

Finding the Adequacy of Surgery of Head and Neck Cancers in Pakistan

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ABSTRACT

Objective: To assess the proportion of adequate surgery in head and neck cancers. Study design: This Observational study was conducted in RHC Raiwind, District Lahore during June 2019 to June 2020 with the collaboration of Cancer Care center in Lahore. Methodology: One fifty nine patients of age more than 20-65 years of either sex with confirmed diagnosis of SCC of head and neck were included in the study. Surgery was done upfront in all patients without any preoperative/induction chemotherapy. Data regarding socio-demographic and histopathology findings were noted. Surgery was labelled as inadequate when number of resected lymph nodes recovered were less than 36 and margins of tumor were <5 mm (inadequate). Data was analysed using SPSS version 25.

Results: Of 159 patients, average age was estimated as 46.57 ± 9.73 years. Less than 36 lymph nodes were

recovered in 84 patients (52.8%) after neck dissection. A total of 64 patients had inadequate margins (40.3%), 77 had adequate margins (48.4%) and 18 had positive margins (11.3%) on histopathological examination. Overall, 56 patients had adequate surgery (35.2%) and 103 had inadequate surgery (64.7%).

Conclusion: More than half of the patients with HNSCC had inadequate surgery. Hence, inadequate surgery can lead to poor loco-regional disease control, increased chances of recurrence and overall poor prognosis.

Key words: Adequate surgery, Adequate margins, Carcinomas, Head and neck cancers, Perineural invasion

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INTRODUCTION

Head and neck cancers are highly prevalent malignancies worldwide, occur more commonly in developing countries during to consumption of tobacco, alcohol and cigarette. Infection with Human Papilloma Virus (HPV), especially type 16 is a risk factor for oropharyngeal cancers. In US incidence of Human Papilloma Virus associated oropharyngeal cancers is increasing, while incidence of other causes related head and neck cancers is declining (NIH, 2020). In Southeast Asia, Head and neck cancers comprise about 1/3 of all cancers and higher incidence is among individuals who consume smokeless tobacco. Other causes include betel quid, salted foods and occupational exposure to asbestos, wood dust etc. Approximately 90% of the oral cavity cancers are Squamous Cell Carcinomas (SCC) (Niaz K, et al., 2017; Khan SZ, et al., 2020).

Surgical resection is an integral part of the multimodal treatment approach for HNCs and the ultimate aim of resection is to achieve the target of loco regional control with adequate surgical margins along with resection adequate number of lymph nodes (Cheng CY, et al., 2020). Because of its sensitive anatomical location after treatment patient may become unable to swallow, breath, chew, and speak for variable period of time so multidisciplinary care is required which includes oncologist, ENT oncological surgeon, radiation oncologist, speech therapist etc. (Clarke P, et al., 2016).

Histologically the margin of greater 5 mm is said to be adequate, less than 5 mm is considered as inadequate and less than 1 mm is said to be positive margins (Janjua OS, et al., 2013; Gokavarapu S, et al., 2014). Histologic status of surgical margins is a strong predictor for prognosis in a variety of malignant tumors. Histopathological findings showing margins involvement suggests that resection was inadequate and patient needs to undergo either adjuvant radiotherapy and chemotherapy or re-excision of the primary site

(Williams MD, 2016). While re-excision is the preferred option which insists on importance of removal of tumor with adequate margins (Sarin R, et al., 2018).

Hence, the goal of the current research was therefore to determine the proportion of adequate surgery of head and neck cancers in the tertiary care hospital in Karachi, Pakistan as in this particular anatomical site surgery is backbone of multi-modal treatment plan and inadequate surgery ultimately results in poor loco-regional control, exposure to chemo radiotherapy and overall poor prognosis. Our research can help improving surgical management and overall prognosis of head and neck cancers.

METHODOLOGY

This observational study was conducted in RHC Raiwind, District Lahore during June 2019 to June 2020 with the collaboration of Cancer Care center in Lahore. Sample size of 159 was calculated by using open a sample size calculator by taking statistics of clear margin as 42.9% (Janjua OS, et al., 2013), absolute precision as 7.7% and 95% confidence level. All patients of age 20-65 years of both sexes with confirmed diagnosis of SCC of head and neck (HNSCCs) were included using non-random consecutive sampling approach. Patients with salivary gland tumors, CNS tumors, nasopharynx tumors, tumors of lacrimal glands and ophthalmological tumors were excluded from the study. All histologies except Squamous Cell Carcinoma were also excluded.

