مقاله تحقیقی

نتایج درمانی و عوامل ایپیدمیولوژیک در سرطان زبان در ۱۱۰ بیمار مراجعه گنده به انسیستو کانسر تهران

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چکیده

اهداف: کانسر زبان یکی از تابع‌های کنسرهای ناحیه حفره دهان می‌باشد که به‌طور متوسط سنی بیماران حدود ۶۰–۷۰ سال می‌باشد.

روش‌های تغییر درمانی تعداد ۱۱۰ بیمار مبتلا به کانسر زبان در استیت‌کانسر تهران در سال‌های ۱۹۹۹–۲۰۰۳ مراجعه کرد یونیک. در یک مطالعه کلیه‌گیری کلیه‌گیری شد. بیماران تحت درمان با جراحی، با رادیوتراپی، یا کمربن‌لیوم تحت درمان قرار گرفتند.

پایه‌دهنده مطالعه سنی آن در اواخر وسط ۷۷ ساله (سال ۹۳–۹۲ در محدوده) بود. ۵۸ بیمار (44/4٪) زن و ۵۵ بیمار (55/6٪) مرد بودند. درمان آن‌ها در ۱۲ بیمار (10/9٪) رادیوتراپی توسط کمربن‌لیوم، درمان کمربن‌لیوم نمودار جوانان ۸ بیمار ۳۰ (7/6٪) بود. میانگین دور دردایی بیماران رادیوتراپی شده بود. ۴۸ بیماران بطور متوسط تحت تابع ۱۰۰ دیگری (7/9 ٪) می‌باشد که متوسط زمان عید ۹‌ماه (۶/۳‌ماه) بود.

نتیجه گیری: عود موضعی و منطقه‌ای در تومورهای حرفه دهان یک مشکل اساسی بینی می‌باشد که مطالعات وسیع‌تر و آنالیزی دقیق ترجمه دست‌بسته به بهترین مودالیته درمانی مورد تایب می‌باشد.

کلمات کلیدی: کانسر زبان – جراحی – رادیوتراپی

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Treatement Results and Epidemiologic Factors in Oral Tongue Cancer: Analysis of 110 Patients in Cancer Institute of Tehran

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ABSTRACT

Background: Tongue cancer is one of the most common cancers of the oral cavity, excluding lip, and the median age of the patients is approximately 60 years.

Methods: Treatment results of a total of 110 patients with oral tongue cancer admitted to cancer Institute of Tehran University between 1999-2003 were retrospectively analyzed. The patients were treated by surgery or radiotherapy or chemotherapy in a curative setting.

Results: The median age at the time of first visit was 67 years (range 27-91 years). 51 patients (46.4%) were female and 59 (53.6%) were male. Primary treatment was surgery in 86 patients (78.2%), radiotherapy alone in 12 patients (10.9%), chemotherapy (as neo adjuvant therapy) in 3 patients (2.7%) and chemotherapy (as neo adjuvant therapy) in 8 patients (7.3%).

Median dose of radiation in patients who received radiotherapy was 6000CGY in the range of (5000-7500 CGY).

Median of follow-up of patients was 10 months in range of (1-78) months.

Conclusion: Local and loco-regional recurrence remains a major clinical problem in oral cavity tumors. Additional studies and detailed analysis of the selection criteria and treatment outcomes across trials are needed to define the best treatment modalities.

Keywords: Tongue Neoplasm; Surgery; Radiotherapy
INTRODUCTION

Tongue cancer is one of the most common cancers of the oral cavity, excluding lip, and the median age of the patients is approximately 60 years. The most common pathology in cancer of oral tongue is squamous cell carcinoma and the most common symptoms are pain and speech problems with more rapid onset than any other oral cavity cancer. Lymphatic metastases from oral tongue cancer are most frequently seen and occur in about 15–75% of cases. Although surgical excision has been the mainstay of treatment, combined surgery and adjuvant radiation therapy to include the primary site and regional nodes is commonly used for more advanced (stages III and IV) cancers, and is being used increasingly for small stage II tumors that exhibit pathologic indicators of lymph-node metastasis or peri neural invasion(1). In this study, 110 patients with oral tongue cancer whom were treated with surgery or radiotherapy with or without chemotherapy were thoroughly evaluated.

METHODS

Files of all patients with Tongue cancer treated in cancer institute by surgery or radiotherapy with or without chemotherapy in a curative setting during the period of 1999-2003 were retrospectively reviewed. All patients, tumor and treatment characteristics were registered. The period of follow-up was calculated from the start of patients’ first modality of treatment to the date of last follow-up or visit or death. Loco regional relapse was defined as the appearance of cancer on the scar or remaining tissue of tongue or regional lymph nodes areas. All other relapse locations were assumed to be distant metastases. All statistical analyses were done with SPSS package program, version 11.2.

