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RECENT ADVANCES IN SURGERY



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SURGERY 39

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Chapter 6

Neck dissection in head and neck cancers

Anshuman Singh, Akshay Anand, Abhinav Arun Sonkar

INTRODUCTION

Surgery has been the first-line management modality for most cancers of the head and neck except for cancers of a few primary sites such as posterior third of tongue, nasopharynx and a few subsites of the larynx. Chemotherapy and radiotherapy are used either as adjuncts to surgery or for palliation in cases of advanced disease, radiation has also been used as a modality equivalent to surgery in select cases. The surgical approach in any cancer of the head and neck involves resection of the primary tumor along with neck dissection for evaluation of the cervical lymph nodes for any evidence of metastasis, which if found involved, the expected survival is reduced to half. This highlights the significance of neck dissection as an equally important component of the treatment of any cancer of the head and neck. The extent of cervical lymph node dissection of cancers of the head and neck has long been a matter of debate. Their importance, evaluation strategies and recent developments are discussed under the subsequent sections.

IMPORTANCE OF LYMPHATIC INVOLVEMENT

Lymph node metastasis is the single most important prognostic factor in malignancies of the upper aerodigestive tract. More than 50% cases of squamous cell carcinoma of the oral cavity have lymph node metastases and the presence of nodal metastases reduces survival by nearly 50%.[1] Reports from the American Cancer Society indicate that squamous cell carcinomas (SCCs) of the oral cavity and pharynx have regionally disseminated disease in nearly 40% of patients.[2] Cancers of these regions are characterized by poor prognosis with an overall 5-year survival rate of only about 50–60% even after successful treatment of the primary tumor. This dismal outcome even after successful treatment of the primary tumor and poor long-term prognosis is probably due to high rates of regional recurrences due to inadequate treatment of lymphatic metastases which usually occur early in the course of the disease. The presence of regional lymph nodal metastases acts as an indicator of the ability of the primary tumor to metastasize locoregionally or systemically.[3] This may explain the dramatic fall in survival rate which occurs with the involvement of the locoregional lymph nodes in cancers of the head and neck. There is a continuous decrease in the 5-year survival rates as the stage of disease progresses from 83% in early stage (stage I and II), to 62% in regionally advanced disease (III, IVa, IVb) to approximately 38% in distant metastatic disease (stage IVc).[4] Early and regionally advanced disease can benefit from adequate dissection of the neck nodes with higher 5-year survival rates. Thus knowledge of locoregional lymphatic drainage and histopathological examination of cervical lymph nodes play the most important role in adequate control of disease alongside treatment of the primary tumor.

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EVALUATION OF CERVICAL LYMPH NODES: DIAGNOSTIC DILEMMA IN CLINICALLY N0 (CN0) NECK

Lymphatic drainage of the head and neck involves a complex architecture of approximately 300 lymph nodes; as a result an assured diagnosis of lymphatic metastasis in primary tumors of the head and neck remains a challenge. Lymphatic metastasis from head and neck primaries usually occurs in a sequential and predictable manner. Patients with primary malignancy of the oral cavity with no clinical evidence of lymph nodal metastasis preoperatively are the patient group in which estimation of the pattern and sequence of nodal metastasis is required to decide on the extent of clearance of neck nodes required.

The risk of clinically undetectable micrometastasis in patients with clinically node-negative disease varies with different primary sites and so does the extent of lymph node clearance that is required. Furthermore, none of the current diagnostic modalities, including clinical examination, have adequate sensitivity and specificity to avoid the need for surgical staging of cervical lymph node status. The sensitivity of inspection and palpation alone for detection of cervical nodes is 60–70% while the corresponding values of magnetic resonance imaging (MRI) and computed tomography (CT) are between 65% and 88%.[5,6] Merritt et al.[7] in a systematic review of studies comparing palpation with CT found a sensitivity of 75% and 83% and a specificity of 81% and 83% for palpation and CT, respectively.

