

Clinical and Imaging Assessment, Staging and Decision Making in Laryngeal Cancers

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Abstract

Cancer of the larynx has numerous implications—respiration, swallowing and speech, besides disability, vocational, recreational, etc. There are numerous treatment options which have been proven to be effective with randomized controlled trials and meta-analysis'. Often, the choice of modality offered to the patient is tailored to the patient's requirements as regard to his/her domestic, vocational and recreational environment. Although we may have a plethora of options for patients belonging to each stage of the disease, there are certain guidelines which must be adhered to in order to prevent any compromise of oncological safety. This article focuses on the planning of the treatment options based on various assessment modalities.

Keywords: Larynx, cancer, treatment.

INTRODUCTION

The larynx is the most complex of the mucosal lined structures of the upper aerodigestive tract. Its important roles in speech, swallowing, and airway protection make the treatment considerations of cancers of this structure varied and controversial. The larynx is bordered by the oropharynx superiorly, the trachea inferiorly, and the hypopharynx laterally and posteriorly. The larynx is comprised of a cartilaginous frame work, and is subdivided vertically by the vocal cords into the supraglottic, glottic, and subglottic subsites. The supraglottic larynx includes the epiglottis, which has both lingual and laryngeal surfaces, the false vocal cords, the arytenoids cartilages, and the aryepiglottic folds. Anterior to the supraglottis is the pre-epiglottis space. This is a complex space with a rich lymphatic network that contributes to the early and bilateral spread of tumors that arise from supraglottic structures to upper, middle, and lower jugular chain lymph nodes.

The glottic larynx describes the true vocal cords, and where they come together anteriorly at the anterior commissure, as well as where they meet the mobile laryngeal cartilages at the posterior commissure. The glottic larynx extends from the ventricle to 1 cm below the level of the true cords. The vocal cords are lined with stratified squamous epithelia, which contrasts with the pseudo stratified ciliated respiratory mucosa lining the remainder of the larynx. Glottic laryngeal cancers tend to metastasize unilaterally and spread regionally less commonly than supraglottic tumors do. Between the thyroid cartilage and

the vocal cord lies the paraglottic space, which is continuous with the pre-epiglottis space. This serves as a pathway for submucosal spread of tumors from the glottis to the supraglottis, or vice versa, which is known as transglottic spread. The subglottic larynx starts 1 cm below the vocal folds and continues to the inferior aspect of the cricoid cartilage. While it is rare for tumors to arise initially in the subglottis, tumors arising in the supraglottic or glottic larynx commonly spread in a “transglottic” fashion to involve the subglottic larynx. Subglottic tumors tend to metastasize to paratracheal (Level VI) as well as middle or lower jugular lymph (Levels III and IV) node groups.¹

CLINICAL ASSESSMENT

History Taking²

h/o Main symptoms: Progressive continuous hoarseness. Hoarseness is unremitting and may be fluctuating in very early stage of the disease. Sensation of foreign body in the throat can also occur along with cough and irritation of the throat.

h/o Etiology: H/O tobacco and/or alcohol in any form.

h/o Complications: Pain is a late feature and referred pain to the ear is an ominous sign s/o cartilage invasion. Dyspnoea and stridor indicates obstruction of the airway and usually indicates advanced disease. Rarely patients present with hemoptysis when bleeding occurs from the epiglottis and in late cases symptoms of fetor and/or anorexia may be apparent.

H/o Associated Pathologies: Dysphagia indicates involvement of pharynx and may be a presenting feature of transglottic disease with extension into the pyriform sinus through the paraglottic space

H/o Treatment Taken: History of any treatment taken for the present disease or in the past for any malignant lesion of the upper aerodigestive tract should be noted.

Specific Clinical Examination before Definitive Treatment²

All patients require a general ENT examination with particular attention focussed on the examination of the larynx. It is important to examine and assess the mobility of larynx. Movements of the vocal cords, the arytenoids joints and the whole hemilarynx should be assessed. The mobility of the medial visceral compartment of the neck upon the prevertebral fascia should be assessed along with the presence of laryngeal crepitus. Examination of the neck should be performed for palpable lymphadenopathy and particular attention should be to the first echelon nodal draining areas in levels II, III and IV. In addition, direct extension of tumor should be felt for extending through or posterior to the thyroid cartilage, or in the subglottic area into the thyroid gland.

