



Guidelines for the Treatment of Laryngeal Cancer from the Korean Society of Head and Neck Surgery

Jeon Yeob Jang^{1,*} · Geun-Jeon Kim^{2,*} · Sang-Yeon Kim² · Min-Su Kim³ · Dong Kun Lee⁴ · Minsu Kwon⁵ · Dongbin Ahn⁶ · Myung Jin Ban⁷ · Young Kang⁸ · Ho-Ryun Won⁹ · Jae Won Chang⁹ · Dong Won Lee¹⁰ · Ki Nam Park¹¹ · Yeon Soo Kim¹² · Ah Ra Jung¹³ · Jungirl Seok¹⁴ · Hye Ran Lee¹⁵ · Sung-Chan Shin¹⁶ · Chang Myeon Song¹⁷ · Gil Joon Lee⁶ · Jihye Kwak⁶ · Soo Yeon Jung¹⁸ · Bo Hae Kim¹⁹ · Dong-Hyun Lee² · Nayeon Choi²⁰ · Eun Kyung Jung²¹ · Yong Tae Hong²² · Hyun-Bum Kim² · Seung Hoon Han²³ · Su Il Kim²⁴ · Ji Won Kim²⁵ · Yoon-Jong Ryu²⁶ · Heejin Kim²⁷ · Sung Joon Park²⁸ · Hanaro Park²⁹ · Eun-Jae Chung¹⁴ · Seung-Kuk Baek¹² · Jun-Ook Park² · Kwang-Jae Cho²

Department of Otorhinolaryngology-Head and Neck Surgery,

¹*Ajou University School of Medicine, Suwon, Korea*

²*College of Medicine, The Catholic University of Korea, Seoul, Korea*

³*CHA Bundang Medical Center, CHA University School of Medicine, Seongnam, Korea*

⁴*Dong-A University College of Medicine, Busan, Korea*

⁵*Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea*

⁶*School of Medicine, Kyungpook National University, Daegu, Korea*

⁷*Soonchunhyang University College of Medicine, Cheonan, Korea*

⁸*ThanQ Seoul Center for Thyroid-Head and Neck Surgery and Medicine, Seoul, Korea*

⁹*Chungnam National University College of Medicine, Daejeon, Korea*

¹⁰*Daegu Catholic University School of Medicine, Daegu, Korea*

¹¹*Soonchunhyang University College of Medicine, Bucheon, Korea*

¹²*Korea University College of Medicine, Seoul, Korea*

¹³*Nowon Eulji Medical Center, Eulji University School of Medicine, Seoul, Korea*

¹⁴*Seoul National University Hospital, Seoul National University College of Medicine, Seoul, Korea*

¹⁵*International St. Mary's Hospital, Catholic Kwandong University College of Medicine, Incheon, Korea*

¹⁶*Pusan National University Hospital, Pusan National University School of Medicine, Busan, Korea*

¹⁷*Hanyang University College of Medicine, Seoul, Korea*

¹⁸*Ewha Womans University College of Medicine, Seoul, Korea*

¹⁹*Dongguk University Ilsan Hospital, Goyang, Korea*

²⁰*Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea*

²¹*Chonnam National University Hwasun Hospital, Chonnam National University Medical School, Hwasun, Korea*

²²*Jeonbuk National University Medical School, Jeonju, Korea*

²³*Hallym University Dongtan Sacred Heart Hospital, Hallym University College of Medicine, Hwaseong, Korea*

²⁴*Kyung Hee University Hospital at Gangdong, College of Medicine, Kyung Hee University, Seoul, Korea*

²⁵*Inha University College of Medicine, Incheon, Korea*

²⁶*Kangwon National University School of Medicine, Chuncheon, Korea*

²⁷*Hallym University Sacred Heart Hospital, Hallym University College of Medicine, Anyang, Korea*

²⁸*Chung-Ang University Gwangmyeong Hospital, Chung-Ang University College of Medicine, Seoul, Korea*

²⁹*Samsung Changwon Hospital, Sungkyunkwan University School of Medicine, Changwon, Korea*

Objectives. Effective treatment of laryngeal cancer requires clinical decision-making that balances survival outcomes with the preservation of essential functions, such as voice and swallowing. This study, led by the Clinical Practice Guideline Committee of the Korean Society of Head and Neck Surgery, aims to establish evidence-based recommendations to guide surgeons in optimizing treatment decisions for patients with laryngeal cancer.

Methods. A literature search was performed in the PubMed, Embase, Cochrane Library, and KoreaMed databases by a literature search expert and subsequently reviewed by a panel of 39 committee experts. The Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) method was employed to assess the quality of evidence and develop and report the recommendations. The strength of each recommendation reflects the guideline panel's confidence that the benefits of an intervention outweigh its risks for the target population. After drafting the guidelines, Delphi questionnaires were distributed to members of the Korean Society of Head and Neck Surgery and an external reviewer panel.

Results. In total, 15 evidence-based recommendations are provided, addressing six critical aspects of laryngeal cancer treatment: early-stage treatment, treatment of locally advanced cancer, neck management, adjuvant therapy, swallowing rehabilitation, and salvage treatment for recurrent tumors.

Conclusion. The guidelines provide evidence-based, validated recommendations to support clinicians in making optimal treatment decisions for laryngeal cancer.

Keywords. Guidelines; Laryngeal Cancer; Laryngectomy; Organ Preservation; Neck Dissection

INTRODUCTION

According to statistical data from the Korean National Cancer Center, the prevalence rate of laryngeal cancer in 2021 was 24.7 cases per 100,000 individuals [1]. Although its incidence has gradually declined in tandem with decreasing smoking rates, laryngeal cancer remains a significant public health concern. The National Comprehensive Cancer Network (NCCN) guidelines outline both surgical and nonsurgical treatment approaches for laryngeal cancer [2]. Historically, surgical interventions, especially total laryngectomy (TL), have adversely affected patients' quality of life due to the loss of voice. In response, non-surgical, organ-preserving strategies emerged as standard treatment modalities based on randomized controlled trials (RCTs), such as those conducted by the Veterans Affairs Administration and the Radiation Therapy Oncology Group (RTOG 91-11) [3,4]. None-

theless, concerns regarding inferior survival outcomes with non-surgical approaches underscore the need for precise clinical decision-making [5-7].

To address these challenges, the Korean Society of Thyroid-Head and Neck Surgery (KSTHNS) developed surgical treatment guidelines for laryngeal cancer in 2017 [8]. These guidelines, primarily based on narrative literature reviews and expert consensus, included 62 recommendations across 32 categories. Although they significantly advanced clinical practice, the need for more robust, evidence-based guidelines soon became apparent.

Recently, the Korean National Cancer Center initiated a project to develop evidence-based clinical practice guidelines for laryngeal cancer treatment using systematic reviews, meta-analyses, and the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) methodology. Comprehensive methodological consultations during the development pro-

• Received January 9, 2025

Revised March 9, 2025

Accepted April 5, 2025

• Corresponding author: **Kwang-Jae Cho**

Department of Otorhinolaryngology-Head and Neck Surgery, College of Medicine, The Catholic University of Korea, 222 Banpo-daero, Seocho-gu, Seoul 06591, Korea

Tel: +82-31-820-3797, Fax: +82-31-847-0038

Email: entckj@catholic.ac.kr

• Co-Corresponding author: **Jun-Ook Park**

Department of Otorhinolaryngology-Head and Neck Surgery, College of Medicine, The Catholic University of Korea, 222 Banpo-daero, Seocho-gu, Seoul 06591, Korea

Tel: +82-2-2030-4559, Fax: +82-2-2030-4632

Email: junook2000@catholic.ac.kr

*These authors contributed equally to this study.

HIGHLIGHTS

- The guidelines provide comprehensive, evidence-based recommendations for laryngeal cancer management, developed through a systematic literature review, meta-analysis, and expert consensus.
- In addition to prioritizing oncologic control, the guidelines emphasize preserving essential functions such as voice and swallowing, and favor organ-preserving strategies when feasible.
- The recommendations are tailored to disease stage, patient condition, and treatment goals to achieve optimal outcomes.

cess revealed that the current clinical practice guidelines did not adequately address certain topics covered in the 2017 guidelines [8]. Therefore, these new guidelines are not intended as an update to the earlier surgical treatment guidelines but rather as a complementary resource. The systematic approach and evidence-based recommendations derived from key questions (KQs) and meta-analyses are expected to support clinical decision-making effectively. It is important to note that these guidelines are intended to supplement, not replace, clinical judgment or resolve medico-legal issues; they serve as an adjunct to sound clinical reasoning.

MATERIALS AND METHODS

Target population

These guidelines apply to patients diagnosed with laryngeal cancer who have either early-stage or locally advanced disease and are candidates for curative-intent treatment via surgery, radiation therapy (RT), or chemoradiotherapy. Patients with systemic metastases or unresectable disease due to extensive local progression are excluded.

Organization of the committee

The guidelines were developed by the Guideline Committee of the Korean Society of Head and Neck Surgery (KSHNS). A task force comprised five teams, totaling 39 experts, was appointed. The task force chairman (JOP) and vice-chairman (JYJ) were designated by the President of KSHNS (KJC), with the Committee's approval. The committee received support from a literature search expert and a methodology expert from the Korean Cancer Management Guideline Network (KCGN) to optimize protocols for literature search, systematic review, meta-analysis (if applicable), and guideline development methodologies. Committee members convened via conference calls and regularly scheduled online or face-to-face meetings to review and evaluate each stage of the guideline development process.

Literature search and quality assessment

A systematic literature search was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. A literature search expert searched the PubMed, Embase, Cochrane Library, and KoreaMed databases between December 25, 2022, and April 17, 2023, using relevant keywords—including MeSH and Emtree terms—and Boolean operators (AND, OR, NOT) to refine the strategy. The retrieved studies underwent screening and eligibility assessment to exclude duplicates, irrelevant studies, and those lacking sufficient comparisons or details. The selection process followed two approaches based on the availability of systematic reviews for each KQ: (1) If an appropriate systematic review was identified for a KQ, the studies it included were used in guideline develop-

ment, supplemented by additional original studies published after the review's search period to ensure up-to-date evidence; (2) If no systematic review was available for a KQ, a comprehensive search for original studies covering the entire period was performed.

Two committee members independently reviewed the final study selection to determine inclusion or exclusion. The search strings for each KQ and the number of retrieved documents are provided in Supplementary Material 1, and the final PRISMA table for each KQ appears in Supplementary Material 2.

Quality assessment of the literature, meta-analysis, and the grading of recommendations

GRADE approach was used to assess evidence quality and develop and report recommendations. Prior to the guideline meeting, committee members received training on this process through online modules, publications, and presentations, supported by the KCGN. Among the selected studies, the quality of systematic reviews was evaluated using A Measurement Tool to Assess Systematic Reviews (AMSTAR) II [9]. The Risk of Bias for Non-randomized Studies (RoBANS) II tool was applied to assess non-RCTs and observational studies, while the Cochrane Risk of Bias (RoB) 2.0 tool was used for RCTs [10,11]. Two committee members independently assessed the quality of the evidence, and any disagreements were resolved through discussion. The final quality assessment results are summarized in Supplementary Material 3.

Meta-analyses were performed for KQs with sufficient data for evidence synthesis. This encompassed KQs A1, A2, B1, C1, D1, and F2 (Table 1). Meta-analysis and statistical analyses were conducted using Review Manager (RevMan) version 5.3 (The Cochrane Collaboration). Summary statistics for dichotomous outcomes were based on unadjusted odds ratios (ORs) and adjusted hazard ratios (HRs) with 95% CIs. Heterogeneity was assessed using the I^2 statistic, and effect sizes were pooled using a random-effects or fixed-effects model, depending on the heterogeneity level. A P -value of <0.05 was considered statistically significant.

Each recommendation's level of evidence was determined according to the GRADE criteria. High-level evidence indicates strong confidence that the estimated effect approximates the true effect, while moderate evidence suggests that the estimate is likely close to the actual effect, although some variation is possible. Low evidence reflects significant uncertainty, and very low evidence (derived from expert consensus) indicates that no direct evidence is available, with recommendations based solely on the formal agreement of the guideline committee.

The Delphi method was used to establish consensus, particularly regarding the balance of benefits and harms. A panel comprising KSHNS members and five multidisciplinary consultation experts reviewed the recommendations using an online questionnaire. Sixteen recommendations were presented, and panel

Table 1. Organization of the KSHNS guidelines for the treatment of laryngeal cancer

Location key	Section	Item
A	Treatment for early-stage (T1–T2) laryngeal cancer	
A1	What is the appropriate treatment for early-stage glottic cancer?	R1-2
A2	What is the appropriate treatment for early-stage supraglottic cancer?	R3-4
B	Treatment for locally advanced laryngeal cancer (T3–T4)	
B1	What is the role of total laryngectomy in locally advanced laryngeal cancer?	R5
B2	What is an appropriate larynx-preservation therapy in locally advanced laryngeal cancer?	R6
C	Management of the neck	
C1	Is prophylactic neck dissection necessary for patients with clinically lymph node-negative laryngeal cancer?	R7-9
C2	What is the appropriate extent of neck dissection in patients with clinically lymph node-positive laryngeal cancer?	R10-12
D	Adjuvant therapy	
D1	Does adjuvant therapy improve treatment outcomes in patients with laryngeal cancer following surgical resection?	R13
E	Swallowing rehabilitation	
E1	What is the role of swallowing rehabilitation in patients with laryngeal cancer?	R14
F	Salvage treatment for recurrent laryngeal cancer	
F1	What are the salvage treatment options for locally recurrent laryngeal cancer?	R15
F2	Does elective neck dissection improve oncological outcomes in salvage treatment for locally recurrent laryngeal cancer?	R16

KSHNS, Korean Society of Head and Neck Surgery.

members were asked to indicate their agreement by selecting “fully agree,” “agree,” “neither agree nor disagree,” “disagree,” or “totally disagree.” A recommendation was accepted if at least two-thirds of the panel responded with “fully agree” or “agree.” In the first round, 66 responses were received, achieving consensus on 15 of the 16 recommendations. The recommendation that did not meet the threshold was revised based on expert feedback and redistributed for a second round, in which 42 experts participated. The remaining recommendation was subsequently finalized through panel consensus.

GUIDELINES

Table 1 summarizes the organization of the Guidelines for the Treatment of Laryngeal Cancer, and a summary of the recommendations is provided in Supplementary Material 4.

A. Treatment for early-stage (T1–T2) laryngeal cancer

A1. What is the appropriate treatment for early-stage glottic cancer?

Recommendation 1

For early-stage glottic cancer, both surgical treatment and radiation therapy can be considered as initial treatment. (Strong recommendation, low-quality evidence)

Recommendation 2

Transoral surgery is the preferred surgical treatment method in early-stage glottic cancer. (Conditional recommendation, low-quality evidence)

The primary goal in treating early glottic cancer (T1–T2) is to achieve local disease control while preserving the larynx and its functions, particularly voice. The principal treatment modalities include transoral laser surgery (TOS), open partial laryngectomy, and external radiation therapy (XRT) [12-15]. Open partial laryngectomy, which encompasses vertical partial laryngectomy and supracricoid partial laryngectomy, has demonstrated oncological outcomes comparable to those of TOS and XRT in early-stage laryngeal cancer [14,16-18]. However, open partial laryngectomy inevitably results in morbidities such as dysphagia and scarring and is generally reserved for patients with contraindications to XRT, recurrent disease, poor laryngeal exposure, or anterior commissure involvement. Consequently, this study excludes patients treated with open partial laryngectomy.

