IMPACT OF PROPHYLACTIC LYMPH NODE DISSECTION DURING SALVAGE TOTAL LARYNGECTOMY

IMPACT DU CURAGE GANGLIONNAIRE PROPHYLACTIQUE LORS D'UNE LARYNGECTOMIE TOTALE DE RATTRAPAGE

S. Ayadi^{1,2}, Y. Hbaieb^{1,2}, G. Youssfi^{1,2}, F. Grati^{2,3}, M.Mnejja^{1,2}, B. Hammami^{1,2}, A. Chaabouni^{1,2}, I. Charfeddine^{1,2} 1: Otorhinolaryngology, head and neck surgery Department, Habib Bourguiba university Hospital, Sfax, Tunisia

2: University of Sfax, Sfax medical school, LR23ES01 Laboratory, Tunisia

3: Anesthesia department, Habib Bourguiba University Hospital, Sfax, Tunisia

_ ABSTRACT _

Introduction: We aimed to evaluate the prevalence of occult node metastasis in squamous cell carcinoma (SCC) of the larynx and to identify its predictive factors.

Methods: Our study is retrospective. We included all patients treated with salvage total laryngectomy (STL) for SCC of the larynx, clinically and radiologically classified as cN0, in the otolaryngology and head and neck surgery, radiotherapy and medical oncology departments of the Habib Bourguiba University Hospital of Sfax, over a period of 30 years (1993-2023).

Results: We included 16 cases of STL with an average annual incidence of 0.53 cases/year. A clear male predominance was noted with a sex ratio of 15 (15M/1F). The average age at the time of STL was 61 ± 13.3 years [41-81 years]. At the end of the initial treatment, continued tumour progression was observed in 8 patients (50%) and tumour recurrence in 8 patients (50%).

All patients had functional bilateral lymph node dissection (levels II, III, and IV). Eight patients underwent bilateral level VI dissection (50%). Pathological examination confirmed lymph node invasion ipsilateral to the tumor with pN+ capsular rupture in 5 patients (31.2%) with a median number of 2 positive nodes. Three patients presented with capsular rupture of pR+ nodes (18.7%). Four patients (25%), all pN+, died of their disease and overall survival and disease-free survival were 70% at 1 year. The presence of occult N+ lymph node metastases was linked to poor overall and disease-free survival (p=0.001).

The presence of pN+ lymph node metastases was statistically linked to supraglottic and subglottic recurrences.

Conclusion: The positivity of N+ metastases was linked to supraglottic and subglottic recurrences in a statistically significant manner, although in the literature the rate of occult metastases is higher for rT3-T4 and supraglottic involvement.

Keywords: Squamous cell carcinoma; Larynx; Lymph node metastasis; Lymph node dissection; Prognostic

RÉSUMÉ

Introduction: Nous avons évalué la prévalence des métastases ganglionnaires occultes dans le carcinome épidermoïde (CE) du larynx, et avons identifié ses facteurs prédictifs.

Méthodes: Notre étude est rétrospective. Nous avons inclus tous les patients traités par laryngectomie totale (LT) de rattrapage pour un CE du larynx, classé N0 cliniquement et radiologiquement, dans les départements d'oto-rhinolaryngologie, de chirurgie cervico-faciale, de radiothérapie et d'oncologie médicale de l'Hôpital Universitaire Habib Bourguiba de Sfax, sur une période de 30 ans (1993-2023).

Résultats: L'étude a inclus 16 cas avec une incidence annuelle moyenne de 0,53 cas/an. Une nette prédominance masculine a été observée avec un ratio de 15 hommes pour 1 femme (15H/1F). L'âge moyen au moment de la LT de rattrapage était de 61 ± 13,3 ans [41 ans - 81 ans]. À la fin du traitement initial, une progression tumorale persistante a été observée chez 8 patients (50 %) et une récidive tumorale chez 8 patients (50 %).