However, ultrasonography (US) allows a detailed evaluation of the intranodal architecture and when coupled with US guided aspiration cytology, its sensitivity and specificity are 80% and 98% respectively with the added advantage of repeatability whenever required.[8] Hence, US is considered superior to both CT and MRI for preoperative evaluation of lymphatic metastasis. However, 15–25% patients with occult micrometastasis in neck nodes could be missed even on sonography. Giancarlo et al.[9] comparing palpation with US found no difference between the methods with a sensitivity of only 82% and specificity of 80% for palpation. Haberal et al.[10] reported a sensitivity of 64%, 72%, and 81% and a specificity of 85%, 96% and 96%, for palpation, US and CT. The addition of positron emission tomography (PET) in the preoperative armamentarium has not been demonstrated to be superior to other modalities. A meta-analysis showed that PET examination may achieve a sensitivity of up to 80% and a specificity of 86%, although, it may miss nearly half of the cases which later prove to be positive for lymphatic metastasis, when neck dissection is performed.[11] The routine clinical application of PET for nodal evaluation of head and neck cancers including clinically N0 neck is not supported by the literature to date.[12] The only established advantage of PET-CT is in detection of residual disease post chemoradiation where it has a higher sensitivity and specificity than CT or MRI, with a higher negative predictive value for detection of malignancy. This has further been proven by retrospective pathological evaluation of neck dissection specimens post chemoradiation which demonstrated a correlation with PET scan results.[13,14] In patients who have a clinically negative neck post chemoradiation, PET-CT performed 12 weeks post chemotherapy is 90% reliable and further imaging becomes optional.[15,16] For patients with equivocal PET-CT results, a recent study suggests a repeat PET-CT 4–6 weeks later may help to identify those patients who can be safely kept under observation without the need for surgery for suspected disease progression or residual disease.[17]

The gold standard for evaluation of neck nodes is histopathological examination after neck dissection. The 15–25% of patients that harbor occult micrometastases (<2 mm) may be missed on routine microscopic examination. Immunohistochemistry for cytokeratin 5 and 14, are an important adjunct to the routine microscopic examination in the detection of such

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cases. Another option is the use of quantitative RT-PCR for cytokeratins in nodal specimens. Although it may further improve the diagnostic accuracy for the occult micrometastasis[18,19] its routine use has been questioned keeping in mind the cost-effectiveness of the procedure.

EVOLUTION OF SURGERY FOR CERVICAL LYMPH NODE METASTASES

Neck dissection, as first described by Jawdynski in the 19th century underwent several changes until Crile described the concept of "radical neck dissection" (RND) in 1905 and this has been the gold standard for clinically palpable neck metastasis for many decades. It involves removal of ipsilateral levels I to V nodes along with the sternocleidomastoid muscle, internal jugular vein, and spinal accessory nerve (SAN). This procedure though oncologically superior was associated with significant postoperative morbidity. Most distressing was the classical "shoulder syndrome" due to sacrifice of the SAN which resulted in shoulder droop, scapular dyskinesia and pain around the shoulder joint. In 1962, Suarez introduced the concept of modified radical neck dissection (MRND); with preservation of sternocleidomastoid, internal jugular vein and the SAN, either one, two or all of these structures. The biggest advantage of MRND was preservation of SAN. The change in surgical technique is intrinsic to the philosophy of preventive treatment and led to dramatic improvement in the postoperative functional and cosmetic results without significant loss in the therapeutic efficacy. The advent of MRND led to sparing of the SAN, which due to the prevention of shoulder syndrome led to a considerable reduction in postoperative morbidity associated with RND without any significant reduction in the therapeutic efficacy. Subsequently, an improved understanding of the pattern of lymphatic spread in neck nodes led to conservation of uninvolved nodes, a concept that was called selective neck dissection. It involved removal of only those levels, which were at highest risk of metastasis while sparing the rest of the nodes unlike RND and MRND, which involved removal of all nodes from level, I to V irrespective of their involvement. As of now, surgery for cervical nodal metastases can be broadly classified into two categories for better understanding: (1) comprehensive neck dissection (for clinically N+ cases) and (2) selective neck dissection (for clinically N0 cases).[20]

Comprehensive neck dissection involves the surgical removal of all the structures in the lateral aspect of neck and includes the following procedures:

- Classic RND (levels I to V nodes, sternocleidomastoid muscle, internal jugular vein, SAN, and submandibular salivary gland)
- Extended RND (i.e. resection of additional regional lymph nodes or sacrifice of other structures such as cranial nerves, muscles, or skin in addition to the structures removed in classical RND)
- Modified radical neck dissection type I (MRND-I), with selective preservation of the SAN
- Modified radical neck dissection type II (MRND-II), with preservation of the SAN and the sternocleidomastoid muscle but resection of the internal jugular vein.
- Modified radical neck dissection type III (MRND-III), with preservation of the SAN, internal jugular vein, and sternocleidomastoid muscle.

