



A CLINICOPATHOLOGIC STUDY TO ASSESS THE EXTENT OF SHRINKAGE OF HEAD AND NECK CANCER SPECIMEN

General Surgery

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ABSTRACT

BACKGROUND: According to the last report of World Health Organization in 2014, cancer of the oral cavity and pharynx constitute the seventh most common cancer in the world and is the ninth leading cause of cancer related deaths. Squamous cell carcinoma (SCC), with a high morbidity and mortality rate, constitutes 90% of the oral cavity tumors. Among the several prognostic factors of SCC, the status of surgically resected margins plays a key role with respect to both local recurrence rate and overall survival.

AIM: To study the extent of shrinkage of head and neck cancer specimen immediately post resection and after formalin fixation.

MATERIALS AND METHODS: This is a prospective clinicopathological analysis of 215 biopsy proven head and neck carcinoma patients conducted in a tertiary cancer center over a period of 2 years.

RESULT: In the present study, mean age of the patients was 48.4 years and male to female ratio was 3.16:1. Adequate margin was seen 73.49% cases, close margin in 23.25% and positive margin in 3.72 % cases. The rate of overall shrinkage cut margin in specimen was 37.74 %, 30.95 % and 31.89% in carcinoma buccal mucosa, carcinoma alveolus and carcinoma tongue respectively with an overall margin positivity rate of 3.72 %.

CONCLUSION: In conclusion, there is a significant difference among resection margins based on tumor anatomical location. Margins shrinkage following resection and processing should be considered at the time of initial resection. Tumors located in the buccal mucosa show significantly greater discrepancies than tumors of other sites. These findings suggest that it might be prudent to consider oral site when outlining margins to ensure adequacy of resection.

KEYWORDS

INTRODUCTION

According to the last report of World Health Organization in 2014, cancer of the oral cavity and pharynx, in combination, are the seventh most common cancer in the world and the ninth most common cause of death by cancer. Globally lip and oral cancers together comprise of 9.7% of all the cancers¹. Incidence of oral cancer is much higher in developing countries than developed countries which can be attributed to more popular chewable forms of tobacco in this region². About 90% of oral cavity tumors are squamous cell carcinomas³.

Its annual incidence is estimated about 529,000 new cases/ year⁴, and its survival rate at 5 years, for most countries, is around 50%⁵. Numerous clinical and histopathologic factors have been considered as prognostic at the SCC⁶. Among them, one of the most relevant, with respect to the overall survival and recurrence rate, is the status of surgical margin of resection^{7,8,9,10}.

In 1978 when Looser et al⁷ defined the term “positive surgical margin”, diverse concepts such as “close margins”, “involved margins” or “clear margins”, among others, have been introduced in the literature without a general consensus^{11,12,13,14}.

In fact, even today, there are no universal guidelines that permit different pathologists to adopt the same histologic criteria regarding to surgical margin^{7,15,16,17,18}.

This lack of agreement on what should constitute an “adequate” or “safe” margin of resection have led to each pathology department to classify surgical margins according to its own experience or internal guidelines, thereby hampering the comparison of the results obtained in the different studies and its extrapolation to the clinical practice¹⁵. A recent systematic review concluded that a histopathologic margin of at least 5 mm is the minimum acceptable margin size that should be achieved in any oral SCC¹⁹. Currently, following the surgical standard, it has been established that a macroscopic surgical margin of 1 to 2 cm obtained intra-operatively is enough extent to obtain a free-tumor margin (5 mm at present) in the oral cavity and oropharynx^{6,20,21}.

AIMS & OBJECTIVES

AIM: To study the extent of shrinkage of head and neck cancer specimen immediately post resection and after formalin fixation.

OBJECTIVES:

- To study the extent of shrinkage of cut mucosal margins of head and neck cancer specimens immediate post resection and during grossing after formalin fixation.
- To study the effect of duration of formalin fixation on shrinkage of cut mucosal margins of head and neck cancer specimens.

- To study the extent of tumor shrinkage after formalin fixation.
- To study the effect of tumor location on degree of cut mucosal margin shrinkage.

