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Oral Cancer in Jordan: A Retrospective Study of 118 Patients

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Aim. To evaluate clinical features, diagnosis, and treatment of oral cancer in Jordan.

Method. We retrospectively analyzed the medical records 118 consecutive patients treated for oral cancer from 1989 until 1998.

Results. The age of the patients ranged from 35 to 90 years (median 62.5 years); three quarters were men. Ninety patients (76%) were smokers and 6 (5%) drank alcohol. The floor of the mouth was the most common site for oral cancer, followed by the tongue. The male/female ratio was 3.1:1. The majority of T1 tumors were treated by surgical excision, T2 tumors by surgery or radiotherapy, and T3 and T4 tumors without evidence of nodal disease by radiotherapy. Patients with nodal disease were treated primarily by surgery. In the absence of nodal disease, T1, T2, T3, and T4 tumors had 5-year survival rates of 95%, 95%, 81%, and 25%, respectively, whereas the patients with nodal disease had a poorer prognosis, with survival rates of 37%, 29%, 12% and 0% for T1, T2, T3, and T4, respectively. The 5-year survival rate decreased from 80% to 20% as the stage of disease progressed from I to IV. The overall 5-year survival for all stages of disease was 62/118 (53%). Patients treated with surgery alone (5-year survival rate 62%), and those treated with postoperative radiotherapy (5-year survival rate 81%) did better than patients treated with radiotherapy alone (31%).

Conclusion. Complete surgical resection combined with radiotherapy results in the best therapeutic outcome.

Key words: *carcinoma, squamous cell; Jordan; mouth neoplasms; neoplasm metastasis; survival rate; tongue neoplasms; tumor treatment*

Oral cancer is one of ten most frequent cancers worldwide (1). The incidence of the tongue cancer seems to be increasing in the USA (2), and in Scotland (3), where cancer in the rest of the mouth is likewise increasing (4).

The clinician's dilemma is differentiating cancerous lesions from a multitude of other ill-defined, controversial, and poorly understood lesions that also occur in the oral cavity. Most oral lesions are benign, but many have an appearance that may be easily confused with malignant lesions and some are now considered premalignant because they have been statistically correlated with subsequent cancerous changes. Conversely, some malignant lesions seen in an early stage may be mistaken for a benign change (5). Early carcinomas are probably asymptotic and subsequent manifestations are commonly misinterpreted because they mimic many benign lesions and the discomfort is minimal. Professional consultation is thus often delayed, increasing the chance for local spread and regional metastases. Emphasis must be placed on gaining access to high risk individuals for periodic oral examinations and educational efforts to increase the skill of primary health care providers in recognizing this problem (5).

The most common malignant neoplasm of the oral cavity is squamous cell carcinoma, which accounts for 90% of the total number of malignant oral lesions. Therefore, the problem of oral cancer is primarily that of pathogenesis, diagnosis, and management of squamous cell carcinoma originating from the oral mucosal surface.

Oral tumor presenting with nodal metastases would appear to have a less favorable prognosis (6). The effect of an elective neck dissection when there is no demonstrable disease is equivocal, some authors suggesting that it is beneficial (7), and others showing that there is no improvement in survival rate (8).

The aim of this investigation was to retrospectively evaluate the clinical features, diagnosis, treatment, and follow-up of oral cancer patients in Jordan.

Patients and Methods

This was a retrospective analysis of 118 patients with oral cancer who were referred to the Department of Oral and Maxillofacial surgery and histopathologically diagnosed and treated between 1989 and 1998. This study was based on the analysis of the hospital charts, referral letters, radiological studies, operative reports, pathological reports, and radiation therapy. The patients were analyzed according to