Tous les patients ont bénéficié d'un curage ganglionnaire bilatéral fonctionnel (niveaux II, III et IV). Huit patients ont également subi un curage bilatéral du niveau VI (50 %). L'examen anatomopathologique a confirmé une invasion ganglionnaire ipsilatérale à la tumeur avec rupture capsulaire pN+ chez 5 patients (31,2%), avec un nombre médian de 2 ganglions positifs. Trois patients présentaient une rupture capsulaire des ganglions pR+(18,7%). Quatre patients (25%), tous pN+, sont décédés de leur maladie. La survie globale et la survie sans maladie étaient de 70 % à 1 an. La présence de métastases ganglionnaires occultes (N+) était associée à une mauvaise survie globale et sans maladie (p = 0,001).

Auteur correspondant: Sirine Ayadi Mail: sirine_ayadi@medecinesfax.org La présence de métastases ganglionnaires pN+ était statistiquement liée aux récidives supraglottiques et sousglottiques.

Conclusion: La positivité des métastases N+ était significativement associée aux récidives supraglottiques et sousglottiques, bien que dans la littérature, le taux de métastases occultes soit plus élevé pour les rT3-T4 et les atteintes supraglottiques.

Mots-clés: Carcinome épidermoïde; Larynx; Métastases ganglionnaires; Curage ganglionnaire; Pronostic

INTRODUCTION _

Salvage total laryngectomy (STL) refers to the surgical treatment of persistent or recurrent laryngeal squamous cell carcinoma (SCC), initially treated with (chemo) radiation (1). Salvage surgery is the preferred curative treatment for patients when re-irradiation is not possible (2,3).

STL is a major surgical procedure, with a high rate of functional complications, particularly pharyngostoma (4), and oncological complications resulting from incomplete resection of damaged tissues in irradiated areas (5).

Lymph node dissection (LND) is systematically performed during STL surgery when cervical lymph nodes (cN+) are present in the local extension assessment. However, the need for LND in patients classified as cN0 remains controversial, and no consensus has yet been established (6,7).

Some authors agreed on the need of LND for patients with advanced local recurrence or progression (rT3-rT4) and for supraglottic tumours (8–10), given the high rates of occult metastases (>20%) (11,12), the benefit in terms of overall survival (7,13,14) and the lower rate of postoperative complications (11,15,16).

On the other hand, several authors were not in favour of systematic LND during STL, reporting low rates of occult metastases (<10%) (10,11,17,18) and no systematic benefit in terms of survival (1,18–21). Overall, there was general agreement that scar complication rates (mainly fistulas) were higher when LNDs were performed in association with STL (17,22,23).

The aims of this study were to describe the functional and carcinological results of LTR surgery with LND, to evaluate the prevalence of occult node metastasis in laryngeal SCC and to identify the predictive factors for occult metastases of the lateral sector in cN0 patients proposed for STL.

METHODS

We report a retrospective study of patients treated in the otolaryngology and head and neck surgery, radiotherapy and medical oncology departments of the Habib Bourguiba University Hospital in Sfax, over a period of 30 years (1993-2023).

We considered as STL any total laryngectomy (TL), or total pharyngo-laryngectomy (TPL), performed in patients with laryngeal SCC initially treated with curative radiotherapy or combined with chemotherapy. We included patients who were clinically and radiologically classified as cN0 at the time of STL with LND and who presented with a persistent or recurrent tumor after initial treatment. Patients were classified as N0 based on clinical evaluation and Computed Tomography (CT), which showed the absence of cervical adenopathy.

We consider "persistent disease "to be the continued progression of the tumour within 6 months of primary curative treatment, while "recurrent disease "is the reappearance of the tumour more than 6 months after completion of primary treatment.

We excluded patients from the study, if they had a tumor classified as glottic T1 during the initial assessment, an incomplete initial treatment, cervical lymphadenopathy (cN+) on the extension assessment before STL, an unresectable tumor, or a tumor type other than SCC.

We collected the following clinical and histological data: age, sex, initial tumour characteristics, initial treatment protocol, relapse staging, time interval between the end of initial treatment and STL, post-operative complications, possible tumour recurrence and estimated survival.

Tumors and relapse stages were assessed according to the 2017 International TNM Classification by the Union for International Cancer Control (UICC)(24). The classification of the disease was performed by a multidisciplinary committee including ENT, maxillofacial surgeons, radiation oncologists and medical oncologists.

All patients in the current study underwent bilateral neck dissection, specifically involving the removal of levels II, III, and IV. We recorded whether the lymph node dissection (LND) was radical or functional, as well as whether sectors I and/or V were also dissected. Level VI dissection was performed if there was subglottic involvement measuring 5 millimeters or more.

