

Preoperative Radiotherapy of Maxillary Sinus Cancer

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Purpose : This study was to evaluate the effectiveness of preoperative radiotherapy in maxillary sinus cancer.

Materials and Methods : A retrospective analysis was done for 42 patients with maxillary sinus cancer who were treated with radiation with or without surgery from April 1986 to September 1996. There were 27 male and 15 female patients. Patients' age ranged from 24 to 75 years (median 56 years). Stage distribution showed 2 in T2, 19 in T3, and 21 in T4 lesions. The histologic type was squamous cell carcinoma in 38, undifferentiated carcinoma in 1, transitional cell carcinoma in 1, and adenoid cystic carcinoma in 2 patients. All patients were treated with radiation initially with a dosage range of 50.4-70.2 Gy (median 70.2 Gy) before further evaluation of remnant disease. Eleven patients were given induction chemotherapy (2 cycles of 5-fluorouracil and cisplatin) concurrently with radiotherapy. Six to eight weeks after radiotherapy with or without chemotherapy, computerized tomography (CT) of paranasal sinus was taken to evaluate remnant disease. If the CT finding showed remnant disease, a Caldwell-Luc procedure was done to get the specimen of suspicious lesions. A radical maxillectomy was done if the specimen was proven to contain malignancy. In contrast periodic follow-up examination was done without any radical surgery if the tissue showed only granulation tissue. Follow-up period ranged from 3 to 92 months with a median 16 months.

Results : Nine (21.4%) patients showed complete response (CR) and 33 patients (78.6%) showed persistent disease (PER) to initial radiotherapy. Among the 9 CR patients, 7 patients had no evidence of disease (NED), 1 patient had local failure, and 1 patient had regional failure. Among 33 PER patients, salvage total maxillectomy was done in 10 patients, and the surgery was not feasible or refused in 23 patients. Following the salvage radical surgery, 2 patients were NED and 8 patients were PER status. Overall and disease-free survival rate at 5 years was 23.1% and 16.7%, respectively. The only factors associated with the overall survival rate was the response to radiotherapy ($p < 0.01$).

Conclusion : The only factors associated with the overall survival rate was the response to radiotherapy. We could omit a radical mutilating surgery by preoperative irradiation in 7 of 42 patients (21.4%) so as to preserve their facial integrity.

Key Words : Maxillary sinus cancer, Preoperative radiotherapy

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INTRODUCTION

Cancer of the maxillary sinus comprises less than 1% of all malignancies and 14% of all malignant head and neck tumors. Surgery alone is effective in the early lesions, which are rarely seen in the clinic. For most of the patients with advanced and moderately advanced lesions, the combined treatment of radiation and surgery is the only effective method of cure. With such treatment, the five-year survival rate has been raised to about 50%.^{1,2)} However, radical surgery confers significant mutilation to the patients. In maxillary cancer, cosmesis is another important factor to influence the selection of treatment. Aggressive surgery for maxillary cancer is associated with functional and cosmetic morbidity related to resection of the palate, maxilla and orbital contents. If we can omit major surgery by effective preoperative irradiation, we can preserve the facial integrity of the patients and improve the quality of their life. This study was to evaluate the effectiveness of preoperative radiotherapy in maxillary sinus cancer.

MATERIALS AND METHODS

To evaluate the effectiveness of preoperative radiation therapy with or without chemotherapy, a retrospective analysis was done for the patients with cancer of the maxillary sinus treated between April 1986 to September 1996.

The patients included in this analysis were those who had biopsy-proven malignancy. The patients rejected from this analysis were those who had neck disease at presentation. A total of 42 patients were analyzed. There were 27 males and 15 females in this analysis. Age ranged from 24 to 75 years (median 56 years). There were 38 patients with squamous cell carcinoma, 2 patients with adenoid cystic carcinoma, 1 patient with transitional cell carcinoma, and 1 patient with undifferentiated carcinoma. Clinical diagnostic staging work-up included medical history, physical ex-

amination, CBC, chest x-rays, and CT of paranasal sinus. The staging was done according to American Joint Committee on clinical staging system.³⁾ There were 2 in T2, 19 in T3, and 21 in T4 lesions. According to ECOG scale, all patients were estimated as H0 or H1 (Table 1).

