

Clinical and Therapeutic Aspects of Squamous Cell Carcinoma of Oral Tongue

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Forty nine patients with squamous cell carcinoma of oral tongue were reviewed retrospectively for the evaluation of clinical manifestation and for the comparison between therapeutic modalities. The gross shape of the tumor was infiltrative in 22, ulcerative in 12, and ulceroinfiltrative type in 10 patients. Direct extension of the tumor was most commonly to the floor of the mouth. The incidence of nodal metastasis generally increased with tumor stage. 55% of the patients showed neck nodal metastasis at the time of diagnosis. Ipsilateral subdigastric node were most commonly involved, followed by submandibular nodes. The 5-year survival rate of patients treated with surgery and radiotherapy was 58.7% in contrast to 21.6% in radiation alone group. Overall 5-year survival rate was 31%. In radiation alone group, half of the patients in stage I, II were locally controlled. But the local control in stage III, IV was much inferior to early lesions. Especially, of 4 patients combined with implantation technique, 3 were completely controlled. 5-year survival rate of these implanted patients was 50%. 49.4% of patients treated over 7,000 cGy survived 5 years. This was significant in contrast to 6.4% of the group treated below 7,000 cGy. The most common sites of failures were primary sites. In early lesions primary radiotherapy with implantation would be an appropriate treatment in cancer of oral tongue, operation reserved for radiation failure. Operation and adjuvant radiotherapy is recommended in cases of advanced disease.

Key Words: Oral tongue, Radiotherapy, Implantation

INTRODUCTION

Carcinomas of the oral tongue accounts for 10-15% of all head and neck cancers^{1,2)}. The treatment of squamous cell carcinoma of the oral tongue has been consisted primarily of surgery and radiation. In the same stage of disease, cure rates are almost equal between the two treatment modalities. But the technique of irradiation is still limited to the external beam alone though, in some cancer centers, implantation radiotherapy was performed in selected cases.

The purpose of this study was to review the clinical manifestations and our experiences with radiation therapy in the treatment of cancer of the oral tongue and the comparison data between the two treatment modalities. So the proper method to minimize the functional disability and cosmetic problem in the treatment of cancer of the oral tongue was discussed.

MATERIAL AND METHOD

The records of 58 patients with cancer of the anterior two-thirds of the tongue treated in the department of Radiation Oncology, Yonsei Cancer Center, Yonsei University Hospital, from January 1976 to March 1984 were reviewed retrospectively.

Of those 58 patients, one case of adenocarcinoma and one case of adenoid cystic carcinoma were excluded. Also excluded are 4 patients who had incomplete treatment and 3 patients who refused treatment.

A total of 49 biopsy-proved squamous cell carcinoma of the oral tongue had a minimum follow-up period of two and a half years. This is considered adequate since 90% of local recurrences appear within two years after treatment³⁾.

There were 41 males and 8 females. The age of the patients ranged from 20 to 73 years with an average of 53.7 years. Two-thirds of the patients were between fifty and seventy years of age.

The clinical stage was determined retrospectively according to the classification proposed by

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the American Joint Committee for Cancer Staging System⁹). The survival rates were calculated from Kaplan-Meyer's life table method.

RESULTS

Distribution of patients according to the tumor and node stage is shown in Table 1. The incidence of nodal disease generally increased with T-stage but it was not significant.

Initial neck node presentation is also depicted in Figure 1. 55% (27/49) of the patients were presented with neck nodal metastasis. Ipsilateral subdigastric node involvement was the most common, followed by submandibular node. Submandibular and subdigastric node involvement were also the most common in contralateral neck. Posterior cervical chain metastasis was found in one patient.

Treatment consisted of radiotherapy, either alone or with operation. As shown in Table 2, 38 patients (77.6%) were treated with radiation alone, 11 patients (22.4%) were treated with radiation and surgery. 7 patients in advanced stage had received

induction chemotherapy with bleomycin or methotrexate or cis-platin which were not considered to effect the local control and survival, and disregarded in this study.

Included in operation and radiation group are those who were treated with salvage radiotherapy; one in stage III recurred at primary site after two months of hemiglossectomy, and one in stage IV recurred at ipsilateral midjugular node after seven months of partial resection of tongue with upper neck dissection. There were relatively even distribution of patients according to stage in operation plus radiation group. But in the radiotherapy alone group 15/38 (39.5%) were in stage IV.