All nodes were examined whole by series of 5 micrometre cross-sections, without immunohistochemical analysis, to determine the presence/ absence, number and location of metastases.

The collected data were computerized on the statistical computer program SPSS 26 for Windows®. We expressed quantitative variables as means after checking the normality of distribution or as median if the normality of distribution was not checked. We expressed the qualitative variables in frequencies.

We studied the relationship between epidemiologicalclinical, histological and biological parameters and the postoperative evolution (failure of decannulation and late false airway).

In order to study the oncological results of STL with LND and to identify the risk factors for occult metastases of the lateral sector in cN0 patients, statistical analysis IMPACT OF PROPHYLACTIC LYMPH NODE DISSECTION DURING SALVAGE TOTAL LARYNGECTOMY

was performed using a χ^2 test or Fisher's exact test for categorical variables and an independent t-test or a Mann-Whitney rank-sum test for continuous variables. Overall survival was calculated from the date of surgery to the date of last news. Disease-free survival was calculated from the day of achieving complete remission until the onset of relapse or last news. Estimates of overall survival and disease-free survival were made using the Kaplan Meier method.

RESULTS -

alottic

in the II A sector (Table 2).

A total of 16 cases of STL were reported during the study period, with a mean annual incidence of 0.53 cases/year.

A male predominance was found, with a sex ratio of 15 (15M/1F). The mean age at the time of salvage surgery was 61 ± 13.3 years [41 - 81 years].

The initial tumor was limited to the glottic level in 4 cases (25%), Supraglottic - glottic in 4 cases (25%), extended to the 3 glottic levels in 8 cases (50%) (Table 1)

Table 1: Initial tumor sublocation $(n = 16)$.						
Sublocation	Number of cases	Percentage				
Supraglottic - Glottic	4	25%				

4

25%

3 glottic level850%Total16100%Initially, the TNM classification showed that 6 patients
had T2 and T3 tumors and 4 patients had T4a tumors.
One patient had a right upper jugulo-carotid adenopathy

Table 2: TNM classification of the initial tumor

Sublocation	Number of cases	Percentage
Supraglottic - Glottic	4	25%
glottic	4	25%
3 glottic level	8	50%
Total	16	100%

Exclusive radiotherapy was performed in 6 patients (37.5%). The irradiation field was cervical, only affecting the tumor bed for pure glottic tumors classified T2N0M0 in 4 patients (25%). Chemotherapy concomitant with radiotherapy was performed in the other 10 patients (62.5%), including 6 patients classified T3 (37.5%) and 4 patients classified T4a (25%).

At the end of the initial treatment, continued tumor progression was observed in 8 patients (50%). The average delay was 2 months [2 to 10 months]. Tumor recurrence was observed in 8 patients (50%). The average delay was 2 years [7 to 56 months] after the end of the initial treatment.

All patients underwent pan endoscopy with biopsies under general anaesthesia. The tumor was:

- Glotto-supraglottic in 8 cases (50%),
- Reaching all three levels of the larynx in 8 cases (50%).
- With extension to the pyriform sinus in one case (6.3%).
- Laryngeal CT scan was performed in all cases. It showed:
- tumor extension to the hyo-thyro-epiglottic area in 8 cases (50%),
- cartilaginous lysis of the thyroid cartilage in 12 cases (75%), with extra-laryngeal extension to the prelaryngeal muscles in 8 cases (50%),
- extension to the pyriform sinus in one patient (6.3%),
 and the absence of lymph node involvement.

Regarding relapse, the TNM staging was rT3 in 4 patients (25%), and rT4 in 12 patients (75%). All patients were rN0 (Table 3).

Table 3: rTNM classification of tumor at relapse.

Initial TNM Classification		rTNM Classification	Number of cases	Percentage	
Т	T2	rT3	2	12,5%	
		rT4	4	25%	
	T3	rT3	2	12,5%	
		rT4	4	25%	
	T4	rT4	4	25%	
N	NO	rNO	15	93,8%	
	N1	rNO	1	6,3%	
М	MO	rMO	15	93,8%	
		rM1	1	6,3%	

For progressive tumor, the average time between the end of initial treatment and STL was 6 months [2 to 36 months]. For tumor recurrence, the average time between the end of initial treatment and STL was 2 years and 4 months [7 to 48 months]. The overall mean time between the end of initial treatment and STL was 2 years with extremes ranging from 2 months to 4 years. Among the 16 patients who underwent salvage surgery, 15 patients had a TL, and 1 rT4 patient with extension to the pyriform sinus had a TPL. A total thyroidectomy was associated in 8 patients (50%), those with subglottic involvement.

