Analysis of Survival Rates Following Primary Surgery of 178 Consecutive Patients with Oral Cancer in a Large District General Hospital

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Received: 20 January 2016 / Accepted: 17 June 2016 / Published online: 8 July 2016
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Abstract

Purpose The aim of this study is to present the survival rates in patients treated for oral cancer with primary surgery in a large district general hospital. We discuss the influence of the most significant prognostic factors on survival and compare our results with larger centres specializing in the management of oral cancer.

Methods All patients diagnosed with oral cancer from 1995 to 2006 and were treated in the Department had their details entered prospectively onto a computerized database. Demographic details of patients, type of treatment, pathological stage of tumor (TNM), local and regional recurrence rate, overall survival, disease specific survival and incidence of involved margins were recorded and calculated.

Results Of the 178 patients, 96 (54 %) were alive and free of oral cancer 5 years after surgery. Forty-four patients died of oral cancer (24.7 %) but 38 (21.3 %) died of other causes. The overall survival rate after primary surgery in relation to stage was: I 84 %, II 71 %, III 36 % and IV 28 %.

Discussion As almost half of our patients presented with advanced cancer and had discouraging survival rates, we emphasize the need for early recognition of the disease. Advanced disease signifies difficulty in obtaining clear margins which actually indicates a higher recurrence rate. 25 % of our patients died of oral cancer within 5 years of surgery which highlights the poor prognosis that recurrence carries after treatment. Effective educational campaign

with purpose to raise oral cancer awareness and earlier referral may result in improvement of survival.

Keywords Oral cancer · Survival rates · Recurrence · Surgical margins

Introduction

In spite of the advances in the management of oral cancer over the last 20 years the prognosis has not changed significantly and curability depends mainly on the stage of disease [1]. The presence of cervical lymph node metastases remains a predictive factor of paramount importance for regional recurrence and overall survival in patients treated for oral squamous cell carcinoma, with extra-capsular spread remaining a powerful indicator of tumour aggression [2–6]. The status of the resection margins has been well reported to influence the survival rate of head and neck cancer patients [7–10]. Vascular, perineural and bony invasion represent other prognostic factors that influence survival after surgical treatment of cancer of the oral cavity [11].

A slight decrease in the mortality rates of oral cancer following surgery has been recorded over the last two decades. However, the reported results demonstrate heterogeneity with the overall 5-year survival rate to range from 41 to 79.5 % [12]. More recently, tumor thickness has been suggested to signify another important prognostic factor associated with overall survival [13].

In this study, the senior author employed a consistent protocol in the management of patients presenting with histologically proven squamous cell carcinoma in which surgery was offered as the primary treatment modality with the majority of patients undergoing wide resection of the

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primary tumour and simultaneous selective neck dissection (SND). The oncological defects were mainly reconstructed by vascularized free tissue transfer techniques.

The aim of this study is to present the overall and disease specific 5 year survival rates in patients treated for oral cancer with primary surgery in a 12-year period. In addition, the influence of the most significant prognostic factors on survival is discussed and results compared with larger centers specializing in the management of oral cancer.

Patients and Methods

All patients diagnosed with oral squamous cell carcinoma from 1995 to 2006 who were treated only by the senior surgeon of the service had their details entered prospectively onto a computerized database. The data was meticulously collected by the senior surgeon of the Unit who also had responsibility for tumor resection and overall patient care. The data was then analysed retrospectively. The follow-up ranged from 5 to 11 years after initial treatment and consisted of monthly clinical visits in the first year, bimonthly in the second year, every 3 months in the third year, every 4 months in the fourth year, twice per year in the fifth year and every year onwards. The study received approval by the Research and Development Office of the hospital.

The preferred method of treatment consisted of elective tracheostomy for the early postoperative period for cases where significant oedema was expected, radical resection of the primary tumor aiming for a 1 cm margin when possible, preservation of the mandibular continuity by means of marginal mandibulectomy when suitable, low threshold for pull through or lip-split and mandibulotomy techniques for access when needed. Supraomohyoid (SOHND) neck dissection (levels I, II, III) were used routinely for patients with N0 status especially where tumour thickness was greater than 4 mm but patients with SCC of the oral tongue underwent extended supra-omohyoid neck dissection (I–IV). Incisional biopsy was used to judge the tumour thickness preoperatively.

