

INDIAN COUNCIL OF MEDICAL RESEARCH



CONSENSUS DOCUMENT FOR MANAGEMENT OF LARYNX AND HYPOPHARYNX CANCERS

*Prepared as an outcome of ICMR Subcommittee on
Larynx and Hypopharynx Cancers*



Indian Council of Medical Research
2017

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Indian Council of Medical Research,
Ansari Nagar, New Delhi – 110029
2017

Disclaimer

This consensus document represents the current thinking of experts on the topic based on available evidence. This has been developed by national experts in the field and does not in any way bind a clinician to follow this guideline. One can use an alternate mode of therapy based on discussions with the patient and institution, national or international guidelines. The mention of pharmaceutical drugs for therapy does not constitute endorsement or recommendation for use but will act only as a guidance for clinicians in complex decision –making.

Dr. Soumya Swaminathan
Secretary,
Department of Health Research
and Director General, ICMR

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Dr. Neeraj Tandon : Head (Publication & Information)

Compiled & Edited by : Dr. Tanvir Kaur, Dr. Paul Sebastian

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Foreword

I am glad to write this foreword for Consensus Document for Management of Larynx and Hypopharynx Cancers. The ICMR had constituted sub-committees to prepare consensus document for management of various cancer sites. This document is the result of the hard work of various experts across the country working in the area of oncology.



This consensus document on management of larynx and hypopharynx cancers summarizes the modalities of treatment including the site-specific anti-cancer therapies, supportive and palliative care and molecular markers and research questions. It also interweaves clinical, biochemical and epidemiological studies.

The various subcommittees constituted under Task Force project on Review of Cancer Management Guidelines worked tirelessly in formulating site-specific guidelines. Each member of the subcommittee's contribution towards drafting of these guidelines deserves appreciation and acknowledgement for their dedicated research, experience and effort for successful completion. We hope that this document would provide guidance to practicing doctors and researchers for the management of patients suffering from larynx and hypopharynx cancers and also focusing their research efforts in Indian context.

It is understood that this document represents the current thinking of national experts on subject based on available evidence. Mention of drugs and clinical tests for therapy do not imply endorsement or recommendation for their use, these are examples to guide clinicians in complex decision making. We are confident that this first edition of Consensus Document on Management of Larynx and Hypopharynx Cancers would serve the desired purpose.

(Dr. Soumya Swaminathan)
Secretary, Department of Health Research
and Director-General, ICMR

Message

I take this opportunity to thank Indian Council of Medical Research and all the expert members of the subcommittees for having faith and considering me as chairperson of ICMR Task Force project on guidelines for management of cancer.



The Task Force on management of cancers has been constituted to plan various research projects. Two sub-committees were constituted initially to review the literature on management practices. Subsequently, it was expanded to include more sub-committees to review the literature related to guidelines for management of various sites of cancer. The selected cancer sites are lung, breast, oesophagus, cervix, uterus, stomach, gallbladder, soft tissue sarcoma and osteo-sarcoma, tongue, acute myeloid leukemia, acute lymphoblastic leukemia, CLL, Non Hodgkin's Lymphoma-high grade, Non Hodgkin's Lymphoma-low grade, Hodgkin's Disease, Multiple Myeloma, Myelodysplastic Syndrome and Pediatric Lymphoma. All aspects related to management were considered including, specific anti-cancer treatment, supportive care, palliative care, molecular markers, epidemiological and clinical aspects. The published literature till December 2016 was reviewed while formulating consensus document and accordingly recommendations are made.

Now, that I have spent over a quarter of a century devoting my career to the fight against cancer, I have witnessed how this disease drastically alters the lives of patients and their families. The theme behind designing of the consensus document for management of cancers associated with various sites of body is to encourage all the eminent scientists and clinicians to actively participate in the diagnosis and treatment of cancers and provide educational information and support services to the patients and researchers. The assessment of the public-health importance of the disease has been hampered by the lack of common methods to investigate the overall; worldwide burden. ICMR's National Cancer Registry Programme (NCRP) routinely collects data on cancer incidence, mortality and morbidity in India through its co-ordinating activities across the country since 1982 by Population Based and Hospital Based Cancer Registries and witnessed the rise in cancer cases. Based upon NCRP's three year report of PBCR's (2012-2014) and time trends on Cancer Incidence rates report, the burden of cancer in the country has increased many fold.

In summary, the Consensus Document for management of various cancer sites integrates diagnostic and prognostic criteria with supportive and palliative care that serve our three part mission of clinical service, education and research. Widespread use of the consensus documents will further help us to improve the document in future and thus overall optimizing the outcome of patients. I thank all the eminent faculties and scientists for the excellent work and urge all the practicing oncologists to use the document and give us valuable inputs

(Dr. G.K. Rath)
Chairperson
ICMR Task Force Project

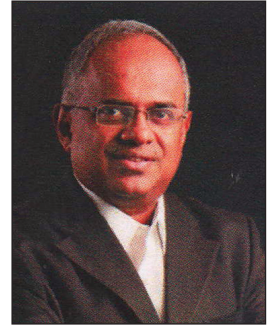
Preface

The past two decades have witnessed a sea-change in the management paradigm of larynx and hypopharynx cancers, notable among which is the establishment of chemotherapy based treatment protocols. This has given way to improved non-surgical laryngeal preservation and Quality of Life (QOF) in those patients who succeed the treatment in terms of survival and preservation of laryngeo-esophageal function.

In this context the initiative of Indian Council of Medical Research (ICMR) to setup a task force to develop a consensus document for management of larynx and hypo-pharynx cancers which would contain evidence based, cost effective practical guidelines that can be implemented in our country should be appreciated.

I thank each and every member of the group who has contributed to the development of this document. I also wish to offer my gratitude to Dr. G.K. Rath and Dr. Tanvir Kaur for their constant encouragement and support.

On the whole it is expected that this document will help multi-disciplinary management teams across the nation involved in the management of laryngeal and hypo-pharyngeal cancers.



(Dr. Paul Sebastian)
Chairman

Sub-committee on Larynx and Hypopharynx Cancer

Preface

Cancer is a leading cause of death worldwide. Globally Cancer of various types effect millions of population and leads to loss of lives. According to the available data through our comprehensive nationwide registries on cancer incidence, prevalence and mortality in India among males cancers of lung, mouth, oesophagus and stomach are leading sites of cancer and among females cancer of breast, cervix are leading sites. Literature on management and treatment of various cancers in west is widely available but data in Indian context is sparse. Cancer of gallbladder and oesophagus followed by cancer of breast marks as leading site in North-Eastern states. Therefore, cancer research and management practices become one of the crucial tasks of importance for effective management and clinical care for patient in any country. Hence, the need to develop a nationwide consensus for clinical management and treatment for various cancers was felt.



The consensus document is based on review of available evidence about effective management and treatment of cancers in Indian setting by an expert multidisciplinary team of oncologists whose endless efforts, comments, reviews and discussions helped in shaping this document to its current form. This document also represents as first leading step towards development of guidelines for various other cancer specific sites in future ahead. Development of these guidelines will ensure significant contribution in successful management and treatment of cancer and best care made available to patients.

I hope this document would help practicing doctors, clinicians, researchers and patients in complex decision making process in management of the disease. However, constant revision of the document forms another crucial task in future. With this, I would like to acknowledge the valuable contributions of all members of the Expert Committee in formulating, drafting and finalizing these national comprehensive guidelines which would bring uniformity in management and treatment of disease across the length and breadth of our country.



(Dr. R.S. Dhaliwal)
Head, NCD Division

Acknowledgement

The Consensus Document on Management of Cancer is a concerted outcome of effort made by experts of varied disciplines of oncology across the nation. The Indian Council of Medical Research has constituted various sub committees to formulate the document for management of different cancer sites. The Task Force on Management of Cancers has been constituted to formulate the guidelines for management of cancer sites. The sub-committees were constituted to review the literature related to management and treatment practices being adopted nationally and internationally of different cancer sites. Besides larynx and hypopharynx, the selected cancer sites are that of lung, breast, oesophagus, cervix, uterus, stomach, gall bladder, soft tissue sarcoma and osteo-sarcoma, tongue, acute myeloid leukaemia, ALL, CLL, NHL-high grade, NHL-low grade, HD, MM, MDS, and paediatric lymphoma. All aspects related to treatment were considered including, specific anti-cancer treatment, supportive care, palliative care, molecular markers, epidemiological and clinical aspects.



This document represents a joint effort of large number of individuals and it is my pleasure to acknowledge the dedication and determination of each member who worked tirelessly in completion of the document.

I would like to take this opportunity to thank Dr. GK Rath, chairperson, ICMR Task Force on Guidelines for Management of Cancer for his constant guidance and review in drafting the consensus document. The chairperson of subcommittee is specially acknowledged in getting the members together, organizing the meetings and drafting the document.

I would like to express gratitude to Dr. Soumya Swaminathan, Secretary, Department of Health Research and Director General, Indian Council of Medical Research, for taking her special interest and understanding the need of formulating the guidelines which are expected to benefit the cancer patients.

I would like to acknowledge here the initiative undertaken with the able guidance of Dr. Bela Shah. I would like to thank Dr. RS Dhaliwal for his support and coordination in finalizing this document. I would like to acknowledge the assistance provided by administrative staff. This document is the result of the deliberations by subcommittees constituted for this purpose. The guidelines were further ratified by circulation to extended group of researchers and practitioners drawn from all over the country. It is hoped that these guidelines will help the practicing doctors to treat cancer patients effectively and thus help them to lead a normal and healthy life.

The ICMR appreciatively acknowledges the valuable contribution of the members for extending their support in formulating these guidelines. The data inputs provided by National Cancer Registry Programme are gratefully acknowledged.

