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SQUAMOUS CELL CARCINOMA OF THE ORAL CAVITY

An unselected material from a 5-year period

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Abstract

Three hundred and four patients with squamous cell carcinomas of the oral cavity were treated at the Finsen Institute in cooperation with the ENT-surgical departments between 1978 and 1982. The primary treatment consisted of radiotherapy alone in 74%, surgery alone in 4%, and a combination of radiotherapy and surgery in 15% of the patients. Two per cent received other treatment (cryotherapy), 5% did not complete the planned radiotherapy, and 1% were not treated at all. Of 203 patients with tumour remnant or first recurrence, 45% were operated, 2% received radiotherapy, and 2% combined treatment. This treatment strategy made 38% of the patients free of disease in the follow-up period ($3\frac{1}{2}$ to 8 years) or until the patients died from other causes. Fifty-nine per cent of the patients died from their oral carcinomas. Tumour size (T), lymph node status (N), and tumour stage were as expected important prognostic factors.

Key words: Oral carcinoma, radiotherapy, surgery, survival.

In Copenhagen it has for many years been a tradition to give primary radiotherapy with curative intent to most patients with squamous cell carcinoma of the oral cavity. Surgery has been reserved for a minority with small and selected tumours, and for remaining or recurrent tumour after radiotherapy.

A retrospective study of this treatment stategy in an unselected material of patients concsecutively referred to the Finsen Institute and the ENT-surgical departments is now presented.

Material

In the 5-year period from 1978 to 1982, 304 patients with invasive squamous cell carcinoma of the oral cavity were referred for treatment. There were 129 females (with 23 to 91 years of age, average 69 years), and 175 males (with 37 to 91 years of age, average 65 years).

The tumour locations in the oral cavity are specified in Table 1, and the most frequent tumour localizations were: the floor of the mouth (30%), the tongue (29%) and the mandibular gingiva (19%). Females presented more often with a tumour in the palate or cheek, whereas males had tumour in the floor of the mouth or in the tongue more often than females.

Prior to therapy all the patients were examined at a joint conference by radiotherapists and otolaryngologists for clinical tumour classification and treatment planning.

The TNM distribution is shown in Table 1. Most patients had T2 tumours (37%), and the rest had an almost even distribution of T1 (19%), T3 (22%) and T4 (22%) tumours. Concerning clinical lymph node status, 67% were classified as N0, 19% as N1, 1% as N2, and 12% as N3. There were only minor differences between the two sexes. Only one patient had distant metastases (lung) at the time of diagnosis (T4, N1, M1). Seventeen per cent of the patients had stage I disease, 25% stage II, 26% stage III, and 32% stage IV. Thus, 58% of our patients had advanced disease with tumours in stage III or IV at the time of referral. There were only minor differences between males and females in this respect.

Treatment

Radiotherapy was administered as external irradiation by cobalt-60 from two lateral opposed (and sometimes wedged) fields to the target volume, which included the tumour with a margin of 2 cm and the subdigastric, submandibular and mid-jugular lymph node areas. In case of

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Table 1

Tumour characteristics

	No. of patients			
	Male	Female	All	%
Tumour localization				
Tongue (anterior 2/3)	53	34	87	28
Palate	6	11	17	6
Gingiva, upper jaw	7	6	13	4
Gingiva, lower jaw	29	30	59	19
Floor of mouth	64	26	90	30
Cheek	16	22	38	12
TNM-classification				
T1	37	21	58	19
T2	56	58	114	37
T3	46	20	66	22
T4	36	30	66	22
N0	112	93	205	67
N1	34	25	59	19
N2	1	2	3	1
N3	28	9	37	12
M0	174	129	303	100
M1	1	–	1	–
Stage				
I	33	18	51	17
II	34	42	76	25
III	48	32	80	26
IV	60	37	97	32

mid-jugular node metastases, the field extended to the supraclavicular region.

The daily dose in the target volume was 1.8–2.0 Gy with 5 fractions a week up to a total dose of 64–68 Gy in 6–7 weeks. In a few cases, the treatment was given with 2 larger fractions weekly up to a biologically equivalent total dose (1). Primary external irradiation with curative intent was given to 73% of the patients (Table 2).

