Use of Larynx-Preservation Strategies in the Treatment of Laryngeal Cancer: American Society of Clinical Oncology Clinical Practice Guideline Update
Introduction

• Based on SEER data for the period 2006-2012, the estimated overall 5-year survival rate for patients with larynx cancer was only 60.7% and has not changed appreciably over the past several decades.

• When analyzed by tumor stage, cure rates for patients diagnosed with limited disease (T1,2) are excellent ranging from 80-90%. Unfortunately, a majority of patients are still diagnosed with locally advanced (T3,4) disease or regional nodal metastases, where survival rates are generally less than 50%.

• In 2006, an ASCO expert panel reviewed evidence supporting treatment strategies that were intended to preserve laryngeal function and published comprehensive guidelines for use of such strategies in both limited and advanced disease settings.

• The purpose of this guideline update is to review the recent literature since publication of the 2006 guidelines and evaluate the prior recommendations to determine if they still represent the state of the art in larynx preservation approaches for patients with laryngeal cancer.
ASCO Guideline Development Methodology

The ASCO Clinical Practice Guidelines Committee guideline process includes:

• a systematic literature review by ASCO guidelines staff
• an expert panel provides critical review and evidence interpretation to inform guideline recommendations
• final guideline approval by ASCO CPGC

The full ASCO Guideline methodology supplement can be found at:

www.asco.org/head-neck-cancer-guidelines
Clinical Questions

This clinical practice guideline addresses five overarching clinical questions:

1. What are the larynx-preservation treatment options for limited stage (T1, T2) primary site disease that do not compromise survival and what are the considerations in selecting among them?

2. What are the larynx-preservation treatment options for advanced stage (T3, T4) primary site disease that do not compromise survival and what are the considerations in selecting among them?

3. What is the appropriate treatment of the regional cervical nodes for patients with laryngeal cancer who are treated with an organ-preservation approach?

4. Are there methods for prospectively selecting patients with laryngeal cancer to increase the likelihood of success of larynx preservation?

5. What are the best measures to evaluate airway, voice and swallowing function to determine the best function preservation treatment or to recommend laryngectomy, and for the pre and post-treatment assessment of function?
Target Population and Audience

Target Population
Patients with laryngeal cancer

Target Audience
Medical Oncologists, Radiation Oncologists, Surgeons, Nurses, Speech Pathologists, Oncology Pharmacists
Summary of Recommendations

CLINICAL QUESTION 1
What are the larynx-preservation treatment options for limited stage (T1, T2) primary site disease that do not compromise survival and what are the considerations in selecting among them?

Recommendation 1.1 [Unchanged]
All patients with T1, T2 laryngeal cancer should be treated, at least initially, with intent to preserve the larynx.

Recommendation 1.2 [Unchanged]
T1, T2 laryngeal cancer can be treated with radiation or larynx-preserving surgery with similar survival outcomes. Selection of treatment depends on patient factors, local expertise, and the availability of appropriate support and rehabilitative services. Every effort should be made to avoid combining surgery with radiation therapy because functional outcomes may be compromised by combined-modality therapy; single-modality treatment is effective for limited-stage, invasive cancer of the larynx.
Summary of Recommendations

**Recommendation 1.3 [NEW]**
The success of the larynx-preservation approach may be higher with initial larynx-preserving surgery compared to radiation based on retrospective studies; however, this may be subjected to patient selection factors. In experienced hands, endoscopic resections are preferred because of equal or better outcomes compared to open partial laryngectomy unless there are issues with tumor exposure or safety of the endoscopic approach. (Type: evidence-based; benefits outweigh harms; Evidence quality: intermediate; Strength of Recommendation: moderate).

**Recommendation 1.4 [UPDATED]**
Surgical excision of the primary tumor with intent to preserve the larynx should be undertaken with the aim of achieving tumor-free margins. Surgery that anticipates the need for postoperative radiation therapy to treat close or involved tumor margins or widespread dysplasia is not an acceptable treatment approach. (Type: evidence-based; benefits outweigh harms; Evidence quality: strong; Strength of Recommendation: high).

**Recommendation 1.5 [Unchanged]**
Local tumor recurrence after radiation therapy may be amenable to salvage by organ-preservation surgery but total laryngectomy will be necessary for a substantial proportion of patients, especially those with index T2 tumors.

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Summary of Recommendations

**Recommendation 1.6 [Unchanged]**
Combined chemotherapy and radiation approaches may be used for larynx preservation for selected patients with limited stage and (1) unfavorable or deeply invasive T2; (2) T2 N+ cancers; (3) for whom total laryngectomy may be the only surgical option; (4) in whom the functional outcome after larynx-preserving surgery is expected to be unsatisfactory; (5) for whom surgical expertise for such procedures is not available.

