Management of early laryngeal and hypopharyngeal cancers

Punita Lal
Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow
World War 1 History

- 1886 – Crown Prince Frederick, Germany developed Laryngeal cancer.
- Advised Laryngectomy. Refused.
- Died 1888
- Succeeded by Kaiser Wilhelm II, who along with Otto von Bismark – Military rule in Germany.
- Led World war I

Could a Radiation oncologist have prevented World War I?
• 11,000 new cases of laryngeal cancer per year in the U.S.
• Accounts for 25% of head and neck cancer and 1% of all cancers
• Most prevalent in the 6th and 7th decades of life
• 4:1 male predilection; Downward trend post WWII
• Due to increasing public acceptance of female smoking
Sub-sites

Supraglottic  - Epiglottis
               - AE fold
               - Arytenoid
               - False cords
               - Ventricles
Glottic       - Vocal cord

Subglottic
Subtypes

- Glottic Cancer: 59%
- Supraglottic Cancer: 40%
- Subglottic Cancer: 1%
- Most subglottic masses are extension from glottic carcinomas
Risk Factors

90% of patients with laryngeal cancer have a history of both
Histological Types

- 85-95% - squamous cell carcinoma
- Histology linked to tobacco and alcohol abuse
- Characterized by epithelial nests surrounded by inflammatory stroma
- Keratin Pearls - pathognomonic
Anatomy

- Lamina of cricoid
- Epiglottis
Anatomy
Natural History

- Supraglottic tumors more aggressive:
  - Pre-epiglottic space/ LN/ hypopharynx, glossoepiglottic fold and tongue base
- Glottic tumors grow slower and metastasize late - paucity of lymphatic drainage
- Metastasize after they have invaded adjacent structures with better drainage
- Subglottic space extension - poor prognosis
- Increases chance of B/L LN & mediastinal extension
Presentation

- Hoarseness
  - Most common symptom
  - Small irregularities in the vocal fold and chronic use of tobacco and alcohol – change in voice

Supraglottic tumors - dysphagia
Methods of determining gross tumor

- Visual inspection
- Palpation
- Endoscopy
- CT scan – axial, sagittal and coronal reconstructs
- T2 MRI
- PET scans
Clinical evaluation

- Indirect mirror exam and/or flexible laryngoscope evaluation
- Videostrobe laryngoscopy may be needed to follow up these subtler lesions

Goals:
- to confirm histopath
- Map the disease & regional nodes & potential metastatic disease
- Stage the lesion
Indirect Laryngoscopy

- Overview of larynx / hypopharynx.
- Excellent color & depth perception

Disadvantage:
- difficult patients
- hidden areas

Malignant lesions can appear as friable, fungating, ulcerative masses or be as subtle as changes in mucosal color
Direct laryngoscopy

Standard of care
- extent of the disease
- vocal cord mobility
- visualise hidden areas
- Palpate crico arytenoid joint
- biopsy – obvious & suspicious areas

Rigid telescopic examination – 90°/70°
Advantages: - simple
- added magnification
- better optical resolution
- higher sensitivity
- better contrast

Flexible fibre optic endoscopy

Limitation of endoscopy – PES/PGS/ Cartilage involvement
## Staging - Primary Tumor (T)

<table>
<thead>
<tr>
<th>TX</th>
<th>Minimum requirements to assess primary tumor cannot be met</th>
</tr>
</thead>
<tbody>
<tr>
<td>T0</td>
<td>No evidence of primary tumor</td>
</tr>
<tr>
<td>Tis</td>
<td>Carcinoma in situ</td>
</tr>
</tbody>
</table>
## Staging - Supraglottis

<table>
<thead>
<tr>
<th>T1</th>
<th>Tumor limited to one subsite of supraglottis with normal vocal cord mobility</th>
</tr>
</thead>
<tbody>
<tr>
<td>T2</td>
<td>Tumor involves mucosa of more than one adjacent subsite of supraglottis or glottis, or region outside the supraglottis (e.g. mucosa of base of the tongue, vallecula, medial wall of piriform sinus) without fixation</td>
</tr>
<tr>
<td>T3</td>
<td>Tumor limited to larynx with vocal cord fixation and or invades any of the following: postcricoid area, preepiglottic tissue, paraglottic space, and/or minor thyroid cartilage erosion (e.g. inner cortex)</td>
</tr>
<tr>
<td>T4a</td>
<td>Tumor invades through the thyroid cartilage and/or invades tissue beyond the larynx (e.g. trachea, soft tissues of neck including deep extrinsic muscles of the tongue, strap muscles, thyroid, or esophagus)</td>
</tr>
<tr>
<td>T4b</td>
<td>Tumor invades prevertebral space, encases carotid artery, or invades mediastinal structures</td>
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</tbody>
</table>
## Staging - Glottis