ENDOSCOPIC EVALUATION³

- Indirect laryngoscopy/Hopkins telescopic/flexible laryngoscopy: To assess cord mobility and the extent of mucosal disease. Any focal abnormality seen should be drawn in the notes.
- Direct laryngoscopy: To define the exact extent of the disease, assess areas not well seen on IDL/Hopkins namely anterior commissure; pyriform fossa and post-cricoid and obtain a biopsy.
- Microlaryngoscopy: For early cord lesions and also to obtain a biopsy.

RADIOLOGIC INVESTIGATIONS³

- Barium swallow: To map the mucosal extent of disease. Postcricoid involvement well seen.
- Imaging CT/MRI scan: Mandatory before conservative laryngectomy/laryngeal preservation therapy. Gives information regarding:
 1. Extent of disease
 2. Cartilage invasion

3. Extralaryngeal spread
4. Para/Pre-epiglottis spaces
5. Tumor volume
6. Nodal disease
 - CT scan preferred for cartilage erosion.
 - MRI preferred for soft tissue invasion.

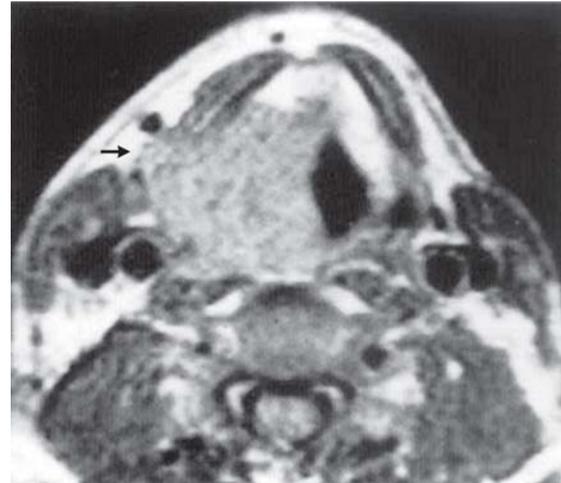


Fig. 1: Carcinoma of the larynx eroding the thyroid cartilage and of the cord results from neoplastic infiltration or from paralysis of extending into the soft tissue of the neck shown on an axial T section⁴

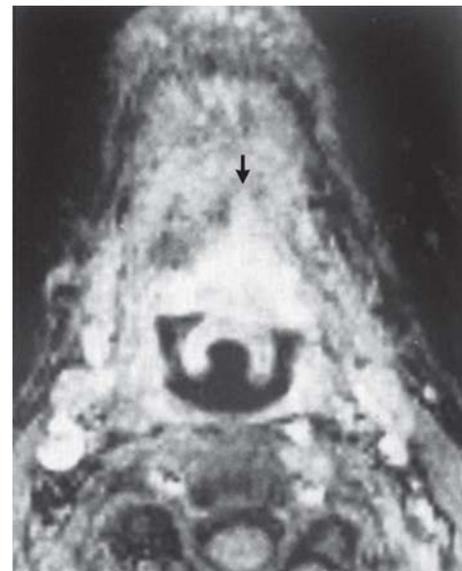


Fig. 2: A gradient-echo FLASH section with gadolinium enhancement showing extension of a laryngeal carcinoma into the base of the tongue⁴

- PET (CT) for evaluating post treatment residual or recurrent disease.
- Speech counseling.

AJCC STAGING OF CARCINOMA OF THE LARYNX¹

Site	Subsites
Supraglottis	Suprahyoid epiglottis
	Infrahyoid epiglottis
	Aryepiglottic folds (laryngeal aspect)
	Arytenoids
Glottis	Ventricular bands (false cords)
	True vocal cords, including anterior and posterior commissures, including the region 1 cm below the plane of the true vocal folds
	Subglottis
Subglottis	Region extending from 1 cm below the true vocal folds to the cervical trachea

Primary Tumor (T)

TX	Primary tumor cannot be assessed.
T0	There is no evidence of primary tumor.
Tis	Carcinoma is <i>in situ</i>

Supraglottis

- T1 Tumor is limited to one subsite of the supraglottis with normal vocal cord mobility.
- T2 Tumor invades mucosa of more than one adjacent subsite of the supraglottis or glottis or region outside the supraglottis (e.g. mucosa of base of tongue, vallecula, medial wall of pyriform sinus), without fixation of the larynx.
- T3 Tumor is limited to the larynx with vocal cord fixation and/or invades any of the following: postcricoid area, pre-epiglottic tissues, paraglottic space, and/or minor thyroid cartilage erosion (e.g. inner cortex).
- T4a Tumor invades through the thyroid cartilage and/or invades tissues beyond the larynx (e.g. trachea, soft tissues of neck, including deep extrinsic muscle of the tongue, strap muscles, thyroid, or esophagus).
- T4b Tumor invades prevertebral space, encases the carotid artery, or invades mediastinal structures.

