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CHANGING ASPECTS IN THE TREATMENT OF SQUAMOUS CELL CARCINOMA OF THE ORAL TONGUE

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Abstract

Two groups of patients were compared. In group 1, consisting of 304 patients treated from 1958 to 1972 (minimum observation time of 5 years), the local and regional control rate was 35 per cent. In group 2, consisting of 126 patients treated 1978 to 1983 (median observation time of 58 months), the local and regional control rate was 60 per cent ($p<0.0001$). The local and regional control rates were improved for all stages, but the differences were significant only for stages T1N0, T2N0, T3N0 and TXN2,3. The actuarial survival rates also showed improvement in group 2 patients. The incidence of treatment failure, with regard to the neck alone or tongue and neck combined, decreased from 51 per cent to 27 per cent with the newer techniques. The greatest improvement was observed in patients with T1N0 and T2N0 tumors. There was also a decrease in the failure rates in patients with the more advanced tumors.

Key words: Tongue, neoplasms; squamous cell carcinoma, radiation therapy, surgery, prognosis.

During the 1930's a method evolved of inserting high intensity radium needles in a single plane into the tumor of the tongue. This method required only limited resources with just 3 to 4 days of hospitalization and was therefore relatively economic. Radiation mucositis developed after the patient was discharged. When the patient returned, the tumor had either completely or partially regressed.

Regardless of the response, a partial glossectomy was performed on most of the patients after a median interval of 3 months after the irradiation, providing tissue in the operative specimen for histologic examination. Whereas this method resulted in high degree of control of the primary site of the early stage carcinomas (86 per cent in T1N0), it was less satisfactory in more advanced tumors (56 per cent local control in T2N0 and 36 per cent in T3N0) (18). Because of the lack of adequate dosimetry and often incomplete coverage of all the tumor extent, the method was rarely applicable in larger tumors. A further disadvantage was that the method did not encompass treatment of occult metastases in the lymph nodes of the neck of many patients. Consequently, a large number of patients returned with neck node metastases, which were frequently fixed due to extracapsular growth of tumor into the soft tissues and the internal jugular vein. The incidence of conversion of a clinically negative neck to a neck with obvious palpable metastatic nodes after treatment (N0→N+), was found to be as high as 45 per cent in patients with T1N0 tumors and 49 per cent in those with T2N0 tumors (17). Such conversions were associated with a poor prognosis and a control rate of only 23 per cent. Only 1/3 of the patients were considered operable.

The new method initiated in 1978, expanded to include even more advanced tumors, consisted of 3 parts:

1) Initiation of treatment with high energy external irradiation, encompassing both the primary tumor and the regional neck nodes even in patients who had a clinically negative neck. The primary purpose was to eradicate occult tumor cells in the lymphatics outside the primary tumor, and at the same time reduce the volume of the tumor in the tongue and of any palpable nodes, if present.

2) Interstitial irradiation of the primary tumor of the tongue with radioactive iridium (^{192}Ir) implanted through guide needles and prefabricated plastic templates to insure proper placement, followed by computerized dose calculation. The goal was to deliver a high dose throughout the tumor volume with the hope of providing a cancericidal effect in a larger number of patients. Previous studies had shown that the five-year survival rate was significantly better for preoperatively irradiated patients in

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Table 1

Squamous cell carcinoma of the oral tongue. Incidence of clinical stages. Sites of failure at time of death. Local-regional control rates

Category	1958–1972							1978–1983							
	Incidence		Sites of failure			Control		Incidence		Sites of failure			Control		*p-value
	No.	Per cent	T	N	TN	No.	Per cent	No.	Per cent	T	N	TN	No.	Per cent	
T1N0	94	31	8	21	7	58	62*	36	29	2	4	1	29	81*	<.01
T2N0	61	20	8	6	20	27	44*	25	20	2	1	0	22	88*	<.001
T3N0	36	12	14	2	14	6	17*	16	13	2	4	2	8	50*	<.01
T4N0	2	0.7	2	0	0	0	0*	11	9	5	1	0	5	45*	NS
T1,2N1	21	7	5	2	7	7	33*	6	5	1	2	1	2	33*	NS
T3,4N1	53	17	2	1	42	8	15*	15	12	3	2	5	5	33*	NS
T1–4N2,3	35	12	3	2	29	1	3*	17	13	1	2	9	5	29*	<.01
M1	2	0.7	0	0	2	0	0	0	0						
Total	304		42	34	121	107	35*	126		16	16	18	76	60*	<.001
Per cent			14	11	40					13	13	14			
				51							27				

whom there was complete histologic eradication of the primary tumor on examination of the operative specimen (16).

3) Partial glossectomy with removal of residual induration in the tongue since it was difficult to determine whether the induration was due to fibrosis or residual tumor. Hemiglossectomy was occasionally necessary in patients with large tumors. Radical neck dissection was performed in patients with operable neck node metastases.

The purpose of this paper is to analyze the results of the new type of therapy and to compare them with the results obtained in the previous group.