Table 2

Primary treatment

	No. of patients	%
External irradiation	222	73
External irradiation + radium mold	1	–
Radium mold	2	1
Surgery	12	4
Preoperative irradiation + surgery	29	10
Operation + postoperative irradiation	8	3
Preop. irradiation + surgery + postop. irradiation	5	2
External irradiation not completed	16	5
Other treatment	5	2
No treatment	4	1
Total	304	101

Surgery was performed either as simple excision of the tumour, or as larger resections, sometimes requiring reconstruction. The excision or resection was combined with neck lymph node dissection, when metastases were suspected, or when the surgical procedure included the lymph node area in the reconstruction.

The larger operations were especially used for recurrence after radiotherapy, and primary surgery was performed in 14 patients only (4%), who had highly selected and small tumours.

A combination of radiotherapy and surgery was used in 42 patients (15%), who either received preoperative external irradiation up to a dose of 20–40 Gy in 2–4 weeks, immediately preceding the operation (10%), or given postoperative external irradiation to the operation area up to a dose of 64–66 Gy in 6–7 weeks (3%). A few patients (2%) received a combination of pre- and postoperative irradiation, up to a total dose of 66–68 Gy. The external irradiation could not be completed as planned for 5% of our patients (Table 2). These were patients with large tumours and a bad general condition, and they died shortly after the treatment.

It is evident from this unselected material, that we had very high ambitions as to treatment with curative intent. Only 4 patients out of 304 were excluded from such treatment, in spite of the fact that 58% of the patients had stage III or IV disease. None of the patients had chemotherapy as primary treatment.

Results

Results of primary treatment. The patients who had tumour persisting more than 8 weeks after primary treatment or had recurrent tumour were examined again at a joint conference in order to decide on further treatment. In our material, 203 patients (66%) had tumour remnant or recurrence after the primary treatment, as shown in Table 3. Out of the tumour remnants or recurrences 73% were located in the primary site, 21% in both primary site and neck nodes, and 5% in the neck nodes only. Distant metastases were rare (1%)

Treatment of recurrences. If the patient had been primarily operated, external irradiation was given with curative

Table 3

Location of tumour remnant or first recurrence

	No. of patients	%
Primary tumour (T)	149	73
Neck lumph nodes (N)	9	5
Both (T + N)	42	21
Distant metastases (M)	2	1
All sites (T + N + M)	1	–
Total	203	100

intent at recurrence. If necessary this treatment was followed by a new operation (Table 4). In case of tumour remnant or recurrence after radiotherapy, radical surgery was performed if possible. In fact, 45% of all patients with a first recurrence were operated and 48% of the patients with a second recurrence (Table 4).

Some patients with incurable recurrences got chemotherapy, thus 33 patients (16%) with first recurrence and 11 patients (18%) with later recurrence received such treatment, usually bleomycin or methotrexate and 5-fluorouracil. Long-term remissions were rare and the treatment was, at best, purely palliative (2). About one-third of the patients with first recurrence received no treatment, as they had inoperable tumours and their general conditions were too poor for chemotherapy.

Results of all treatment modalities. The final results of this treatment strategy are shown in Table 5. All patients were followed for at least $3\frac{1}{2}$ years and up to 8 years,

Table 4

Treatment of tumour remnant or recurrence

	First treatment		Second treatment	
	No. of patients	%	No. of patients	%
Surgery	91	45	29	48
Surgery + radiotherapy	3	2	–	–
Radiotherapy	5	2	3	5
Chemotherapy	33	16	11	18
Chemotherapy + radiotherapy	2	1	1	2
Other treatment	2	1	2	3
No treatment	67	33	15	24
Total	203	100	61	100

Table 5

Results of treatment

	No. of patients					
	Stage					
	I	II	III	IV	All	%
Free of disease after primary treatment	29	15	14	10	68	22
Free of disease after first recurrence treatment*	7	16	7	7	37	12
Free of disease after second recurrence treatment*	1	7	4	1	13	4
Died of oral carcinoma	13	36	54	75	178	59
Unknown (not evaluated after treatment)	1	2	1	3	7	2
Lost to follow-up	–	–	–	1	1	–
Total	51	76	80	97	304	100

* Recurrence includes tumour remnant and recurrences.