N1 stage disease was also treated with a SOHND. A modified radical neck dissection was performed in patients with N2/N3 disease. Assessment of disease is based on clinical examination and modern imaging modalities (CT&MRI head & neck). This treatment protocol is in accordance with the head and neck cancer multidisciplinary team guidelines in the U.K. All patients were presented and discussed at a multidisciplinary tumour board comprising surgeons, radiation oncologists, medical oncologists, and other allied health care professionals dedicated to the overall treatment and prevention of head

and neck cancer. Primary reconstruction with free tissue transfer was performed considering the type of defect and the performance status of patients. Routine intra-operative frozen sections of the resection margins and an effort to deliver the specimen in continuity are also preferred techniques by the senior surgeon.

The surgical specimens were pinned out on a cork board before fixation in 10 % buffered formalin. The specimens were examined in the laboratory one to two days after fixation. All histologically assessed sections were stained with haematoxylin and eosin. A margin positive for presence of invasive squamous cell carcinoma was considered as involved. A margin with carcinoma in situ was considered as involved however margins with dysplasia were not considered involved. Close margins (<5 mm) were considered as uninvolved. Patients were offered post-operative adjuvant treatment—radiotherapy dependent on the histological outcome. Factors influencing post operative therapy included involved margins, bone, perineural and/or vascular invasion at the primary site. In the neck dissection analysis, multiple level nodal involvement and extracapsular spread were considered indicators for adjuvant therapy.

Demographic details of patients, anatomical site, treatment modality, pathological stage of tumor (TNM), local and regional recurrence rate, overall and disease specific 5 year survival, and incidence of involved margins were recorded and calculated. Descriptive statistics and statistical analysis for significance were performed with the SPSS version 17.0 software (Chicago, IL). *P* values <0.05 were regarded to be significant.

Results

During the period studied, 178 patients were prospectively enlisted for this study. One hundred and seven were males (60 %) and 71 females (40 %). The average number of newly diagnosed patients undergoing surgery by the senior author per year was 15 (range 9–32). The age groups and distribution of patients with respect to age is shown in Fig. 1.

Fig. 1 Distribution of patients with respect to age

Table 1 Anatomical sites of tumours (%)

Lower lip	20 (11.2 %)
Tongue	52 (29.2 %)
Floor of mouth	46 (25.8 %)
Palate	17 (9.5 %)
Buccal mucosa	13 (7.3 %)
Retromolar region	10 (5.6 %)
Mandibular/alveolus	13 (7.3 %)
Oropharynx/tonsil	7 (4 %)
Total	178

The anatomical site of the tumours is shown in Table 1. The mean age was 56.3 years and the most frequent age group was the 70–79 years one.

One hundred and seventy eight patients received primary surgery for treatment of their oral cancer with curative intention. Of these, 96 (54 %) were alive and free of oral cancer 5 years after surgery. Forty-four patients died

of oral cancer (24.7 %) and 38 (21.3 %) died of other causes in the same period of time (Fig. 2). The disease specific survival rate was 75.3 %. Table 2 compares survival rates with other centres.

One hundred and seven male patients received primary surgery with curative intent. Of these patients, 73 survived and 34 died. The male survival rate 5 years after surgery was 68 %. Seventy one female patients were submitted to primary surgery. Of these patients, 47 were alive and 24 died 5 years after surgery. The female survival rate after surgery was 66 % (Fig. 3). No statistically significant differences were observed in relation to sex in postoperative survival rates.