Material and Methods

All consecutively admitted patients with histologically verified squamous cell carcinoma of the oral tongue were included in the study: 304 patients from the beginning of 1958 to the end of 1972 (group 1), and 126 patients from the beginning of 1978 to the end of 1983 (group 2). The annual number of new patients was about 20 in both groups. The median age was 68 years for men and 70 years for women in group 1 and 65 and 72 years respectively in group 2, ranging from 29 to 93 years. The male/female ratio was 1.43 (179 males, 125 females) in group 1, and 2.15 (86 males and 40 females) in group 2. The clinical symptoms and signs were comparable. The presenting complaints were: an ulcer on the tongue in 55 per cent of the women and 66 per cent of the men; a lump or growth on the tongue in 13 per cent of the women and 23 per cent of the men. Pain, soreness when eating, discomfort from wearing dentures and irritation from the teeth, were other frequent complaints. Some patients had teeth extracted before the diagnosis was made. The dental profession played an increasingly important role in diagnosing these tumors at an early stage. Leukoplakia preceded the diagnosis of carcinoma in 9 patients (4 women, 5 men).

The UICC staging system was used (6). All stages were assigned by the senior author, retrospectively in group 1, prospectively in group 2. The distribution of patients within the different stages was similar in the two groups with an incidence of approximately 50 per cent of early stages (T1N0, T2N0) (Table 1). All patients were followed-up, either in the outpatient clinic or by the referring physicians. There is no evidence that this disease has changed its clinical manifestations over the years, and the two groups should therefore be comparable.

In group 1, a dose of approximately 80 Gy at a distance of 0.5 cm from the single plane of radium needles was administered over a period of 24 to 48 h in the early stage tumors. The more advanced tumors were treated with a median dose of approximately 48 Gy of external high energy radiation in periods varying from 16 to 53 days (from 2 to 4 Gy a day) (20, 21). Partial glossectomy was performed in patients with early stage tumors after a median interval of about 3 months.

In group 2, external high energy irradiation was administered at a rate of 2 Gy middle tumor dose per day 5 days a week (or the CRE equivalent, i.e. 2.35 Gy 4 days a week) for a total middle tumor dose of 48 to 70 Gy, the lower dose being reserved for preoperative irradiation or in combination with ^{192}Ir implants (Table 2). The dose of interstitial irradiation from ^{192}Ir varied from 15 to 30 Gy according to the isodose curve which was deemed adequate to cover the tumor volume determined by palpation under general anesthesia. The confines of the tumor had previously been tattooed, to aid the surgeon when the residual infiltration was to be removed, usually within 6 weeks after completion of radiation therapy. Guide nee-

Table 2

Median radiation dosages 1978–1983 at 2 Gy, 5 days a week, or the equivalent CRE 2.35 Gy/day, 4 times a week. Gy to primary tumor/Gy to neck

	External irrad. alone	Preop. ext. irrad. + surgery	Postop. ext. irrad. + surgery	Extern. irrad. + ^{192}Ir	Extern. irrad. + ^{192}Ir + surgery
T1N0	–	55/50	56/47	50/50+25	50/47+30
T2N0	–	50	60/50	50 +27	55/47+30
T3N0	70/50	48	–	55 +26	56/47+29
T4N0	70/50	56/44	–	60/50+24	50/50+30
N1	60/50	70/50	60/50	65/50+20	63/47+20
N2,3	68/50	65/55	–	70/54+15	58/50+25

Table 3

Local control of the tumor in the tongue and regional control of the lymph nodes in the neck, after different methods of treatment analyzed according to stage including those patients who were salvaged after conversion from a negative to a positive neck, following radical neck dissection and postoperative external irradiation

	Conversion from N0 to N+ 1978–1983					
	T1N0	T2N0	T3N0	T4N0	Total	%
Surgical resection alone (partial glossectomy)	5/15**	1/3*	1/1	–	7/19	37
External irradiation alone	–	–	0/1	0/1	0/2	0
Preoperative external irradiation + surgery	0/3	1/3*	1/1	0/3	2/10	20
Surgery + postoperative external irradiation	2/10	2/7*	–	–	4/17	24
External irradiation + radioactive iridium	0/2	0/3	1/2	0/3	1/10	10
External irradiation + radioactive iridium + surgery	1/6*	0/8	4/11*	1/3	6/28	21
Surgery + postoperative radioactive iridium	–	0/1	–	–	0/1	0
Chemotherapy alone methotrexate 50 mg once a week	–	–	–	0/1	0/1	0
Total	8/36	4/25	7/16	1/11	20/88	
Per cent	22	16	44	9	23	

* One patient salvaged by radical neck dissection and postoperative irradiation. Total 7/20 (35%).
** Two patients salvaged.

For comparison:			
Conversion N0→N+ 1958–1972	T1N0	T2N0	T3N0
Total patients	42/94	31/61	15/36
Per cent	45	51	42

dles were inserted into the tissues of the tongue, through plastic templates to insure correct placement of the ^{192}Ir filaments 1 cm apart. The position of the filaments was fixed by sutures. Orthogonal roentgen films were taken and computerized dose calculation was performed. The median total tumor dose in the tongue, adding external and interstitial irradiation, varied between 75 and 85 Gy delivered over a period of 6 to 8 weeks (Table 2).