**Recommendation 1.7 [UPDATED]**
Limited-stage laryngeal cancer constitutes a wide spectrum of disease. The clinician must exercise judgment when recommending treatment in this category. For a given patient, factors that may influence the selection of treatment modality include extent and volume of tumor; vocal cord mobility, involvement of the anterior commissure; lymph node metastasis; the patient’s age, occupation, pretreatment voice, and swallowing function; patient preference and compliance; and the availability of expertise in radiation therapy or surgery. Optimal outcomes require specialized skill, judgement and expertise. Poorly performed open or endoscopic surgery or radiation therapy will raise the risk for recurrence or the need to add additional modalities of therapy to achieve disease control. (Type: evidence-based; benefits outweigh harms; Evidence quality: intermediate; Strength of Recommendation: moderate).

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Summary of Recommendations

CLINICAL QUESTION 2
What are the larynx-preservation treatment options for advanced stage (T3, T4) primary site disease that do not compromise survival and what are the considerations in selecting among them?

Recommendation 2.1 [REWORDED]
Organ-preservation surgery, combined chemotherapy and radiation, and radiation therapy alone, all with further surgery reserved for salvage, offer the potential for larynx preservation without compromising overall survival. Anticipated success rates for larynx preservation, associated toxicities, and suitability for a given patient will vary among these approaches. Selection of a treatment option will depend on patient factors including age, co-morbidities, preferences, socio-economic factors, local expertise, and the availability of appropriate support and rehabilitation services.

Recommendation 2.2 [NEW]
For selected patients with extensive T3 or large T4a lesions and/or poor pretreatment laryngeal function, better survival rates and quality of life may be achieved with total laryngectomy rather than organ preservation approaches and may be the preferred approach. (Type: evidence-based; benefits outweigh harms; Evidence quality: strong; Strength of Recommendation: high).

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Summary of Recommendations

**Recommendation 2.3 [Unchanged]**
All patients should have multidisciplinary evaluation regarding their suitability for a larynx-preservation approach, and they should be apprised of these treatment options. No larynx preservation approach offers a survival advantage compared with total laryngectomy and appropriate adjuvant treatment.

**Recommendation 2.4 [UPDATED]**
A minority of patients with T3-T4 primary-site disease will be suitable for specialized organ-preservation surgical procedures, such as a supracricoid partial laryngectomy. The addition of postoperative radiation therapy will compromise functional outcomes. Induction chemotherapy before organ-preservation surgery is not recommended outside of a clinical trial. (Type: evidence-based; benefits outweigh harms; Evidence quality: intermediate; Strength of Recommendation: moderate).

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Summary of Recommendations

**Recommendation 2.5 [UPDATED]**
Concurrent chemoradiation therapy offers a significantly higher chance of larynx preservation than does radiation therapy alone or induction chemotherapy followed by radiation albeit at the cost of higher acute in-field toxicities and without improvement in overall survival. The best available evidence supports the use of cisplatin as the drug of choice in this setting. (Type: evidence-based; benefits outweigh harms; Evidence quality: high; Strength of Recommendation: strong).

**Recommendation 2.6 [UPDATED]**
There is insufficient evidence to indicate that survival or larynx-preservation outcomes are improved by the addition of induction chemotherapy before concurrent treatment or the use of concurrent treatment with altered fractionation radiation therapy in this setting. (Type: evidence-based; benefits outweigh harms; Evidence quality: intermediate; Strength of Recommendation: moderate).

**Recommendation 2.7 [Unchanged]**
For patients who desire larynx-preservation therapy but are not candidates for organ-preservation surgery or chemoradiation, radiation therapy alone is an appropriate treatment. With this last approach, survival is similar to that associated with chemoradiation therapy when timely salvage surgery is incorporated, but the likelihood of larynx preservation is lower.
Summary of Recommendations

CLINICAL QUESTION 3
What is the appropriate treatment of the regional cervical nodes for patients with laryngeal cancer who are treated with an organ-preservation approach?

**Recommendation 3.1 [Unchanged]**
Most patients with T1, T2 lesions of the glottis and clinically negative cervical nodes (N0) do not require routine elective treatment of the neck.

**Recommendation 3.2 [Unchanged]**
Patients with advanced lesions of the glottis and all patients with supraglottic lesions should have elective treatment of the neck, even if clinically N0.

**Recommendation 3.3 [UPDATED]**
Patients with clinically involved regional cervical nodes (N+) who are treated with definitive radiation therapy or chemotherapy and radiation therapy and who have a complete clinical, radiologic and metabolic imaging (PET-CT at 12 weeks or later after therapy) do not require elective neck dissection. (Type: evidence-based; benefits outweigh harms; Evidence quality: strong; Strength of Recommendation: high).
Summary of Recommendations

**Recommendation 3.4 [UPDATED]**
Patients with equivocal FDG uptake should undergo neck dissection. The risks and cost of expectant observation versus surgery should be discussed with the patient. (Type: evidence-based; benefits outweigh harms; Evidence quality: strong; Strength of Recommendation: high).

