# "INCIDENCE OF METASTATIC INVOLVEMENT OF CAROTID SHEATH IN ORAL SQUAMOUS CELL CARCINOMA"-A Cross Sectional type of study.

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Abstract: Background: Surgery is the most well established mode of initial definitive treatment for a majority of oral cancers. Over the past few decades, the surgical technique of neck dissection has evolved from Radical neck dissection to Modified radical neck dissection and then to Selective Neck Dissection.

Objectives: The main purpose of this research is to evaluate the incidence of pathologic incursion of the carotid sheath, when noticed grossly uninvolved while doing surgery in the patients with neck dissection for head and neck squamous cell carcinoma (HNSCC).

Methods: 80 neck dissections will be performed. Carotid Sheath will be removed separately and methodically evaluated by well experienced head and neck pathologists by performing hematoxylin and Eosin staining and Immunohistochemistry Analysis with Markers like Pancytokeratin and CD34 for tumour infiltration and the occurrence of lymphatic tissue. Hence, if found negative than it will strongly indicate that we can modify the neck dissections limiting up to the level of carotid sheath.

Results: Carotid Sheath is not grossly involved, removal of Carotid Sheath is not recommended. Histologically Carotid Sheath may harbour dilated lymphatic vessels, lymphocytes aggregates and neutrophils. Carotid Sheath, however, would not harbour any metastatic tumour emboli from primary Oral Squamous Cell Carcinoma.

Conclusion: Not only for surgical safety but also for the shield it provides post operatively against adjuvant radiation therapy and any infection in neck and even trickling of saliva down the neck postoperatively by protecting vital structures it encases like Common carotid artery, Vagus Nerve and Internal jugular vein. So far there is paucity of data in presence of metastatic involvement of carotid Sheath. This study will give basis for preservation of Carotid sheath during neck dissection which will reduce postoperative morbidities in head and neck squamous cell carcinoma patients.

Keywords: Metastasis, Carotid Sheath, Oral Squamous Cell Carcinoma.

## **Introduction:**

"Oral squamous cell carcinoma (OSCC)" potentially metastasizes to loco-regional lymphatic stations and basins in an orderly and predictable pattern. The most important prognostic factor in Oral squamous cell carcinoma is Cervical lymphnode Metastasis<sup>(1,2)</sup>.Comprehensive management includes removal of primary tumor suitable neck dissection followed by radiotherapy, chemotherapy, or combination therapy. Surgical management of neck corresponds to complete removal of metastatic lymphnode or part of neck where metastasis likely to appear.

In Patients with nodal neck diseases, extention of neck dissection is debatable. Traditionally, Radical neck dissection was recommended for all patients with pathologically affected lymphnodes. However, recently, selective neck dissections(level I-IV) are recommended and considered as more conservative approach <sup>(3,4)</sup>. Routinely during neck dissection, complete removal of carotid sheath is considered as it harbors loco-regional lymphatic stations and basins. IJV and CA are shielded by Carotid Sheath from various infectious agents and saliva . Carotid Sheath act as a fibroelastic tissue barrier in post operative period <sup>(5,6)</sup>. The Carotid Sheath with vital structures makes the structures prone to damage while working in that plane <sup>(7)</sup>. Pathalogical involvement of Carotid Sheath intra operatively has been reported very little . Failure to remove the diseased Lymph nodes may lead to recurrence.

Deep Cervical fascia constitutes Carotid Sheath which majorly covers the important structures of neck. It encorporates important structures like Common Carotid Artery and its branches, Internal Jugular Vein and X<sup>th</sup> cranial nerve i.e Vagus. Vagus is found posteriorly inbetween the carotid artery and Internal jugular vein. Ansa cervicalis is created by the descendens cervicalis and desending hypoglossi which carries 'C1'(superior root) 'C2' and 'C3' (inferior root) fibres and is encorporated anteriorly,and cervical sympathetic chain is encorporated directly posterior to the carotid sheath in prevertebral fascia. The carotid sheath covers IX, XI and XII nerve which has subdivisons in the upper part. Superiorly Carotid Sheath is fixed to the part of carotid canal and jugular foramen also fibrous adhesions of Internal Jugular Vein adheres to internal surface of Carotid Sheath. On Microscopic examination Carotid Sheath shows constitution of fibroelastic tissue, with varying wall thickness. In the study, Embryologically, it was seen that often there was invasion of fatty tissue and follicles of lymphoid tissue which are in close vicinity to Carotid Sheath.