When planned preoperative external radiation alone was administered, the median dose varied between 48 and 70 Gy to the primary tumor and from 44 to 55 Gy to the neck (Table 2). When postoperative external radiation alone was given, the median dose varied between 56 and 60 Gy to both the tongue and the neck. When no surgery was possible, either external irradiation alone was administered with median dosages varying between 60 and 70 Gy, or external irradiation was followed by interstitial ^{192}Ir irradiation with median dosages varying between 50 and 70 Gy for the external irradiation and between 15 and 27 Gy for the additional ^{192}Ir irradiation. If possible, surgical resection aided by the previous tattooing, was carried out, usually within 6 to 8 weeks, when the radiation mucositis had subsided.

Surgery alone was performed in 20 patients, 15 of whom belonged to the T1N0, 3 to the T2N0, 1 to the T3N0 and 1 to the T2N1 stage (Tables 3 and 4). External irradiation alone was given to 11 patients with advanced tumors. They were considered inoperable and poor risk for interstitial irradiation due to old age, general debility and coexisting diseases.

Preoperative external irradiation followed by surgical resection was administered to 13 patients, 6 of whom had

Table 4

Total incidence of development of metastatic lymph nodes in the neck, including those patients who were salvaged by radical neck dissection and postoperative external irradiation to the neck. Local and regional control of squamous cell carcinoma of the oral tongue according to methods of treatment

Stage	Surgery alone	Ext. irr. alone	Preop. ext. irr. +surgery	Surgery +postop. ext. irr.	Ext. irr. +^{192}Ir	Ext. irr. +^{192}Ir +surgery	Surg. +postop. ^{192}Ir	Chemo-ther. alone	No therapy	Total
T1N0	12/15		2/3	7/10	2/2	6/6				29/36 (81%)
T2N0	3/3		3/3	5/7	3/3	7/8	1/1			22/25 (88%)
T3N0	0/1	0/1	0/1		1/2	7/11				8/16 (50%)
T4N0		1/1	1/3		2/3	1/3		0/1		5/11 (45%)
T2N1	0/1	0/1		2/4						2/6
T3N1				1/2	1/1	0/3				2/6
T4N1		0/2	1/1		0/3	2/3				3/9 (33%)
T3N2						1/1				1/1
T4N2		0/1			1/1					1/2
T1N3		0/1	0/2							0/3
T3N3		0/1				2/3		0/1		2/5
T4N3		1/3			0/2				0/1	1/6
Total	15/20 (75%)	2/11 (18%)	7/13 (54%)	15/23 (65%)	10/17 (59%)	26/38 (68%)	1/1	0/2	0/1	76/126 (60%)

early stage tumors. Surgical resection followed by external irradiation was the treatment method in 23 patients, 17 of whom had early stage tumors. External irradiation followed by interstitial ^{192}Ir irradiation was administered to 17 patients, five of whom had early stage tumors. These patients either refused surgery or were considered poor candidates for resection. The most frequent method was external irradiation immediately followed by interstitial ^{192}Ir irradiation and surgical resection 6 to 8 weeks later. Among 38 patients treated this way, 14 had early stage tumors. In one single patient surgical resection for a T2N0 tumor was followed by ^{192}Ir irradiation (51 Gy/100 h) 5 months later because of nodularity in the scar, resulting in local/regional control on the last examination 26 months later.

Chemotherapy alone (50 mg methotrexate intravenously once a week) was given to two old patients with advanced tumors but without response. One 89-year-old woman with a T4N3 tumor received no treatment at all.

At the time of writing, all patients in group 1 have been followed for at least 5 years and in group 2 for a median of 58 months (ranging from 26 to 83 months). Information regarding the cause of death was obtained from either the attending physician, the Cancer Registry or the death certificate and correlated with the condition of the patient at the time of the last follow-up examination shortly preceding the demise. Very few postmortem examinations were conducted, because most patients died in their homes or in nursing homes.

Statistical methods. Statistical analyses for the local-regional control rates were carried out according to the chi-square or the Fischer exact probability test and for the survival rates employing the log-rank test (12).

When calculating the absolute survival rate no discrimination as to the cause of death was made. The relative survival rate was based on counting only patients registered as dying from their tongue carcinoma as deceased, while deaths from intercurrent disease were counted as patients withdrawn from observation.

The one-year cohorts in the life-table were used when comparing the 2 groups of patients by the log-rank test. This was a modification of the method of PETO et coll. (12), allowing for equal ranking of patients belonging to the same cohort. This method evaluates the expected number of deaths in each group, which are then compared with the observed number through a chi-square test giving the level of significance. The probability that the difference should be due to the chance is expressed as the p-value. A value of less than 0.05 is accepted as statistically significant.