Due to the anatomical structure and the limited submucosal lymphatic networks, cervical lymph node treatment is generally not performed in early glottic cancer, in contrast to other laryngeal subsites [19,20]. The NCCN guidelines for early-stage glottic cancer advocate an organ-preserving strategy—either surgery (with or without neck dissection) or XRT. Numerous studies comparing TOS and XRT have reported similar local control and survival rates, suggesting that posttreatment functional preservation should be a key consideration when selecting a treatment modality for early-stage glottic cancer.

Based on a review of 34 studies, we conducted a meta-analysis comparing the effectiveness of these two treatment modalities [21-54]. The analysis evaluated oncological outcomes, posttreatment voice quality, and other adverse effects, such as the incidence of secondary primary cancers and the overall laryngeal preservation rate (LPR). Oncologically, the local control rate (LCR) for early-stage laryngeal cancer is typically reported to be around 90% [22,55]. Nonetheless, debate persists regarding the oncological superiority of specific treatment modalities, largely due

to the lack of RCTs. According to our meta-analysis, TOS yielded better 5-year overall survival (OS) outcomes (risk ratio [RR], 0.744; 95% CI, 0.671–0.825) [28,29,31,34,36,37,39,41,45,46,50,52]. However, no statistically significant differences were observed between the two groups in terms of disease-specific survival (DSS; RR, 0.825; 95% CI, 0.591–1.152) or disease-free survival (DFS; RR, 1.051; 95% CI, 0.724–1.526). These results are consistent with previous comparative studies and indicate that a definitive oncological superiority between TOS and XRT could not be established.

Regarding residual voice impairment after treatment, TOS typically affects vocal fold vibration by creating surgical scars, and the resulting tissue loss can cause a glottal gap, thereby impairing the voice. This effect is generally correlated with the extent of tissue excision [38]. In contrast, XRT is reported to alter vocal fold vibration by inducing dryness and fibrosis [56]. Prior research has often suggested that XRT yields superior voice outcomes compared to surgical treatment [12,57,58]. Our meta-analysis compared subjective assessments using the Voice Handicap Index and objective voice parameters—including fundamental frequency (F0), jitter, shimmer, noise-to-harmonic ratio, and maximal phonation time (MPT) [21,24,27,31–33,35,38–40,43,45,47,49,51,53]. MPT was evaluated in eight studies, and after excluding one heterogeneous study, it was found to be lower in the TOS group compared to the XRT group (standardized mean difference, –0.748; 95% CI, –1.133 to –0.364). However, no significant differences were noted between the two groups for the other voice parameters.

Regarding adverse effects following treatment, one study evaluated the frequency of secondary primary tumors and the need for salvage laryngectomy during the posttreatment follow-up period. A meta-analysis of six studies examining secondary primary tumors found no statistically significant difference in risk between the two treatment groups (RR, 1.007; 95% CI, 0.442–2.297) [35–37,44,46,48]. However, in the case of salvage laryngectomy, the TOS group exhibited significantly lower risk of undergoing the procedure compared to the XRT group (RR, 0.521; 95% CI, 0.334–0.812), with low heterogeneity observed among the studies (I^2 , 33%; τ^2 , 0.5088; $P=0.10$). These findings are consistent with previous meta-analyses [55,59]. Guimaraes et al. [59] reported that during the posttreatment observation period, individuals in the surgery group had a 1.8% probability of undergoing salvage laryngectomy, whereas those in the XRT group had an 11.8% probability.

We did not find convincing oncological evidence favoring either TOS or XRT. Likewise, aside from MPT, no significant differences were identified in voice-related outcomes—although heterogeneity in measurement timing across studies limited the precision of MPT conclusions. Notably, the rate of salvage TL, which reflects laryngeal preservation, was significantly lower in the TOS group, consistent with previous findings. Overall, most studies included in the meta-analysis were retrospective and

carried a high risk of bias. Oncologically, both surgery and RT produced comparable outcomes, each offering distinct advantages and disadvantages regarding voice preservation and recurrence. Given that both treatments achieved survival rates exceeding 90% for early glottic cancer in most studies, we strongly recommend either treatment option.

A2. What is the appropriate treatment for early-stage supraglottic cancer?

Recommendation 3

For early-stage supraglottic cancer, both surgical treatment and radiation therapy can be considered as initial treatment. (Strong recommendation, low-quality evidence)

Recommendation 4

Conservative laryngeal surgery (transoral surgery or open partial laryngectomy) can be considered as a surgical treatment option for early-stage supraglottic cancer. (Conditional recommendation, low-quality evidence)

For patients with early-stage supraglottic cancer (T1–T2), successful disease control can be achieved through either conservative laryngeal surgery (open partial laryngectomy or TOS) or therapeutic doses of XRT [8,60]. The key factors when selecting initial treatment include improving survival, reducing recurrence, and preserving laryngeal function.

Regarding the comparative effectiveness of surgical treatment and XRT, Patel et al. [61] conducted a systematic literature review and meta-analysis of seven retrospective studies [60,62–67]. Their analysis indicated that disease-specific mortality (OR, 0.43; 95% CI, 0.31–0.60) and 5-year overall mortality (OR, 0.40; 95% CI, 0.29–0.55) were lower in the surgical group than in the XRT group, while the local recurrence rate did not differ significantly between the two [61].

Among the studies in this meta-analysis, Arshad et al. evaluated the largest cohort (2,631 patients) and found that organ-preserving surgery with lymph node dissection resulted in a significantly better survival rate than XRT alone, suggesting that surgical treatment is preferable for early-stage supraglottic cancer [62]. Conversely, Spriano et al. [60] reported a 5-year DFS rate of 88.4% for conservative laryngeal surgery versus 76.4% for radiotherapy in T1–T2 supraglottic cancer (166 patients), without a statistically significant difference. This study also noted that complications related to chronic aspiration occurred in 3% of patients undergoing conservative surgery, with a higher risk in those receiving more extensive surgery than in those treated with XRT [60]. Since all the studies included in the meta-analysis were retrospective, the level of evidence is very low, making definitive conclusions difficult.

Overall, there is no significant evidence-based difference in

oncologic outcomes between surgical treatment and XRT for early-stage supraglottic cancer (T1–T2). Moreover, no study has yet compared the functional outcomes of these two modalities. Therefore, taking into account both patient-specific factors and the benefits and risks of treatment, surgical treatment and RT remain viable initial options; the most appropriate choice should be determined through shared decision-making between the treatment team and the patient.

B. Treatment for locally advanced laryngeal cancer (T3–T4)

B1. What is the role of total laryngectomy in locally advanced laryngeal cancer?

Recommendation 5

Total laryngectomy can be selected as an initial treatment in locally advanced laryngeal cancer to achieve better locoregional control and survival. (Conditional recommendation, low-quality evidence)

The larynx is essential for respiration, phonation, and swallowing; therefore, in advanced laryngeal cancer, survival must be balanced with functional preservation. TL, the primary surgical treatment modality for locally advanced laryngeal cancer, inevitably leads to a significant decline in quality of life [68,69]. Following prospective randomized trials on laryngeal preservation—including studies by the Veteran's Affairs [3] and RTOG 91-11 [4], which demonstrated that primary RT and chemoradiation were not inferior to surgery—laryngeal preservation treatments have become a dominant modality in managing locally advanced laryngeal cancer [70,71]. However, because these preservation treatments have not independently improved survival [69,70], the optimal primary treatment modality remains debated.

A number of studies have compared oncologic outcomes of TL and organ preservation treatments in locally advanced laryngeal cancer. We conducted a meta-analysis evaluating OS, DFS, DSS, and locoregional control (LRC). Our analysis of 17 studies revealed that primary TL significantly reduced risk compared to concurrent chemoradiation therapy (CCRT) for patients with T3 and T4 stages (HR, 0.77; 95% CI, 0.66–0.90; $P<0.00001$) [6,71–83]. In a subgroup analysis for T4 stage, the risk for reduced OS was significantly higher in the CCRT group compared to the TL group (HR, 1.40; 95% CI, 1.20–1.57; $P<0.00001$) [6,70,73,78,81,82]. These findings are consistent with previous studies, which consistently show the superiority of primary TL for OS in T4-stage disease [69–71,78,83]. Current NCCN guidelines also recommend primary surgery as the preferred treatment for T4a patients [2]. Additionally, in a meta-analysis of five studies on LRC, the primary TL group demonstrated a significantly lower risk compared to the CCRT group (HR, 0.58; 95% CI, 0.38–0.88; $P=0.01$) [74,76,77,82,84], although stage-specific subgroup analysis was not feasible. No significant differences between TL and CCRT were observed for DFS and DSS, and

stage-specific analysis could not be performed [71–74,76,77, 85–87].

Uncertainty remains regarding the management of T3 disease. In our meta-analysis of OS for T3 cases, no significant difference was found between the primary TL and CCRT groups (HR, 1.19; 95% CI, 0.83–1.70; $P=0.33$) [70,73,81], which is consistent with prior analyses and systematic reviews [69,70,83]. The NCCN guidelines also consider non-surgical treatment modalities as equally feasible for T3 cases, including those potentially suitable for TL [88].

Studies on quality of life have consistently highlighted that TL results in loss of natural phonation and introduces psychological and social challenges due to the creation of a permanent tracheostomy [68–71,78,83,89,90]. Furthermore, during treatment decision-making, patients may refuse such life-altering surgery or have comorbidities—especially in older patients—that make aggressive surgery less tolerable [78]. Conversely, non-surgical treatments also come with quality-of-life concerns, such as dietary restrictions caused by radiation-induced oral mucositis and xerostomia [89], and a lower rate of improvement in dysphagia in the CCRT group compared to the surgical group (75.4% vs. 53.8%, $P<0.001$) [90]. Ganly et al. [91] reported that salvage TL performed after initial CCRT failure was associated with significantly higher local complications due to delayed wound healing (45% vs. 25%, $P=0.02$) and increased rates of pharyngocutaneous fistula (53% vs. 36%, $P=0.08$) compared to initial TL.

In summary, although debate persists over the initial application of TL versus laryngeal-preserving treatments, the superior OS outcomes and lower local recurrence rates observed with TL support its use as an initial treatment for locally advanced laryngeal cancer, especially in T4-stage disease. However, because surgical feasibility and tolerance for postoperative quality-of-life reductions vary among patients, treatment choice must consider factors such as whether the disease is T3 or T4, the patient's need for voice function in social activities, age, and comorbidities. Therefore, the recommendation remains conditional. Therefore, a careful selection of initial treatment modalities, tailored to individual patient characteristics and disease burden, is crucial for achieving the optimal balance between oncologic outcomes and quality of life in the management of locally advanced laryngeal cancer.

B2. What is an appropriate larynx-preservation therapy in locally advanced laryngeal cancer?

Recommendation 6

(A) Larynx-preservation therapy (concurrent chemoradiation therapy or larynx-preservation surgery) can be applied depending on the patient's condition (T stage, age, underlying diseases, social activities, etc.). (Conditional recommendation, low-quality evidence)

(B) Larynx-preservation surgery can be performed in selected T3–T4 cancers without extensive tongue base invasion, bilateral cricoarytenoid unit impairment, or inferior extension to the cricoid cartilage, although the risk of post-operative morbidity such as dysphagia and aspiration should be carefully considered. (Conditional recommendation, low-quality evidence)

Managing locally advanced laryngeal cancer (T3–T4) presents significant challenges. This discussion is based on a comprehensive review of treatment options, with a focus on larynx-preservation therapies compared to TL. TL is often regarded as the standard treatment for T4 tumors because of its superior OS and local control outcomes. Previous studies have shown that TL reduces the risk of death compared to CCRT [69,71,83,92]. Specifically for T4 tumors, TL demonstrated significantly better OS than CCRT [69,70,92]. In contrast, CCRT is a viable option for T3 tumors, providing oncologic outcomes comparable to TL; in subgroup analysis, no significant OS difference was observed between TL and CCRT for T3 tumors [69,70]. CCRT is especially beneficial for patients prioritizing laryngeal function preservation or those at high surgical risk. A recent meta-analysis found no significant difference in DFS between TL and CCRT, although heterogeneity was moderate ($I^2=69\%$) [69]. Similarly, no significant difference in DSS was observed between TL and CCRT (with high heterogeneity, $I^2=89\%$) [69,71], while TL achieved better local control than CCRT with low heterogeneity ($I^2=20\%$) [69].

The choice of therapy for locally advanced laryngeal cancer should be individualized, taking into account patient-specific factors and tumor characteristics such as age, comorbidities, lung and swallowing function, and the extent of local invasion and nodal involvement [93]. Partial laryngectomy may be considered for selected T3–T4 tumors that do not invade critical structures extensively; in selected cases, partial laryngectomy has shown oncologic outcomes comparable to TL and CCRT [94]. A recent study suggests that surgery with adjuvant therapy is preferred for patients with T4a tumors, whereas patients with T3 tumors can be managed with either surgery or definitive CCRT/RT to preserve laryngeal function [83].

Recent advances in transoral surgery, including laser surgery and transoral robotic surgery (TORS), have shown promise as effective larynx-preservation strategies in locally advanced laryngeal cancer [95,96]. These minimally invasive techniques offer benefits such as reduced surgical morbidity, shorter recovery times, and potentially better functional outcomes regarding voice and swallowing. Laser surgery enables precise tumor excision with minimal damage to adjacent tissues, while TORS provides improved visualization and dexterity. For selected patients, these approaches may serve as useful alternatives, preserving laryngeal function without compromising oncologic control. However, their indications and long-term oncologic safety have not yet been fully established.

In conclusion, while TL offers superior outcomes for T4 tumors, CCRT and partial laryngectomy provide viable alternatives for T3 or selected T4 cases, allowing laryngeal function to be preserved without sacrificing oncologic control. This tailored approach is essential for optimizing outcomes in patients with advanced laryngeal cancer.

C. Management of the neck

C1. Is prophylactic neck dissection necessary for patients with clinically lymph node-negative laryngeal cancer?

The indications and extent of prophylactic neck dissection or irradiation in patients with clinically lymph node-negative laryngeal cancer remain topics of ongoing debate. The decision to pursue prophylactic neck treatment is typically based on the primary subsite of laryngeal cancer, its T stage, and the estimated risk of occult lymph node metastases (LNM). Directly analyzing the impact of neck dissection extent on survival in laryngeal cancer is challenging; therefore, indirect evidence was derived by examining the pooled incidence of LNM at each neck level. Prophylactic treatment is generally considered when this risk reaches 15%–20% or higher. The risk varies by primary site and stage, with glottic cancers typically exhibiting sparse lymphatic drainage and a lower incidence of occult LNM [97]. Expected survival benefits, as well as potential functional and cosmetic morbidity from prophylactic treatment, are comprehensively considered for each patient.