Selective neck dissection involves removal of selected groups of lymph nodes at risk of micrometastasis in a clinically N0 neck.[21,22] This operation comprises:

- Supraomohyoid neck dissection (SOHND), which encompasses dissection of lymph nodes at levels I, II, and III (and sometimes superior portion of level IV)[20] preferred in SCCs of oral cavity.

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- Jugular node dissection, which includes dissection of lymph nodes at levels II, III, and IV preferred in primary tumors of pharynx.
- Anterolateral neck dissection, which includes dissection of lymph nodes at levels I, II, III, and IV preferred in primary tumors of tongue.
- Posterolateral neck dissection, which includes lymph nodes in the suboccipital triangle, posterior triangle of the neck, level V, and the deep jugular chain of lymph nodes at levels II, III, and IV for melanomas and squamous carcinomas of the posterior scalp.
- Central compartment neck dissection, which involves clearance of lymph nodes at level VI in the central compartment of the neck adjacent to the thyroid gland and in the tracheoesophageal groove for thyroid cancer preferred in thyroid malignancies.

THERAPEUTIC APPROACH IN CLINICALLY N0 CANCERS: ROLE OF ELECTIVE VERSUS THERAPEUTIC NECK DISSECTION

The question arises as to why in clinically N0 neck, the nodes need to be treated? When lymph node involvement is not found clinically or by imaging, but the risk of microscopic metastases (15–20% or more) is higher than the risk associated with addition of a surgical procedure and its morbidity, neck dissection becomes a viable option.

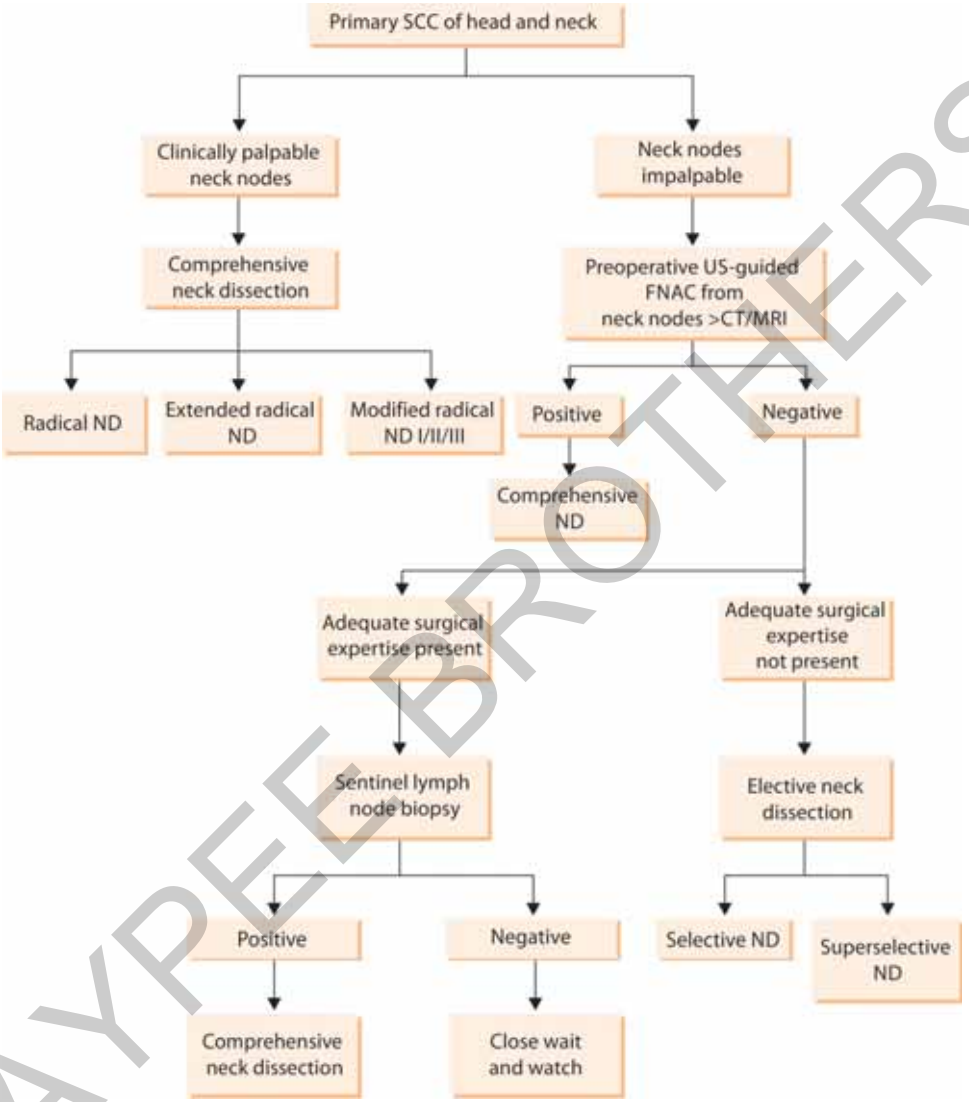
The involvement of lymph nodes is dependent on many factors which includes the T stage which reflects tumor burden or invasiveness and is thus correlated with the risk of nodal metastasis for any given primary site.[3] Overall, the risk for metastasis is less than 15% for T1, 15–30% for T2, 30–50% for T3 and up to 75% for T4 head and neck primary SCCs. For a particular T stage, the subset of disease with endophytic and poorly differentiated tumors have greater risk of nodal metastasis than exophytic and well-differentiated tumors respectively **(Flowchart 6.1)**. Tumor thickness, however, is considered an independent risk factor for nodal metastasis in tumors of tongue and floor of mouth with 4 mm being considered the cut off, with thicker tumors bearing greater risk.[3]

