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Significance of post-resection tissue shrinkage on surgical margins of oral squamous cell carcinoma

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ABSTRACT

Background: Resecting oral squamous cell carcinoma (SCC) with an appropriate margin of uninvolved tissue is critical in preventing local recurrence and in making decisions regarding postoperative radiation therapy. This task can be difficult due to the discrepancy between margins measured intraoperatively and those measured microscopically by the pathologist after specimen processing.
Material and methods: A total of 61 patients underwent resective surgery with curative intent for primary oral SCC were included in this study. All patients underwent resection of the tumor with a measured 1-cm margin. Specimens were then submitted for processing and reviewing, and histopathologic margins were measured. The closest histopathologic margin was compared with the in situ margin (1 cm) to determine the percentage discrepancy.
Results: The mean discrepancy between the in situ margins and the histopathological margins of all close and positive margins were 47.6% for the buccal mucosa (with a *P* value corresponding to 0.05 equaling 2.1), which is statistically significant, 4.8% for the floor of mouth, 9.5% for the mandibular alveolus, 4.8% for the retromolar trigon, and 33.3% for the tongue.
Conclusion: There is a significant difference among resection margins based on tumor anatomical location. Margins shrinkage after resection and processing should be considered at the time of the initial resection. Tumors located in the buccal mucosa show significantly greater discrepancies than tumors at other sites. These findings suggest that it is critical to consider the oral site when outlining margins to ensure adequacy of resection. Buccal SCC is an aggressive disease, and should be considered as an aggressive subsite within the oral cavity, requiring a radical and aggressive resective approach.

1. Introduction

Surgery is the most well-established mode of initial definitive treatment for a majority of oral cancers, and has been the accepted method of treatment for well over a century (Shah and Gil, 2009).

The surgeon's objective is, ideally, to eliminate disease by resecting as little tissue as possible and to obtain a margin clear of tumor. Margin status in oral squamous cell carcinoma (SCC) has been found to be an independent predictor for recurrence and patient survival (Yahalom et al., 2008).

One of the most important but difficult aspects of cancer surgery is ensuring complete removal of the tumor at the primary site. It has been shown that failure to achieve a clear surgical margin results in increased risk of local recurrence and a subsequent reduced chance of survival (Kurita et al., 2008).

Assessment of the resection margins forms an important part of the pathological examination of surgical specimens in patients undergoing surgery with curative intent for most forms of malignant disease, including oral SCC. Although the histopathologic status of the resection margins has long been used as a potential

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indicator of local recurrence and survival, there is still considerable uncertainty concerning many aspects of resection margins. including their nomenclature and definition, and the influence of anatomical and histological factors (Woolgar and Triantafyllou, 2005).

The optimal width of the surgical margin for oral cancer has always been an issue of debate. Microscopic tumor at the inked resection margin increases the chance of local recurrence by a factor of 2 or more in most series. The term "positive margin" should be reserved for patients with microscopic tumor at the inked resection margin (Nason et al., 2009).

There are 2 explanations for the positive margin phenomenon. The first is that microscopic tumor may extend beyond the clinically visible and palpable tumor. Resection of a 1-cm margin of clinically normal tissue around the tumor is carried out to achieve at least 5 mm of histopathologically normal tissue; however, this is not always sufficient. Finger extensions or islands of tumor may invade out of the main mass of tumor, resulting in a margin that is closer than anticipated. Alternatively, tissue retraction that occurs after resection and pathologic processing of the specimen may cause the margin of tissue to decrease in size. A combination of these phenomena may also occur (Cheng et al., 2008).

Boonstra et al. (1983) evaluated cervical tissue shrinkage by formaldehyde fixation, paraffin wax embedding, cutting, and mounting. They concluded that shrinkage did not differ significantly in the different directions and resulted in an average shrinkage of respectively 2.7% and 12.6% of the original dimensions. In the calculation of the total shrinkage, these alterations can be neglected, since the changes, although not consistent, are small. It follows that in morphometric studies, a total shrinkage of about 15% of the original dimensions has to be taken into consideration.

Chen et al. (2012) conducted a study to investigate whether formalin fixation is associated with the shrinkage of head and neck cancer specimens. They found that the average decreases in length, width, and depth after formalin fixation were 1.50 mm (4.40%), 1.52 mm (6.18%), and 0.67 mm (4.10%), respectively. There was no significant difference in the shrinkage percentages associated with gender, age, tumor site, tumor size, or histology.