Recommendation 7

If lymph node metastasis is clinically negative in early-stage (T1–T2) laryngeal cancer confined to the glottis, prophylactic neck dissection is not mandatory. (Conditional recommendation, low-quality evidence)

The initial search identified 868 studies on occult neck LNM in laryngeal cancer. Among these, only 10 studies specifically addressed glottic cancer, encompassing a total of 2,192 patients [97–106]. Regardless of T stage, the overall pooled incidence of occult metastasis in glottic cancer was 9% (95% CI, 5.6–14.7; $I^2=91\%$). In five studies reporting data on the T1–T2 stage [97, 99–102], the pooled incidence was 6% (95% CI, 0.1–12; $I^2=88\%$). For the subgroup with T3 stage of glottic cancer [98–102], the pooled incidence was 15.6% (95% CI, 7.6–23.6; $I^2=30\%$). For T4 stage disease [98–102], the pooled incidence was 46.5% (95% CI, 20.6–72.4; $I^2=67\%$).

Recently, with the introduction of non-surgical organ preservation treatments such as definitive RT and transoral surgery for early-stage glottic cancer, avoiding unnecessary neck dissection and minimizing the radiation field have become increasingly important to prevent treatment-related morbidities [107]. In this context, the low probability of occult neck LNM in T1–T2 glottic cancer suggests that prophylactic neck dissection may be omitted. This approach helps to avoid unnecessary procedures and

potential complications, thereby preserving the patient's quality of life.

However, these results do not directly assess the impact of prophylactic neck dissection on survival. The decision to perform neck dissection should be based on various clinical factors, and therefore, the strength of the recommendation remains conditional.

Recommendation 8

If lymph node metastasis is clinically negative in early-stage (T1–T2) laryngeal cancer involving the supraglottis, prophylactic neck dissection including levels II–III can be considered. (Conditional recommendation, low-quality evidence)

The lymphatic drainage of the larynx differs significantly between the supraglottic and glottic regions. The supraglottis has a dense lymphatic network that drains via the thyrohyoid membrane into the first-echelon lymph nodes at levels II and III. In contrast, the glottis—particularly the free edge of the true vocal cords—has a sparse lymphatic network and is nearly devoid of lymphatic vessels. Since the 1960s, several studies have highlighted these differential drainage patterns, emphasizing the rich lymphatic presence in the supraglottis compared to the minimal lymphatic structures in the vocal cords [108-110].

In our analyses, 23 studies specifically addressing supraglottic cancer, with a total of 2,235 patients, were reviewed [100-102, 111-130]. In T1–T2 tumors, the pooled incidence of occult LNM was 15.1% (95% CI, 12–18.3; $I^2=0\%$). For the subgroup of T3 supraglottic cancer, the pooled incidence of occult metastasis was 23.1% (95% CI, 16.6–29.7; $I^2=65\%$). Given the higher incidence of LNM in supraglottic cancer compared to glottic cancer at similar T classifications (15.1% vs. 6% in T1–T2 tumors and 23.1% vs. 15.6% in T3 tumors), prophylactic neck dissection may be warranted in early-stage (T1–T2) supraglottic cancer. This increased risk underscores the importance of addressing potential lymph node involvement to ensure comprehensive treatment and improve patient outcomes.

Our analysis further indicates a pooled incidence of 0.8% (95% CI, 0–3.3; $I^2=48\%$) for level I and only 1% (95% CI, 0–3.3; $I^2=48\%$) for level IV, suggesting that routine elective treatment of these levels may be unnecessary. Similarly, the pooled incidence for level V was 2.3% (95% CI, 1.1–3.5; $I^2=37\%$), which supports their exclusion from routine dissection.

Recommendation 9

If lymph node metastasis is clinically negative in advanced stage (T3–T4) laryngeal cancer, prophylactic neck dissection including levels II–III should be considered. (Conditional recommendation, low-quality evidence)

Twenty studies on laryngeal cancer without specifying a subsite—including a total of 3,916 patients—were reviewed [102,131-

149]. The pooled incidence of occult neck LNM in advanced-stage (T3–T4) laryngeal cancer was 20.8% (95% CI, 15.5–26.1; $I^2=61\%$). This substantial risk supports the need for prophylactic neck dissection in patients with advanced-stage laryngeal cancer who do not exhibit clinically apparent ipsilateral neck LNM. The increasing risk of occult metastases with advancing T stage highlights the importance of this approach in ensuring comprehensive treatment and improving patient outcomes.

C2. What is the appropriate extent of neck dissection in patients with clinically lymph node-positive laryngeal cancer?

Recommendation 10

If ipsilateral lymph node metastasis is clinically evident, comprehensive neck dissection or selective neck dissection including at least levels II, III, and IV should be performed. (Strong recommendation, low-quality evidence)

Although no large-scale randomized studies have established the optimal treatment for laryngeal cancer with clinically positive LNM, modified radical neck dissection (MRND) involving levels I–V is commonly performed. However, studies indicate that metastasis to levels I (1.8%–5%) and V (2%–11%) is infrequent in laryngeal cancer [131,150,151]. Allegra et al. [152] reported neck recurrence in 6 of 58 patients (10.3%) with laryngeal cancer and LNM who underwent selective neck dissection (SND)—all within previously dissected areas. Similarly, Lohuis et al. performed SND including levels II–V in 48 patients with laryngeal and hypopharyngeal cancer, reporting six cases of recurrence, five of which occurred within previously dissected regions [151]. Brazilian Head and Neck Cancer Study Group [153] compared MRND and SND (levels II–V) in 132 patients with T2–T4N0M0 supraglottic and transglottic cancer and found no significant differences in 5-year survival, recurrence rate, complications, or hospital stay. However, Santos et al. [154] reported higher neck recurrence rates after SND in patients with T3 or higher primary tumors and N2b or higher neck metastasis, advising caution in such cases. Furthermore, when extranodal extension (ENE) is present, resection of the spinal accessory nerve, internal jugular vein, and sternocleidomastoid muscle may be necessary.

A literature search on LNM for unilateral neck dissection in supraglottic cancer yielded only a few studies. In an earlier study, Candela et al. [131] found that metastasis in laryngeal cancer was most common in levels II–IV. In supraglottic cancer with clinical LNM, 5% and 6% of 119 patients had metastasis in levels I and V, respectively, while postoperative confirmation showed 11% in level I and none in level V. Choi et al. [155] analyzed 78 cases (39 of which were supraglottic cancer) and noted that the two cases with level I metastasis were salvage surgeries; both node-negative and node-positive patients had very low frequencies of level I involvement. Consistent with this, Buckley and

MacLennan [156] and Gallo et al. [157] reported that most metastases in laryngeal cancer occurred in levels II–V, with few cases at levels I and V. Multiple other studies have also indicated a low frequency of metastasis at levels I and V [158–162]. However, most of these studies were retrospective and lacked bias assessments, making the evidence low-quality. Nevertheless, given the high probability of metastasis in levels II, III, and IV when lymph node involvement is present, performing neck dissection that includes at least these levels is necessary, warranting a strong recommendation.

Recommendation 11

If ipsilateral lymph node metastasis is clinically apparent in laryngeal cancer confined to the glottis, contralateral prophylactic neck dissection is not mandatory. (Conditional recommendation, low-quality evidence)

Prophylactic neck dissection in head and neck cancer is generally considered when the rate of occult metastasis is 15%–20% or higher. If the tumor crosses the midline and invades the contralateral side, elective treatment of the contralateral neck may be necessary [8]. In locally advanced glottic cancer (T3–T4) that extends beyond the midline, and in transglottic cancer—which involves both the supraglottic and subglottic regions—the lymphatic spread pattern may be similar to that of primary cancers in these areas, suggesting that contralateral prophylactic neck dissection could be warranted.

Amar et al. [163] studied 104 laryngeal cancer patients who underwent surgery and found that in unilateral glottic cancer without midline involvement, the contralateral occult metastasis rate was only 3.5%, suggesting that contralateral prophylactic dissection is unnecessary. Bottcher et al. [147] investigated occult metastasis rates in 28 advanced laryngeal cancer patients who underwent TL with prophylactic neck dissection for transglottic cancer, finding occult metastasis in 24.9% of cases—14.2% on the ipsilateral side and 10.7% on the contralateral side. They also noted that previous studies observed no contralateral metastasis when the primary tumor did not cross the midline [164].

Given these rates, current evidence does not support routine contralateral prophylactic neck dissection in glottic cancer with ipsilateral lymph node metastasis. However, due to the lack of well-designed prospective comparative studies, the level of evidence remains low and the recommendations are conditional.

Recommendation 12

If ipsilateral lymph node metastasis is clinically apparent in laryngeal cancer involving the supraglottis, contralateral prophylactic neck dissection including levels II–IV should be considered. (Conditional recommendation, moderate-quality evidence)

Studies on prophylactic contralateral neck dissection in supraglottic cancer consistently show that surgery reduces recurrence and improves survival compared to observation, without significantly increasing complications. Ferlito et al. [160] found that prophylactic contralateral neck dissection improved survival and recurrence management. Weber et al. [165] reported a recurrence rate of 20% in the observation group compared to 9% in the surgical group, with 2-year survival rates of 76% versus 72%, respectively, favoring surgery. Gallo et al. [157] analyzed 24 surgical versus 103 observational cases, noting that 9 of 24 had pathologic lymph node metastasis while 40 of 103 in the observation group developed local recurrence; however, 5-year survival rates did not differ significantly. Chiu et al. [166] compared 202 observational with 115 surgical cases, demonstrating a lower 2-year recurrence rate (7.8% vs. 20%) and higher 2-year survival (83% vs. 72%) in the surgical group. Although these studies were retrospective, each included over 100 patients and provided moderate-level evidence.

Regarding the extent of surgery, Bottcher et al. [147] reported contralateral neck metastasis only in levels IIA, III, and IV, although their analysis was limited to six patients. Gross et al. [167] analyzed 65 patients and found that approximately 20% had metastasis in contralateral level IIB, suggesting that surgical intervention in this area may be necessary. Dundar et al. [168] observed that contralateral level IIB metastasis occurred only when level IIA was also involved, making intraoperative detection challenging because preoperative assessments showed no LNM. Additional studies generally support performing lymph node dissection in contralateral levels II–IV [129,169,170].

Regarding complications of contralateral prophylactic neck dissection, two retrospective studies compared complication rates in supraglottic cancer patients with unilateral neck metastasis who underwent selective dissection versus observation. Gregor et al. [171] found no significant differences in complications or sequelae between the groups. Similarly, Gallo et al. [157] compared 24 surgical and 103 observational cases and reported no significant differences in complications or 5-year survival rates between the two groups. The surgical procedure typically involves SND of levels II–IV, with potential complications including injury to the spinal accessory nerve.

D. Adjuvant therapy

D1. Does adjuvant therapy improve treatment outcomes in patients with laryngeal cancer following surgical resection?

Recommendation 13

(A) Adjuvant therapy (radiation therapy or chemoradiation therapy) following radical surgery can be considered for patients with advanced stage (III–IV) disease and/or risk factors such as vascular invasion, perineural invasion, or multiple nodal metastases. (Conditional recommendation, low-quality evidence)

(B) Adjuvant chemoradiotherapy should be considered for patients with laryngeal cancer and positive surgical margins or extranodal extension. (Conditional recommendation, high-quality evidence)

Although the optimal adjuvant therapy strategy (radiation versus chemoradiation) after radical surgery for advanced laryngeal cancer remains unclear, its benefits in stage III and IV head and neck squamous cell carcinoma (HNSCC) are well established [172-175]. A meta-analysis assessing the impact of adjuvant RT in advanced laryngeal cancer identified 13,359 abstracts from multiple databases (PubMed, Embase, Cochrane Library, KoreaMed) using terms related to laryngeal cancer and radiotherapy. After screening, three studies were included. Despite high heterogeneity ($I^2=78\%$), patients who underwent postoperative RT ($n=596$) showed significantly improved 5-year OS compared to those who had surgery alone ($n=930$) (RR, 0.90; 95% CI, 0.84–0.97) [92,176,177]. Additionally, postoperative RT reduced recurrence rates (RR, 0.36; 95% CI, 0.14–0.90; $I^2=0\%$) [176,177]. These findings suggest that adjuvant RT after radical surgery improves clinical outcomes in advanced laryngeal cancer. However, in pT3N0 laryngeal cancer without other adverse pathological features, its use should be carefully weighed against potential risks [175,92].

Previous studies have identified high-risk factors that benefit from adjuvant therapy after HNSCC surgery, including ENE, positive or close margins, pT3/pT4 primary tumors, pN2/pN3 nodal disease, perineural invasion, vascular invasion, and lymphatic invasion [178]. Two major RCTs investigating optimal postoperative therapy for advanced resectable HNSCC have been conducted. The RTOG 9501 trial demonstrated that adjuvant CCRT improved LRC and DFS compared to adjuvant RT alone in patients with multiple LNM (>2), ENE, and microscopic positive margins [172]. Similarly, the EORTC 22931 trial reported that CCRT improved progression-free and OS by reducing locoregional relapse in patients with pT3/pT4 tumors (except T3N0 laryngeal cancer), ENE, positive margins, perineural involvement, or vascular invasion [173]. A comparative analysis of RTOG 9501 and EORTC 22931 concluded that adjuvant CCRT is most beneficial for patients with positive margins or ENE, rather than those with multiple LNM [174,179]. Based on these findings with high-quality evidence, CCRT is recommended post-surgery for patients with ENE, with or without positive margins [178]. Additionally, CCRT may be considered for vascular invasion, perineural invasion, or multiple nodal metastases when its benefits are evident [178].

In summary, postoperative RT or CCRT may be considered for advanced (stage III–IV) laryngeal cancer with multiple nodal metastases, perineural, vascular, or lymphatic invasion; however, CCRT is preferred over RT when positive margins or ENE are present. Given the higher risk of severe adverse events associated with CCRT in HNSCC, patients should be thoroughly in-

formed before proceeding with adjuvant therapy [172,173].

E. Swallowing rehabilitation

E1. What is the role of swallowing rehabilitation in patients with laryngeal cancer?

Recommendation 14

Swallowing rehabilitation may be useful for dysphagia after surgical or nonsurgical treatment for laryngeal cancer. (Conditional recommendation, very low-quality evidence)

Swallowing difficulties are common following both surgical and nonsurgical treatments for laryngeal cancer, often necessitating rehabilitation [180-183]. After partial laryngectomy, aspiration occurs in up to 74% of patients, with recovery typically taking 4–6 weeks; more extensive resections may require a longer recovery period [184-186]. Although supracricoid partial laryngectomy is associated with a high incidence of dysphagia, swallowing function often improves within 3 months post-surgery [183,187]. TL can affect swallowing due to reduced pharyngeal wall contraction and pharyngoesophageal pressure; however, most patients resume a normal diet within 1 month if no complications occur [188]. In addition, RT may cause fibrosis and radionecrosis, impairing tongue and pharyngeal muscle function and leading to dysphagia [189]. Swallowing rehabilitation after laryngeal cancer treatment typically includes posture adjustments, swallowing maneuvers, and bolus modification. Techniques such as the supraglottic, super-supraglottic, Masako, Mendelsohn, and effortful swallowing maneuvers can help reduce aspiration, especially following partial laryngectomy or radiotherapy [180-182,190]. Rehabilitation strategies are tailored based on the extent of structural changes and the severity of dysphagia, often assessed through barium swallow tests.

