# Current philosophy in the surgical management of neck metastases for head and neck squamous cell carcinoma

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**ABSTRACT:** Neck dissection is an important treatment for metastases from upper aerodigestive carcinoma; an event that markedly reduces survival. Since its inception, the philosophy of the procedure has undergone significant change from one of radicalism to the current conservative approach. Furthermore, nonsurgical modalities have been introduced, and, in many situations, have supplanted neck surgery. The refinements of imaging the neck based on the concept of neck level involvement has encouraged new philosophies to evolve that seem to benefit patient outcomes particularly as this relates to diminished morbidity. The purpose of this review was to highlight the new paradigms for surgical removal of neck metastases using an evidence-based approach. © 2014 Wiley Periodicals, Inc. *Head Neck* **37:** 915–926, 2015

**KEY WORDS: neck dissection, head and neck squamous cell carcinoma, neck metastasis, clinically negative neck, clinically positive neck**

## INTRODUCTION

The importance of cervical lymph node metastases as a prognostic factor in patients with head and neck squamous cell carcinoma (HNSCC) has long been recognized.[1] Their presence decreases survival by approximately 50% and improper management of these metastases increases regional failure. However, this does not mean that lymph node metastases are the only cause of poor prognosis. The discrepancy between a successful initial treatment of tumor and poor long-term prognosis is also related to comorbidities of the patients, recurrent primary tumor, second primaries, and distant metastases developing in the further course of the disease.[2]

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The radical neck dissection was introduced in the late 19th century[3–5] and represented the workhorse of treatment of cervical lymph node metastases for many decades. Starting in 1952, Suárez began to use a modified technique by preserving nonlymphatic structures. He named this procedure the "functional" or "conservative" neck dissection.[6] The foundation of this evolution was gleaned from his studies of the fascial compartments of the neck, together with the evidence, which demonstrated that nonlymphatic structures, such as muscles, nerves, and the internal jugular vein, were rarely directly involved by cancer. In 1985, Byers[7] reported on the removal of only the cervical lymph node groups that were at greatest risk for containing metastasis. Although this procedure was referred to as a modified neck dissection, it was subsequently more appropriately termed a "selective neck dissection," suggesting a more directed approach to reducing tumor burden in the neck compartments affected by metastases.

Patients undergoing neck dissection may suffer from some degree of morbidity, especially shoulder dysfunction, even after the application of these modifications to

TABLE 1. Current terminology of lymph node groups within levels.[9,10]

| Level | Content and boundaries |
|---|---|
| Level I (Submental and submandibular) | The lymph nodes between the mandible and hyoid bone. The posterior (lateral) boundary is the vertical plane defined by the posterior edge of the submandibular gland. This level is divided into 2 sublevels. |
| Sublevel IA (Submental) | The lymph nodes within the triangular boundary of the anterior belly of the digastric muscles and the hyoid bone. |
| Sublevel IB (Submandibular) | The lymph nodes within the boundaries of the anterior belly of the digastric muscle, the stylohyoid muscle, and the body of the mandible. The submandibular gland is usually included within the specimen when the lymph nodes of this triangle are removed. |
| Level II (Upper jugular) | The lymph nodes located around the upper third of the internal jugular vein and spinal accessory nerve, extending from skull base to the level of the inferior border of the hyoid bone. The anterior (medial) boundary is the vertical plane defined by the posterior edge of the submandibular gland and the posterior (lateral) boundary is the posterior border of the sternocleidomastoid muscle. |
| Sublevel IIA | The lymph nodes located anterior (medial) to the spinal accessory nerve. |
| Sublevel IIB | The lymph nodes located posterior (lateral) to the spinal accessory nerve. |
| Level III (Middle jugular) | The lymph nodes located around the middle third of the internal jugular vein extending from the inferior border of the hyoid bone (above) to the inferior border of the cricoid cartilage (below). The anterior (medial) boundary is the lateral border of the sternohyoid muscle, and the posterior (lateral) boundary is the posterior border of the sternocleidomastoid muscle. |
| Level IV (Lower jugular) | The lymph nodes located around the lower third of the internal jugular vein extending form the inferior border of the cricoid cartilage (above) to the clavicle below. The anterior (medial) boundary is the lateral border of the sternohyoid muscle and the posterior (lateral) boundary is the posterior border of the sternocleidomastoid muscle. |
| Level V (Posterior triangle group) | The lymph nodes located along the lower half of the spinal accessory nerve and the transverse cervical artery. The supraclavicular nodes are also included in the posterior triangle group. The superior boundary is formed by the sternocleidomastoid and trapezius muscles, the inferior boundary is the clavicle, the anterior (medial) boundary is the posterior border of the sternocleidomastoid muscle, and the posterior (lateral) boundary is the anterior border of the trapezius muscle. This level is also divided at the level of anterior cricoid arch into sublevels VA and VB. |
| Sublevel VA | Contents of level V above the level of anterior cricoid arch. |
| Sublevel VB | Contents of level V below the level of anterior cricoid arch. |
| Level VI (Anterior compartment group or central group) | The pretracheal and paratracheal nodes, precricoid (Delphian) node, and the perithyroidal nodes, including the lymph nodes along the recurrent laryngeal nerves. The superior boundary is the hyoid bone, the inferior boundary is the suprasternal notch, and the lateral boundaries are the common carotid arteries. |
| Level VII (Upper mediastinal group) | Contains the paratracheal lymph nodes and fibro-fatty tissue located between the suprasternal notch and the innominate artery. |

neck dissection. More recently, super-selective neck dissections, which are dissections limited to 2 levels, have been developed and applied clinically. A growing body of evidence indicates that favorable oncologic and functional results can be obtained when these procedures are used in the proper setting.

