Sentinel Lymph Node Biopsy Versus Elective Neck Dissection in Evaluation of N0 Neck in Patients with Oral and Oropharyngeal Squamous Cell Carcinoma.

A meta-analysis study
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List of abbreviations

OCSCC	:	Oral cavity squamous cell carcinoma
OPSCC	:	Oropharyngeal squamous cell carcinoma
cN+	:	Clinical node positive.
cN0	:	Clinical node negative.
CT	:	Computed tomography.
DWI	:	Diffusion weighted Imaging.
false +ve	:	False positive.
false –ve	:	False negative.
FDG-PET	:	Fluorodeoxyglucose positron emission tomography.
HNSCC	:	Head and neck squamous cell carcinoma.
LN	:	Lymph nodes.
MRI	:	Magnetic resonance imaging.
PET	:	Positron emission tomography.
PET/CT	:	Combined positron emission tomography and computed tomography.
QUADAS	:	Quality assessment for studies of diagnostic accuracy.
SCC	:	Squamous cell carcinoma.
SN	:	Sentinel node.
SLN	:	Sentinel lymph node.
SNB	:	Sentinel node biopsy.
SLNB	:	Sentinel lymph node biopsy.
SND	:	Selective neck dissection.
SNET	:	Sentinel node European trial.
END	:	Elective neck dissection.
ENI	:	Elective neck irradiation.

ECS	:	Extracapcular spread.
Tc99	:	Technetium-99
true +ve	:	True positive.
true –ve	:	True negative.
US	:	Ultrasound.
USgFNAC	:	Ultrasound guided fine needle aspiration cytology.
~	:	Nearly

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INTRODUCTION

Oral cavity squamous cell carcinoma (OCSCC) and oropharyngeal squamous cell carcinoma (OPSCC) are considered an important part of the global burden of cancer, mainly due to the widespread use of tobacco and alcohol. [(1)]

The most important prognostic factor is the presence of cervical lymph node metastases, which can decrease the 5-year survival rates to lower than 50%. [(2)]

Exact staging of the neck is therefore crucial in managing this type of cancer. Staging by palpation and imaging techniques (e.g. MRI, CT, ultrasound-guided fine needle aspiration cytology (USgFNAC) are not sensitive enough in detecting micrometastases, resulting in a high incidence of occult metastases in the neck. [(3)] In the literature rates between 23% and 43% have been reported. [(4)] Because of this, elective neck dissection (END) is the standard of care in clinically negative necks (cN0) of early stage (T1/T2) oral cavity and oropharyngeal squamous cell carcinomas in most institutions. However, this implies over treatment and treatment associated morbidity in the majority of patients. Sentinel lymph node biopsy (SLNB) has emerged as an alternative or additional staging procedure. [(5)]

The sentinel node concept states that the spread of a tumor is embolic in nature, via the lymphatics to the first-echelon lymph node(s) encountered in the regional draining basin. These represent the lymph nodes most likely to harbor occult metastases, and are designated the sentinel lymph nodes. [(6)]

By definition, the sentinel lymph node is the first draining lymph node to receive lymphatic drainage from a

primary tumor of a specific site. In case of lymphatic spread, the lymphatic drain will first pass to the SLN. All the following nodes may be reached only subsequently by the disease. [7]

Excisional biopsy and pathological evaluation of the SLNs therefore allows for prediction of the disease status of the remaining cervical lymph node basin, potentially avoiding the need for a neck dissection. Sentinel lymph nodes need not be those closest to the tumor, and there may be multiple SLNs. With the application of early dynamic lymphoscintigraphy (LSG), lymphatic channels are usually visualized, and nodes on a direct drainage pathway may be distinguished. The practical approach may include the combination of available detection techniques. [6]

SLNB is a minimally invasive technique, performed in conjunction with radiotracer injection and lymphoscintigraphy. This allows the surgeon to identify and excise targeted upper echelon lymph nodes that drain the site of a primary malignancy for the laboratory detection of what would otherwise be subclinical nodal metastases. This technique offers a less invasive means of staging lymphatic basins in a patient with a primary malignancy, and permits detailed histological,immunohistochemical, and molecular examination of at least the first echelon (Frequently second and rarely third) lymph node basin for clinically occult micro- and conventional metastases(clinical-stage N0). Use of this technique may potentially avoid overtreatment of patient with oral or oropharyngeal squamous cell carcinoma who undergo elective neck dissection and are subsequently declared pathological N0, and hence reduce neck dissection-associated morbidity. [8]

Classically, neck dissection has been divided into: a) therapeutic, when it treats lymph node metastases found during physical exam or imaging studies; b) elective, when

lymph node metastases is not found clinically or by imaging, but the risk of microscopic metastases is higher than the risk associated with addition of a surgical procedure and its morbidity.