Materials And Research Methodology Study Design

This is a hospital based prospective clinicopathological study of 215 patients with operable head and neck carcinoma conducted on the basis of data collected clinically during surgery and pathologically in a tertiary care institute

Duration Of Study

1st October 2016 to 31st November 2018

Inclusion Criteria:

- All biopsy proven head and neck operable cancer cases including where radical surgery was done with curative intent both upfront and/ or after neoadjuvant treatment.

Exclusion Criteria:

- All head and neck cancer cases where adequate margin was not taken and additional margins were then removed.
- All patients of head and neck cancer who did not give consent for the study.

METHOD:

All the patients included underwent routine blood investigations, chest X Ray, CECT neck from base of skull to clavicle with bone window/ or MRI neck pre operatively and for follow up.

Resection was done with the aim of keeping the cut margin at a minimum arbitrary value of 10 mm. Immediately after resection of specimen, the cut margin were recorded with a pliable scale without any stretching of mucosa.

OBSERVATIONS AND RESULTS

Total 215 patients were included in the study with mean age of 48.4 years and male to female ratio of 3.16:1. Adequate margin was seen 73.49% cases, close margin in 23.25% and positive margin in 3.72 % cases. The rate of overall shrinkage cut margin in specimen was 37.74 %, 30.95 % and 31.89% in carcinoma buccal mucosa, carcinoma alveolus and carcinoma tongue respectively with an overall margin positivity rate of 3.72 %.

Table No. 1: Distribution Of Cases W.r.t Site Of Cancer, Sex And Side.

SITE OF TUMOR	NUMBER OF CASES	MALE/FEMALE	SIDE INVOLVED
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CARCINOMA BUCCAL MUCOSA	99	MALE 78	RIGHT SIDE 41
		FEMALE 21	LEFT SIDE 37
CARCINOMA ALVEOLUS	77	MALE 53	RIGHT SIDE 24
		FEMALE 24	LEFT SIDE 29
CARCINOMA TONGUE	39	MALE 33	RIGHT SIDE 8
		FEMALE 6	LEFT SIDE 16
			RIGHT SIDE 21
			LEFT SIDE 12
			RIGHT SIDE 3
			LEFT SIDE 3

Table No. 2: Distribution Of Patients According To Tnm Staging

T STATUS	N STATUS	OVERALL STAGING
T ₁	35	N ₀ 117
T ₂	57	N ₁ 30
T ₃	22	N ₂ 66
T ₄	99	N ₃ 00
		STAGE I 28
		STAGE II 36
		STAGE III 22
		STAGE IVA 127

MARGINS**Table No. 4:** Immediate Post Resection Margins

MARGIN	AVERAGE(in mm)	RANGE (in mm)
ANTERIOR	17.2	10-55
POSTERIOR	17.55	10-70
MEDIAL	16.06	10- 60
LATERAL	15.38	9- 75

Table No. 5: Post Formalin Fixation Margins

MARGIN	AVERAGE(in mm)	RANGE (in mm)
ANTERIOR	11.50	1- 50
POSTERIOR	11.67	1- 55
MEDIAL	10.24	1- 45
LATERAL	10.04	1- 57

Table No. 6: Margin Shrinkage

SIDES	IMMEDIATE POST OPERATIVE MARGIN(mm)	MARGIN AFTER FORMALIN FIXATION (mm)	SHRINKAGE (%)
ANTERIOR	17.20	11.50	33.14
POSTERIOR	17.55	11.67	27.33
MEDIAL	16.06	10.24	36.24
LATERAL	15.38	10.04	34.72

Table No. 7: Mucosal Cut Margin Shrinkage In Relation To Location Of Tumor

TUMOR SITE	POST OPERATIVE MARGIN(mm)	MARGIN AFTER FIXATION (mm)	SHRINKAGE (%)
BUCCAL MUCOSA	15.55	9.68	37.74
ALVEOLUS	15.07	10.41	30.95
TONGUE	21.72	14.79	31.89

Table No. 8: Tumor Diameter Shrinkage

POST OPERATIVE	10 mm – 130 mm	Average: 44.72 mm
AFTER FIXATION	8 mm – 120 mm	Average: 39.76 mm
OVERALL SHRINKAGE: 11.1 %		

Effect Of Delay In Pathological Grossing

13 patients were operated prior to next day holiday. Grossing hence was done on 3rd day with average formalin exposure time being 48 hours.