**Recommendation 3.5 [Unchanged]**
Patients with clinically involved cervical nodes who are treated with surgery for the primary lesion should have neck dissection. If there are poor-risk features, adjuvant concurrent chemoradiation therapy is indicated.

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Summary of Recommendations

CLINICAL QUESTION 4
Are there methods for prospectively selecting patients with laryngeal cancer to increase the likelihood of success of larynx preservation?

Recommendation 4.1 [UPDATED]
There are no validated markers that consistently predict outcomes of larynx-preservation therapy. However, patients with a non-functional larynx (e.g. extensive T3 or T4a) or tumor penetration through cartilage into surrounding soft tissues are considered poor candidates for a larynx-preservation approach. Primary surgery, usually total laryngectomy, is recommended in this setting. (Type: evidence-based; benefits outweigh harms; Evidence quality: intermediate; Strength of Recommendation: moderate).

Recommendation 4.2 [UPDATED]
Selection of therapy for an individual patient requires assessment by the multidisciplinary team, as well as consideration of voice, and swallowing function, patient comorbidity, psychosocial situation and preferences, and local therapeutic expertise. The multidisciplinary team should include surgical oncology, medical oncology, radiation oncology, speech pathology, radiology, pathology, nursing, dietetics, psychology, and a variety of rehabilitative services including dental/prosthodontics, smoking cessation, or other ancillary services as required for such things as pain management, and psychosocial support. (Type: evidence-based; benefits outweigh harms; Evidence quality: intermediate; Strength of Recommendation: moderate).
Recommendation 4.3 [Unchanged]
Continued cigarette smoking is associated with a worse outcome after therapy. Patients should be encouraged to abstain from smoking after the diagnosis and monitored and recommended for smoking cessation programs as necessary throughout and following treatment.

CLINICAL QUESTION 5 [NEW]
What are the best measures to evaluate airway, speech and swallowing function to determine best function preservation treatment or laryngectomy and for the post treatment assessment of function?

Recommendation 5.1
As part of a comprehensive pretreatment evaluation, all patients should undergo an assessment of voice and swallowing function, voice (use and requirements), and counseling regarding potential impact on quality of life, voice, and swallowing with treatment options. (Type: evidence-based; benefits outweigh harms; Evidence quality: strong; Strength of Recommendation: high).
Summary of Recommendations

Recommendation 5.2
Pretreatment voice and swallowing assessments should establish the functional impact of tumor volume and extent and stage of disease on voice and swallowing outcomes. (Type: evidence-based; benefits outweigh harms; Evidence quality: intermediate; Strength of Recommendation: moderate).

Recommendation 5.3
Instrumental, performance status, and quality of life measures of voice and swallowing should be used to evaluate pre- and post-treatment function. Multiple assessment tools are available for voice and swallowing. Routine methods of assessment include self-recorded and/or expert-rated voice-quality measures, voice-related quality of life tools, videostroboscopy, radiographic (videofluoroscopic) or fiber-optic laryngoscopic evaluation of swallowing, and dietary assessment. (Type: evidence-based; benefits outweigh harms; Evidence quality: intermediate; Strength of Recommendation: moderate).
Patient and Clinician Communication

- The nuances of treatment selection, assessments of pretreatment voice and swallowing, and public awareness of new organ preservation treatment and decision-making have increased to the point that careful and individualized discussion with patients and family by the multidisciplinary treatment team are critical elements of modern care.

- Establishing good communications between all members of the care team is essential to a good outcome, and good communication is a shared responsibility.

- Advances in care and electronic medical documentation have encouraged greater participation by patients in communication and the coordination of care by the other members of a modern treatment team.

- Treatment plans need to be articulated in the medical record. Responsibilities for each component of care and follow up need to be defined and understood by the patient and primary care providers.

- Patients should be empowered to participate in their care, treatment plans, and surveillance schedules and to share any other concerns regarding ongoing care, side effects, overall prognosis and other issues that may impact their cancer recovery and quality of life.
Cost Implications

- Cost of care is a major consideration that should take into account the frequency and necessity of surveillance activities and cost of secondary salvage procedures in addition to the cost of initial treatment modalities.

- Assessing cost implications of chemoradiation vs. total laryngectomy as initial treatment of patients with advanced disease is difficult as type of chemotherapy, hospital setting and likelihood of high cost complications will determine overall costs of organ preserving approaches.

- True costs in terms of patient burden and quality of life, return to work, and health utilities for loss of laryngeal function however, are difficult to measure and compare.
Additional Resources

More information, including a Data Supplement, a Methodology Supplement, slide sets, and clinical tools and resources, is available at

www.asco.org/head-neck-cancer-guidelines

Patient information is available at www.cancer.net
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