Table 6

Follow-up

	No. of patients					
	Stage					
	I	II	III	IV	All	%
Alive and free of disease	26	24	7	5	62	20
Died without cancer	8	13	14	10	45	15
Died of a second cancer but without oral cancer	3	1	4	3	11	4
Died without evaluation	1	2	1	3	7	2
Lost to follow-up	–	–	–	1	1	–
Died of oral carcinoma	13	36	54	75	178	59
Total	51	76	80	97	304	100

except for one patient who was lost to follow-up in a foreign country with the status of remnant tumour after surgery and radiotherapy.

After primary treatment, 22% of the patients were persistently free of disease. After treatment of tumour remnant or first recurrence, another 12% became free of disease, and after the second or further treatment for recurrence, 4% became free of disease. In all, 38% of all patients reached a stage in which they were clinically free of disease.

Fifty-nine per cent of the patients died of their oral carcinomas, and 2% were not evaluated concerning cause of death, as they died shortly after the treatment.

Table 6 shows the follow-up for these patients; 20% were still alive and free of disease $3\frac{1}{2}$ to 8 years after treatment. Fifteen per cent of the patients died of intercurrent diseases without recurrence of oral carcinomas. Four per cent died of a second cancer (lung, gastrointestinal or prostate), but without recurrence of their oral carcinomas.

Fig. 1 shows the crude survival rate for the whole material, divided into males and females; there was no

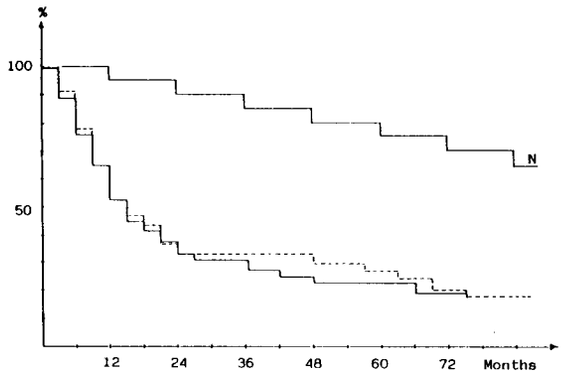

Fig. 1. Crude survival for 129 female (– – –) and 175 male (——) patients with oral carcinoma. The upper curve (——N) represents survival in the general population standardized for sex and age distribution in the study population.

difference in survival between the 2 sexes. A survival curve for the general population adjusted for sex and age distribution in the study material is also shown. There were no striking differences in survival between different age groups or between different tumour locations. There were significant survival differences between the different stages (Fig. 2). Three-year crude survival in stage I was 65%, in stage II 45%, in stage III 17%, and in stage IV only 6%.

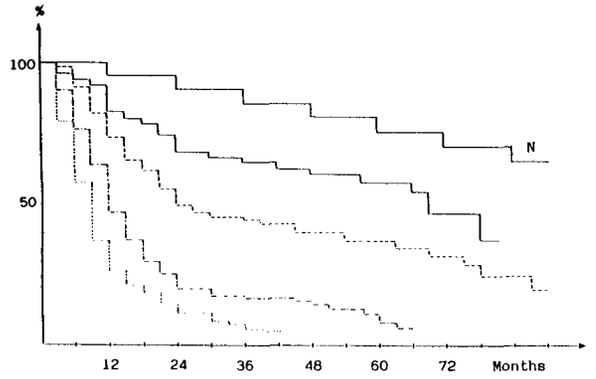

Fig. 2. Crude survival for primary tumours stage I (——), stage II (– – –), stage III (–·–·–) and stage IV (· · ·). The upper curve (– N) is survival for the general population standardized for sex and age distribution in the study population.