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1</td>
<td>Tumor limited to the vocal cord(s) (may involve anterior or posterior commissure) with normal mobility</td>
</tr>
<tr>
<td>T1a</td>
<td>Tumor limited to one vocal cord</td>
</tr>
<tr>
<td>T1b</td>
<td>Tumor involves both vocal cords</td>
</tr>
<tr>
<td>T2</td>
<td>Tumor extends to supraglottis and/or subglottis, and/or with impaired vocal cord mobility</td>
</tr>
<tr>
<td>T2a</td>
<td>Tumor limited to the larynx with vocal cord fixation and/or invades paraglottic space, and/or minor thyroid cartilage erosion (e.g. inner cortex)</td>
</tr>
<tr>
<td>T2b</td>
<td>Tumor invades through the thyroid cartilage, and/or invades tissues beyond the larynx (e.g. trachea, soft tissues of the neck including deep extrinsic muscles of the tongue, strap muscles, thyroid, or esophagus)</td>
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**AJCC 6th edition, 2006 – T2a – with cord mobility & T2b – with impaired mobility**
Aim of treatment – desirable end points

- Local control
- **Organ preservation**
  - Organ preservation possible by surgery and radiotherapy
  - Organ preservation ≠ Function preservation
  - Functions – speech, deglutition and breathing.
Patient related factors influencing decision

-KPS
-Co-morbidities
-Tracheostomy
-Age

Nutritional support required before, during and after radiation treatment.
Decision tree – stagewise management

- Early disease
  - Ca-in-situ
    - RT/Laser/striping
  - T1 glottis
    - RT/Laser/striping
  - Other T1 & T2
    - Preserv Surg Or RT

- N0 – No treatment in T1 and select T2 glottic cases. Single modality treatment.
Laser Surgery versus Radiotherapy for T1–T2N0 Glottic Cancer: A Meta-Analysis

Yan Feng  Binquan Wang  Shuxin Wen
Otorhinolaryngology, Head and Neck Surgery, The First Affiliated Hospital of Shandong Medical University, Taiyuan, China

- CO2 laser
- Accurate review of margins difficult
- AC – not adequately dissected
- Residual hoarseness +
Stripping/ cordectomy

- Tis lesions
- T1a & b lesions
- Strong consideration for RT in Tis lesion post stripping recurrence
- Web formation
- Voice quality diminishes on repeated stripping
- Median time to rec 2-3yrs. Need close follow up.

Laryngeal preservation surgery – partial laryngectomy

- T2 (esp unfavourable) lesions
- Expensive; skill
- Voice quality – poor
• T1/T2 – suitable for OP. RT or surgery - 85-95% cures.
• Surgery - shorter treatment period; worse voice outcomes; RT as reserve
• RT- 6-7 wks.
• T1/T2 – RT = Larynx preserv Sx
• T1/T2 – No elective nodal RT
• T1/T2 SGL – Treat the neck
Management of T1–T2 Glottic Carcinomas

T1–T2 glottic carcinomas may be treated with conservative surgery or radiotherapy. The goals of treatment are cure and laryngeal voice preservation. The aim of the current study was to review the pertinent literature and discuss the optimal management of early-stage laryngeal carcinoma. Literature review indicated that the local control, laryngeal preservation, and survival rates of patients were similar after transoral laser resection, open partial laryngectomy, and radiotherapy. Voice quality depended on the extent of resection for patients undergoing surgery; results for patients undergoing laser resection for limited lesions were comparable to the corresponding results for patients receiving radiotherapy, whereas open partial laryngectomy yielded poorer results. Costs were similar for laser resection and radiotherapy, but open partial laryngectomy was more expensive. Patients with well defined lesions suitable for transoral laser excision with a good functional outcome were treated with either laser or radiotherapy. The remaining patients were optimally treated with radiotherapy. Open partial laryngectomy was reserved for patients with locally recurrent tumors. Cancer 2004;100:1786–92.