A systematic literature review identified three studies on swallowing rehabilitation [180-182]. Among them, two prospective studies included head and neck cancer patients in general, rather than focusing specifically on laryngeal cancer, while one retrospective study examined swallowing rehabilitation following supracricoid partial laryngectomy. Due to significant heterogeneity in patient populations, a meta-analysis was not feasible, and a narrative literature review was conducted instead. Lewin et al. [181] found that despite initial severe dysphagia following supracricoid partial laryngectomy, most patients regained oral intake with appropriate rehabilitation strategies. Hajdu et al. [180] reported that swallowing exercises during radiotherapy improved quality of life and functional outcomes, although they did not significantly affect penetration-aspiration scores. Messing et al. [182] indicated that prophylactic swallowing exercises in patients undergoing chemoradiotherapy led to early improvements in oromotor function and swallowing efficiency. These findings suggest that structured swallowing rehabilitation may enhance functional recovery and improve swallowing outcomes in patients

with laryngeal cancer.

However, several limitations were noted. Most studies included mixed cohorts of head and neck cancer patients, limiting their applicability specifically to laryngeal cancer. In addition, the retrospective nature of the only laryngeal cancer-specific study further reduced its generalizability. Variability in treatment approaches, rehabilitation protocols, and evaluation time points also contributed to inconsistencies among studies. Given the limited availability of high-quality, controlled studies focused exclusively on laryngeal cancer, the current evidence remains very low in quality, supporting only a conditional recommendation for swallowing rehabilitation. Despite these limitations, the existing data suggest that swallowing rehabilitation may be beneficial for managing dysphagia following surgical or nonsurgical treatment of laryngeal cancer. However, due to differences in dysphagia assessment tools, evaluation time points, and small sample sizes across studies, determining the precise effectiveness of swallowing rehabilitation remains challenging. Nonetheless, the available evidence supports its clinical benefit, highlighting the need for further well-designed, prospective studies to establish more definitive guidelines.

F. Salvage treatment for recurrent laryngeal cancer

F1. What are the salvage treatment options for locally recurrent laryngeal cancer?

Recommendation 15

- (A) Total laryngectomy should be considered for most patients with locally recurrent cancer when larynx-preserving strategy is not feasible due to patient and tumor characteristics. (Strong recommendation, low-quality evidence)
- (B) Open partial laryngectomy can be considered for selected patients with locally recurrent laryngeal cancer in whom one or two cricoarytenoid units can be preserved. (Conditional recommendation, very low-quality evidence)
- (C) Transoral surgery may be considered for well-selected patients with localized and limited recurrent tumors, providing precise preoperative assessment to ensure adequate exposure and complete resectability. (Conditional recommendation, very low-quality evidence)
- (D) Radiation therapy/concurrent chemoradiation therapy is an available salvage modality for eligible patients unless it was used in the initial treatment. (Conditional recommendation, very low-quality evidence)

The larynx is generally more amenable to salvage surgery than other head and neck subsites, with salvage total laryngectomy (STL) remaining the primary treatment for locally recurrent, advanced-stage laryngeal cancer. STL is indicated for rT3 tumors associated with cricoarytenoid unit or hemilaryngeal fixation, or extension to the paraglottic/pre-epiglottic spaces, hypopharynx, or subglottis, as well as for rT4a tumors with extralaryngeal spread

or cricoid cartilage infiltration [191-194]. STL is also recommended for patients who are poor candidates for laryngeal conservation surgery because of advanced age or compromised cardiopulmonary function—even in cases of smaller tumors [191-194]. Reported 5-year survival rates for STL range from 37.7% to 59% for OS, 54.9% to 68.7% for DSS, and 42.1% to 83% for DFS [191,192,194-196]. However, STL carries a high complication rate, particularly following prior RT with or without chemotherapy. A 2017 systematic review and meta-analysis of 3,292 patients from 50 studies reported an overall complication rate of 67.5%, with pharyngocutaneous fistula being the most common complication, occurring in 5.6% to 73% of cases (pooled incidence, 28.9%) [197].

Open partial laryngectomy has gained acceptance as a salvage option in selected cases, offering acceptable survival outcomes while preserving the larynx. A 2018 meta-analysis by De Virgilio et al. [198], which included 251 patients from 11 studies, reported a 79% 5-year OS, 80% 3-year DFS, 92% 2-year local control, and an 85.2% LPR for salvage supracricoid partial laryngectomy in recurrent laryngeal cancer [198]. Notably, 27.1% of patients had rT3-T4 disease. A 2022 review by Shapira et al. [199], analyzing 323 patients from 15 studies, found a 90.4% laryngectomy-free survival rate after open supracricoid partial laryngectomy, supporting the use of open partial laryngectomy as a viable salvage option following RT failure. Similarly, Lucioni et al. [200] (2016) reported 82% OS, 82% DSS, and a 70% LPR after salvage partial laryngectomy for patients who failed primary transoral laser microsurgery (TLM), suggesting its safety in this setting. However, most studies on salvage open partial laryngectomy are retrospective and involve small patient cohorts (often fewer than 30 patients), which introduces potential selection and publication biases. Surgeons should take these limitations into account when interpreting the favorable outcomes.

TLM is a valuable salvage option for locally recurrent laryngeal cancer, particularly in early-stage recurrence after primary RT/CCRT or TLM. In rT1-T2 disease following RT/CCRT, salvage TLM has demonstrated OS rates ranging from 52.6% to 100.0%, DSS from 67.9% to 100.0%, LCR from 42.0% to 100.0%, and LPR from 63.0% to 100.0% [201-209]. For rT1-T2 disease following primary TLM, reported outcomes include OS of 61.6%–90.0%, DSS of 79.6%–100.0%, LCR of 57.5%–70.2%, and LPR of 38.5%–85.0% [210-213]. A 2023 systematic review and meta-analysis by Russo et al. [214], which included 235 patients undergoing salvage TLM after RT/CCRT and 271 patients after primary TLM, reported pooled 3-year LCR, DSS, and LPR rates of 53.9%, 67.8%, and 73.5% after RT/CCRT, and 53.2%, 77.0%, and 83.7% after primary TLM, respectively. While some studies have explored salvage TLM for rT3-T4a disease, success in these cases depends on strict patient selection, precise preoperative assessment, and significant surgical expertise to ensure adequate exposure and complete resection.

RT/CCRT can also be used as salvage treatment for eligible

patients if surgery was used as the primary treatment. However, data on salvage RT/CCRT outcomes after failed first-line surgical treatment remain limited, and its effectiveness for recurrent laryngeal cancer following initial surgery cannot be guaranteed. A 2021 study by Akbaba et al. [215], which included 75 patients who underwent salvage RT/CCRT for recurrent hypopharyngeal and laryngeal cancer after primary surgery alone, reported a 5-year local progression-free survival of 75%, OS of 64%, distant progression-free survival of 82%, and an LPR of 100%.

F2. Does elective neck dissection improve oncological outcomes in salvage treatment for locally recurrent laryngeal cancer?

Recommendation 16

Elective neck dissection can be considered in selected patients with locally recurrent laryngeal cancer who are at high risk for regional recurrence, including those with supraglottic or transglottic involvement and advanced rT category. (Conditional recommendation, very low-quality evidence)

An evaluation was conducted on the rate of occult metastasis in patients with locally recurrent laryngeal cancer who underwent salvage laryngectomy (TL) with prophylactic neck dissection for a clinically N0 neck. The analysis included 22 studies [216-237]. The rate of occult metastasis was assessed in patients who underwent neck dissection; however, a meta-analysis was not feasible, and results were derived through quantitative synthesis. An evaluation was conducted on the rate of occult metastasis in patients with locally recurrent laryngeal cancer who underwent salvage laryngectomy (TL) with prophylactic neck dissection for a clinically N0 neck. The analysis included 22 studies.

Next, a meta-analysis was performed to evaluate DSS rates in relation to neck dissection performed alongside TL. Five studies were included [219,220,227,231,234]. The DSS rate was 64.9% (range, 56.4%–100%) in patients who underwent elective neck dissection, compared to 70.5% (range, 54.6%–100%) in those who did not. The meta-analysis found no significant difference in DSS between the two groups (RR, 0.96; 95% CI, 0.78–1.19), likely due to variations in patient numbers, primary tumor sites (supraglottic, transglottic, glottic), disease stage, and evaluation time points. Furthermore, a meta-analysis of OS rates was conducted using data from eight studies [217-220,227,231,236,237]. The OS rate was 62.9% (range, 42.9%–100%) in patients who underwent elective neck dissection, compared to 60.4% (range, 36.2%–100%) in those who did not. No significant difference in OS was found between the two groups (RR, 1.01; 95% CI, 0.86–1.17). A meta-analysis of regional recurrence rates was conducted using data from nine studies [216-219,223,226,233,234,237]. The regional recurrence rate was 7.7% (range, 0%–18.8%) in patients who underwent elective neck dissection, compared to 9.2% (range, 0%–30.8%) in those who did not. This meta-analysis also found no significant difference in regional recurrence

rates between the two groups (RR, 0.69; 95% CI, 0.40–1.21).

An assessment of complications associated with neck dissection performed alongside TL was also conducted. Commonly evaluated complications included pharyngocutaneous fistula, wound hematoma, and infection. Some studies additionally assessed chyle leakage and prolonged feeding tube use. Despite variations in complication types and assessment timings across studies [216-218,220,222,223,231,233,237], the meta-analysis revealed no significant difference in complication rates between groups with and without neck dissection (RR, 1.25; 95% CI, 0.84–1.87).

Two papers included in the systematic review reported differences in occult metastasis rates and corresponding survival rates based on the primary tumor site. Birkeland et al. (2016) [225] found a higher occult metastasis rate of 28% in the supraglottis compared to other subsites ($P<0.00$). Koss et al. [227] reported occult metastasis rates of 60% in the supraglottis ($P=0.02$) and 30% in the transglottis, with correspondingly lower survival rates ($P=0.02$). Birkeland et al. [225] also reported that higher primary tumor stages at recurrence were associated with increased occult metastasis rates: 10% for T1–T2, 15.7% for T3, and 34% for T4 ($P<0.00$). Most studies in this review focused on cases where initial treatment involved RT or chemoradiotherapy. Further evaluation is needed to determine the applicability of these findings to cases where surgical management was the primary treatment.

Concluding remarks

The management of laryngeal cancer requires a careful balance between achieving optimal oncologic outcomes and preserving essential functions such as voice and swallowing. The Korean Society of Head and Neck Surgery, with support from the KCGN, has developed new guidelines for laryngeal cancer management. A key limitation of these guidelines is the lack of active involvement by a multidisciplinary committee during the development process, underscoring the need for future revisions that incorporate broader expertise. Additionally, most key recommendations are based on low-quality evidence and are conditional in nature, making it difficult to provide a clear decision flow. This limitation should be addressed by generating high-quality evidence through future research. Nevertheless, these guidelines—developed through systematic literature review, meta-analysis, and expert consensus, with methodological consultation based on GRADE criteria—offer evidence-based recommendations intended to assist clinicians in making informed treatment decisions.

CONFLICT OF INTEREST

Jeon Yeob Jang and Seung-Kuk Baek are editorial board members of the journal but were not involved in the peer reviewer selection, evaluation, or decision process of this article. No oth-

er potential conflicts of interest relevant to this article were reported.

ACKNOWLEDGMENTS

This work was supported by Research fund of National Cancer Center, Republic of Korea (NCC-2112570).

We thank the Korean Cancer Management Guideline Network (KCGN), Soo Young Kim, MD, PhD (Department of Family Medicine, Kangdong Sacred Heart Hospital, Hallym University College of Medicine, Seoul, Korea), and Seong Ouk Lee (special librarian) for the technical support.

ORCID

Jeon Yeob Jang	https://orcid.org/0000-0002-9047-4896
Geun-Jeon Kim	https://orcid.org/0000-0002-5032-5853
Sang-Yeon Kim	https://orcid.org/0000-0003-3745-5124
Min-Su Kim	https://orcid.org/0000-0001-8311-4174
Dong Kun Lee	https://orcid.org/0000-0002-7296-1420
Minsu Kwon	https://orcid.org/0000-0003-0772-0708
Dongbin Ahn	https://orcid.org/0000-0002-4977-7406
Myung Jin Ban	https://orcid.org/0000-0003-2069-2422
Young Kang	https://orcid.org/0000-0002-0911-8326
Ho-Ryun Won	https://orcid.org/0000-0002-5135-2474
Jae Won Chang	https://orcid.org/0000-0002-6596-931X
Dong Won Lee	https://orcid.org/0000-0003-1653-8975
Ki Nam Park	https://orcid.org/0000-0001-6641-3981
Yeon Soo Kim	https://orcid.org/0000-0002-7862-1662
Ah Ra Jung	https://orcid.org/0000-0001-5647-1184
Jungirl Seok	https://orcid.org/0000-0001-6473-6015
Hye Ran Lee	https://orcid.org/0000-0003-0722-419X
Sung-Chan Shin	https://orcid.org/0000-0003-2329-0648
Chang Myeon Song	https://orcid.org/0000-0001-5267-0135
Gil Joon Lee	https://orcid.org/0000-0002-3344-1879
Jihye Kwak	https://orcid.org/0000-0003-3063-7603
Soo Yeon Jung	https://orcid.org/0000-0001-7497-3057
Bo Hae Kim	https://orcid.org/0000-0002-4645-0678
Dong-Hyun Lee	https://orcid.org/0000-0003-4049-2823
Nayeon Choi	https://orcid.org/0000-0002-0962-0594
Eun Kyung Jung	https://orcid.org/0000-0001-5371-3598
YongTae Hong	https://orcid.org/0000-0001-7584-5823
Hyun-Bum Kim	https://orcid.org/0000-0003-1802-8952
Seung Hoon Han	https://orcid.org/0000-0001-7156-993X
Su Il Kim	https://orcid.org/0000-0002-9647-3034
Ji Won Kim	https://orcid.org/0000-0003-1587-9671
Yoon-Jong Ryu	https://orcid.org/0000-0003-0864-409X
Heejin Kim	https://orcid.org/0000-0001-6157-3636
Sung Joon Park	https://orcid.org/0000-0001-6370-5997
Hanaro Park	https://orcid.org/0000-0001-6804-0760

Eun-Jae Chung	https://orcid.org/0000-0003-3918-7717
Seung-Kuk Baek	https://orcid.org/0000-0002-4751-0337
Jun-Ook Park	https://orcid.org/0000-0001-7118-3463
Kwang-Jae Cho	https://orcid.org/0000-0002-5396-8459

AUTHOR CONTRIBUTIONS

Conceptualization: JYJ, GJK, SYK, MSK, DKL, MK, DA, EJC, SKB, JOP, KJC. Methodology: JYJ, GJK, SYK, MSK, DKL, MK, DA, MJB, YK, HRW, JWC, DWL, KNP, YSK, ARJ, JS, HRL, SCS, CMS, GJL, JK, SYJ, BHK, DHL, NC, EKJ, YTH, HBK, SHH, SIK, JWK, YJR, HK, SJP, HP, EJC, SKB, JOP, KJC. Formal analysis: JYJ, GJK, SYK, MSK, DKL, MK, DA. Data curation: JYJ, GJK, SYK, MSK, DKL, MK, DA, MJB, YK, HRW, JWC, DWL, KNP, YSK, ARJ, JS, HRL, SCS, CMS, GJL, JK, SYJ, BHK, DHL, NC, EKJ, YTH, HBK, SHH, SIK, JWK, YJR, HK, SJP, HP. Visualization: JYJ, GJK. Project administration: JOP, KJC. Writing—original draft: JYJ, GJK. Writing—review & editing: JYJ, GJK, JOP, KJC. All authors read and agreed to the published version of the manuscript.

