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Management of oral cancer: a clinical retrospective study of our experience list of authors

Abstract

Purpose: Treatment of the oral cancer consisted of a multiple modality therapy, however; the final outcome still poor. The aim of the current retrospective study is to assess survival outcomes with different Multidisciplinary strategies management of oral squamous cell carcinoma and to obtain valid criteria for therapeutic decision-making.

Patients and methods: patients with oral squamous cell carcinoma from 2005 to 2010 were enrolled in our study. The patients were treated by the same team and grouped according to the treatment strategy. Group A: the patients were treated by surgical excision, management of neck, postoperative radiotherapy. While in Group B: the patients were treated by surgical excision, management of neck, postoperative chemo-radiotherapy. Data collection: Demographic (age, sex, site & Side), treatment modality, and survival data was obtained.

Results: A total 88 patients were enrolled in our study. Disease specific survival rate (mean) in group A was 2.1 y and 3.8 y in group B. disease free survival (mean) was 1.7 y in group A and 2.3 in group B. Metastases free survival (mean) was 1.6 y in group A and 2.7 in group B. recurrence rate of group A was 35% while in group B 20%.

Conclusion: Adjuvant treatment modalities should be applied and implemented in cases with unclear margins and lymphatic spread. Postoperative adjuvant chemo-radiotherapy shows better performance with improves survival outcomes in oral cancer. Neck dissection associated with better survival and recurrence rates.

Keywords: oral cancer, anesthetic management, surgical excision, reconstruction, management of neck, postoperative chemo-radiotherapy

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Abbreviations: SCCs, squamous cell carcinomas; OSCC, oral squamous cell carcinoma; TNM, tumor, node and metastasis; CRT, chemo-radiotherapy; RT, radiotherapy; SD, mean; MACH-NC, meta-analysis of chemotherapy on head and neck cancer; cN0, clinical proven metastases; Gy, grey

Introduction

Oral cancer located in the mouth, tongue or oropharynx is a significant health problem throughout the world. It's the eight most common cancers worldwide with 300.000 new cases reported annually.[1] The overall five-year-survival rate for patients with oral cancer stagnated for the last 20 years.[2]

Squamous cell carcinomas (SCCs) of the lip and oral cavity comprise 90-95% of all oral malignancies. Hidden regional metastasis in oral squamous cell carcinoma (OSCC) is prevalent in at least 30% of cases.[3]

Five year survival rates for early stage localized disease are over 80% but this drops to 40% where disease has spread to the neck and to below 20% for distant metastatic disease. Early intervention is appropriate. Factors affecting the prognosis of oral cancer are based on tumor, node and metastasis (TNM) classification which stages the patient according to the size of the primary tumor and the presence of loco-regional and distant metastases. Additional prognostic histopathological information includes tumor depth, grade and surgical margin status, as well as cohesiveness (pattern of invasion) and the presence of peri neural or lympho vascular invasion.[4]

Traditional treatment for head and neck cancer comprises surgery and radiotherapy. Surgery remains the mainstream treatment for the management of oral cancer because radical radiotherapy is associated with substantial local side effects such as xerostomia whilst the risk of osteoradio necrosis in tumors close to the mandible cannot be underestimated. However, as with the treatment of most malignancies, there has been a shift towards increased use of concurrent chemo-radiotherapy as part of an organ preservation strategy. This has altered the frontline treatment for most of the anatomical sites of the head and neck including the oropharynx.[4]

The basis of adding concurrent chemotherapy to adjuvant RT is that advanced tumors respond better to concurrent CRT rather than to RT alone.[5–9]

The outcomes of the treatment affect not only the aesthetics but may also compromise the functions. According to literature surgical management has better prognosis.[10–12]

The treatment options expanded in 2004 when two international trials showed the addition of postoperative chemotherapy to radiation improved outcomes. These trials were, however not oral cavity site specific. The aim of the current study was to give description of our experience with Multidisciplinary strategy based therapy of oral

cancer in our hospitals. The specific aim was to determine if the addition of postoperative chemotherapy improves survival compared to other treatment regimens.

Patients and methods

The institutional ethics committee of the host institution reviewed and approved the study. Patients with oral cancer from 2005 to 2010 were enrolled in our study. Two Multidisciplinary strategies were used. First Multidisciplinary strategy consisted of, surgical excision, management of neck, postoperative radiotherapy (RT). Second Multidisciplinary strategy consisted of, surgical excision, management of neck, postoperative chemo-radiotherapy (CRT). The patients were treated by the same team and grouped according to the treatment strategy.