Glottis

- T1 Tumor is limited to the vocal cords(s) (may involve anterior or posterior commissure), with normal mobility.
- T1a Tumor is limited to one vocal cord.
- T1b Tumor involves both vocal cords.

- T2 Tumor extends to the supraglottis and/or subglottis, and/or with impaired vocal cord mobility.
- T3 Tumor is limited to the larynx with vocal cord fixation and/or invades paraglottic space, and/or minor thyroid cartilage erosion (e.g. inner cortex).
- T4a Tumor invades through the thyroid cartilage and/or invades tissues beyond the larynx (e.g. trachea, soft tissues of the neck, including deep extrinsic muscle of the tongue, strap muscles, thyroid, or esophagus).
- T4b Tumor invades prevertebral space, encases the carotid artery, or invades mediastinal structures.

Subglottis

- T1 Tumor is limited to the subglottis.
- T2 Tumor extends to the vocal cord(s), with normal or impaired mobility.
- T3 Tumor is limited to the larynx with vocal cord fixation.
- T4a Tumor invades cricoid or thyroid cartilage and/or invades tissues beyond the larynx (e.g. trachea, soft tissues of neck, including deep extrinsic muscles of the tongue, strap muscles thyroid, or esophagus).
- T4b Tumor invades prevertebral space, encases the carotid artery, or invades mediastinal structures.

Neck

- N0 No regional lymph node metastasis
- N1 Ipsilateral lymph node metastasis ≤ 3 cm
- N2 Lymph node metastasis in a single ipsilateral lymph node > 3 cm and ≤ 6 cm, or in multiple lymph nodes none more than 6 cm (including bilateral nodal metastasis)
- N2A Lymph node metastasis in single ipsilateral lymph node > 3 cm and ≤ 6 cm
- N2B Lymph node metastasis in multiple ipsilateral lymph nodes all ≤ 6 cm
- N2C Lymph node metastasis in bilateral or contralateral lymph nodes all ≤ 6 cm
- N3 Lymph node metastasis > 6 cm

FACTORS AFFECTING THE CHOICE OF TREATMENT FOR EARLY GLOTTIC CANCERS⁵

Tumor Factors

- Mobility of vocal cord
- Anterior commissure involvement

- Depth of cord invasion
- Extent of tumor involvement of cord
- Proximity of supraglottic cancer to commissure
- Differentiation of tumor
- Exophytic vs. Endophytic

Patient Factors

- Patient wishes
- Medical condition
- Occupation
- Distance from treatment facilities
- Mental status of patient

Health Care Factors

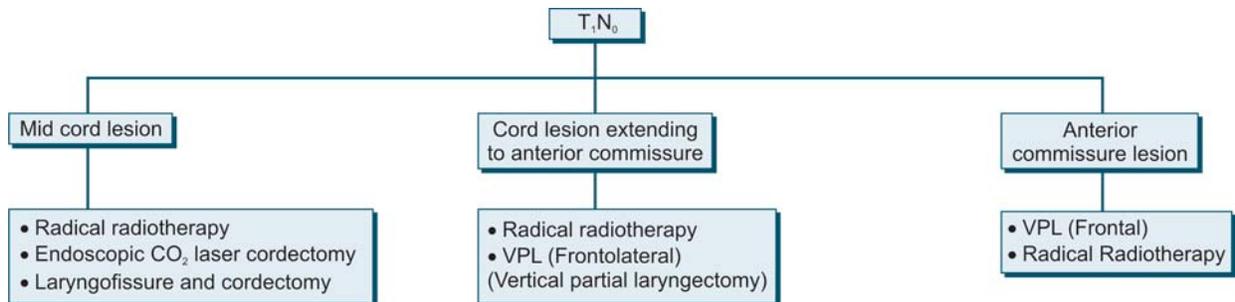
- Team approach to treatment
- Skills of surgeon and radiation oncologist
- Modern radiation facilities
- Availability of support services

Early larynx lesion		
RT	vs	Surgery
• Anosmia		• None
• Xerostomia		• None
• Dysphagia		• None
• Loss of taste		• None
• Prolonged treatment		• Short treatment
• Good voice		• Hoarse voice

