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Executive Summary of the American Radium Society Appropriate Use Criteria for Management of Early Glottic Cancer
A Review

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IMPORTANCE Stage I squamous cell carcinoma (SCC) of the glottic larynx carries a favorable prognosis after treatment with endoscopic surgery or radiation therapy (RT). In addition to tumor control, goals of therapy include preservation of voice quality, swallow function, and breathing. Multidisciplinary consensus guidelines are needed to assist clinicians in treatment selection and the appropriate use of both surgical and radiation-based techniques.

OBSERVATIONS Treatment of clinical T1N0 glottic SCC has evolved over time, with advances in both transoral laser microsurgery and RT designed to become more targeted and reduce the overall treatment burden for patients. When selecting a treatment option, consideration should be given to patient-specific factors, including tumor position/extent, age, and medical and psychosocial factors. This 16-member multidisciplinary American Radium Society (ARS) Head and Neck Cancer Appropriate Use Criteria (AUC) expert panel performed a review of the English-language medical literature from 2000 to 2022 to inform consensus guidelines. Clinical case variants were developed to represent commonly encountered clinical scenarios, and the RAND/UCLA appropriateness method was used to rate the appropriate use of various treatments. The modified Delphi method was used to reach consensus recommendations, which were approved by the ARS Executive Committee and subject to public comment per established ARS procedures.

CONCLUSIONS AND RELEVANCE Given the range of treatment options available, early glottic SCC management should be done in a multidisciplinary fashion including otolaryngologists and radiation oncologists. The ARS Head and Neck AUC expert panel created an appropriate-use consensus document by performing a literature review of the current treatment strategies for stage I glottic SCC, providing recommendations regarding the appropriateness of surgery or RT for various clinical scenarios and highlighting areas of controversy and uncertainty.

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More than 12 000 new cases of laryngeal cancer are diagnosed annually in the US, with approximately 60% originating from the true glottis.[1] Stage I glottic squamous cell carcinoma (SCC) has favorable 5-year local control (LC) and cancer-specific survival; thus, treatment goals include optimizing tumor control while also preserving voice quality, swallow function, and breathing.[2] Given the recent evolution of both surgical and radiation treatment options, an appropriate-use consensus document was created based on a literature review of current treatment strategies for stage I (T1a-bN0) glottic SCC with representative clinical scenarios. The aims of this review are to (1) comprehensively evaluate existing prospective and large retrospective clinical studies of clinical T1N0 glottic SCC using a formalized methodologic approach and reported using the Preferred Reporting Items for Systematic Review and Meta-Analyses Protocol (PRISMA-P)[3] and (2) provide multidisciplinary panel recommendations regarding the appropriateness of surgery or radiation therapy (RT) for various clinical scenarios, highlighting areas of controversy and uncertainty.

Methods

Relevant studies of T1 glottic SCC published from January 1, 2000, to April 15, 2022, were identified via librarian-guided search using Medical Subject Headings and OVID Medline and SCOPUS (eAppendix 1 in the Supplement). The PICO (participants, interventions, comparators, outcomes) framework was used to identify relevant studies, including randomized trials, nonrandomized prospective trials, and retrospective studies (eAppendix 2 in the Supplement). Included studies reported oncologic or quality of life end points for

T1N0 glottic SCC from 30 or more patients if prospective or 100 or more patients if retrospective. For comparative studies (those including patients treated with both surgery and radiation), we limited inclusion of prospective studies to those containing 30 or more patients in each group and for retrospective studies with 100 or more patients total. Covidence software was used for article screening and selection (**Figure**). A few studies that were not identified through the formal search are referenced in the text for context but not included in the evidence table (eAppendix 4 in the Supplement) or as supporting evidence for appropriateness rating. The findings of the included studies were summarized to present a current state of the literature.

The American Radium Society (ARS) Head and Neck Appropriate Use Criteria (AUC) multidisciplinary panel was comprised of 16 site experts, including 13 radiation oncologists, 2 head and neck surgeons, and 1 otolaryngologist. Panelists convened and reviewed the relevant literature. Clinical case variants (**Table 1** and **Table 2**)[4-48] were designed by 4 of us (M.E.S., S.M., A.A., and D.N.M.) and finalized by panel consensus to represent common clinical scenarios and treatment options. The RAND/UCLA appropriateness method[49] was used to rate each treatment and the modified Delphi[50] method was used to achieve consensus over 2 rounds of voting.[51] The composed document was then reviewed and approved by the ARS AUC Executive Panel and subject to public comment before final approval.

Discussion

RT in the Management of T1N0 Glottic Cancer

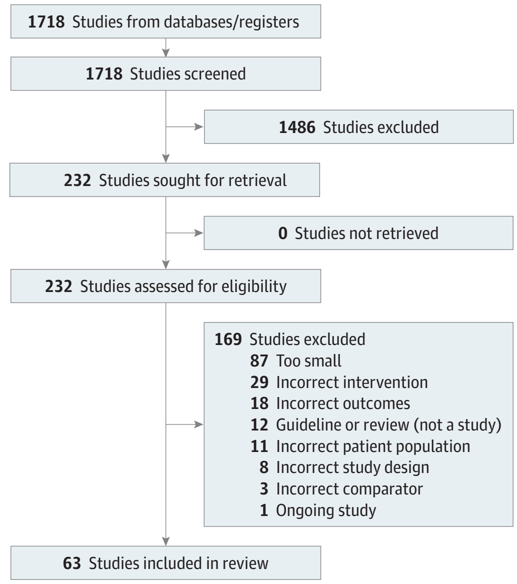
Subtopic 1: External Beam RT (2- or 3-Dimensional) Using Traditional Field Borders Targeting the Whole Glottic Larynx

RT has traditionally included most of the larynx to account for movement during treatment delivery using a 5 × 5-cm field, referring to typical size of the field borders on a plain film. Multiple prospective and retrospective studies of standard RT for T1N0 glottic SCC using 1.8 to 2.0 Gy per day, generally up to 60 to 70 Gy, reported 5-year LC of 77% to 92%.[19-39] Regional nodal failures were rare.[21,22,24,26,27] Most radiotherapy failures were salvaged with total laryngectomy or, rarely, with partial laryngectomy or cordectomy. Together with low rates of regional or distant metastatic spread and the availability of curative salvage options, cause-specific survival rates were high, ranging from 90% to 100%.[22,23,28,30,35,39]

Moderate Hypofractionation With Traditional RT Fields (2- or 3-Dimensional) to the Whole Glottic Larynx | Three prospective randomized trials[36,37,39] and 1 prospective cohort study[38] compared accelerated/moderately hypofractionated RT (using 2.2 to 2.4 Gy per fraction) vs standard fractionation for early glottic SCC. Three studies showed a 5% to 15% LC benefit[36,37,39] in favor of hypofractionation, with 1 of these showing the benefit reached significance.[36] Neither acute nor late toxic effects was different between arms in the 3 randomized studies. These studies generally concluded that hypofractionation should be offered given comparable tumor control and convenience.

Additionally, we identified 3 retrospective studies of moderate hypofractionation with doses greater than 3 Gy per fraction to the whole larynx from the Christie and Royal Marsden Hospitals[52] (3.125 to 3.28 Gy per fraction over 16 fractions), the Birmingham

Figure. PRISMA Flow Diagram of Study Selection



experience[23] (3.125 Gy per fraction over 16 fractions), and the Tata Memorial Hospital experience[53] (3.30 to 3.43 Gy per fraction over 15 to 16 fractions). These studies reported 5-year LC of 88% to 93%.

Acute and Late Effects of RT Using Traditional Field Borders Targeting the Whole Glottic Larynx | Acute toxic effects include inflammation of the skin, laryngeal, and pharyngeal tissues within the treatment field leading to erythema; acute mucosal pain; difficulty swallowing; and, rarely, difficulty breathing due to laryngeal edema. Radiation exposure of the minor salivary glands of the aerodigestive tract can lead to increased/thickened pharyngeal secretions and long-term throat dryness. The studies identified in this literature search showed that 2- and 3-dimensional RT was well tolerated, with a typical incidence of Common Terminology Criteria for Adverse Events grade 3 or higher toxic effects between 0% and 5%.[25,27,29,30,36,38]

Late effects of treatment, including RT-related second malignant neoplasms, can be challenging to define due to long lag time, variability in toxic effect assessment across studies, and loss to follow-up. Twelve of 21 RT studies using standard or moderate hypofractionation less than 3 Gy per day reported late complications; most were low grade, ranging from 0% to 28%.[20,24,33,36,38,54] These included hypothyroidism, dysphagia not impairing a safe oral diet, xerostomia, persistent dysphonia (more than 6 months), and benign polypoid corditis. High-grade late toxic effects were infrequently reported and ranged from 0% to 2%.[20,24,33,36,38,54] These included persistent laryngeal edema, cartilage necrosis, need for tracheostomy (temporary or permanent), dysphagia necessitating percutaneous gastrostomy tube placement (temporary or permanent), and airway fibrosis or stenosis requiring surgery.