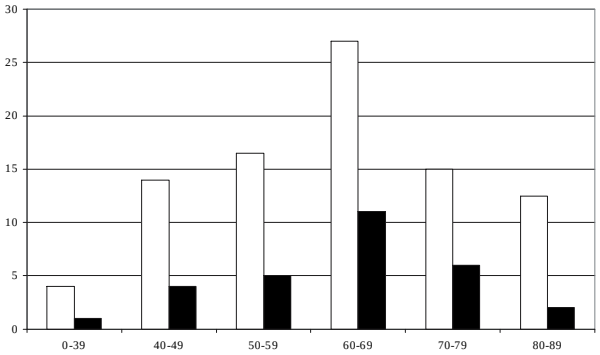

Figure 1. Age and sex distribution of patients with oral cancer. Open bars, men; closed bars, women.

the sex, age, histopathological type of the tumor, site, localization, size of the tumor, therapeutic approaches, and follow up information. The follow up information was available for 97 patients, and the follow up period was from 6 months to 9 years (median 6.5 years). There were 89 men and 29 women with a mean age of 62.5 years (range 35-90 years).

Tumors were staged clinically according to the 1992 classification of the International Union against Cancer (UICC) (9). Distribution by stage according to the UICC classification was as follows: 20 (17%) patients in stage I, 34 (29%) patients in stage II, 38 (32%) patients in stage III, and 26 (22%) patients in stage IV. None of them had evidence of distant metastasis at the time of initial examination.

Treatment comprised surgery, radiotherapy, or their combination. Surgery alone was used for 57 patients who underwent local excision together with radical or supraomohyoid neck dissection. Sixteen patients were treated by surgical treatment combined with radiotherapy. Forty-five patients were treated by radiotherapy alone. Radical neck dissection was performed in 53 patients, and supraomohyoid neck dissection in 20 patients. Fifty eight (49%) patients had cervical lymph node metastases. Survival curves were calculated according to the Kaplan-Meier method (10), and the differences were tested at the $p<0.05$ level of significance.

Results

The age of the patients ranged from 35 to 90 years, with a mean age of 62.5 years. The male/female ratio was 3.1:1. Most of the patients were in the 60-79 age group (59, 50%), followed by those in the 50-59 age group, and 14 (9%) were over 80 years of age (Fig. 1). The histological classification was squamous cell carcinoma in 113 (96%), adenocystic carcinoma in 3 (2.5%) cases, and mucoepidermoid carcinoma and fibrosarcoma in a case each.

Squamous cell carcinomas were classified histologically into well differentiated tumors in 52 (44%) patients, moderately differentiated in 50 (42%) patients, and poorly differentiated in 16 (14%) patients.

Table 1. Distribution of patients (N, %) by the site of oral cancer

Site	Men	Women	Total
Floor of mouth	31 (26)	9 (8)	40 (34)
Tongue	19 (16)	8 (7)	27 (23)
Lower alveolar ridge	17 (14)	6 (5)	23 (19)
Upper alveolar ridge	9 (8)	1 (1)	10 (9)
Gingiva	5 (4)	2 (2)	7 (6)
Buccal mucosa & buccal sulcus	4 (3)	2 (2)	6 (5)
Palate	4 (3)	1 (1)	5 (4)
Total	89 (100)	29 (100)	118 (100)

There was a total of 28 (24%) non-smokers (24 woman and 4 men), whereas 65 (55%) of the patients, mostly men, were smokers.

The majority of pipe smokers were 22 (19%) men, and 3 (2%) men smoked cigars. Most of the patients (112, 95%) did not drink alcohol, and only 6 males were drinkers.

Symptoms and Referrals

The patients complained of pain in 36 (30%) cases, 15 (13%) had tenderness, 12 (10%) experienced swelling, and 15 (13%) had burning sensation. A color change was observed by 20 (17%) patients. There were no symptoms in 20 (17%) patients and they were unaware of any abnormality.

Duration of the symptoms varied between 1 and 4 weeks in 4 (3%) of cases, 1-3 months in 47 (40%), 4-10 months in 46 (39%), and 1-3 years in 6 (5%) patients. Information about duration of symptoms was not obtained from 15 (13%) patients.