Of 38 patients treated with radiotherapy alone, 26 (38%) were treated with external beam only (Table 3). Most of the techniques were dependent on external radiotherapy. 3 patients in stage II treated with interstitial implantation were delivered 5,000 cGy by external beam and 3,000 cGy by implantation. One patient in stage I with implantation received

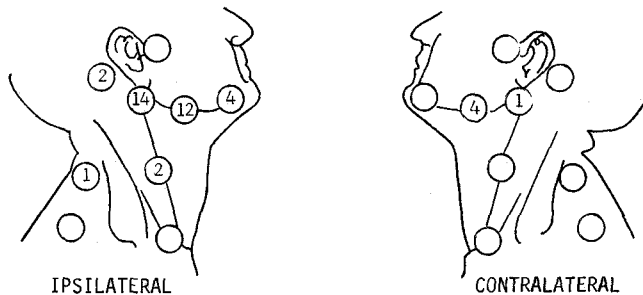
Table 1. T and N Stage

	T1	T2	T3	T4	Total
N0	8	10	3	1	22
N1	1	7	4	4	16
N2a	—	—	1	—	1
N2b	1	1	3	—	5
N3b	1	1	1	2	5
Total	11	19	12	7	49

Table 2. Treatment Modality

Stage	No.	RT alone	OP + RT
I	8	6	2
II	10	8 (1)*	2 **
III	14	9	5 (1)*
IV	17	15 (4)*	2** (1)*
Total	49	38	11

() * No. of induction chemotherapy
 ** One received salvage radiotherapy



No	N1	N2a	N2b	N3b	N1-N3 / Total
22	16	1	5	5	27 / 49 = 55%

Fig. 1. Node presentation at diagnosis.

ed 500 cGy external and 6,500 cGy interstitial radiotherapy.

The overall five-year actuarial survival was 31% as depicted in Figure 2. The 5-year survival rate (5-YSR) in stage I was 36.8%, stage II 58.8%, stage III 31.7%, and stage IV 14.9%. The 5-YSR in surgery plus radiation and radiotherapy alone group were 58.7%, 21.6% respectively (Fig. 3).

Table 4 shows the local control rate in the

Table 3. Radiotherapy Technique

Stage	External	External + IOC*	External + Imp**	Total
I	3	2	1	6
II	4	1	3	8
III	6	3	—	9
IV	13	2	—	15
Total	26	8	4	38

* Intraoral cone, ** Implantation

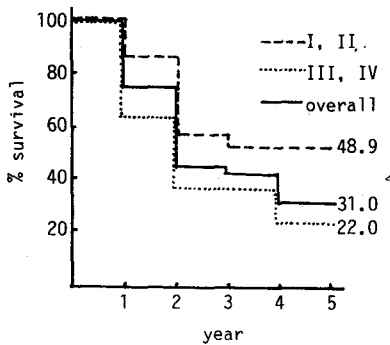


Fig. 2. Overall 5 YSR by stage

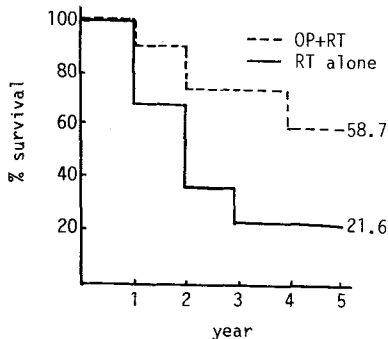


Fig. 3. Overall 5 YSR by treatment modality.

evaluable patients. 5 of 11 (45%) in stage I, II were controlled by radiotherapy alone. In the group of patients with stage III, IV (i.e., advanced stage), only 4 of 18 (22%) were controlled by radiotherapy in contrast to 4 of 6 (67%) controlled by operation plus radiation. Especially one stage I patient and two stage II patients who were treated with implantation were controlled by radiotherapy alone. Overall local control rate by radiation alone was 31%.

The 5-YSR according to radiotherapy technique are illustrated in Table 5. The 5-YSR in the group of external irradiation alone was 16.9%, with intraoral cone 42.3%, and with implantation 50%. But it may not be statistically significant because of the small sample size.