One concern regarding higher dose per fraction to the whole larynx is excess toxic effects. The retrospective data are mixed. One experience of moderate hypofractionation with doses of 3 Gy or greater per day described similar late toxic effects to several series of doses less than 3 Gy.[52] Another series described higher late toxic

Table 1. Clinical Condition: Healthy Patients With Unilateral (T1a) Glottic Squamous Cell Carcinoma (SCC)

Treatment	Rating category[a] Final tabulations 1	2	3	4	5	6	7	8	9	Group median rating	Disagreement	Sources	Study quality[c,d]	SOE[c]	SOR[c,e]
Variant 1: A patient aged 45 y with SCC superficially involving the middle one-third of the right TVF has vocal folds that are freely mobile and display normal vibratory function on videostroboscopy. There is good visualization of the tumor with direct laryngoscopy. Rate the appropriateness of the following treatments to achieve optimal tumor control while maintaining best laryngeal function:															
Total laryngectomy	11	3	0	1	0	0	0	0	0	1	No	NA	NA	Expert consensus	↑
Endoscopic/transoral laser microsurgery	0	0	0	0	0	0	3	8	4	8	No	Breda et al,[4] 2015; Brøndbo and Benninger,[5] 2004; Brøndbo et al,[6] 2007; Canis et al,[7] 2015; Djukic et al,[8] 2019; Motta et al,[9] 2005; Peretti et al,[10] 2004; Resuli and Cansiz,[11] 2020; Cabrera-Sarmiento et al,[12] 2021; Eckel et al,[13] 2000; Grant et al,[14] 2007; Peretti et al,[15] 2001; Hamzany et al,[16] 2021; Lechien et al,[17] 2022; Zhang et al,[18] 2018	2	Strong	↑
3D conformal RT using traditional field borders with standard fractionation (eg, 2 Gy per fraction to 66 Gy)	0	0	0	1	4	5	3	1	1	5[b]	Yes	Agarwal et al,[19] 2009; Al-Mamgani et al,[20] 2014; Al-Mamgani et al,[21] 2013; Cacicedo et al,[22] 2013; Cheah et al,[23] 2009; Chera et al,[24] 2010; Itoh et al,[25] 2016; Jin et al,[26] 2002; Kim et al,[27] 2012; Mendenhall et al,[28] 2001; Motegi et al,[29] 2015; Mourad et al,[30] 2013; Mucha-Małecka et al,[31] 2019; Sert et al,[32] 2019; Short et al,[33] 2006; Smee et al,[34] 2010; Tong et al,[35] 2012	2	Moderate	-
3D conformal RT using traditional field borders using moderate hypofractionation (eg, 2.25 Gy per fraction to 63 Gy)	0	0	0	0	1	1	6	4	3	7	No	Kodaira et al,[36] 2018; Moon et al,[37] 2014; Salas-Salas et al,[38] 2020; Yamazaki et al,[39] 2006	1	Strong	↑
IMRT to whole larynx with standard or moderate hypofractionation	0	0	0	1	2	1	6	5	0	7	No	Cetinayak et al,[40] 2019; Mishra et al,[41] 2022; Mohamed et al,[42] 2020; Zumsteg et al,[43] 2015	2	Moderate	-
Hypofractionated IMRT to single (involved) vocal fold, (3.63 Gy per fraction in 16 fractions to 58.08 Gy)	0	1	4	5	2	3	0	0	0	5[b]	Yes	Al-Mamgani et al,[44] 2015; Tans et al,[45] 2022	2	Limited	↓
SBRT to lesion only	3	4	6	1	1	0	0	0	0	3	No	Sher et al,[46] 2019; Sher et al,[47] 2025; Sanguineti et al,[48] 2025	1	Limited	↑
Variant 2: A patient aged 55 y with no tobacco use history who lectures daily presents with hoarseness and a SCC involving the entire left TVF and the anterior commissure. Bilateral vocal fold mobility is normal. There is severe impairment in vibratory mucosal function of the left TVF. Results of CT is negative for paraglottic involvement. There is good visualization of the tumor with direct laryngoscopy under anesthesia. Rate the appropriateness of the following treatments to achieve optimal tumor control while maintaining best laryngeal function:															
Endoscopic/transoral laser microsurgery	0	0	1	2	3	6	3	0	0	6	No	Breda et al,[4] 2015; Brøndbo and Benninger,[5] 2004; Brøndbo et al,[6] 2007; Canis et al,[7] 2015; Djukic et al,[8] 2019; Motta et al,[9] 2005; Peretti et al,[10] 2004; Resuli and Cansiz,[11] 2020; Cabrera-Sarmiento et al,[12] 2021; Eckel et al,[13] 2000; Grant et al,[14] 2007; Peretti et al,[15] 2001; Hamzany et al,[16] 2021; Lechien et al,[17] 2022; Zhang et al,[18] 2018	2	Strong	-
3D conformal RT using traditional field borders	0	0	0	0	0	0	10	3	2	7	No	Agarwal et al,[19] 2009; Al-Mamgani et al,[20] 2014; Al-Mamgani et al,[21] 2013; Cacicedo et al,[22] 2013; Cheah et al,[23] 2009; Chera et al,[24] 2010; Itoh et al,[25] 2016; Jin et al,[26] 2002; Kim et al,[27] 2012; Mendenhall et al,[28] 2001; Motegi et al,[29] 2015; Mourad et al,[30] 2013; Mucha-Małecka et al,[31] 2019; Sert et al,[32] 2019; Short et al,[33] 2006; Smee et al,[34] 2010; Tong et al,[35] 2012; Kodaira et al,[36] 2018; Moon et al,[37] 2014; Salas-Salas et al,[38] 2020; Yamazaki et al,[39] 2006	1	Strong	↑

(continued)

Table 1. Clinical Condition: Healthy Patients With Unilateral (T1a) Glottic Squamous Cell Carcinoma (SCC) (continued)

Treatment	Rating category[a] Final tabulations 1	2	3	4	5	6	7	8	9	Group median rating	Disagreement	Sources	Study quality[c,d]	SOE[c]	SOR[c,e]
IMRT to whole larynx	0	0	0	0	0	0	9	4	2	7	No	Cetinayak et al,[40] 2019; Mishra et al,[41] 2022; Mohamed et al,[42] 2020; Zumsteg et al,[43] 2015	2	Moderate	-
Hypofractionated IMRT to single (involved) vocal fold and involved anterior commissure, (3.63 Gy per fraction in 16 fractions to 58.08 Gy)	0	1	4	3	4	2	1	0	0	5[b]	Yes	Al-Mamgani et al,[44] 2015; Tans et al,[45] 2022	2	Limited	↓
SBRT to lesion only	4	4	5	2	0	0	0	0	0	2	No	Sher et al,[46] 2019; Sher et al,[47] 2025; Sanguineti et al,[48] 2025	1	Limited	↑
RT with concurrent cisplatin	7	4	1	3	0	0	0	0	0	2	No	NA	NA	NA	↑

Abbreviations: 3D, 3-dimensional; CT, computed tomography; IMRT, intensity-modulated radiotherapy; NA, not applicable; RT, radiation therapy; SBRT, stereotactic body radiotherapy; SOE, strength of evidence; SOR, strength of recommendation; TVF, true vocal fold.

[a] Rating categories 1 to 3 were defined as usually not appropriate; 4 to 6, may be appropriate; and 7 to 9, usually appropriate.

[b] Per the RAND/UCLA appropriateness method, disagreement (ie, the variation of the individual ratings from the median rating) indicates panel disagreement on the final recommendation. Group median rating is set automatically to 5.

[c] For more information on study quality, SOE, and SOR, see eAppendix 2 in the Supplement.

[d] Study quality values range from 1 (well designed and accounts for common biases) to 4 (not useful as primary evidence).