(Dr. Tanvir Kaur)
Program Officer & Coordinator

Members of the Sub-Committee

Chairman

Dr.Paul Sebastian
Director,
Regional Cancer Centre
Thiruvananthapuram-695011

Members

Dr. G.K. Rath, Head, National Cancer Institute
& Chief,
Dr.B.R.A.Institute of Rotary Cancer Hospital
All India Institute of Medical Sciences
New Delhi

Prof. Sushmita Ghoshal
Department of Radiotherapy
Post Graduate Institute of Medical Education &
Research
Chandigarh

Dr. Moni Abhraham Kuriakose
Professor & Director
Surgical Oncological Services
Mazumdar Shaw Cancer Institute
Narayana Hrudayalaya
Bangalore

Dr. Kumar Prabhash
Professor,
Medical Oncology
Tata Memorial Hospital
Mumbai

Dr.Alok Thakkar, Professor
Department of Otolaryngology & Head & Neck
Surgery
AIIMS, New Delhi

Dr. Cessal Thomachan Kainickal
Associate Professor, Radiation Oncology
Regional Cancer Centre
Thiruvananthapuram

Dr. Vishal Rao U.S
Surgical Oncologist - Head & Neck
Health Care Global (HCG),Bangalore

Dr. Kuddush Ahmed
Head & Neck Oncologist
Dispur Oncology Centre
Dispur Hospitals, Ganeshguri
Guwahati

Dr. Subharamanium Iyer
Professor & Head
Division of Reconstructive Surgery & Head &
Neck Institute
Amrita Institute of Medical Sciences,
Kochi

Dr. Prathamesh Pai
Professor
Department of Head Neck Surgical oncology
Tata memorial Hospital
Mumbai

Dr. K. Ramadas
Professor
Department of Radiotherapy
& Medical Superintendent
Regional Cancer Centre
Medical College,
Thiruvananthapuram

Dr. Ashok M.Shenoy
Professor & Head
Department of Head Neck Oncology Surgery,
Kidwai Memorial Institute of Oncology,
Bangalore

Dr. Bipin Thomas Varghese (Convenor)
Additional Professor
Division of Surgical Oncology
(Head & Neck services)
Regional Cancer Centre
Thiruvananthapuram

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1. Introduction

Laryngeal cancer is the second most common Head and Neck Cancer with >1,59,000 new cases and 90,000 cancer deaths world wide and it forms 2% of all cancers. Laryngeal cancers are more common (9:1) among men with a higher incidence in South Asia. Conservative surgery or radiotherapy (RT) offers equal cure rates in its early stage although radiation therapy (RT) is more popular worldwide. For intermediate and advanced staged tumors, total laryngectomy with post operative RT was the standard of care until the Veterans Administration Larynx Study in 1991 and other subsequent organ preservation trials which established the role of combination of chemotherapy with radiation in the upfront treatment of locally advanced laryngeal cancers (stage III and early IV a). Hypopharyngeal cancers although managed in the same lines, are more aggressive and liable for treatment failure and low survival. The incidence of hypopharyngeal cancers is relatively high in India (approximately 11% against 1% worldwide, among males)¹⁻⁴.

1.1 Epidemiology¹⁻⁴: The age adjusted incidence rates of laryngeal and hypopharyngeal cancers from population based cancers registries (PBCR) in India and the international comparison is as follows. Source: Three Year report of Population Based Cancer Registration (2009-2011), Incidence and Distribution of Cancer 2013, Report of 25 PBCR's in India, Indian Council of Medical Research 2013).

Larynx (ICD_10: C32)

Males: East Khasi Hills District (11.1) had the highest Age adjusted rate (AAR) followed by Aizawl District (9.5) and Kamrup urban District, in Assam (8.2).

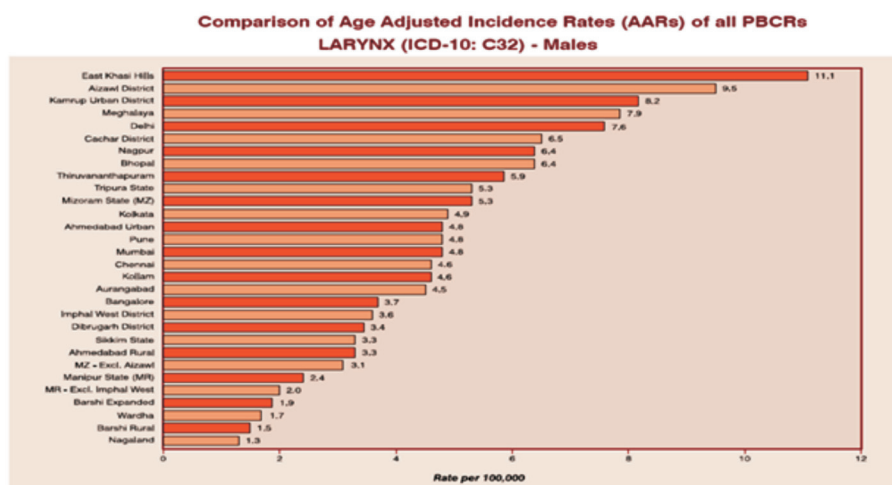


Fig. - 1

International Comparison

Males: Basque Country, Spain was the top with an AAR of 16.1. East Khasi Hills District of Meghalaya had an AAR of 11.1 from India.

GLOBOCAN estimates of world Age standardised incidence rate (ASR) for the year 2008 give the highest AAR of 8.3 per 100,000 for Central and Eastern Europe in males.

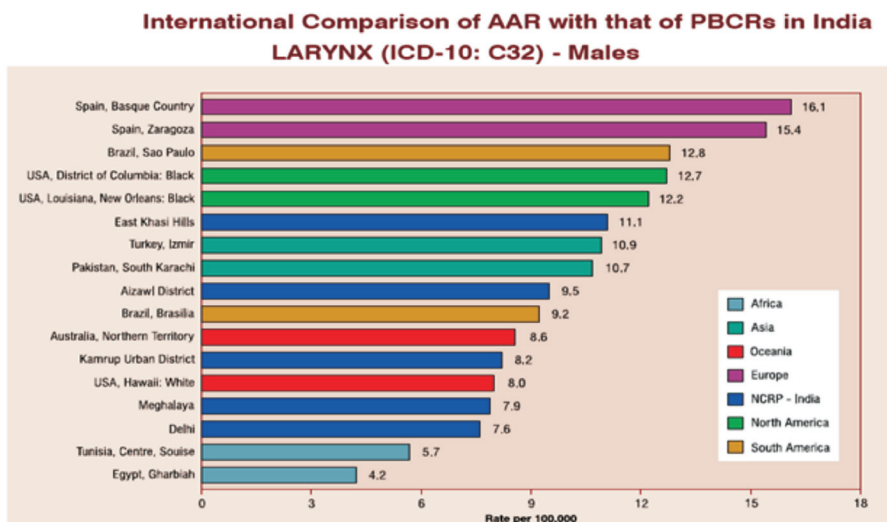


Fig. - 2

Hypopharynx (ICD-10 C12-C13)

Males: The AARs of East Khasi Hills District of Meghalaya (21.5) and the state of Meghalaya as a whole (17.4) were higher followed by Aizawl District (15.4) of Mizoram.

Females: Kamrup Urban District (Assam) showed the highest AAR (3.6) followed by Cachar District (Assam) (2.6).

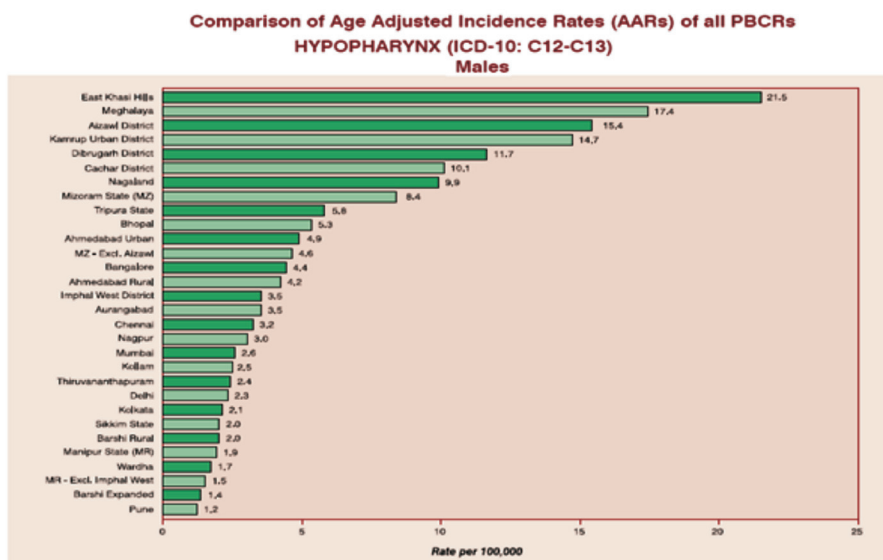


Fig. - 3

**Comparison of Age Adjusted Incidence Rates (AARs) of all PBCRs
HYPOPHARYNX (ICD-10: C12-C13)
Females**

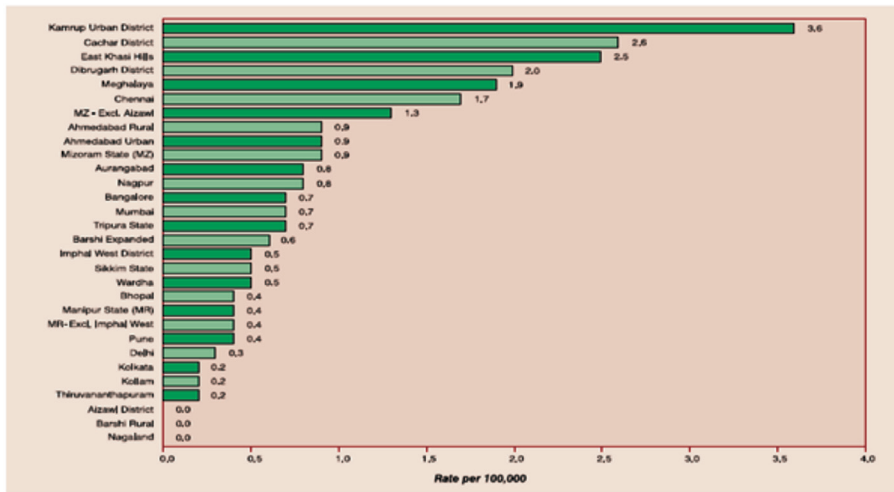


Fig. - 4

International Comparison

Males: East Khasi Hills had the highest AAR (21.5) among all the Indian and International PBCRs. The top five positions were occupied by five Indian PBCR's

Females: Kamrup Urban District (Assam) had the highest AAR (3.6) followed by four more Indian PBCRs among all the Indian and International PBCRs.