Piffer et al in  $1980^{(8)}$  had demonstrated that the Carotid Sheath constitutes tissue of fibroelastic origin . KhafifHefetz (2004), Kolomvo's (2010) , Chaturvedi (2012), and Palliyalil M(2017) stated that Carotid Sheath constitutes vascular tissue of fibrofatty origin. There is lack of evidences which claims its removal during dissection of neck .The current prospective studies aims at investigating relationship of tumor characteristics such as site, size, stage, grade of the tumor which can conclude on removal or preservation of Carotid Sheath .

## **Objectives:**

- To evaluate the incidence of metastatic involvement of Carotid Sheath by Oral Squamous Cell Carcinoma.
- To evaluate the possible correlation of Tumor related risk factors (Site, Size, Depth of Tumor invasion, T-Stage and Histopathological grading) with metastatic Carotid Sheath involvement
- To evaluate the possible correlation of nodal characteristics (Number of cervical nodes, extracapsular spread and perinodal extension) with metastatic Carotid Sheath involvement

## Methodology:

## **Trial Study Design:**

After taking approval from Institutional Ethics committee(Ref no-DMIMS(DU)/IEC/2018-19/7502),the current study will be performed in Department of Oral surgery, SPDC and H ,Wardha.80 patients will be selected from Department of Oral surgery, SPDC, Wardha after taking informed consent .It is CROSS-SECTIONAL TYPE OF STUDY

## **INCLUSION CRITERIA:**

All Patients with Oral Squamous Cell Carcinoma of head and neck who have undergone neck dissections in Sharad Pawar Dental College, Wardha.

- 1. Subjects with histopathologically confirmed ofOral Squamous Cell Carcinoma
- 2. Patients with resectable primary Oral Squamous Cell Carcinoma.
- 3. Patients who do not have any history of any previous treatment such as Surgery, Chemotherapy, Radiotherapy, or both.
- 4. Patients in whom primary tumor extirpation, Neck dissection is performed with a curative intent.

## **EXCLUSION CRITERIA:**

1. Patients who are not fit for undergoing treatment under General Anesthesia.

- 2. Patients in whom primary tumour excision was performed without neck dissection.
- 3. Patients with Multiple Primary Tumors.
- 4.  $T_{4b}$  tumours extending to the infra temporal fossa, maxillary sinus, orbit and base of tongue.
- 5. Subjects having carotid bruit or with masses in neck which are in close vicinity to carotid sheath
- 6. Subjects having any mass in neck region which is encircling  $>270^{\circ}$  carotid artery.

The data will be collected from Sharad Pawar Dental College and Hospital. In this Crosssectional study, histopathologically confirmed cases of Squamous cell carcinoma will undergo neck dissection. 80 patients from the Out Patient Department (OPD) of the Department of Oral and Maxillofacial Surgery, Sharad Pawar Dental College and Hospital, Sawangi(M), Wardha will be included. The data collection will be done from October 2018 to May 2020.

Informed consent will be filled from all the patients who will be involved in this study, who will undergo neck dissections. Histologically proven OSCC cases will be considered and the extent of the disease will be staged by TNM staging (clinically, Acc to AJCC 7<sup>th</sup> EDITION)<sup>(9)</sup>. The Carotid sheath harvesting will be performed according to established surgical oncologic principles, in this procedure, Extension will be done for removal of Carotid sheath superiorly and inferiorly extending from posterior belly of Digastric and upto level of superior belly of Omohyoid muscle (mid-jugular Lymphnode) respectively. Fixation of resected specimen will be done by using 10% formalin and will be sent to Oral Pathology and Microbiology Department, Sharad Pawar Dental College and Hospital. . The probability for cancer cells, present within the lymphatic vessels on the resected specimen of carotid sheath will be analysed by monoclonal Ab pan-cytokeratin which will show microscopic changes for metastasis. Microsections (5µ serial section) staining by Haematoxylin & Eosin will be analysed by pathologist under light microscope. The positive specimens will be analysed by Immunohistochemistry Staining to rule out presence of occult metastasis which invades carotid sheath and harbours intra-luminal emboli of metastasis in lymphatic vessels. 4µ thick sections will be taken on silane coated slides and analysed using IHC markers by CD34 and pancytokeratin Lymphatic vessels and blood vessels can be differentiated by some characteristic features which includes- 1) Irregular thin borders 2) Absence of tunica media 3) Lack of RBC's in the lumen. Possibility of cancer cells present in lymphatics, analysed by monoclonal Ab pan-cytokeratin which will show microscopic changes for metastasis along with Immunohistochemistry marker CD34.

Outcome: To avoid removal of Carotid Sheath in cases where nodal invasion is absent. Conservation of Carotid Sheath will protect the important structures in neck region and minimize the post-surgical sequelae.

