

Stage IV oral cavity carcinoma

Is conventional radical treatment an option?

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ABSTRACT

Objective: To evaluate the outcome of radical treatment for patients with stage IV squamous cell carcinoma of the oral cavity.

Methods: Using head and neck tumor database, 57 patients with stage IV non-metastatic invasive squamous cell carcinoma of the oral cavity treated with curative intent at King Faisal Specialist Hospital and Research Center, Riyadh, Kingdom of Saudi Arabia, between July 1992 and June 1998, were identified and retrospectively reviewed.

Results: Our cohort of patients consisted of 33 males and 24 females, with a median age of 65 years. The primary sites were alveolus (26), tongue (22), buccal mucosa (6), floor of mouth (2) and retromolar trigone (one). Definitive radiotherapy was used in 7 patients, surgery in 17 and combined modality in 33. With a

median follow-up for surviving patients of 53-months, the actuarial 5-year overall survival and relapse free survival was 20% and 14%. Tumors arising from the alveolus showed a better outcome as compared to the rest of oral cavity sites with an overall survival and relapse free survival of 32% and 26% compared to 8% and 4% (p value=0.0057 and 0.0038).

Conclusion: Advanced oral cavity tumors are aggressive neoplasms with a poor outcome to conventional treatment modalities. New approaches like neoadjuvant or concurrent chemoradiotherapy with or without surgery need to be considered and evaluated in prospective studies.

Keywords: Oral cavity carcinoma, surgery, radiotherapy.

Saudi Med J 2002; Vol. 23 (9): 1095-1098

Malignant oral cavity tumors represent approximately 26% of all head and neck cancers diagnosed annually in the Kingdom of Saudi Arabia (KSA).¹ The majority of cases are advanced, and palliatively treated. The ideal goal for head and neck cancer treatment is to eradicate known disease while limiting both functional and cosmetic deformity. Despite aggressive combined modality treatment utilizing surgery and radiation, still the majority of patients eventually develop locoregional

recurrence or occasionally distant metastasis. As a result of low successful salvage rates, the overall prognosis is very poor and the outcome is usually dismal.²⁻⁴ Recently several clinical trials evaluating the role of neoadjuvant chemotherapy prior to radiation or surgery, or using chemotherapy concurrently with radiation, showed promising results; however some were subject to patient selection biases.⁵⁻⁷ In this retrospective review we report King Faisal Specialist Hospital and Research

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Received 25th March 2002. Accepted for publication in final form 3rd June 2002.

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Centre (KFSH & RC), Riyadh, KSA experience of radical treatment for stage IV oral cavity carcinoma.

Methods. The medical records of all adult patients (16 years or above) with stage IV squamous cell carcinoma of the oral cavity treated with curative intent at KFSH & RC between July 1992 and June 1998 were identified using head and neck tumor database. In total, 57 patients were available for analysis, constituting 3% (57/1861) of all head and neck cancer cases seen during that period. Of the 57 patients, there were 33 men and 24 women. Their ages ranged from 19 to 80 years with a median of 65 years. The primary sites were alveolus, (26) tongue (22), buccal mucosa (6), floor of mouth (2) and retromolar trigone (1). Thirty-five patients (61%) were from Gizan region, KSA, and 86% of them admitted chewing shamma. Presenting symptoms, clinical findings, and tumor stage are summarized in **Tables 1 & 2**. All patients were seen at multi-disciplinary combined head and neck oncology clinic, and jointly evaluated by a head and neck cancer surgeons and radiation oncologists. They all had a biopsy proven histological diagnosis, reviewed by an expert pathologist at KFSH & RC, and were re-staged according to 1997 American Joint Committee of Cancer (AJCC) criteria based on physical examination, routine laboratory tests, chest radiograph, computerized tomography scan of the head and neck, liver ultrasound, and bone scan. All recurrences were confirmed pathologically.

Treatment. All patients were treated with curative intent. Seventeen patients had surgical resection, 7 had radical radiotherapy alone, and 33 underwent combined modality treatment (radical surgery followed by radiotherapy). Surgery included primary tumor excision and neck node dissection. Radiation therapy treatment fields encompassed all the gross tumors or tumor bed with safety margin

and both sides of the neck to a total dose of 6600-7000 centigray (cGy) using conventional fractionation. Areas at risk for microscopic disease were treated to 4500-5000 cGy. Postoperative irradiation was tailored to cover the area at high risk for recurrence to a total dose of 5000-6000 cGy.

Statistical methods. Overall survival (OS) was calculated from the date of diagnosis to the date of last follow-up or death from any cause, and relapse free survival (RFS) from the date of treatment completion to recurrence date. Patients lost to follow-up were censored at the time of last visit. Survival curves were plotted using the method of Kaplan and Meier, and compared using the log rank test. Differences were considered significant if the two-tailed $p < 0.05$. All analyses were performed using Statistical Package of Social Sciences (SPSS) software version 10.