## Current classification of neck dissections and lymph node groups in the neck

The current and widely used classification and terminology of neck dissections was introduced in 1991[8] by a committee of the American Head and Neck Society and the American Academy of Otolaryngology–Head and Neck Surgery, and this terminology was updated in 2002[9] and 2008.[10] In the last update, lymph nodes in the neck were grouped in levels, as shown in Table 1.[9,10]

In the 1991 classification, neck dissections were classified as radical, modified radical, extended, and selective neck dissection. This classification recognized 4 types of selective neck dissections; lateral, posterolateral, supraomohyoid and anterior. However, in 2002, the committee recommended that the use of a more simplified and flexible classification be substituted for specific names. The rationale behind this change was the emergence of numerous variations in the compartmentalization and extent of neck dissections. According to the new recommendation, the acronym "SND" refers to "selective neck dissection" and the removed lymph node groups are depicted in brackets. For example, the "lateral neck dissection" of the 1991 classification is designated as SND (II–IV).

Recently, Ferlito et al[11] proposed a new classification for neck dissections, in which the procedures are not classified as radical, modified radical, and selective. Instead, any type of neck dissection is recorded as "ND" and node levels and nonlymphatic structures removed are indicated in brackets. For example, a radical neck dissection is designated as ND (I–V, SCM, IJV, CN XI), and a lateral neck dissection as ND (II–IV). The main advantage of this classification is that any type of neck dissection may be precisely described. For example, removal of a nonlymphatic structure during a selective neck dissection can be reported with this classification scheme, which was not possible with the previous methodology. It is

TABLE 2. The past and current classifications of neck dissection.[8–11]

| 1991 Classification | 2002 Classification | 2008 Update | 2011 Classification proposed by Ferlito et al. |
|---|---|---|---|
| (Committee for Head and Neck Surgery and Oncology of the American Academy of Otolaryngology–Head and Neck Surgery) | (American Head and Neck Society and Committee for Head and Neck Surgery and Oncology, American Academy of Otolaryngology–Head and Neck Surgery) | (American Head and Neck Society and Committee for Head and Neck Surgery and Oncology, American Academy of Otolaryngology–Head and Neck Surgery) | (Members of International Head and Neck Scientific Group) |
| Radical neck dissection | Radical neck dissection | Classification and terminology of neck dissection has not changed. | Any neck dissection is designated as "ND" and the removed lymph node levels or sublevels and/or non-lymphatic structures are denoted in parentheses |
| Modified radical neck dissection | Modified radical neck dissection | New recommendations have been made regarding the following: | |
| Selective neck dissection<br>• Supraomohyoid<br>• Lateral<br>• Posterolateral<br>• Anterior | Selective neck dissection: each variation is depicted by "SND" and the use of parentheses to denote the levels or sublevels removed | - Boundaries between levels I and II and between levels III/IV and VI<br>- Terminology of the superior mediastinal nodes (level VII)<br>- The method of submitting surgical specimens for pathologic analysis | |
| Extended neck dissection | Extended neck dissection | | |

anticipated that this proposed classification will soon gain international popularity and acceptance and will become a uniform international classification system endorsed by various head and neck societies (Table 2[8–11]).

## Neck dissection for head and neck squamous cell carcinoma with clinically negative neck

**Oral cavity squamous cell carcinoma with clinically negative neck.** Occult metastases have been demonstrated in 20% to 44%[12–20] of patients with oral cavity squamous cell carcinoma (SCC) whose neck is staged N0. Because there is general agreement that elective neck dissection is indicated when the risk of occult metastases exceeds 15% to 20%, most patients with clinically N0 oral cavity SCC undergo elective neck dissection. This approach results in overtreatment of the majority of patients.

Alternatively, an observation policy reserving neck dissection for salvage of regional recurrence can be followed. Studies have differed as to the value of such an observation compared to elective neck dissection. In a 1996 study of 47 patients with oral cavity SCC staged N0 treated between 1987 and 1992 and followed by observation of the neck using conventional methods (mostly palpation and patient self-observation), Andersen et al[21] reported that approximately two thirds of the patients developed N2 or N3 recurrent neck disease. The authors concluded that close follow-up is therefore essential to obtain comparable results with elective neck dissection.

A disease-specific survival advantage has been demonstrated toward elective neck dissection in a meta-analysis comparing elective neck dissection versus observation in clinically N0 oral cavity cancer.[22] However, in another review article, Monroe and Gross[23] reported that the current literature lacks evidence to support an advantage of elective neck dissection over a policy of watchful waiting.

The chief factor in determining the usefulness of follow-up by "observation" is the quality of initial and follow-up examination of the neck as well as a rigorous postoperative examination schedule. Flach et al[24] recently reported the results of observation ($n = 234$) versus elective neck dissection ($n = 51$) in a series of 285 patients with clinically N0 oral cavity cancer, after initial diagnostic workup using ultrasound-guided fine-needle aspiration cytology (FNAC) to detect occult lymph node metastases. In the observation group, 27.8% developed delayed metastases. Most of these delayed metastases required modified radical neck dissection followed by adjuvant radiotherapy. However, 5-year disease-specific and overall survival rates were almost identical for patients undergoing neck dissection for delayed metastases after observation (80.0% and 62.8%, respectively) and for patients undergoing elective neck dissection (81.3% and 64.2%, respectively). It is noteworthy that, in this study, ultrasound-guided FNAC was used during follow-up for early detection of initially missed metastases.