Diagnostically the most definite approach for accurate evaluation of cervical lymph nodes is histopathological examination of the lymph nodes. The timing of neck dissection in clinically N0 neck has been a matter of debate for a long time. Whether to perform prophylactic "elective" neck dissection at the time of primary surgery or following a close wait and watch policy after excision of the primary tumor and performing "therapeutic" neck dissection only once nodal relapse occurs, has been a long-standing debate. Both procedures have their merits and drawbacks. Elective dissection has many advantages such as accurate evaluation of occult micrometastases, delineation of the extent of lymphatic metastases and identification of poor prognostic factors for nodal recurrence (extracapsular spread, perineural or perivascular invasion, tumor emboli in lymphatics, central necrosis) and consequently selecting the patients for adjuvant radiotherapy. On the other hand, it leads to high number of negative neck dissections and associated morbidity. Therapeutic neck dissection has the advantage of avoiding unnecessary neck dissections but with the associated risk of nodal relapse, which may sometimes be advanced enough to be inoperable.

Studies to date do not provide a definitive indication to support management decision-making. The most effective way to evaluate the usefulness of elective neck dissection is to conduct a randomized controlled trial (RCT). To date there are 5 RCTs performed with this objective. Vandenbrouck et al.[23] in a randomized setting showed no significant advantage of elective neck dissection over close observation and follow-up. Fakih et al.[24] in their study

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Flowchart 6.1 Algorithm for management of neck nodes in primary squamous cell carcinomas (SCCs) of head and neck.



(FNAC: Fine-needle aspiration cytology; CT: Computed tomography; MRI: Magnetic resonance imaging; ND: Neck dissection).

indicated therapeutic advantage in terms of better overall and disease-free survival for the group of elective neck dissection. Kligerman et al.[25] in another randomized study with 67 cases and recently a multicenter randomized trial by Yuen et al.[26] described similar results in favor of elective neck dissection. The results in all the above-mentioned studies had limitations of small sample size. In 2015, D'Cruz et al.[27] in a large randomized study brought an end to the controversy when their analysis of 496 patients clearly proved an absolute overall survival benefit of 12.5% and a disease-free survival benefit of 23.6% for elective neck

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dissection in clinically N0 SCCs of the oral cavity over close wait and watch policy followed by therapeutic neck dissection at the time of nodal relapse. The superior benefit in the trial led to early termination of the study. Recently a meta-analysis combining the above five RCTs concluded there was an overall as well as disease-free survival benefit in favor of elective neck dissection.[28] Thus the evidence to date favors elective neck dissection performed at the time of resection of the primary tumor, which confers an overall survival benefit in patients with early stage, clinically node-negative oral squamous cell carcinoma. The extent of elective neck dissection to be carried out depends on the associated risk of lymphatic metastasis, which in turn depends on the location, and extent of the primary tumor as previously discussed. In primary tumors of the oral cavity with cN0 neck, the highest chance of nodal metastases is to the levels I to III lymph node levels and it is very rare for skip metastasis to occur to levels IV or V in the absence of involvement of level I, II or III. The incidence of skip metastases at level IV rises from 3% to 28%, depending upon the specific site of the primary tumor.[29,30]

