

## SQUAMOUS CELL CARCINOMA OF THE MAXILLARY SINUS AND THE ORAL PART OF THE UPPER JAW

### Comparison of treatment results

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The treatment results were compared in 77 patients with maxillary sinus squamous cell carcinoma (MC) and 53 patients with squamous cell carcinoma arising from the oral part of the upper jaw (OC). Both sets of patients received radiotherapy alone, or radiotherapy combined with surgery and/or chemotherapy. Computerized tomography was useful for the definition of the treatment volume. Intraarterial chemotherapy was given in 89 of 130 patients and in these patients the total radiation dose was reduced by about 10 Gy. No difference was found in the 5-year survival rate between the MC (65%) and the OC (66%) groups. The cumulative incidence of local failure was higher in MC (36%) than in OC (26%), whereas the ultimate incidence of neck node metastasis was higher in OC (43%) than in MC patients (18%). Half of the inoperable patients (9/18) were older than 80 years and had contraindications to anaesthesia and major surgery. The local recurrence rate was high in the inoperable MC patients (6/8). Contralateral sinus cancers occurred in 4 patients in the MC group.

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Carcinomas arising from the maxillary antrum (MC) and from the oral part of the upper jaw (OC) are from practical point of view often categorized as cancers of the upper jaw (1, 2). Several reports have been published during recent years concerning both OC (3-5) and MC (6-10).

Even in MC and OC from biological point of view should be regarded as separate entities, the treatment modalities are quite similar for these two types of tumor and a comparison of the treatment results may therefore

be of interest. In Japan, surgical resection, radiotherapy, and intraarterial infusion of 5-FU (trimodal combination therapy) are currently the most common treatment modalities (6-8). The selection of appropriate treatment for each case has probably led to improved therapeutic results in both types of tumor, although other problems following treatment have become apparent.

#### Material and Methods

The subjects of this analysis were patients with squamous cell carcinoma of the maxillary sinus (MC) and oral part of the upper jaw (OC), treated at the Department of Radiology of Tokyo Medical and Dental University between 1980 and 1988. The parameters investigated included local recurrence, regional and/or distant metastasis, treatment complications, and some prognostic factors. The study included 130 patients: 77 MC (50 males and 27 females) and 53 OC, (36 males and 17 females). Excluded among the sinus tumors due to diverging histology were 10 malignant lymphomas, 3 undifferentiated carcinomas,

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2 extramedullary plasmacytomas, 2 adenoid cystic carcinomas, 2 malignant fibrous histiocytomas, 2 embryonal cell sarcomas, and one adenocarcinoma. Ten malignant lymphomas, 3 adenoid cystic carcinomas, 2 anaplastic carcinomas, 2 malignant melanomas and one each of undifferentiated carcinoma, sarcoma, and mucoepidermoid carcinoma, were excluded from the OC group as not representing squamous cell carcinoma.

Pretreatment examinations included chest x-rays, plain skull x-rays, orthopantomograms, and dental x-rays, as well as CT of the maxillary sinus and neck region. Concerning the CT diagnosis, patients with a soft tissue mass occupying the maxillary sinus, with or without maxillary antral wall destruction, were diagnosed as having MC, whereas patients with an upper gum or hard palate tumor with alveolar or hard palate bone destruction were diagnosed as having OC.

Based on the UICC TNM system (1987) (9), 77 MC cases were classified as follows: one as stage I, 7 as stage II, 27 as stage III, and 42 as stage IV. Similarly classified the number of OC cases at stages I, II, III and IV were 3, 20, 14, and 16 respectively (8). At first presentation, neck metastasis was found in 15/53 (28%) of OC cases and in 3/77 (4%) of MC cases.