Results

The local-regional control rates, including conversions NO→N+ that remained under control after neck dissection, increased from an overall of 35 to 60 per cent from the period 1958 to 1972 compared with 1978 to 1983 (Tables 1, 3), a difference which is statistically significant

($p<0.0001$). The differences are also significant for the subgroups of patients with T1N0, T2N0, T3N0 and TXN2,3 tumors. The local-regional control rates increased for T1N0 tumors from 62 to 81 per cent, for T2N0 from 44 to 88 per cent, for T3N0 from 17 to 50 per cent and for TXN2,3 tumors from 3 to 29 per cent. The control rates for T3,4N1 tumors increased from 15 to 33 per cent, but the number of patients was too small for the difference to be statistically significant. The percentage of patients who died with lymph node metastases in the neck decreased from 51 to 27 per cent while the percentage with local recurrence limited to the tongue remained unaltered (14 and 13 per cent respectively). The percentage of patients who developed simultaneous tongue and neck recurrences decreased from 39 to 14 per cent.

A separate analysis of group 2 showed that in patients with T1N0 tumors the same degree of control with surgery alone (12/15=80 per cent) was obtained, as with surgery and /or radiation therapy (17/21=81 percent).

In the subgroup treated with external irradiation and ^{192}Ir interstitial radiation therapy with or without surgery, the disease of all 8 patients was controlled. In the group of patients with T2N0 tumors, the disease of all but 3 patients was controlled (22/25=88 per cent). The 3 failures were in the subgroups which had surgery and irradiation (2 had had primary surgery and postoperative external irradiation and 1 preoperative external interstitial ^{192}Ir irradiation followed by surgery). In 50 per cent (8/16) of the patients with T3N0 tumors the disease was controlled. Thirteen of these had received external irradiation and ^{192}Ir (2 alone, 11 with surgery added) and 8 were controlled. None of the 3 treated with the other methods achieved control. In patients with T4N0 tumors, 45 per cent (5/11) had local-regional tumor control (2 of 4 with surgery and external beam, 3 of 6 with external + interstitial irradiation and surgery). One patient received weekly doses of 50 mg methotrexate without response. In the group of patients with neck node metastases, 12 of 38 (32 per cent) obtained local-regional tumor control (7/21 with mobile nodes and 5/17 with fixed nodes). In summary, 84 per cent (51/61) of the patients with early stage (T1N0, T2N0) tumors were controlled locally and regionally, as compared with 38 per cent (25/65) of the patients with more advanced tumors.

Surgery alone controlled the tumor in 15 of 20 (75 per cent) patients with predominant early stage tumors. External irradiation alone controlled the tumor in 2 of 11 (18 per cent) patients with advanced stage tumors. Preoperative external irradiation and surgery controlled 7 of 13 (54 per cent) and postoperative irradiation after primary surgery controlled the tumor in 15 of 23 (65 per cent) patients. The former group consisted of about 50 per cent early stages, whereas in the latter group approximately 75 per cent were early stages. External irradiation and ^{192}Ir interstitial irradiation controlled the tumor in 10 of 17 (59 per cent) patients. All five T1N0 and T2N0 tumors were controlled, but only 5 of the 12 remaining, more advanced tumors were controlled. External irradiation, ^{192}Ir irradiation and surgery controlled the tumor in 26 of 38 (68 per cent) of the patients. Thirteen of 14 patients with T1N0 and T2N0 had their tumors controlled, whereas 13 of the remaining 24 (54 per cent) patients with more advanced tumors had local and regional tumor control ($p=0.08$).

Conversion from a clinically negative to a positive neck (N0→N+). With surgery alone 37 per cent (7/19 patients) developed subsequent metastatic neck nodes and 6 of these had early stage tumors (5 of 15 T1N0 converting) (Table 4). Three patients were salvaged by subsequent neck dissection, 2 in the T1N0 category and 1 in the T2N0 category. None of the 2 patients treated with external irradiation alone developed neck node metastases. Preoperative external irradiation followed by surgery was associated with subsequent neck node metastases in 2 of 10 patients. One of these patients, who had a T2N0 tumor, was salvaged by neck node dissection. Surgery followed by postoperative external irradiation was performed in 17 patients, 4 of whom developed neck node metastases. One of these patients, with a T2N0 tumor, was salvaged by neck node dissection. External irradiation and interstitial ^{192}Ir irradiation without surgery was followed by N0→N+ conversion in 1 of 10 patients. External irradiation and interstitial ^{192}Ir irradiation followed by partial glossectomy resulted in the development of neck node metastases in 6 of 28 (21 per cent) patients. Four of 11 patients in this group had T3N0 tumors and one of 3 had T4N0 tumors. Only 1 of 14 (7 per cent) patients with T1N0, T2N0 tumors treated in this manner developed N0→N+ conversion. One patient with a T1N0 and another with a T3N0 tumor were salvaged by neck dissection.

Summary: Of 36 patients with T1N0 tumors in group 2, 8 converted (22 per cent) as compared to 42 of 94 (45 per cent) in group 1 (18). Of 25 patients with T2N0 tumors in group 2, 4 converted (16 per cent) compared to 31 of 61 (51 per cent) in group 1 (18). The conversion rates for T3N0 tumors were similar in the two groups (44 and 42 per cent respectively). The overall conversion rate in group 2 was 23 per cent (20/88). The salvage rate after rescue neck dissection was 35 per cent (7/20), similar to the 33 per cent previously reported for T1,2,3N0 patients (18).

