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Importance of Intraoperative Frozen Section Biopsy in Head and Neck Surgical Oncology

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Review Article

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ABSTRACT

Purpose: This particular study aimed to determine the importance of intraoperative frozen section pathology of head and neck cancers in order to examine the reliability of the frozen section. Frozen section biopsy technique often helps a rapid diagnosis of a mass during surgery, which in turn may help a surgeon to know the status of the margins of his resection before closing.
Objective: The study was done to achieve tumour free surgical margin after resection of oral squamous cell carcinoma (OSCC). The study also examines to determine positive margins and their relation to tumour size, grade, and stage of oral squamous cell carcinoma.
Method: This cross-sectional study was done in 179 patients with oral sqamous cell carcinoma.
Results: Overall, 179 patients who underwent surgery for oral cavity cancers were included; 116 (65.2%) were males. The mean (+standard deviation) age of the included participants was 57.4 + 16.1 years. The most common tumour subsite was the tongue (n ¼ 71, 39.2%). The frozen, negative intraoperative malignancy and the postoperative safe surgical margin did not significantly differ.
Conclusion: The intra-operative frozen section biopsy plays an important role in Achieve tumour free surgical margin in the resection of oral squamous cell carcinoma. In this study, it was also noted that the number of positive margins increased in relation to increased tumour size and tumour stage (cTNM).

Keywords: Neck Surgical Oncology, Intraoperative, Frozen Section, Biopsy.

Introduction

Locoregional control and treatment outcomes for primary oral cancers and cervical lymph node metastases have improved markedly with improvements in imaging diagnosis, advances in multidisciplinary treatment applying surgical therapy, radiotherapy, and chemotherapy, and the development of supportive therapies for oral cancer treatment.[1-3] However, despite these advances, the primary lesion recurs in several cases. Therefore, control of the primary lesion is a major concern for oral surgeons, as recurrent lesions are difficult to control and markedly compromise the quality of life of the patients. In surgical therapy for oral cancers, the

resection range for the primary lesion is determined based on the TNM classification following evaluation of the clinical findings and images from contrast-enhanced-computed tomography (CT), contrast-enhanced magnetic resonance imaging (MRI), positron Emission tomography-CT and ultrasonography.[1] The safety margins of the resected primary lesion are confirmed during surgery by palpation and from intraoperative frozen Section histological analysis (FS). However, the resection range varies among operators; the usefulness of FS has not been verified and the primary lesion recurs in several cases.

As regards the methods used for evaluating the safety margins of the resected primary lesions, the 2013 guidelines for the treatment of oral cancer[1] described vital Lugol staining as being useful for mucosal lesions in cancer of the tongue. The recurrence rate of the primary lesions was found to be lower among patients for whom the non-Lugol-stained region was included in the resection field compared to those for whom there was no vital Lugol staining in the resected lesions. Although the examination of all the surgical margins of the resected primary lesions in FS is difficult and the scope of the evaluation is limited, investigating the presence or absence of residual tumor tissue in the resected margin appears to be useful. Surgery with per-operative frozen section biopsy to ensure tumour free margin is better than radiotherapy alone or surgery combined with postoperative radiotherapy. Because radiotherapy can not ensure the total eradication of squamous cell carcinoma. Postoperative radiotherapy not only produces various hazards on the general condition of the patient but also complicates the primary surgical site. In a study on surgery vs surgery and radiotherapy, Loree and Strong reported that local recurrence rates in patients with positive margins who underwent radiotherapy were greater than local recurrence rates in comparable patients with negative margins not receiving postoperative radiotherapy. They also mentioned that adjuvant postoperative radiotherapy was not effective to control local recurrence in the presence of positive margins. Resection of involved margins in a second surgical procedure is often unacceptable and/or impractical. For this reason, in situations where a positive margin is found (by paraffin preparation), the use of postoperative radiotherapy is advocated as early as possible at full therapeutic dosage. So, one can easily understand the importance of frozen section biopsy.

Methods: This was a retrospective study of 179 patients who were diagnosed with oral squamous cell carcinoma between September 2018 and December 2019 at our tertiary center. Patients were included if they had a diagnosis of primary oral cavity squamous cell carcinoma. Patients were excluded if they did not have squamous cell carcinoma as a result of pathology findings; had undergone surgery or prior radiotherapy; did not have detailed pathological information available in their files. At least one day before the operation the surgeon had to inform the pathology department. Pathological requisition form on which minimum important information of the patient and approximate time for FS are written. After 1 to 2 minutes, the embedded tissue and cryomatrix turned frosted white in colour and hard. The tissue block (small specimen) was cut into 5-6 micron thickness by using a rotary microtome. The sectioned tissues were picked up, placed in the same numbered slide, and was then placed into Carnoy's fixative containing coplin jar. The sections were stained by quick haematoxylin and eosin stain. The sections were examined microscopically. Results were recorded on the frozen section request form. FS result was informed to the surgeon. Total Frozen Section Biopsy as Intraoperative Procedure.

procedure was completed within about 15-20 minutes. In case of any positive margin, 2nd sample from the positive site of the lesion was sent for further histopathological examination.