The pathological margins are reported to be much smaller than the pre-resection margins; this is largely attributed to the margin shrinkage following resection, and less commonly to the presence of microscopic neoplastic foci beyond the palpable and visual margins. The problem of margin shrinkage has been dealt with at other sites, but has not been analyzed and quantified in oral cavity cancers (Mistry et al., 2005).

Cheng et al. (2008) found a significant difference between margins measured at the time of surgical resection of oral SCC and the margins measured after histopathologic review.

The aim of this prospective study was to evaluate the surgical resection of oral SCC and the possible difference and discrepancy between in situ margins (measured at the time of surgical resection) and post-resection margins at the time of pathological processing and interpretation.

2. Material and methods

This prospective study was performed in the Oral and Maxillofacial Surgery Department, Faculty of Oral and Dental Medicine, Cairo University, and the Surgical Oncology Department, Faculty of Medicine, Menofia University, between September 2006 and January 2014 after approval by the hospital's Ethics Committees. It involved surgical resection of primary oral SCC in 61 patients.

Following a thorough clinical examination and routine preoperative laboratory tests, a search of locoregional and distant metastases were done with computed tomography (CT), magnetic resonance imaging (MRI), bone scanning, and abdominal ultrasonography. Inclusion criteria included primary oral SSC with no previous treatment and good general condition allowing a major surgical procedure. Patients with locoregional recurrence or distant metastases were excluded from the study.

The studied groups were 61 patients: 39 males (63.9%) and 22 females (36.1%), with a male to female ratio 1.8:1. The age of the patients ranged from 35 to 69 years, with a mean of 51.6 ± 7.07 years. The tumor site was the tongue in 20 cases (32.8%), mucosa of alveolar margin of the mandible in 13 (21.3%), buccal mucosa in 15 (24.6%), retromolar in 6 (9.8%), floor of mouth in 3 (4.9%), and mucosa of alveolar margin of the maxilla in 4 (6.6%) (Table 1).

The borders of the tumor were determined by visual inspection and palpation and were then marked with marking ink. Adequate surgical margin of at least 10 mm from the tumor margin was marked circumferentially for subsequent resection using a metric ruler and/or caliper at 10 mm from the clinically detectable tumor, as illustrated in Fig. 1. These measurements were used to guide tissue resection. Care was taken to flatten the surrounding mucosa without stretching it. Two sterile black silk sutures were placed over the tumor margin and the proposed resection margin. The distance between the 2 sutures was measured using a measuring caliper and recorded as the in situ resection margin. The specimen was resected using electrocautery with 3-dimensional clearance, and carefully incorporating both the sutures in the resected specimen. After resection, the specimen was examined, and the distance was measured again and recorded (Mistry et al., 2005).

In cases in which the primary site was the buccal mucosa invading the buccinator muscle, with or without clinical palpable LN, the excision included the skin, buccinator muscle, and buccal fat pad, together with the marginal mandibular branch *en bloc* with radical neck dissection (Fig. 2).

Frozen section biopsy samples were taken intraoperatively to assess resection adequacy. In the case of positive margins of frozen section analysis, additional tissue was taken. However, this additional tissue was not included in the margin discrepancy analysis.

For regional control, neck management includes radical neck dissection (RND), modified radical neck dissection (FND), and/or supraomohyoid neck dissection, depending on the primary tumor size and location, clinical presentation, and involvement of cervical lymph nodes. Postoperatively, patients with unfavorable pathologic features including involved margin, nodal extracapsular extension, more than 2 positive cervical nodes, perineural invasion, or

Table 1
Patients' demographic characteristics.

Studied variable	*n*	%	Mean	Range
Age, years			51.6	35–69
Total patients	61			
Male	39	63.9%		
Female	22	36.1%		
Tumor site				
Buccal mucosa	15	24.6%		
Tongue	20	32.8%		
Mandible alveolus	13	21.3%		
Retromolar trigon	6	9.8%		
Floor of mouth	3	4.9%		
Maxillary alveolus	4	6.6%		
Tumor stage				
T1	4	6.6%		
T2	47	77%		
T3	5	8.2%		
T4	5	8.2%		
Nodal stage				
N0	55	90.2%		
N1	6	9.8%		