Finally, although all these strategies have attempted to avoid unnecessary neck dissections, the number of negative END could still be as high as 80%. [9]

The amount and quality of information currently available does not offer a definitive answer to the question of the prognostic effect of END. Furthermore, the recent introduction of sentinel lymph node biopsy in the diagnosis and treatment of head and neck cancer,has brought back the old question regarding the clinical usefulness of elective neck dissection. [9]

SLNB is an alternative to END for the management of T1/T2 N0 oral and oro-pharyngeal squamous cell carcinomas and is also finding application to head and neck cancer at other sites.The main clinical aim of sentinel node biopsy is to achieve better staging and there is now evidence that the procedure reduces morbidity. [10] In recent studies using radiotracers, the diagnostic accuracy and the localization rate reaches almost 100%. [11]

Because of the need to accurately stage the neck and to treat only those most likely to benefit from therapy, much interest has arisen in sentinel lymph node biopsy (SLNB). The validity of the concept of SLNB is based on the fact that tumor cells will spread from the primary site to a single node or group of nodes (the sentinel nodes), before progressing to the remainder of the lymph nodes. [12] **i.e.** if the sentinel node is positive for disease, the patient's neck is considered to harbor disease whether any further deposits are found on

histological examination subsequently and therefore there are **no false-positive cases in this scenario**.

Meta-analysis is the statistical method used in this study to determine the overall diagnostic value of SLNB versus END in evaluation of CN0 neck in patients with OCSCC and OPSCC.

Meta-analysis is a quantitative statistical procedure that synthesizes finding across many studies, overcoming the problems of small samples and diverse outcomes and programs. **(13)**

Aim of the work

The Aim of this work is to assess:

The overall diagnostic value of sentinel lymph node biopsy versus elective neck dissection in evaluation of cN0 neck in patients with oral and oropharyngeal squamous cell carcinoma.

Review of literature

Anatomy of Cervical Lymph Node Groups:

The patterns of spread of cancer from various primary sites in the head and neck to the cervical lymph nodes (LN) have been documented by retrospective analysis of large series of patients undergoing neck dissection. The nodal groups at risk for involvement are widespread throughout the neck, extending from the mandible and skull base superiorly to the clavicle inferiorly and from the posterior triangle of the neck laterally to the midline viscera and then to the contralateral side of the neck. It is now recommended that the lymph node groups in the neck be categorized according to the level system originally described by the Memorial Sloan-Kettering Group **(Fig.1)**. [14]

Division of Neck Levels By Sublevels :

The 2001 report of the American Head and Neck Society's Neck Dissection Committee recommended the use of sublevels for defining selected LN groups within levels I, II, and V on the basis of the biologic significance, independent of the larger zone in which they lay. These are outlined in **(Fig. 1)** as sublevels IA (submental nodes), IB (submandibular nodes), IIA and IIB (together composing the upper jugular nodes), VA (spinal accessory nodes), and VB (transverse cervical and supraclavicular nodes). The boundaries for each of these sublevels are defined in **Table 1.** [14]

(Table 1) Lymph Node Groups Found within the Six Neck Levels and the Six Sublevels (fig.1)

Lymph Node Group	Description
Submental (sublevel I_A)	LN within the triangular boundary of the anterior belly of the digastric muscles and the hyoid bone; these nodes are at the greatest risk of harboring metastases from cancers arising from the floor of the mouth, anterior oral tongue, anterior mandibular alveolar ridge, and lower lip.
Submandibular (sublevel I_B)	LN within the boundaries of the anterior belly of the digastric muscle, the stylohyoid muscle, and the body of the mandible, including the preglandular and postglandular nodes and the prevascular and postvascular nodes. The submandibular gland is included in the specimen when the lymph nodes within this triangle are removed. These nodes are at greatest risk for harboring metastases from cancers arising from the oral cavity, the anterior nasal cavity, and the soft tissue structures of the midface and the submandibular gland.
Upper jugular (sublevels II_A and II_B)	LN located around the upper third of the internal jugular vein and the adjacent spinal accessory nerve, extending from the level of the skull base above to the level of the inferior border of the hyoid bone below. The anterior (medial) boundary is the stylohyoid muscle (the radiologic correlate is the vertical plane defined by the posterior surface of the submandibular gland), and the