Sentinel lymph node biopsy (SLNB) has evolved as a possible alternative for elective neck dissection or "watchful waiting" in oral cancer. A recently published decision analysis study of different strategies for management of the N0 neck in early oral cavity SCC identified the sentinel lymph node procedure as the most cost-effective strategy.[25] This option offers a high accuracy in the detection of occult nodal metastasis[26–28] and excellent long-term disease control at the neck site in patients undergoing SLNB only.[29,30]

Although elective neck dissection may provide a better survival rate, most patients with a clinically N0 neck do not have occult metastases, and a neck dissection puts them at risk of unnecessary morbidity. Thus, the need to identify patients who have occult metastases without doing a neck dissection is apparent.[31] Today, the most commonly used parameter to predict which patients are

more likely to have occult metastases and need elective neck dissection is tumor thickness. A meta-analysis of studies published before 2009 showed that occult lymph node metastases are significantly more common when the thickness of the primary tumor is >4 mm.[32] Tumor thickness can be evaluated with frozen section and the decision about neck dissection can be made intraoperatively. However, in a recent evaluation of multiple parameters potentially predicting lymph node metastases in patients undergoing a thorough search for occult metastases by SLNB, tumor thickness failed to achieve significance. The authors therefore concluded that the neck in oral cavity SCC should be treated irrespective of tumor thickness and depth of invasion; preferably by SLNB.[33] Future predictors may include tests based on molecular features of the primary tumor.[31,34]

A radical or modified radical neck dissection is not necessary for management of the clinically N0 neck in oral cavity cancers because comparable results can be obtained with selective neck dissections.[35] Levels I and III and sublevel IIA are at the highest risk for metastases; thus neck dissection for oral cavity SCC with a clinically negative neck should encompass these levels.

Current literature demonstrates that metastases to sublevel IIB from oral cavity cancers are rare.[36,37] However, sublevel IIB metastases may be found in up to 22%, when other levels, especially sublevel IIA, are involved.[37,38] This finding has been reported for tongue cancer but not for other oral cavity subsites.[37,38] Although sublevel IIB metastases from oral cavity cancers are rare, there is no prospective outcome data to support preservation of sublevel IIB.

There is also controversy about the incidence of level IV metastases from oral cavity cancers in the literature. In some reports, the incidence of level IV metastases is as high as 15%, which may justify routine dissection of this level.[39,40] However, there are other reports demonstrating a low incidence of metastases in level IV.[41,42] It is noteworthy that a significant proportion of neck recurrences occur because of skip metastases to levels III or IV,[43] which is a finding that may support inclusion of level IV for prevention of neck recurrences. Currently, the management of level IV is not clear in clinically N0 oral cavity cancer, given the discrepancy between the frequently reported low incidence of metastases in level IV and the occurrence of neck recurrences because of skip metastases to this level. However, when other levels are not involved, routine inclusion of this level in selective neck dissection may not be justified owing to the low incidence of isolated nodal metastasis at level IV in these tumors.[44–46] There is a general consensus that level V should not be included in the neck dissection in these patients because level V is rarely involved in oral cavity cancers.[47]

In 34.4% (42 of 122) of early oral cancer patients with a positive sentinel node, additional nonsentinel node metastases were found on subsequent neck dissection. Because 92.9% (39 of 42) of these additional lymph node metastases were located in the same or adjacent level, super-selective neck dissection may be considered.[48] However, more studies are needed to confirm these data and to improve patient selection.

The submandibular gland, which, unlike the parotid, does not contain lymph nodes, is rarely involved in early stage (stages I–II) oral cavity cancers. Any involvement would be by direct invasion, thus, the gland can be preserved in selective neck dissections in its absence.[49–51] However, it is important to remove all the submandibular lymph nodes, which are the first echelon lymph nodes of oral cavity, when preserving the submandibular gland to avoid a neck recurrence. This is sometimes difficult to perform without removal of the gland, especially when nodal disease is located medial to the mylohyoid muscle or subjacent to the jaw in the posterior aspect of the submandibular triangle.

**Laryngeal squamous cell carcinoma with clinically negative neck.** Because of different embryologic origins, supraglottic, glottic, and subglottic compartments have different lymphatic drainage pathways. The supraglottic larynx has a rich lymphatic network and drains bilaterally into the upper and middle jugular lymph nodes, whereas the vocal folds have sparse lymphatic channels. The glottic and the subglottic regions drain into the lower jugular, prelaryngeal, and pretracheal lymph nodes. Because of these anatomic features, metastases from the supraglottic larynx cancer can occur even in the early stages of cancer; however, metastases from early glottic lesions are rare.[52,53] Consequently, indications differ for elective treatment of the neck in supraglottic and glottic-subglottic cancers.