All patients were treated with radiation with a dosage range of 50.4–70.2 Gy (median 70.2 Gy), five times a week, 1.8 Gy daily before further evaluation of remnant disease. Radiation therapy fields included ipsilateral paranasal sinus and/or orbit. A paired wedge technique was used with 6 MV X-ray. The eye was not shielded when the tumor grossly involved the orbit. All patients were contoured and computer-assisted dosimetry was used with wedges and bolus to insure adequate dose distribution within the tumor volume. Eleven patients were given induction chemotherapy (2 cycles of 5-fluorouracil and cisplatin) concurrently with radiotherapy. Six to eight weeks after radiotherapy with or without chemotherapy, computerized tomography (CT) of paranasal sinus was taken to evaluate remnant disease. Response was judged as complete response (CR) when all

Table 1. Patient Characteristics

Characteristics	No of patients
Age (in years)	
Median	56
Range	24–75
Sex	
Female	15
Male	27
Histology	
Squamous	38
Undifferentiated	1
Transitional	1
Adenoid cystic	2
T stage	
T2	2
T3	19
T4	21
RT Dose (Gy)	
Median	70.2
Range	50.4–70.2
Follow-up (months)	
Median	16
Range	3–92

RT : radiotherapy

clinical evidence of the tumor had disappeared, and as persistent (PER) when there was any evidence of tumor masses. If the CT finding showed remnant disease, a Caldwell-Luc procedure was done to get the specimen of suspicious lesions. A radical maxillectomy was done if the specimen was proven to contain malignancy and exenteration of the orbital contents was performed if the orbit was invaded either. Periodic follow-up examination was done without any radical surgery if the tissue showed only granulation tissue. Follow-up period ranged from 3 to 92 months (median 19 months) and no one was lost to follow-up.

Survival was calculated by Kaplan-Meier method and analyzed by logrank test.⁴⁾ Overall and disease-free survival rate were calculated from the beginning of the first treatment to the date of death and date of the first failure, respectively. All contingency tables were evaluated by chi-square test.⁵⁾

RESULTS

CR was noted in 9/42 patients (21.4%) and PER in 33/42 patients (78.6%) after initial radiotherapy with or without chemotherapy. Among 9 patients with CR to initial treatment, 7 patients had no evidence of disease (NED), 1 patient had local failure, and 1 patient had regional failure after 3 and 11 months, respectively. Among 33

PER patients, salvage total maxillectomy was done in 10 patients, and the surgery was not feasible or refused in 23 patients. Following the salvage radical surgery, 2 patients were NED and 8 patients were PER status. We could omit a radical mutilating surgery by preoperative irradiation in 7 of 42 patients (21.4%) so as to preserve their facial integrity (Table 2).

Overall and disease-free survival rate at 5 years was 23.1% and 16.7%, respectively (Fig. 1). Median survival time was 21 months.

The only prognostic factor associated with the overall survival rate was the response to

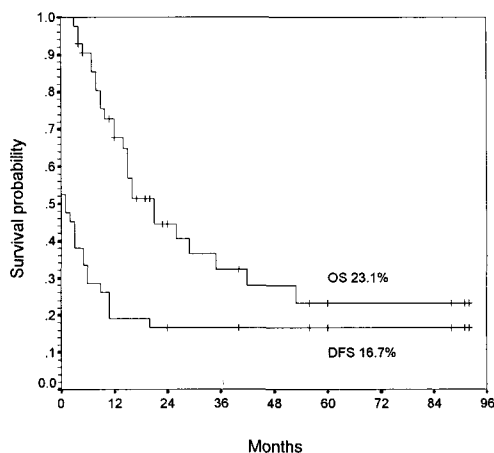


Fig. 1. Overall and disease-free survival for all patients.