[e] Per American Radium Society SOR rating guidelines, ↑ indicates strong recommendation; – indicates moderate recommendation; and ↓ indicates weak recommendation.

effects, with 28% of patients experiencing persistent late laryngeal edema, disproportionately those treated with larger RT field sizes (greater than 36 cm^2) and telecobalt therapy, where dose is often less uniform than with higher energy megavoltage photons (4 to 6 MV).[53]

Voice Outcomes With RT Using Traditional Field Borders Targeting the Whole Glottic Larynx | Both subjective and objective voice parameters generally improved after RT, with less improvement in patients who smoked. Three studies of conventional RT reported voice outcomes.[19-21] In the largest, 233 patients were administered the Voice Handicap Index (VHI), a commonly used and validated tool for patient assessment of voice quality, with an average baseline score of 37.[20] Scores deteriorated during RT, with the highest (worst) scores at the end of treatment (mean score, 52.2). Rapid improvement was noted thereafter, with VHI scores improving beyond baseline approximately 4 to 6 weeks following treatment. Two years after RT, mean VHI score was 18 in the whole group and 11 in those who quit smoking, a significant improvement from pretreatment. In a smaller prospective study, a history of smoking, anterior commissure involvement and larger RT volumes resulted in poorer voice parameters following RT.[19]

Subtopic 2: Intensity Modulated Radiotherapy Targeting the Whole Glottic Larynx

Intensity-modulated radiotherapy (IMRT) is a technique in which the intensity of multiple beams is modified during radiation delivery, allowing for precise sculpting of the dose around the target while minimizing high-dose exposure to surrounding normal tissues. In the 2000s, several groups described long-term adverse effects of RT on the carotid arteries, namely stenosis and elevated risk of transient ischemic attacks/cerebrovascular events.[55-57] IMRT was proposed to minimize exposure to the carotid arteries, though initially there was some concern that the conformality of this technique could lead to marginal failures.

This search identified 4 studies of whole-larynx IMRT for early glottic cancer,[40-43] including 1 prospective cohort study and 3 retrospective studies. Although clinical target volume definitions were different between these studies, they closely mimicked what was intended to be treated with traditional glottic RT fields. They reported similar high LC rates with IMRT as seen with 2- and 3-dimensional techniques. High-dose exposure to carotid arteries was significantly reduced, although rates of cerebrovascular events were not consistently reported given their late onset.

Subtopic 3: Image-Guided IMRT Targeting the Involved Vocal Fold

Radiation Targeting a Single-Vocal Fold | RT for early glottic cancer continues to evolve with interest in reducing the anatomical extent of treatment using image guidance to account for motion during treatment. This review identified no studies of standard to moderately hypofractionated RT (ie, 3 Gy or less per day) to smaller volumes, such as an involved lesion or single vocal fold. In a study from the Netherlands,[44] 111 consecutive patients received single vocal cord irradiation (SVCI) using 5-9 IMRT beams to a dose of 58.08 Gy in 16 fractions, 3.63 Gy per fraction.[52,53] The clinical target volume was the entire vocal fold with expansion to include target motion. Planning target volume, a margin applied to account for patient setup,

Table 2. Patients With Comorbidities and/or Limited Visualization of T1 Glottic Squamous Cell Carcinoma (SCC)

Treatment	Rating category[a] Final tabulation 1	2	3	4	5	6	7	8	9	Group median rating	Disagreement	Sources	Study quality[c,d]	SOE[c]	SOR[c,e]
Variant 3: A patient aged 75 y with multiple medical conditions, including COPD requiring home oxygen and recent STEMI with stents requiring dual antiplatelet therapy (recommendation to continue for at least 6 mo), presents with an SCC superficially involving the anterior one-third of the right TVF; the left TVF is clear. Bilateral vocal fold mobility is normal with moderate reduction in mucosal vibratory function on videostroboscopy at the lesion. Office visualization of the anterior tumor extent is challenging. Rate the appropriateness of the following treatments to achieve optimal tumor control while maintaining best laryngeal function:															
Total laryngectomy	7	3	4	0	1	0	0	0	0	2	No	NA	NA	Expert consensus	↑
Endoscopic/transoral laser microsurgery	0	1	7	1	4	2	0	0	0	5[b]	Yes	Breda et al,[4] 2015; Brøndbo and Benninger,[5] 2004; Brøndbo et al,[6] 2007; Canis et al,[7] 2015; Djukic et al,[8] 2019; Motta et al,[9] 2005; Peretti et al,[10] 2004; Resuli and Cansiz,[11] 2020; Cabrera-Sarmiento et al,[12] 2021; Eckel et al,[13] 2000; Grant et al,[14] 2007; Peretti et al,[15] 2001; Hamzany et al,[16] 2021; Lechien et al,[17] 2022; Zhang et al,[18] 2018	2	Strong	-
3D conformal RT using traditional field borders	0	0	0	0	0	2	7	3	3	7	No	Agarwal et al,[19] 2009; Al-Mamgani et al,[20] 2014; Al-Mamgani et al,[21] 2013; Cacicedo et al,[22] 2013; Cheah et al,[23] 2009; Chera et al,[24] 2010; Itoh et al,[25] 2016; Jin et al,[26] 2002; Kim et al,[27] 2012; Mendenhall et al,[28] 2001; Motegi et al,[29] 2015; Mourad et al,[30] 2013; Mucha-Małecka et al,[31] 2019; Sert et al,[32] 2019; Short et al,[33] 2006; Smee et al,[34] 2010; Tong et al,[35] 2012; Kodaira et al,[36] 2018; Moon et al,[37] 2014; Salas-Salas et al,[38] 2020; Yamazaki et al,[39] 2006	1	Strong	↑
IMRT to whole larynx	0	0	0	0	0	1	6	7	1	8	No	Cetinayak et al,[40] 2019; Mishra et al,[41] 2022; Mohamed et al,[42] 2020; Zumsteg et al,[43] 2015	2	Moderate	-
Hypofractionated IMRT to single (involved) vocal fold (3.63 Gy per fraction in 16 fractions to 58.08 Gy)	0	0	5	3	4	2	0	0	0	5[b]	Yes	Al-Mamgani et al,[44] 2015; Tans et al,[45] 2022	2	Limited	↓
SBRT to lesion only	0	3	10	0	2	0	0	0	0	3	No	Sher et al,[46] 2019; Sher et al,[47] 2025; Sanguineti et al,[48] 2025	1	Limited	↑
Variant 4: A patient aged 75 y with ongoing tobacco smoking, history of cervical spine surgery with limited neck extension, and moderate to severe asymptomatic carotid artery stenosis presents with an SCC involving the middle one-third of the right TVF. Vocal folds are freely mobile and display normal vibratory function on videostroboscopy. There is incomplete visualization of the tumor with direct laryngoscopy under anesthesia, including with an anterior commissure laryngoscope. Rate the appropriateness of the following treatments to achieve optimal tumor control while maintaining best laryngeal function:															
Total laryngectomy	10	2	2	0	0	0	1	0	0	1	No	NA	NA	Expert consensus	↑
Open partial laryngectomy	0	5	7	1	1	1	0	0	0	3	No	NA	NA	Expert opinion	↑
Endoscopic/transoral laser microsurgery	0	5	7	0	1	1	1	0	0	3	No	Breda et al,[4] 2015; Brøndbo and Benninger,[5] 2004; Brøndbo et al,[6] 2007; Canis et al,[7] 2015; Djukic et al,[8] 2019; Motta et al,[9] 2005; Peretti et al,[10] 2004; Resuli and Cansiz,[11] 2020; Cabrera-Sarmiento et al,[12] 2021; Eckel et al,[13] 2000; Grant et al,[14] 2007; Peretti et al,[15] 2001; Hamzany et al,[16] 2021; Lechien et al,[17] 2022; Zhang et al,[18] 2018	2	Strong	↑
3D conformal RT using traditional field borders	0	0	0	1	0	1	9	3	1	7	No	Agarwal et al,[19] 2009; Al-Mamgani et al,[20] 2014; Al-Mamgani et al,[21] 2013; Cacicedo et al,[22] 2013; Cheah et al,[23] 2009; Chera et al,[24] 2010; Itoh et al,[25] 2016; Jin et al,[26] 2002; Kim et al,[27] 2012; Mendenhall et al,[28] 2001; Motegi et al,[29] 2015; Mourad et al,[30] 2013; Mucha-Małecka et al,[31] 2019; Sert et al,[32] 2019; Short et al,[33] 2006; Smee et al,[34] 2010; Tong et al,[35] 2012; Kodaira et al,[36] 2018; Moon et al,[37] 2014; Salas-Salas et al,[38] 2020; Yamazaki et al,[39] 2006	1	Strong	↑
IMRT to whole larynx (carotid sparing)	0	0	0	0	0	1	5	6	3	8	No	Cetinayak et al,[40] 2019; Mishra et al,[41] 2022; Mohamed et al,[42] 2020; Zumsteg et al,[43] 2015	2	Moderate	-