As a result, in a clinically node-negative disease with primary tumor of the oral cavity, selective clearance of the levels I, II and III (supraomohyoid neck dissection) is usually sufficient without the need for comprehensive neck dissection. For cancers of the body of the tongue dissection should also involve removal of level IV lymph nodes keeping in mind the greater metastatic potential and more aggressive nature of the disease probably due to greater density of lymphatics. Studies have even reported isolated involvement of level IV lymph nodes only (skip metastasis) in primary lesions of the tongue in 10% of cases without involvement of level I to III lymph nodes. Similarly for primary tumors of the lateral part of oropharynx, hypopharynx and larynx with clinically undetectable nodes, the highest chances for micrometastasis is to the levels II, III, and IV with rare chance of skip metastasis to level I or V. Involvement of level V with primary lesions of oral cavity and clinically negative nodes is exceedingly rare. Thus in cases of clinically N0 of head and neck cancer, selective neck dissection is performed and it has been proven in many studies that nodal metastasis beyond the confines of an appropriate selective neck dissection is rare (<10%).[30-32]

LEVEL IIB DISSECTION AND ROLE OF SUPER SELECTIVE NECK DISSECTION

Level IIB removal has generated a lot of controversy and is discussed in the literature bearing in mind the high-risk of injury to the SAN during dissection of this group, as well as the low probability of its involvement in lymphatic metastasis of head and neck primaries. In selective neck dissection, shoulder function impairment has been observed in 21–60% of cases despite preservation of the SAN.[33,34] This functional injury despite anatomic integrity is probably due to close proximity of the SAN to the level IIB nodes and stretching of the nerve due to dissection performed in its vicinity. Level IIB nodal metastasis has been documented to be 5–10% in cN0 neck undergoing elective neck dissection.[35-37] It has also been stated that the oral cavity does not drain directly into level IIB[20,38,39] and also it is rarely involved in isolation. When involved it is accompanied by either clinically identifiable metastasis to other levels or occult metastasis of level IIA.

In a recent study, de Vicente et al.[40] described the prevalence of metastasis at level IIB was 0% in pathological proven N0 necks and 3.4% in pathological N+ necks, with an overall prevalence of 1.8% in oral cancer. Villaret et al.[41] in a multicentric trial has stated that the oral cavity has the highest overall prevalence of level IIB metastasis (10%) among head and neck SCCs, but these metastases are only found in 2% of cN0 cases. Pantvaidya et al.[42]

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described similar findings in tongue cancers (5%) and cancers of the retromolar trigone (6.2%) as subsites. Based on a meta-analysis, the frequency of nodal metastasis to level IIB in previously untreated OSCC is 6.0% (95% CI: 3.5–8.6).[43] Based on these findings, it can be concluded that inclusion of level IIB when performing elective neck dissection in cN0 cases might be unnecessary and can be avoided without significant risk of relapse, to prevent postoperative shoulder disability.

It has been established that an appropriately indicated selective neck dissection can achieve the same oncologic outcomes as modified therapeutic ones. An even more explicit neck dissection, termed superselective neck dissection, involves the compartmental removal of the fibrofatty tissue contents within the defined boundaries of two or fewer contiguous neck levels. Evidence from retrospective studies suggests that superselective neck dissection is oncologically proposed for two indications: (1) elective treatment of clinically N0 neck and (2) salvage treatment of persistent lymph node disease after chemoradiotherapy.[44] Evidence-based trials with a large number of cases can justify the idea of this type of neck dissection, which is presently a futuristic concept. This concept has led to further investigation of the role of preserving level IIB nodes during selective neck dissection for oral cavity cancers (other than cancer tongue) with clinically N0 neck to prevent SAN related injury. Robbins et al. have indicated that selective and superselective neck dissection, which spare function and minimize morbidity, are viable therapeutic alternatives for patients with residual disease confined to 1 level after various chemoradiation protocols.[45]