Referrals were as follows: 99 (84%) by their dentists, and 19 (16%) by their physicians. In 11 (9%) cases there was no delay in referral, 13 (11%) were referred with a delay of 1-4 weeks, 40 (34%) with 1-3 months delay, 28 (24%) with a delay of 4-9 months, and 17 (14%) with a delay of 1-3 years. Information about the delay in referral could not be obtained for 9 (8%) of the patients. In cases with delayed referral, patients themselves were the cause in 91 (77%) cases, whereas a dentist caused the delay in 11 (9%), and a physician in 6 (5%) cases.

Localization

The site of intra-oral cancer is shown in Table 1. Cancer of the floor of the mouth was observed in 40 (34%), and cancer of the tongue in 27 (23%) of cases. Mucosal changes adjacent to the tumor were observed in 45 (38%) of cases, leukoplakia was noted in 36 (31%),

Table 2. Distribution of patients with oral cancer by TNM classification, stage grouping, and the total incidence of regional lymph node metastases

TNMD	N0		N1		N2-N3		Total incidence of nodal metastases
	No.	Stage	No.	Stage	No.	Stage	
T1	20	I	4	II	4	IV	8/28 (29%)
T2	20	II	10	II	4	IV	14/34 (41%)
T3	6	III	22	III	2	IV	24/40 (60%)
T4	4	IV	8	IV	4	IV	12/16 (75%)
Total	60		44		14		58/118 (49%)

erythroplakia in 5 (5%), and lichen planus in 2 (2%). There were no changes in the adjacent tissue in 73 (62%) patients.

Metastases

Metastases in lymph nodes were found in 45 (38%) out of 118 patients at presentation or subsequent treatment of the primary tumor, and 13 (11%) patients had no clinically evident nodal metastases but positive histological finding after surgery. Thus, 58 (49%) of 118 patients with oral cancer had lymph node metastases. The prevalence of metastases increased significantly with the progression of the primary tumor (Table 2): from 29% in T1 to 75% in T4 lesions ($p<0.001$). Lymphatic spread of tumors was found in 29% of T1 tumors, 41% of T2 tumors, 60% of T3 tumors, and 75% of T4 tumors. The prevalence of cervical lymph node metastases according to the degree of tumor differentiation was 7/52 (13%) of grade I, 37/50 (74%) of grade II, and 14/16 (87%) of grade III.

Local or neck recurrences of the tumors were encountered in 20 (17%) cases. Recurrence developed four times as often in those patients in whom lymph nodes were microscopically positive for metastases (16/58, 28%), as compared with those in whom nodes were negative (4/60, 7%).

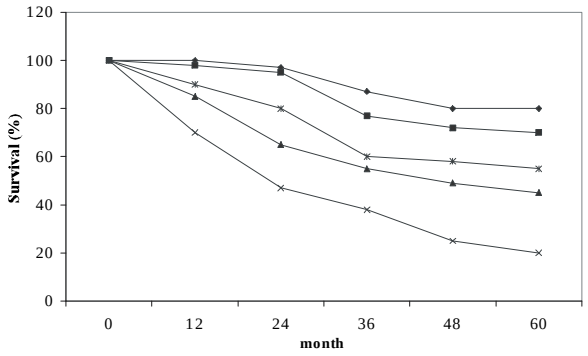

Figure 2. Survival rate of patients with oral cancer according to the stage of disease. Rhomb, stage I (n=20), square, stage II (n=34), triangle, stage III (n=38), cross, stage IV (n=26), and asterisk, total (n=118).

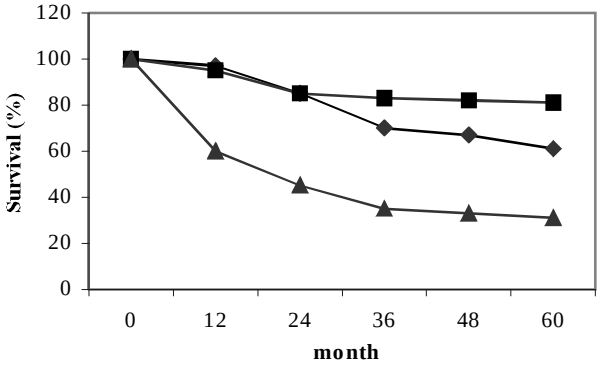

Figure 3. Survival of patients with oral cancer according to the treatment modality. Square, surgery and radiation; rhomb, surgery alone; triangle, radiation alone.