All patients had functional LND involving sectors II, III and IV bilaterally.

Eight patients with subglottic involvement underwent bilateral level VI dissection.

For reinforcement of the neo-pharynx suture, a flap was used in all cases. The flap used was a pedicled pectoralis major muscle flap in 10 patients (62.5%), and a loco-regional rotation flap in the rest of the patients.

Pathological examination revealed well-differentiated SCC in all cases. Twelve patients had a complete resection (R0) and 4 patients presented microscopically tumoral margins (R1).

Pathological examination confirmed lymph node invasion ipsilateral to the tumor with pN+ capsular rupture in 5 patients (31.2%) with a median number of 2 positive nodes (Table 4).

Three patients presented with capsular rupture of pR+ nodes (18.7%). The RMD was negative in all cases.

Table 4: Cross-distribution TNM, rTNM and N+ R+.

NR		rTNM		
	T2N0	ТЗ		rT4N0
		NO	N1	
N+ R+	1	1	1	3
N+ R-	1	1	-	2

The infectious complications were mainly marked by an infection of the edges of the tracheostomy which appeared after an average delay of 10 days.

Pharyngo-cutaneous fistulas were observed in 8 patients with two patients having microscopic positive margins in the pharyngeal resection margins (R1). The average time to onset was 11 days.

The mean follow-up was 2 years and 4 months with extremes ranging from 4 months to 6 years and 8 months.

At the end of our study, 11 patients were still alive: 8 in remission and 3 living with the disease. Four patients (25%), all N+, died of their disease and one patient was lost to follow-up.

Overall survival averaged 17 ± 13 months [4 months to 4 years and 4 months]. Overall survival was 70% at 1 year, 3 years and 5 years (Figure 1).



Figure 1: Kaplan-Meier curve: overall survival

The presence of N+ lymph node metastases was linked to poor overall survival (p=0.001) (Figure 2).



Figure 2: Kaplan-Meier curve: overall survival according to lymph node metastases.

The presence of occult N+ lymph node metastases was associated to supraglottic and subglottic recurrences (p= 0,001, p=0,026 respectively).

DISCUSSION

The incidence of occult lymph node metastases varies widely between studies, ranging from 0 to 32%. The rate found in our study (31.2%) is among the highest reported in various series (13,14,20,25–28). In a 2020 metaanalysis, including more than 1100 patients with relapse of laryngeal SCC after radiotherapy or radio-chemotherapy, the rate of occult lymph node metastasis was 11% (29).

Performing a lateral cervical node dissection is the rule for N+ necks. However, for the N0 neck, performing a LND remains controversial in STL (30).

Supporters of non-practicing a LND base their arguments on the low overall rate of occult metastases, ranging from 4 to 17%, and on the higher rate of complications in the case of LND (18,25).

However, some authors consider that lateral dissection improves survival. Lateral neck dissection also helps to prepare the recipient site, as these authors also prefers the use of vascularised tissue for pharyngeal reconstruction (30).

In cases of occult lymph node involvement, the diseasefree survival at 5 years varies from 56% to 100%, and the overall survival at 5 years varies from 33% to 75% (8,10,13,20,27,28).

In our study, the presence of occult pN+ lymph node metastases, was linked to poor overall survival (20% vs 100% at 1 year) (p=0.001).

Although, Lin et al. (31) showed that performing LND significantly reduces disease-specific survival. A more recent study including a larger number of patients found a benefit (in multivariate analysis) in terms of overall survival and without recurrence in favour of performing a neck dissection for locally advanced cN0 laryngeal tumors (14). Furthermore, the risk of regional recurrence appears to be reduced by more than 50% (18).

Leong et al. (32) and Klozar et al. (33) also found that lymphatic extension was a major prognostic factor for overall survival and disease-specific survival.