SUPPLEMENTARY MATERIALS

Supplementary materials can be found online at <https://doi.org/10.21053/ceo.2025.00009>.

REFERENCES

1. Park EH, Jung KW, Park NJ, Kang MJ, Yun EH, Kim HJ, et al. Cancer statistics in Korea: incidence, mortality, survival, and prevalence in 2021. *Cancer Res Treat*. 2024 Apr;56(2):357-71.
2. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Head and Neck Cancers version 1.2025. NCCN; 2024.
3. Department of Veterans Affairs Laryngeal Cancer Study Group; Wolf GT, Fisher SG, Hong WK, Hillman R, Spaulding M, et al. Induction chemotherapy plus radiation compared with surgery plus radiation in patients with advanced laryngeal cancer. *N Engl J Med*. 1991 Jun;324(24):1685-90.
4. Forastiere AA, Goepfert H, Maor M, Pajak TF, Weber R, Morrison W, et al. Concurrent chemotherapy and radiotherapy for organ preservation in advanced laryngeal cancer. *N Engl J Med*. 2003 Nov;349(22):2091-8.
5. Megwalu UC, Sikora AG. Survival outcomes in advanced laryngeal cancer. *JAMA Otolaryngol Head Neck Surg*. 2014 Sep;140(9):855-60.
6. Grover S, Swisher-McClure S, Mitra N, Li J, Cohen RB, Ahn PH, et al. Total laryngectomy versus larynx preservation for T4a larynx cancer: patterns of care and survival outcomes. *Int J Radiat Oncol Biol Phys*. 2015 Jul;92(3):594-601.
7. Choi YS, Park SG, Song EK, Cho SH, Park MR, Park KU, et al. Comparison of the therapeutic effects of total laryngectomy and a larynx-preservation approach in patients with T4a laryngeal cancer and thyroid cartilage invasion: a multicenter retrospective review. *Head*

- Neck. 2016 Aug;38(8):1271-7.
8. Korean Society of Thyroid-Head and Neck Surgery Guideline Task Force; Ahn SH, Hong HJ, Kwon SY, Kwon KH, Roh JL, et al. Guidelines for the surgical management of laryngeal cancer: Korean Society of Thyroid-Head and Neck Surgery. *Clin Exp Otorhinolaryngol*. 2017 Mar;10(1):1-43.
 9. Shea BJ, Reeves BC, Wells G, Thuku M, Hamel C, Moran J, et al. AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. *BMJ*. 2017 Sep;358:j4008.
 10. Seo HJ, Kim SY, Lee YJ, Park JE. RoBANS 2: a revised risk of bias assessment tool for nonrandomized studies of interventions. *Korean J Fam Med*. 2023 Sep;44(5):249-60.
 11. Sterne JA, Savovic J, Page MJ, Elbers RG, Blencowe NS, Boutron I, et al. RoB 2: a revised tool for assessing risk of bias in randomized trials. *BMJ*. 2019 Aug;366:14898.
 12. Mendenhall WM, Werning JW, Hinerman RW, Amdur RJ, Villaret DB. Management of T1-T2 glottic carcinomas. *Cancer*. 2004 May;100(9):1786-92.
 13. de Virgilio A, Greco A, de Vincentiis M. The role of cricohyoidoepiglottopexy in the era of transoral laser surgery and radio/chemotherapy. *Acta Otorhinolaryngol Ital*. 2014 Jun;34(3):209.
 14. Marcotullio D, de Vincentiis M, Iannella G, Bigelli C, Magliulo G. Surgical treatment of T1b glottic tumor, 10-years follow-up. *Eur Rev Med Pharmacol Sci*. 2014 Apr;18(8):1212-7.
 15. Allegra E, Lombardo N, La Boria A, Rotundo G, Bianco MR, Barrera T, et al. Quality of voice evaluation in patients treated by supracricoid laryngectomy and modified supracricoid laryngectomy. *Otolaryngol Head Neck Surg*. 2011 Nov;145(5):789-95.
 16. Jadeed R, Westhofen M. Outcomes of frontolateral vertical partial laryngectomy in T1b glottic carcinomas. *Acta Otolaryngol*. 2021 Jan;141(1):99-105.
 17. Page C, Mortuaire G, Mouawad F, Ganry O, Darras J, Pasquesoone X, et al. Supracricoid laryngectomy with cricohyoidoepiglottopexy (CHEP) in the management of laryngeal carcinoma: oncologic results: a 35-year experience. *Eur Arch Otorhinolaryngol*. 2013 May;270(6):1927-32.
 18. Wang Y, Li X, Pan Z. Analyses of functional and oncologic outcomes following supracricoid partial laryngectomy. *Eur Arch Otorhinolaryngol*. 2015 Nov;272(11):3463-8.
 19. Pressman J, Dowdy A, Libby R, Fields M. Further studies upon the submucosal compartments and lymphatics of the larynx by the injection of dyes and radioisotopes. *Ann Otol Rhinol Laryngol*. 1956 Dec;65(4):963-80.
 20. Ermis E, Teo M, Dyker KE, Fosker C, Sen M, Prestwich RJ. Definitive hypofractionated radiotherapy for early glottic carcinoma: experience of 55Gy in 20 fractions. *Radiat Oncol*. 2015 Sep;10:203.
 21. Ahn SH, Kim JH, Lee SH, Kim WJ, Kim DH, Park YH, et al. Comparison of voice outcomes in early glottic cancer patients after laser surgery or radiotherapy. *Korean J Otorhinolaryngol-Head Neck Surg*. 2012 Nov;55(11):701-6.
 22. Brady JS, Marchiano E, Kam D, Baredes S, Eloy JA, Park RC. Survival impact of initial therapy in patients with T1-T2 glottic squamous cell carcinoma. *Otolaryngol Head Neck Surg*. 2016 Aug;155(2):257-64.
 23. Carvalho GB, Kohler HF, Lira RB, Vartanian JG, Kowalski LP. Survival results of 3786 patients with stage I or II laryngeal squamous cell carcinoma: a study based on a propensity score. *Braz J Otorhinolaryngol*. 2022 May-Jun;88(3):337-44.
 24. Cragle SP, Brandenburg JH. Laser cordectomy or radiotherapy: cure rates, communication, and cost. *Otolaryngol Head Neck Surg*. 1993 Jun;108(6):648-54.
 25. De Santis RJ, Poon I, Lee J, Karam I, Enepekides DJ, Higgins KM. Comparison of survival between radiation therapy and trans-oral laser microsurgery for early glottic cancer patients; a retrospective cohort study. *J Otolaryngol Head Neck Surg*. 2016 Aug;45(1):42.
 26. Epstein BE, Lee DJ, Kashima H, Johns ME. Stage T1 glottic carcinoma: results of radiation therapy or laser excision. *Radiology*. 1990 May;175(2):567-70.
 27. Gandhi S, Gupta S, Rajopadhye G. A comparison of phonatory outcome between trans-oral CO2 laser cordectomy and radiotherapy in T1 glottic cancer. *Eur Arch Otorhinolaryngol*. 2018 Nov;275(11):2783-6.
 28. Goor KM, Peeters AJ, Mahieu HF, Langendijk JA, Leemans CR, Verdonck-de Leeuw IM, et al. Cordectomy by CO2 laser or radiotherapy for small T1a glottic carcinomas: costs, local control, survival, quality of life, and voice quality. *Head Neck*. 2007 Feb;29(2):128-36.
 29. Hirayama M, Takahashi H, Yao K, Inagi K, Nakayama M, Makoshi T, et al. Clinical study of T1a glottic-type cancer. *Acta Otolaryngol Suppl*. 2002;(547):67-71.
 30. Jotic A, Stankovic P, Jesic S, Milovanovic J, Stojanovic M, Djukic V. Voice quality after treatment of early glottic carcinoma. *J Voice*. 2012 May;26(3):381-9.
 31. Kono T, Saito K, Yabe H, Uno K, Ogawa K. Comparative multidimensional assessment of laryngeal function and quality of life after radiotherapy and laser surgery for early glottic cancer. *Head Neck*. 2016 Jul;38(7):1085-90.
 32. Krengh M, Policarpo M, Manfreda I, Aluffi P, Gambaro G, Panella M, et al. Voice quality after treatment for T1a glottic carcinoma: radiotherapy versus laser cordectomy. *Acta Oncol*. 2004;43(3):284-9.
 33. Laoufi S, Mirghani H, Janot F, Hartl DM. Voice quality after treatment of T1a glottic cancer. *Laryngoscope*. 2014 Jun;124(6):1398-401.
 34. Liang QW, Peng L, Liao J, Huang CX, Wen WP, Sun W. Comparison of survival outcomes of different treatment options for cT1-2, N0 glottic carcinoma: a propensity score-weighted analysis. *Front Surg*. 2022 May;9:902817.
 35. Loughran S, Calder N, MacGregor FB, Carding P, MacKenzie K. Quality of life and voice following endoscopic resection or radiotherapy for early glottic cancer. *Clin Otolaryngol*. 2005 Feb;30(1):42-7.
 36. Low TH, Yeh D, Zhang T, Araslanova R, Hammond JA, Palma D, et al. Evaluating organ preservation outcome as treatment endpoint for T1aN0 glottic cancer. *Laryngoscope*. 2017 Jun;127(6):1322-7.
 37. Mahler V, Boysen M, Brøndbo K. Radiotherapy or CO(2) laser surgery as treatment of T(1a) glottic carcinoma? *Eur Arch Otorhinolaryngol*. 2010 May;267(5):743-50.
 38. McGuirt WF, Blalock D, Koufman JA, Feehs RS, Hilliard AJ, Greven K, et al. Comparative voice results after laser resection or irradiation of T1 vocal cord carcinoma. *Arch Otolaryngol Head Neck Surg*. 1994 Sep;120(9):951-5.
 39. Milovanovic J, Djukic V, Milovanovic A, Jotic A, Banko B, Jesic S, et al. Clinical outcome of early glottic carcinoma in Serbia. *Auris Nasus Larynx*. 2013 Aug;40(4):394-9.
 40. Nunez Batalla F, Caminero Cueva MJ, Senaris Gonzalez B, Llorente Pendas JL, Gorris Gil C, Lopez Llamas A, et al. Voice quality after endoscopic laser surgery and radiotherapy for early glottic cancer: objective measurements emphasizing the Voice Handicap Index. *Eur Arch Otorhinolaryngol*. 2008 May;265(5):543-8.
 41. O'Hara J, Whitmarsh A, Pring M, Thomas S, Ness A. Quality of life following treatment for T1a glottic cancer with surgery or radiotherapy: outcomes from the Head and Neck 5000 cohort. *Clin Otolaryngol*. 2022 Jan;47(1):67-74.
 42. Ozturk K, Turhal G, Durusoy D, Sahin E, Akagunduz O, Eyigor S, et al. Long-term swallowing outcomes of radiotherapy and transoral laser microsurgery for T1 glottic cancer treatment. *Clin Otolaryngol*. 2021 Mar;46(2):340-6.
 43. Peeters AJ, van Gogh CD, Goor KM, Verdonck-de Leeuw IM, Lan-