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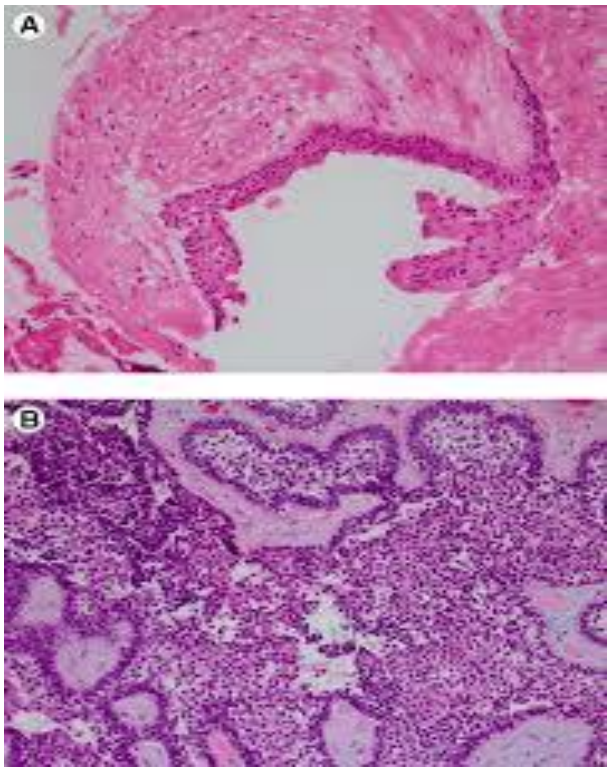

Results: Overall, 179 patients who underwent surgery for oral cavity cancers were included; 116 (64.2%) were males, 63 (35.8%) females, and the mean (+SD) age was 57.4 + 16.1years. The most common tumour subsite was the tongue (n ¼ 69, 39.2%), followed by the lower lip (n ¼ 34, 18.8%), the floor of the mouth (n ¼ 18, 10%), the hard palate (n ¼ 18, 10%), the retromolar trigon (n ¼ 16, 8.8%), the lower gingiva (n ¼ 15, 8.3%), and the upper gingiva (n ¼ 9, 4.9%; Table 1). The mean (+SD) number of lymph nodes examined and affected lymph nodes were 27.8 + 22.4 and 3.0 + 2.2, respectively. The mean (+SD) DOI was 11.9 + 8.5 (range 1-40) mm. Overall, 50 (27.6%), 72 (39.8%), 22 (12.2%), and 37 (20.4%) patients had grades of 1, 2, 3, and 4, respectively. Perineural invasion, lymphovascular invasion, and WPOI were observed in 88 (48.6%), 43 (23.8%), and 11 (6.1%) patients, respectively. Finally, extranodal extension was positive in 41 (22.7%) patients.

Discussion: It is very important to achieve clean surgical margins in cancer surgery. Even if surgeons remove the tumor macroscopically, their aim is to confirm a negative microscopic surgical margin. Frozen section examination is the most common technique that is used clinically to assess surgical margins. In addition to time and staff occupation, increased cost due to over-sampling, and increased surgical time, Mannelli et al reported that they might miss the positive surgical margin. However, in our study, the results for both positive and negative frozen examination of surgical margins were found to be compatible with the postoperative pathology. Due et al reported that 2% to 10% of frozen results, which were defined as negative based on the intraoperative findings, could be positively detected in the postoperative pathology. In our study, it was observed that there was a high agreement between frozen investigations that were reported as negative based on the intraoperative findings and the exact pathology, thus confirming that our findings are consistent with those reported in the recent literature. We found that as long as the number of frozen examinations increased, the accordance also increased. Due et al suggested that sampling from the surgical bed should be better defined for intraoperative frozen examination.[5,6] Although this is an option, as the number of frozen

examinations increases, the rate at which the pathologist misdiagnoses samples will decrease. Although increasing the number of frozen sections has disadvantages such as increasing the duration of surgery and increasing the cost of the frozen examination, these disadvantages are not outweighed when considering postoperative surgical margin positivity and retreatment. We identified that the sensitivity and specificity of the frozen section evaluations were 99% and 96%, respectively. While these results are compatible with some of those previously published, they are very optimistic compared to other studies. Our findings might be impacted by the sampling method used, including where the samples were taken from; this is an important factor that affects frozen results. There are 3 accepted sampling techniques: specimen-driven, tumor-bed, or a combination of both of these approaches.[4] The specimen-driven approach increases the surgical defect and indicates that the resection is complete if the frozen result is negative compared to the specimen technique.[6] However, this technique causes false results as the surgeon obtains the frozen sections from the deeper side of the tumor bed.[8] This illusion is due to the withdrawal of the retraction of the deep soft tissue, especially in cases where the defect is large, such as in T2-4 oral squamous cell carcinoma. Recent studies emphasize the superiority of the specimen- driven technique compared to the tumor bed technique. We used the specimen-driven approach and thus believe that this had an impact on the high level of compliance.[7]

Frozen section examination is a very frequently used technique but fluorescence-guided optical imaging spectroscopy or Raman spectroscopy, narrow-band imaging, and optical coherence tomography are new techniques that are used for intraoperative frozen examination of surgical margins. Although each of these techniques has its own characteristics, their superiority in examining whether there is a tumor at the surgical margin is still not understood. In conclusion, our FS method appears to be useful for resecting tumors with reliable safety margins for tissues retaining anatomical continuity, such as the tongue.[9,10] The macroscopic observation of cross-sections of the resected tumor specimens is easy and the surgical margins may be readily investigated.[11] However, this method is insufficient for determining a resection range in tissues containing soft tissue and jaw bone, such as upper and lower gingival tumors, and other methods to control primary lesions must be investigated.

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