RESULTS

A total of 110 patients with oral tongue cancer had been treated by surgery or radiotherapy or chemotherapy or combination of these treatment modalities. The median age at the time of first visit was 67 years (range 27-91 years). 51 patients (46.4%) were female and 59 (53.6%) were male. Frequency of pathology was: Well differentiated squamous cell carcinoma in 63 patients(57.3%), moderately differentiated squamous cell carcinoma in 33 patients(30%), poorly differentiated squamous cell carcinoma in 7 patients(6.4%), adenoid cystic carcinoma in 2 patients(1.8%), sarcoma in 1 patients(0.9%), undifferentiated carcinoma in 2 patients(1.8%) and verrucous carcinoma in 2 patients(1.8%).

Chief complaint of patients was: feeling of mass in the tongue in 51 patients (46.4%) and ulceration of oral tongue in 56 patients (50.9%) and in 3 patients was not recorded.

According to 2002 American Joint Committee on cancer (AJCC) TNM staging system for the lip and oral cavity:

- 8 patients (7.3%) were T1, 32 patients (29.1%) were T2, 48 patients (43.6%) were T3, 7 patients (6.4%) were T4 and 15 patients (13.6%) were Tx.
- 51 patients (46.4%) were N0, 6 patients (5.5%) were N1, 12 patients (10.9%) were N2, 12 patients (10.9%) were N3 and 28 patients (25.5%) were Nx.

Primary treatment was surgery in 86 patients (78.2%), radiotherapy alone in 12 patients (10.9%), chemo radiation in 3 patients (2.7%) and chemotherapy (as neo adjuvant therapy) in 8 patients (7.3%).

Frequency of type of surgery was: tumor resection in 38 patients (34.5%), tumor resection plus lymph node dissection in 52 patients (47.3%) and tumor resection and lymph node dissection and flap in 3 patients (2.7%).

The overall and loco regional disease-free survival rates were calculated using the Kaplan – Meier method and compared using the log rank test.
In regard of adjuvant therapy 42 patients didn’t receive any thing (38.2%). 13 patients received chemo radiation as adjuvant therapy (11.8%). 43 patients received radiotherapy alone (39.1%). Only 3 patients treated by chemotherapy after surgery (2.7%). In 9 patients after primary chemo radiation surgery were done as adjuvant treatment (8.2%). Brach therapy with 197 iridium was done in 3 patients (2.7%) in addition to external beam radiation which all of them received 1500eGY. Median dose of radiation in patients who received radiotherapy was 6000CGY in the range of (5000-7500).

Median follow-up of patients were 10 months in range of (1-78) months. 23 patients had recurrence after treatment (20.9%). Median time of recurrence was 9 months in the range of (3-36) months. After recurrence treatment modalities were as below: chemotherapy in 5 patients (4.5%), chemotherapy followed by surgery in 1 patient (0.9%), radiotherapy alone in 1 patient (0.9%), surgery followed by chemotherapy in 1 patient (0.9%), surgery followed by radiotherapy in 1 patient (0.9%) and surgery alone in 3 patients. In the follow –up of patients 2 patients had distant metastases (0.9%) and 2 patients died (0.9%).

**DISCUSSION**

Tongue cancers account for 25% of oral cavity squamous cell carcinomas and, although surgical excision has been the mainstay of treatment, combined surgery and adjuvant radiation therapy to include the primary site and regional nodes is commonly used for most advanced (stages III and IV) cancers, and is being used increasingly for small stage II cancers that exhibit pathologic indicators of lymph-node metastasis or peri neural invasion. For stage I cancers, surgical excision is effective and expeditious with good preservation of function. For stage II lesions that are infiltrative, hemiglossectomy achieves excellent tumor control rates and can be combined with modified dissection of neck nodes (supraomohyoid dissections) to provide accurate staging information and determination of the need for adjuvant radiation. (1) In our study surgery were wildly used even for advanced tumors (T3) and hemiglossectomy together with lymph node dissection were the most common surgical procedure. Hicks et al. reported the results of 79 patients with squamous cell carcinoma of the oral tongue treated with surgery alone. Clinically, 69% of the patients presented with stage I/II disease and 31% with stage III/IV. Survival by pathological stage I–IV was 89%, 95%, 76%, and 65%, respectively. Surgical therapy ranged from partial to total glossectomy. Local recurrence was observed in 15% of patients with close margins (<1 cm) and 9% of patients with adequate margins (≥1 cm). The incidence of pathological node-positive (N+) disease was 6%, 36%, 50%, and 67% for T1, T2, T3, and T4 tumors, respectively. Twenty-five percent of patients undergoing elective neck dissection were pathological N+. All pathological confirmed nodal disease was at level II or I. Of the 43 patients with clinical N0 disease, 16% subsequently developed regional recurrence, all of whom were surgically salvaged. The authors concluded that adequate margins were crucial to local control and, because of the high rate of occult disease (41%), prophylactic treatment of regional lymphatic for primary clinical disease of T2 or greater was necessary. (2)