Sample size: 80 Patients

# **Expected Results:**

In cases where Carotid Sheath is not grossly involved, removal of Carotid Sheath is not recommended. Histologically Carotid Sheath may harbour dilated lymphatic vessels, lymphocytes aggregates and neutrophils. Carotid Sheath, however, would not harbour any metastatic tumour emboli from primary Oral Squamous Cell Carcinoma.

## **Discussion:**

Oral Squamous Cell Carcinoma is the most frequent of head and neck malignancies in which Surgically performing neck dissection remains a standardized treatment, which is associated with certain morbidity and mortality. Many studies on oral squamous cell carcinoma have been reported from this region<sup>10,11,12</sup>. Lohe et al reported on evaluation of correlation of serum lipid profile in patients with oral cancer and precancer<sup>13</sup>. Studies on different biochemical factors associated with oral cancer were reported by Mallick et al <sup>14</sup>, Chole et al<sup>15</sup> and Korde et al<sup>16</sup>. Agrawal et al reported about Touch Imprint Cytology as an alternative to frozen section in intraoperative assessment of cervical metastasis in oral squamous cell carcinoma<sup>17</sup>. Various procedure are planned to remove the lymph nodes of the neck thereby sacrificing anatomical structures of the neck which are associated with functional and aesthetical losses. Carotid sheath has been assessed for being a potential area of metastasis. However literature shows nearly no evidence of this trait. It is important to know the correlation of carotid sheath and the lymphoid aggregates which was mentioned in the review of literature.Piffer et al in 1980<sup>(8)</sup> had demonstrated that the Carotid Sheath constitutes tissue of fibroelastic origin . Khafif Hefetz (2004), Kolomvo's (2010) and Chaturvedi (2012), Palliyalil M(2017) stated that Carotid Sheath constitutes vascular tissue of fibrofatty origin. There is lack of evidences which claims its removal during dissection of neck. Preserving the sheath helps in decreasing the operative time and stress as well as escaping of direct action on the carotid artery and vital structures encased by the carotid sheath. The present prospective study will help us to evaluate the incidence of metastatic involvement of Carotid Sheath, in Oral Squamous Cell Carcinoma patients and if no such involvement seen than preservation of Carotid Sheath will help by avoiding damage to vital structures during neck dissections, Reduce operating time and also act as postoperative barrier against postoperative radiations and infections to vital structures.

# **Conclusion:**

Therefore this study which will be conducted on Oral Squamous Cell Carcinoma patients who will undergo neck dissection and if they have no invasion of the tumor into the carotid sheath, so it will strongly indicate that we can modify the neck dissections limiting upto the level of carotid sheath and sparing it intact for major advantages it offers . Not only for surgical safety but also for the shield it provides post operatively for further adjuvant radiation therapy

## **References:**

- [1] Sagowski C, Kehrl W, Metternich FU, Wenzel S. The prognostic impact of metastatic pattern of lymph nodes in patients with oral and oropharyngeal squamous cell carcinomas. European Archives of Oto-Rhino-Laryngology. 2004 May 1;261(5):270–5.
- [2] Johnson JT, Myers EN. Extracapsular spread of squamous carcinoma in cervical metastasis. In: Jacobs C, editor. Cancers of the Head and Neck [Internet]. Boston,

MA: Springer US; 1987 [cited 2019 Dec 11]. p. 11–20. Available from: http://link.springer.com/10.1007/978-1-4613-2029-6\_2