(continued)

Table 2. Patients With Comorbidities and/or Limited Visualization of T1 Glottic Squamous Cell Carcinoma (SCC) (continued)

Treatment	Rating category[a] Final tabulation 1	2	3	4	5	6	7	8	9	Group median rating	Disagreement	Sources	Study quality[c,d]	SOE[c]	SOR[c,e]
Hypofractionated IMRT to single (involved) vocal fold, (3.63 Gy per fraction in 16 fractions to 58.08 Gy)	0	0	5	4	3	3	0	0	0	5[b]	Yes	Al-Mamgani et al,[44] 2015; Tans et al,[45] 2022	2	Limited	↓
SBRT to lesion only	3	5	6	0	1	0	0	0	0	2	No	Sher et al,[46] 2019; Sher et al,[47] 2025; Sanguineti et al,[48] 2025	1	Limited	↑
Variant 5: A patient aged 65 y with a 50-pack-year tobacco use history has hoarseness and SCC involving the anterior one-third of both TVFs and the anterior commissure with extensive leukoplakic changes and carcinoma in-situ involving the posterior right TVF. Bilateral vocal fold mobility is normal with diffuse mild impairment in vibratory function. There is good visualization of the tumor with direct laryngoscopy under anesthesia. Rate the appropriateness of the following treatments to achieve optimal tumor control while maintaining best laryngeal function:															
Total laryngectomy	4	4	4	1	0	2	0	0	0	2	No	NA	NA	Expert consensus	↑
Endoscopic/transoral laser microsurgery	0	1	7	6	0	1	0	0	0	5[b]	Yes	Breda et al,[4] 2015; Brøndbo and Benninger,[5] 2004; Brøndbo et al,[6] 2007; Canis et al,[7] 2015; Djukic et al,[8] 2019; Motta et al,[9] 2005; Peretti et al,[10] 2004; Resuli and Cansiz,[11] 2020; Cabrera-Sarmiento et al,[12] 2021; Eckel et al,[13] 2000; Grant et al,[14] 2007; Peretti et al,[15] 2001; Hamzany et al,[16] 2021; Lechien et al,[17] 2022; Zhang et al,[18] 2018	1	Strong	-
3D conformal RT using traditional field borders	0	0	0	0	0	0	6	6	3	8	No	Agarwal et al,[19] 2009; Al-Mamgani et al,[20] 2014; Al-Mamgani et al,[21] 2013; Cacicedo et al,[22] 2013; Cheah et al,[23] 2009; Chera et al,[24] 2010; Itoh et al,[25] 2016; Jin et al,[26] 2002; Kim et al,[27] 2012; Mendenhall et al,[28] 2001; Motegi et al,[29] 2015; Mourad et al,[30] 2013; Mucha-Małecka et al,[31] 2019; Sert et al,[32] 2019; Short et al,[33] 2006; Smee et al,[34] 2010; Tong et al,[35] 2012; Kodaira et al,[36] 2018; Moon et al,[37] 2014; Salas-Salas et al,[38] 2020; Yamazaki et al,[39] 2006	1	Strong	↑
IMRT to whole larynx	0	0	0	1	0	1	5	6	2	8	No	Cetinayak et al,[40] 2019; Mishra et al,[41] 2022; Mohamed et al,[42] 2020; Zumsteg et al,[43] 2015	2	Moderate	-
SBRT to lesion only	5	3	6	1	0	0	0	0	0	2	No	Sher et al,[46] 2019; Sher et al,[47] 2025; Sanguineti et al,[48] 2025	1	Limited	↑
RT with concurrent cisplatin	4	5	3	3	0	0	0	0	0	2	No	NA	NA	Expert consensus	↑

Abbreviations: 3D, 3-dimensional; COPD, chronic obstructive pulmonary disease; CT, computed tomography; IMRT, intensity-modulated radiotherapy; NA, not applicable; RT, radiation therapy; SBRT, stereotactic body radiotherapy; SOE, strength of evidence; SOR, strength of recommendation; STEMI, ST-elevation myocardial infarction; TVF, true vocal fold.

[a] Rating categories 1 to 3 were defined as usually not appropriate; 4 to 6, may be appropriate; and 7 to 9, usually appropriate.

[b] Per the RAND/UCLA appropriateness method, disagreement (ie, the variation of the individual ratings from the median rating) indicates panel disagreement on the final recommendation. Group median rating is set automatically to 5.

[c] For more information on study quality, SOE, and SOR, see eAppendix 2 in the Supplement.

[d] Study quality values range from 1 (well designed and accounts for common biases) to 4 (not useful as primary evidence).

[e] Per American Radium Society SOR rating guidelines, ↑ indicates strong recommendation; – indicates moderate recommendation; and ↓ indicates weak recommendation.

was 3 mm axially and 5 mm superiorly and inferiorly with daily cone-beam computed tomography; the median planning target volume was 12.5 mL. There were 2 in-field local failures translating to 5-year LC of 97.1%. Salvage total laryngectomy was successful in both patients. With a median follow-up of 41 months, there were no acute grade 3 toxic effects and no late grade 4 to 5 toxic effects. Late grade 3 toxic effects were seen in 7 patients (6.5%); 2 (1.9%) with severe hoarseness and 5 (4.6%) with laryngeal radionecrosis. In summary, the Netherlands experience demonstrates preservation of high rates of LC with significant reduction in treatment volume compared with traditional fields. There were no excess marginal failures noted in this disease predisposed to field cancerization. Late toxic effects were similar to traditional fields with moderate hypofractionation (2.2 to 2.4 Gy per day), although on the higher end with regard to laryngeal radionecrosis.[45,58]

Radiation Targeting Lesion Only Using Stereotactic Ablative Radiotherapy | After the literature search, 2 additional studies relevant to this topic were published. They provided insight into further reducing treatment volume to lesion only using stereotactic ablative radiotherapy (SABR), generally defined as highly precise treatment concentrated over 1 to 5 sessions.[46-48] A phase 2 study of SABR for Tis-T2 lesions delivered 42.5 Gy in 5 fractions, twice per week, to small tumors (smaller than 10 mL; median volume, 5.9 mL) in patients without active smoking and 58.08 Gy in 16 fractions for all others. There were 2 in-field failures, 1 in each group, bringing the cumulative local failure rate to 8% at 2 years. There were no grade 3 or higher toxic effects reported.

Another phase 1/2 trial of T1 glottic cancer in Italy[48] treated the involved one-third of the true vocal fold to 36 Gy in 3 fractions every other day; the remainder of the true vocal fold received 30 Gy in 3 fractions. The 4-year LC was 100%. Six patients (18.2%) developed mucosal/soft tissue or cartilage necrosis at a median of 14.9 months from treatment, leading to accrual suspension. Four of 6 patients with necrosis continued to smoke after treatment. The 4 patients with mucosal/soft tissue necrosis healed with conservative therapy and medical therapy. In summary, SABR to the involved lesion only is under investigation but not standard of care. LC rates are promising despite a significant reduction in treatment volume, mirroring endoscopic surgical technique. There are early concerns regarding increased risk of tissue necrosis, particularly in patients who continue to smoke after treatment. Longer-term follow-up in a larger number of patients is needed.

Surgical Management of Early Glottic Cancer

Open surgical techniques have generally been supplanted by endoscopic laser microsurgery following its introduction in 1972 by Strong and Jako[59] for management of benign laryngeal lesions. By 1975, Strong[60] reported using the CO_2 surgical laser and microscope for 11 patients with early malignant lesions of the vocal fold. Advancements in lighting, magnification, and laser technology (which reduced spot sizes) facilitated more precise excision of vocal fold cancers with reduced surrounding tissue trauma. The most commonly used laser type in transoral laser microsurgery (TLM) for malignant lesions is the CO_2 laser, known as a cutting or ablating laser, as its 10 600-nm wavelength is absorbed by water. Newer photoangiolytic lasers specifically target hemoglobin and are used for their effectiveness in targeting the angiogenesis of dysplastic and superficial invasive laryngeal cancers. Pulsed and super-pulsed settings allow millisecond pauses in the laser fluence to allow cooling of target and surrounding tissues to minimize fibrosis and poor voice outcomes associated with deeper and wider thermal injury.