**International Comparison of AAR with that of PBCRs in India
HYPOPHARYNX (ICD-10: C12-C13)**

Males

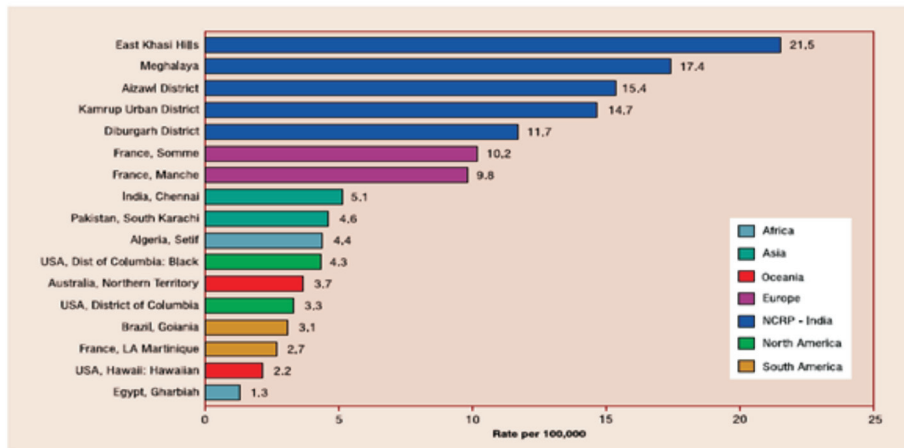


Fig. - 5

**International Comparison of AAR with that of PBCRs in India
HYPOPHARYNX (ICD-10: C12-C13)**

Females

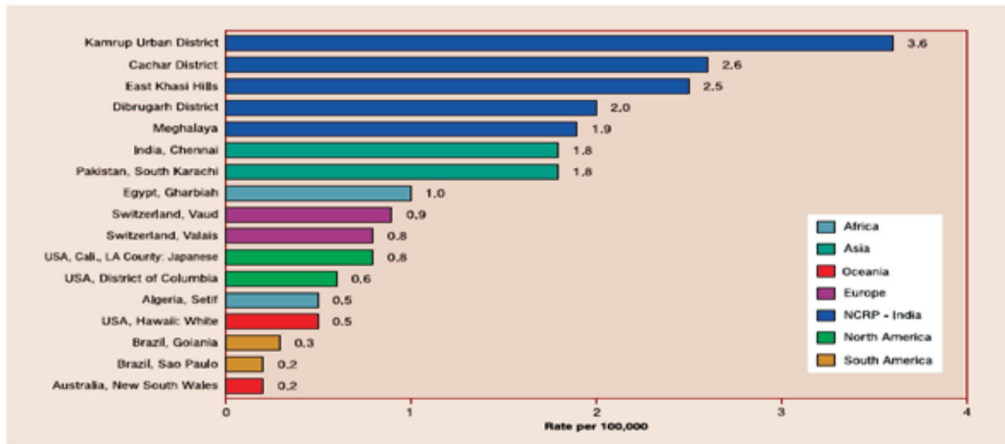


Fig. - 6

2.1 Diagnostic Workup

Larynx is anatomically divided into

1. Supraglottic larynx
2. Glottis
3. Subglottis

Approach to laryngeal Carcinoma⁵⁻⁴⁴

Detailed history should include hoarseness, difficulty in breathing, (stridor), choking spells (aspiration), difficulty in swallowing (dysphagia) or pain while swallowing (odynophagia), foreign body sensation and ear ache. Presence of tracheostomy tube or nasogastric tube needs to be documented. Proper documentation of performance and nutrition status is needed.

Detailed clinical examination of primary and neck should be carried out in addition to a general examination. ENT evaluation includes indirect laryngoscopy (IDL) examination and endoscopic evaluation. Check list for ENT examination are the following

- Primary site
- Nature of growth
- Extension into sub sites of larynx
- Mobility of vocal cord
- Involvement of Anterior commissure
- Extension to Oropharynx
- Extension into Hypopharynx including post cricoid
- Airway evaluation
- Laryngeal crepitus
- Function of larynx

Larynx Function: Points to be noted include

- Tracheostomy for airway obstruction.
- Aspiration requiring hospitalisation up to 6 weeks
- Poor (non-serviceable) Voice
- Dysphagia requiring nasogastric tube insertion / gastrostomy feeding procedures

Table 1. Investigations for laryngeal cancer

Ideal	Essential
<ul style="list-style-type: none"> • X - ray Chest PA view • Complete blood count , Renal function test, Liver function test • Direct laryngoscopy and biopsy • CT Scan of neck* • MRI is useful only in selected patients** • CT Thorax or PET scan is not recommended in the initial evaluation 	<ul style="list-style-type: none"> • X-ray Chest PA • CT Scan* • Blood counts • Endoscopy and biopsy
<p>* CT Scan can be avoided in patients with T1a mid cord lesion without involvement of anterior commissure when radiotherapy is planned.</p> <p>** MRI is more sensitive in determining cartilage involvement but CT Scan is more specific. MRI is better in assessing soft tissue involvement¹⁰</p>	<p>* CT Scan is essential for planning surgical conservation¹⁰⁻¹² and usually high resolution scan with 1 mm slices are required.</p> <p>* CT Scan is advised based on the economic status, stage of the disease, intend of treatment and expertise available</p>

The basic details to be evaluated in the CT scan are the following

- Site of the disease
- Larynx
- Anterior commissure
- Post cricoid region
- Other sub sites of larynx
- Cartilages involvement & extent of involvement
- Thyroid gland
- Carotid artery involvement
- Tumor volume
- Pre-epiglottic space
- Paraglottic space
- Extensions
- Oropharynx or oesophagus
- Extra laryngeal spread
- Pre vertebral fascia involvement
- Lymph Node

2.2 Staging

Table 2 (a, b & c)

Table 2a. **2010 American Joint Committee on Cancer Staging**¹³

PRIMARY TUMOR (T)	
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Tis	Carcinoma <i>in situ</i>
SUPRAGLOTTIS	
T1	Tumor limited to one subsite of supraglottis with normal vocal cord mobility
T2	Tumor invades mucosa of more than one adjacent subsite of supraglottis 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 limited to larynx with vocal cord fixation and/or invades any of the following: postcricoid area, preepiglottic tissues, paraglottic space, and/r 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 muscles of the tongue, strap muscles, thyroid, or esophagus)
T4b	Tumor invades prevertebral space, encases carotid artery, or invades mediastinal structures
GLOTTIS	
T1	Tumor limited to one (T1a) or both (T1b) vocal cord(s) (may involve anterior or posterior commissure) with normal mobility
T2	Tumor extends to supraglottis and/or subglottis, and/or with impaired vocal cord mobility
T3	Tumor 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 neck including deep extrinsic muscles of the tongue, strap muscles, thyroid, or esophagus)
T4b	Tumor invades prevertebral space, encases carotid artery, or invades mediastinal structures
SUBGLOTTIS	
T1	Tumor limited to the subglottis
T2	Tumor extends to vocal cord(s) with normal or impaired mobility
T3	Tumor limited to larynx with vocal cord fixation
T4a	Tumor invades cricoid or thyroid cartilage and/or 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 carotid artery, or invades mediastinal structures

Table 2b

NODAL DISEASE (N)	
NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis in a single ipsilateral lymph node, 3 cm or less in greatest dimension
N2	Metastasis in single ipsilateral lymph node, more than 3 cm but no more than 6 cm in greatest dimension; or in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension; or in bilateral or contralateral lymph nodes, no more than 6 cm in greatest dimension
N2a	Metastasis in single ipsilateral lymph node, more than 3 cm but no more than 6 cm in greatest dimension
N2b	Metastasis in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension
N2c	Metastasis in bilateral or contralateral lymph nodes, none more than 6 cm in greatest dimension
N3	Metastasis in a lymph node more than 6 cm in greatest dimension

Table 2c. Overall Stage Grouping

Stage 0	Tis	N0	M0
Stage I	T1	N0	M0
Stage II	T2	N0	M0
Stage III	T3	N0	M0
	T1-T3	N1	M0
Stage IVA	T4a	N0-N1	M0
	T1-T4a	N2	M0
Stage IVB	Any T	N3	M0
	T4b	Any N	M0
Stage IVC	Any T	Any N	M1

2.3 Treatment

Goals of treatment

Multidisciplinary team for treatment includes radiation oncologist, surgical oncologist, medical oncologist, radiologist, pathologist, speech therapist, nutrition specialist and clinical psychologist

Major goals of treatment of carcinoma larynx are the following

1. To maximize cure
2. Preserve the function of Larynx
3. Preserve the quality of voice
4. Maintain good quality of life
5. Palliation of symptoms in patients with incurable disease

The management is divided into

- A. Management of Early Laryngeal Disease (Stage I, II)
- B. Management of Moderately Advanced Laryngeal disease (Stage III, IVa)
- C. Management of Very Advanced Laryngeal Disease (Stage IVb, IVc)

2.4 Stage-wise treatment

A. Management of early laryngeal disease (Stage I, II)

Intention of treatment is to achieve maximum cure with good quality of voice. The options are based on patient preference and expertise available. Treatment modality is either radiotherapy or surgery. There is no significant difference in outcome between radiotherapy or surgery. Quality of voice is generally better with Radiotherapy.

Treatment options for early laryngeal disease $T_{1-2}N_0$ ⁵⁻⁸

Glottic Carcinoma ($T_{1-2}N_0$)

1. External beam radiotherapy or
2. Transoral laser microsurgery / open partial laryngectomy.

Patients who undergo surgery should have negative margins. Surgery with involved margin followed by post-operative radiotherapy is not an acceptable approach. In early glottis carcinoma (T1, T2N0) disease, there is no need to address the lymph nodes.

Choice is based on expertise available in the Centre

Supraglottic Larynx (T₁₋₂N₀)

1. External beam radiotherapy or
2. Transoral laser microsurgery / open partial laryngectomy.

Proper evaluation of neck should be done in patients who are undergoing surgery, & because of a higher propensity for bilateral lymph node involvement a prophylactic bilateral neck dissection may be needed. Radiotherapy (RT) is generally preferred because laryngeal function can be better preserved and neck nodes can be more easily tackled by this modality.

Subglottis (T₁₋₂N₀)

External beam radiotherapy.

B. Management of moderately advanced laryngeal disease (Stage III, IV)

Management of advanced laryngeal cancer is a therapeutic challenge. Stage III and Stage IV constitute advanced laryngeal cancer. The aim of treatment of Stage III (sometimes referred to as Intermediate stage) and Stage IVa disease is to achieve cure and preserve laryngeal function¹³⁻²⁶. Palliative treatment is generally offered for patients with Stages IVb and IVc.

Treatment option for locally advanced laryngeal cancer

T₁₋₂N₁ (Stage III)

1. Concurrent chemo radiation* (CCRT)
2. Anti Epidermal Growth EGFR monoclonal antibody²⁷⁻²⁹ + RT
3. Radical Radiation (Altered Fractionation)⁹
4. Conservation Surgery + Neck dissection +/- RT or CT+RT (margin positive / Extra Capsular Spread (ECS)).

T₁₋₂N₂ (Stage IVa)

1. Concurrent chemo radiation* (CCRT)
2. Anti EGFR monoclonal antibody + RT
3. Radical RT
4. Conservation Surgery + Neck dissection + RT or CT+RT (margin positive / Extra Capsular Spread (ECS)).

Ideal treatment is concurrent chemoradiation. Proper patient selection is the corner stone of treatment. Patient should have good performance status (0,1) with good renal function. Anti EGFR antibody + RT should be considered only if the patient not fit for chemo RT either by poor performance status or impaired renal function.