Metastases of laryngeal cancer usually occur in levels II, III, and IV, whereas levels I and V are rarely involved.[9,54–56] Thus, selective neck dissection (II–IV) has been used widely with great success in the past 20 years for the management of the neck in clinically N0 laryngeal cancer, achieving a neck recurrence rate as low as 1.7%.[57]

Although the spinal accessory nerve is preserved during selective neck dissection of levels II to IV, it has been demonstrated that the nerve's function may be impaired after surgery.[58,59] This is attributed in great part to retraction of the nerve during clearance of the contents of sublevel IIB or devascularization of the nerve by dissection. In prospective studies, the rate of sublevel IIB metastases in patients with clinically N0 laryngeal cancer ranged between 0% and 3.2%.[36,60–65] Given the low rate of metastases, dissection of sublevel IIB is not indicated in patients with clinically N0 laryngeal cancer.[66] This modification helps to minimize accessory nerve dysfunction without reducing the oncologic safety of the neck dissection.[67]

The rate of metastases to level IV in patients with clinically N0 laryngeal cancer is also low.[62,68] Thus, it is possible to omit level IV dissection and avoid complications such as chylous fistula and phrenic nerve injury. Based on these observations, it seems that patients with supraglottic cancer could be treated with a neck dissection procedure that encompasses 2 levels: II and III. This procedure has become known as a "super-selective neck dissection" and is defined as the removal of 2 or less contiguous neck levels.[69] When super-selective neck dissection is used as part of the primary treatment, it is important to point out that the presence of positive nodal

disease found within the neck dissection specimen could be an indication for postoperative adjuvant radiation therapy, and/or extension of the neck dissection if the nodal disease is recognized intraoperatively.

Recently, Medina et al[70] reported that level VI metastases were frequent in patients with primary subglottic carcinomas, advanced glottic, and certain advanced supraglottic carcinomas, and recommended that selective neck dissection should be extended to include level VI in these patients. In general, extension of the neck dissection to level VI should be considered in laryngeal SCC with gross subglottic extension.

In summary, should primary surgical therapy be selected for laryngeal cancer, the current literature supports sublevel IIA to level III dissection in clinically N0 supraglottic cancers[65,71] and no elective neck dissection for early stage tumors limited to the glottis.[53] Level IV dissection is required in transglottic and primary subglottic cancers. The dissection should be extended to include level VI in patients with primary subglottic carcinomas, as well as other advanced tumors with significant subglottic extension.

**Oropharyngeal and hypopharyngeal squamous cell carcinoma with clinically negative neck.** As compared to oral cavity or laryngeal cancers, management of the clinically N0 neck in these cancers is less clear. The use of organ preservation protocols for these cancers has increased in the past few decades. As many of these patients are successfully treated with nonsurgical measures, it is difficult to draw conclusions on elective neck dissection in patients with oropharyngeal and hypopharyngeal cancer with a clinically N0 neck. The emergence of transoral video and robot-assisted resection of selected oropharyngeal carcinomas has renewed interest in surgical treatment.

The risk of metastases to cervical lymph nodes is high in oropharyngeal cancer, with an overall incidence of 92%, and an incidence of 39% for the clinically N0 neck,[72] which suggests the need for elective treatment in the majority of the latter. However, the efficacy of elective neck treatment in clinically N0 oropharyngeal cancer has not yet been demonstrated with prospective studies, and observation is used as an option in some centers. In a series of 49 patients with clinically N0 oropharyngeal cancer, neck recurrence rates were 10% and 24% for the elective neck dissection and observation groups, respectively.[73] However, only 50% of the patients with recurrences in the observation group could be successfully salvaged. Although a statistically significant advantage of elective neck dissection was not demonstrated in this study, it seems to offer better disease-specific survival in patients with clinically N0 oropharyngeal cancer who are surgically treated.

Oropharyngeal cancers usually drain into level II, III, and IV lymph nodes, as well as retropharyngeal and parapharyngeal lymph nodes,[74,75] and dissection of levels II, III, and IV would be appropriate for clinically N0 oropharyngeal cancer.

The relevance of the lymph nodes in sublevel IB in the management of the neck in patients with oropharyngeal carcinomas has been a matter of debate for some time. However, several studies suggest that these nodes need consideration in patients with clinically obvious metastases in other lymph node levels of the neck and in patients with carcinomas of the base of the tongue. In the study by Candela et al,[76] metastases in level I nodes were found in only 2% of the cases that had undergone radical neck dissection for SCC of the oropharynx clinically staged N0. Level IV nodes were involved in 8% of the cases. Wiegand et al[77] studied 77 patients with oropharyngeal cancer in order to determine whether level I and sublevel IIB need to be dissected in these patients. They found that none of the patients with clinically N0 necks had metastases in level I or sublevel IIB. On the other hand, 12.8% of the patients with cN+ neck had metastases in level I.[77] Others have reported similar results.[78] Vartanian et al[79] studied 81 patients with oropharyngeal carcinoma and, even though they do raise the issue of including level I when performing a selective neck dissection for these patients, in their concluding paragraph they state: "Even if our results are based on a small cohort, they suggest that patients with base of tongue carcinoma should have a supraomohyoid neck dissection, which includes neck level I, II, and III, rather than a lateral neck dissection."

Gross et al[72] found that the majority of the metastases were located in levels II and III. However, sublevel IIB metastases range between 2.5% and 6% in oropharyngeal cancers,[36,72,80] suggesting that this sublevel can be omitted during elective neck dissection. In their series of 348 patients with oropharyngeal cancer, metastases were present in sublevel IIB in 2.5% and 25% of patients with clinically N0 and clinically positive necks, respectively.[72] The authors concluded that removal of sublevel IIB is not necessary in patients with T1 or T2 tumors with clinically N0 necks. However, dissection of sublevel IIB was recommended in patients with advanced primaries, with the primary tumor in the tonsil, with bulky disease at sublevel IIA, or when the neck is clinically positive either unilaterally or bilaterally. The same study found level IV metastases to be also rare in patients with clinically N0 oropharyngeal cancer, occurring in about 1% of the cases.[45] It seems that a more limited dissection confined to sublevel IIA and level III may be appropriate for some carefully selected patients with clinically N0 oropharyngeal cancer, but this must be supported with prospective studies with higher numbers of patients.