In contrast to traditional en-bloc resection, TLM allows for piecemeal resection, thus tighter margins and less disruption of normal anatomy. Another advantage is the potential for more accurate assessment of the lesion's depth invasion. In comparison, en-bloc resection may underestimate the depth of invasion, leaving a close or positive margin. Experts suggest peripheral margins as narrow as 1 mm are adequate when resecting small glottic tumors. Healing of defects occurs by secondary intention.[61]

To standardize language for the extent of TLM resection, the European Laryngological Society (ELS) categorized cordectomy procedures from type I to type V, with higher numbers representing greater depth and extent to which the vocal fold was resected,[62] with a subsequent addition of a type VI category of resection.[63] From superficial to deep, the vocal fold is comprised of the epithelium, superficial lamina propria (also known as the Reinke space), intermediate lamina propria, deep lamina propria, and finally the vocalis muscle (also known as the thyroarytenoid muscle). The intermediate and deep lamina propria together are known as the vocalis ligament. Several studies identified in this literature search described outcomes by ELS classification (eAppendix 3 in the Supplement).

Our search identified 16 articles on endoscopic laser microsurgery for T1N0 glottic SCC: 8 retrospective studies,[4-11] 4 prospective observational cohorts or case series,[12-15] and 4 prospective studies.[16-18] One of the prospective studies was a randomized study comparing CO_2 TLM and low-temperature radiofrequency ablation for T1a glottic cancer.[18]

Expected Tumor Control Rates With TLM

In contrast to radiation studies, the TLM literature generally stratified outcomes by T1a vs T1b tumors, due to the different ELS cordectomy types for unilateral vs bilateral lesions and associated differences in tumor control and voice outcomes. LC was 87% to 98% for T1a lesions and 67% to 93% for T1b lesions. Studies reporting LC for T1 tumors (not separated by T1a vs T1b) showed an 85% to 93% LC. Larynx preservation rates in these series were 80% to 98%.

Risk factors associated with increased local failure after TLM were anterior commissure involvement[8] (although not universally[12]), T1b tumors,[8] tumors requiring type Vb and VI cordectomies,[8] lateral extension of tumor,[10] and involvement of the roof of the ventricle and/or false vocal fold.[10]

Acute Effects of Endoscopic Laser Surgery

Acute adverse effects following TLM for T1 glottic cancer were infrequent, ranging from 0% to 5%.[5,7-9,11-13,15] These included tongue and/or airway edema requiring corticosteroids and/or temporary tracheostomy, bleeding requiring electrocoagulation, second procedures to remove granulation tissue, temporary nasogastric tube placement, and infection. Airway fires and laser skin burns have been reported but are relatively rare due to protocolized safety measures, including draping the face and eyes with saline-soaked surgical towels, use of an endotracheal tube resistant to laser ignition, protecting the endotracheal tube from laser energy delivery, and keeping O_2 concentration in the endotracheal tube to 30% FiO_2 or lower.[61]

Box. Appropriate-Use Recommendations Derived From the Variant Voting Results by the Multidisciplinary Panel

Special Considerations for Radiation Therapy for Early Glottic Cancer

1. Young patients with resectable disease and good anticipated postoperative laryngeal function may benefit from surgical management due to the risk of second malignant neoplasm and late effects.
2. Patients with prior head and neck RT have increased risks of acute and late effects (eg, need for tracheostomy, dysphagia, lower cranial neuropathy, and impaired voice quality). The radiation oncologist should evaluate the prior RT plan for the delivered dose to the larynx and adjacent tissues. Full-dose reirradiation of the larynx should be avoided.
3. Patients unwilling or unable to attend daily radiation treatments (eg, unreliable transportation, extended distance from RT center) may not be ideal candidates for multiweek courses of RT as LC declines with extended overall treatment time[24] or an incomplete RT course. Continued efforts toward optimizing safety and efficacy of shorter RT regimens will hopefully lessen this burden.
4. For patients with a prior TIA or cerebrovascular accident, high-grade carotid stenosis, or multiple vascular risk factors, consideration should be given to a carotid-sparing RT technique or a primary surgical approach.
5. Active connective tissue disease, such as scleroderma, should prompt consideration of surgery, if possible, due to concern for heightened soft tissue reactions, both acute and late. For well-controlled or mild connective tissue disease, RT is not necessarily a contraindication, but adverse effects may be heightened.[74]
6. In patients with significant claustrophobia, the treatment mask can pose a challenge. Anxiolytics can be helpful in addition to modification of the mask (eg, open-face mask) while maintaining its ability to ensure a reproducible treatment position. Less rigid external immobilization in combination with surface guidance may also be an option.
7. Implanted cardiac devices are generally positioned in the upper chest, sufficiently away from an early larynx RT field to be at low risk of damage, but care should be taken to accurately model and minimize dose to these devices to ensure the RT dose is within prespecified manufacturer limits.

Technical/Oncologic Considerations With Endoscopic Surgery

1. High-quality surgery requires the ability to transorally visualize the tumor and wider laryngeal structure. Limiting factors may include poor neck extension, eg, due to severe arthritis or prior spinal surgery; short thyromental distance; and limitations to oral access, such as trismus or unfavorable dental, mandibular, and/or tongue anatomy.[77,78]
2. TLM excision of more extensive tumors (multifocal dysplasia or invasion, field cancerization, or wide extent of in-situ disease around the index lesion) may lead to positive surgical margins and/or compromised functional outcomes related especially to voice and sometimes to swallow. In some cases, there may be a need for adjuvant radiotherapy or, rarely, salvage open surgery.
3. Another stated contraindication is the inability to preserve at least 1 arytenoid because failure to do so leaves the posterior aspect of the larynx incompetent and at increased risk for long-term aspiration.
4. Other TLM considerations are limitations in a patient's ability to tolerate general anesthesia (eg, severe cardiac or respiratory comorbidities).
5. For TLM, coordination between the surgeon and anesthesiologist is critical, particularly regarding bulky or obstructive tumors that could cause bleeding or airway obstruction.

Abbreviations: LC, local control; RT, radiation therapy; TIA, transient ischemic attack; TLM, transoral laser microsurgery.

Late Effects of Endoscopic Surgery

Late effects of endoscopic surgery were rarely reported. In one study, 1 of 118 patients (0.8%) developed synechiae in the anterior commissure, treated with lysis of the web with a laser and silicone stenting for 4 weeks.[5] In another series, 1 of 285 patients (0.4%) developed glottic stenosis following transoral laser surgery requiring an open surgery to restore an adequate airway.[13] In another series, 3 of 228 patients (1.3%) developed cartilage necrosis after repeat TLM for granulation tissue in the anterior commissure, leading to laryngeal stenosis and tracheostomy placement (unknown if permanent).[11] Time of onset was not specified but interpreted to be outside of the acute recovery window of the initial procedure.

Surgical Margin Status With Endoscopic Laser Surgery

Ideally, TLM specimens are oriented and labeled ex vivo to indicate to the pathologist where to assess the final margin. Specialized pathologic and surgical expertise is preferred as surgical margins are often difficult to accurately assess in laser-resected specimens given small tissue specimens, tissue retraction, and carbonization and potential lack of orientation of piecemeal specimens.[64,65]

Surgical margin status following initial resection was reported in 6 of 16 surgical series.[4,6-8,15,66] Positive surgical margins rates resulting in repeat TLM procedures varied widely from 1.3% to 43.1%, with most in the 15% to 20% range. However, due to the complexity in interpreting the pathology specimens, at least 2 studies showed that positive or close margins were not associated with poorer clinical outcomes.[6,7] Regardless, some patients may benefit from referral for adjuvant radiotherapy if there are concerns about repeat TLM to clear margins and potentially worse voice outcomes.

Voice Outcomes With Endoscopic Laser Microsurgery

Voice quality following endoscopic surgery was characterized in 5 studies included in the literature review.[5,16-18,66] Four studies assessed voice quality both before and after surgery. Hamzany et al[16] performed a prospective study of male patients with early glottic cancer. Voice outcomes were assessed using the VHI; perceptual grade of dysphonia, roughness, and breathiness; and acoustic and aerodynamic parameters. In patients undergoing ELS cordectomy types I to III, VHI, grade of dysphonia, and breathiness significantly improved from presurgery to 3 and 6 months after treatment. Patients undergoing types I to III cordectomy had better 6-month values for VHI, perceptual grade of dysphonia, and acoustic and aerodynamic voice measures compared with those undergoing types IV to VI cordectomy. In patients undergoing ELS cordectomy types IV to VI, only VHI significantly improved from presurgery to 3 and 6 months after treatment.