In other studies (34,35), the percentage of patients surviving after a 2-year follow-up based on the pN analysis is as follows: 88.1%: pN0 group; 65.4%: N+ group without capsular rupture; 46.2%: N+ R+ group (only 1 lymphadenopathy) and 15.4%: N+ R+ group (more than one lymphadenopathy).

A mathematical model based on a meta-analysis including morbidity, mortality, risk of lymph node recurrence and overall survival based on a rate of occult metastases between 0 and 8% was proposed by Hilly et al. (14). According to their model, the recovery rate for STL was between 50% and 65%, whether or not it was associated with LND. The authors did not recommend systematic LND when performing STL in the case of an N0 neck. Given the morbidity of the lymph node procedure in the salvage setting, and the lack of benefit in terms of regional control or overall survival, some teams no longer systematically perform LND during STL. The decision to proceed with neck dissection at stage N0 must weigh up the benefits of increased survival against the possibility of increased post-operative complications. Nevertheless, results from two recent meta-analyses have not demonstrated the likelihood of a pharyngocutaneous fistula or the clear benefit of neck dissection in terms of survival (29,31).

The main objection to a LND is that the rate of pathologically confirmed occult metastases, even in advanced recurrences, is less than 10% as well as a higher risk of complications (17,18).

Bohannon et al. (18) performed a survival analysis comparing patients with or without LND. There was no survival benefit in patients undergoing LND (52% vs 48% at 2 years).

The lack of benefit in terms of overall survival for N0 patients receiving LND during STL has been similarly observed in other studies (10,17,20).

A time between the end of treatment and salvage surgery of less than one year and positive lymph node status at initial management was for Lee et al. (7) factors indicating the need for LND and were influential on specific survival and local disease control.

In the presence of clinical and/or radiological evidence of lymph node involvement, therapeutic LND is systematically performed. On the other hand, in the case of an N0 neck, the systematic performance of a LND remains controversial.

Most studies do not randomize patients to account for inherent selection bias, including those that do not demonstrate the benefit of neck dissection (17,18,36,37). The ineffectiveness of LND could simply be a reflection of how well it can distinguish between groups that require and do not require this neck dissection. Reviews agree that a subgroup of patients may benefit from neck dissection; however, due to the heterogeneity of the studies, it is not possible to perform a subgroup analysis. As a result, the approach to the patient (tumor characteristics, prior treatment, patient preferences, comorbidities) and the treatment facility (access to surgical resources) should be tailored to each individual.

In addition to treatment of the primary disease, treatment of the neck (surgery plus or minus irradiation if not received during initial treatment) is justified if positive lymph nodes are found at the time of recurrence. The prognosis is reserved, though, as many of these patients will eventually experience distant or cervical failure (36,38).

For patients submitted to LND, Hilly et al. (14) found a survival benefit. This benefit was limited to recurrent T3/T4 and not recurrent T1/T2, pointing to a potential benefit of LND for improving survival rates and disease control. However, Lin et al. (31) emphasize that survival data must be interpreted with caution, as many studies, which included small numbers of patients, are unable to detect a survival advantage, and the distribution of T stages between treated and observed necks is often not homogeneous. In patients undergoing STL, previous research has identified tumor stage, tumor site, and pathologically positive (pN+) lateral neck disease as predictors of survival (38).

In order to verify that paratracheal node dissection (PTND) offers a survival advantage independent of these variables, Farlow et al. (39) conducted a multivariate analysis. In cN0 subjects, PTND was linked to better overall survival (p = 0.03, HR = 0.60) after adjusting for tumor stage, tumor site, and pathologically positive lateral neck disease.

The lateral neck status has no bearing on the survival benefit. Obviously, since the risk of occult metastasis or regional failure is very low, early glottic recurrences will not justify a neck dissection (37). An elective neck dissection may be justified in cases of supraglottic subsite and advanced recurrences, which frequently show occult metastases in neck dissection specimens (28% and 34%, respectively) or will more frequently spread to the neck in the absence of treatment (18).

According to Anwar et al. (40), patients undergoing STL with advanced local disease at recurrence may benefit from an LND; supraglottic tumors may justify LND; less advanced recurrences (rT1-2) may benefit from an observation policy for the neck, and more advanced recurrences (rT3–4) may benefit from LND.

