



American Society of Clinical Oncology

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Use of Larynx-Preservation Strategies in the Treatment of Laryngeal Cancer

American Society of Clinical Oncology
Clinical Practice Guideline

Introduction

- ASCO convened an Expert Panel to develop recommendations regarding the appropriate application of larynx-preservation therapies.
- The guideline focuses only on invasive laryngeal cancers with squamous cell carcinoma histology and is most applicable to supraglottic and glottic tumors.
- The AJCC Cancer Staging Manual (6th Edition, 2002) is the TNM system used to summarize the guideline recommendations by T stage.
- Treatment of M1 disease is not considered in the guideline.

Guideline Methodology

- An ASCO Expert Panel completed a review of the pertinent literature through November 2005:
 - ✓ MEDLINE
 - ✓ CANCERLIT
 - ✓ Cochrane Collaboration Library

Guideline Methodology (cont'd): Panel Members

- David G. Pfister, MD, *Co-Chair* Memorial Sloan-Kettering Cancer Center
- Gregory T. Wolf, MD, *Co-Chair* University of Michigan Hospital
- David J. Adelstein, MD Cleveland Clinic Foundation
- Kie-Kian Ang, MD, PhD UT MD Anderson Cancer Center
- Gary L. Clayman, MD UT MD Anderson Cancer Center
- Susan G. Fisher, PhD University of Rochester
- Arlene A. Forastiere, MD Johns Hopkins University, The Sidney Kimmel Cancer Center
- Louis B. Harrison, MD Beth Israel Health Care System
- Scott A. Laurie, MD The Ottawa Hospital Regional Cancer Centre
- Jean-Louis Lefebvre, MD Centre Oscar-Lambret
- Nancy Leupold Support for People with Oral and Head and Neck Cancer (SPONHC)
- Marcy A. List, PhD University of Chicago
- William M. Mendenhall, MD University of Florida
- Bernard O'Malley, MD Princeton Radiology Association
- Marshall R. Posner, MD Dana-Farber Cancer Institute
- Michael A. Schwartz, MD Oncology Hematology Associates
- Snehal Patel, MD Memorial Sloan-Kettering Cancer Center
- Gregory S. Weinstein, MD University of Pennsylvania Medical Center

Background

Parts of the larynx:

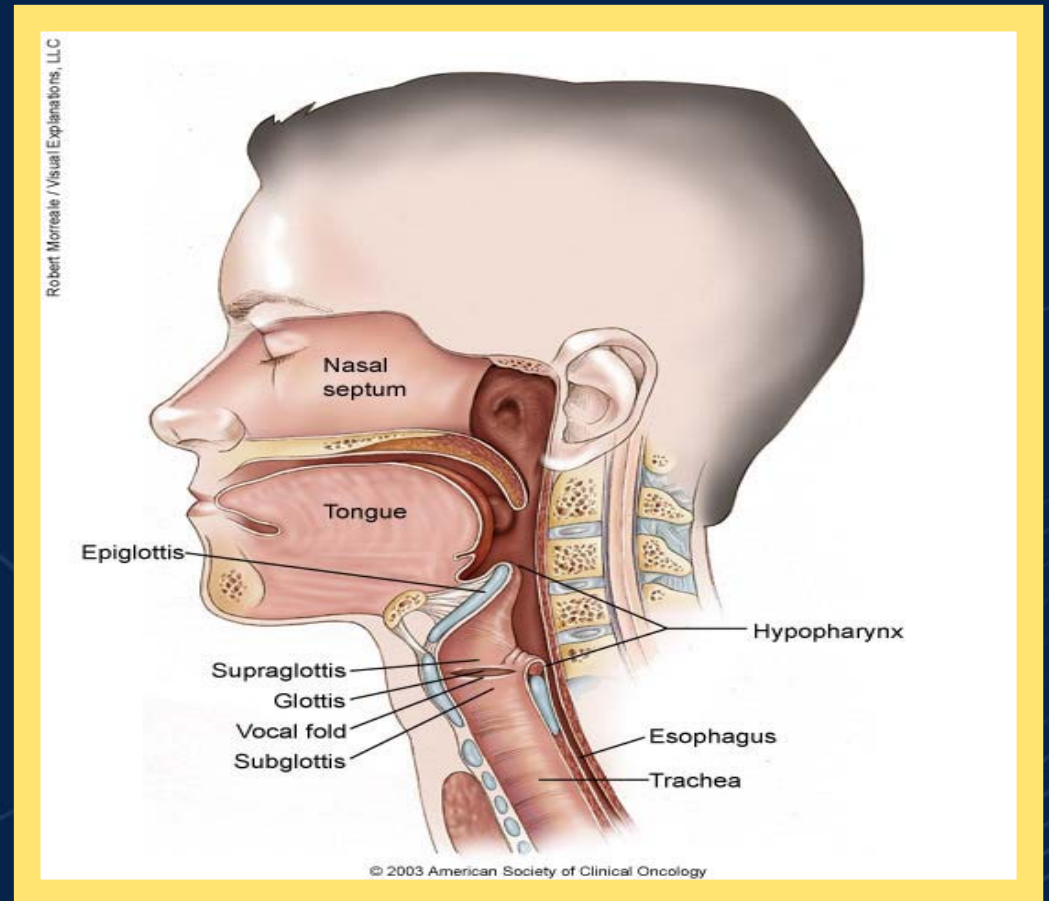
➤ **Supraglottis**

(epiglottis, arytenoids, aryepiglottic folds, false cords)

➤ **Glottis**

(true cords, anterior and posterior commissures)

➤ **Subglottis**



Background (cont'd)

- New cases of laryngeal cancer to be diagnosed (U.S., 2005):
9,880
- Newly diagnosed cases that will lead to death (U.S., 2005):
3,770
- 95% of laryngeal cancers are invasive with squamous cell carcinoma as the predominant histologic type
- 40% of patients will have stage III or IV laryngeal cancer (upon first evaluation)
- 25% of healthy people are willing to trade a 20% absolute difference in survival for the opportunity to save their voice

Background (cont'd)

- Most cases of laryngeal cancer are associated with alcohol and/or tobacco use.
- Continued tobacco and/or alcohol use complicates treatment and facilitates medical comorbidity and the development of second primary cancers.



Background (cont'd)

- **Larynx-preservation options include:**
 - Radiation therapy
 - Chemoradiation therapy
 - Function-preserving partial laryngectomy procedures
- **Total laryngectomy is recognized as one of the surgical procedures most feared by patients. Common sequelae:**
 - Social isolation
 - Job loss
 - Depression

Background (cont'd)

Larynx-Preservation:

- ▣ Focuses on maintaining the function of the larynx though part may be removed
- ▣ Applies only to patients with resectable disease
- ▣ Includes endoscopic resections and open techniques
- ▣ Involves the careful consideration of survival, function, quality of life and costs.
- ▣ Requires a team with special expertise for effective treatment application:
 - ◆ Head and neck surgery
 - ◆ Radiation Therapy
 - ◆ Medical Oncology
 - ◆ Pathology
 - ◆ Nursing
 - ◆ Audiology
 - ◆ Social Services
 - ◆ Nutrition
 - ◆ Tobacco Cessation
 - ◆ Management of Medical Comorbidities
 - ◆ Speech and Swallowing Physiology/Rehabilitation

Guideline Questions

1. What are the larynx-preservation treatment options for limited stage (T1, T2) primary site disease that do not compromise survival? 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? What are the considerations in selecting among them?
3. What is the appropriate treatment of the regional cervical nodes in 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 successful larynx preservation?

What are the larynx-preservation treatment options for limited stage (T1, T2) primary site disease that do not compromise survival?

- All patients with T1-T2 laryngeal cancer should be treated, at least initially, with intent to preserve the larynx.
- Treatment selection depends on patient factors, local expertise, and availability of support and rehabilitation services.
- Radiation or Larynx-Preservation Surgery
 - Single-modality treatment is effective for limited stage, invasive larynx cancer. Avoid combining surgery with radiation therapy as combined-modality therapy may compromise functional outcomes.

Treatment Options for Limited Stage (T1, T2) Cancer (cont'd)

- Surgical excision of the primary tumor with intent to preserve the larynx should be done with the aim of achieving tumor-free margins.
 - “Narrow-margin excision” followed by postoperative radiation therapy **IS NOT** an acceptable treatment approach.

Treatment Options for Limited Stage (T1, T2) Cancer (cont ' d)

- Should a local tumor recur after radiation therapy, organ-preservation surgery may be helpful. However, total laryngectomy may be necessary for a substantial proportion of these patients, especially those with index T2 tumors.
- While induction chemotherapy has been investigated as a treatment for laryngeal cancer, further clinical trial research is needed before the Panel can make a recommendation for this treatment option.