Verbal informed consent was obtained from all the eligible patients. Surgery was performed upfront in all patients without any preoperative induction/chemotherapy. Data regarding age, gender, residence, occupation, ethnicity and addiction was noted on pre-designed proforma. Detailed findings of histopathology including site and size of tumor, nodal status, metastasis, stage and grade of tumor were noted. Histopathological examination was carried out to assess the margin status. Surgical margins were labelled as adequate when no tumor

was found within 5 millimetres of the resection margin, inadequate(close) when tumor was presented with 1 to 5 millimetres and positive (involved) when distance was less than 1 millimetre. Surgery was labelled as inadequate when number of resected lymph nodes recovered were less than 36 and margins of tumor were <5 millimetres (inadequate).

SPSS version 25 was used to analyse data. Mean and standard deviation were reported for numeric variables, whereas counts and proportions were reported for categorical variables.

RESULTS

Of 159 patients with HNSCCs the mean age was estimated as 46.57 ± 9.73 years (Range: 22-70 years). Most of the patients were males (n=132, 83%), urban residents (n=140, 88.1%), outdoor workers (n=133, 83.6%) and Urdu speaking (n=75, 47.2%) respectively. Of 159 patients, 71 were smokers (44.7%), 82 were gutka consumers (51.6%), 38 were pan consumers (23.9%), 5 were betel nut consumers (3.1%) and 15 were naswar users (9.4%) respectively (Table 1).

Table 1: Socio-demographic profile (n=159)

Variables	Mean ± SD
Age in years	46.57 ± 9.73
	n (%)
Gender	
Male	132(83)
Female	27(17)
Residence	Retrospective
Urban	140 (88.1)
Rural	19 (11.9)
Occupation	Retrospective
Indoor	26(16.4)
Outdoor	133(83.6)
Ethnicity	
Sindhi	19(11.9)
Urdu	75(47.2)
Punjabi	52(32.7)
Pashto	1(0.6)
Baloch	12(7.5)
Addiction history	Retrospective
Smoking	71(44.7)
Gutka	82(51.6)
Pan	38(23.9)
Betel nut	5(3.1)
Naswar	15(9.4)

The buccal mucosa was the commonest site of tumor (n=92, 57.9%), followed by tongue (n=62, 39%) respectively. On radiological assessment, 91 patients had stage III of tumor (n=91, 57.2%) and in initial biopsy most of the patients had grade II of tumor (n=135, 84.9%). Of 159 patients, less than 36 lymph nodes were recovered in 84 patients (52.8%) after neck dissection. A total of 64 patients had inadequate margins (40.3%), 77 had adequate margins (48.4%) and 18 had positive margins (11.3%) on histopathological examination. About 56 patients had perineural invasion (35.2%) and 43 patients had lymphovascular invasion (27%). On pathological examination 75 patients had stage III of tumor (47.2%) and 110 patients had grade III of tumor (61.6%). Overall, 56 patients had adequate surgery (35.2%) and 103 had inadequate surgery (64.7%) (Table 2).

Table 2: Characteristics of tumor and frequency of adequate surgery (n=159)

Variables	n (%)
Site of tumor	15(9.4)
Tongue	62(39)
Buccal Mucosa	92(57.9)
Oropharynx	5(3.1)
Stage (Radiology)	15(9.4)
I	6(3.8)
II	22(13.8)
III	91(57.2)
IV	40(25.2)
Grade (Biopsy)	15(9.4)
I	8(5)
II	135(84.9)
III	16(10.1)
Recovered lymph nodes	15(9.4)
<36	84(52.8)
≥36	75(47.2)
Surgical margins	15(9.4)
Positive	18(11.3)
Inadequate	64(40.3)
Adequate	77(48.4)
Yes	43(27)
No	116(73)
Perineural invasion	15(9.4)
Yes	56(35.2)
No	103 (64.8)
Stage (Pathological)	15(9.4)
I	6 (3.8)
II	31(19.5)
III	75(47.2)
IV	47(29.6)
Grade	15(9.4)
I	2(1.3)
II	47(29.6)
III	110(69.2)
Surgery	15(9.4)
Adequate	56(35.2)
Inadequate	103(64.7)

DISCUSSION

One of the challenges of cancer resection in head and neck is the complete removal of the tumor from the primary site, and the failure to do so may result in a 2-fold increase in the likelihood of local-regional recurrence (Mahvi DA, *et al.*, 2018). The goal of Head and Neck Cancers treatment is therefore to safely remove the tumor with clear margins and to preserve the associated morbidity and with minimal cosmetic disfigurement. Surgery is quiet challenging in head and neck region as this anatomical site has neurovascular bundles and important cosmetic features.