Recently, the French ENT Society do not recommend a systemic LND linked to STL (41). Meanwhile, the American recommendations of the National Comprehensive Cancer Network (NCCN) in 2023 (42) do not take a position on the treatment of lymph nodes in their decision tree.

Limitations of our study

The main limitation of our study is the small number of patients with cN0 status who underwent LND, which may be insufficient for subgroup analysis. This limitation could be attributed to the improved outcomes of radiotherapy.

CONCLUSION .

Although the literature contains a wide range of incidences of occult metastases, the positivity rate probably depends on the proportion of supraglottic tumors included in the series. Our study has confirmed that the higher the proportion of supraglottic tumours, the higher the rate of occult metastases. Occult N+ metastases were associated with recurrence in the supraglottic region and at all 3 laryngeal levels, despite the fact that in the literature the rate of occult metastases is higher for rT3-T4 and supraglottic involvement.

Informed consent: Written informed consent was obtained from the patients for their anonymized information to be published in this article.

Funding: The author(s) received no financial support for the research, authorship, and/or publication of this article.

Declaration of Conflict of Interests: The author(s) declared that they have no potential conflicts of interest with respect to the investigation, authorship, and/or publication of this article.

REFERENCES:

- Sanabria A, Silver CE, Olsen KD, Medina JE, Hamoir M, Paleri V, et al. Is elective neck dissection indicated during salvage surgery for head and neck squamous cell carcinoma? Eur Arch Oto-Rhino-Laryngol Off J Eur Fed Oto-Rhino-Laryngol Soc EUFOS Affil Ger Soc Oto-Rhino-Laryngol - Head Neck Surg. 2014;271(12):3111-9.
- Wong LY, Wei WI, Lam LK, Yuen APW. Salvage of recurrent head and neck squamous cell carcinoma after primary curative surgery. Head Neck. 2003;25(11):953-9.
- Julieron M, Temam S. [Locoregional recurrence of ORL cancer: the place of surgery]. Bull Cancer (Paris). 2004;91(11):863-9.
- Virtaniemi JA, Kumpulainen EJ, Hirvikoski PP, Johansson RT, Kosma VM. The incidence and etiology of postlaryngectomy pharyngocutaneous fistulae. Head Neck. janv 2001;23(1):29-33.
- Clark JR, de Almeida J, Gilbert R, Irish J, Brown D, Neligan P, et al. Primary and salvage (hypo)pharyngectomy: Analysis and outcome. Head Neck. août 2006;28(8):671-7.
- Teymoortash A, Bohne F, Kissing L, Daniel H, Kurt B, Wilhelm T, et al. Oncological and surgical outcome of total laryngectomy in combination with neck dissection in the elderly. Eur Arch Oto-Rhino-Laryngol Off J Eur Fed Oto-Rhino-Laryngol Soc EUFOS Affil Ger Soc Oto-Rhino-Laryngol - Head Neck Surg. 2016;273(7):1825-33.
- Lee DJ, Kwon KH, Chung EJ, Park IS, Kim JH, Rho YS. The role of elective neck dissection during salvage surgery in head and neck squamous cell carcinoma. Acta Otolaryngol (Stockh). 2013;133(8):886-92.
- Yao M, Roebuck JC, Holsinger FC, Myers JN. Elective neck dissection during salvage laryngectomy. Am J Otolaryngol. 2005;26(6):388-92.
- 9. Wax MK, Touma BJ. Management of the N0 neck during salvage laryngectomy. The Laryngoscope. 1999;109(1):4-7.
- Farrag TY, Lin FR, Cummings CW, Koch WM, Flint PW, Califano JA, et al. Neck management in patients undergoing postradiotherapy salvage laryngeal surgery for recurrent/persistent laryngeal cancer. The Laryngoscope. 2006;116(10):1864-6.
- Pezier TF, Nixon IJ, Scotton W, Joshi A, Guerrero-Urbano T, Oakley R, et al. Should elective neck dissection be routinely performed in patients undergoing salvage total laryngectomy? J Laryngol Otol. 2014;128(3):279-83.
- Solares CA, Fritz MA, Esclamado RM. Oncologic effectiveness of selective neck dissection in the N0 irradiated neck. Head Neck J Sci Spec Head Neck. 2005;27(5):415-20.
- 13. Koss SL, Russell MD, Leem TH, Schiff BA, Smith RV. Occult nodal disease in patients with failed laryngeal preservation undergoing surgical salvage. The Laryngoscope. 2014;124(2):421-8.
- Hilly O, Gil Z, Goldhaber D, Amit M, Biadsee A, Popovtzer A, et al. Elective neck dissection during salvage total laryngectomy--a beneficial prognostic effect in locally advanced recurrent tumours. Clin Otolaryngol Off J ENT-UK Off J Neth Soc Oto-Rhino-Laryngol Cervico-Facial Surg. 2015;40(1):9-15.