The following self-explanatory flow diagram shows the management protocols:³

GLOTTIS

Aim of treatment: To maximize cure and to preserve voice



Radical radiotherapy: Small, localized fields covering only the larynx with margins, after appropriate immobilization and planning. Dose: 55Gy/16ft/3weeks or 60gy/24ft/5week

Note:

- Control rates: Radiotherapy = Endoscopic laser surgery = VPL
- Voice quality: Radiotherapy > Endoscopic laser surgery > PVL
- Surgery preferred in: Young patient, verrucous lesion when quality of voice is not a major factor
- Nodes need not be addressed as incidence of metastasis is very low.

VERTICAL PARTIAL LARYNGECTOMY⁵

Advanced Glottic Cancers³

Stage III – T1-2 N1/T3N0-1

- Concomitant CT + RT
- Surgery: Vertical Partial Laryngectomy/Near-Total laryngectomy/Total laryngectomy + RT
- Radical radiotherapy in patients with low GC/poor performance status who might not tolerate CT+RT

Stage IV – T4a N0-1/ T1-4aN2-3

- Surgery: Near-Total laryngectomy/Total laryngectomy + RT
- Concomitant CT+RT
- Radical radiotherapy in patients with low GC/poor performance status who might not tolerate CT+RT

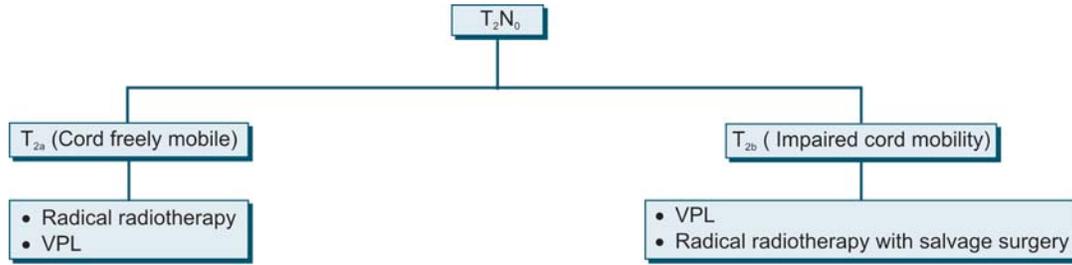
NECK NODES

N0-1 nodes are managed with RT if the primary is treated with RT. If surgery is the primary treatment, modified neck dissection for N1 nodes is recommended.

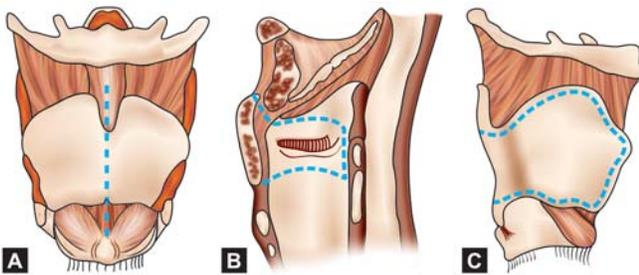
Elective Neck Dissection⁶

Elective treatment of cervical lymph node metastasis is generally recommended when the risk of occult disease is around 15 to 20 percent. Candela and colleagues demonstrated that the nodal groups at risk from laryngeal cancer are at levels II, III and IV.⁵Level I was rarely involved in isolation and level V was never involved alone. This tends to support the removal of levels II, III and IV, the so-called jugular node dissection or lateral neck dissection.

Contd...



- If radiotherapy is the primary treatment, neck to be treated with RT.
- If surgery is the primary treatment, ipsilateral neck to be sampled.



Figs 3A to C: (A) A midline thyrotomy is used to access the larynx when the anterior commissure is uninvolved by tumor, (B) Cut section of the larynx demonstrating the extent of mucosal resection in a vertical partial laryngectomy, (C) External view showing resection of the thyroid ala

N2-3 nodes need MND/RND with Postoperative chemoradiotherapy. If radiotherapy is the primary treatment, neck dissection follows radiotherapy 4-6 weeks later if

residual nodes persist, or electively irrespective of nodal status.³

EARLY SUPRAGLOTTIC CANCER

Management depends on nodal disease, pulmonary reserve and exact site and extent of the disease as shown in the following flow diagram.³