Multidisciplinary Approach to Treatment Selection for Early Glottic Cancer

Treatment for T1N0 glottic SCC has evolved over the past several decades and should be approached in a multidisciplinary fashion involving both surgeons and radiation oncologists. When selecting a treatment option, consideration should be given to each patients' unique circumstances with regard to tumor position and distribution, age, and medical and psychosocial factors (Table 1 and Table 2).

Conventional RT, typically less conformal than IMRT, continues to be the most commonly used RT technique with excellent LC and voice and swallowing outcomes; it remains a standard of care.[67]

Radiation techniques have since evolved to include IMRT with the goal of reducing overall toxic effects, namely late vascular events, by mitigating dose to the carotid arteries.[55-57]

Additional work has evaluated whether RT can be delivered successfully to a reduced anatomic region, such as the involved vocal fold or lesion only. Thus far, the highest quality study of image-guided SVCI used a higher dose per fraction (3.63 Gy) than the more commonly used regimens of 3 Gy or less. LC and toxic effects appeared similar to conventional RT and IMRT targeting the whole larynx.[45] The VOCAL study[68] is a multicenter phase 2 study using milder, more commonly used regimens of 5 fractions per week over 4 to 6 weeks, randomizing patients to either vocal fold only RT or complete larynx RT. This study will more clearly assess outcomes of common whole-larynx RT regimens when applied to a single vocal fold.

Lastly, studies aimed to shorten the duration of RT using high dose per fraction in 5 or fewer treatments have had mixed results, with some concern for higher rates of late toxic effects, particularly in patients with active smoking.[46-48] With any new technique targeting significantly smaller volumes, patient selection is key, particularly in glottic cancer where multifocality and field cancerization can occur. Accurate and precise treatment delivery are also vital to account for tumor motion with respiration and swallowing, as is an adequate planning target volume expansion to account for setup variation and high-quality daily image guidance.

Surgical approaches have also evolved and are minimally invasive to optimize voice preservation and maintain swallow function. TLM studies demonstrated high rates of LC with excellent voice quality outcomes. Future innovations will include the use of a variety of laser types and techniques and improved visualization technologies to further refine treatment outcomes.[16,17]

Unfortunately, there are limited randomized data comparing transoral surgery with RT. In, to our knowledge, the only prospective randomized trial available comparing these modalities, 56 patients with T1a glottic carcinoma were randomized to transoral CO_2 laser surgery or conventional RT (66 Gy in 33 fractions). Postsurgical biopsies were taken to ensure complete (R0) resection. Two-year voice outcomes using the GRBAS (grade, roughness, breathiness, asthenia, strain) scale showed less breathiness and asthenia in the RT arm. There were no differences in self-rating of hoarseness, but patients in the RT arm reported less impact of voice quality on their daily living activities. At 5 years, there were no differences with regard to overall survival, disease-specific survival, and recurrence-free survival.[69] Several retrospective studies and prospective cohorts have also compared surgery with RT finding similar cancer-related and voice outcomes in most studies.[70-75] An ongoing phase 3 multicenter study in Switzerland (VoiceS)[76] plans to randomize 34 patients with unilateral stage 0 or I glottic larynx cancer to transoral CO_2 laser surgery vs SVCI.[44]

The variants in this article (Table 1 and Table 2) provide clinical scenarios of varying tumor and patient characteristics for T1N0 glottic SCC. Each table shows panelist voting results, with areas of consensus and disagreement regarding the appropriateness of each treatment. Appropriate-use recommendations derived from the variant voting results by the multidisciplinary panel are summarized in the Box. The range of opinions within the panel reflect decision-making nuances that factor into treatment recommendations.

Conclusions

Given multiple treatment options, early glottic SCC management should be done in a multidisciplinary fashion including otolaryngologists and radiation oncologists. The ARS Head and Neck AUC expert panel created an appropriate-use consensus document by performing a literature review of current treatment strategies for stage I glottic SCC and provided recommendations regarding the appropriateness of surgery or RT for various clinical scenarios, highlighting areas of controversy and uncertainty.

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REFERENCES

1. American Cancer Society. Key statistics for laryngeal and hypopharyngeal cancers. Accessed February 29, 2024. https://www.cancer.org/cancer/types/laryngeal-and-hypopharyngeal-cancer/about/key-statistics.html

2. Forastiere AA, Ismaila N, Wolf GT. Use of larynx-preservation strategies in the treatment of laryngeal cancer: American Society of Clinical Oncology Clinical Practice Guideline Update Summary. *J Oncol Pract*. 2018;14(2):123-128. doi:10.1200/JOP.2017.027912

3. Shamseer L, Moher D, Clarke M, et al; PRISMA-P Group. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. *BMJ*. 2015;350:g7647. doi:10.1136/bmj.g7647

4. Breda E, Catarino R, Monteiro E. Transoral laser microsurgery for laryngeal carcinoma: survival analysis in a hospital-based population. *Head Neck*. 2015;37(8):1181-1186. doi:10.1002/hed.23728

5. Brøndbo K, Benninger MS. Laser resection of T1a glottic carcinomas: results and postoperative voice quality. *Acta Otolaryngol*. 2004;124(8):976-979. doi:10.1080/00016480410017413

6. Brøndbo K, Fridrich K, Boysen M. Laser surgery of T1a glottic carcinomas; significance of resection margins. *Eur Arch Otorhinolaryngol*. 2007;264(6):627-630. doi:10.1007/s00405-006-0233-5

7. Canis M, Ihler F, Martin A, Matthias C, Steiner W. Transoral laser microsurgery for T1a glottic cancer: review of 404 cases. *Head Neck*. 2015;37(6):889-895. doi:10.1002/hed.23688

8. Djukic V, Milovanović J, Jotić AD, et al. Laser transoral microsurgery in treatment of early laryngeal carcinoma. *Eur Arch Otorhinolaryngol*. 2019;276(6):1747-1755. doi:10.1007/s00405-019-05453-1

9. Motta G, Esposito E, Motta S, Tartaro G, Testa D. CO(2) laser surgery in the treatment of glottic cancer. *Head Neck*. 2005;27(7):566-573. doi:10.1002/hed.20135

10. Peretti G, Piazza C, Bolzoni A, et al. Analysis of recurrences in 322 Tis, T1, or T2 glottic carcinomas treated by carbon dioxide laser. *Ann Otol Rhinol Laryngol*. 2004;113(11):853-858. doi:10.1177/000348940411301101

11. Resuli AS, Cansiz H. Advantages of transoral endoscopic diode laser microsurgery for the treatment of early-stage glottic laryngeal cancers. *Int J Cancer Manag*. 2020;13(2):e97928. doi:10.5812/ijcm.97928

12. Cabrera-Sarmiento JA, Vázquez-Barro JC, González-Botas JH, Chiesa-Estomba C, Mayo-Yáñez M. T1b glottic tumor and anterior commissure involvement: is the transoral CO_2 laser microsurgery a safe option? *Ear Nose Throat J*. 2021;100(1_suppl):68S-72S. doi:10.1177/0145561320937238

13. Eckel HE, Thumfart W, Jungehülsing M, Sittel C, Stennert E. Transoral laser surgery for early glottic carcinoma. *Eur Arch Otorhinolaryngol*. 2000;257(4):221-226. doi:10.1007/s004050050227

14. Grant DG, Salassa JR, Hinni ML, Pearson BW, Hayden RE, Perry WC. Transoral laser microsurgery for untreated glottic carcinoma. *Otolaryngol Head Neck Surg*. 2007;137(3):482-486. doi:10.1016/j.otohns.2007.05.064

15. Peretti G, Nicolai P, Piazza C, Redaelli de Zinis LO, Valentini S, Antonelli AR. Oncological results of endoscopic resections of Tis and T1 glottic carcinomas by carbon dioxide laser. *Ann Otol Rhinol Laryngol*. 2001;110(9):820-826. doi:10.1177/000348940111000904

16. Hamzany Y, Crevier-Buchman L, Lechien JR, Bachar G, Brasnu D, Hans S. Multidimensional voice quality evaluation after transoral CO_2 laser cordectomy: a prospective study. *Ear Nose Throat J*. 2021;100(1_suppl):27S-32S. doi:10.1177/0145561320906328

17. Lechien JR, Crevier-Buchman L, Circiu MP, Lisan Q, Hans S. Evolution of voice quality in type 1-2 transoral CO_2 laser cordectomy: a prospective comparative study. *Laryngoscope*. 2022;132(7):1421-1426. doi:10.1002/lary.29924