Overall immediate post operative margin was 20.40 mm. Overall margin during grossing was 11.13 mm. The margin shrinkage came out to be 45.42 % with an overall tumor shrinkage of 24.42 %. There was only 10.24 % shrinkage in tumor diameter with 24 hours of formalin exposure.

Table No. 9: Overall Mucosal Cut Margin And Tumor Shrinkage In Relation To Duration Of Formalin Exposure

Formalin Exposure	No. of Patients	Immediate Post op Margin (Average) in mm	Margin After Fixation in mm	Percent Shrinkage in Margin	Percent Tumor Shrinkage
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24 hours	202	16.33	10.85	33.50	10.24
48 hours	13	20.40	11.13	45.42	24.42

DISCUSSION

In the current study, we found a difference between margins measured at the time of surgical resection of oral SCC and the margins measured after histopathological review. Furthermore, we found a significant difference among margin discrepancies based on tumor anatomical location.

In a study of 52 oral cancer cases, by Mohiyuddin et al²², the average decrease in tumor margins measured after fixation in formalin was found to be statistically significant ($P < 0.05$) in 65% of cases. Of the 52 patients, 13 patients had closest pathological margin less than 5 mm (close margins) while 39 patients had the pathological margin ≥ 5 mm. In the present study also, 25 % cases had close margins.

The average surgical margin shrinkages estimated by Pangare et al²³ were 18.7% anteriorly, 14.9% posteriorly, 23.6% medially, and 23.9% laterally. In our study, average shrinkage in anterior margin irrespective of tumor location was 33 %, posterior was 32.9 %, medial margin shrinkage was 36.2 % and lateral margin shrinkage being 34.7 %.

Mistry et al¹⁷ published a study on 27 patients with oral SCC of the tongue and buccal mucosa where analyzed the distances pre-resection and post-resection and reported a mean shrinkage of 3.18 mm (22.7%). However, El-Fol et al²⁴ described a mean discrepancy between intraoperative margins and 155 histopathologic margins exclusively analyzing all close and positive margins. In this study, the mean discrepancy for buccal mucosa was 47.6%, 33.3% for the tongue, 9.5% for the mandibular alveolus, and 4.8% for both, retromolar trigone and floor of the mouth.

In our study the overall shrinkage cut margin in specimen of carcinoma buccal mucosa was 37.74 %. 30.95 % shrinkage in cut margin was seen in specimen of carcinoma alveolus. In specimen of carcinoma tongue there was 31.89 % shrinkage in cut margin.

In a study of 1,522 cases of aerodigestive tract carcinoma, Lee et al²⁵ discovered that the oral cavity was most likely site to have margins involved with residual tumor. The rate of positive margins in the same study for oral cancers was 15%. In our study, margin positivity rate was 3.72 %.

The results of our study show a significant difference between margins measured at the time of surgical resection of oral SCC and the margins measured after histopathological review. Furthermore, we found a significant difference among margin discrepancies based on tumor anatomical location.

CONCLUSION:

In conclusion, tissue shrinkage on surgical margins of resection in oral SCC is a tangible phenomenon. The highest percentage of retraction occurs at the time of resection. There is a significant difference among resection margins based on tumor anatomical location. Margins shrinkage following resection and processing should be considered at the time of initial resection. Tumors located in the buccal mucosa show significantly greater discrepancies than tumors of other sites.

We recommend that margin distance be measured in millimeters and recorded on the surgical pathology report. Positive margins should be surgically cleared whenever possible. If this is not feasible, chemoradiotherapy is superior to adjuvant radiotherapy alone.

Limitations Of The Study

The study was carried out on a small sample size. Studies using larger samples are needed to quantify these findings.