T₃N₀₋₁ (Stage III), T₃N₂ (Stage IVa)

There are two treatment options for this group of patients without laryngeal dysfunction.

Organ preservation approach.

Surgery +/- adjuvant radiotherapy RT or Concurrent chemo radiation (CCRT +RT), If margin is positive or perinodal extension).

1. Organ preservation approach

Organ preservation should be considered for all patients who have good laryngeal function and intact laryngeal framework. The treatment options are:

- i. Concurrent chemo radiation (CCRT) is the standard treatment. .

If the patient cannot tolerate concurrent chemoradiation

- ii. Anti EGFR monoclonal antibody with Radical Radiotherapy
- iii. Induction chemotherapy followed by radical radiotherapy- assess the response after chemotherapy¹⁶⁻²⁴
- iv. Radical Radiotherapy by altered fractionation.

2. Surgery +/- Adjuvant radiotherapy based on clinical and histopathological features

- i. Conservation laryngeal surgery in highly selected patients.
- ii. Total Laryngectomy (TL) / near total laryngectomy (NTL) - where adequate margins can be achieved with preservation of atleast one innervated cricoarytenoid joint.

Proper patient selection is of prime importance for concurrent chemoradiation. If patients are not suitable for CCRT surgical options should be offered. Hemilaryngectomy & Transoral laser microsurgery should be done with extreme caution only in those centres with expertise and documented track record of success. NTL ± Neck Dissection (ND) adjuvant RT or CT-RT is a viable alternative in trained hands when the disease is lateralized to one side without interarytenoid involvement. Patients with laryngeal dysfunction are candidates for total laryngectomy followed by post-operative radiotherapy / chemoradiotherapy.

Evaluation after concurrent chemoradiation: Ref Annexure 2

Treatment of T4aN₀₋₂ (Stage IVa)

Moderately Advanced disease with or without cartilage involvement

Standard treatment for T4a disease with cartilage involvement is total laryngectomy³⁷⁻³⁹ and bilateral elective neck dissection (Level II-IV in clinically node negative neck and Level II-V in a clinically node positive neck) and adjuvant therapy. Voice Rehabilitation should be offered to all suitable patients. Voice Rehabilitation: Ref Annexure 3.

If expertise is available, conservation laryngeal surgery (supracricoid laryngectomy with cricohyoidopexy or cricohyoidoepigottopexy) or near total laryngectomy (NTL) with adjuvant radiotherapy may be considered in highly selected group of patients.

Adjuvant therapy in Stage IVa is usually radiotherapy. Adjuvant chemoradiation is indicated in those with margin positive or nodes with extra capsular spread⁴⁰⁻⁴². Good performance status is a prerequisite for adjuvant chemo radiation.

Concurrent chemo RT may be suitable for a patient with good performance status, adequate laryngeal function and a disease that has not penetrated the thyroid cartilage and a patient who refuses surgery. Adjuvant Therapy: Ref Annexure 1

A practical approach^{43,44} for bulky T4a cancers with involvement of adjacent hypopharynx without laryngeal penetration would be a sequential regime where neoadjuvant chemotherapy (Taxane based multidrug therapy) is given and response assessed. If there is more than 50% response the treatment is consolidated with concurrent chemoradiation however if the response is stable disease or progression total laryngectomy should be considered.

C. Management of Very Advanced Laryngeal Cancer (IVb, IVc)

Treatment of T_{4b} or N₃ (Stage IV_b)

In general these patients are treated with palliative intent. Treatment with curative intent may be considered in patients with good performance status. Situations where radical approach is considered in stage IVB disease are

1. T_{1-4a} primary with operable N₃ node in a patient with good performance status. Primary surgery and post operative adjuvant therapy or standard chemo radiotherapy may be considered or neoadjuvant chemotherapy followed by chemoradiation (those with partial response to NACT can be triaged to surgery and adjuvant arm).
2. Selected T4b disease where nodal burden is low. Standard Chemo RT or induction chemo therapy followed by chemoradiation may be considered (sequential regime).

Elective neck dissection may be considered for patients with N₃ disease with operable residual disease after chemo radiation provided primary is in clinical remission.

In the remaining subset of patients with good performance status individualised decisions may be taken from the following options

1. Induction chemotherapy and response assessment followed by chemoradiation (Sequential-chemoradiotherapy in responders without laryngeal cartilage penetration)
2. Total laryngectomy and post operative adjuvant may be an alternative strategy in border line operable cases.

Stage IVC

Patients with stage IV C disease are candidates for palliative treatment. Decision regarding local radiotherapy or systemic treatment is based on the clinical situation.

Summary of Composite staging and treatment options in Laryngeal cancer (Table 3a & b)

	Stage T1	Stage T2	Stage T3	Stage T4a	Stage T4b
N0	I	II	III	IVA	IVB
N1	III	III	III	IVA	IVB
N2	IVA	IVA	IVA	IVA	IVB
N3	IVB	IVB	IVB	IVB	IVB
M1	IVC	IVC	IVC	IVC	IVC
<ul style="list-style-type: none"> ■ Early Disease -RT/Surgery (outcomes are equal) ■ T3 disease -concurrent chemo radiation ■ M1 palliative treatment ■ Stage III- Concurrent Chemo RT 			<ul style="list-style-type: none"> ■ T4a Surgery -- Post op RT (cartilage involvement) ■ T4b Palliative treatment /radical approach in selected cases ■ Stage IVb Radical approach in selected patients 		

Follow up

Objectives of follow up are

1. Detect early recurrences
2. Evaluation and management of morbidity
3. Detection of second primary.

Clinical examination including ENT evaluation is done once in 3 months for the first two years. Once in 4-6 months from third to fifth year. Yearly follow up after 5 years. TSH evaluation should be done after 6 months of radiation and periodically.

Summary

Before embarking on treatment, proper evaluation of performance and nutrition status is very essential. Intention of treatment in early disease is to achieve maximum cure with minimum morbidity. Based on the tumour factors, treatment can be either radiotherapy or conservative laryngeal surgery in early disease. In addition the treatment decision should take into account patients preference expertise available, social support, functional status of the larynx, performance of the patient and the affordability of the patient. Proper clinical evaluation and CT scan of neck are mandatory in deciding treatment options in locally advanced laryngeal cancer. In patients with good performance and normal creatinine clearance, concurrent chemo radiation is the standard of care in stage III and IVa disease without cartilage involvement and with a functional larynx. Patients with cartilage involvement (T4a) should generally be subjected to primary surgery followed by postoperative radiotherapy. Following surgery, Patients with high risk features such as margin positive disease, extra capsular spread should receive post operative chemo radiation. Patients with good performance status with stage IVb disease may be considered for radical approach on an individual basis. Patients with Stage IVc are candidates for palliative approach.

Practical aspects in Ca Larynx

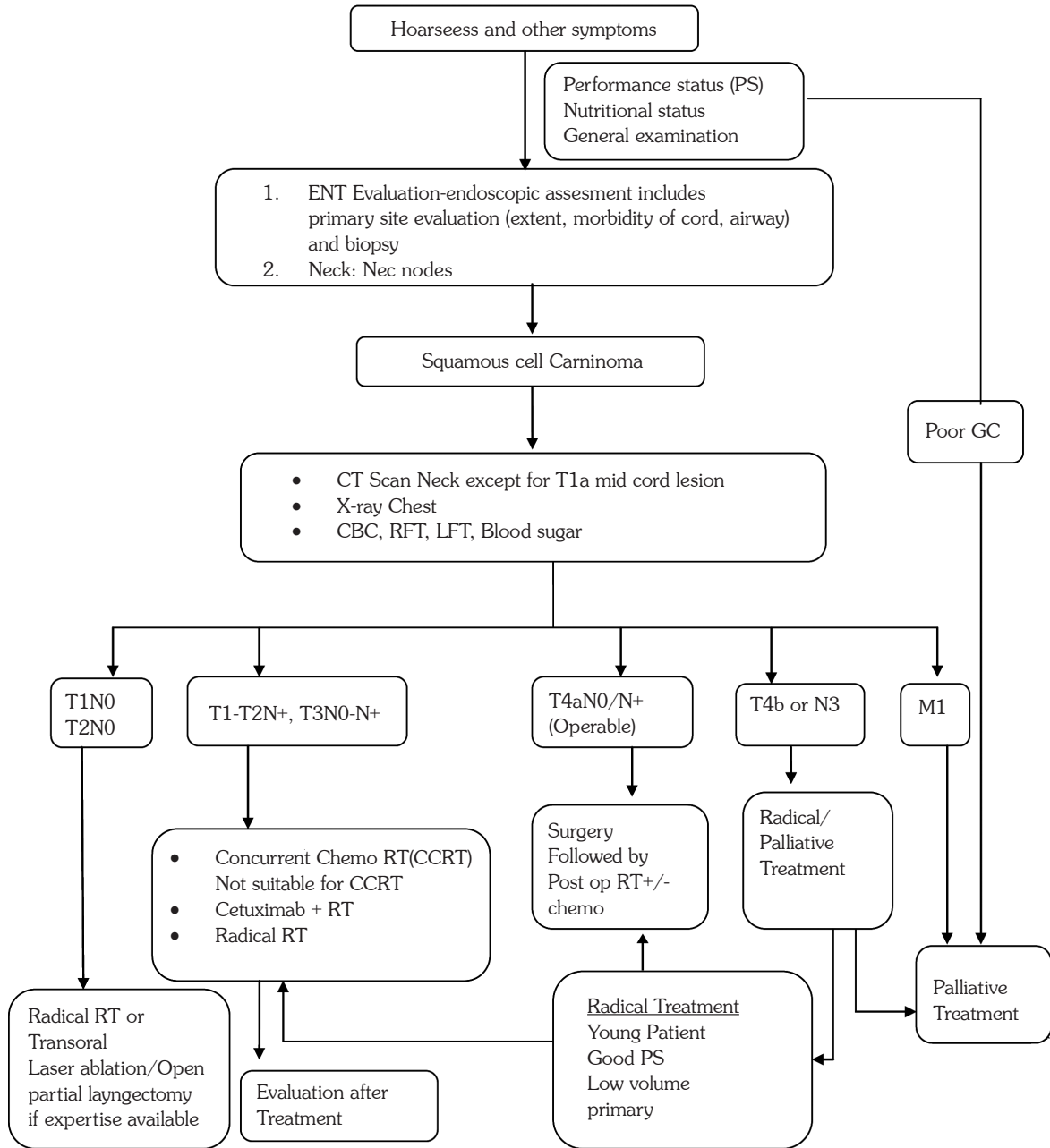
1. Proper Biopsy from the primary site for tissue diagnosis is mandatory
2. Accurate staging is the most important step in the management.