With the recent trend to treatment of carcinomas of the oropharynx with transoral conventional or video and robot-assisted resection, the management of the N0 neck has renewed importance. In that regard, the study by Olzowy et al[81] provides pertinent information. This study is unique in that it reports findings of bilateral comprehensive neck dissections performed in a large cohort of patients with oropharyngeal SCCs. They found that the prevalence of bilateral lymph node metastases was <15% only in T1 tumors of the base of the tongue and soft palate and in T1 and T2 tumors of the tonsillar fossa. This information suggests that when such tumors are resected, only the lymph nodes in the ipsilateral side of the neck need to be addressed. On the other hand, when larger tumors are resected, both sides of the neck must be addressed, especially if the intent of the clinician is to use surgery as the single treatment modality.

The use of SLNB has become established for early oral cavity cancer and can be recommended as an alternative to selective neck dissection for the patients with T1 to 2 N0 disease. SLNB is also a safe and accurate staging modality to select patients with clinically stage I/II oropharyngeal SCC with occult lymph node disease for elective neck dissection, although the proportion of oropharyngeal carcinomas is considerably lower compared to the oral cavity in most studies. The propagation of SLNB was less extensive in oropharyngeal cancer because of 2 main reasons. First, in many centers, all oropharyngeal cancers are treated by primary (chemo)radiation regardless of the initial stage, and, second, only oropharyngeal cancers accessible for preoperative transoral injection of the radio tracer qualify for the SLNB procedure. This might change in the future with the currently observed revival of transoral surgery with the robot. Nonetheless, there are studies that included a considerable number of oropharyngeal cancer for SLNB, showing equally good results for this subsite as for oral cavity. The promising reported short-term results of one of these studies published a few years ago have meanwhile been sustained by a recently published long-term follow-up. Patients with negative SLNB and no elective neck dissection achieve an excellent neck control rate that compares favorably with reports on primary elective neck dissection. The neck control rate in sentinel node-negative patients is superior to that in sentinel node-positive patients, which is reflected in superior disease-specific survival.[30] In addition, a prospective consecutive cohort analysis has demonstrated that even small tumor deposits only detectable by the extensive histopathologic workup of the SLNB protocol have a significant impact on tumor control and survival in early oral and oropharyngeal SCC.[82]

Regarding the possibility of metastases in the retropharyngeal nodes, it is commonly accepted today that these are rarely found in patients whose neck is otherwise free of metastases. Consequently, these nodes do not need to be included for clinically N0 necks. However, in patients with pathologic nodal disease in other levels of the neck, the prevalence of retropharyngeal metastases has been reported to be as high as 23%.[83,84] Recently, Moore et al[85] reported the results of a retrospective analysis of 72 patients with oropharyngeal SCC treated with transoral oropharyngectomy, neck dissection, and retropharyngeal node dissection. They concluded that in patients with tonsillar cancer, the risk of retropharyngeal metastases is negligible in the presence of clinically T1 to 2, N0 to N2a disease, with a negative computed tomography (CT) and positron emission tomography (PET)-CT. They estimate that 40% of patients meet these criteria and may safely forego treatment of the retropharyngeal nodes. They also estimate that approximately 10% of patients will have positive imaging and for those patients a retropharyngeal node dissection at the time of surgery is recommended to treat macroscopic disease. In the remaining patients at risk for retropharyngeal node involvement, adjuvant radiotherapy is generally indicated based on other adverse features, and the retropharyngeal nodes can be incorporated into the treatment field.

The various subsites of the hypopharynx have different lymphatic drainage pathways. For the pyriform sinuses, the direction of drainage is to the upper, midjugular, and spinal accessory chains. The inferior portions of the hypopharynx and postcricoid regions drain into the paratracheal, paraesophageal, and supraclavicular lymph nodes. Lymphatic drainage from the posterior hypopharyngeal wall is to the retropharyngeal and midjugular nodes.[86] Confirming these observations, Candela et al[76] reported that lymph nodes in levels II, III, and IV were most frequently involved in patients with oropharyngeal or hypopharyngeal cancers and isolated skip metastases outside of these levels were very rare (0.3%). The prevalence of paratracheal lymph node metastasis ranges in the reported series of laryngeal, hypopharyngeal, and (cervical) esophageal cancers, from 1% to 59%, depending on stage, subsite, and extension.[87] When paratracheal lymph nodes were electively removed, metastases were found in 8.2% of the patients with hypopharyngeal cancer.[88] In light of these limited data, it seems that removal of levels II, III, and IV along with paratracheal lymph nodes is appropriate in patients with clinically N0 hypopharyngeal cancer. However, paratracheal lymph node metastases may develop independently from lymph node metastases at other lymph node levels. Plaat et al[89] found paratracheal lymph node metastases in 4 of 25 patients (16%) with laryngeal, hypopharyngeal, and esophageal cancer, who had undergone neck dissection and were found to have no metastases in the lateral (I–V) neck levels. In the study of Timon et al,[90] 5 of 13 patients with laryngeal, hypopharyngeal, and esophageal cancer, and paratracheal lymph node metastases had only paratracheal lymph node metastases with the other cervical lymph nodes free of disease. Moreover, the diagnostic value of CT, magnetic resonance imaging (MRI), and fluorodeoxyglucose-PET/CT for detection of metastases in level VI is poor.[91,92]

Recently, Sakai et al,[93] reporting the incidence of sublevel IIB metastases in patients with hypopharyngeal cancer, found involvement in 13.3% of the clinically positive necks and 0% of the clinically N0 necks. The authors concluded that sublevel IIB may be preserved during neck dissection in patients with clinically N0 hypopharyngeal cancer.