The MC patients were treated by 4 MV x-rays using wedge filter portals at 90 degrees for tumors of the maxillary antrum, with the eye shielded at treatment from the anterior portal, depending on the degree of the orbital invasion. Forty-seven among 53 OC patients who had bone destruction with or without sinus involvement were treated by 4 MV x-rays using either wedge filter portals at 90 degrees or by parallel opposing portals. External radiation therapy consisted of 2.5 Gy per day, 4 times per week. The total external radiation dose in the tumors for both sets of patients ranged from 30 Gy to 60 Gy with a median dose of 50 Gy; 30 Gy was given for OC who were irradiated preoperatively and 50 Gy in 5 weeks was given for patients treated by combined treatment. Eight MC and 10 OC were inoperable and treated by external radiotherapy alone and given 60 Gy in 6 weeks. Nine (3 MC and 6 OC) among these 18 inoperable patients were older than 80 years and had contraindication to general anesthesia and/or major surgery. Six OC cases with superficial lesions on CT were treated with either  $^{198}\text{Au}$  grain mold or interstitial implantation without surgical excision.

Surgical excision of the primary lesion was performed in 69 of the MC patients. Surgical excision of the tumor was also performed in 37 OC patients who were diagnosed as having bone destruction on CT. Most of these operations involved partial maxillectomy, but total maxillectomy including orbital extraction was performed in 10 of the MC patients. Intraarterial chemotherapy using 5-FU (5-fluorouracil), infused via the superficial temporal artery, was administered in 66 MC and 23 OC patients, with 5-FU doses ranging from 1.5 g to 5.9 g, with a median

dose of 4.5 g in 5 weeks. Clinically negative necks were not irradiated or dissected and were followed to the appearance of node metastasis.

Local recurrences in both the MC and OC patients were treated by surgery and/or irradiation, including intracavitary brachytherapy, and by other modalities including chemotherapy. Regional neck metastases in either set of patients were mainly treated by radical neck dissection or by irradiation and/or chemotherapy.

Disease specific survival was calculated according to Kaplan and Meier, and the differences were analysed by the generalized Wilcoxon's test. Multivariate analysis of prognostic factors by multiple regression analysis was performed for the various stage, sex, age, total dose administered, type of surgery, and/or chemotherapy.

### Results

There was no difference in sex distribution between the two groups, but the average age of the OC patients was approximately 10 years higher than of the MC patients.

The MC and OC disease specific survival curves are shown in Fig. 1 and the survivals by stage in Figs. 2 and 3. There was no statistical difference between the disease specific curves for MC patients (5 years; 65%) and the OC patients (5 years; 66%). There was a statistical difference ( $p = 0.07$ ) in the 10-year survival rate between stage II and stage IV MC patients. In the 7-year survival, a difference was noted in the OC patients between stage II and stage IV ( $p = 0.09$ ), and between stage II and stage III ( $p = 0.03$ ).

The incidence of local failure in the MC patients was 36% (28/77) and it was higher in non-operated patients (6/8) than in operated patients (20/69). There was no obvious relation between radiation dose and the recurrence rate in the MC group. The incidence of local failure in the OC patients was 26% (14/53) and there was no obvious

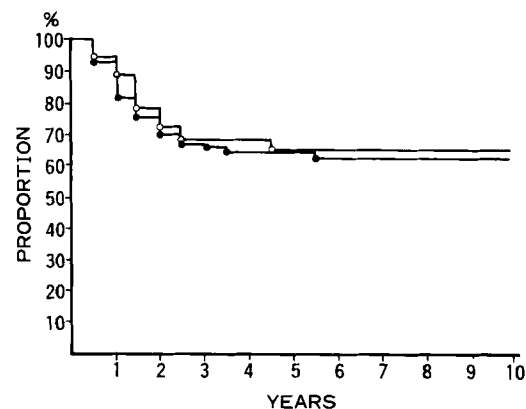


Fig. 1. Disease specific survival curves of 77 patients with maxillary sinus carcinoma (—●—) and 53 with oral carcinoma in the upper jaw (—○—).

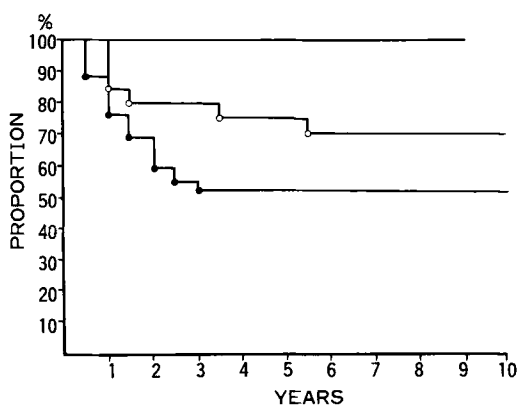


Fig. 2. Disease specific survival by stage of patients with maxillary sinus carcinoma, according to the UICC clinical classification (1987). —○—: Stage I+II (n=8); - -○-: stage III (n=27); —●—; Stage IV (n=42).