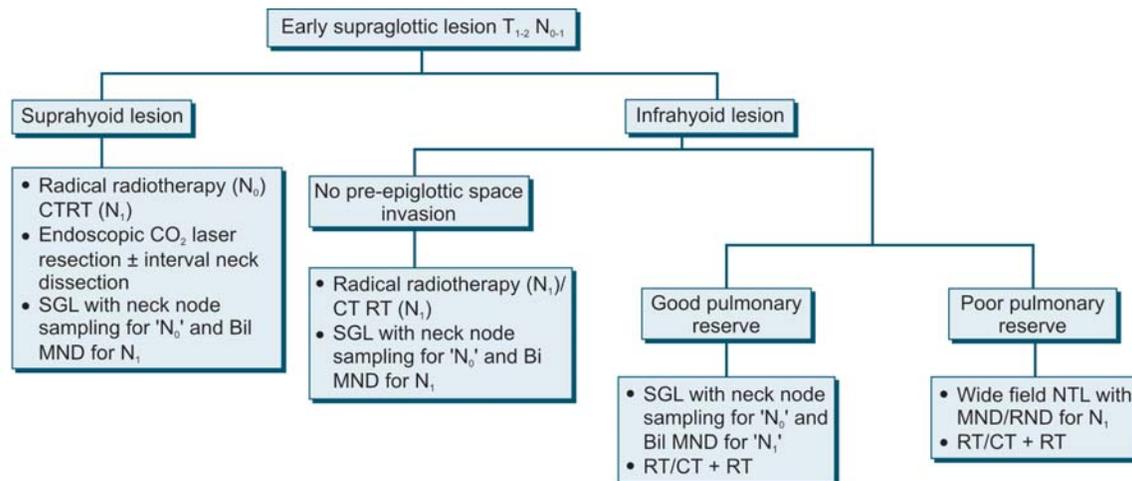
ADVANCED SUPRAGLOTTIC CANCER

SUPRAGLOTTIS

Surgery is preferred over radiotherapy in cases with

- Large volume disease
- Cartilage erosion

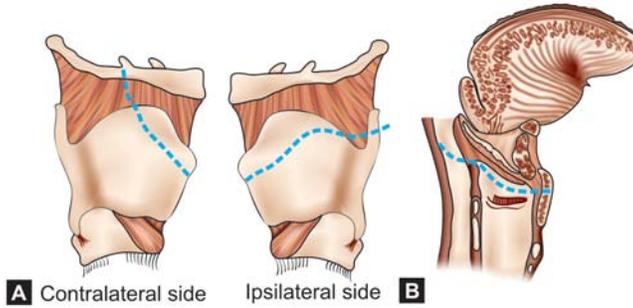
Flow Chart 1



RT = Radiotherapy
CT = Chemotherapy
SGL = Supraglottic laryngectomy

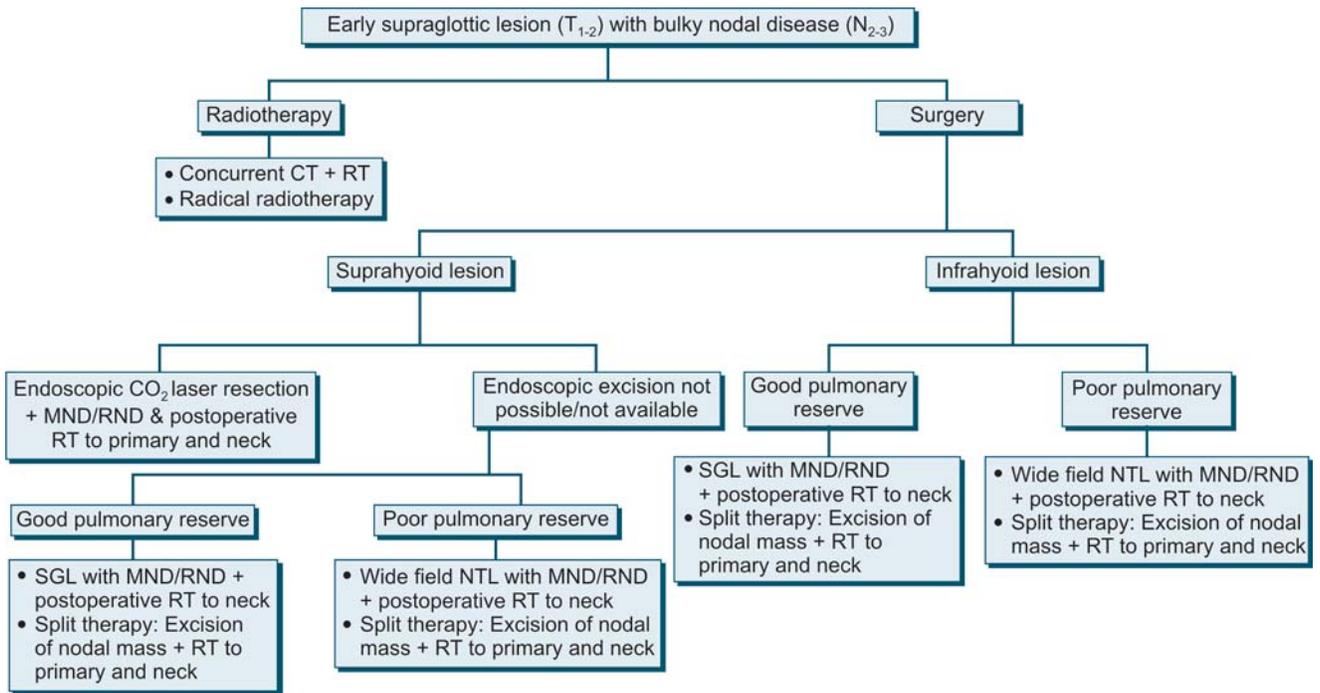
MND = Modified neck dissection
NTL = Near-total laryngectomy