- gendijk JA, Mahieu HF. Health status and voice outcome after treatment for T1a glottic carcinoma. *Eur Arch Otorhinolaryngol*. 2004 Nov;261(10):534-40.
44. Puram SV, Bhattacharyya N. Surgery versus radiation for T1 glottic carcinoma: second primary considerations. *Laryngoscope*. 2019 Dec;129(12):2713-5.
 45. Remmelts AJ, Hoebbers FJ, Klop WM, Balm AJ, Hamming-Vrieze O, van den Brekel MW. Evaluation of lasersurgery and radiotherapy as treatment modalities in early stage laryngeal carcinoma: tumour outcome and quality of voice. *Eur Arch Otorhinolaryngol*. 2013 Jul;270(7):2079-87.
 46. Schrijvers ML, van Riel EL, Langendijk JA, Dikkers FG, Schuurin E, van der Wal JE, et al. Higher laryngeal preservation rate after CO2 laser surgery compared with radiotherapy in T1a glottic laryngeal carcinoma. *Head Neck*. 2009 Jun;31(6):759-64.
 47. Sjogren EV, van Rossum MA, Langeveld TP, Voerman MS, van de Kamp VA, Friebel MO, et al. Voice outcome in T1a midcord glottic carcinoma: laser surgery vs radiotherapy. *Arch Otolaryngol Head Neck Surg*. 2008 Sep;134(9):965-72.
 48. Spector JG, Sessions DG, Chao KS, Haughey BH, Hanson JM, Simpson JR, et al. Stage I (T1 N0 M0) squamous cell carcinoma of the laryngeal glottis: therapeutic results and voice preservation. *Head Neck*. 1999 Dec;21(8):707-17.
 49. Tamura E, Kitahara S, Ogura M, Kohno N. Voice quality after laser surgery or radiotherapy for T1a glottic carcinoma. *Laryngoscope*. 2003 May;113(5):910-4.
 50. Thurnher D, Erovic BM, Frommlet F, Brannath W, Ehrenberger K, Jansen B, et al. Challenging a dogma: surgery yields superior long-term results for T1a squamous cell carcinoma of the glottic larynx compared to radiotherapy. *Eur J Surg Oncol*. 2008 Jun;34(6):692-8.
 51. van Gogh CD, Verdonck-de Leeuw IM, Wedler-Peters J, Langendijk JA, Mahieu HF. Prospective evaluation of voice outcome during the first two years in male patients treated by radiotherapy or laser surgery for T1a glottic carcinoma. *Eur Arch Otorhinolaryngol*. 2012 Jun;269(6):1647-52.
 52. Wang WL, Zheng HW, Zhang LH, Yu LS. Effect of treatment modality on the long-term survival of patients with early glottic squamous cancer: a retrospective cohort study based on the SEER database. *Ann Transl Med*. 2022 Apr;10(8):440.
 53. Wedman J, Heimdal JH, Elstad I, Olofsson J. Voice results in patients with T1a glottic cancer treated by radiotherapy or endoscopic measures. *Eur Arch Otorhinolaryngol*. 2002 Nov;259(10):547-50.
 54. Zhan C, Yang X, Song X, Yan L. Radiotherapy vs surgery for T1-2N0M0 laryngeal squamous cell carcinoma: a population-based and propensity score matching study. *Cancer Med*. 2018 Jul;7(7):2837-47.
 55. Higgins KM, Shah MD, Ogaick MJ, Enepekides D. Treatment of early-stage glottic cancer: meta-analysis comparison of laser excision versus radiotherapy. *J Otolaryngol Head Neck Surg*. 2009 Dec;38(6):603-12.
 56. Roh JL, Kim AY, Cho MJ. Xerostomia following radiotherapy of the head and neck affects vocal function. *J Clin Oncol*. 2005 May;23(13):3016-23.
 57. Dey P, Arnold D, Wight R, MacKenzie K, Kelly C, Wilson J. Radiotherapy versus open surgery versus endolaryngeal surgery (with or without laser) for early laryngeal squamous cell cancer. *Cochrane Database Syst Rev*. 2002;(2):CD002027.
 58. Kadish SP. Can I treat this small larynx lesion with radiation alone?: update on the radiation management of early (T1 and T2) glottic cancer. *Otolaryngol Clin North Am*. 2005 Feb;38(1):1-9.
 59. Guimaraes AV, Dedivitis RA, Matos LL, Aires FT, Cernea CR. Comparison between transoral laser surgery and radiotherapy in the treatment of early glottic cancer: a systematic review and meta-analysis. *Sci Rep*. 2018 Aug;8(1):11900.
 60. Spriano G, Antognoni P, Piantanida R, Varinelli D, Luraghi R, Cerizza L, et al. Conservative management of T1-T2N0 supraglottic cancer: a retrospective study. *Am J Otolaryngol*. 1997 Sep-Oct;18(5):299-305.
 61. Patel KB, Nichols AC, Fung K, Yoo J, MacNeil SD. Treatment of early stage Supraglottic squamous cell carcinoma: meta-analysis comparing primary surgery versus primary radiotherapy. *J Otolaryngol Head Neck Surg*. 2018 Mar;47(1):19.
 62. Arshad H, Jayaprakash V, Gupta V, Cohan DM, Ambujakshan D, Rigual NR, et al. Survival differences between organ preservation surgery and definitive radiotherapy in early supraglottic squamous cell carcinoma. *Otolaryngol Head Neck Surg*. 2014 Feb;150(2):237-44.
 63. Sessions DG, Lenox J, Spector GJ. Supraglottic laryngeal cancer: analysis of treatment results. *Laryngoscope*. 2005 Aug;115(8):1402-10.
 64. Jones AS, Fish B, Fenton JE, Husband DJ. The treatment of early laryngeal cancers (T1-T2 N0): surgery or irradiation? *Head Neck*. 2004 Feb;26(2):127-35.
 65. Orus C, Leon X, Vega M, Quer M. Initial treatment of the early stages (I, II) of supraglottic squamous cell carcinoma: partial laryngectomy versus radiotherapy. *Eur Arch Otorhinolaryngol*. 2000 Nov;257(9):512-6.
 66. Santos CR, Kowalski LP, Magrin J, Fogaroli RC, Santos JC, Saboia MV, et al. Prognostic factors in supraglottic carcinoma patients treated by surgery or radiotherapy. *Ann Otol Rhinol Laryngol*. 1998 Aug;107(8):697-702.
 67. Spector JG, Sessions DG, Emami B, Simpson J, Haughey B, Fredrickson JM. Squamous cell carcinomas of the aryepiglottic fold: therapeutic results and long-term follow-up. *Laryngoscope*. 1995 Jul;105(7 Pt 1):734-46.
 68. Hanna E, Sherman A, Cash D, Adams D, Vural E, Fan CY, et al. Quality of life for patients following total laryngectomy vs chemoradiation for laryngeal preservation. *Arch Otolaryngol Head Neck Surg*. 2004 Jul;130(7):875-9.
 69. Tang ZX, Gong JL, Wang YH, Li ZH, He Y, Liu YX, et al. Efficacy comparison between primary total laryngectomy and nonsurgical organ-preservation strategies in treatment of advanced stage laryngeal cancer: a meta-analysis. *Medicine (Baltimore)*. 2018 May;97(21):e10625.
 70. Bates JE, Amdur RJ, Morris CM, Hitchcock KE, Dziegielewski PT, Boyce BJ, et al. Curative-dose chemoradiotherapy versus total laryngectomy for stage T3-T4 squamous cell carcinoma of the larynx: an "apples-to-apples" analysis of the national cancer database. *Am J Clin Oncol*. 2019 Jun;42(6):527-33.
 71. Kohler HF, de Carvalho GB, Kowalski LP. Impact of treatment modality on survival in patients with stage IV laryngeal cancer: a population-based propensity score analysis. *Am J Otolaryngol*. 2020 Nov-Dec;41(6):102626.
 72. Bussu F, Micciche F, Rigante M, Dinapoli N, Parrilla C, Bonomo P, et al. Oncologic outcomes in advanced laryngeal squamous cell carcinomas treated with different modalities in a single institution: a retrospective analysis of 65 cases. *Head Neck*. 2012 Apr;34(4):573-9.
 73. Dziegielewski PT, O'Connell DA, Klein M, Fung C, Singh P, Alex Mlynarek M, et al. Primary total laryngectomy versus organ preservation for T3/T4a laryngeal cancer: a population-based analysis of survival. *J Otolaryngol Head Neck Surg*. 2012 Apr;41 Suppl 1:S56-64.
 74. Hsin LJ, Fang TJ, Tsang NM, Chin SC, Yen TC, Li HY, et al. Tumor volumetry as a prognostic factor in the management of T4a laryngeal cancer. *Laryngoscope*. 2014 May;124(5):1134-40.
 75. Patel UA, Howell LK. Local response to chemoradiation in T4 larynx cancer with cartilage invasion. *Laryngoscope*. 2011 Jan;121(1):106-10.

76. Rades D, Schroeder U, Bajrovic A, Schild SE. Radiochemotherapy versus surgery plus radio(chemo)therapy for stage T3/T4 larynx and hypopharynx cancer: results of a matched-pair analysis. *Eur J Cancer*. 2011 Dec;47(18):2729-34.
77. Rosenthal DI, Mohamed AS, Weber RS, Garden AS, Sevak PR, Kies MS, et al. Long-term outcomes after surgical or nonsurgical initial therapy for patients with T4 squamous cell carcinoma of the larynx: a 3-decade survey. *Cancer*. 2015 May;121(10):1608-19.
78. Stokes WA, Jones BL, Bhatia S, Oweida AJ, Bowles DW, Raben D, et al. A comparison of overall survival for patients with T4 larynx cancer treated with surgical versus organ-preservation approaches: a National Cancer Data Base analysis. *Cancer*. 2017 Feb;123(4):600-8.
79. Timme DW, Jonnalagadda S, Patel R, Rao K, Robbins KT. Treatment selection for T3/T4a laryngeal cancer: chemoradiation versus primary surgery. *Ann Otol Rhinol Laryngol*. 2015 Nov;124(11):845-51.
80. Timmermans AJ, de Gooijer CJ, Hamming-Vrieze O, Hilgers FJ, van den Brekel MW. T3-T4 laryngeal cancer in The Netherlands Cancer Institute; 10-year results of the consistent application of an organ-preserving/-sacrificing protocol. *Head Neck*. 2015 Oct;37(10):1495-503.
81. Timmermans AJ, van Dijk BA, Overbeek LI, van Velthuisen ML, van Tinteren H, Hilgers FJ, et al. Trends in treatment and survival for advanced laryngeal cancer: a 20-year population-based study in The Netherlands. *Head Neck*. 2016 Apr;38 Suppl 1:E1247-55.
82. Vengalil S, Giuliani ME, Huang SH, McNiven A, Song Y, Xu W, et al. Clinical outcomes in patients with T4 laryngeal cancer treated with primary radiotherapy versus primary laryngectomy. *Head Neck*. 2016 Apr;38 Suppl 1:E2035-40.
83. Wushouer A, Li W, Zhang M, Lei D, Pan X. Comparison of treatment modalities for selected advanced laryngeal squamous cell carcinoma. *Eur Arch Otorhinolaryngol*. 2022 Jan;279(1):361-71.
84. Nguyen-Tan PF, Le QT, Quivey JM, Singer M, Terris DJ, Goffinet DR, et al. Treatment results and prognostic factors of advanced T3: 4 laryngeal carcinoma: the University of California, San Francisco (UCSF) and Stanford University Hospital (SUH) experience. *Int J Radiat Oncol Biol Phys*. 2001 Aug;50(5):1172-80.
85. Bryant GP, Poulsen MG, Tripcony L, Dickie GJ. Treatment decisions in T3N0M0 glottic carcinoma. *Int J Radiat Oncol Biol Phys*. 1995 Jan;31(2):285-93.
86. Karatzanis AD, Psychogios G, Waldfahrer F, Kapsreiter M, Zenk J, Velegakis GA, et al. Management of locally advanced laryngeal cancer. *J Otolaryngol Head Neck Surg*. 2014 Jan;43(1):4.
87. Porter MJ, McIvor NP, Morton RP, Hindley AC. Audit in the management of T3 fixed-cord laryngeal cancer. *Am J Otolaryngol*. 1998 Nov-Dec;19(6):360-4.
88. National Comprehensive Cancer Network. Head and neck cancer (version 4.2024) [Internet]. National Comprehensive Cancer Network; 2024 [cited 2025 Apr 1]. Available from: https://www.nccn.org/professionals/physician_gls/pdf/head-and-neck.pdf
89. Boscolo-Rizzo P, Maronato F, Marchiori C, Gava A, Da Mosto MC. Long-term quality of life after total laryngectomy and postoperative radiotherapy versus concurrent chemoradiotherapy for laryngeal preservation. *Laryngoscope*. 2008 Feb;118(2):300-6.
90. Lee MY, Belfiglio M, Zeng J, Fleming CW, Koyfman S, Joshi NP, et al. Primary total laryngectomy versus organ preservation for locally advanced T3/T4a laryngeal cancer. *Laryngoscope*. 2023 May;133(5):1122-31.
91. Ganly I, Patel S, Matsuo J, Singh B, Kraus D, Boyle J, et al. Postoperative complications of salvage total laryngectomy. *Cancer*. 2005 May;103(10):2073-81.
92. Graboyes EM, Zhan KY, Garrett-Mayer E, Lentsch EJ, Sharma AK, Day TA. Effect of postoperative radiotherapy on survival for surgically managed pT3N0 and pT4aN0 laryngeal cancer: analysis of the National Cancer Data Base. *Cancer*. 2017 Jun;123(12):2248-57.
93. Kim D, Kim N, Koh S, Chung MK, Son YI, Oh D, et al. Oncological and functional outcomes of larynx-preserving surgery for hypopharyngeal cancer: a comparison with definitive radiation-based treatment. *Cancer Res Treat*. 2022 Jan;54(1):84-95.
94. Campo F, Mazzola F, Bianchi G, Mancio V, Ralli M, Greco A, et al. Partial laryngectomy for naïve pT3N0 laryngeal cancer: systematic review on oncological outcomes. *Head Neck*. 2023 Jan;45(1):243-50.
95. Wang CC, Lin WJ, Liu YC, Chen CC, Wu SH, Liu SA, et al. Transoral robotic surgery for pharyngeal and laryngeal cancers: a prospective medium-term study. *J Clin Med*. 2021 Mar;10(5):967.
96. Forastiere AA, Ismaila N, Lewin JS, Nathan CA, Adelstein DJ, Eisbruch A, et al. Use of larynx-preservation strategies in the treatment of laryngeal cancer: American Society of Clinical Oncology clinical practice guideline update. *J Clin Oncol*. 2018 Apr;36(11):1143-69.
97. Patel TR, Eggerstedt M, Toor J, Tajudeen BA, Husain I, Stenson K, et al. Occult lymph node metastasis in early-stage glottic cancer in the national cancer database. *Laryngoscope*. 2021 Apr;131(4):E1139-46.
98. Yang CY, Andersen PE, Everts EC, Cohen JI. Nodal disease in purely glottic carcinoma: is elective neck treatment worthwhile? *Laryngoscope*. 1998 Jul;108(7):1006-8.
99. Elo J, Balatoni Z, Kotai Z, Bartfai R. Considerations in the treatment of the node-negative (N0) neck in glottic carcinomas. *Pathol Oncol Res*. 2002 Dec;8(4):257-61.
100. Pinilla M, Gonzalez FM, Lopez-Cortijo C, Arellano B, Herrero J, Trinidad A, et al. Management of N0 neck in laryngeal carcinoma: impact on patient's survival. *J Laryngol Otol*. 2003 Jan;117(1):63-6.
101. Zhang B, Xu ZG, Tang PZ. Elective lateral neck dissection for laryngeal cancer in the clinically negative neck. *J Surg Oncol*. 2006 May;93(6):464-7.
102. Deganello A, Gitti G, Meccariello G, Parrinello G, Mannelli G, Gallo O. Effectiveness and pitfalls of elective neck dissection in N0 laryngeal cancer. *Acta Otorhinolaryngol Ital*. 2011 Aug;31(4):216-21.
103. Erdag TK, Guneri EA, Avincsal O, Sarioglu S, Ecevit MC, Guneri A, et al. Is elective neck dissection necessary for the surgical management of T2N0 glottic carcinoma? *Auris Nasus Larynx*. 2013 Feb;40(1):85-8.
104. Heng Y, Xu C, Lin H, Zhu X, Zhou L, Zhang M, et al. Management of clinically node-negative glottic squamous cell carcinoma patients according to risk-scoring model for occult lymph node metastases. *Laryngoscope Investig Otolaryngol*. 2022 Mar;7(3):715-22.
105. Mehel DM, Akgul G, Ozdemir D, Celebi M, Turgut NF, Aydemir S, et al. Neck metastasis in transglottic laryngeal carcinomas. *J Exp Clin Med*. 2022;39(1):189-93.
106. Wong SN, Lau FT, Chung JC, Tsang RK. Retrospective review on role of neck dissection in laryngectomy of patients with N0 laryngeal carcinoma. *OTO Open*. 2022 Sep;6(3):2473974X221127903.
107. Ferlito A, Rinaldo A. Controversies in the treatment of N(0) neck in laryngeal cancer: neck dissection, no surgery or sentinel lymph node biopsy? *ORL J Otorhinolaryngol Relat Spec*. 2000 Nov-Dec;62(6):287-9.
108. Welsh LW. The normal human laryngeal lymphatics. *Ann Otol Rhinol Laryngol*. 1964 Sep;73(3):569-82.
109. Welsh LW, Welsh JJ. Laryngeal lymphatics, human in vivo studies. *Trans Am Acad Ophthalmol Otolaryngol*. 1963 Jul-Aug;67:524-9.
110. Welsh JJ, Welsh LW, Rizzo TA. Laryngeal spaces and lymphatics: current anatomic concepts. *Ann Otol Rhinol Laryngol Suppl*. 1983 Jul-Aug;92(4_suppl):19-31.
111. Levendag P, Vikram B. The problem of neck relapse in early stage supraglottic cancer: results of different treatment modalities for the clinically negative neck. *Int J Radiat Oncol Biol Phys*. 1987 Nov;13(11):1621-4.
112. Ramadan HH, Allen GC. The influence of elective neck dissection