In a survey conducted at United States among American Head and Neck Society members stated that surgical margin of greater 5 millimetres is sufficient, whereas some stated that surgical margins greater than 1 millimetre is also safe (Meier JD, *et al.*, 2005). This variation can

be observed in head and neck surgesons globally. Some authors showed that surgical margins greater than 5 millimetres are adequate in pharynx and oral cavity (Hinni ML, *et al.*, 2013). Whereas Liao *et al.* said greater 7 millimetres surgical margins are safe for oral cavity to provide good prognosis (Liao CT, *et al.*, 2008). Another research showed that less than 5 mm surgical margins is a significant predictor for loco-recurrence (Loree TR and Strong EW, 1990). Yamada *et al.* suggested that 5 mm of clear surgical margin should be the reference of the oral Squamous Cell Carcinoma (OSCC) surgery (Yamada S, *et al.*, 2016). A meta-analysis also suggested that a 5 mm margin is the least acceptable surgical margin size in Oral Squamous Cell Carcinoma (Anderson CR, *et al.*, 2015). Hence, the 5 mm distance has remained the frequent consensus distance for Oral squamous cell carcinoma as also reported by National Comprehensive Cancer Network Head and Neck Cancers guideline (Yamada S, *et al.*, 2016; NCCN, 2015). In the present study, we also considered greater than 5 mm surgical margins as clear, safe and adequate. Our findings showed that 48.4% of the patients with HNSCCs had adequate margins. Similar results were observed in the research by Janjua, *et al.* that 43% of the patients had complete clear margins (Janjua OS, *et al.*, 2013). Overall, our analysis shows a large number (>60%) of cases of inadequate surgery than other related studies (Janjua OS, *et al.*, 2013; Cheng A, *et al.*, 2008). Another research showed that 6% of Oral Squamous Cell Carcinoma patients managed with surgery had positive margins and 30 percent had a surgical margin of 0.1-2.2 mm. These findings may be due to the extent of the resection and the way in which the specimen is oriented, handled and preserved. A further determinant that may influence the margins after surgery is the shrinkage of normal tissue and tissues from different anatomical locations may experience varying shrinkage rates (Zanoni DK, *et al.*, 2017). In one study, overall survival in Head and Neck Cancers was found to be 35 months if lymph nodes dissected were <15, 63 months if dissected lymph nodes were 15-39 and 73.4 months if dissected lymph nodes were >40 (Merz S, *et al.*, 2018). This showed clinical significance of number of examined lymph nodes. According to one more study the number of lymph nodes examined rather than involved lymph nodes is associated with improved survival. Minimum 10 lymph nodes should be removed and with each additional lymph node mortality is found to be decreased until number of resected lymph nodes reaches up to 35. No significant advantage was observed beyond 35 lymph nodes (Ho AS, *et al.*, 2017). So it is determined that adequate number of lymph nodes should be removed in order to completely and precisely stage the cancer which will ultimately decide the prognosis and need for adjuvant treatment.

Adequate surgeries help in identifying accurate pathological stage and potentially de-intensify postoperative chemotherapy and radiotherapy. Surgical outcome depends on many factors including clinical stage, surgical expertise, anatomical site and health care equipment's availability at the treatment center (Golusiński W and Kardach EG, 2019). Further studies should be conducted in order to evaluate whether surgical margins and recovered lymph nodes has prognostic significance or not. More studies should be conducted to evaluate the proportion of adequate surgeries in different areas of Pakistan in order to evaluate and predict the overall prognosis of head and neck cancers in Pakistan. As in our setup huge numbers of patients come with inadequate surgery which leads to unnecessary exposure with chemotherapy and radiotherapy. Thus, conducting cancer surgery, it should be kept in mind that removal of tumor with adequate margins and dissection of adequate number of lymph nodes is necessary to achieve successful loco-regional control, improve overall survival and decrease extra burden on tertiary care hospitals delivering post-operative radiotherapy and chemotherapy.

CONCLUSION

More than half of the patients with head and neck squamous cell carcinoma had inadequate surgery. Hence, inadequate surgery can lead to poor loco-regional disease control, increased chances of recurrence and overall poor prognosis. We need more tertiary care setups that can provide best surgical management with better health care facilities in order to achieve better control over this highly prevalent malignancy.