Table 2. Response to Treatment and Outcome

CR 9	↙ ↘	NED 7	
		LRF 2	
PER 33	↙ ↘	TM 10	NED 2
			PER 8
		PER 23	

CR : Complete response
 NED : No evidence of disease
 LRF : Locoregional failure
 PER : Persistent disease
 TM : Total maxillectomy

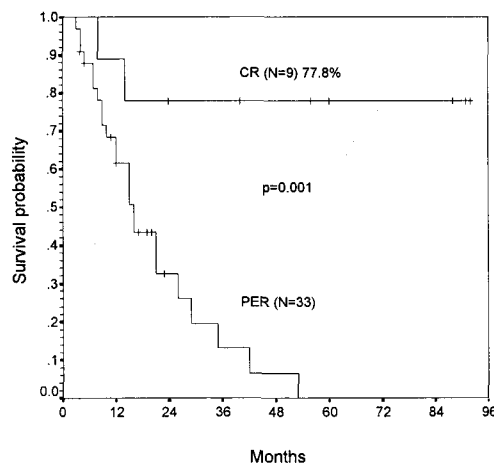


Fig. 2. Overall survival by response to radiotherapy.

Table 3. Prognostic Factors Predicting Overall Survival

Factors	p value
Response to RT	p=0.001
Modality	N.S.
Sex	N.S.
Age	N.S.
Radiation dose	N.S.
Histology (Squamous vs. Non-squamous)	N.S.

RT : Radiotherapy
N.S. : Not significant

Table 4. Characteristics of CR Patients vs. PER Patients

Characteristics	CR (N=9)	PER (N=33)
Sex		
Male	3	24
Female	6	9
Histology		
Squamous	9	29
Non-Squamous	0	4
T Stage		
T2	0	2
T3	4	15
T4	5	16
Chemotherapy		
+	2	9
-	7	24
RT dose (Gy)		
50.4	1	0
59.4	1	1
70.2	7	32

CR : Complete response
PER : Persistent disease

radiotherapy ($p < 0.01$, Fig. 2). Chemotherapy did not impact survival rate. Radiation dose and histologic type did not impact survival rate, either (Table 3). The characteristics of 9 CR patients and 33 PER patients to initial treatment are described in Table 4. We could not find any significantly different factor between CR patients and PER patients.

Treatment was tolerated quite well in most cases. No case of severe complications was observed.

DISCUSSION

Malignant tumors of the maxillary sinus have a

notoriously bad prognosis. No definite agreement has been reached concerning the optimum treatment for patients with maxillary sinus carcinoma. Improvements in the field of surgery, radiotherapy, and chemotherapy are not reflected in a higher survival percentage. The 5-year survival rate of 35–50% is highly disappointing. Surgery alone is effective in the very early lesions, which rarely are seen in the clinic. In advanced disease, especially T4 disease, it is almost impossible to resect the tumor completely. Therefore, preoperative radiation therapy is indispensable for patients with such advanced disease.¹²⁾ Radiation therapy plays an important role in sterilizing malignant cells that cannot be removed by operation.^{1, 2, 8, 16)} Hu et al.¹³⁾ reported preoperative radiotherapy was obviously superior than postoperative radiotherapy.

A serious problem of a radical surgery is that it imposes a major facial mutilation^{9, 11, 15)} Because of its mutilating nature, therefore, appropriateness of using total maxillectomy should be seriously considered. Preoperative radiotherapy has a possible role in maintaining facial integrity of the patients with maxillary cancer. In our group of patients, radiation therapy with or without chemotherapy actually excluded the necessity of a maxillectomy in 7 of 42 patients (21.4%). In other words, we could omit 7 unnecessary radical surgeries by effective preoperative treatment. Moreover, among the 10 patients who underwent salvage radical surgery, not all but only 2 of them was rescued.

Five-year overall and disease-free survival rate of 23.1% and 16.7%, in this study are lower than previously reported data. In patients with maxillary cancer treated with combined surgery and radiation, the 5-year survival rate varies between 30–50%.^{8, 16)} Our poor result may be accounted for the high proportion of advanced disease. In comparison with other series, our group of patients had a very high proportion of advanced disease, i.e., 50% had T4 tumors (Table 1).