- on neck relapse in NO supraglottic carcinoma. *Am J Otolaryngol*. 1993 Jul-Aug;14(4):278-81.
113. Petrovic Z, Krejovic B, Janosevic S. Occult metastases from supraglottic laryngeal carcinoma. *Clin Otolaryngol Allied Sci*. 1997 Dec; 22(6):522-4.
 114. Guney E, Yigitbasi OG. Management of N0 neck in T1-T2 unilateral supraglottic cancer. *Ann Otol Rhinol Laryngol*. 1999 Oct;108(10): 998-1003.
 115. Tu GY. Upper neck (level II) dissection for N0 neck supraglottic carcinoma. *Laryngoscope*. 1999 Mar;109(3):467-70.
 116. Amoros Sebastia LI, Carrasco Llatas M, Lopez Molla C, Pla Mocho-li A, Ferrer Ramirez MJ, Estelles Ferriol JE, et al. Treatment of the NO neck in supraglottic cancer. *Acta Otorrinolaringol Esp*. 2003 Oct;54(8):577-83.
 117. Fiorella R, Di Nicola V, Fiorella ML, Russo C. "Conditional" neck dissection in management of laryngeal carcinoma. *Acta Otorhinolaryngol Ital*. 2006 Dec;26(6):356-9.
 118. Rodrigo JP, Cabanillas R, Franco V, Suarez C. Efficacy of routine bilateral neck dissection in the management of the N0 neck in T1-T2 unilateral supraglottic cancer. *Head Neck*. 2006 Jun;28(6):534-9.
 119. Cagli S, Yuce I, Guney E. Is routine inclusion of level IV necessary in neck dissection for clinically N0 supraglottic carcinoma? *Otolaryngol Head Neck Surg*. 2007 Feb;136(2):287-90.
 120. Cagli S, Yuce I, Yigitbasi OG, Guney E. Is routine bilateral neck dissection absolutely necessary in the management of N0 neck in patients with supraglottic carcinoma? *Eur Arch Otorhinolaryngol*. 2007 Dec;264(12):1453-7.
 121. Yuce I, Cagli S, Bayram A, Guney E. Occult metastases from T1-T2 supraglottic carcinoma: role of primary tumor localization. *Eur Arch Otorhinolaryngol*. 2009 Aug;266(8):1301-4.
 122. Lawson G, Matar N, Nollevaux MC, Jamart J, Krug B, Delos M, et al. Reliability of sentinel node technique in the treatment of N0 supraglottic laryngeal cancer. *Laryngoscope*. 2010 Nov;120(11):2213-7.
 123. Csanady M, Czigner J, Vass G, Jori J. Transoral CO2 laser management for selected supraglottic tumors and neck dissection. *Eur Arch Otorhinolaryngol*. 2011 Aug;268(8):1181-6.
 124. Jia S, Wang Y, He H, Xiang C. Incidence of level IIB lymph node metastasis in supraglottic laryngeal squamous cell carcinoma with clinically negative neck: a prospective study. *Head Neck*. 2013 Jul; 35(7):987-91.
 125. Ma H, Lian M, Feng L, Li P, Hou L, Chen X, et al. Factors contributing to lymph node occult metastasis in supraglottic laryngeal carcinoma cT2-T4 N0M0 and metastasis predictive equation. *Chin J Cancer Res*. 2014 Dec;26(6):685-91.
 126. Djordjevic V, Bukurov B, Arsovic N, Dimitrijevic M, Jesic S, Nestic V, et al. Prospective case-control study of efficacy of bilateral selective neck dissection in primary surgical treatment of supraglottic laryngeal cancers with clinically negative cervical findings (N0). *Clin Otolaryngol*. 2016 Dec;41(6):634-9.
 127. Wang SX, Ning WJ, Zhang XW, Tang PZ, Li ZJ, Liu WS. Predictors of occult lymph node metastasis and prognosis in patients with cN0 T1-T2 supraglottic laryngeal carcinoma: a retrospective study. *ORL J Otorhinolaryngol Relat Spec*. 2019;81(5-6):317-26.
 128. Zhang Y, Xu S, Liu W, Wang X, Wang K, Liu S, et al. Rational choice of neck dissection in clinically N0 patients with supraglottic cancer. *Head Neck*. 2020 Mar;42(3):365-73.
 129. Kurten CH, Zioga E, Gauler T, Stuschke M, Guberina M, Ludwig JM, et al. Patterns of cervical lymph node metastasis in supraglottic laryngeal cancer and therapeutic implications of surgical staging of the neck. *Eur Arch Otorhinolaryngol*. 2021 Dec;278(12):5021-7.
 130. Jia S, Wang Y, He H, Xiang C. Efficacy of superselective neck dissection (IIA and III) for supraglottic laryngeal cancer with clinically negative neck. *J Cancer Res Clin Oncol*. 2022 Jun;148(6):1457-63.
 131. Candela FC, Shah J, Jaques DP, Shah JP. Patterns of cervical node metastases from squamous carcinoma of the larynx. *Arch Otolaryngol Head Neck Surg*. 1990 Apr;116(4):432-5.
 132. Kligerman J, Olivatto LO, Lima RA, Freitas EQ, Soares JR, Dias FL, et al. Elective neck dissection in the treatment of T3/T4 N0 squamous cell carcinoma of the larynx. *Am J Surg*. 1995 Nov;170(5):436-9.
 133. Leon X, Quer M, Orus C, Sancho FJ, Bague S, Burgues J. Selective dissection of levels II-III with intraoperative control of the upper and middle jugular nodes: a therapeutic option for the N0 neck. *Head Neck*. 2001 Jun;23(6):441-6.
 134. Spriano G, Piantanida R, Pellini R, Muscatello L. Elective treatment of the neck in squamous cell carcinoma of the larynx: clinical experience. *Head Neck*. 2003 Feb;25(2):97-102.
 135. Coskun HH, Erisen L, Basut O. Selective neck dissection for clinically N0 neck in laryngeal cancer: is dissection of level IIB necessary? *Otolaryngol Head Neck Surg*. 2004 Nov;131(5):655-9.
 136. Khafif A, Fliss DM, Gil Z, Medina JE. Routine inclusion of level IV in neck dissection for squamous cell carcinoma of the larynx: is it justified? *Head Neck*. 2004 Apr;26(4):309-12.
 137. Elsheikh MN, Mahfouz ME, Salim EI, Elsheikh EA. Molecular assessment of neck dissections supports preserving level IIB lymph nodes in selective neck dissection for laryngeal squamous cell carcinoma with a clinically negative neck. *ORL J Otorhinolaryngol Relat Spec*. 2006 Apr;68(3):177-84.
 138. Lim YC, Choi EC, Lee JS, Koo BS, Song MH, Shin HA. Is dissection of level IV absolutely necessary in elective lateral neck dissection for clinically N0 laryngeal carcinoma? *Oral Oncol*. 2006 Jan;42(1): 102-7.
 139. Katilimis H, Ozturkcan S, Ozdemir I, Tuna B, Guvenc IA, Ozkul Y. Is dissection of levels 4 and 5 justified for cN0 laryngeal and hypopharyngeal cancer? *Acta Otolaryngol*. 2007 Nov;127(11):1202-6.
 140. Mnejja M, Hammami B, Bougacha L, Chakroun A, Charfeddine I, Khahir A, et al. Occult lymph node metastasis in laryngeal squamous cell carcinoma: therapeutic and prognostic impact. *Eur Ann Otorhinolaryngol Head Neck Dis*. 2010 Nov;127(5):173-6.
 141. Xu Y, Fei M, Wang J, Zheng L, Chen Y, Liu Q. Clinical significance of micrometastases in lymph nodes from laryngeal squamous cell carcinoma. *Am J Otolaryngol*. 2012 Jul-Aug;33(4):402-7.
 142. Furtado de Araujo Neto VJ, Cernea CR, Aparecido Dedivitis R, Furtado de Araujo Filho VJ, Fabiano Palazzo J, Garcia Brandao L. Cervical metastasis on level IV in laryngeal cancer. *Acta Otorhinolaryngol Ital*. 2014 Feb;34(1):15-8.
 143. Tsushima N, Hayashi R, Shinozaki T, Tomioka T, Okano W, Ikeda M. The role of elective neck dissection for cT4aN0 glottic squamous cell carcinoma. *Jpn J Clin Oncol*. 2019 Jun;49(6):525-8.
 144. Cayonu M, Tuna EU, Acar A, Dinc AS, Sahin MM, Boynuegri S, et al. Lymph node yield and lymph node density for elective level II-IV neck dissections in laryngeal squamous cell carcinoma patients. *Eur Arch Otorhinolaryngol*. 2019 Oct;276(10):2923-7.
 145. Riviere D, Mancini J, Santini L, Loth Bouketala A, Giovanni A, Dessi P, et al. Nodal metastases distribution in laryngeal cancer requiring total laryngectomy: therapeutic implications for the N0 Neck. *Eur Ann Otorhinolaryngol Head Neck Dis*. 2019 Jun;136(3S):S35-8.
 146. Shi Y, Zhou L, Tao L, Zhang M, Chen XL, Li C, et al. Management of the N0 neck in patients with laryngeal squamous cell carcinoma. *Acta Otolaryngol*. 2019 Oct;139(10):908-12.
 147. Bottcher A, Betz CS, Bartels S, Schoennagel B, Munscher A, Bubmann L, et al. Rational surgical neck management in total laryngectomy for advanced stage laryngeal squamous cell carcinomas. *J Cancer Res Clin Oncol*. 2021 Feb;147(2):549-59.
 148. Anderson EM, Luu M, Lu DJ, Chung EM, Gay C, Scher KS, et al. Predicting pathologic lymph node positivity in cN0 pharynx and larynx cancers. *Laryngoscope*. 2023 Jul;133(7):1660-6.
 149. Bayir O, Toptas G, Saylam G, Izgi TC, Han U, Keseroglu K, et al. Occult lymph node metastasis in patients with laryngeal cancer and

- relevant predicting factors: a single-center experience. *Tumori*. 2022 Oct;108(5):439-49.
150. dos Santos CR, Goncalves Filho J, Magrin J, Johnson LF, Ferlito A, Kowalski LP. Involvement of level I neck lymph nodes in advanced squamous carcinoma of the larynx. *Ann Otol Rhinol Laryngol*. 2001 Oct;110(10):982-4.
 151. Lohuis PJ, Klop WM, Tan IB, van Den Brekel MW, Hilgers FJ, Balm AJ. Effectiveness of therapeutic (N1, N2) selective neck dissection (levels II to V) in patients with laryngeal and hypopharyngeal squamous cell carcinoma. *Am J Surg*. 2004 Feb;187(2):295-9.
 152. Allegra E, Franco T, Domanico R, La Boria A, Trapasso S, Garozzo A. Effectiveness of therapeutic selective neck dissection in laryngeal cancer. *ORL J Otorhinolaryngol Relat Spec*. 2014 Jun;76(2):89-97.
 153. Brazilian Head and Neck Cancer Study Group. End results of a prospective trial on elective lateral neck dissection vs type III modified radical neck dissection in the management of supraglottic and transglottic carcinomas. *Head Neck*. 1999 Dec;21(8):694-702.
 154. Santos AB, Cernea CR, Inoue M, Ferraz AR. Selective neck dissection for node-positive necks in patients with head and neck squamous cell carcinoma: a word of caution. *Arch Otolaryngol Head Neck Surg*. 2006 Jan;132(1):79-81.
 155. Choi EC, Kim YH, Kim DY, Lee SY, Hong WP. Is it necessary to dissect level I in laryngeal and hypopharyngeal squamous cell carcinoma? *Korean J Otolaryngol* 1999 Jul;42(7):882-5.
 156. Buckley JG, MacLennan K. Cervical node metastases in laryngeal and hypopharyngeal cancer: a prospective analysis of prevalence and distribution. *Head Neck*. 2000 Jul;22(4):380-5.
 157. Gallo O, Fini-Storchi I, Napolitano L. Treatment of the contralateral negative neck in supraglottic cancer patients with unilateral node metastases (N1-3). *Head Neck*. 2000 Jul;22(4):386-92.
 158. Ferlito A, Kowalski LP, Silver CE, Shaha AR, Rinaldo A, Byers RM. The use and misuse of level IA dissection for head and neck cancer. *Acta Otolaryngol*. 2002 Jul;122(5):553-5.
 159. Ferlito A, Silver CE, Rinaldo A, Smith RV. Surgical treatment of the neck in cancer of the larynx. *ORL J Otorhinolaryngol Relat Spec*. 2000 Jul-Aug;62(4):217-25.
 160. Ferlito A, Rinaldo A, Silver CE, Robbins KT, Medina JE, Rodrigo JP, et al. Neck dissection for laryngeal cancer. *J Am Coll Surg*. 2008 Oct;207(4):587-93.
 161. Santoro R, Franchi A, Gallo O, Burali G, de' Campora E. Nodal metastases at level IIb during neck dissection for head and neck cancer: clinical and pathologic evaluation. *Head Neck*. 2008 Nov;30(11):1483-7.
 162. Riviere D, Mancini J, Santini L, Giovanni A, Dessi P, Fakhry N. Lymph-node metastasis following total laryngectomy and total pharyngolaryngectomy for laryngeal and hypopharyngeal squamous cell carcinoma: frequency, distribution and risk factors. *Eur Ann Otorhinolaryngol Head Neck Dis*. 2018 Jun;135(3):163-6.
 163. Amar A, Chedid HM, Franzi SA, Rapoport A. Neck dissection in squamous cell carcinoma of the larynx: indication of elective contralateral neck dissection. *Braz J Otorhinolaryngol*. 2012 Apr;78(2):7-10.
 164. Bottcher A, Olze H, Thieme N, Stromberger C, Sander S, Munscher A, et al. A novel classification scheme for advanced laryngeal cancer midline involvement: implications for the contralateral neck. *J Cancer Res Clin Oncol*. 2017 Aug;143(8):1605-12.
 165. Weber PC, Johnson JT, Myers EN. The impact of bilateral neck dissection on pattern of recurrence and survival in supraglottic carcinoma. *Arch Otolaryngol Head Neck Surg*. 1994 Jul;120(7):703-6.
 166. Chiu RJ, Myers EN, Johnson JT. Efficacy of routine bilateral neck dissection in the management of supraglottic cancer. *Otolaryngol Head Neck Surg*. 2004 Oct;131(4):485-8.
 167. Gross BC, Olsen SM, Lewis JE, Kasperbauer JL, Moore EJ, Olsen KD, et al. Level IIB lymph node metastasis in laryngeal and hypopharyngeal squamous cell carcinoma: single-institution case series and review of the literature. *Laryngoscope*. 2013 Dec;123(12):3032-6.
 168. Dundar R, Aslan H, Ozbay C, Basoglu S, Guvenc IA, Ogredik EA, et al. The necessity of dissection of level IIb in laryngeal squamous cell carcinoma: a clinical study. *Otolaryngol Head Neck Surg*. 2012 Mar;146(3):390-4.
 169. Elteley AM, Abou-Zeid MA, Abdelmalek ME, Nassar AA. Assessment of occult nodal micrometastases to the clinically negative contralateral neck in locally advanced supraglottic squamous cell carcinoma. *Indian J Otolaryngol Head Neck Surg*. 2022 Sep;74(3):369-374.
 170. Ozturkcan S, Katilmis H, Ozdemir I, Tuna B, Guvenc IA, Dundar R. Occult contralateral nodal metastases in supraglottic laryngeal cancer crossing the midline. *Eur Arch Otorhinolaryngol*. 2009 Jan;266(1):117-20.
 171. Gregor RT, Oei SS, Hilgers FJ, Hart AA, Balm AJ, Keus RB. Management of cervical metastases in supraglottic cancer. *Ann Otol Rhinol Laryngol*. 1996 Nov;105(11):845-50.
 172. Cooper JS, Pajak TF, Forastiere AA, Jacobs J, Campbell BH, Saxman SB, et al. Postoperative concurrent radiotherapy and chemotherapy for high-risk squamous-cell carcinoma of the head and neck. *N Engl J Med*. 2004 May;350(19):1937-44.
 173. Bernier J, Domenge C, Ozsahin M, Matuszewska K, Lefebvre JL, Greiner RH, et al. Postoperative irradiation with or without concomitant chemotherapy for locally advanced head and neck cancer. *N Engl J Med*. 2004 May;350(19):1945-52.
 174. Cooper JS, Zhang Q, Pajak TF, Forastiere AA, Jacobs J, Saxman SB, et al. Long-term follow-up of the RTOG 9501/intergroup phase III trial: postoperative concurrent radiation therapy and chemotherapy in high-risk squamous cell carcinoma of the head and neck. *Int J Radiat Oncol Biol Phys*. 2012 Dec;84(5):1198-205.
 175. Mattioli F, Fermi M, Molinari G, Capriotti V, Melegari G, Bertolini F, et al. pT3 N0 laryngeal squamous cell carcinoma: oncologic outcomes and prognostic factors of surgically treated patients. *Laryngoscope*. 2021 Oct;131(10):2262-8.
 176. Ampil FL, Nathan CO, Lian TS, Caldito G, Milligan E. Total laryngectomy and T3-T4 laryngeal cancer without other adverse histopathology. *Otolaryngol Head Neck Surg*. 2007 Feb;136(2):296-300.
 177. Deng K, Yao J, Zeng S, Wen M, Huang J, Zhu T, et al. The effect of surgery plus intensity-modulated radiotherapy on treatment in laryngeal cancer: a clinical retrospective study. *J Cancer Res Clin Oncol*. 2022 Feb;148(2):517-25.
 178. Pfister DG, Spencer S, Adelstein D, Adkins D, Anzai Y, Brizel DM, et al. Head and neck cancers, version 2.2020, NCCN clinical practice guidelines in oncology. *J Natl Compr Canc Netw*. 2020 Jul;18(7):873-98.
 179. Bernier J, Cooper JS, Pajak TF, van Glabbeke M, Bourhis J, Forastiere A, et al. Defining risk levels in locally advanced head and neck cancers: a comparative analysis of concurrent postoperative radiation plus chemotherapy trials of the EORTC (#22931) and RTOG (# 9501). *Head Neck*. 2005 Oct;27(10):843-50.
 180. Hajdu SF, Wessel I, Dalton SO, Eskildsen SJ, Johansen C. Swallowing exercise during head and neck cancer treatment: results of a randomized trial. *Dysphagia*. 2022 Aug;37(4):749-62.
 181. Lewin JS, Hutcheson KA, Barringer DA, May AH, Roberts DB, Holsinger FC, et al. Functional analysis of swallowing outcomes after supracricoid partial laryngectomy. *Head Neck*. 2008 May;30(5):559-66.
 182. Messing BP, Ward EC, Lazarus CL, Kim M, Zhou X, Silinonte J, et al. Prophylactic swallow therapy for patients with head and neck cancer undergoing chemoradiotherapy: a randomized trial. *Dysphagia*. 2017 Aug;32(4):487-500.
 183. Lips M, Speyer R, Zumach A, Kross KW, Kremer B. Supracricoid