Note: Conservation surgery/Laser preferred in young patient, unwilling to attend 6 weeks of RT

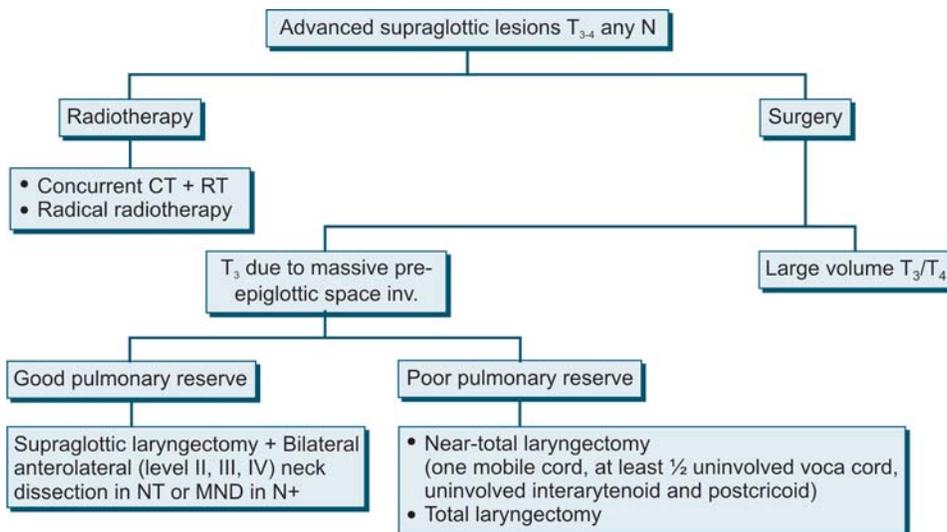


Figs 4A and B: Diagram demonstrating the extent of resection during supraglottic partial laryngectomy⁵

Flow Chart 2



Flow Chart 3



- Bulky nodal disease
- Gross pre epiglottis space involvement
- General condition not permitting concurrent chemoradiotherapy

Management of Neck Nodes

N0

Bilateral neck nodes need to be addressed either with surgery lateral neck dissection (II-IV) or RT.

N1

Bilateral Comprehensive/anterolateral neck dissection (II-IV) + Postoperative RT.

N2-3

Bilateral MND/RND (on side of greater disease) + Post-operative RT.

Small primary (radiocurable T1-2) with large resectable disease (N2-3) may be considered for neck dissection with RT to primary and neck.

SUBGLOTTIS

The treatment of subglottis is same as for the other subsites and depends on the stage. Thus, early stage I and II are treated with single modality radiotherapy, whereas advanced stage III and IV are treated initially by surgery and then followed by radiotherapy.