It is of interest to compare group 1 and 2 with respect to the failure rates in the neck since this gives an indication of how effective the elective treatment of the neck has been. (Table 1): Patients with T1N0 tumors showed a failure rate at the time of death of 30 per cent (28/94) in group 1 compared to 14 per cent (5/36) in group 2. Among the 5 failures in group 2 there were 3 patients who had been treated with surgery alone. If this subgroup of 'surgery alone' is excluded, only 2 of 21 (10 per cent) of the irradiated patients developed neck node metastases. One additional patient who had received external irradiation, ^{192}Ir interstitial irradiation and partial glossectomy, con-

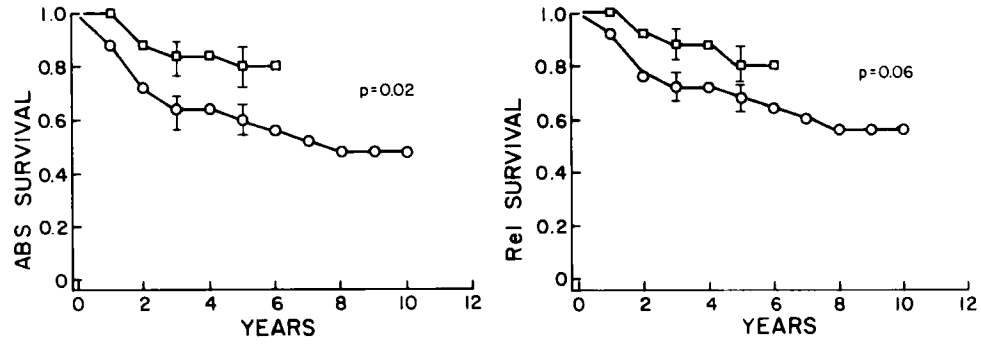

Fig. 1. Absolute and relative survival of patients with T1N0 tumors, 94 treated 1958–1972 (○) and 36 treated 1978–1983 (□).

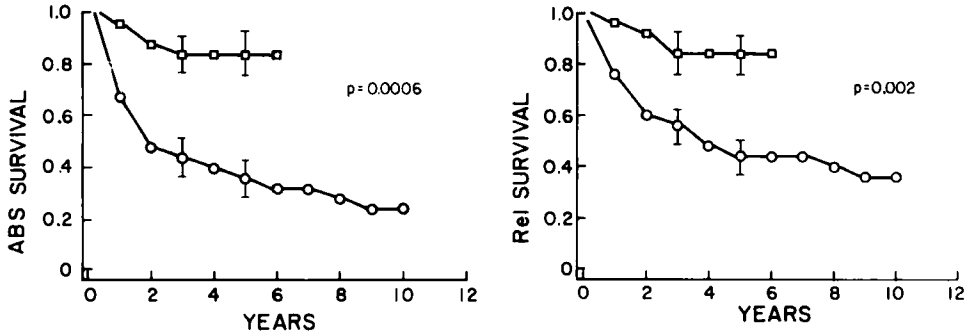

Fig. 2. Absolute and relative survival of patients with T2N0 tumors, 61 treated 1958–1972 (○) and 25 treated 1978–1983 (□).

verted from N0 to N+, but was salvaged by radical neck dissection. The difference between group 1 and 2 (p=0.09) is nearly significant. Similarly, patients with T2N0 tumors showed a failure rate in the neck of 43 per cent (26/61) in group 1 and 4 per cent (1/25) in group 2. This difference is significant (p=0.0006).

Local control related to histology of resected specimen after preoperative radiation therapy. When preoperative irradiation had been given to the 51 patients in group 2 and the pathologist was unable to identify any residual tumor cells in the operative specimen, the disease in 80 per cent (24/30) of the patients remained locally controlled compared with a local control rate of 38 per cent (8/21) in patients with operative specimens positive for residual tumor cells (p=0.003) (Table 5). When the early stage tumors were compared, all 16 patients with T1N0, T2N0 tumors and negative postirradiation histology were controlled. However, the tumors of only 1 of the 4 with positive postirradiation histology remained locally controlled.

Survival. When all patients were considered, both the absolute (crude) and the relative (determinate) survival rates were significantly better in group 2 than in group 1 (Figs 1–8). This was true for both the initial period (≤3 years) and the long-term period (>3 years). When the patients were divided into subgroups according to stage,

Table 5

Local control of squamous cell carcinoma of the oral tongue related to the presence and absence of residual tumor cells in the operative specimen after preoperative irradiation (Group 2)

Stage	Negative histology No. controlled	Positive histology for residual tumor No. treated
T1N0	7/7	1/2
T2N0	9/9	0/2
T3N0	5/7	2/5
T4N0	1/2	1/4
TN1	1/3	2/4
TN2,3	1/2	2/4
Total	24/30*	8/21*
(%)	(80)	(38)

* p=0.003

significant differences in the absolute survival rates were noted in patients with T1N0, T2N0, T3,4N0 and TXN2–3 tumors, and in the relative survival rates in patients with T2N0 and TXN2,3 tumors. The relative survival rates also increased in patients with T1N0, T3N0 and combined T3,4N0 tumors with p-values approaching significance (p