REFERENCES:

- Jemal A, Bray F, Center MM, Ferlay J, Ward E, Forman D. Global cancer statistics. CA: A Cancer Journal for Clinicians [Internet]. Wiley; 2011 Feb 4;61(2):69–90. Available from: <http://dx.doi.org/10.3322/caac.20107>.
- IARC Working Group on the Evaluation of Carcinogenic Risks to Humans, IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, vol. 89, World Health Organization, 2007.
- J. Watkinson and R. Gilbert, "Stell & Maran's textbook of head and neck surgery and oncology," in Lip and Oral Cavity Cancer, p. 549, CRC Press, 2012.
- Stewart BW, Wild CP. World Cancer Report 2014. World Health Organization: Geneva; 2014.
- Warnakulauriya S. Global epidemiology of oral and oropharyngeal cancer. Oral

- Oncology [Internet]. Elsevier BV; 2009 Apr;45(4-5):309–16. Available from: <http://dx.doi.org/10.1016/j.oraloncology.2008.06.002>
6. Massano J, Regateiro FS, Januário G, Ferreira A. Oral squamous cell carcinoma: Review of prognostic and predictive factors. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology* [Internet]. Elsevier BV; 2006 Jul;102(1):67–76. Available from: <http://dx.doi.org/10.1016/j.tripleo.2005.07.038>.
 7. Looser KG, Shah JP, Strong EW. The significance of “positive” margins in surgically resected epidermoid carcinomas. *Head & Neck Surgery* [Internet]. Wiley; 1978 Nov;1(2):107–11. Available from: <http://dx.doi.org/10.1002/hed.2890010203>.
 8. Yahalom R, Dobriyan A, Vered M, Talmi YP, Teicher S, Bedrin L. A prospective study of surgical margin status in oral squamous cell carcinoma: A preliminary report. *Journal of Surgical Oncology* [Internet]. Wiley; 2008 Dec 15;98(8):572–8. Available from: <http://dx.doi.org/10.1002/jso.21034>.
 9. Kurita H, Nakanishi Y, Nishizawa R, Xiao T, Kamata T, Koike T, et al. Impact of different surgical margin conditions on local recurrence of oral squamous cell carcinoma. *Oral Oncology* [Internet]. Elsevier BV; 2010 Nov;46(11):814–7. Available from: <http://dx.doi.org/10.1016/j.oraloncology.2010.08.014>.
 10. Hinni ML, Ferlito A, Brandwein-Gensler MS, Takes RP, Silver CE, Westra WH, et al. Surgical margins in head and neck cancer: A contemporary review. Eisele D, editor. *Head & Neck* [Internet]. Wiley; 2012 Sep 3;35(9):1362–70. Available from: <http://dx.doi.org/10.1002/hed.23110>.
 11. McMahon J, O'Brien C., Pathak I, Hamill R, McNeil E, Hammersley N, et al. Influence of condition of surgical margins on local recurrence and disease-specific survival in oral and oropharyngeal cancer. *British Journal of Oral and Maxillofacial Surgery* [Internet]. Elsevier BV; 2003 Aug;41(4):224–31. Available from: [http://dx.doi.org/10.1016/s0266-4356\(03\)00119-0](http://dx.doi.org/10.1016/s0266-4356(03)00119-0).
 12. Nason RW, Binahmed A, Pathak KA, Abdoh AA, Sándor GKB. What is the adequate margin of surgical resection in oral cancer? *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology* [Internet]. Elsevier BV; 2009 May;107(5):625–9. Available from: <http://dx.doi.org/10.1016/j.tripleo.2008.11.013>.
 13. Woolgar JA, Triantafyllou A. A histopathological appraisal of surgical margins in oral and oropharyngeal cancer resection specimens. *Oral Oncology* [Internet]. Elsevier BV; 2005 Nov;41(10):1034–43. Available from: <http://dx.doi.org/10.1016/j.oraloncology.2005.06.008>.