In conclusion, current literature suggests that sublevel IIB may be preserved in either oropharyngeal or hypopharyngeal cancer with clinically negative neck. A superselective neck dissection confined to sublevel IIA and level III may be appropriate for carefully selected patients with clinically N0 oropharyngeal cancer, with the exception of patients with advanced primaries, with the primary tumor in the tonsil, or with a clinically positive neck either unilaterally or bilaterally. A neck dissection for hypopharyngeal cancer with clinically negative neck should encompass sublevel IIA, and levels III and IV along with the paratracheal lymph nodes.

**Squamous cell carcinoma of other head and neck primary sites with clinically negative neck.** The current literature lacks sufficient data regarding neck dissection for clinically N0 mucosal SCC of other less commonly affected head and neck primary sites, such as paranasal sinuses and temporal bone. Nasopharyngeal carcinoma differs in many

aspects from other head and neck cancers, and neck dissection is only used for salvage of the residual neck disease after (chemo)radiotherapy.

Recently, Takes et al[94] published a review of management of the N0 neck for SCC of the maxillary sinus. Although the studies included in this review were heterogeneous in terms of stage, histopathology, and treatment, the authors noted that the rates of failure of the untreated N0 neck were high enough to warrant elective treatment in many published series. The recommended treatment was neck dissection in patients undergoing free flap reconstruction, where the neck would have already been opened, or irradiation of the neck along with the primary site, in other patients.

## Neck dissection for head and neck squamous cell carcinoma with clinically positive neck

The traditional surgical management of the clinically positive neck has been the radical neck dissection. The modified radical neck dissection, developed in the 1960s, also called a comprehensive dissection of all lateral lymph node levels, began to replace the standard radical neck dissection. Until recently, the radical and modified radical neck dissections were considered as the necessary and correct treatment for the surgical management of lymph node metastases of HNSCC.[95,96] However, in many cases of clinically positive neck, a radical or modified radical neck dissection turns out to be overtreatment because not all of the palpable or detectable nodes are pathologically positive and not all (sub)levels of the neck are involved.[97] In addition, there is little chance of cure of a patient with involvement of all 5 node levels with SCC. Kowalski and Carvalho[98] retrospectively analyzed radical neck dissection specimens of 164 patients with oral cavity cancer with a clinically N1 or N2a neck and found a high false-positive rate (57.4% pN0) in N1 patients with a clinically positive node in level I. Similarly, Simental et al[99] reported a false-positive rate of 32% in patients who were initially staged as clinically positive (with palpation and radiology studies only for some patients). However, much will depend on the diagnostic means that are used to stage the neck.[100]

After popularization of the selective neck dissections for the elective management of the clinically N0 neck, some surgeons explored the efficacy of selective neck dissections in the setting of the clinically positive neck, in an effort to reduce morbidity of neck dissection without reducing oncologic safety.[101] The first reports were on the clinically N1 neck, but there are a considerable number of studies regarding management of N2 or even N3 necks with selective neck dissections in the recent literature.

Selective neck dissection for the clinically positive neck may be considered as an adequate removal of gross tumor, or may be used as a pathological staging procedure before planned radiotherapy of the neck.[102] The histopathological report offers vital information for planning of adjuvant radiotherapy after selective neck dissection: irradiation volume design, selection of dose levels, and eventual intensification of irradiation by concurrent administration of chemotherapy should be based on the extent of disease (number, size, and spatial distribution of positive nodes in the neck) and eventual presence of extracapsular tumor spread.[103,104] In this context, the number of all retrieved lymph nodes is an indicator of adequacy of surgery and is related to the reliability of prognostic information obtained at histopathological examination of dissected specimen. However, a current Cochrane analysis by Bessell et al[105] found no evidence that radical neck dissection (a greater extent of dissection) increases overall survival compared to conservative neck dissection surgery.

In one of the leading articles about management of clinically positive neck with selective neck dissection, Andersen et al[106] reported the results of 129 selective neck dissections in 106 patients with previously untreated clinically N1 to N3 HNSCC. The regional control rate was 94.3%. There were only 6 recurrences on the side of selective neck dissection (5%). The authors emphasized the importance of careful selection of patients without massive adenopathy and concluded that nodal fixation, gross extracapsular spread, history of previous neck surgery, or radiotherapy are relative contraindications for this approach.

In a group of 191 patients with HNSCC with clinically positive neck disease, Santos et al[107] performed 34 selective neck dissections in 28 patients. There were 4 recurrences (11.8%) after selective neck dissection. One of these patients was stage N1, 2 were N2b, and 1 was pN2c. Regional recurrence rates were higher in patients with advanced T classification versus early T classification disease. The authors also stressed the importance of careful patient selection and noted that regional recurrence is high in patients with advanced T classification and/or N2b classification disease.

In a retrospective analysis of 65 patients with HNSCC and a clinically positive neck who underwent selective neck dissection, researchers from the University of Pittsburgh[99] found 8 recurrences (12.3%), but their association with N or T classification was not reported. Four recurrences could be managed by salvage surgery with a resultant overall regional control rate of 93.9%.

Recently, the use of selective neck dissection in the treatment of the clinically positive neck with involvement of nonlymphatic structures[108] has been reported. In most patients, the nodal disease was confined to 2 or fewer neck levels. Regional recurrence rates were 0% and 13% for primary treatment and postradiation cases, respectively. Although these results are very encouraging, this is the only study on the "extended" use of selective neck dissection and needs to be supported with further studies.