- Furuta Y, Homma A, Oridate N, Suzuki F, Hatakeyama H, Suzuki K, et al. Surgical complications of salvage total laryngectomy following concurrent chemoradiotherapy. Int J Clin Oncol. 2008;13:521-7.
- Scotton W, Cobb R, Pang L, Nixon I, Joshi A, Jeannon JP, et al. Post-operative wound infection in salvage laryngectomy: does antibiotic prophylaxis have an impact? Eur Arch Oto-Rhino-Laryngol Off J Eur Fed Oto-Rhino-Laryngol Soc EUFOS Affil Ger Soc Oto-Rhino-Laryngol - Head Neck Surg. 2012;269(11):2415-22.
- Basheeth N, O'Leary G, Sheahan P. Elective neck dissection for N0 neck during salvage total laryngectomy: findings, complications, and oncological outcome. JAMA Otolaryngol Neck Surg. 2013;139(8):790-6.
- Bohannon IA, Desmond RA, Clemons L, Magnuson JS, Carroll WR, Rosenthal EL. Management of the N0 neck in recurrent laryngeal squamous cell carcinoma. The Laryngoscope. 2010;120(1):58-61.
- Yirmibesoglu E, Fried D, Shores C, Rosenman J, Weissler M, Hackman T, et al. Incidence of subclinical nodal disease at the time of salvage surgery for locally recurrent head and neck cancer initially treated with definitive radiation therapy. Am J Clin Oncol. 2013;36(5):475-80.
- Freiser ME, Ojo RB, Lo K, Saint-Victor S, Bollig C, Nayak CS, et al. Complications and oncologic outcomes following elective neck d issection with salvage laryngectomy for the N0 neck. Am J Otolaryngol. 2016;37(3):186-94.
- Temam S, Koka V, Mamelle G, Julieron M, Carmantrant R, Marandas P, et al. Treatment of the N0 neck during salvage surgery after radiotherapy of head and neck squamous cell carcinoma. Head Neck. 2005;27(8):653-8.
- Dedivitis RA, Aires FT, Cernea CR, Brandão LG. Pharyngocutaneous fistula after total laryngectomy: systematic review of risk factors. Head Neck. 2015;37(11):1691-7.
- Dagan R, Morris CG, Kirwan JM, Werning JW, Vaysberg M, Amdur RJ, et al. Elective neck dissection during salvage surgery for locally recurrent head and neck squamous cell carcinoma after radiotherapy with elective nodal irradiation. The Laryngoscope. 2010;120(5):945-52.
- 24. Brierley JD, Gospodarowicz MK, Wittekind C. TNM Classification of Malignant Tumours. John Wiley & Sons; 2017. 272 p.
- Birkeland AC, Rosko AJ, Issa MR, Shuman AG, Prince ME, Wolf GT, et al. Occult Nodal Disease Prevalence and Distribution in Recurrent Laryngeal Cancer Requiring Salvage Laryngectomy. Otolaryngol--Head Neck Surg Off J Am Acad Otolaryngol-Head Neck Surg. 2016;154(3):473-9.
- Bernard SE, Wieringa MH, Meeuwis CA, Baatenburg de Jong RJ, Sewnaik A. Elective neck treatment during salvage (pharyngo) laryngectomy. Eur Arch Oto-Rhino-Laryngol Off J Eur Fed Oto-Rhino-Laryngol Soc EUFOS Affil Ger Soc Oto-Rhino-Laryngol - Head Neck Surg. 2019;276(4):1127-33.