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Radiotherapy

• UK - RT standard of care – TIS, T1/2
• Parallel opp fields
• T1 - 5cm – thyroid promontory to lower border C5
• T2 - 6cm – Hyoid to cricoid

No IMRT done routinely!
Steps of Larynx (T1/2) Radiotherapy

Patient counseling

Patient positioning and Immobilization

• Simulation and/or Imaging

• Target definition & planning

• Treatment delivery
Patient positioning

- Comfortable
- Supine
- Neutral head position
- Laser alignment
- Indexing
Patient positioning devices
Immobilization

- Appropriate to anatomy
- Restrict movement
- Comfortable!
- Coordinate system
What are the problems in immobilization?

- Neck rest versus neck shape
- Loosening of cast due to weight loss
- Difficult individual patient positioning
- Short neck

Gap between neck, upper thorax and table with standard neck rest

Wrong neck rest
What do radiation portals depend upon?

- Location of the primary and stage
- LN- location, size and laterality
Beam energy and accessories

- 4-6 MeV
- Cobalt-60
- 10-20° Wedge pair

Bolus
Missing tissue Compensator
Definitive radiotherapy for early (T1-T2) Glottic Squamous cell carcinoma: a 20 year Cleveland clinic experience

Mohammad K Khan¹, Shlomo A Koyfman², Grant K Hunter², Chandana A Reddy² and Jerrold P Saxton²

Figure 1. Example of Arrangement & Weighting of Fields (1A) and Comparison of Non-Bulky vs. Bulky Tumor (1B).
Radiation dose schedules

Conventional RT Phased treatment

Tis – rec post stripping
- 60Gy/30fr or eq

T1 glottis
- 60Gy/30fr or eq

≥ T2
- 70Gy/35fr/6-7wks or eq
  - <42cm² – 55Gy/20fr/4wks
  - >42cm² – 64Gy/32fr/61/2wks
Status of IMRT in early glottic ca.

No sparing of vital structures – not recommended routine clinical setting

Published in final edited form as:

SIMPLE CAROTID-SPARING INTENSITY-MODULATED RADIOTHERAPY TECHNIQUE AND PRELIMINARY EXPERIENCE FOR T1–2 GLOTTIC CANCER

David L. Rosenthal, M.D., Clifford D. Fuller, M.D., Jerry L. Barker Jr., M.D., Bryan Malony, M.S., John A. Garci, C.M.D., Jan B. Lewis, Ph.D., P. Christopher Holzinger, M.D., C. Richard Stainey, M.D., Steven J. Frank, M.D., David L. Schwartz, M.D., William H. Morrison, M.D., Adam S. Garden, M.D., and K. Kim Ang, M.D., Ph.D.
*Department of Radiation Oncology, University of Texas M. D. Anderson Cancer Center, Houston, TX

Fig. 1.
Composite carotid artery dose-volume histogram (n = 4) showing mean (solid line) and 95% confidence interval (shaded region) for virtual plan (red = intensity-modulated radiotherapy, blue = opposed lateral).

Fig. 2.
Stereotyped isodose plans for (a) lateral field setup and (b) intensity-modulated radiotherapy.
Reasons for failure

- Diffuse Tis lesions
- Ant commissure failure with megavoltage beam underdosage – **Bolus; No shell cut outs; No wedge.**
- Short neck – high shoulder – **Use of wedge oblique arrangement.**
Total Laryngectomy - Salvage

• Post RT failures

• Speech rehabilitation – TEP; electro larynx; eso speech
Early Supraglottic carcinoma

- RT standard of care
- Cover bilateral lymph nodes – level II -IV
- 5 year LC rate T1 -100%; T2 -83%
Supraglottic laryngectomy

- Select group
- T1,2, or 3 if only by preepiglottic space invasion
- Mobile cords
- No anterior commissure involvement
- Good cardiac & pulmonary reserves
- No tongue base disease past circumvallate papillae
- Apex of pyriform sinus not involved
## Outcome - Glottis & Supraglottis

<table>
<thead>
<tr>
<th>5 year survival</th>
<th></th>
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<tbody>
<tr>
<td>Stage I</td>
<td>&gt;95%</td>
</tr>
<tr>
<td>Stage II</td>
<td>85-90%</td>
</tr>
</tbody>
</table>
Conclusions

- Worst complication is tumor recurrence
- Pre treatment assessment & staging crucial
- Radiotherapy = Laryngeal preservation surgeries
- Results excellent. Pay attention to disease, planning and treatment delivery
Carcinoma of the Hypopharynx - early tumors
Hypopharynx - Anatomy

- Lies behind and lateral to larynx from hyoid bone to crico pharyngeal junction at C6 level.