After histological analysis of the specimens, the tumor resection margin was involved in 6 cases and all these cases recurred. Recurrence occurred in 12 out of 110 patients with free surgical margins (>0.5 cm) and in 9 out of 62 patients with close surgical margin (<0.5 cm), the difference being not statistically significant (Chi square, p value 0.48). Table 3 shows the recurrence rate in relation

Fig. 2 Postoperative survival rates for male and female patients at 5 years post op **Table 2** Survival data for oral cancer in different centres

Author	Year	Institute	No patients	% Patients treated with surgery	% DSS	% OS
Rogers	2008	Liverpool, UK	489	100	74	56
Kessler	2008	Erlangen, Germany	128	100	83	69
Koo	2006	Seoul, South Korea	127	100	76	71
Aksu	2006	Istanbul, Turkey	61	100	49	46
Turner	1996	Manchester, UK	333	0	55	43
Jones	1993	Liverpool, UK	126	0	64	37
Tytor	1990	Bergen, Norway	176	76	53	28
Loree	1990	Memorial, USA	398	100	–	57
Smith (Current)	2014	Northampton, UK	178	88	75	54

Fig. 3 Overall and disease specific survival at 5 years for 178 patients after primary surgery

Table 3 Recurrence rate in relation to incidence of involved margins

	Smith 2014 (%)	Eckardt 2004 (%)	Woolgar 1999 (%)	Rogers 2008 (%)
Involved margins	3	12.9	5	16.7
Recurrence	15	19.8	19	21

Table 4 Incidence of patients who received adjuvant radiotherapy in relation to the stage of the disease

Stage	
I	16 %
II	31 %
III	41 %
IV	56 %

to the incidence of involved margins in this unit and comparing the results with two large head and neck cancer centres.

The distribution of patients according to stage was: 25 % in stage I, 24 % in stage II, 9 % in stage III, 42 % in stage IV. The overall 5 year survival rate after primary surgery in relation to stage was: I 84 %, II 71 %, III 36 % and IV 28 %, respectively. pN0 was identified in 42 (24 %) of the patients with an overall survival of 77 % whereas pN+ was identified in 136 (76 %) patients with an overall survival of 32 %.

Post operative radiotherapy was given in 16 % of Stage I disease, 31 % of Stage II disease, 41 % of Stage III disease and 56 % of Stage IV disease (Table 4). 32 % of

advanced stage patients were deemed not sufficiently fit to withstand the intensity of radiotherapy with curative intent (radical) and received palliative treatment. 12 % declined or interrupted their treatment. These patients did not affect the recurrence rate. The disease specific survival rate following surgery according to stage is outlined in Table 5 and compared to two other studies published from large head and neck cancer centres.

Discussion

Acquiring and collecting accurate data on survival of patients with oral cancer is a challenge and health authorities repeatedly maintain that such data can only be meaningful when collected and analysed in large centralized units. This study including its outcomes challenges this concept in as much as diligent data collection coupled with a reasonable throughput of surgical activity is capable of achieving outcomes comparable to larger centres.

Although cure and survival are of paramount importance for patients, assessing surgical outcomes based entirely on the overall survival hides several pitfalls. Oral cancer patients are frequently elderly and the majority has co-morbidities which make them susceptible to other diseases and premature death, as demonstrated in this study. Nearly as many patients die from other diseases (21.3 %) as from oral cancer (24.7 %) (Fig. 2). Many of our patients are heavy smokers and abuse alcohol, reflected in the prevalent anatomical sites in the UK of oral tongue and floor of mouth. These facts influence the reported success of treatment as the survival of these patients can be less than 5 years after surgery. Therefore, disease specific survival is a much more accurate indicator of the surgical outcome but at the same time more difficult to record since it requires confirmation of absence of oral cancer at the time of death [4].

Data from the present study is valid as the migration of patients treated in this Unit and analyzed is minimal. It reports the disease specific survival following surgery at 75 %. Advanced initial stage, notably a prevalence of Stage IV disease and the presence of pathological nodal metastases are the two most important prognostic factors influencing outcome. These conclusions are in agreement with other studies from centers internationally known as specialized in oral cancer surgical treatment [14, 15].