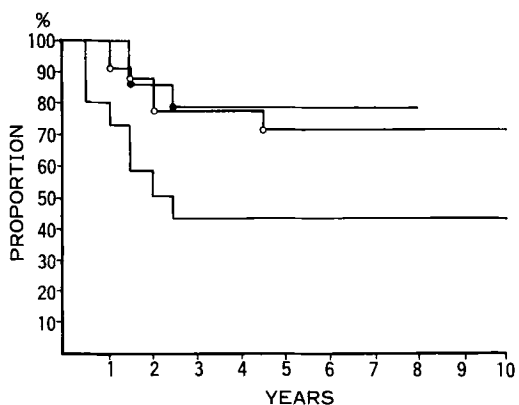


Fig. 3. Disease specific survival by stage of patients with oral carcinoma in the upper jaw according to the UICC clinical classification (1987). —○—: Stage I+II (n=23); —●—: Stage III (n=14); —: Stage IV (n=16).

difference between operated patients (10/37) and non-operated patients (4/16) (Fig. 4). The dose of 5-FU had no discernible relation to the local control rate but the total radiation dose to the primary lesion was in these patients reduced by about 10 Gy. All but 3 cases of the local recurrences in the MC patients occurred within 20 months, with the remaining three occurring at 21, 26, and 71 months after the initial treatment.

The local recurrence was successfully treated in 4 (17%) out of 24 recurrences in MC patients and in 2 (15%) out of 13 in the OC patients. Of the 24 local recurrences in the MC patients, 9 were treated by surgery, which proved successful in only one patient, and further 8 were irradiated, with successful results in three patients. Two of these three radiation-salvaged cases developed brain necrosis and underwent successful surgery for removal of the necrosis at 1 and 3 years respectively after the second radiation treatment. However, one of them got motor aphasia and periodic epileptic seizures postoperatively. Out of the 14

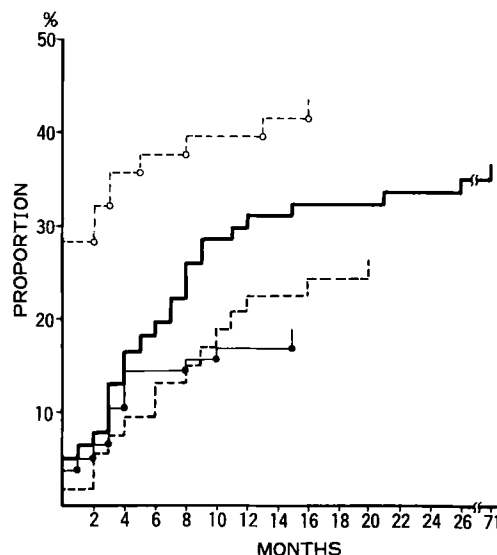


Fig. 4. Cumulative incidence (proportion) of local recurrence and neck node metastasis after treatment. Maxillary sinus carcinoma: —: local recurrence, - - -: neck node meta. Oral carcinoma in the upper jaw: —●—: local recurrence, —○—: neck node meta.

cases with local recurrence in OC group, 3 were operated, 6 irradiated, and one laser-treated, treatment was successful in only on operated case and in the laser-treated patient.

A rather low cumulative incidence of neck metastases was noted in the MC patients (14/77 = 26%). In contrast, the cumulative incidence of neck metastases in the OC group was high (23/53 = 43%). In both groups, the neck metastases occurred within 16 months after initial treatment. In the MC group, radical neck dissection was performed in 8 of the 14 patients, and was successful in 7 cases. In the OC group, 21 of the 23 patients with neck metastasis underwent a radical neck dissection, but only in 11 patients with successful result. In only two of the 77 MC patients was a distant metastasis the first relapse.

