmoid sinuses: A reevaluation of surgical resection. Am J Surg 126:469-476, 1973

=국문초록=

원발성 상악동 편평상피암의 방사선치료

서울대학교 의과대학 치료방사선과학교실 · 이비인후과학교실*

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1979년 2월부터 1986년 9월까지 서울대학교 병원 치료방사선과에서 치료받은 상악동의 편평상피암 환자 73예를 분석하였다. 41예에서는 수술과 수술후 또는 수술전 방사선치료를 병용하여 치료하였고 32예에서는 방사선치료만을 주치료로 시행하였다.

전체환자의 5년 생존율은 40.4%였으며 방사선치료만을 주치료로 시행한 집단의 5년 생존율은 22.1%였고 수술과 방사선치료를 함께 시행한 집단의 5년 생존율은 65.3%였다.

치료 후 사망이 확인된 환자 가운데 상세한 치료실패 과정을 알 수 있었던 31예 중 잔류병소를 포함 국소치유실패를 나타냈던 경우가 22예(71.0%)였고 경부임파절 재발로 인한 치유실패가 6예(19.3%)였으며 원격전이로 인한 치유실패가 3예(9.7%)에서 나타났다.

그러므로, 상악동 암의 국소치유율을 증가시켜서 생존율을 높이기 위해서는 계획된 수술과 방사선치료의 병용요법이 필요할 것으로 생각된다.