It should be noted that 2 of the studies mentioned above[99,107] reported relatively high rates of regional failure, which may reflect undertreatment of these patients and the need for more careful patient selection. Based on observations from the current literature, it seems that selective neck dissection is feasible in selected patients with clinically positive neck disease and theoretically in some with involvement of nonlymphatic structures. In addition, because postoperative radiotherapy or chemoradiotherapy is routinely administered in these cases, including all neck levels in the radiation fields, this may be sufficient to achieve good control rates in undissected levels.

Furthermore, modern radiation equipment and contemporary principles of radiotherapy planning allow more selective and accurate dose delivery to different nodal regions in the neck with simultaneous advantage of reducing morbidity and taking into consideration the risk level of individual nodal regions for harboring residual tumor cells.[109] With concurrent administration of systemic therapy, when appropriate, adjuvant radiotherapy seems to effectively compensate for less extensive surgery. However, these findings should be interpreted with caution because we still need prospective studies with larger number of patients to further clarify the role of selective neck dissection in the case of the clinically positive neck.

## Neck dissection after primary chemoradiation for head and neck squamous cell carcinoma

In the early years of the era of organ preservation, the initial strategy was to perform a planned neck dissection for all cases with an initially positive neck, regardless of the response to chemoradiotherapy. In the following years, evidence has accumulated that a planned neck dissection in complete responders who initially presented with N1 neck disease is not necessary. However, debate continues about routine performance of planned neck dissection for complete responders who initially presented with bulky ($\geq$N2a) neck disease. The need for an algorithm to clearly identify the patients who are likely to benefit from a planned neck dissection is apparent, because the morbidity of surgery after chemoradiation is significant. Planned neck dissection may be beneficial only for those patients who have persistent or recurrent resectable disease in the neck alone.[110] In those patients with complete clinical response, the operation is usually unnecessary. Moreover, in patients with incurable disease caused by local or distant failure, neck dissection would add nothing but additional morbidity, except in certain situations in which palliative surgery would prevent serious complications, such as a carotid blowout. It is also noteworthy that therapeutic effects of chemoradiation continue after completion of the treatment and sampling of cervical lymph nodes may reveal false-positive results for up to 12 weeks.[111] Not surprisingly, the time window of 8 to 12 weeks postchemoradiation was found optimal for response evaluation with different diagnostic tools, such as CT, MRI, or PET,[112] although not perfect. van der Putten et al[113] found in patients with suspicion of regional residual or recurrent disease after chemoradiation a sensitivity of 80% and specificity of only 42% for ultrasound-guided FNAC.

However, delay of neck dissection beyond the 12-week point relegates these patients to the "salvage" group, rather than the "planned" neck dissection group. A higher incidence of major complications was reported by Lavertu et al.[114] when neck surgery was performed later than 12 weeks compared to 4 to 12 weeks after radiotherapy. The question remains as to whether the higher incidence of complications among patients undergoing salvage neck dissection is compensated for by the elimination of unnecessary neck surgery in patients who have responded completely to nonsurgical treatment. In addition, it has been generally considered that delay of surgical intervention in the neck to 12 weeks or later after chemoradiation reduces disease control in the neck in addition to increasing the risk of treatment-related complications.[115] Some authors have found the extent of neck dissection to be more important than the timing of surgery with regard to the incidence of complications.

The routine management of recurrent or residual neck disease after radiotherapy (or chemoradiation) in patients with nasopharyngeal carcinoma has been to perform a radical neck dissection. Recently, Zhang et al[116] reported their experience with recurrent or residual regional metastases of nasopharyngeal carcinoma. Patients with residual disease had better outcomes than patients with recurrent disease. There were 70 patients with residual neck disease and 42 of these patients had 1 single persistent lymph node during the course of the treatment. Although the researchers had performed a radical neck dissection in every case, they concluded that residual disease limited to 1 single lymph node might be managed with a selective neck dissection.

Recently, Ferlito et al[117] performed an extensive review of the literature in order to evaluate the necessity of planned neck dissection in the case of complete response to (chemo)radiation. The review revealed 24 articles reflecting an advantage of planned neck dissection. All of these studies were retrospective and treatment strategies were considerably heterogeneous, including radiotherapy alone, radiotherapy twice daily, and chemoradiotherapy, applied in various regimens. Among these 24 studies, regional failure rates varied considerably, ranging from 0% to 38%. On the other hand, the review reported 26 articles in which an advantage of planned neck dissection could not be demonstrated. Most of these studies were also retrospective with regional failure rates ranging between 0% and 16%, which were comparable with regional failure rates of planned neck dissection. In this review, the authors emphasized the importance of radiologic evaluation, especially PET-CT, in detection of persistent or recurrent neck disease. The authors concluded that planned neck dissection for patients with a complete response after chemoradiation, based on PET-CT evaluation 12 weeks after the end of treatment, cannot be justified.

Although the traditional treatment philosophy for patients with recurrent or persistent neck disease after (chemo)radiation had been to perform a comprehensive neck dissection, there is emerging evidence that most patients can be effectively treated with a selective neck dissection.[118–120] However, the results of most of these studies included patients with pretreatment bulky neck disease who had both complete and incomplete responses to chemoradiation. Recently, Dhiwakar et al[121] reported their results with selective neck dissection performed as an early salvage only for patients with clinically persistent neck disease after chemoradiation. Sixty-nine selective neck dissections were performed on 62 patients and pathological examination revealed residual disease in 32 specimens (46%). Residual disease was confined to levels II and III in the majority of the cases (88%). There were 4 neck recurrences (6%), but only 1 of these occurred in the operated neck, which was staged N3 before treatment.