Table 5 Overall survival in relation to stage of disease

	Stage I (%)	Stage II (%)	Stage III (%)	Stage IV (%)
Smith (current)	84	71	36	28
Rogers	76	68	65	37
Garzino	80	78	48	42

Despite the difficulties in comparing outcomes from different units because of the differences in the studied populations and the variability of treatment, an attempt at comparative data is made with published literature from other centers (Table 2). It is interesting to see that the reported survival rates of the current study arising from a smaller unit are close to outcomes from larger volume centres.

A significant prognostic factor for patients treated for oral cancer remains the presence of nodal metastases [2–4]. In the present study, the prognosis in N0 patients (77 %) was twice as high as for those with one or more cervical lymph node metastasis (32 %). This well-established relationship between metastasis in the lymph nodes of the neck and reduced survival rates has been confirmed by many authors who have all reported similar decreases in survival due to the metastatic load of the regional lymph nodes [4, 12, 14–18].

The status of the resection margin is of paramount importance in survival of patients treated surgically for oral cancer and this has been well reported [7–10]. Local recurrence has been identified as the major cause of death in oral cancer patients after radical surgery [14, 19]. In their study, Woolgar et al. [14] reported that 50 % of their patients presented with stage III/IV disease and this is in accordance with our results (49 %). Obtaining clear margins in advanced disease is obviously more technically demanding especially for tumors located in the posterior third of the oral cavity. However, clearance of the primary tumour can be achieved by surgeons working in centres where the throughput is lower than larger centralized units. Nevertheless, early recognition is of great significance in an effort to achieve clear margins which emphatically affects survival.

As local recurrence represents one of the major parameters to affect survival adversely, minimizing the incidence of relapse should eventually lead to improved survival rates. Oral squamous cell carcinoma infiltrates local structures including blood and lymph vessels [20]. The presence of residual cancer cells in the postoperative surgical field can be attributed to these specific features of the tumour's biological behavior. Consequently, local recurrence develops as a result of incomplete tumor resection. Snow showed that involved resection margins is an important prognostic factor with respect to recurrence in oral cancer patients and this was later confirmed by Slootweg et al. [21, 22].

Several more recent studies have demonstrated the need for in-continuity resections with purpose to remove the lingual nodes and the lymphatic tracts between the primary site and the cervical lymph nodes [23–25]. There is suspicion and evidence to suggest that involvement of these intermediate nodes worsens prognosis [23, 26, 27]. These

tissues can be removed with preservation of the greater part of the mylohyoid and the digastric muscles thereby reducing the postoperative morbidity. Our findings indicate that a low incidence of involved margins (3 %) can lead to a similarly low recurrence rate (15 %) and subsequently to improved control of the disease (Table 3).

Despite the fact that malignant infiltration of the resection margin is thought to indicate the most relevant predictive factor for local recurrence [28, 29], obtaining clear margins does not preclude the possibility of a recurrent tumor. Interestingly, Brennan et al. [30] using molecular biology techniques of histopathological cancer-free resection margins, detected clonal populations of infiltrating p53 gene mutant cells in 52 % of the studied specimens. These evidence suggest that a clinical margin of 1 cm in oral cancer resection may not be adequate. Additionally, the routine use of intra-operative frozen sections of the resection margins is justified in light of these findings.

Conclusion

The results of the current study support the prognostic value of the staging system. As almost half of our patients present with advanced cancer and had discouraging survival rates in comparison to patients who present with early disease (Table 3), we cannot emphasize enough the critical need for early recognition of the disease. Advanced disease signifies increased difficulty in obtaining clear margins which actually indicates a higher recurrence rate. This study also revealed that 25 % of patients died of oral cancer within 5 years of surgery which highlights the poor prognosis that recurrence carries after surgical treatment. This is in agreement with the fact that more than 75 % of recurrent oral squamous cell carcinomas develop within 2 years after primary surgery [31–33]. As almost half of our patients presented with advanced cancer and had discouraging survival rates in comparison to patients who came to us early, we cannot emphasize enough the critical need for early recognition of the disease.

Compliance with Ethical Standards

Conflict of interest The authors of this paper have no conflict of interest.

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