18. Zhang Y, Wang B, Sun G, Zhang G, Lu L, Liang G. Carbon dioxide laser microsurgery versus low-temperature plasma radiofrequency ablation for T1a glottic cancer: a single-blind randomized clinical trial. *Biomed Res Int*. 2018;2018:4295960. doi:10.1155/2018/4295960

19. Agarwal JP, Baccher GK, Waghmare CM, et al. Factors affecting the quality of voice in the early glottic cancer treated with radiotherapy. *Radiother Oncol*. 2009;90(2):177-182. doi:10.1016/j.radonc.2008.09.016

20. Al-Mamgani A, van Rooij PH, Mehilal R, Verduijn GM, Tans L, Kwa SL. Radiotherapy for T1a glottic cancer: the influence of smoking cessation and fractionation schedule of radiotherapy. *Eur Arch Otorhinolaryngol*. 2014;271(1):125-132. doi:10.1007/s00405-013-2608-8

21. Al-Mamgani A, van Rooij PH, Woutersen DP, et al. Radiotherapy for T1-2N0 glottic cancer: a multivariate analysis of predictive factors for the long-term outcome in 1050 patients and a prospective assessment of quality of life and voice handicap index in a subset of 233 patients. *Clin Otolaryngol*. 2013;38(4):306-312. doi:10.1111/coa.12139

22. Cacicedo J, Casquero F, del Hoyo O, et al. Definitive radiotherapy for T1 glottic squamous cell carcinoma: a 15-year Cruces University Hospital experience. *Clin Transl Oncol*. 2013;15(11):925-931. doi:10.1007/s12094-013-1025-1

23. Cheah NL, Lupton S, Marshall A, Hartley A, Glaholm J. Outcome of T1N0M0 squamous cell carcinoma of the larynx treated with short-course radiotherapy to a total dose of 50 Gy in 16 fractions: the Birmingham experience. *Clin Oncol (R Coll Radiol)*. 2009;21(6):494-501. doi:10.1016/j.clon.2009.02.008

24. Chera BS, Amdur RJ, Morris CG, Kirwan JM, Mendenhall WM. T1N0 to T2N0 squamous cell carcinoma of the glottic larynx treated with definitive radiotherapy. *Int J Radiat Oncol Biol Phys*. 2010;78(2):461-466. doi:10.1016/j.ijrobp.2009.08.066

25. Itoh Y, Kubota S, Kawamura M, et al. A multicenter survey of stage T1 glottic cancer treated with radiotherapy delivered in 2.25-Gy fractions in clinical practice: an initial 5-year analysis. *Nagoya J Med Sci*. 2016;78(4):399-406. doi:10.18999/nagjms.78.4.399

26. Jin J, Liao Z, Gao L, Huang X, Xu G. Analysis of prognostic factors for T(1)N(0)M(0) glottic cancer treated with definitive radiotherapy alone: experience of the cancer hospital of Peking Union Medical College and the Chinese Academy Of Medical Sciences. *Int J Radiat Oncol Biol Phys*. 2002;54(2):471-478. doi:10.1016/S0360-3016(02)02920-6

27. Kim TG, Ahn YC, Nam HR, et al. Definitive radiation therapy for early glottic cancer: experience of two fractionation schedules. *Clin Exp Otorhinolaryngol*. 2012;5(2):94-100. doi:10.3342/ceo.2012.5.2.94

28. Mendenhall WM, Amdur RJ, Morris CG, Hinerman RW. T1-T2N0 squamous cell carcinoma of the glottic larynx treated with radiation therapy. *J Clin Oncol*. 2001;19(20):4029-4036. doi:10.1200/JCO.2001.19.20.4029

29. Motegi A, Kawashima M, Arahira S, et al. Accelerated radiotherapy for T1 to T2 glottic cancer. *Head Neck*. 2015;37(4):579-584. doi:10.1002/hed.23641

30. Mourad WF, Hu KS, Shourbaji RA, Woode R, Harrison LB. Long-term follow-up and pattern of failure for T1-T2 glottic cancer after definitive radiation therapy. *Am J Clin Oncol*. 2013;36(6):580-583. doi:10.1097/COC.0b013e318256f5fd

31. Mucha-Małecka A, Chrostowska A, Urbanek K, Małecki K. Prognostic factors in patients with T1 glottic cancer treated with radiotherapy. *Strahlenther Onkol*. 2019;195(9):792-804. doi:10.1007/s00066-019-01481-2

32. Sert F, Kaya I, Ozturk K, Esassolak M. Patterns of failure for early-stage glottic carcinoma: 10 years' experience in conformal radiotherapy era. *J Cancer Res Ther*. 2019;15(3):576-581. doi:10.4103/jcrt.JCRT_692_17

33. Short S, Krawitz H, Macann A, et al. TN/TN glottic carcinoma: a comparison of two fractionation schedules. *Australas Radiol*. 2006;50(2):152-157. doi:10.1111/j.1440-1673.2006.01559.x

34. Smee RI, Meagher NS, Williams JR, Broadley K, Bridger GP. Role of radiotherapy in early glottic carcinoma. *Head Neck*. 2010;32(7):850-859. doi:10.1002/hed.21262

35. Tong CC, Au KH, Ngan RK, et al. Definitive radiotherapy for early stage glottic cancer by 6 MV photons. *Head Neck Oncol*. 2012;4:23. doi:10.1186/1758-3284-4-23

36. Kodaira T, Kagami Y, Shibata T, et al; Radiation Therapy Study Group of the Japan Clinical Oncology Group. Results of a multi-institutional, randomized, non-inferiority, phase III trial of accelerated fractionation versus standard fractionation in radiation therapy for T1-2N0M0 glottic cancer: Japan Clinical Oncology Group Study (JCOG0701). *Ann Oncol*. 2018;29(4):992-997. doi:10.1093/annonc/mdy036

37. Moon SH, Cho KH, Chung EJ, et al. A prospective randomized trial comparing hypofractionation with conventional fractionation radiotherapy for T1-2 glottic squamous cell carcinomas: results of a Korean Radiation Oncology Group (KROG-0201) study. *Radiother Oncol*. 2014;110(1):98-103. doi:10.1016/j.radonc.2013.09.016

38. Salas-Salas BG, Domínguez-Nuez DJ, Cabrera R, Ferrera-Alayón L, Lloret M, Lara PC. Hypofractionation vs. conventional radiotherapy fractionation in the conservative treatment of T1 glottic cancer: a prospective cohort study. *Clin Transl Oncol*. 2020;22(1):151-157. doi:10.1007/s12094-019-02118-7

39. Yamazaki H, Nishiyama K, Tanaka E, Koizumi M, Chatani M. Radiotherapy for early glottic carcinoma (T1N0M0): results of prospective randomized study of radiation fraction size and overall treatment time. *Int J Radiat Oncol Biol Phys*. 2006;64(1):77-82. doi:10.1016/j.ijrobp.2005.06.014

40. Cetinayak O, Dogan E, Kuru A, et al. Outcome of early-stage glottic laryngeal carcinoma patients treated with radical radiotherapy using different techniques. *J Oncol*. 2019;2019:8640549. doi:10.1155/2019/8640549

41. Mishra AK, Sinha VR, Suhag V, Nilakantan A. Evaluation of voice after definitive radiotherapy in patients of early stage squamous cell carcinoma of larynx (glottis): a prospective observational study. *Indian J Otolaryngol Head Neck Surg*. 2022;74(suppl 2):2386-2394. doi:10.1007/s12070-020-02193-1

42. Mohamed ASR, Smith BD, Smith JB, et al. Outcomes of carotid-sparing IMRT for T1 glottic cancer: comparison with conventional radiation. *Laryngoscope*. 2020;130(1):146-153. doi:10.1002/lary.27873

43. Zumsteg ZS, Riaz N, Jaffery S, et al. Carotid sparing intensity-modulated radiation therapy achieves comparable locoregional control to conventional radiotherapy in T1-2N0 laryngeal carcinoma. *Oral Oncol*. 2015;51(7):716-723. doi:10.1016/j.oraloncology.2015.02.003

44. Al-Mamgani A, Kwa SL, Tans L, et al. Single vocal cord irradiation: image guided intensity modulated hypofractionated radiation therapy for T1a glottic cancer: early clinical results. *Int J Radiat Oncol Biol Phys*. 2015;93(2):337-343. doi:10.1016/j.ijrobp.2015.06.016