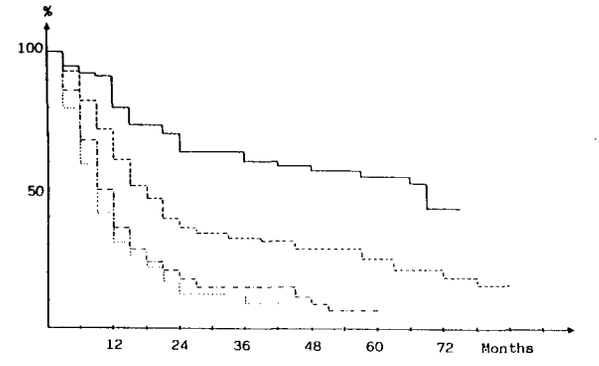

Fig. 3. Crude survival for primary tumours classified as T1 (——), T2 (– – –), T (–·–·–) and T4 (· · ·), UICC 1978.

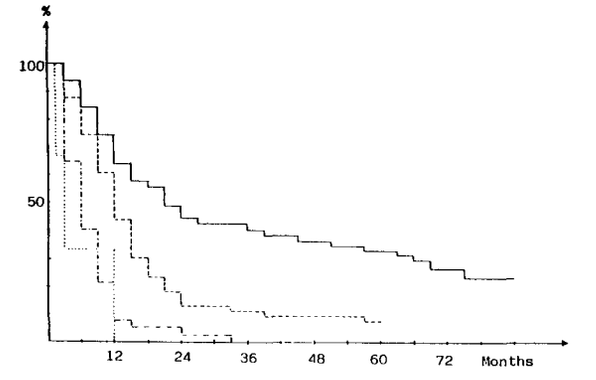

Fig. 4. Crude survival for primary lymph node status N0 (——), N1 (– – –), N2 (· · ·) and N3 (–·–·–), UICC 1978.

Significant survival differences were also found between the T1, T2 and T3 groups but not between T3 and T4 (Fig. 3). N0 and N1 had a better survival than N2 and N3 patients (Fig. 4). Log rank test was used for comparison of survival (3).

Discussion

It is difficult to compare our results with other reports which are often selected according to special tumour locations in the mouth (4, 5), or by treatment modalities (6, 7).

We found a similar crude survival for men and women, which is unusual in head and neck cancer. However, the distribution of age, tumour size and stage were very equal in men and women in our material. As expected, the treatment results in the less advanced stages were much better than in the more advanced ones (Table 5). Disease-free survival was in stage I 73% (37/51 patients) and in stage II 50% (38/76 patients), while the results in stages III and IV were very poor.

In Copenhagen there has been a tradition of treating both operable and inoperable oral carcinomas with primary radiotherapy, radical surgery being used mainly for locoregional tumour remnants or recurrences. The intention has been to cure the patients with a minimum of functional or cosmetic sequelae. This explains why only 4% in the present series were primarily operated.

Preoperative radiotherapy and surgery are described to give good results, at least in minor tumours of the tongue (4, 5, 8), but as mentioned by Snow (9), three randomized trials have failed to demonstrate higher survival for patients receiving preoperative radiotherapy than for patients treated by surgery alone (10–12). There are therefore divergent opinions concerning the value of preoperative radiotherapy.

Larger tumours (T3 and T4) are seldom sufficiently treated by radiotherapy alone, and in many cases tumour remnants persist and surgery must be performed anyway. There may be a reduction in tumour size after radiotherapy that can facilitate the surgery but surgical complications are also more frequent after radiotherapy. Primary surgery also for these tumours, followed by radiotherapy, might yield better results (13, 14) and therefore we have now a more aggressive surgical attitude even to the larger tumours, which sometimes are primarily operated and given postoperative radiotherapy.

Another possibility of obtaining better treatment results is to change the radiotherapeutic treatment schedule to accelerated fractionation with 2 fractions per day, as reported by Wang et al. (15). Interstitial implantation of radioactive sources (most often iridium-192) may achieve a high local tumour dose and may be used alone or in combination with external irradiation (6, 7, 16).

Chemotherapy before or in conjunction with radiotherapy has also been investigated. Several agents used as

single drugs or as combination chemotherapy have been tried (17, 18), but no improvement in survival has so far been demonstrated. One of the most promising chemotherapeutic treatment schedules has been reported by Kish et al. (19, 20) and others (21, 22).

The Danish Head and Neck Cancer Group has started a prospective, randomized trial with cisplatinum and 5-flourouracil before radiotherapy or surgery for treatment of squamous cell carcinomas of the oral cavity in stage II–IV.

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