Treatment Options for Limited Stage (T1, T2) Cancer (cont'd)

- Concurrent chemoradiation therapy may be used for selected patients under one of the following conditions:
 - Stage III, T2 N+ cancer patients for whom total laryngectomy is the only surgical option,
 - Larynx-preservation surgery is expected to yield an unsatisfactory functional outcome, OR
 - Organ-preservation surgical expertise is unavailable.

Treatment Options for Limited Stage (T1, T2) Cancer (cont'd)

- Because limited stage laryngeal cancer constitutes a wide spectrum of disease, the clinician must exercise sound judgment when recommending treatment.
- Factors that may influence treatment modality include:
 - Extent and volume of tumor
 - Involvement of the anterior commissure
 - Lymph node metastasis
 - Patient age, occupation, preference, and compliance
 - Availability of expertise in radiation therapy or surgery
 - History of malignant lesion in the head and neck

What are the larynx-preservation treatment options for advanced stage (T3, T4) primary site disease that do not compromise survival?

- Larynx-preservation options that offer potential without compromising survival (further surgery reserved for salvage):
 - Organ-preservation surgery
 - Concurrent chemoradiation therapy
 - Radiation therapy alone
- No larynx-preservation approach offers a survival advantage compared with total laryngectomy and appropriate adjuvant treatment
- Treatment selection depends on patient factors, local expertise, and the availability of support and rehabilitation services

Treatment Options for Advanced Stage (T3, T4) Cancer (cont'd)

- All patients should be evaluated for larynx-preservation suitability and apprised of their treatment options/effects
- Specialized Organ-Preservation Surgery (e.g., supracricoid partial laryngectomy):
 - Postoperative radiation therapy will compromise anticipated functional outcomes
 - Induction chemotherapy is not recommended before organ-preservation surgery and is not recommended outside of a clinical trial
 - A minority of patients are suitable

Treatment Options for Advanced Stage (T3, T4) Cancer (cont'd)

- Concurrent Chemoradiation Therapy
 - At the cost of higher toxicities this option offers a significantly higher chance of larynx-preservation than when radiation therapy alone or induction chemotherapy followed by radiation
 - Best available evidence supports the use of **cisplatin**
- 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 chemotherapy with altered fractionated radiation therapy in this setting.

Treatment Options for Advanced Stage (T3, T4) Cancer (cont'd)

- Radiation Therapy (only)
 - Appropriate for patients who desire larynx-preservation therapy but are not candidates for surgery or chemoradiation therapy.
 - Survival is similar to that associated with chemoradiation therapy when salvage surgery is incorporated, but the likelihood of larynx preservation is lower.

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

- T1-T2 Glottic Lesions (N0)
 - Most patients **do not** require routine elective treatment of the neck
- Advanced Glottic/Supraglottic Lesions (even if clinically N0)
 - Requires elective treatment of the neck
- Involved Regional Cervical Nodes (N1)
 - Neck dissection depends on clinical response to definitive radiation therapy or chemoradiation therapy. If a complete response to therapy is not achieved, neck dissection is recommended.

Treatment of Regional Cervical Nodes (cont'd)

- Involved Regional Cervical Nodes (N2 or N3)
 - Neck dissection is recommended for these patients regardless of clinical response to radiation or chemoradiation therapy
 - No standard imaging approach has been validated to significantly improve on clinical decision-making in this setting
 - Salvage surgery for recurrent disease in the neck is rarely successful if required
 - Patients who have had an apparent complete response to radiation or chemoradiation therapy and choose to be followed up with expectant observation should be made aware of the risks in this setting

Treatment of Regional Cervical Nodes (cont'd)

- Clinically Involved Cervical Nodes
 - When treated with surgery for the primary lesion, neck dissection is recommended
 - Adjuvant concurrent chemoradiation therapy is indicated if there are poor-risk features

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

- Patients with tumor penetration through cartilage into soft tissues are considered poor candidates for a larynx-preservation approach. Total laryngectomy is usually recommended in these cases.
- Patients should be encouraged to abstain from smoking following the diagnosis and throughout treatment due to negative outcomes associated with continued cigarette smoking following radiation therapy.