3. Performance status, nutritional assessment, social and family support are key factors in deciding treatment.
4. In T1 or T2 vocal cord, proper attention to be taken to rule out minimal T3 disease and subglottic extension and thyroid cartilage involvement in anterior commissure disease.
5. CT scan is mandatory to rule out T3 and T4 disease.
6. Patients with laryngeal dysfunction are not candidates for organ preservation approaches.
7. Organ preservation approach should be avoided in patients having cartilage destruction.
8. Proper patient selection is needed for concurrent chemoradiation in T3 disease.
9. Organ preservation approach should be considered for all T3 disease with good laryngeal function.
10. Avoid unnecessary biopsy for patients who have laryngeal edema after chemoradiation.
11. Avoid unnecessary investigations and costly chemotherapy in patients who are candidates for palliative approach.
12. Patients should be counselled regarding symptoms and signs of relapse after primary treatment.

Consensus statement on practice

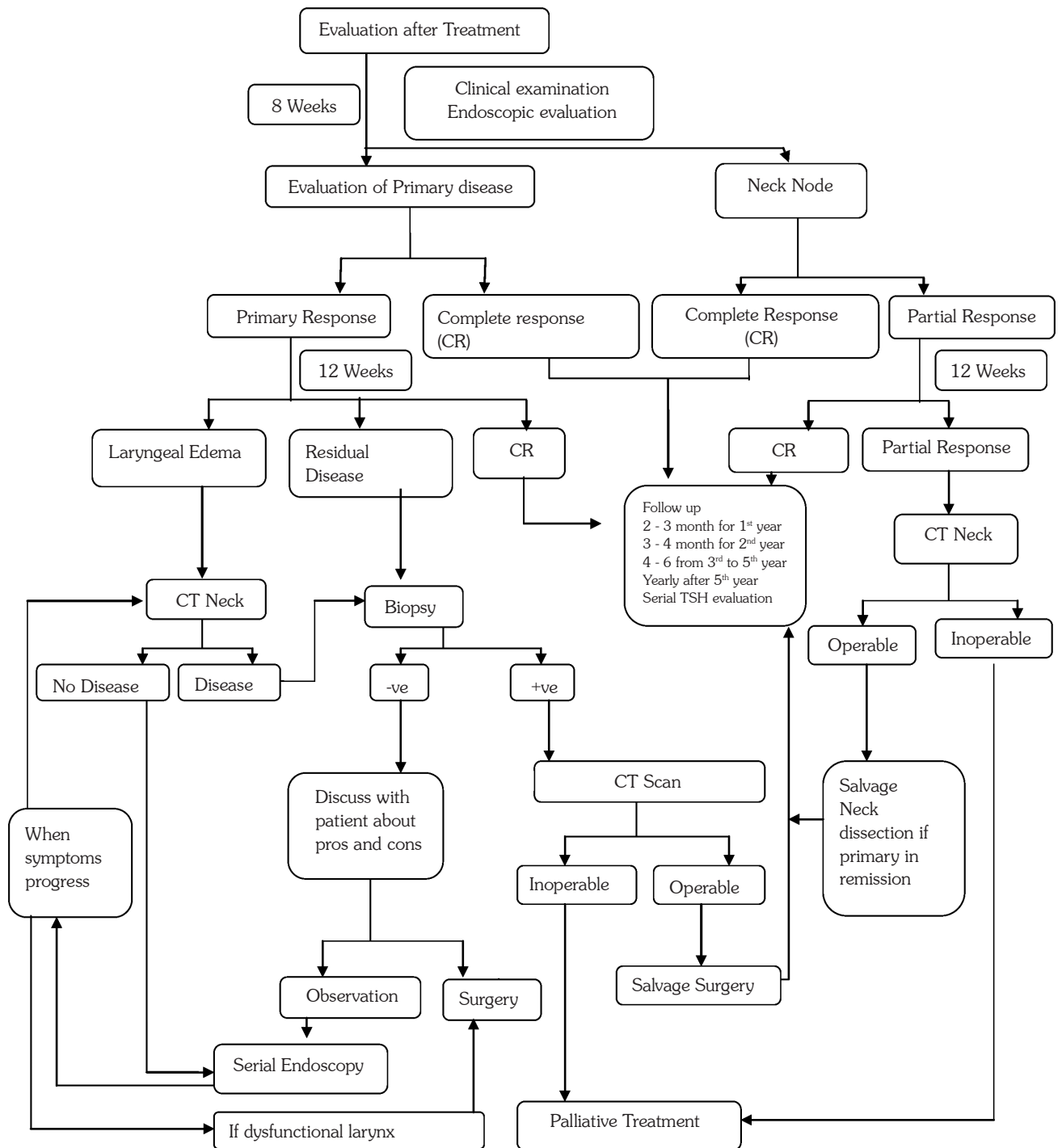
Flow chart 1.

Comprehensive Algorithm for Management of Laryngeal Cancer



Flow chart - 2

Comprehensive Algorithm for follow up of Organ preservation approach in Laryngeal Cancer



3.1 Diagnostic work up

Hypopharynx is divided into

Pyriiform sinus

Post-cricoid region

Posterior pharyngeal wall

Cancer of Larynx and hypopharynx differs in many aspects as depicted in the table below

Table 4. Comparison of laryngeal and hypopharyngeal cancer

	Larynx	Hypopharynx
Symptoms	Early	Late
Nutrition	Good	Poor
Laryngeal preservation	Good	Poor
Nodal involvement	Less	High
Systemic disease	Less common	Increased systemic metastasis
Relapse	Less	More

Approach to a patient with hypopharyngeal cancer

Proper history taking and general examination is important. Documentation of extent of dysphagia, performance and nutritional status assessment is absolutely necessary. Evaluation of primary disease includes indirect laryngoscopy (IDL) and endoscopic evaluation. Neck should be examined for cervical lymph nodes. Detailed clinical examination of primary site and neck should be carried out in addition to a general examination and endoscopic evaluation. Check list for ENT examination are the following

- Primary site
- Nature of growth
- Extension into sub sites of hypopharynx
- Mobility of vocal cord
- Extension to Oropharynx
- Extension into oesophagus

- Airway evaluation
- Laryngeal crepitus
- Function of larynx

Larynx Function: Points to be noted include

- Tracheostomy for airway obstruction.
- Aspiration requiring hospitalisation up to 6 weeks
- Poor (non-serviceable) Voice
- Dysphagia requiring nasogastric tube insertion / gastrostomy feeding procedures

Table 5. Investigations for hypopharyngeal cancer

Ideal	Essential
<ul style="list-style-type: none"> • X -ray Chest PA view • Complete blood count , Renal Function test, Liver function test • Direct laryngoscopy and biopsy • CT Scan of neck • MRI is useful only in selected patients * • CT Thorax or PET scan is not recommended in the initial evaluation ** 	<ul style="list-style-type: none"> • X-ray chest PA • CT Scan^{*56,10-12} • Blood counts • Endoscopy and biopsy
<p>* MRI is useful in</p> <ol style="list-style-type: none"> 1. To document inner perichondrial involvement 2. Patients planned for conservation surgery 3. To delineate prevertebral fascia involvement <p>MRI is selected when CT findings are ambiguous</p> <p>**Except in T3 and T4 and N+ locally advanced cases with lower neck node metastasis (level 4,5) and in cases where a gastric pull up is planned.</p>	<p>* CT Scan is essential for planning surgical conservation⁵⁻⁶ and usually high resolution scan with 1 mm slices are required.</p> <p>* CT Scan is advised based on the economic status, stage of the disease, intend of treatment and expertise available</p>

The basic details to be evaluated in the CT scan are the following

- Site of the disease
- Tumor volume
- Larynx
- Paraglottic space
- Post cricoid region
- Extensions
- Other sub sites of hypopharynx
- Oropharynx or oesophagus
- Cartilages involvement & extent of involvement
- Extra laryngeal spread
- Thyroid gland
- Pre vertebral fascia involvement
- Carotid artery involvement
- Lymph Nodes

MRI is more sensitive in determining cartilage involvement but CT Scan is more specific. MRI is better in assessing soft tissue involvement^{10,11}.

3.2 Staging

2010 American Joint Committee on Cancer Staging¹³ (Table 6a, b & c)

Table 6a

PRIMARY TUMOUR (T)

T1	Tumour limited to one subsite of hypopharynx and 2 cm or less in greatest dimension
T2	Tumour invades more than one subsite of hypopharynx or an adjacent site, or measures more than 2 cm but not more than 4 cm in greatest diameter without fixation of the hemilarynx
T3	Tumour more than 4 cm in greatest dimension or with fixation of the hemilarynx or extension to oesophagus
T4a	Tumour invades thyroid/cricoid cartilage, hyoid bone, thyroid gland, or central compartment soft tissue
T4b	Tumour invades the prevertebral fascia, encases the carotid artery, or involves mediastinal structures

Table 6b. LYMPH NODE (N)

NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis in a single ipsilateral lymph node, 3 cm or less in greatest dimension
N2	Metastasis in single ipsilateral lymph node, more than 3 cm but no more than 6 cm in greatest dimension; or in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension; or in bilateral or contralateral lymph nodes, no more than 6 cm in greatest dimension
N2a	Metastasis in single ipsilateral lymph node, more than 3 cm but no more than 6 cm in greatest dimension
N2b	Metastasis in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension
N2c	Metastasis in bilateral or contralateral lymph nodes, none more than 6 cm in greatest dimension
N3	Metastasis in a lymph node more than 6 cm in greatest dimension
DISTANT METASTASIS (M)	
M0	No distant metastasis (no pathologic M0; use clinical M to complete stage group)
M1	Distant metastasis

Table 6c. OVERALL STAGE GROUPING

Stage 0	Tis	N0	M0
Stage I	T1	N0	M0
Stage II	T2	N0	M0
Stage III	T3	N0	M0
	T1-T3	N1	M0
Stage IVA	T4a	N0-N1	M0
	T1-T4a	N2	M0
Stage IVB	Any T	N3	M0
	T4b	Any N	M0
Stage IVC	Any T	Any N	M1

3.3 Treatment

Goals of Treatment

Multidisciplinary team for treatment includes radiation oncologist, surgical oncologist, medical oncologist, radiologist, pathologist and speech therapist. Goals of treatment are the following

- Maximize cure
- Organ preservation when possible

- Provide good quality of life
- Palliation of symptoms in patients with incurable disease.