In an earlier study, 602 patients treated for cancer of the mobile tongue at the Curie institute were evaluated. Sixteen percent had T1, 48% T2, and 36% T3 lesions. Sixty-four percent had no palpable nodes (N0). The primary tumor region was treated in the majority of patients by radium implant alone or in association with external radiotherapy, and the cervical lymph nodes were treated primarily by surgery. The 5-year survival rate for T1, T2 and T3 tumors was 80%, 56% and 25%, respectively. Fifty-nine percent of those with clinically negative neck nodes survived 5 years. Recurrence at the primary site alone or associated with neck failure was 14% for T1, 22% for T2 and 29% for T3 lesions, and 70% of recurrences occurred within 1 year. Although 13%
of patients who had recurrence at the primary site were alive at 5 years, 33% of those who had salvage surgery were rescued. Two percent of patients required surgery for radiation necrosis. The results showed that radiotherapy alone was a good alternative for the management of primary lesions of mobile tongue cancers. (3)

In a Japanese study that evaluated the results of treatment for early mobile tongue cancer in patients less than 40 years of age, the 5-year local control rate for the younger age group was 78%, which was not significantly different from those of the 2 older groups. The incidence of regional lymph-node metastasis was 32% for T1 and 48% for T2 lesions, and 56% for males and 24% for females. The regional failure rate of young males was significantly higher than those of the 2 older groups: 32% for middle age and 22% for old age ($P = 0.001$). In this study, male gender was found to be a risk factor for lymph-node metastasis and low cause-specific survival (4). We did not find any correlation between gender and treatment results.

Although a combination of chemotherapy with surgery and radiotherapy has improved cure rates in some other head-and-neck cancers, its role in the management of oral cavity tumors is less clear. KIRITA treated 48 oral cavity tumors with concurrent neo adjuvant chemo-radiotherapy followed by surgery. Although 5-year overall survival was reported as 81.3%, the complication rate of this treatment was high and the functional state of the patients was not described (5). In another study, a clinical complete response was achieved in 50% of 69 patients who were treated with neo adjuvant chemotherapy followed by concurrent chemo-radiation. Fifty-three patients had surgery after chemo-radiation and the complete response rate was 54%. The complete response rate of the entire group was 46%. The 3-year disease-free survival rate was reported as 73%. An important point of this study was the high amount of toxicity; grade 3–4 mucositis was seen in 59% of patients. (6)

Regarding the poor prognosis of patients with locally advanced disease, in the 1990s a number of studies investigating the role of concurrent chemo-radiation in the adjuvant setting were performed, but the overall results of these small trials did not show a significant benefit in terms of local control and survival (8) and (9). As our study that chemo radiation have been used in only a few patients. But in 2004 the results of 2 large prospective randomized trials changed the situation markedly (10, 11). The first study was the Radiation Therapy Oncology Group (RTOG) 9501/Intergroup trial (12) that randomized 459 patients to receive either radiotherapy alone (60–66 Gy in 30–33 fractions over a period of 6–6.6 weeks) or the same regimen plus concurrent cisplatin (100 mg/m$^2$ on days 1, 22 and 43). The results showed that the rate of local and regional control was significantly higher in the combined-therapy group than in the group given radiotherapy alone, with a 2-year rate of local and regional control of 82% in the combined-therapy group as compared to 72% in the radiotherapy group ($P = 0.01$). Disease-free survival was also significantly longer in the combined-therapy group than in the radiotherapy group ($P = 0.04$), but the overall survivals were not significantly different ($P = 0.19$). These results showed that in high-risk patients with resected head-and-neck cancer, concomitant postoperative chemo radiotherapy significantly improved the rates of local and regional control and disease-free survival. The combined treatment was, however, associated with a significant increase in adverse grade 3 effects (34% versus 77%, $P < 0.001$). The European Organization for Research and Treatment of Cancer (EORTC) trial 22931 also tested the efficacy of the same chemotherapy regimen in 167 patients, and demonstrated that adjuvant postoperative concomitant chemotherapy with cisplatin and radiotherapy is more likely to control loco-regional disease and yield disease-free survival than postoperative radiotherapy alone. (11)

Local and loco-regional recurrence remains a major clinical problem in oral cavity tumors. Surgery in relapse is associated with significant and sometimes unacceptable morbidity. Re-irradiation is also often difficult because of the limited tolerance of normal tissue structures. In a study by SCHWARTZ, a salvage rate of 21% was
reported for recurrent oral cavity tumors. The salvage cure rate by surgery was significantly better than by non-surgical treatments such as radiotherapy \((P = 0.008)\). (7) We also had significant rate of recurrence (20%) and most of recurrence were treated with surgery but with we need prospective trials to and more follow-up to show our salvage cure rate.

CONCLUSION

In conclusion, small mucosal oral cavity tumors can be successfully treated by radiotherapy or surgery with similar results. Local control rate for T3 and T4 lesions is poor with surgery or radiotherapy alone, so combined surgery and postoperative radiation therapy is the treatment of choice for these patients. Extensive nodal disease (N2 or N3 neck) is rarely salvaged by radiotherapy or surgery alone, and the combination of node dissection and postoperative radiotherapy is the appropriate treatment in such patients also.

The results of the RTOG 9501 and EORTC 22391 trials demonstrated the potential benefits of concomitant postoperative chemo radiotherapy in high-risk operable head-and-neck cancer. Additional studies and detailed analysis of the selection criteria and treatment outcomes across these 2 trials are needed to define the real role of chemo-radiotherapy in patients with operable, locally advanced disease and the best treatment modalities.
## REFERENCES