REFERENCES

1. Head and Neck Cancers. National Cancer Institute (NIH). 2020.
2. Niaz K, Maqbool F, Khan F, Bahadar H, Ismail Hassan F, Abdollahi M. Smokeless tobacco (paan and gutkha) consumption, prevalence, and contribution to oral cancer. *Epidemiology and health*. 2017; 39: e2017009.
3. Khan SZ, Farooq A, Masood M, Shahid A, Khan IU, Nisar H, *et al.* Smokeless tobacco use and risk of oral cavity cancer. *Turk J Med Sci*. 2020; 50(1): 291-297.
4. Cheng CY, Sun FJ, Liu CJ. The influence of cervical lymph node number of neck dissection on the prognosis of the early oral cancer patients. *J Dent Sci*. 2020; 15(4): 519-525.
5. Clarke P, Radford K, Coffey M, Stewart M. Speech and swallow rehabilitation in head and neck cancer: United Kingdom national multidisciplinary guidelines. *J Laryngol Otol*. 2016; 130(S2): S176-S80.
6. Janjua OS, Ahmed W, Qureshi SM, Khan TS, Ahmed A, Alamgir W. Assessment of margins in resection specimens for head and neck malignancies. *J Coll Physicians Surg Pak*. 2013; 23(4): 265-268.
7. Gokavarapu S, Chander R, Parvataneni N, Puthamakula S. Close margins in oral cancers: Implication of close margin status in recurrence and survival of pT1N0 and pT2N0 oral cancers. *Int J Surg Oncol*. 2014; 2014: 545372.
8. Williams MD. Determining adequate margins in head and neck cancers: Practice and continued challenges. *Curr Oncol Rep*. 2016; 18(9): 54.
9. Sarin R, Somsekhar SP, Kumar R, Pawan G, Sumeet J, Pramoj J, *et al.* Practical consensus recommendations for tumor margins and breast conservative surgery. *South Asian J Cancer*. 2018; 7(2): 72-78.
10. Mahvi DA, Liu R, Grinstaff MW, Colson YL, Raut CP. Local cancer recurrence: The realities, challenges, and opportunities for new therapies. *CA Cancer J Clin*. 2018; 68(6): 488-505.
11. Meier JD, Oliver DA, Varvares MA. Surgical margin determination in head and neck oncology: current clinical practice. The results of an International American Head and Neck Society Member Survey. *Head Neck*. 2005; 27(11): 952-958.
12. 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. *Head Neck*. 2013; 35(9): 1362-1370.
13. Liao CT, Chang JT, Wang HM, Ng SH, Hsueh C, Lee LY, *et al.* Analysis of risk factors of predictive local tumor control in oral cavity cancer. *Ann Surg Oncol*. 2008; 15(3): 915-922.
14. Loree TR, Strong EW. Significance of positive margins in oral cavity squamous carcinoma. *Am J Surg*. 1990; 160(4): 410-414.
15. Yamada S, Kurita H, Shimane T, Kamata T, Uehara S, Tanaka H, *et al.* Estimation of the width of free margin with a significant impact on local recurrence in surgical resection of oral squamous cell carcinoma. *Int J Oral Maxillofac Surg*. 2016; 45(2): 147-152.

16. Anderson CR, Sisson K, Moncrieff M. A meta-analysis of margin size and local recurrence in oral squamous cell carcinoma. *Oral Oncol.* 2015; 51(5): 464-469.
17. Head and Neck Cancers; Principles of surgery. National Comprehensive Cancer Network Inc (NCCN). 2015; 9: 3.
18. Cheng A, Cox D, Schmidt BL. Oral squamous cell carcinoma margin discrepancy after resection and pathologic processing. *J Oral Maxillofac Surg.* 2008; 66(3): 523-539.
19. Zaroni DK, Migliacci JC, Xu B, Katabi N, Montero PH, Ganly I, *et al.* A proposal to redefine close surgical margins in squamous cell carcinoma of the oral tongue. *JAMA otolaryngology-head and neck surgery.* 2017; 143(6): 555-560.
20. Merz S, Timmesfeld N, Stuck BA, Wiegand S. Impact of lymph node yield on outcome of patients with head and neck cancer and pNo neck. *Anticancer Res.* 2018; 38(9): 5347-5350.
21. Ho AS, Kim S, Tighiouart M, Gudino C, Mita A, Scher KS, *et al.* Metastatic lymph node burden and survival in oral cavity cancer. *J Clin Oncol.* 2017; 35(31): 3601-3609.
22. Golusiński W, Kardach EG. Current role of surgery in the management of oropharyngeal cancer. *Front Oncol.* 2019; 9: 388.