IMPACT OF PROPHYLACTIC LYMPH NODE DISSECTION DURING SALVAGE TOTAL LARYNGECTOMY

- Asimakopoulos P, Thompson CSG, Hogg GE, Evans AS, Adamson RM, Vernham GA, et al. Surgical and pathological outcomes of elective neck dissection during salvage total laryngectomy. Clin Otolaryngol Off J ENT-UK Off J Neth Soc Oto-Rhino-Laryngol Cervico-Facial Surg. 2019;44(3):375-8.
- Hussain T, Kanaan O, Höing B, Dominas N, Lang S, Mattheis S. The role of elective neck dissection during salvage laryngectomy - a retrospective analysis. Laryngorhinootologie. 2018;97(10):694-701.
- 29. Gross JH, Vila PM, Simon L, Rizvi ZH, Zenga J, Jackson RS, et al. Elective neck dissection during salvage laryngectomy: A systematic review and meta-analysis. The Laryngoscope. 2020;130(4):899-906.
- Silverman DA, Puram SV, Rocco JW, Old MO, Kang SY. Salvage laryngectomy following organ-preservation therapy - An evidence-based review. Oral Oncol. 2019;88:137-44.
- Lin C, Puram SV, Bulbul MG, Sethi RK, Rocco JW, Old MO, et al. Elective neck dissection for salvage laryngectomy: A systematic review and meta-analysis. Oral Oncol. 2019;96:97-104.
- Leong SC, Kartha SS, Kathan C, Sharp J, Mortimore S. Outcomes following total laryngectomy for squamous cell carcinoma: one centre experience. Eur Ann Otorhinolaryngol Head Neck Dis. 2012;129(6):302-7.
- Klozar J, Cada Z, Koslabova E. Complications of total laryngectomy in the era of chemoradiation. Eur Arch Oto-Rhino-Laryngol Off J Eur Fed Oto-Rhino-Laryngol Soc EUFOS Affil Ger Soc Oto-Rhino-Laryngol - Head Neck Surg. 2012;269(1):289-93.
- 34. Ramroth H, Schoeps A, Rudolph E, Dyckhoff G, Plinkert P, Lippert B, et al. Factors predicting survival after diagnosis of laryngeal cancer. Oral Oncol. 2011;47(12):1154-8.

- Barroso Ribeiro R, Ribeiro Breda E, Fernandes Monteiro E. Prognostic significance of nodal metastasis in advanced tumors of the larynx and hypopharynx. Acta Otorrinolaringol Esp. 2012;63(4):292-8.
- Sandulache VC, Vandelaar LJ, Skinner HD, Cata J, Hutcheson K, Fuller CD, et al. Salvage total laryngectomy after external-beam radiotherapy: A 20-year experience. Head Neck. 2016;38(Suppl 1):1962-8.
- Deganello A, Meccariello G, Bini B, Paiar F, Santoro R, Mannelli G, et al. Is elective neck dissection necessary in cases of laryngeal recurrence after previous radiotherapy for early glottic cancer? J Laryngol Otol. 2014;128(12):1089-94.
- BirkelandAC, BeesleyL, Bellile E, RoskoAJ, Hoesli R, Chinn SB, et al. Predictors of Survival after Total Laryngectomy for Recurrent/Persistent Laryngeal Squamous Cell Carcinoma. Head Neck. 2017;39(12):2512-8.
- Farlow JL, Birkeland AC, Rosko AJ, VanKoevering K, Haring CT, Smith JD, et al. Elective Paratracheal Lymph Node Dissection in Salvage Laryngectomy. Ann Surg Oncol. 2019;26(8):2542-8.
- 40. Anwar M, Dewidar H, Hareedy A, Gebril NE, Nassar A. Role of elective neck dissection with salvage laryngectomy. Egypt J Otolaryngol. 2022;38(1):55-61.
- SFORL. Recommandation pour la pratique clinique organisation du parcours de soins en cancérologie des VADS. Société Française d'Oto-Rhino-Laryngologie et de Chirurgie de la Face et du Cou; 2019.
- 42. Caudell JJ, Gillison ML, Maghami E, Spencer S, Pfister DG, Adkins D, et al. NCCN Guidelines® Insights: Head and Neck Cancers, Version 2.2023. J Natl Compr Cancer Netw JNCCN. 2023;20(3):224-34.