Group A: The patients were treated by surgical excision, management of neck, followed by adjuvant RT within 6-8 weeks post-operatively.

Group B: The patients were treated by surgical excision, management of neck, post-operative adjuvant CRT within 6-8 weeks of their operation.

Inclusion criteria: Patients with oral cancer proved by Biopsy. Patients without previous history of any treatment on oral cancer.

Exclusion criteria: Patients treated by another surgical team, patients with oral cancer with previous treatment. Patients lost during postoperative radiotherapy or chemo radiotherapy, or lost during the follow-up period. Refusal of prescribed treatment and treatment with palliative intent. Cases of oral cancer included all cancers of the oral cavity (i.e., those found on the lips, tongue, buccal mucosa, retro molar region, palate, and other areas of the oral cavity). Cases of tonsillar carcinomas and pharyngeal cancers were not included. Surgical resections were consisted of tumor ablation with variations of primary closure, loco-regional or free tissue transfer reconstruction, and unilateral or bilateral neck dissection.

Data collection

Demographic (age, sex, site), treatment modality, and survival data was obtained from patients diagnosed with oral cancer from 2005-2010 in the Al-Azhar University hospitals. The medical records of the patients were reviewed to determine the TNM classification and staging, age, gender, race, occupation, symptoms, habits (tobacco and alcohol consumption), and site of the primary tumor. However, it was not possible to analyze alcohol and tobacco use in terms of quantity, quality and frequency of use.

The primary outcome measure was set as overall survival rate (the time from the first date of treatment to the date of death or last known date the patient was alive). Secondary outcomes included disease-specific, disease-free, and metastases-free survival as per treatment group. Disease-specific survival was defined as the time from the first day of treatment to death as a result of the disease. Death caused by the primary cancer was therefore considered to be disease specific death. Disease-free survival was calculated from the first day of treatment to the date of disease recurrence. Thus, if patients died without any evidence of disease, they were considered disease free at the time of death. Metastasis-free survival was defined as the time from the first day of treatment to the date of distant metastasis detection.

Statistical analysis

The data were analyzed with the help of Instat (Graph Pad, CA, and USA) statistical software. Mean (SD), medians, and percentages were calculated for the summarized data. Probabilities of <0.05 were accepted as significant.

Results

A total 88 patients were enrolled in our study. Demographic distribution was as the following, 38 patients with OSCC of tongue, 8 patient with SCC of the floor of the mouth, 26 patients with OSCC of alveolar gingiva, 8 patients with SCC of the maxillary tuberoses, 6 patients with SCC of the retro molar area and one patient with SCC of the buccal mucosa which were confirmed by the histopathological examination. Ultrasonography-guided cytology, CT &/or MRI was used for evaluation of the lymph-node status at the time of diagnosis. The follow-up period range from 1.5 year to 5 years with average of 3.8 years.

Group A: A total of 43 patients were enrolled in the group. 32 patients (74.5%) were male and 11 patients (25.5%) were female. The patient's age ranged from 39 to 71 years (mean +SD= 53.98 ± 6.9).

Group B: A total of 45 patients were enrolled in the group. 30 patients (66.7%) were male and 15 patients (33.3%) were female. The patients age ranged from 42 to 65 years (mean +SD= 55.71 ± 5.41).

According to TNM system, 4 patients in group A and 3 in group B were stage I, 9 patients in group A and13 in group B were stage II, 7 patients in group A and 9 in group B were stage III, 11 patients in group A and 7 in group B were stage IVA, 8 patients in group A and 5 in group B were stage IVB, and 4 patients in group A and 8 in group B were stage IVC. Statistical analysis showed non-significant difference between both of the study groups regarding TNM system (P-Value = 0.65).

Group A: Histopathologically; Well-differentiated OSCC accounted for 65% the samples examined (28 patients), moderately differentiated 28% (12 patients) and poorly differentiated OSCC 7% (3 patients). Among the cases of group a patients, 23 patients (53%) unilateral had neck dissections and 11 patients (25.5%) bilateral had neck dissections performed? Of which, 71% were positive and 29% were negative. 9 patients (21%) had no neck management.

Group B: Well-differentiated OSCC accounted for 69% the samples examined (31patients), moderately differentiated 22% (10 patients) and poorly differentiated OSCC 9% (4 patients). Among the cases of group A patients, 21 patients (47%) unilateral had neck dissections, and13patients (29%) bilateral had neck dissections performed. Of which, 70.6% were positive and 29.4% were negative. While 11 patients (24%) had no neck management.