Postirradiation monitoring for more than 3 years of the eye on the diseased side was possible for more than 3 years in 37 MC patients. Out of 8 patients, in whom the eye was shielded when the anterior portal was exposed, 2 developed cataract that was successfully treated by surgery. In 18 out of 29 patients, in whom an eye was included in both the lateral and anterior portals, clinical evidence of subsequent cataract was detected and 12 of these patients underwent successful cataract surgery. Furthermore, in one patient, severe blepharitis developed 3 years after irradiation and the eye had to be enucleated.

A multivariate analysis of the prognostic factors was performed for all 130 cases, and the age ( $p = 0.02$ ) and clinical stage ( $p = 0.01$ ) were significant. Age had a significant association to the prognosis in both the MC ( $p = 0.06$ ) and OC ( $p = 0.07$ ) groups. The strong association to age could, at least probably, be explained by the

fact that 9 out of 14 patients who were older than 80 years were not operated but only received radiation therapy with or without chemotherapy. The clinical stage was also found to significantly correlate to the prognosis in the MC group ( $p = 0.08$ ).

Second cancers were found in 17 of the 77 MC patients and in 8 of the 53 OC patients. In one of these 8 OC patients, a synchronous buccal mucosal cancer was found. In 4 of the 17 MC patients with metachronous second cancer, a first primary carcinoma had developed in the contralateral maxillary antrum and had been successfully treated 5 to 17 years prior to their second maxillary antral carcinoma. The three other antecedent cancers in the MC group represented breast cancer, tongue cancer, and esophageal cancer. Of 10 cancers that subsequently developed in the MC patients, three were gastric cancers, two esophageal cancers, two hepatic cancers, one tongue cancer, one laryngeal cancer, and one malignant lymphoma. In the OC group, the 4 antecedent cancers included 2 gastric cancers, one sigmoid colon cancer, and one esophageal cancer. Three cancers that subsequently developed in the OC patients represented pulmonary carcinoma, prostatic cancer, and esophageal cancer.

### Discussion

The clinical and biological differences between MC and OC have been known since several decades and are mentioned in several reports and text books (2–5). The introduction of CT has made it easier to differentiate between these two types of tumor and adequate radiation treatment fields (10).

Some well-known differences between MC and OC, apart from anatomical sites, could be verified in the present analysis. An age difference was thus found and the OC patients were on average about 10 years older than the MC patients. In this connection it should be mentioned that the incidence of oral cancers among older persons in Japan has been increasing (5). We had to choose non-invasive treatment methods for very old patients and patients with physical and mental complications (10). Age was strongly related to the prognosis in both MC and OC patients. The cumulative incidence of neck node metastases was twice as high in the OC patients than in the MC patients. However, in the OC group, there was often a favorable therapeutic response (52%) to neck dissection. We thus found that cervical lymph node metastasis was not necessarily connected with a poor prognosis in agreement with reports by other authors (1, 12, 13). The cumulative incidence of local recurrence was relatively low (26%) in OC patients compared to that in MC patients (36%). The survival curves were quite similar for MC and OC patients.

Another difference between the two groups concerned the site where the second primary cancer occurred. Con-

cerning MC patients, a high incidence of second cancer in the contralateral maxillary sinus has been reported (14, 15). Four such cases were found in our 77 MC cases. However, second primary cancers in the upper aerodigestive tract occurred with about equal frequency in the MC and OC groups.

A characteristic common for these two groups is the high incidence of local failures (10). Local failure seems to be the greatest risk for these patients which mainly explain the still relatively poor long-term results. In the present series, salvage treatment gave successful result in only 17% of the MC patients and 15% of the OC patients. This can be compared with successful salvage treatment of neck node metastasis in 54% of the MC and 48% of the OC cases. In our series most local recurrences appeared within two years after treatment. However, local recurrences have been reported to occur also after a 5-year disease-free period (10). Since the introduction of trimodal combination therapy, there seems to be a reduction of the incidence of late local recurrence (13). If this possible reduction is due to chemotherapy or improved surgical radicality is not known. The incidence of distant metastasis as first relapse is, according to all experience, low in both MC and OC and was observed in only 2 of our 130 patients. This seems to support a previous suggestion that partial maxillectomy does not increase the risk of distant metastasis (12).

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