The management is divided into

- A. Management of Early Hypopharyngeal Disease (Stage I, II)
- B. Management of Moderately Advanced Hypopharyngeal Disease (Stage III, IVa)
- C. Management of very Advanced Hypopharyngeal Disease (Stage IVb, IVc)

3.4 Stage wise treatment

A. Management of Early Hypopharyngeal Disease (Stage I, II)

Early disease (T1N0, T2N0)

- External Beam Radiotherapy
- Transoral Laser Microsurgery/open conservation surgery

The intention is to achieve maximum cure with minimum morbidity. Modality of treatment depends on patient's preference and expertise available. In general radiotherapy (RT) is preferred. Standard dose of RT is 66-70 Gy over 6-7 weeks. The target volume is entire neck.

Surgical treatment includes either transoral laser microsurgery in suitable cases or partial laryngopharyngectomy plus neck dissection- unilateral or bilateral antero-lateral neck (level II-IV) dissection depending on the location of the tumour.

B. Management of Moderately Advanced Hypopharyngeal disease (III, IVA)

Stage III and IVA [T₁₋₂ N₁/N₂]

- Concurrent Chemoradiation
- Radical radiotherapy(conventional /altered fractionation radiotherapy)
- Partial laryngopharyngectomy + Neck dissection ± Adjuvant treatment

Stage III and IVA (T₃, N₀₋₂)

These patients can be treated either by

1. Organ preservation approach
2. Surgery followed by post-operative radiotherapy

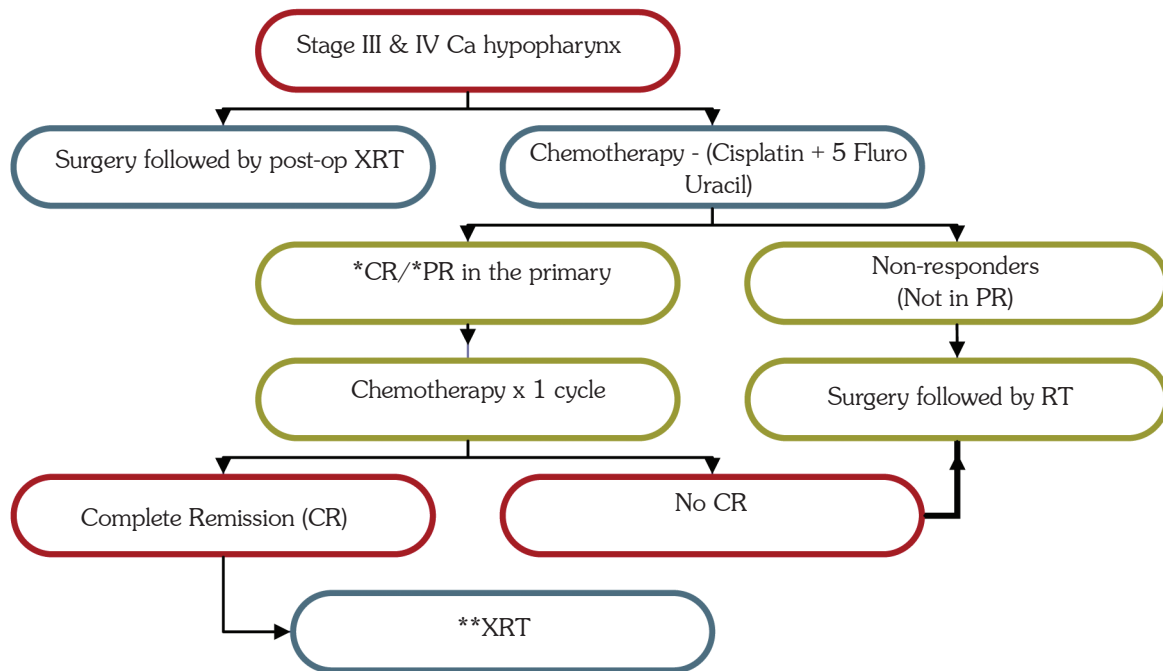
1. Organ preservation in Ca Hypopharynx

Organ preservation approach may be considered only in patients with intact laryngeal framework and preserved laryngeal function. Basically there are two approaches to organ preservation.

- a) Induction chemotherapy with response based treatment
- b) Concurrent chemoradiation

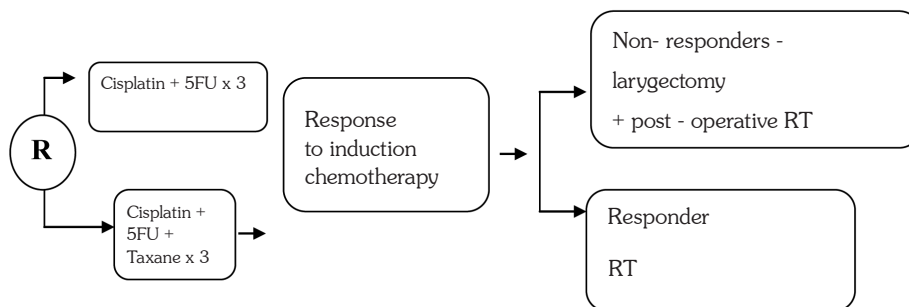
a) Induction chemo followed by organ preservation approach depending on response. The response of the primary is the most deciding factor in deciding the further treatment. There are two evidence based induction protocols available and they are given below. Good compliance is necessary for the success of induction chemotherapy protocols.

Flow chart 3. Hypopharyngeal Ca – European Organisation for Research and Training in Cancers (EORTC) protocol41:



*CR – Complete Remission, *PR – Partial Remission ** Radical Radiotherapy

Flow Chart 4. GORTEC 2000 -0135 laryngeal preservation trial protocol



Induction chemotherapy protocols are mainly applicable for pyriform sinus tumours. Advanced posterior pharyngeal wall and post cricoid are generally managed with concurrent chemoradiation.

b) Concurrent chemoradiation

Patient should have good performance status, adequate renal function, good family and social support and a functioning larynx without total or near total dysphagia. Patients with dysfunctional larynx and absolute dysphagia are better candidates for surgery (if operable)

2. Surgery followed by adjuvant radiation or chemoradiation

Surgery involves either total or near-total laryngectomy with partial pharyngectomy with reconstruction of the pharynx either with primary closure or a pharyngoplasty with a flap (pedicled pectoralis major myocutaneous flap or free flap either radial artery forearm or anterolateral thigh). Voice rehabilitation should be offered to all suitable patients depending on their affordability and availability of services as outlined in Annexure 3.

Stage IVA (T4a, N0-N2) with or without cartilage involvement

These patients are primarily treated with surgery and not candidates for organ preservation approaches. The surgical treatment includes Near-Total Laryngectomy / Total Laryngectomy with partial or total (circumferential) pharyngectomy with bilateral neck dissection followed by post-operative radiotherapy³⁶⁻³⁹. Most of the patients will require pharyngeal reconstruction with vascularised flaps (pharyngeal patch). In cases where there is a discontinuity of the pharynx with the oesophagus (circumferential pharyngectomy) a tubed skin flap Pectoralis Major Myo Cutaneous (PMMC) /Free Radial Forearm or Antero Lateral Thigh (ALT) Flap or visceral interposition (free jejunum / pedicled colon) or a gastric transposition may be required depending on the availability of intact cervical oesophageal stump All patients require post-operative radiotherapy in stage IVA disease. Indications for adjuvant post operative chemo RT are margin positive disease and extra capsular spread. Good Performance status is a prerequisite for adjuvant chemo radiation. Patients, who refuse surgery or are medically inoperable, are treated with concurrent chemoradiation or radiation. Options of voice rehabilitation (Annexure 3) should to be given to patients undergoing total laryngectomy. In patients with uninvolved cartilage, induction chemotherapy followed by chemo-radiation for responders and surgery for non-responders is an option.

C. Management of Very Advanced Hypopharyngeal Disease (IVb, IVc)

Stage IVB disease- T4B or N3 disease

In general these patients are treated with palliative intent. Situations where radical approach is considered in stage IVB disease are T1-4a primary disease with an operable N3 disease (surgery and post operative adjuvant) or low volume T4b disease (chemo RT) in a patients with good performance status. In the remaining patients, decisions regarding sequential chemotherapy and upfront surgery with adjuvant treatment (in borderline inoperable cases) can be taken on a case to case basis.

Stage IV-C

Patients with stage IV C disease are candidates for palliative treatment. Decision regarding local radiotherapy or systemic treatment is based on the clinical situation

Table 7. Composite staging and summary of treatment of Hypopharyngeal cancer

	Stage T1	Stage T2	Stage T3	Stage T4a	Stage T4b
N0	I	II	III	IVA	IVB
N1	III	III	III	IVA	IVB
N2	IVA	IVA	IVA	IVA	IVB
N3	IVB	IVB	IVB	IVB	IVB
M1	IVC	IVC	IVC	IVC	IVC
<p>■ Early Disease RT/Surgery ■ Induction /Concurrent Chemo RT ■ M1 palliative treatment</p>			<p>■ Surgery Post op RT(cartilage involvement) ■ Palliative treatment / *Radical approach in selected group of patients</p>		
* Young patient with good performance status, low volume primary disease and resectable nodal disease					

Practical aspects in Ca Hypopharynx

1. Biopsy from the primary site is mandatory.
2. Accurate staging is the most important step in the management.
3. Performance status, Nutritional status & Family support are key factors in deciding treatment..
4. CT Scan is mandatory to rule out T3 disease.
5. Organ preservation approach should be avoided in patients having cartilage destruction.
6. Patients with laryngeal dysfunction are not candidates for organ preservation.
7. Organ preservation approach should be considered for all T3 disease with good laryngeal function.
8. Proper patient selection is needed for concurrent chemoradiation
9. Avoid unnecessary investigations and costly chemotherapy in patients who are candidates for palliative approach
10. Patients should be counselled regarding symptoms and signs of relapse