As shown in Table 6, in the group treated with radiation alone, the 5-YSR of those delivered above and below 7,000 cGy were 49.4% and 0.4% respec-

Table 4. Local Control Rate

Stage	RT alone	OP + RT
I	2/5 (1/1)*	1/1
II	3/6 (2/3)*	1/1
III	1/5	3/4
IV	3/13	1/2
Total	9/29	5/8

() * Number of implantation

Table 5. 5 YRS by Radiotherapy Technique

	No.	5 YRS (%)
Ext *	26	16.9
Ext + ICO **	8	42.3
Ext + Imp ***	4	50.0

* External
** Intraoral cone
*** Implantation

Table 6. 5 YSR by Radiation Dose in Radiotherapy alone Group

Dose (cGy)	No.	5 YSR (%)
< 7000	24	6.4
≥ 7000	14	49.4

p < 0.01

Table 7. Pattern of Failure

Failure site	RT alone (%)	OP + RT (%)
Local	12 (31)	1 (9)
Regional	1 (3)	1 (9)
Locoregional	7 (18)	1 (9)
D.M. *	—	—
None	4 (11)	7 (63)
Unknown	14 (37)	1 (9)
Total	38	11

* Distant metastasis

tively. This was statistically significant ($p < 0.01$). Only 19% of those below 7,000 cGy lived 2 years in contrast to 63.5% of those over 7,000 cGy.

Pattern of failure after treatment is also demonstrated in Table 7. Of 38 patients treated with radiotherapy alone, 12 (31%) recurred locally at primary site and 7 (18%) failed in the regional neck nodes. Most failures were found in primary and nodal areas.

DISCUSSION

Squamous cell carcinoma of the oral tongue is a common type of oral cancer and includes lesions arising from the mobile portion of the tongue anterior to the circumvallate papillae. The gross shape of the tumor showed infiltrative type in 22 patients, ulcerative type in 12, ulceroinfiltrative in 10, others such as fungating type in 5. According to histologic grade, well differentiated tumors were found in 13 patients, moderately well differentiated in 5, poorly differentiated in 5, and undetermined in 26.

Most frequent symptoms were lump in 16 patients, ulceration in 15 patients, and pain in 14 patients. Posterolateral border of the tongue was the most common primary site in 84% of patients in our study. The floor of the mouth was the most frequently involved site by direct extension in 8 of stage IV patients. The tumor also extended to the mandible, base of tongue, anterior pillar, and adjacent buccal mucosa in 2, 2, 1, and 1 patients, respectively.

The tongue is endowed with a rich supply of lymphatics and squamous cell carcinoma of this anatomic site tends to have developed lymph node metastases when initially diagnosed. Though clinically positive nodes were found in 35-40% in other reports^{5,6}, 55% of the patients had already

spread to nodes at the time of presentation in our study. As shown in Table 1, similar to other report, the incidence of nodal disease generally increased with T-stage.

Distant metastases were not found at the time of diagnosis in our study. But Suzanne et al⁷ reported that distant metastases were found in 14% of patients and the most common site of metastasis was lung followed by bone, liver, and brain. They also reported that the risk of developing distant metastasis did not increase with advancing stage.

It is generally accepted⁸ that operation and irradiation produced similar local control rates and decisions must be based on functional and cosmetic loss and patient preference in the case of early T1 and T2 lesions. Irradiation is usually selected for larger T1 lesions and for T2 lesions to preserve normal speech and swallowing. Wide local excision is the treatment of small well-circumscribed lesions.

Lesions of a large surface involvement with minimal infiltration can be cured with radiation therapy alone, and glossectomy is reserved for radiation failure. On the other hand advanced lesions can be managed by planned combined surgery and irradiation. In our study primary radiotherapy was tried for early lesions in only a small number of patients. Of 38 patients who were treated with radiation therapy alone, only 14 were stage I, II, compared to 24 of stage III, IV.

The local control rate in our study showed 22% of stage III, IV disease treated with irradiation alone compared to 66.7% treated with surgery plus radiation. These results are also comparable with other studies^{6,9}. Dan White et al reported¹⁰ 21% failure rate after surgery for stage III, IV oral tongue cancer versus 59% failure rate after radiotherapy for the same-staged patients. Surgery should be the initial treatment in patients with lesions of stage III, IV, rather than radiotherapy. The surgical procedure should be tailored to adequately remove the gross and microscopic diseases, if possible. Postoperative radiotherapy is indicated if necessary. From these data, it appears that radiation therapy is the primary treatment for the early stage tumors rather than advanced lesions which require combined surgery plus radiotherapy.