Statistical analysis between both of the study group showed non-significant differences regarding the histopathological classification of the OSCC and the number of the patient treated by the neck dissection (P-value = 0.89 & 0.66 alternatively).

Disease specific survival rate (mean) in group A was 2.1y and 3.8y in group B. disease free survival (mean) was 1.7y in group A and 2.3 in group B. Metastases free survival (mean) was 1.6 y in group A and 2.7 in group B. Recurrence rate of group A was 35% while in

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group B 20%. Group B showed highly significant better outcome in comparison with group A (P-value <0.0001).

Moreover, group B showed significant better outcome in comparison with group A in relation to the recurrence. In terms of, group B showed less number of recurrences (9 patients) than group A (15 patients) (P-value=0.0125) (Table 1).

In our study, the patients treated with neck dissection showed better overall survival rate and less recurrence rate in relation to patients without neck dissection.

Table 1 Characteristic features of the tumor and treatment by the groups

Variable	Group A	Group B	p-value
Site of the OSCC			
Tongue	16(37.2%)	22(48.9%)	
Floor of the mouth	5(11.6%)	3(6.7%)	
Alveolar mucosa	11(25.5%)	15(33.3%)	0.296
Maxillary tuberosity	5(11.6%)	3(6.7%)	
Retromolar area	5(11.6%)	2(4.4%)	
Buccal mucosa	1(2.3%)	0(0%)	
TNM Stages			
Stage I	4(9.3%)	3(6.7%)	
Stage II	9(21%)	13(29%)	
Stage III	7(16.3%)	9(20%)	0.65
Stage IVA	11(25.5%)	7(15.5%)	
Stage IVB	8(18.6%)	5(11%)	
Stage IVC	4(9.3%)	8(17.8%)	
Histopathological Study			
Well differentiated OSCC	28(65%)	31(69%)	
Moderate differentiated OSCC	12(28%)	10(22%)	0.89
Poorly differentiated OSCC	3(7%)	4(9%)	
Neck Dissection			
Unilateral	23(53%)	21(47%)	0.66
Bilateral	11(25.5%)	13(29%)	
No neck dissection	9(21%)	11(24%)	
Positive Neck	17(71%)	24(70.6%)	0.62
Negative Neck	7(29%)	10(29.4%)	
Overall Survival Rate (mean)	3.5 Y	4.1 Y	<0.0001
Disease-Specific Survival (mean)	2.1 Y	3.8 Y	<0.0001
Disease-Free Survival (mean)	1.7 Y	2.3 Y	<0.0001
Metastases-Free Survival (mean)	1.6Y	2.7Y	<0.0001
Recurrence (No of patients)	15(35%)	9 (20%)	0.0125

Discussion

In treating OCC, the goals are provided for best functional results and minimal risk of serious complications. Treatment advances are partly responsible for improvement in survival. Therefore a bigger number of survivors run into long-term consequences of cancer treatment. Nowadays managing and preventing squeal after surgery, radiation therapy with or without chemotherapy, are paramount. Treatment complications depend on specific site and stage of primary tumor, as well as treatment technique. Palliative care is offered to patients who either have incurable disease, or are medically unfit to be subjected to potentially curative treatment. Pain relief, chemotherapy and sometimes radiotherapy or surgery may be useful for these patients, who will be assessed and managed by a palliative care team.[13]

Currently, surgery and radiotherapy are the two treatment options available with curative potential, and may be used alone or in combination. Surgery will involve complete excision of the tumor along with a surrounding margin of normal tissue, and, where indicated, some or all of the ipsilateral and occasionally contra lateral cervical lymph nodes.

Radical excision in the surgical treatment of neoplasm considered as the most important principle in oncologic surgery. The completeness of removal clearly requires a cuff of healthy tissue around the neoplastic tissue, whose dimensions generally vary depending on several factors such as the district or type of tumor. These basic principles also apply oral squamous cell carcinoma (OSCC). Local recurrence in head and neck malignant neoplasm scan is influenced by the involvement of resection margins.[14–16]

In our study, surgical excision was aimed to complete removal of the primary tumor with adequate safety margin to provide a free surgical margin. This followed by reconstruction of the surgical defect by local flaps. Radiotherapy preferentially kills dividing cells, and for those patients treated by radiotherapy, the aim is to kill every cancer cell. Both the primary tumor and the regional lymph nodes can be included in the treatment field**.** A full course of radiotherapy is typically expressed in the usual units as being about 60 Grey (Gy) (1Gy=100rads), which is fractionated into 30daily doses of 2Gy each over six weeks. Radiotherapy has the advantage of organ preservation and is currently the primary modality used to treat some cases of tonsillar, soft palate, and pharyngeal SCC. However, significant and potentially disabling side effects may follow the use of radiotherapy in the head and neck region, including mucositis, xerostomia and osteoradio necrosis.[17]