Follow up

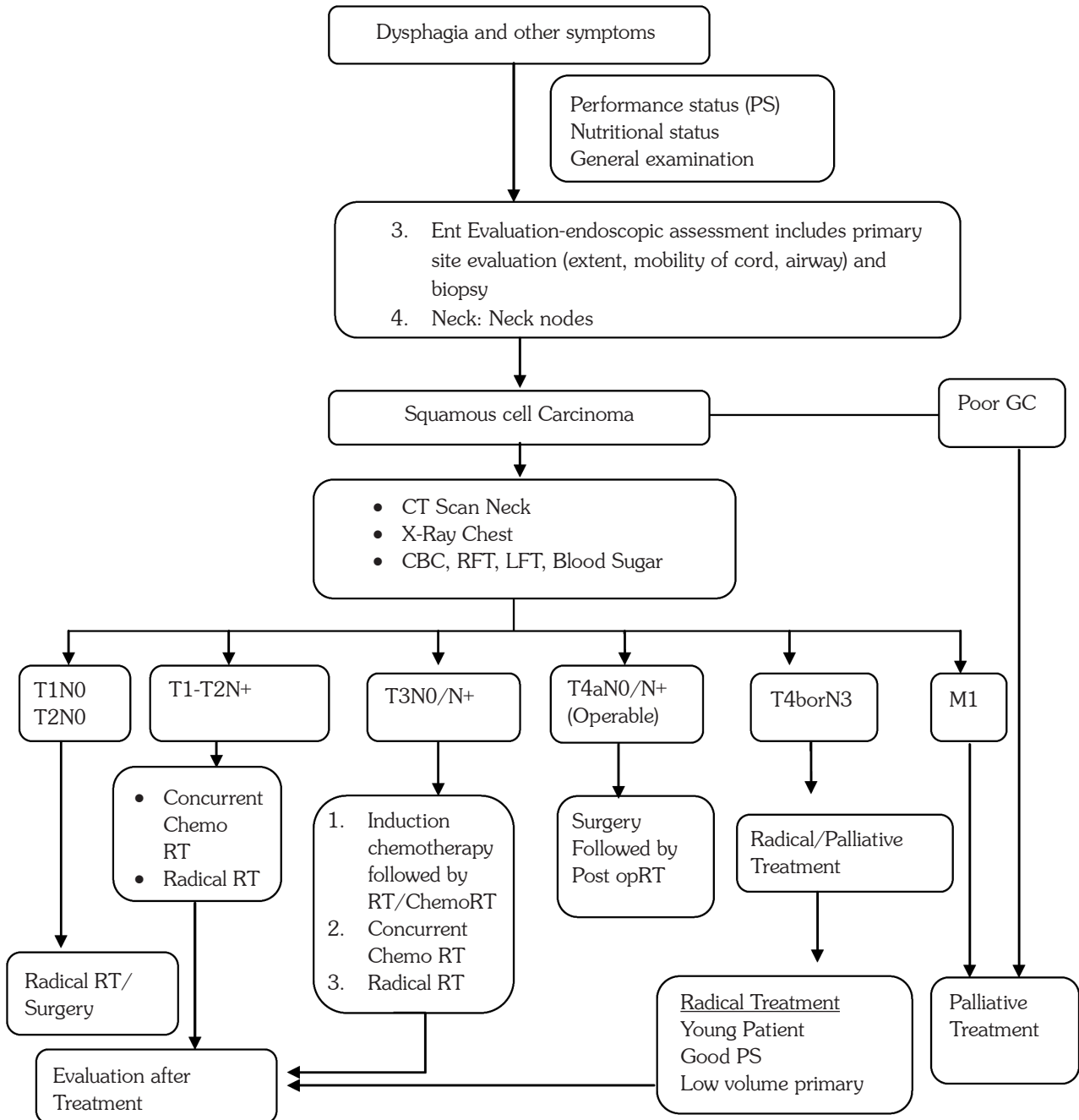
Objectives of follow up are

1. Detection of early recurrences
2. Evaluation of morbidity
3. Detection of second primary.

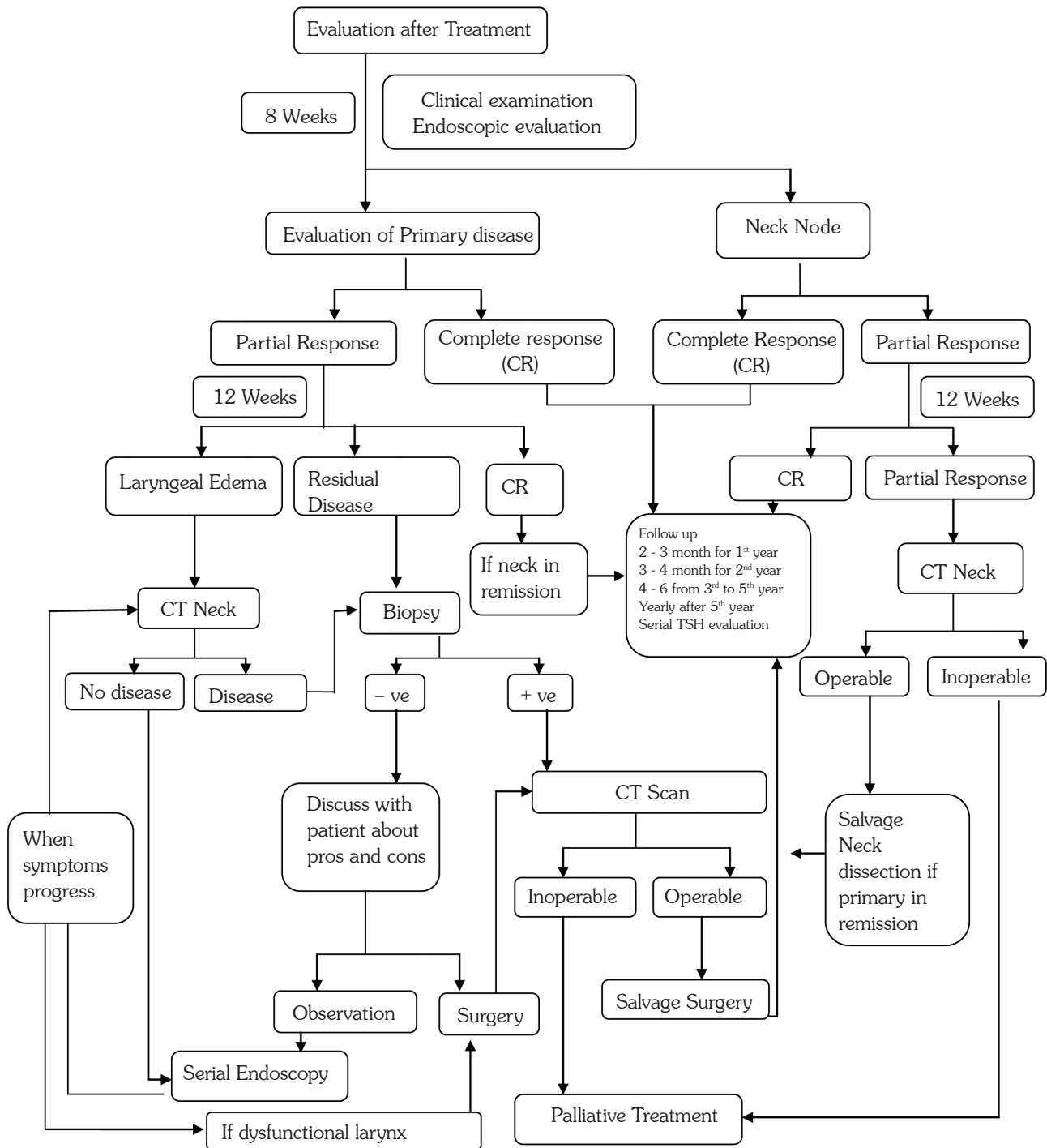
Clinical examination including ENT evaluation is done once in 3 months for the first two years followed by once in 4-6 months from third to fifth year. Yearly follow up after 5 years. TSH evaluation should be done periodically

CONSENSUS STATEMENT ON PRACTICE

Flow Chart 5. Comprehensive Algorithm for Management of Hypopharyngeal Cancer



Flow Chart 6. Comprehensive Algorithm for follow up of Organ preservation approach



4.1 Altered vs conventional fractionation regimes

Accelerated radiotherapy is a reasonable alternative to conventional radiotherapy in early disease⁸. In advanced disease, hyperfractionation is found to be superior in terms of locoregional control and over all survival compared to conventional radiotherapy³³.

4.2 Salvage Surgery for failed organ preservation protocols

Salvage surgery is the only option available to tackle a failed organ preservation protocol ie recurrence or an irreversible life threatening post radiation sequelae (eg. severe laryngo-oesophageal dysfunction secondary to chondroradionecrosis or laryngopharyngo-oesophageal fibrosis). The 'equalising effect' of salvage surgeries in organ preservation protocols in attaining comparable figures to the traditional upfront surgical (total laryngectomy) protocols for intermediate and advanced staged diseases have not been adequately quantified. Although in trial settings good results have been reported²⁹ there are ample evidence to suggest that salvage surgery especially those performed for early failures carries a higher morbidity³²⁻³⁶.

4.3 Palliation in larynx and hypopharynx cancers⁴⁵⁻⁵¹

For patients with late stage disease laryngeal and hypopharyngeal cancer, good nursing care and palliative measures such as pain control and interventions to help them eat and breathe are crucial; those who are expected to live for a significant period may benefit from palliative surgery, radiotherapy or chemotherapy.

Patients can also be encouraged to participate in ethically approved clinical trials.

4.4 Management of acute events

4.4.1 Acute major airway obstruction

The onset of laryngeal obstruction may be slow if due to tumour growth, but acute if precipitated by haemorrhage or infection. Most patients would have previous radical RT. Lumen patency can be restored by interventional procedures e.g. tracheostomy or laser therapy for endoluminal lesions. Other options include external beam radiotherapy. Correction of hypoxia with oxygen or 4:1 helium: oxygen mixture, which has a lower viscosity than air and can reduce respiratory effort. Dexamethasone at a starting dose of 16 mg daily may be helpful. Benzodiazepine can be used to reduce anxiety or panic, e.g. diazepam 5-10mg IV, midazolam 2.5-5mg IV or SC. Nebulized normal saline helps to facilitate removal of sticky sputum. Palliative sedation may be considered if symptoms are refractory to treatment.

Tracheostomy is considered for appropriate patients in order to maintain airway patency and to allow

expectoration of secretions. The indications of tracheostomy include bilateral vocal cord paralysis, laryngectomy, and tumour occluding the airway. Basic care of tracheostomy includes:

1. Humidification of inspired air e.g. steam inhalation;
2. Clearing of secretions by regular deep-breathing exercises and chest physiotherapy;
3. Suctioning for viscid secretions or mucous plugs.

Whilst doing tracheostomy care should be taken to place the incision appropriately considering salvage procedure in future. The tracheal opening should also be placed between third and fourth ring to facilitate a proper near-total shunt in suitable patients. Following tracheostomy care of the skin surrounding the stoma should be taken with antiseptic barrier dressing between the tracheostomy tube and skin.

4.4.2 Acute tracheostomy obstruction

Tracheostomy can be blocked acutely by bleeding from tracheostomal recurrence or severe crusting of secretions. If blockage occurs, the inner tube of tracheostomy should be removed, followed by suctioning through the outer tube of. Re-suctioning can be repeated with instillation of 5ml of normal saline into the tube if necessary. If obstruction persisted, one can remove and clean or replace the outer tube. If the outer tube has to be removed, the tracheal dilator must be available in hand.

4.4.3 Massive arterial bleeding

There is a higher risk of massive arterial bleeding in patients with eroding tumours close to carotid arteries. Unconsciousness and death may occur rapidly before sedation is allowed. If time allows, patient should be sedated with midazolam or diazepam intravenously or intramuscularly. It is important to note that drugs given subcutaneously are poorly absorbed in circulatory shutdown. A dark green cloth is helpful in camouflaging blood, and to reduce the visual impact on relatives and staff.