Many authors^{9,11,12} reported the required optimum dose to control the tumors of oral tongue since the concept of optimum dose was defined by Paterson¹³. Fu and Chan demonstrated⁹ minimum tumor dose 6,000 cGy for T1 lesions and 6,500 cGy for T2 lesions with interstitial radium implants

alone. They also reported, from their study of 25 patients, all of 12 cases received combined total dose of 7,500 cGy with interstitial and external irradiation achieved local control, but only 4 of 13 patients who received a total dose of less than 7,500 cGy achieved local control. The local control rate was significantly higher for those patients who received a minimum tumor dose of more than 4,000 cGy from interstitial radium implants. In our data the 5-YSR of patients who received at least 7,000 cGy regardless of the radiation technique was higher than the group less than 7,000 cGy (Table 6). Our 5-YSR 49.4% in the group over 7,000 cGy would have been raised if interstitial implantation therapy was added to external beam irradiation.

Improvement in results may come about by the use of implants of flexible Iridium-192 which allow afterloading techniques to be used and permit better dosimetry than other methods^{14,19}.

The use of induction chemotherapy may be of benefit to the radiotherapy though it was not beneficial in our patients. A reduction in tumor size would be expected to improve the oxygen supply to the residual tumor. The increase in oxygen delivery and tumor growth fraction would result in the enhanced efficacy of radiotherapy. Some compounds such as cis-platin may be retained within tumor cells and have intrinsic radiosensitization properties in several reports^{16,17}. The role of induction chemotherapy needs to be evaluated.

Site of failure was consisted mostly of primary site with or without regional nodes (Table 7). Alan et al¹⁹ showed that the control rate decreases with increasing size of tumor, and also reported implant combined with external beam therapy gives control superior to the other methods used because a higher tumor dose is achieved, which will be discussed later. One more reason to this is that our patients who were irradiated were mainly composed of advanced diseases (Table 2).

Survival varied with irradiation technique. Fu et al.¹¹ in a review of 32 years' experience, reported that the overall control rate of the primary lesion after initial treatment was 50%. The local control rate with radon or radium implants alone demonstrated that 45% of stage I, II disease were locally controlled. Of these early lesions, patient with stage I disease was completely controlled but unfortunately 4 months later, left midjugular node failure was noted. Of 3 patients with stage III disease treated with implantation, one patient was not controlled because he had poorly differentiated, ulcerative deep tumor of 4 cm size and survived one year and

one month. The other two patients were controlled completely and alive for 3 year and 2 months, 5 years and 2 months respectively. Our 5-YSR by radiotherapy technique is seen in Table 5. This figure was generally identical with Fu's report¹¹. Interstitial therapy appears to be essential if maximal local control and longer survival are to be obtained. External beam alone gives inferior cure rates even in early lesions. It is well documented that the control is improved if a great proportion of the treatment is by interstitial therapy¹⁹.

In conclusion, because the most common site of failure after treatment was the primary site, either alone or with neck disease, the interstitial implantation is required for higher local control and to make the total dose at least 7,000 cGy. Primary operation with adjuvant radiotherapy is recommended when it comes to advanced disease. In early lesions primary radiotherapy would be more appropriate in terms of functional and cosmetic preservation and local control, operation reserved for radiation failures.

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== 국문초록 ==

구강 설 편평 상피 세포암의 임상적, 치료적 고찰

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김 귀 언 · 노 준 규

구강 내 설(舌)암은 설(舌)의 전방 삼분의 이에서 발생하는 것으로 근치적 요법으로는 수술과 방사선 치료가 그 근간을 이루어 왔으며, 같은 병기에서 두 요법간의 완치율은 거의 동일한 것으로 보고되고 있다. 특히 조기병소(T1, T2)에서는 이 두 요법 간에 비슷한 국소 퇴치율을 보이므로 치료법의 선택에는 그 치료로 인해 발생하는 기능적 손상 및 미용적 결손을 최소화 하는데 역점을 두어야 할 것이다. 그러므로 큰 기능적 손상 없이 용이하게 절제할 수 있는 첨단부 및 배부의 작은 병소를 제외하고 대부분의 조기병소는 방사선 요법으로 정상적인 발성 및 연하작용을 유지하며 치료할 수 있다. 그러나 비교적 진행된 병소(late T2, T3) 중 하부 침윤이 심하지 않으면 방사선 치료만으로 완치될 수 있으며 수술은 방사선 치료 후 재발암의 구원요법으로 유보해 두는 것이 바람직할 것이다.

방사선 치료의 방법으로는 외부 조사법 외에 자입요법 등이 있으나 최대의 국소 퇴치를 위해서는 자입요법이 필수적인 것으로 나타났다. 이러한 자입요법으로 치료기간을 단축할 수 있음은 말할 것도 없고 투여되는 선량을 증가시킴으로서 국소 퇴치율의 향상을 기대하고 나아가 생존율을 높일 수가 있을 것이다.