Results. With a median follow-up for surviving patients of 53 months (range 8-74 months), data was available for all patients, except one lost to follow-up. This patient was free of disease at last visit 8 months after his treatment. Forty patients (70%) developed locoregional recurrence, and 6 (11%) had post-treatment residual disease. Forty-five patients (79%) died, 44 (77%) from oral cavity carcinoma, and one (2%) from unrelated cause. All recurrences were locoregional, with a median time of 9 months (range 2 - 67 months). The 5 year actuarial OS was 20% and RFS was 14% (**Figures 1 & 2**). Overall survival and RFS were significantly higher in patients with carcinoma of the alveolus 32% and 26% as compared to the rest of the oral cavity tumors 8% and 4%, ($p=0.0057$ and $p=0.00038$). Combined modality treatment using surgery followed by radiotherapy showed a trend for better locoregional control and survival as compared to single modality. Overall survival and RFS were 24% and 19% for the combined approach as compared to 18% and 11% for

Table 1 - Patients presenting symptoms and shamma using habit.

Symtoms	n (%)
Pain	46 (81)
Ulcer	45 (79)
Dysphagia	9 (16)
Neck mass	9 (16)
Dysarthria	3 (5)
Shamma using habit	30 (53)
n - number	

Table 2 - Patients clinical stage.

T stage	Nodal stage			
	N 0	N 1	N 2	N 3
T1	0	0	0	0
T2	0	0	5	0
T3	0	0	8	0
T4	19	16	8	1
T - tumor, n - nodal				

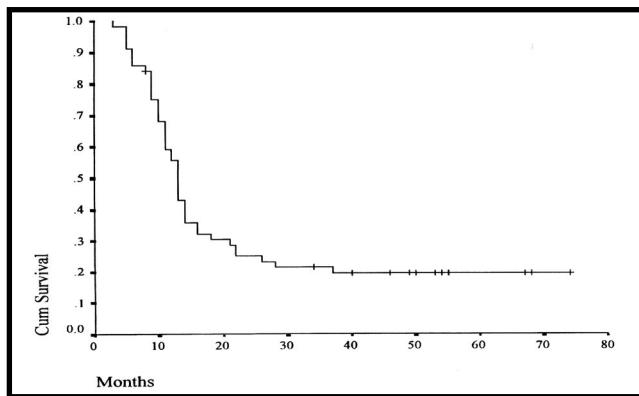


Figure 1 - Overall survival.

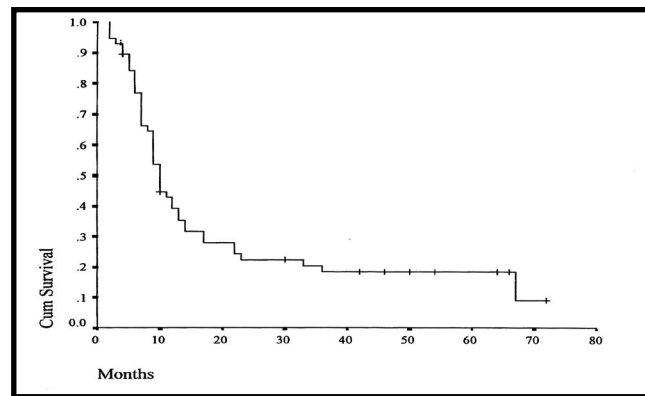


Figure 2 - Relapse free survival.

single modality ($p = 0.11$ and $p=0.19$). Age and sex showed no impact on either OS and RFS.

Discussion. Oral cavity tumors are the most common neoplasms in the Gizan region of KSA. They represent 13% of all cancers and 72% of head and neck cancers diagnosed annually in this area.¹ Several studies have attributed this high incidence to "shamma" using habit.⁸⁻¹⁰ 'Shamma' is a crude mixture of powdered tobacco, slaked lime, ash, oil, spices and other flavoring additives. An animal model study carried out at our institute has demonstrated its carcinogenic effects and it is believed that long-term users may develop oral cavity cancer.¹⁰ Oral cavity tumor has generally been considered a disease of the elderly with a male to female ratio 10:1. However with the increasing use of tobacco and alcohol by the female population, the ratio has now come down to 1.5.¹¹⁻¹⁵ Our study shows a male to female ratio of 1.38:1. This high incidence in females in the Saudi community is roughly in line with the data from the western societies, but the reasons are entirely different. Alcohol is not used in the country for religious and social background while smoking amongst females is almost negligible. The high incidence (61%) in our patients cohort is confined to one geographical region, where the shamma chewing habit is believed to be similar in both sexes. Our 5-year OS and RFS results of 20% and 14% are somewhat disappointing, but it is generally in line with other reported studies. It has been reported to be as low as 16-18%.^{2,4} Excluding patients with carcinoma of the alveolus, the 5-year OS (8%) and RFS (4%) results are even much worse. This is related to the advanced stage of disease at presentation, indicating the needs to look for other methods, other than conventional, to improve our results. Stage migration and lack of lymphatic drainage in alveolus tumor can explain the significantly superior treatment outcome compared to the rest of oral cavity tumors. Our data clearly shows