4.5 Management of chronic problems

4.5.1 Pain control

Elucidation of underlying causes of pain is important. Pain can result from deep tissue infiltration, cranial nerve involvement, tumour ulceration, or the effects of surgery or radiotherapy such as mucositis or fibrosis. Psychosocial factors can contribute to pain. Analgesics can be prescribed according to the WHO analgesic ladder.

NSAIDs may be helpful especially in the presence of bone involvement and inflammation. Tricyclic antidepressants or anti-convulsants can be given for neuropathic pain, and steroids as an anti-inflammatory agent. Antibiotics e.g. metronidazole can be used to cover anaerobic organism infections. Local radiotherapy and nerve block may be considered for pain control in appropriate candidates.

4.5.2 Swallowing disorders and aspiration

Artificial feeding via a fine-bore nasogastric tube or PEG (percutaneous endoscopic gastrostomy tube) has to be considered in appropriate cases. Carers/family members should be educated on the correct method of feeding.

Formal assessment by speech therapist and Video Fluoroscopic Swallowing Study (VFSS) are better assessment for aspiration. In presence of aspiration, it is important to maintain a good oral hygiene in order to reduce the bacterial colonisation. Specific swallowing strategies include feeding patient at an upright position, dividing the food into small boluses, feeding slowly, etc. In patients with immobile hemi

pharynx it is helpful to tilt or turn the head towards the paralysed side to open the contralateral normally functioning lateral food channel. For those with reduced tongue control, the postural compensation techniques or exercises may be helpful. Other measures such as dietary modification with foods of pasty consistency may reduce risk of aspiration.

4.5.3 Fungating wounds

The aim of treatment is to control pain, odour, prevent bleeding and to provide psychological support. Odour and discharge can be reduced by antibiotic (e.g. metronidazole) either topically or systemically, adequate ventilation, and the use of special dressing materials. Local RT may have a haemostatic effect for wound with bleeding. Palliative Surgery can be anticipated as a measure for treatment of fungating wounds in carefully selected patients with optimal results achieved.

1. Comparisons of radical RT with conservation surgery in early larynx.
2. Proper identification of patients suitable for concurrent chemoradiation (CCRT).
3. Induction chemo followed chemoradiation vs CCRT for very advanced operable larynx/hypopharynx cancers
4. Altered fractionation vs Chemoradiation
5. Translational research with Prognostic & Predictive markers
6. Selection of cases suitable cases for primary surgery/non-surgical organ preservation based on functional scoring of larynx, tumor morphometry and volumetry (in cc)
7. 3 wkly/wkly cisplatin for concurrent CT-RT

Annexure 1: Standard Radiotherapy & Chemotherapy Schedules

Clinical target volume includes entire neck. Standard dose is 60Gy/30fr. Spinal cord is shielded after 40-42Gy. Posterior neck is boosted using electrons if facility is available.

1. Radical Dose is 66-70 Gy in 33-35 fr to primary disease and involved nodes and 50 - 54 Gy to uninvolved nodal region.
2. Standard post-operative dose is 60 Gy in 30 fr. High risk region with positive margin or extra capsular extension should be boosted up to 66 Gy along with concurrent cisplatin
3. Palliative radiotherapy dose 30 Gy in 10 fr or 20 Gy in 5 fr

Chemotherapy Schedules along with radiotherapy*Concurrent Chemo radiation*

1. Three weekly: Cisplatin 80 -100 mg / m² IV (Day1, Day 22, Day 43) along with radical radiotherapy
2. Weekly: Cisplatin 30-40mg/m² weekly along with radical radiotherapy

Neoadjuvant Chemotherapy followed by radiation / chemoradiation

1. Cisplatin 80-100 mg / m² IV Day 1 and 5 F U 750-1000 mg / m² IV Day 1 to Day 5 as 24 hr infusion x 2 cycles followed by radical radiotherapy or chemoradiation with cisplatin.
2. Taxane based multidrug therapy is considered usually three weekly. Docetaxel 75mg/m² D1, Cisplatin 100mg/m² D1 and 5FU1000 mg/m²/d D1-4 followed by radical radiotherapy or chemoradiation with cisplatin.

Targeted Therapy

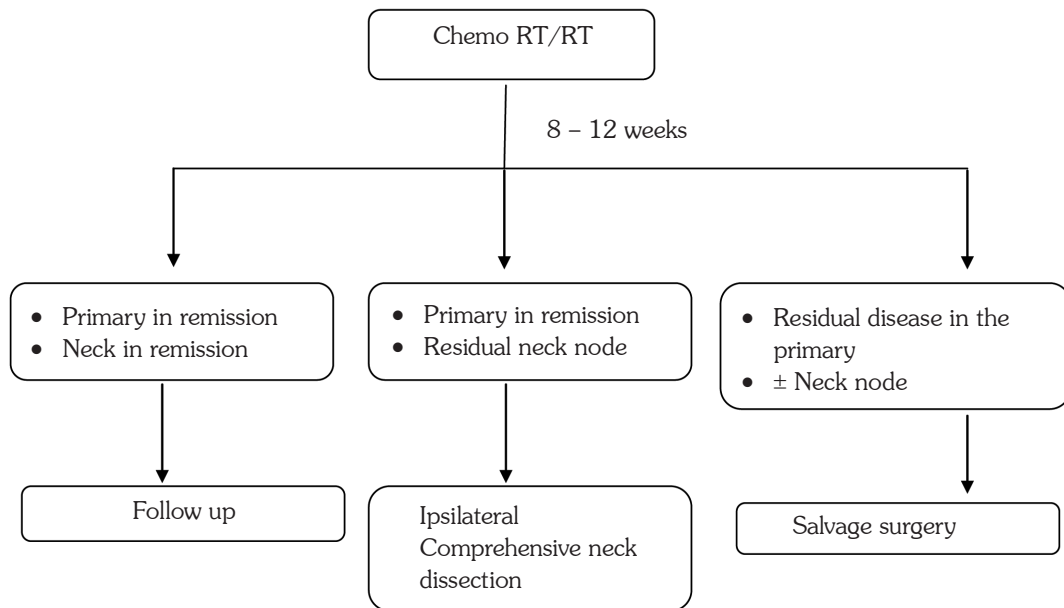
Cetuximab 400 mg / m² IV one week before radiotherapy and 250 mg / m² IV weekly along with radical radiotherapy.

Nimotuzumab 200mg weekly.

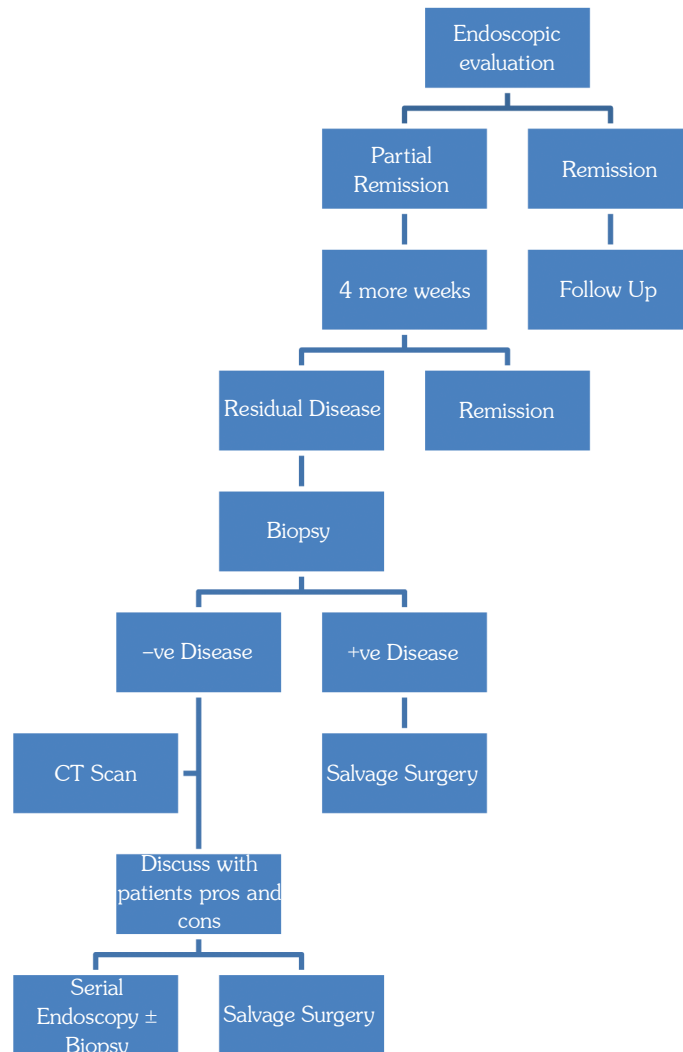
Annexure 2: Evaluation after definitive radiation / concurrent chemoradiation for Ca Larynx / Hypopharynx

Initial evaluation is done after 8-12 weeks. If both primary and neck is in clinical remission, follow up is needed. If primary is in remission and residual nodes are present, patient should undergo ipsilateral comprehensive neck dissection. If there is residual disease in the primary, salvage surgery should be considered with or without neck dissection and is given the flow chart

Flow Chart 7. Flow chart for evaluation of patients undergoing RT / ChemoRT



Flow Chart 8. Flow chart for assessing the primary disease after chemo RT / RT



Protocol for evaluation of Laryngeal edema

- Take CT scan of the Neck
- If endoscopic evaluation shows only edema and CT Scan shows no disease, patient is advised follow up
- Avoid repeat biopsy
- If patients has laryngeal dysfunction then salvage surgery is contemplated

Annexure 3: Voice Rehabilitation

Options of voice rehabilitation should be given to patients undergoing total laryngectomy which include³⁷⁻³⁹

1. Immediate Voice restoration - Primary Tracheo-esophageal puncture (TEP) and insertion of tracheo-esophageal voice prosthesis during laryngectomy (Indwelling type) or after the fistula has formed (indwelling or non indwelling type).

2. Secondary Rehabilitation:

1. Secondary TEP and voice restoration with indwelling or non indwelling tracheo-esophageal voice prosthesis 3 – 6 months after radiation.
2. Oesophageal speech trial and training in suitable cases or Electronic larynx.

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INDIAN COUNCIL OF MEDICAL RESEARCH

Department of Health Research

(Ministry of Health & Family Welfare)

**V. Ramalingaswami Bhawan, Post Box 4911,
Ansari Nagar, New Delhi-110029**

Phone: 91-11-26588980, 26589794, 26588895

E-mail: icmrhqds@sansad.nic.in

Website: <http://www.icmr.nic.in>