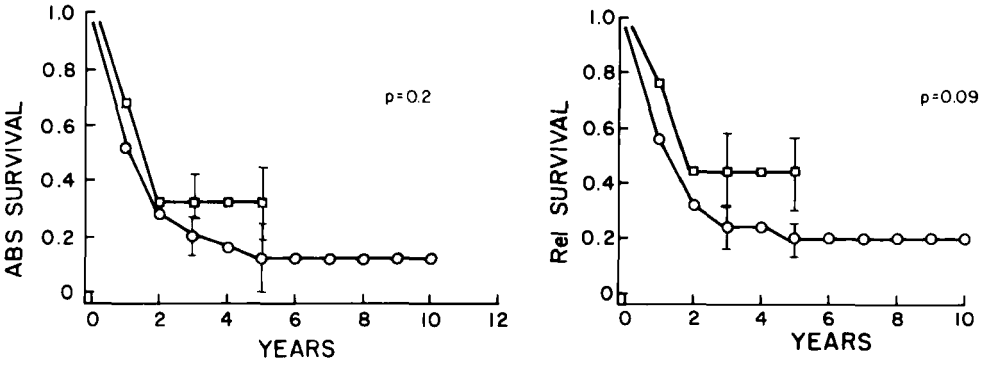

Fig. 3. Absolute and relative survival of patients with T3N0 tumors, 36 treated 1958–1972 (○) and 16 treated 1978–1983 (□).

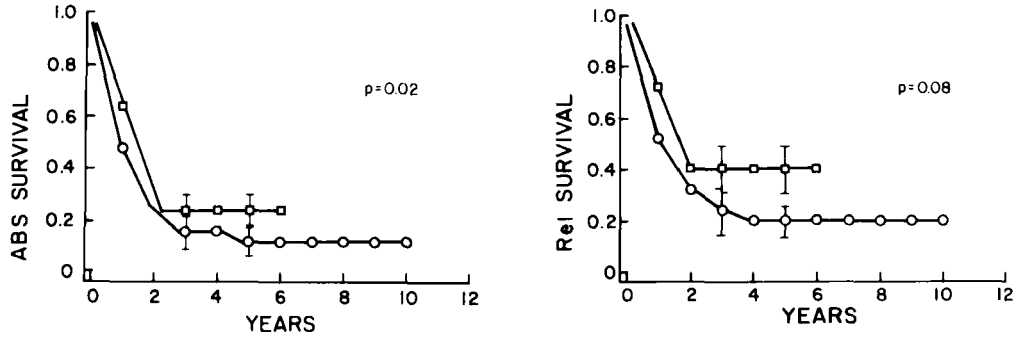

Fig. 4. Absolute and relative survival of patients with T3,4N0 tumors, 36 T3N0 + 2 T4N0 treated 1958–1972 (○) and 16 T3N0 + 11 T4N0 treated 1978–1983 (□).

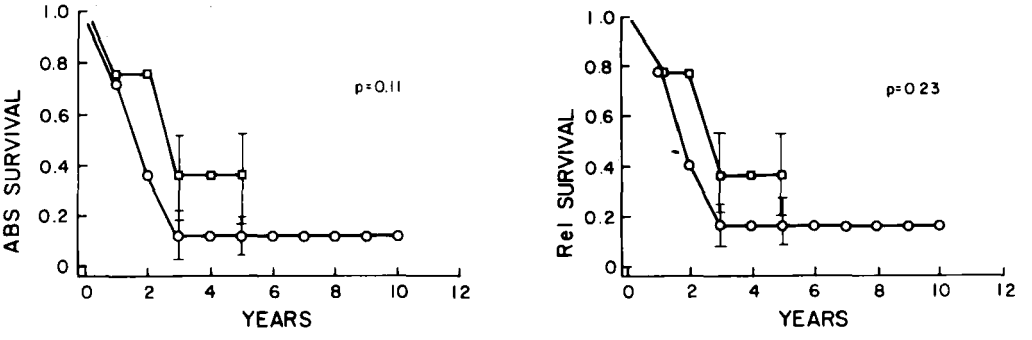

Fig. 5. Absolute and relative survival of patients with T1,2N1 tumors, 21 treated 1958–1972 (○) and 6 treated 1978–1983 (□).

0.06, 0.09, 0.08 respectively). Sex did not influence the results, neither in group 1 (20, 21) nor in group 2. The median survival rates were 26 months in women and 32 months in men and the local-regional control rates were 53 and 60 per cent respectively.

Distant metastases were diagnosed in 26 patients (9 per cent) in group 1 (16) and in 8 patients (6 per cent) in group 2. All except 2 (one T1N0, one T2N0) had been treated for advanced T4 tumors with or without neck node metastases on admission. The two exceptions are of some interest. The first patient, a 63-year-old male radiologist with a T1N0 tumor had been treated with partial glossectomy and the pathologist reported that the margins of resection were free of tumor. The patient was offered postoperative irradiation, but he elected not to accept the offer. One year later he developed a neck node metastasis which was removed locally. Radical neck dissection was performed 18 days later and the operative specimen was reported histologically negative for tumor. He nevertheless received 59 Gy external irradiation to the neck at daily doses of approximately 2 Gy. Fifteen months later he died with both recurrence in the neck and distant metastases.