Table 3. The 5-year survival rates for patients with oral cancer (n, %), and presenting with or without nodal disease

Tumor size	With nodal disease	Without nodal disease	All
T1	3/8 (37.5)	19/20 (95)	22/28 (79)
T2	4/14 (29)	19/20 (95)	23/34 (68)
T3	3/24 (12.5)	13/16 (81)	16/40 (40)
T4	0/12 (0)	1/4 (25)	1/16 (6)
Total	10/58 (17)	52/60 (87)	62/118 (53)

Survival

Survival was directly related to the stage of disease on presentation (Fig. 2). Patients with stage I disease had a 5-year survival rate of 16/20 (80%), patients with stage II disease 24/34 (71%), patients with stage III disease 17/38 (45%), and patients with stage IV disease 5/26 (20%) 5-year survival rate ($p=0.001$). The overall 5-year survival rate for all clinical stages was 62/118 (53%). There was a clear dichotomy between patients with stage I-II disease and patients with stage III-IV disease ($p=0.001$). In accordance with this dichotomy between stage groups differing in N (node) classification, patients who were without clinically palpable regional metastases (87% 5-year survival rate) did better than patients who presented with regional metastases (17% 5-year survival rate, $p=0.003$). Classifying patients according to T status also resulted in prognostically different groups ($p=0.001$). Patients with T1 tumors showed 79% 5-year survival rate compared with only 6% for patients with T4 tumors (Table 3).

The survival rate was correlated with the treatment (Fig. 3). Patients treated with surgery alone had the 5-year survival rate of 35/57 (62%). For the patients who received radiotherapy after surgery, the 5-year survival rate was 13/17 (81%). They did better than patients treated with radiotherapy alone, who had the 5-year survival rate of 14/45 (31%) ($p=0.0001$).

The 5-year survival rate according to the anatomic site was as follows: floor of the mouth 19/40 (47.5%), tongue 16/27 (59%), lower alveolar ridge 10/23 (43%), upper alveolar ridge 6/10 (60%), gingiva 3/7 (43%), buccal mucosa 4/6 (67%), and the palate in 4/5 (80%).

Discussion

The results of this study compare favorably with the overall statistics for oral carcinoma in age, sex distribution, and histopathological findings (11-13).

This disease is most prevalent in men over the age of 45 (13-15), with the average age at diagnosis of approximately 60 years (16). Our study reaffirmed that oral cancer is a disease that mainly affects the older population. However, highest prevalence in patients in their sixth and seventh decade is in contrast to other reports (14,16,17).

The men:women ratio in this study was 3.1:1, which is higher than the ratio reported from other countries: 1.7:1 in England and Wales (14), 1.8:1 in New Zealand (17), and 2:1 in the USA (16). The man to woman ratio

varies from site to site in the oral cavity (18), as we observed in our study.

The most common histologic diagnosis of oral cancer is squamous cell carcinoma, followed by sarcoma (16,19,20). The present study also showed a significant relationship between age and histological diagnosis. These findings are in agreement with those of Pindporg (20), who reported that sarcoma occurs more frequently in younger age group than squamous cell carcinoma.

There is almost universal agreement that carcinoma of the oral cavity is in some way related to the use of tobacco in some form and to the consumption of alcohol (16,21). In this series a high percent of our patients were smokers.

The majority of oral cancers involve the tongue and floor of the mouth (22,23). Hindle et Nally (14) showed that tongue was the commonest site for oral cancer, whereas our study showed that the floor of the mouth was the most frequent site in Jordanian patients, similar to the data from Scotland (21).