ROLE OF SENTINEL LYMPH NODE SAMPLING

The significance of sentinel node sampling was brought into consideration with the aim to reduce the need for elective neck dissection to a minimum, so as to prevent the morbidities associated with it. In head and neck cancers the complex lymphatic architecture and the high density of lymph nodes in the region resulted in failure to accurately determine the first draining nodes. As a result, some authors were of the opinion to remove at least 2–3 sentinel lymph nodes in order to exclude the false-negative results.[19] In an evaluation performed at the Department of Otolaryngology, Marburg, Germany, sampling of only one sentinel lymph node was associated with a false-negative rate of nearly 40%.[46] These results when compared with the complexity of dissection required in the sampling of sentinel nodes often in rather inaccessible areas and subsequent risks of intraoperative damage to non-lymphatic structures, do not support the use of sentinel node biopsy for evaluation of neck nodes in clinically N0 cancers in centers where surgical expertise is inadequate. Thus, as of now, selective node dissection at the time of primary surgery (elective neck dissection) seems to be a better alternative for a staging procedure rather than sentinel lymph node biopsy in centers where surgical expertise for sentinel node biopsy is not available. In centers with adequate surgical expertise, sentinel lymph node biopsy may be considered prior to neck dissection for histopathological examination in cases of cN0 head and neck cancers.

NATIONAL COMPREHENSIVE CANCER NETWORK 2016 GUIDELINES FOR HEAD AND NECK CANCERS

In the 7th edition of the American Joint Committee on Cancer (AJCC) staging manual, the words *resectable* and *unresectable* with respect to head and neck malignancies have been replaced by the terms moderately advanced, i.e. T4a and *very advanced*, i.e. T4b.[47] The reason is that there has never been a consensus regarding the *resectability* of any

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given tumor and it depends to a reasonable extent on the surgical expertise available and existing medical comorbidities. Thus, a designation of stage IV does not always designate unresectable disease. The National Comprehensive Cancer Network (NCCN) panel, in general, recommends single modality treatment with either surgery or radiotherapy for early stage cancers (stage I and II) and combined modality therapy for locally or regionally advanced disease (stage III and IV). However the final decision is guided by the specific site of the primary, stage and the pathologic findings. For neck dissection, NCCN follows the contemporary nomenclature of comprehensive and selective neck dissection based on the number of lymph node groups that are resected.[21] As per the NCCN guidelines, the chief role of selective neck dissections is to determine the patients who are candidates for possible adjuvant therapy (CT/RT or RT alone), although it may be used as treatment when the tumor burden is low, i.e. clinically N0,[48] whilst in cases with neck node metastasis comprehensive neck dissection is the preferred surgical modality. Sentinel node biopsy, although less accurate for floor of mouth cancers,[49,50] can help to identify occult cervical metastases[51-54] and can avoid the morbidities associated with neck dissection in cN0 neck and should be performed in centers with adequate surgical expertise.

CONCLUSION

The extent of lymph node metastasis is the single most important prognostic factor for head and neck cancer. US guided FNAC has been shown to be superior to CT and MRI but histopathological examination of neck nodes still remains the gold standard for assessment of nodal metastasis. The extent of neck dissection depends on the risk of lymphatic metastasis, i.e. site, extent and histomorphology of the primary tumor. Comprehensive and selective neck dissections should be performed when indicated. Elective node dissection has improved efficacy in terms of survival in clinically negative necks. Specific indications for sentinel lymph node biopsy and superselective dissection are still under evaluation.

Key points for clinical practice

- Extent of lymph node metastasis is the most important prognostic factor for head and neck SCC.
- US guided fine-needle aspiration cytology (FNAC) from neck nodes is superior to both CT and MRI scans for detection of nodal metastasis.
- Histopathological examination of neck nodes is gold standard for assessment of nodal metastasis.
- Immunohistochemistry is useful adjunct to HPE for detection of micrometastasis.
- Comprehensive neck dissection is indicated in clinically palpable cervical lymph nodes.
- Selective neck dissection is indicated in clinically undetectable cervical lymph nodes.
- Elective neck dissection is superior to therapeutic neck dissection in cN0 SCC of the oral cavity.
- The extent of neck dissection depends on the risk of lymphatic metastasis, i.e. site, extent and histomorphology of the primary tumor, i.e. elective neck dissection is selective neck dissection.
- Level IIB lymph nodes could be safely excluded while performing elective neck dissection in cN0 SCC of the oral cavity without significant risk of relapse.
- Sentinel LN biopsy could be used in place of elective neck dissection for diagnostic evaluation of neck nodes provided adequate surgical expertise is available.

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