 14. Brandwein-Gensler M, Teixeira MS, Lewis CM, Lee B, Rolnitzky L, Hille JJ, et al. Oral Squamous Cell Carcinoma. *The American Journal of Surgical Pathology* [Internet]. Ovid Technologies (Wolters Kluwer Health); 2005 Feb;29(2):167–78. Available from: <http://dx.doi.org/10.1097/01.pas.0000149687.90710.21>.
 15. Tirelli G, Zaccagna S, Biasotto M, Piovesana M. Erratum to: Open questions and novel concepts in oral cancer surgery. *European Archives of Oto-Rhino-Laryngology* [Internet]. Springer Nature; 2015 Jul 2;273(8):1987–8. Available from: <http://dx.doi.org/10.1007/s00405-015-3695-5>.
 16. Chiou W-Y, Lin H-Y, Hsu F-C, Lee M-S, Ho H-C, Su Y-C, et al. Buccal mucosa carcinoma: surgical margin less than 3 mm, not 5 mm, predicts locoregional recurrence. *Radiation Oncology* [Internet]. Springer Nature; 2010;5(1):79. Available from: <http://dx.doi.org/10.1186/1748-717x-5-79>.
 17. Mistry RC, Qureshi SS, Kumaran C. Post-resection mucosal margin shrinkage in oral cancer: Quantification and significance. *Journal of Surgical Oncology* [Internet]. Wiley; 2005;91(2):131–3. Available from: <http://dx.doi.org/10.1002/jso.20285>.
 18. Loree TR, Strong EW. Significance of positive margins in oral cavity squamous carcinoma. *The American Journal of Surgery* [Internet]. Elsevier BV; 1990 Oct;160(4):410–4. Available from: [http://dx.doi.org/10.1016/s0002-9610\(05\)80555-0](http://dx.doi.org/10.1016/s0002-9610(05)80555-0).
 19. Anderson CR, Sisson K, Moncrieff M. A meta-analysis of margin size and local recurrence in oral squamous cell carcinoma. *Oral Oncology* [Internet]. Elsevier BV; 2015 May;51(5):464–9. Available from: <http://dx.doi.org/10.1016/j.oraloncology.2015.01.015>.
 20. Cheng A, Cox D, Schmidt BL. Oral Squamous Cell Carcinoma Margin Discrepancy After Resection and Pathologic Processing. *Journal of Oral and Maxillofacial Surgery* [Internet]. Elsevier BV; 2008 Mar;66(3):523–9. Available from: <http://dx.doi.org/10.1016/j.joms.2007.08.040>.
 21. Upile T, Fisher C, Jerjes W, El Maaytah M, Searle A, Archer D, et al. The uncertainty of the surgical margin in the treatment of head and neck cancer. *Oral Oncology* [Internet]. Elsevier BV; 2007 Apr;43(4):321–6. Available from: <http://dx.doi.org/10.1016/j.oraloncology.2006.08.002>.
 22. Mohiyuddin SMA, Padiyar BV, Suresh TN, Mohammadi K, Sagayaraj A, Merchant S, et al. Clinicopathological study of surgical margins in squamous cell carcinoma of buccal mucosa. *World Journal of Otorhinolaryngology-Head and Neck Surgery* [Internet]. Elsevier BV; 2016 Mar;2(1):17–21. Available from: <http://dx.doi.org/10.1016/j.wjorl.2016.02.003>.
 23. Pangare TB, Wanknis PP, Bawane SS, Patil MN, Wadhera S, Patowary PB. Effect of Formalin Fixation on Surgical Margins in Patients With Oral Squamous Cell Carcinoma. *Journal of Oral and Maxillofacial Surgery* [Internet]. Elsevier BV; 2017 Jun;75(6):1293–8. Available from: <http://dx.doi.org/10.1016/j.joms.2016.11.024>.
 24. El-Fol HA, Noman SA, Beheiri MG, Khalil AM, Kamel MM. Significance of post-resection tissue shrinkage on surgical margins of oral squamous cell carcinoma. *Journal of Cranio-Maxillofacial Surgery* [Internet]. Elsevier BV; 2015 May;43(4):475–82. Available from: <http://dx.doi.org/10.1016/j.jcms.2015.01.009>.
 25. Lee JG. Detection of residual carcinoma of the oral cavity, oropharynx, hypopharynx, and larynx: a study of surgical margins. *Trans Am Acad Ophthalmol Otolaryngol*. 1974 Jan-Feb;78(1):ORL49-53.