Our study suggested that response to radiation was the most important prognostic factor for

maxillary cancer. Though there was no significantly different prognostic factor between CR patients and PER patients (Table 4), local control should be the main aim of treatment of maxillary cancer. The analysis of patterns of relapse showed that local recurrence was the primary cause of failures in all stages.¹⁴⁾

Although a relatively wide range of radiation doses has been used in the treatment of maxillary carcinomas for combined therapy or radiation therapy alone, most authors advocated 40 to 60 Gy for combined therapy¹⁰⁾ and 60 to 70 Gy for radiation therapy alone.^{17, 18)} In this analysis, radiation dose could not be an issue because most patients received around 70 Gy of radiation. Considering the aggressive nature of maxillary cancer, it seems reasonable to give high-dose radiation up to the tolerance level of the normal tissues. However, one patient who was given 50.4 Gy and the other who was given 59.4 Gy were also controlled by radiotherapy alone for 56 and 60 months, respectively. In the next study, we are to plan to calculate the dose-response curve.

Chemotherapy did not impact survival rate in our study, though we believe CR to initial treatment was accounted for the addition of chemotherapy. Lorusso et al.⁶⁾ reported that maxillary cancer was highly responsive to systemic combination chemotherapy containing cisplatin-based regimens. More through prospective study may be required to settle this issue in the future.

Salvage surgery rescued only 2 of 10 patients (20%). The remaining 8 patients were not salvaged even with the radical surgery. Giri et al.⁷⁾ reported surgery should be an integral part of treatment of maxillary cancer. We also agree with that idea but we may not control the disease even with radical surgery if it is too far advanced.

Radiation therapy with or without chemotherapy excluded the necessity of a maxillectomy in 7 of 42 patients (21.4%). Treatment was tolerated quite well in most cases. No case of severe complications was observed. This kind of treatment for maxillary sinus malignancy seemed to contribute to lower the rate of facial mutilation though it's

not much satisfactory.

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= 국문 초록 =

상악동암에서 수술 전 방사선 치료의 효과

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목 적 : 상악동암에서 수술 전 방사선 치료를 시행함으로써 안면 보존의 가능성이 어느 정도 되는지를 알아보려고 하였다.

대상 및 방법 : 1986년 6월부터 1996년 9월까지 상악동암으로 방사선치료를 받은 42명의 환자를 대상으로 후향적 분석을 시행하였다. 환자의 연령은 24세에서 75세로 중간값은 56세였으며, 남자 27예, 여자 15예였다. 병기별 분포는 T2 2예, T3 19예, T4 21예로 진단 당시 대부분 진행된 상태였다. 조직학적으로는 편평 상피암 38예, 미분화 세포암 1예, 이행 상피암 1예, 선양 낭종암 2예였다. 모든 환자에 대해 동측 부비동을 포함하는 쌍췌기법 방법의 방사선치료를 시행하였다. 방사선 치료선량은 50.4-70.2 Gy로 중간값은 70.2 Gy였다. 11례의 환자에 대해 방사선치료와 유도 화학요법을 병행하였다. 화학요법은 5-fluorouracil과 cisplatin으로 2회 시행하였다. 대상 환자의 추적기간은 3개월에서 92개월로 중간값은 16개월이었다. 방사선치료 후 6 내지 8개월 경과 후 전산화단층촬영을 실시하여 병소의 반응을 평가하였다. 완전관해가 된 경우는 계속 추적검진만 하였으며 병변이 의심되는 경우는 콜드웰-뤼크 수술을 시행하여 확인하였다. 병변이 확인된 경우는 상악동전절제술을 시행하였다.

결 과 : 방사선 및 화학요법 시행 후 9예 (21.4%) 에서 완전관해를 보였고 33예 (88.6%) 에서 잔여병변이 확인되었다. 완전관해를 보인 9예의 환자 중 7예가 국소제어되었으며 2예에서 국소 재발하였다. 잔여병변이 있는 33예의 환자 중 10예에서 근치적 수술이 가능하였고 그 중 2예에서 국소제어가 되었다. 전체 환자의 5년 생존율은 23.1%였고 5년 무병생존율은 16.7%였다. 방사선치료에 대한 반응 ($p < 0.05$) 만이 생존율에 영향을 미치는 유의한 인자였다.

결 론 : 방사선치료에 대한 반응만이 생존율에 영향을 미치는 유의한 인자였다. 전체적으로 7예 (16.7%) 에서 수술 전 방사선치료로 안면보존이 가능하였다.