a trend for inferior result for single modality treatment as compared to combined surgery and radiotherapy. This did not reach statistical significance, most likely due to the small sample size. Krause et al¹⁶ review study had a larger cohort of patients and confirmed the statistical difference in favor of combined modality. Locoregional recurrence is the major site for treatment failure. In most studies, as well as in the current study, recurrences occur within an average of 2 years from treatment;¹⁷⁻¹⁸ this highlights the importance of close follow up in the first few years following treatment. Combined conventional treatment with radiotherapy and surgery has generally shown disappointing results. However, recent reports have indicated that with the addition of chemotherapy as a 3rd modality, either before or after surgery and radiotherapy, locoregional control and survival rates have improved.⁶⁻⁷

In conclusion, advanced oral cavity tumors are aggressive neoplasms with poor outcome to conventional treatment modalities. New approaches, such as neoadjuvant or concurrent chemoradiotherapy with or without surgery need to be considered and evaluated in prospective studies.

References

1. Ministry of Health. Cancer Incident Report 1994-1996. Riyadh (KSA): National Cancer Registry Authority; 1999.
2. Gujrathi D, Kerr P, Anderson B, Nason R. Treatment outcome of squamous cell carcinoma of the oral tongue. *J Otolaryngol* 1996; 25: 145-149.
3. Pugliano F, Piccirillo J, Zequeira M, Fredrickson J, Perez C, Simpson J. Clinical-severity staging system for oral cavity cancer: five-years survival rates. *Otolaryngology Head Neck Surg* 1999; 120: 38-45.
4. Charabi S, Balle V, Charabi B, Berthelsen A, Thomsen J. Squamous cell carcinoma of the oral cavity: The results of the surgical and non-surgical therapeutic modalities in a consecutive series of 156 patients treated in Copenhagen country. *Acta Otolaryngol Suppl* 1997; 529: 226-228.
5. Giralt J, Gonzalez J, del Campo J, Maldonado J, Sanz X, Pamiás J et al. Preoperative induction chemotherapy followed by concurrent chemoradiotherapy in advanced carcinoma of the oral cavity and oropharynx. *Cancer* 2000; 89: 939-945.

6. Kirita T, Ohgi K, Shimooka H, Yamanaka Y, Tatebayashi S, Yamamoto K et al. Preoperative concurrent chemoradiotherapy plus radical surgery for advanced squamous cell carcinoma of the oral cavity: An analysis of long-term results. *Oral Oncol* 1999; 35: 597-606.
7. Kirita T, Ohgi K, Tsuyuki M, Kamikaido N, Yamamoto K, Sugimura M. Preoperative simultaneous cisplatin or carboplatin-based chemotherapy and radiotherapy for squamous cell carcinoma of the oral cavity. *J Surg Oncol* 1996; 63: 240-248.
8. Amer MH, Dauk M, McArthur P, Landmark G, El-Senoussi M. Shamma usage and oral cancer in Saudi Arabia. *Annals of Saudi Medicine* 1985; 5: 135-140.
9. Hannan MA, El Yazigi A, Manik P, Gibson DP, Phillips RL. Genotoxicity of 'shamma', a chewing material suspected of causing oral cancer in Saudi Arabia. *Mutation Research* 1986; 169: 41-46.
10. Sammam M, Bowen I, Taiba K, Antonius J, Hannan M. Mint prevents shamma-induced carcinogenesis in hamster cheek pouch. *Carcinogenesis* 1998; 19: 1795-801.
11. Nyman J, Mercke C, Lindström J. Prognostic factors for local control and survival of cancer of the oral tongue. *Acta Oncol* 1993; 32: 667-673
12. Franceschi D, Gupta R, Spiro RH, Shah JP. *Am J Surg* 1993; 166: 360-365.
13. Shaw J, Candela F, Poddar A. The pattern of cervical lymph node metastasis from squamous carcinoma of the oral tongue. *Cancer* 1990; 66: 109-113.
14. Lydiatt DD, Robbins KT, Byers RM, Wolf PF. Treatment of Stage I and II oral tongue cancer. *Head Neck* 1993; 15: 308-312.
15. MacComb W. reporting end results. *Am J Surg* 1967; 114: 486-488.
16. Krause C, Lee J, Macabe B. Carcinoma of the oral cavity. *Arch Otolaryngol* 1973; 97: 354-358.
17. Nason RW, Anderson BJ, Gujrathi DS, Abdoh AA, Cooke RC. A retrospective comparison of treatment outcome in the posterior and anterior tongue. *Am J Surg* 1996; 172: 665-670.
18. Al-Rajhi N, Khafaga Y, Saleem M, Al-Husseni J, Mourad W, Abuzei M et al. Early Stage Carcinoma of the Oral Tongue: Prognostic Factors For Local Control and Survival. *Oral Oncology* 2000; 36: 508-514.