- [3] Khafif-Hefetz A, Leider-Trejo L, Medina JE, Gil Z, Fliss DM. The carotid sheath: An anatomicophathologic study. Head Neck. 2004 Jul;26(7):594–7.
- [4] Byers RM, Clayman GL, McGill D, Andrews T, Kare RP, Roberts DB, et al. Selective neck dissections for squamous carcinoma of the upper aerodigestive tract: patterns of regional failure. Head Neck. 1999 Sep;21(6):499–505.
- [5] Cleland-Zamudio SS, Wax MK, Smith JD, Cohen JI. Ruptured internal jugular vein: A postoperative complication of modified/selected neck dissection. Head Neck. 2003 May;25(5):357–60.
- [6] Timon CVI, Brown D, Gullane P. Internal jugular vein blowout complicating head and neck surgery. J Laryngol Otol. 1994 May;108(5):423–5.
- [7] Chaturvedi P, Vaishampayan SS, Nair S, Nair D, Pawar P, Kane S. Routine removal of the carotid sheath as part of neck dissection is unnecessary if grossly uninvolved as seen intra-operatively. International Journal of Oral and Maxillofacial Surgery. 2012 May;41(5):576–80.
- [8] Piffer CR. Mesoscopic and microscopic study of the carotid sheath. Acta Anatomica. 1980;106(4):393–9.
- [9] Edge SB, Compton CC. The American Joint Committee on Cancer: the 7th Edition of the AJCC Cancer Staging Manual and the Future of TNM. Ann Surg Oncol. 2010 Jun;17(6):1471–4.
- [10] Chaudhary, Minal, Amol Ramchandra Gadbail, Gaurav Vidhale, Mugdha P. Mankar (Gadbail), Shailesh M. Gondivkar, Madhuri Gawande, and Swati Patil. "Comparison of Myofibroblasts Expression in Oral Squamous Cell Carcinoma, Verrucous Carcinoma, High Risk Epithelial Dysplasia, Low Risk Epithelial Dysplasia and Normal Oral Mucosa." *HEAD & NECK PATHOLOGY* 6, no. 3 (September 2012): 305–13. https://doi.org/10.1007/s12105-012-0335-x.
- [11] Gadbail, Amol Ramchandra, Minal Chaudhary, Madhuri Gawande, Alka Hande, Sachin Sarode, Satyajit Ashok Tekade, Sheetal Korde, et al. "Oral Squamous Cell Carcinoma in the Background of Oral Submucous Fibrosis Is a Distinct Prognosis." Clinicopathological Entity with Better JOURNAL OF ORAL PATHOLOGY & no. (July 448-53. *MEDICINE* 46, 6 2017): https://doi.org/10.1111/jop.12553.
- [12] Korde, Sheetal D., Anjan Basak, Minal Chaudhary, Madhur Goyal, and Anjali Vagga. "Enhanced Nitrosative and Oxidative Stress with Decreased Total Antioxidant Capacity in Patients with Oral Precancer and Oral Squamous Cell Carcinoma." ONCOLOGY 80, no. 5–6 (2011): 382–89. https://doi.org/10.1159/000329811.
- [13] Lohe, Vidya K., Shirish S. Degwekar, Rahul R. Bhowate, Ravindra P. Kadu, and Suwarna B. Dangore. "Evaluation of Correlation of Serum Lipid Profile in Patients with Oral Cancer and Precancer and Its Association with Tobacco Abuse." *JOURNAL OF ORAL PATHOLOGY & MEDICINE* 39, no. 2 (February 2010): 141–48. https://doi.org/10.1111/j.1600-0714.2009.00828.x.

- [14] Mallick, S., R. Patil, R. Gyanchandani, S. Pawar, V. Palve, S. Kannan, K. A. Pathak, M. Choudhary, and T. R. Teni. "Human Oral Cancers Have Altered Expression of Bcl-2 Family Members and Increased Expression of the Anti-Apoptotic Splice Variant of Mcl-1." *JOURNAL OF PATHOLOGY* 217, no. 3 (February 2009): 398–407. https://doi.org/10.1002/path.2459.
- [15] Chole, Revant H., Ranjitkumar N. Patil, Anjan Basak, Kamlesh Palandurkar, and Rahul Bhowate. "Estimation of Serum Malondialdehyde in Oral Cancer and Precancer and Its Association with Healthy Individuals, Gender, Alcohol, and Tobacco Abuse." *JOURNAL OF CANCER RESEARCH AND THERAPEUTICS* 6, no. 4 (December 2010): 487–91. https://doi.org/10.4103/0973-1482.77106.
- Albrecht, U., Stangeb, R., & Schermuly, N. (2020). Efficacy and Safety of The Herbal Combination Containing Tropaeoli Majoris Herba and Armoraciae Rusticanae Radix in Patients Suffering from Uncomplicated, Acute Rhinosinusitis: A Randomized, Double-Blind, Placebo Controlled, Two-Arm, Parallel Group, Phase. Journal of Current Medical Research and Opinion, 3(10), 665-681. https://doi.org/10.15520/jcmro.v3i10.350
- Korde (Choudhari), Sheetal, Gokul Sridharan, Amol Gadbail, and V. Poornima. "Nitric Oxide and Oral Cancer: A Review." *ORAL ONCOLOGY* 48, no. 6 (June 2012): 475–83. https://doi.org/10.1016/j.oraloncology.2012.01.003.
- Agarwal, Anchal, Nitin Bhola, Rajanikanth Kambala, and Rajiv M. Borle. "Touch Imprint Cytology: Can It Serve as an Alternative to Frozen Section in Intraoperative Assessment of Cervical Metastasis in Oral Squamous Cell Carcinoma?" *JOURNAL OF ORAL AND MAXILLOFACIAL SURGERY* 77, no. 5 (May 2019): 994–99. https://doi.org/10.1016/j.joms.2019.01.011.