45. Tans L, Al-Mamgani A, Kwa SLS, et al. Single vocal cord irradiation for early-stage glottic cancer: excellent local control and favorable toxicity profile. *Oral Oncol*. 2022;127:105782. doi:10.1016/j.oraloncology.2022.105782

46. Sher DJ, Timmerman RD, Nedzi L, et al. Phase 1 fractional dose-escalation study of equipotent stereotactic radiation therapy regimens for early-stage glottic larynx cancer. *Int J Radiat Oncol Biol Phys*. 2019;105(1):110-118. doi:10.1016/j.ijrobp.2019.03.010

47. Sher DJ, Avkshtol V, Moon D, et al. Stereotactic ablative radiotherapy for T1 to T2 glottic larynx cancer: mature results from the phase 2 GLoTtic Larynx-SABR trial. *Int J Radiat Oncol Biol Phys*. 2025;121(1):137-144. doi:10.1016/j.ijrobp.2024.07.2147

48. Sanguineti G, D'Urso P, Bottero M, et al. Stereotactic radiation therapy in 3 fractions for T1 glottic cancer. *Int J Radiat Oncol Biol Phys*. 2025;121 (1):145-152. doi:10.1016/j.ijrobp.2024.09.051

49. Fitch K, Bernstein SJ, Aguilar MD, et al. *The RAND/UCLA Appropriateness Method: User's Manual*. RAND Corporation; 2000.

50. Dalkey N. An experimental study of group opinion: the Delphi method. *Futures*. 1969;1: 408-426. doi:10.1016/S0016-3287(69)80025-X

51. Margalit DN, Sacco AG, Cooper JS, et al. Systematic review of postoperative therapy for resected squamous cell carcinoma of the head and neck: executive summary of the American Radium Society appropriate use criteria. *Head Neck*. 2021; 43(1):367-391. doi:10.1002/hed.26490

52. Gowda RV, Henk JM, Mais KL, Sykes AJ, Swindell R, Slevin NJ. Three weeks radiotherapy for T1 glottic cancer: the Christie and Royal Marsden Hospital Experience. *Radiother Oncol*. 2003;68(2): 105-111. doi:10.1016/S0167-8140(03)00059-8

53. Laskar SG, Baijal G, Murthy V, et al. Hypofractionated radiotherapy for T1N0M0 glottic cancer: retrospective analysis of two different cohorts of dose-fractionation schedules from a single institution. *Clin Oncol (R Coll Radiol)*. 2012;24 (10):e180-e186. doi:10.1016/j.clon.2012.07.001

54. Cellai E, Frata P, Magrini SM, et al. Radical radiotherapy for early glottic cancer: results in a series of 1087 patients from two Italian radiation oncology centers. I. the case of T1N0 disease. *Int J Radiat Oncol Biol Phys*. 2005;63(5):1378-1386. doi:10.1016/j.ijrobp.2005.05.018

55. Dorresteijn LD, Kappelle AC, Boogerd W, et al. Increased risk of ischemic stroke after radiotherapy on the neck in patients younger than 60 years. *J Clin Oncol*. 2002;20(1):282-288. doi:10.1200/JCO.2002.20.1.282

56. Haynes JC, Machtay M, Weber RS, Weinstein GS, Chalian AA, Rosenthal DI. Relative risk of stroke in head and neck carcinoma patients treated with external cervical irradiation. *Laryngoscope*. 2002;112(10): 1883-1887. doi:10.1097/00005537-200210000-00034

57. Scott AS, Parr LA, Johnstone PA. Risk of cerebrovascular events after neck and supraclavicular radiotherapy: a systematic review. *Radiother Oncol*. 2009;90(2):163-165. doi:10.1016/j.radonc.2008.12.019

58. Farneti D, Fabbri C, Prencipe SR. Chondroradionecrosis of the larynx. *Curr Opin Otolaryngol Head Neck Surg*. 2019;27(6):463-466. doi:10.1097/MOO.0000000000000586

59. Strong MS, Jako GJ. Laser surgery in the larynx. early clinical experience with continuous CO 2 laser. *Ann Otol Rhinol Laryngol*. 1972;81(6):791-798. doi:10.1177/000348947208100606

60. Strong MS. Laser excision of carcinoma of the larynx. *Laryngoscope*. 1975;85(8):1286-1289. doi:10.1288/00005537-197508000-00003

61. Rubinstein M, Armstrong WB. Transoral laser microsurgery for laryngeal cancer: a primer and review of laser dosimetry. *Lasers Med Sci*. 2011;26 (1):113-124. doi:10.1007/s10103-010-0834-5

62. Remacle M, Eckel HE, Antonelli A, et al. Endoscopic cordectomy. a proposal for a classification by the Working Committee, European Laryngological Society. *Eur Arch Otorhinolaryngol*. 2000;257(4):227-231. doi:10.1007/s004050050228

63. Remacle M, Van Haverbeke C, Eckel H, et al. Proposal for revision of the European Laryngological Society classification of endoscopic cordectomies. *Eur Arch Otorhinolaryngol*. 2007; 264(5):499-504. doi:10.1007/s00405-007-0279-z

64. Yan Y, Olszewski AE, Hoffman MR, et al. Use of lasers in laryngeal surgery. *J Voice*. 2010;24(1): 102-109. doi:10.1016/j.jvoice.2008.09.006

65. Meulemans J, Hauben E, Peeperkorn S, Nuyts S, Delaere P, Vander Poorten V. Transoral laser microsurgery (TLM) for glottic cancer: prospective assessment of a new pathology workup protocol. *Front Surg*. 2020;7: 56. doi:10.3389/fsurg.2020.00056

66. Song W, Caffier F, Nawka T, et al. T1a glottic cancer: advances in vocal outcome assessment after transoral CO_2-laser microsurgery using the VEM. *J Clin Med*. 2021;10(6):1250. doi:10.3390/jcm10061250

67. Amini A, Morgan R, Meyer E, et al. Outcomes between intensity-modulated radiation therapy versus 3D-conformal in early stage glottic cancer. *Head Neck*. 2021;43(11):3393-3403. doi:10.1002/hed.26841

68. Vocal-cord vs. Complete Laryngeal Radiotherapy for Early Glottic Cancer (VOCAL). ClinicalTrials.gov identifier: NCT03759431. Updated March 21, 2025. Accessed February 13, 2025. https://clinicaltrials.gov/study/NCT03759431

69. Pakkanen P, Irjala H, Ilmarinen T, et al. Survival and larynx preservation in early glottic cancer: a randomized trial comparing laser surgery and radiation therapy. *Int J Radiat Oncol Biol Phys*. 2022; 113(1):96-100. doi:10.1016/j.ijrobp.2022.01.010

70. Chung SY, Kim KH, Keum KC, et al. Radiotherapy versus cordectomy in the management of early glottic cancer. *Cancer Res Treat*. 2018;50(1):156-163. doi:10.4143/crt.2016.503

71. Dinapoli N, Parrilla C, Galli J, et al. Multidisciplinary approach in the treatment of T1 glottic cancer. the role of patient preference in a homogenous patient population. *Strahlenther Onkol*. 2010;186(11):607-613. doi:10.1007/s00066-010-2142-1

72. 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;47(1):67-74. doi:10.1111/coa.13849

73. Remmelts AJ, Hoebers 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;270(7):2079-2087. doi:10.1007/s00405-013-2460-x

74. Schrijvers ML, van Riel EL, Langendijk JA, et al. Higher laryngeal preservation rate after CO2 laser surgery compared with radiotherapy in T1a glottic laryngeal carcinoma. *Head Neck*. 2009;31(6): 759-764. doi:10.1002/hed.21027

75. van Gogh CD, Verdonck-de Leeuw IM, Wedler-Peeters 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;269(6): 1647-1652. doi:10.1007/s00405-012-1947-1

76. VoiceS: Voice Quality After Transoral CO2-Laser Surgery Versus Single Vocal Cord Irradiation for Larynx Cancer (VoiceS). ClinicalTrials.gov identifier: NCT04057209. Updated June 24, 2025. Accessed February 13, 2025. https://clinicaltrials.gov/study/NCT04057209

77. Incandela F, Paderno A, Missale F, et al. Glottic exposure for transoral laser microsurgery: proposal of a mini-version of the laryngoscore. *Laryngoscope*. 2019;129(7):1617-1622. doi:10.1002/lary.27525

78. Piazza C, Mangili S, Bon FD, et al. Preoperative clinical predictors of difficult laryngeal exposure for microlaryngoscopy: the Laryngoscore. *Laryngoscope*. 2014;124(11):2561-2567. doi:10.1002/lary.24803