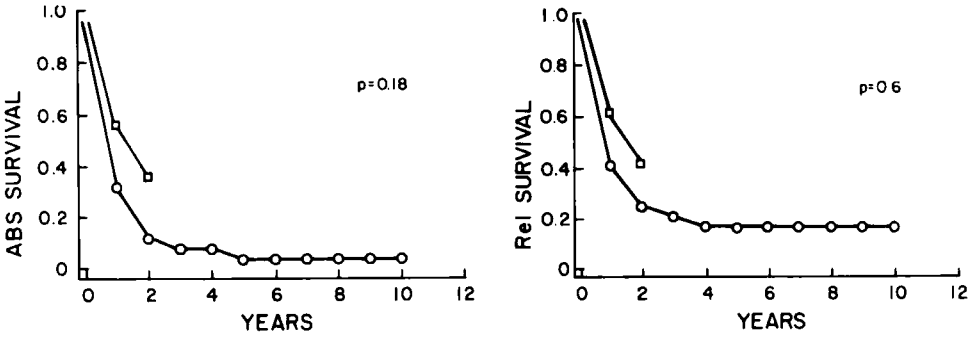

Fig. 6. Absolute and relative survival of patients with T3,4N1 tumors, 53 treated 1958–1972 (○) and 15 treated 1978–1983 (□).

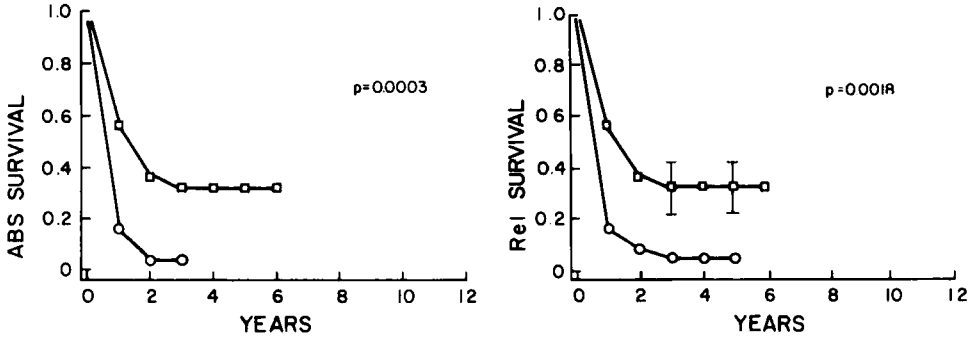

Fig. 7. Absolute and relative survival of patients with T1-4N2,3 tumors, 35 treated 1958–1972 (○) and 17 treated 1978–1983 (□).

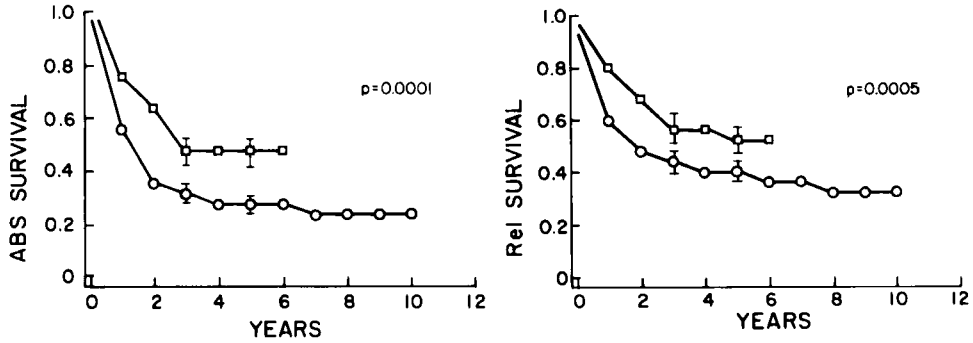

Fig. 8. Absolute and relative survival of all patients, 304 treated 1958–1972 (○) and 126 treated 1978–1983 (□).

The second patient, a 68-year-old female, presented to her local hospital with a T2N0 tumor and was treated with partial glossectomy and suprahyoid, unilateral neck dissection. The pathologist reported that the margins of resection and the nodes in the neck were free of tumor. No additional therapy was offered. Four months later she developed a metastatic node in the neck and was treated with radical neck dissection and 60 Gy of postoperative external irradiation at 2 Gy per day. The tumor had already invaded the internal jugular vein and the extracapsular connective tissues and muscles diffusely. One year later she developed lung and bone metastases and died 32 months after the radiation therapy.

Second primary tumors were diagnosed in 11 patients. Eight of these died of their second primary tumors; carcinoma of the esophagus (n=3), carcinoma of the lung (n=1), stomach (n=1), colon (n=1), rectum (n=1) and plasmocytoma of the retroperitoneal space obstructing the kidney and ureter (n=1). The 3 surviving patients had carcinoma of the hypopharynx, gingiva and opposite tongue respectively and have been followed for 49, 64 and 74 months at this writing.