- laryngectomy and dysphagia: a systematic literature review. *Laryngoscope*. 2015 Sep;125(9):2143-56.
184. Logemann JA, Gibbons P, Rademaker AW, Pauloski BR, Kahrilas PJ, Bacon M, et al. Mechanisms of recovery of swallow after supraglottic laryngectomy. *J Speech Hear Res*. 1994 Oct;37(5):965-74.
 185. Kreuzer SH, Schima W, Schober E, Pokieser P, Kofler G, Lechner G, et al. Complications after laryngeal surgery: videofluoroscopic evaluation of 120 patients. *Clin Radiol*. 2000 Oct;55(10):775-81.
 186. Rademaker AW, Logemann JA, Pauloski BR, Bowman JB, Lazarus CL, Sisson GA, et al. Recovery of postoperative swallowing in patients undergoing partial laryngectomy. *Head Neck*. 1993 Jul-Aug;15(4):325-34.
 187. de Vincentiis M, Minni A, Gallo A, Di Nardo A. Supracricoid partial laryngectomies: oncologic and functional results. *Head Neck*. 1998 Sep;20(6):504-9.
 188. McConnel FM, Mendelsohn MS, Logemann JA. Examination of swallowing after total laryngectomy using manofluorography. *Head Neck Surg*. 1986 Sep-Oct;9(1):3-12.
 189. Lazarus CL, Logemann JA, Pauloski BR, Colangelo LA, Kahrilas PJ, Mittal BB, et al. Swallowing disorders in head and neck cancer patients treated with radiotherapy and adjuvant chemotherapy. *Laryngoscope*. 1996 Sep;106(9 Pt 1):1157-66.
 190. Logemann JA, Pauloski BR, Rademaker AW, Colangelo LA. Supersupraglottic swallow in irradiated head and neck cancer patients. *Head Neck*. 1997 Sep;19(6):535-40.
 191. Vander Poorten V, Meulemans J, Beitler JJ, Piazza C, Kowalski LP, Makitie AA, et al. Salvage surgery for residual or recurrent laryngeal squamous cell carcinoma after (Chemo)radiotherapy: oncological outcomes and prognostic factors. *Eur J Surg Oncol*. 2021 Nov;47(11):2711-21.
 192. Silverman DA, Puram SV, Rocco JW, Old MO, Kang SY. Salvage laryngectomy following organ-preservation therapy: an evidence-based review. *Oral Oncol*. 2019 Jan;88:137-44.
 193. Philippe Y, Espitalier F, Durand N, Ferron C, Bardet E, Malard O. Partial laryngectomy as salvage surgery after radiotherapy: oncological and functional outcomes and impact on quality of life: a retrospective study of 20 cases. *Eur Ann Otorhinolaryngol Head Neck Dis*. 2014 Feb;131(1):15-9.
 194. Holsinger FC, Funk E, Roberts DB, Diaz EM Jr. Conservation laryngeal surgery versus total laryngectomy for radiation failure in laryngeal cancer. *Head Neck*. 2006 Sep;28(9):779-84.
 195. Sullivan CB, Ostedgaard KL, Al-Qurayshi Z, Pagedar NA, Sperry SM. Primary laryngectomy versus salvage laryngectomy: a comparison of outcomes in the chemoradiation era. *Laryngoscope*. 2020 Sep;130(9):2179-85.
 196. Wulff NB, Andersen E, Kristensen CA, Sorensen CH, Charabi B, Homoe P. Prognostic factors for survival after salvage total laryngectomy following radiotherapy or chemoradiation failure: a 10-year retrospective longitudinal study in eastern Denmark. *Clin Otolaryngol*. 2017 Apr;42(2):336-46.
 197. Hasan Z, Dwivedi RC, Gunaratne DA, Virk SA, Palme CE, Riffat F. Systematic review and meta-analysis of the complications of salvage total laryngectomy. *Eur J Surg Oncol*. 2017 Jan;43(1):42-51.
 198. De Virgilio A, Pellini R, Mercante G, Cristalli G, Manciooco V, Giannarelli D, et al. Supracricoid partial laryngectomy for radiorecurrent laryngeal cancer: a systematic review of the literature and meta-analysis. *Eur Arch Otorhinolaryngol*. 2018 Jul;275(7):1671-80.
 199. Shapira U, Warshavsky A, Muhanna N, Oestreicher-Kedem Y, Nachalon Y, Ungar OJ, et al. Laryngectomy-free survival after salvage partial laryngectomy: a systematic review and meta-analysis. *Eur Arch Otorhinolaryngol*. 2022 Jun;279(6):3021-7.
 200. Lucioni M, Bertolin A, Lionello M, Giacomelli L, Rizzotto G, Marioni G. Open partial horizontal laryngectomy for salvage after failure of CO₂ laser-assisted surgery for glottic carcinoma. *Eur Arch Otorhinolaryngol*. 2016 Jan;273(1):169-75.
 201. Quer M, Leon X, Orus C, Venegas P, Lopez M, Burgues J. Endoscopic laser surgery in the treatment of radiation failure of early laryngeal carcinoma. *Head Neck*. 2000 Aug;22(5):520-3.
 202. Del Bon F, Piazza C, Mangili S, Redaelli De Zinis LO, Nicolai P, Peretti G. Transoral laser surgery for recurrent glottic cancer after radiotherapy: oncologic and functional outcomes. *Acta Otorhinolaryngol Ital*. 2012 Aug;32(4):229-37.
 203. Barbu AM, Burns JA, Lopez-Guerra G, Landau-Zemer T, Friedman AD, Zeitels SM. Salvage endoscopic angiolytic KTP laser treatment of early glottic cancer after failed radiotherapy. *Ann Otol Rhinol Laryngol*. 2013 Apr;122(4):235-9.
 204. Casiano RR, Cooper JD, Lundy DS, Chandler JR. Laser cordectomy for T1 glottic carcinoma: a 10-year experience and videostroboscopic findings. *Otolaryngol Head Neck Surg*. 1991 Jun;104(6):831-7.
 205. Steiner W, Vogt P, Ambrosch P, Kron M. Transoral carbon dioxide laser microsurgery for recurrent glottic carcinoma after radiotherapy. *Head Neck*. 2004 Jun;26(6):477-84.
 206. Ansarin M, Planicka M, Rotundo S, Santoro L, Zurlo V, Maffini F, et al. Endoscopic carbon dioxide laser surgery for glottic cancer recurrence after radiotherapy: oncological results. *Arch Otolaryngol Head Neck Surg*. 2007 Dec;133(12):1193-7.
 207. Roedel RM, Matthias C, Wolff HA, Schindler P, Aydin T, Christiansen H. Transoral laser microsurgery for recurrence after primary radiotherapy of early glottic cancer. *Auris Nasus Larynx*. 2010 Aug;37(4):474-81.
 208. Han YJ, Lee HS, Kim SW, Hong JC, Kim ST, Park HS, et al. Transoral laser microsurgery of recurrent early glottic cancer after radiation therapy: clinical feasibility and limitations. *Ann Otol Rhinol Laryngol*. 2012 Jun;121(6):375-82.
 209. Choi SH, Lee KD, Mun HS, Kim SW, Kim YR, Yu TH. Laser salvage surgery for recurrent glottic cancer after radiotherapy. *Korean J Otolaryngol-Head Neck Surg*. 2007 Feb;50(2):139-44.
 210. Roedel RM, Matthias C, Wolff HA, Christiansen H. Repeated transoral laser microsurgery for early and advanced recurrence of early glottic cancer after primary laser resection. *Auris Nasus Larynx*. 2010 Jun;37(3):340-6.
 211. Weiss BG, Bertlich M, Canis M, Ihler F. Transoral laser microsurgery or total laryngectomy for recurrent squamous cell carcinoma of the larynx: retrospective analysis of 199 cases. *Head Neck*. 2017 Jun;39(6):1166-76.
 212. Huang J, Yu Z, Fang J, Chen X, Chen X, Huang Z. Salvage transoral laser microsurgery for early recurrent glottic carcinoma after primary laser treatment. *Acta Otolaryngol*. 2013 May;133(5):531-7.
 213. Forner D, Rigby MH, Corsten M, Trites JR, Pyne J, Taylor SM. Oncological and functional outcomes after repeat transoral laser microsurgery for the treatment of recurrent early glottic cancer. *J Laryngol Otol*. 2020 Feb;1-5.
 214. Russo E, Costantino A, Veneroni MV, Festa BM, Pellini R, Campo F, et al. Transoral laser microsurgery in recurrent laryngeal cancer: a systematic review and meta-analysis. *Laryngoscope*. 2023 Jun;133(6):1425-33.
 215. Akbaba S, Held T, Lang K, Hoerner-Rieber J, Zaoui K, Forster T, et al. Salvage radiotherapy for recurrent hypopharyngeal and laryngeal squamous cell carcinoma (SCC) after first-line treatment with surgery alone: a 10-year single-centre experience. *Radiat Oncol*. 2019 Feb;14(1):34.
 216. Basheeth N, O'Leary G, Sheahan P. Elective neck dissection for no neck during salvage total laryngectomy: findings, complications, and oncological outcome. *JAMA Otolaryngol Head Neck Surg*. 2013 Aug;139(8):790-6.
 217. Bohannon IA, Desmond RA, Clemons L, Magnuson JS, Carroll WR, Rosenthal EL. Management of the N0 neck in recurrent laryngeal squamous cell carcinoma. *Laryngoscope*. 2010 Jan;120(1):58-61.

218. Deganello A, Meccariello G, Bini B, Paia 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 Dec;128(12):1089-94.
219. 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. *Laryngoscope*. 2006 Oct;116(10):1864-6.
220. Freiser ME, Ojo RB, Lo K, Saint-Victor S, Bollig C, Nayak CS, et al. Complications and oncologic outcomes following elective neck dissection with salvage laryngectomy for the N0 neck. *Am J Otolaryngol*. 2016 May-Jun;37(3):186-94.
221. Giese RA, Vural EA, Moreno MA. Outcomes and oncologic considerations for elective neck dissection in patients undergoing salvage laryngectomy. *Otolaryngol Head Neck Surg*. 2014 Sep;151(1_suppl):P61.
222. 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 Mar;128(3):279-83.
223. 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. *Laryngoscope*. 2010 May;120(5):945-52.
224. Amit M, Hilly O, Leider-Trejo L, Popovtzer A, Gutfeld O, Shvero J, et al. The role of elective neck dissection in patients undergoing salvage laryngectomy. *Head Neck*. 2013 Oct;35(10):1392-6.
225. 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*. 2016 Mar;154(3):473-9.
226. 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*. 2015 Feb;40(1):9-15.
227. Koss SL, Russell MD, Leem TH, Schiff BA, Smith RV. Occult nodal disease in patients with failed laryngeal preservation undergoing surgical salvage. *Laryngoscope*. 2014 Feb;124(2):421-8.
228. Pennings RJ, Marres HA, den Heeten A, van den Hoogen FJ. Efficacy of diagnostic upper node evaluation during (salvage) laryngectomy for supraglottic carcinoma. *Head Neck*. 2009 Feb;31(2):158-66.
229. Wax MK, Touma BJ. Management of the N0 neck during salvage laryngectomy. *Laryngoscope*. 1999 Jan;109(1):4-7.
230. Abstracts of the 14th British Academic Conference in Otolaryngology. July 4-7, 2012. Glasgow, United Kingdom. *Clin Otolaryngol*. 2012 Jul;37 Suppl 1:1-223.
231. Yao M, Roebuck JC, Holsinger FC, Myers JN. Elective neck dissection during salvage laryngectomy. *Am J Otolaryngol*. 2005 Nov-Dec;26(6):388-92.
232. Yuen AP, Wei WI, Ho CM. Results of surgical salvage for radiation failures of laryngeal carcinoma. *Otolaryngol Head Neck Surg*. 1995 Mar;112(3):405-9.
233. Bernard SE, Wieringa MH, Meeuwis CA, Baatenburg de Jong RJ, Sewnaik A. Elective neck treatment during salvage (pharyngo) laryngectomy. *Eur Arch Otorhinolaryngol*. 2019 Apr;276(4):1127-33.
234. 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*. 2013 Aug;133(8):886-92.
235. 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 Oct;36(5):475-80.
236. Dasse R, Dupin C, Gorphe P, Temam S, Dupret-Bories A, Vergez S, et al. Proposal for an algorithm to avoid neck dissection during salvage total laryngectomy: a GETTEC multicentric study. *Oral Oncol*. 2022 Oct;133:106026.
237. Gouzos M, Dale O, Sethi N, Foreman A, Krishnan S, Hodge JC. Elective neck dissection for the node-negative neck during salvage laryngectomy: an analysis of survival outcomes and complication rates. *J Laryngol Otol*. 2019 Sep;133(9):788-91.