Indications for Postoperative Radiotherapy

Primary

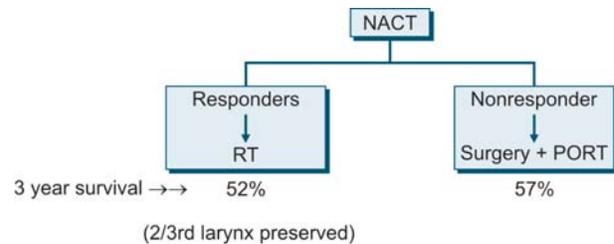
- Large primary – T3 or T4
- Close or positive margins of excision
- Deep infiltrative tumor
- High grade tumor
- Lymphovascular and perineural invasion

Lymph Nodes

- Bulky nodal disease N2/N3
- Extra nodal extension
- Multiple level involvement.

EVOLUTION OF CHEMORADIO THERAPY AND ORGAN PRESERVATION PROTOCOLS

After the discovery of cisplatin in 1970s, the entire decade of 80s tried for various chemotherapy regimens in Head and neck cancer. The VA study⁸ published in 1991 was the first



to suggest that chemotherapy (CT) given as Neoadjuvant (NACT) was helpful in making larynx preservation possible without compromising the survival. The following is the study design of the VA trial:

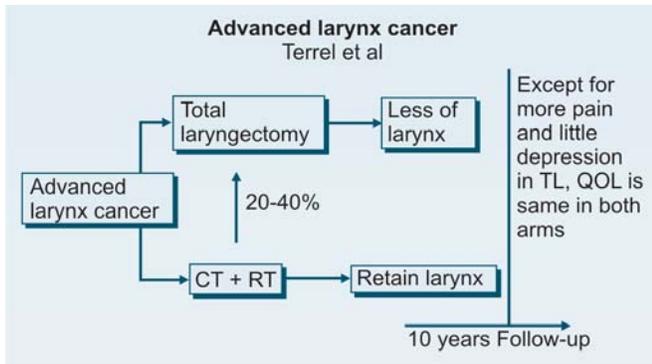
The study confirmed that a treatment strategy involving induction chemotherapy and definitive radiation therapy can be effective in preserving the larynx in a high percentage of patients, without compromising overall survival.⁸

The MACH-NC meta analysis proved that there was no significant benefit associated with adjuvant or neoadjuvant chemotherapy. Chemotherapy given concomitantly to radiotherapy gave significant benefits, but heterogeneity of the results prohibits firm conclusions.⁹ So, RTOG initiated a study to test this hypothesis and the RTOG91-11 randomized control trial was published in 2003 which proved that in patients with laryngeal cancer, radiotherapy with concurrent administration of cisplatin is superior to induction chemotherapy followed by radiotherapy or radiotherapy alone for laryngeal preservation and loco regional control.¹⁰ Hence, the standard organ preservation protocols in the year 2010 employs concomitant chemoradiotherapy over sequential chemoradiotherapy.

REHABILITATION AND QUALITY OF LIFE ISSUES

Recently, Lazarus retrospectively studied patients being treated with chemotherapy and radiation therapy and found that 40 percent had swallowing difficulties.¹¹ Clinical evidence of disorders in the pharyngeal phase of swallowing has been demonstrated in patients who have undergone chemotherapy and radiation therapy for tumors of the upper aerodigestive tract. Specifically, reduced laryngeal closure, reduced laryngeal elevation and reduced posterior tongue base movement relative to age-matched controls has been documented.¹¹

Certainly, patients who successfully undergo chemo/RT treatments to preserve their larynx have a much improved



quality of life relative to patients requiring total laryngectomy.¹²

Nevertheless, it should be realized that anatomic preservation does not always result in functional preservation. Very rarely, total laryngectomy is performed in order to restore the ability to swallow when a larynx is incompetent and non functional but clinically free of cancer. When the patients treated in the Veterans Affairs Laryngeal Cancer Study Group were evaluated, an improved long-term quality of life was seen in the cohort who were randomized to chemotherapy and radiation therapy compared to those treated by surgery and radiation therapy.¹¹

Interestingly, this difference was primarily related to freedom from pain, better emotional well-being and lower levels of depression rather than the preservation of the ability to speak.¹²

Nevertheless, several methods are available to rehabilitate the ability of a patient to communicate following total laryngectomy. Many patients are able to acquire esophageal speech, in which air is swallowed and then used to create a voice. Approximately 2 decades ago a significant advance in the rehabilitation of patients with laryngectomies took place when the tracheoesophageal puncture was developed.¹³

This is a relatively minor procedure where a fistula is created between the trachea and esophagus. A prosthesis with a one way valve is placed into this fistula, which allows the creation of a lung powered voice. In the motivated patient, this voice can be quite good.