Complications (Group 2). Three patients developed osteonecrosis of the mandible without evidence of tumor recurrence; one associated with an orocutaneous fistula which closed after conservative treatment, another with a pathologic fracture, and the third on the basis of severely decayed teeth. A fourth patient developed soft tissue necrosis of the floor of the mouth, which healed slowly with conservative treatment. The prophylactic treatment of healthy teeth with fluor was an important part of the treatment regimen. Severely decayed teeth were extracted before radiation therapy began. Extraction of teeth after completion of radiation therapy was not recommended for fear of osteonecrosis developing. One patient developed severe edema and had to be fed with a nasogastric tube for several weeks until the edema subsided. Xerostomia bothered most patients, some of whom were relieved by the use of artificial saliva. None of the patients required surgery for complications.

Discussion

Squamous cell carcinomas of the oral tongue are known both for their great propensity to infiltrate locally and for their tendency to metastasize early to the lymph nodes of the neck. They are considered to be relatively radioresistant, since when they reach large dimensions, they ulcerate and become necrotic due to poor blood supply and inadequate oxygenation (1–4, 8–10, 13–15). Therefore, the need for a high dose of radiation delivered to the primary tumor to prevent local recurrence has become widely recognized. External high energy irradiation alone has rarely been sufficient to eradicate the larger primary tumors, and additional interstitial irradiation of the residual tumor of the tongue has become mandatory. Whereas external irradiation has served as a good adjuvant to surgical therapy, even better results can be anticipated when interstitial irradiation is added to the primary tumor in the tongue. The use of thin flexible radioactive wires or filaments, widely accepted as a technique tolerated well by most patients, provides an excellent means for local sterilization of the tumor in the tongue (13–15). Furthermore, the need for elective irradiation of the neck of patients without clinically detected lymph node metastases has been widely accepted (1–5, 7, 9, 10).

To meet both these needs, two aspects of radiation therapy have been studied: 1) The initial en bloc irradiation of both the tongue and the neck up to a dose that will eradicate practically all clonogenic tumor cells in the clinically negative neck, and 2) the interstitial irradiation of the primary tumor of the tongue with ^{192}Ir to a high dose.

Our results appear promising when compared with results from other types of therapy, both with respect to local control of the tongue and regional control of the neck. Our ability has improved both histologically to sterilize the tumor in the tongue and to prevent the conversion of a negative to a positive neck. The survival rates seem to be increasing. The question has been raised whether partial glossectomy is really necessary in patients with T1N0, T2N0 in view of the fact that all 5 patients treated with irradiation alone obtained both local and regional control of their tumors. If the patients can be followed closely at monthly intervals by the same experienced physician, observation alone may be justified, and surgery may be performed on demand when the clinical findings make it mandatory. The problem is still under investigation in our institutions.

The advanced squamous cell carcinomas of the oral tongue remain a challenge. Previously, interstitial irradiation and radical surgery were seldom used and most patients died of local persistence or recurrence. With the newer interstitial implantation techniques, even large tumors can be adequately treated and the rate of local control has improved. Surgical resection without such therapy was often considered inadequate because tumor-free margins could not be obtained. However, with the combined external beam and interstitial irradiation an increasing number of operative specimens have been reported histologically negative or containing relatively small numbers of tumor cells. Signs of severe radiation damage near the necrotic centers of the tumors were often seen. Unfortunately, a substantial number of these patients are old and debilitated and suffer from many coexisting diseases which require special treatment. Nutritional adjuvant therapy, usually in the form of added enteral tube feeding, has been of help in enabling them to complete the therapy. It should also be mentioned that ongoing clinical trials with preoperative and preradiotherapy chemotherapy such as cisplatinum and 5-fluorouracil have given promising results as far as the initial regression rates are concerned in advanced head and neck carcinomas. However, further observation is necessary to assess the final value on long-term survival.

Conclusions

The results of treatment of patients with squamous cell carcinoma of the oral tongue seem to depend on several factors: 1) The extent of the tumor. 2) The successful integration of external high energy radiation therapy of both the primary tumor and the neck. 3) Optimal interstitial radiation therapy with accurate placement of radioactive sources (^{192}Ir) within the tumor volume. 4) Exact dose calculation performed by well-trained physicists with the aid of computers. 5) Complete surgical removal of all residual tumors, if present, both in the tongue and the neck. 6) The general condition of the patient and optimal supportive therapy as required.

Complete local sterilization of the primary tumor in the tongue is rarely successful with external radiation therapy alone. With interstitial radiation therapy added, however, complete eradication of all histologically demonstrable tumor cells can be accomplished in most patients with less

advanced squamous cell carcinomas and in over 60 per cent of those with more advanced tumors.

Surgical excision of any residual infiltration provides additional information of possible residual tumor cells and may prevent recurrence in the future. An operative specimen which is negative for residual viable tumor cells is associated with an improved prognosis.

Elective irradiation of the neck of patients with no palpable lymph node metastases, reduces the incidence of later development of neck node metastases in patients with controlled primary tumors. Therapeutic neck irradiation in patients with clinically palpable neck node metastases can eradicate tumor cells in the smaller mobile nodes, but a combination of irradiation and surgical neck dissection is necessary to achieve optimal results in patients with large or fixed nodes.

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