Increase the Likelihood of Successful Larynx Preservation (cont'd)

- Selection of therapy for an individual patient requires:
 - Assessment by multidisciplinary team
 - Consideration of patient comorbidity, psychosocial situation and preferences
 - Availability of local therapeutic expertise

Increase the Likelihood of Successful Larynx Preservation (cont'd)

- Factors Associated with Decreased Larynx-Preservation Outcomes:
 - Male gender
 - Anemia (at start of treatment)
 - Smoking
 - Advanced T stage
 - Clinically detectable impaired vocal cord mobility
 - Subglottic extension
 - Involvement of anterior commissure
 - Large tumor volume
 - Invasion of specific anatomic sites (determined by CT or MRI)

Summary

Type of Cancer	Recommended Treatment	Other Option
T1 Cancer (Glottis)	Endoscopic Resection (selected patients) <u>OR</u> Radiation Therapy	Open organ-preservation surgery
T2 Cancer (Glottis, favorable) [Superior tumor on radiographic imaging, with normal cord mobility]	Open organ-preservation surgery <u>OR</u> Radiation Therapy	Endoscopic resection (selected patients)
T2 Cancer (Glottis, unfavorable) [Deeply invasive tumor on radiographic imaging, with or without subglottic extension, with impaired cord mobility (indicating deeper invasion)]	Open organ-preservation surgery <u>OR</u> Concurrent chemoradiation therapy (selected patients with node-positive disease)	Radiation therapy Endoscopic resection (selected patients)
T1 – T2 Cancer (Supraglottis, favorable) [Superficial invasion on radiographic imaging and preserved cord mobility, and/or a tumor of the aryepiglottic fold with minimal involvement of the medial wall of the pyriform sinus]	Open organ-preservation surgery <u>OR</u> Radiation Therapy	Endoscopic resection (selected patients)
T2 Cancer (Supraglottis, unfavorable) [More locally advanced and invasive]	Open organ-preservation surgery <u>OR</u> Concurrent chemoradiation therapy (selected patients with node-positive disease)	Radiation therapy Endoscopic resection (selected patients)
T3 – T4 Cancers (Glottis or Supraglottis)	Concurrent chemoradiation therapy <u>OR</u> Open organ-preservation surgery (in highly selected patients)	Radiation therapy

☞ This summary table is provided to assist in summarizing the guideline slide set. There are additional recommendations not presented in this table. For a complete review of the guideline specifications, please refer to previous slides in this show or the larynx-preservation guideline directly.

Conclusions

- Larynx-preservation therapy is intended to offer improved function and quality of life for patients with laryngeal cancer, without compromising survival.
- All patients with T1 – T2 laryngeal cancer (with rare exception) should be treated initially with intent to preserve the larynx.
- Patients with T3 or T4 disease (in the absence of tumor penetration through cartilage into soft tissues) should be offered a larynx-preservation treatment option. Concurrent chemoradiation therapy is the most widely applicable approach.
- Selection of treatment for laryngeal cancer should always depend on patient factors, local expertise, and the availability of appropriate support and rehabilitative services.
- Organ-preservation treatments can be difficult to administer, given that many patients have underlying medical comorbidity.

Conclusions (cont'd)

- When treatments yield similar survival endpoints, other outcomes, such as function, quality of life, and cost, become increasingly relevant.
- Preservation of the laryngeal structure is not considered a functional success if persistent dysphagia, aspiration, or chronic tracheostomy results from organ preserving therapy.
- A multidisciplinary team with specialized expertise is necessary to ensure optimal outcomes. The team should fully discuss with the patient the advantages and disadvantages of the larynx-preservation options compared with treatments that include total laryngectomy.

Additional ASCO Resources

- The full text of the 2006 larynx-preservation guideline, this slide set, and additional ASCO resources are available at:
<http://www.asco.org/guidelines/larynx>
- A patient guide is available at
<http://www.cancer.net>

ASCO Guidelines

It is important to realize that many management questions have not been comprehensively addressed in randomized trials and guidelines cannot always account for individual variation among patients. A guideline is not intended to supplant physician judgment with respect to particular patients or special clinical situations and cannot be considered inclusive of all proper methods of care or exclusive of other treatments reasonably directed at obtaining the same results. Accordingly, ASCO considers adherence to this guideline to be voluntary, with the ultimate determination regarding its application to be made by the physician in light of each patient's individual circumstances. In addition, the guideline describes administration of therapies in clinical practice; it cannot be assumed to apply to interventions performed in the context of clinical trials, given that clinical studies are designed to test innovative and novel therapies in a disease and setting for which better therapy is needed. Because guideline development involves a review and synthesis of the latest literature, a practice guideline also serves to identify important questions for further research and those settings in which investigational therapy should be considered.