FUTURE TRENDS

- Concurrent CT + RT (Cisplatinum based)
- NACT(Taxane based) → Response → CT + RT
- Altered fractionation RT :- Hyperfractionated or Accelerated (alone or in combination with CT)
- Molecular targeted therapy(cetuximab) combined with RT or CT or both

The above four competing regimes are at this moment trying to prove each other’s superiority. At this moment based on the available evidence in literature only concurrent CT+RT can be recommended over the other 3 treatment regimes. A dedicated multidisciplinary team (like a tumor board) is strongly recommended in all institutes to test and



Fig. 6: Ideal multidisciplinary team

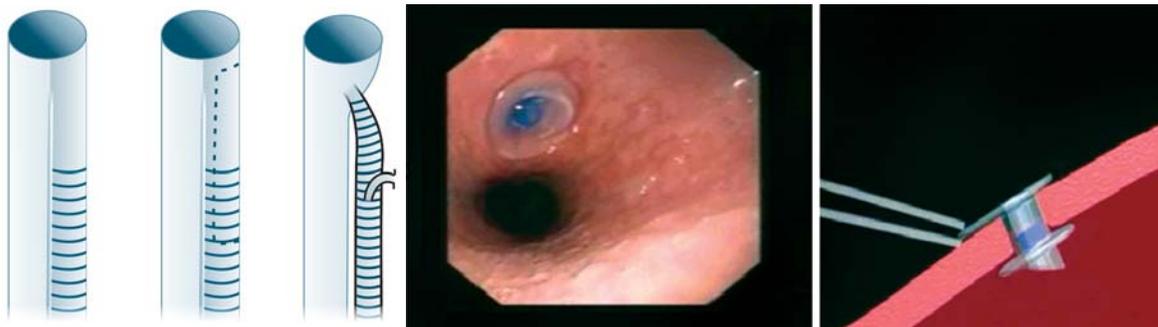


Fig. 5: Tracheoesophageal puncture

prove these new treatment regimens in experimental and clinical settings.

REFERENCES

1. Daniel G. Deschler, Terry Day, in the Pocket Guide to TNM staging of head and neck cancer and neck dissection classification; Published by American Academy of Otolaryngology–Head and Neck Surgery Foundation, Inc. Third Edition 2008
2. John Watkinson, Mark N Gaze, Janet Wilson Chpt 14; in Steel and Maran's head and neck surgery fourth Edition © 2008
3. Evidence Based Management Guidelines for Head and Neck Cancer, Volume IV 2005 Published by Tata Memorial Hospital, 2005.
4. Peter D Phelps. chpt. 47, Pharynx and larynx. In David Sutton's Textbook of Radiology and Imaging
5. William ML, Ydiatt, Daniel DLYdiatt, chpt 9. The larynx in Jatin P Shah and Snehal Patel's American Cancer Society Atlas of Clinical oncology Cancer of the Head and Neck © 2001
6. Candela FC, Shah J, Jaques DP, Shah JP. Patterns of cervical node metastases from squamous carcinoma of the larynx. Arch Otolaryngol Head Neck Surg 1990;116:432-5
7. John F Carew chpt. 8 The larynx in Jatin P Shah and Snehal Patel's American Cancer Society Atlas of Clinical oncology. Cancer of the Head and Neck © 2001.
8. Veterans Affairs Laryngeal Cancer Study Group. NEJM 1991;324:1685-90.
9. Pignon JP. Meta-Analysis of CT on H and N Cancer [MACH-NC]. Lancet 2000;355:949-55.
10. RTOG91-11, Forastier AA, Concurrent CT and RT for organ preservation in advanced laryngeal cancer. NEJM 2003;349:2091-8.
11. Lazarus CL, Logemann JA, Pauloski BR, et al. Swallowing disorders in head and neck cancer patients treated with radiotherapy and adjuvant chemotherapy. Laryngoscope 1996;106(9 Pt 1):1157-66.
12. Terrell JE, Fisher SG, Wolf GT. Long-term quality of life after treatment of laryngeal cancer. The Veterans Affairs Laryngeal Cancer Study Group. Arch Otolaryngol Head Neck Surg 1998;124(9):964-71.
13. Singer MI Blom ED. Tracheoesophageal puncture: A surgical prosthetic method for post laryngectomy speech restoration. Third International Symposium on Plastic Reconstructive Surgery of the Head and Neck, 1979.