The feasibility of performing a super-selective neck dissection for patients after chemoradiation has also been addressed. The initial supporting data was based on the clinical and pathological findings in 177 patients (239 hemi-necks) with clinically positive neck disease treated with concomitant radiation and intra-arterial cisplatin.[122] Comparisons were made between the clinical presence of neck-level specific disease at postchemoradiation restaging and subsequent evidence of pathological disease after neck dissection. Among the 89 patients whose necks were restaged as a partial response, 73 had clinical evidence of residual adenopathy involving only 1 neck level. Fifty-four patients subsequently had a salvage neck dissection, for whom the pathological findings were correlated with the postchemoradiation staging for neck-level specific metastases. Only 2 of the 54 evaluable patients had evidence of pathologic disease extending beyond the single neck level, 1 of whom had disease in the contiguous neck level. The correlations supported the hypothesis that super-selective neck dissection, defined as the removal of 2 or fewer neck levels, is feasible among patients whose residual neck node disease is confined to a single level. In another analysis of clinical outcomes after neck dissection following radiation and intra-arterial cisplatin,[123] the absence of regional recurrence was noted among a small subset (7 patients) in which a super-selective neck dissection was performed. Most recently, the treatment outcomes were reported of a larger series of 35 super-selective neck dissections over a median follow-up of 33 months (range, 8–72 months)[124]; there were 8 recurrences, all of which occurred at either the primary site or at distant sites. There were no isolated recurrences in the neck, although there was 1 patient who was found to have a recurrence in the primary site and neck simultaneously. The projected 5-year disease-specific survival rate for the group was 60%.

In a group of 241 patients with stage IV HNSCC, Cannady et al.[125] performed 67 selective or super-selective neck dissections and 94 radical or modified radical neck dissections. The study lacks important information regarding the indications for neck dissection, the criteria to determine the extent of surgery, and other data, but no difference in regional failure was found based on neck dissection type. Additionally, the authors reported that selective neck dissection would have removed residual disease in most cases if the dissection had encompassed the next distal level in addition to the original levels.

The data show that super-selective neck dissection is an effective treatment strategy applicable to a specific subset of patients after chemoradiation for advanced head and neck cancer.[69] With this latter application, it may be regarded as an adjuvant therapy rather than part of the primary treatment. It is based on the principle that neck levels with clinically absent metastases before treatment, which then receive a therapeutic dose of radiation along with concurrent chemotherapy, should have a very low risk of occult residual metastases after treatment, especially given the reduction of lymph nodes which usually follows radiotherapy. This should obviate the need to surgically remove the nodes from these levels, even though other neck levels had clinically positive disease. On the other hand, it should be kept in mind that in about 20% of the patients undergoing selective neck dissection or super-selective neck dissection for residual disease post-chemoradiation, for adequate resection of the disease in the neck, it is necessary to remove either the internal jugular vein, a portion of the sternocleidomastoid muscle, or even the spinal accessory nerve.[123]

In summary, the current literature suggests that routine planned neck dissection after complete response to chemoradiation is no longer warranted. Furthermore, in many cases of persistent neck disease, the use of selective neck dissection is feasible whereas super-selective neck dissection is an option for patients with residual adenopathy confined to a single neck level.

### Future directions

As the evolution of neck dissection continues, technological developments continue to shape the frontier of treating the neck in HNSCC. Transoral robotic surgery has gained popularity in some centers for treatment of oropharyngeal cancers; similarly, the use of robotic surgery has been introduced in neck dissection.[126,127] The cost-effectiveness and variable availability of this technology will continue to fuel debate as to its accepted utility in treating neck disease. With further dissemination of the surgical technique and potential decrease in cost, robotic surgery of the head and neck may one day enjoy an application as widespread as endoscopic sinus surgery.

SLNB of the cervical lymph nodes followed by neck dissection has been a subject of investigation for many years. A recent review by Thompson et al,[128] identified 26 studies that met inclusion criteria. According to these studies, the pooled sensitivity and negative predictive value of SLNB for all head and neck tumors was 95% and 96%, respectively. In patients with oropharyngeal, hypopharyngeal, and laryngeal tumors, the rates reached 100%. Govers et al[26] found, in a more recent meta-analysis, a sensitivity of 93% for SLNB in early oral cancer. The negative predictive value ranged from 88% to 100%. These findings demonstrate that SLNB is a reliable tool for correctly staging the neck in patients with HNSCC, thus heralding the potential for gaining wide acceptance among the head and neck community.

## CONCLUSIONS

Since its first introduction 125 years ago, neck dissection has evolved considerably, from a procedure associated with significant morbidity to one that preserves function while remaining oncologically effective. Recent studies have clearly demonstrated that sublevel IIB and level V are rarely involved in patients with HNSCC with clinically negative and even clinically positive necks. There is also evidence that the risk of level IV metastases is low in many patients. Today, (super)selective neck dissections omitting these levels are routinely used in many centers. On the other hand, lymph node levels, which are important for disease control but not routinely dissected during neck dissection, such as level VI or the retropharyngeal compartment, need to be addressed in specific tumors. In conclusion, instead of a uniform approach in all settings, the contemporary approach to the neck is increasingly diverse and tailored to the characteristics of the primary tumor, the

rate and location of nodal metastases, and the extent to which this has occurred as determined by imaging studies.

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