The incidence of cervical lymph node metastases at the time of initial treatment varies from 35% (5) to 63% (24). In this context our findings are close to those reported by Khafif et al (8), but lower to those of Montana et al (25), and Correa et al (24) who reported the incidence of 62% and 63%, respectively. McGavran and coworkers (26) found that lymph node metastases occurred more frequently in patients with poorly differentiated carcinoma. In contrast, Rammler and colleagues (27) failed to demonstrate any correlation between the histological grade and lymph node metastasis. In our series, the incidence of lymph node metastases in well-differentiated carcinoma was significantly lower than that of moderately and poorly differentiated carcinoma.

The survival period and cure rate are generally reduced when regional lymph node metastases are present (8,25,28). The prognosis for patients with oral cancer in this study was related to the size of the tumor and presence or absence of cervical nodal disease. The majority of the T1 lesions were surgically excised, with a 5-year survival rate of 79%. Amagasa et al (29) reported a 100% 5-year survival rate for surgically excised T1 tumors, whereas Kanehira et al (30) reported a 75% 5-year survival rate for their T1 patients treated by low dose irradiation and an interstitial implant. Therefore, it would appear that T1 lesions may be adequately managed by surgery or radiotherapy. The 5-year survival rate for patients with a T2 tumor treated in this study was 68%. This is similar to the survival rate of 60% reported by Pukander et al (6), but Amagasa et al (29) claimed a 5-year survival rate of 88.9% in Japanese patients. This would suggest that surgery or radiotherapy would again be equally effective in the management of these tumors. However, in our study, the 5-year survival rates were 62% for surgery and 31% for radiotherapy, although this was not statically significant (p=0.123). T1 tumors showed the lowest incidence of nodal disease in this study, with only 29% developing lymph node metastases. However 45% of T2 lesions, 60% of T3 lesions, and 75% of T4 lesions developed nodal disease. These figures would suggest that for all T3 and T4 lesions an elective neck dissection should be performed as a part of the initial treatment. A poor prognosis is indicated by the development of nodal disease at any stage in the treatment of oral cancer. Pukander et al (6) reported for the group of T1 and T2 lesions to have a 58.5% 5-year survival rate for N0 patients compared with 15.1% for those with nodal disease, Matiakin (31) reported similar, 65.8% 5-year survival rate in the N0 group and 15% in patients with regional metastases. Mitchell and Crighton (32) reported 90% 5-year survival rate in N0 group and 33% in the patients with regional metastases. In this study, patients with T1 or T2 lesions had a 95% 5-year survival rate if they belonged to the N0 group but only 32% when nodal disease was present. These figures would seem to show an improved survival. Cunningham et al (7) supported the concept of an elective neck dissection in patients with stage I and II oral carcinomas, quoting a 3-year survival rate of 88% in patients who underwent elective neck dissection compared with 56% for those who underwent salvage surgery following neck nodes metastases. However Khafif et al (8) found little difference in disease free survival rate for patients treated by elective radical neck dissection compared with delayed radical neck dissection after the clinical appearance of nodes.

Patients survival rates for oral cancer vary, depending on several factors, including the stage of the lesion, lymph node involvement (33), site of primary tumor, histological differentiation of malignancy, and patient's general health and habits (16,21). The findings of this study are consistent with a report (5) that revealed association between the site of oral cancer, patient's characteristics, and diagnostic patterns.

The survival rate, based on clinical staging in this series, closely corresponded with those reported by other authors (34,35). The 5-year survival rates in our series were higher than those reported by Correa and colleagues (24). The overall 5-year survival rates in our series for all clinical stages of disease were 53%, which exceeds that of several large series in the literature (17,27,36). The overall 5-year survival ranged from 25% (15) to 66% (36,37).

The modes of treatment of oral cancer are either by surgical excision (38), with or without a complete or partial neck dissection (39), presurgical or postsurgical radiation (40), radiation alone, or by a combination of these procedures (41). The results obtained by treatment modalities in this series compare favorably with those reported in other studies (25,35,36).

The results of this study indicate that T1 tumors of the oral cavity, if excised with an adequate margin of normal tissue, have good prognosis.

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