The rational of adding concurrent chemotherapy to adjuvant RT is that advanced tumors respond better to concurrent CRT rather than to RT alone. Chemotherapy can sensitize tumors to radiotherapy by inhibiting tumor repopulation, preferentially killing hypoxic cells, inhibiting the repair of sub lethal radiation damage, sterilizing micro metastatic disease outside of the radiation fields and decreasing the tumor mass, which leads to improved blood supply and re oxygenation. While, Fractionated radiotherapy, in turn, may sensitize tumors to chemotherapy by inhibiting the repair of drug-induced damage and by decreasing the size of the tumor mass, leading to improved blood supply and enhanced drug delivery.[5–9]

The Meta-Analysis of Chemotherapy on Head and Neck Cancer (MACH-NC) demonstrated that adding chemotherapy to radiotherapy in both definitive and adjuvant postoperative settings resulted in a 12% reduction in the risk of death from SCCHN, corresponding to an absolute improvement of 4% in 5 years survival. A recent update

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has shown a 19% reduction in the risk of death and an overall 8% improvement in 5-year survival compared with treatment with RT alone. These findings were a result of the use of concurrent chemotherapy.[18]

Currently, three multimodality treatment approaches are used. The first approach is surgery followed by adjuvant concurrent chemo radiotherapy, which enables precise pathologic staging and identification of high-risk features that influence the choice of adjuvant treatment. This approach can have limitations, such as poor organ preservation, depending on the anatomic location (e.g., larynx) and the majority of loco regionally advanced tumors are unresectable, especially if organ preservation is the goal.

The second approach is definitive concurrent chemo radiotherapy with surgery as an optional salvage or completion treatment. Although no pathologic information is obtained with this approach, it has the advantage of improved organ preservation. This benefit is most clearly established for laryngeal cancer but is increasingly recognized for other anatomic locations; however, this approach remains controversial for oral cavity tumors.

The third approach is the use of induction chemotherapy followed by definitive local therapy. Advantages include the potential to decrease the risk of distant failure and a rapid reduction in tumor bulk in responders. A response to induction appears to predict responsiveness to chemo radiotherapy. Nonetheless, this can result in prolonged treatment and additional chemotherapy-related toxic effects from systemic doses. This approach remains controversial, but data from recent clinical trials seem to support its use. The role of this approach in the context of concomitant chemo radiotherapy is currently being investigated in several large, multicenter, randomized trials.[19]

In our study; the addition of adjuvant chemotherapy allowed for significantly increased rates of local control, disease-specific survival, and overall survival, without high incidences of late adverse effects. Moreover, the addition of the adjuvant chemotherapy associated with less recurrence rate.

When nodal metastases are present, nobody can deny the important effect of therapeutic neck dissection in the prognosis of head and neck cancer patients. However, Management of the cN0 in oral cancer has been a matter of discussion. Even in the absence of clinical proven metastases (cN0), there is generally a high rate of occult metastases, which strongly depends on the localization as well as the extent of the primary tumor. Management of the cN0 neck is therefore considered crucial.[20]

Controversies in the treatment of negative neck in oral cancer arise due to different question that facing the surgeons treating such cases, these issues include the following: What is the optimal pre-treatment modality for diagnosing the cervical lymph nodes metastasis? Should a patient with a cN0 neck treated now or wait and see? Should the patient receive an elective neck dissection or should they be treated with elective neck radiation? Are there prognostic factors that can guide us in our decisions in treating the neck? Which modality should be used for treating the neck? What are the future trends? The answer is continuously debated, but surgeons believe management decisions should rely on the incidence of occult metastatic disease for a given tumor and its sub site.[20]

In our study; the overall survival and recurrence rate was significantly better in patients with neck management. Patients without neck dissection showed higher rate of recurrence and less metastases-free survival rate.

One of the limitations of our study is the small number of the patients. However, selection of the patients treated by the same surgical team was aimed to block one of the variables in the current study.

Conclusion

Adjuvant treatment modalities should be applied and implemented in cases with unclear margins and lymphatic spread. Postoperative adjuvant chemo-radiotherapy shows better performance with improves survival outcomes in oral cancer. Neck dissection associated with better survival and recurrence rates.

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Conflicts of interest

The author declares there are no conflicts of interest.

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