- Larynx indents anterior wall of hypopharynx to form horse shoe shaped hollow cavity which forms the central aerodigestive pathway and two lateral fossae ie: pyriform sinuses.
## Hypopharynx - Pathology

- **Pyriform fossa**   - 75-80%
- **Post. Pharyngeal wall**  - 15-20%
- **Post cricoid**   - 5%

- 95% cases - squamous cell carcinoma  
  - 33% - non keratinising  
  - 40% - poorly differentiated

- Minor salivary gland tumors
- Sarcomas
- Lymphoma
Hypopharyngeal cancer- aetiology

• Clinically inaccessible region
• Aggressive in behavior; Abundant lymphatic drainage
• Field cancerisation-12-20 % multiple synchronous
• Nutritionally depleted patients
• Tobacco (smoked/ chewed); Alcohol –co-carcinogen
• Nutritional- deficiency of B-carotenoids, iron deficiency anemia (asso. with dysphagia and glossitis as Plummer Wilson or PKB syndrome)
Lymph node involvement after elective neck diss. In N0 neck-2/3 in T1-T2

- Pyriform fossa
  - Incidence of nodal involvement - 75%
  - Bilateral nodal involvement - 10-14%
  - Clinical N0 neck, found positive - 40-50%

Retropharyngeal nodes +ve in 40% patients with PFF and post. Pharyngeal wall lesions
Hypopharynx- natural history

- Advanced disease at presentation
- Distant mets follow locoregional relapse
- Skip lesions
- Early esophageal spread
- Lymphatic
  - Most common level II followed by level III
  - Involvement of level I, IV, V uncommon
Hypopharynx- distant spread

- Distant metastasis
  - 20-30% within two years despite treatment
  - RTOG analysed effect of locoregional control on distant metastasis
  - Locoregional control at 6 months associated with reduction in incidence of mets.- 43-40%
  - Most common sites – lungs, mediastinal nodes, liver, bone
Cancer Hypopharynx-symptomatology

- Mild non specific sore throat
- Vague discomfort on swallowing
- Neck mass as sole finding in 25% cases
- Referred otalgia characteristic of ca PFF
- Salivary drooling, blood streaked saliva
- Significant wt. loss, poor ODH
- Hoarseness- cricoid, inter-arytenoid space, post-cricothyroid muscles OR Hot potato voice OR Nasal voice
Cancer Hypopharynx—work up

- History
- Physical examination (general, neck, laryngeal crepitus)
  - I.L examination
- Flexible endoscopy and biopsy
- Hemogram, Clinical chemistry
- Imaging barium swallow, chest X Ray, Xray soft tissue neck,
- CT/MRI/USG neck
- FNAC from LN mass
Cancer Hypopharynx- staging

- **Tx** Primary tumor can not be assessed
- **T0** No evidence of primary tumor
- **Tis** Carcinoma in situ
- **T1** Limited to one subsite of hypopharynx, < 2 cm
- **T2** More than one subsite or involving an adjacent site or 2-4 cm, without fixation of larynx
- **T3** More than 4 cm or With fixation of larynx
- **T4** Tumor invades adjacent structures of neck (soft tissues, prevertebral fascia, esophagus, thyroid or cricoid cartilage, thyroid gland)
Cancer Hypopharynx- surgery

- Conservation surgery – size and location, fixity of nodes, medical condition of patient
- **Contraindication**
  - Transglottic extension (mucosa of AE fold and paraglottic space)
  - Cartilage invasion
  - Vocal fold paralysis
  - Pyriform apex or post cricoid invasion
  - Extension beyond laryngeal framework
- Unilateral neck dissection
Hypopharyngeal ca. -RT

- Pyriform sinus
  - T1, T2 lesions
  - Irradiation alone or surgery (PLP + U/L ND) +/- RT

- Posterior Pharyngeal wall
  - T1, T2 lesions
  - Irradiation alone or surgery (PLP + U/L ND) + RT +/- CT

- Post cricoid – early lesion

Optimal treatment yet to be defined
Cancer Hypopharynx—Radiotherapy

- RT alone
  - Small superficial lesions PFS
  - Mendenhall et al reported 64% control in T1/2 lesions (65 - 70Gy in 7 weeks)
  - Best results with
    - Lesions confined to one or two walls
    - Lack bulk
    - Not infiltrate larynx or destroy thyroid cartilage
Cancer Hypopharynx- RT technique

- Larynx, pharynx, neck
- Base of skull to clavicle (PC – 5cm prox esophagus)
- Dose – 70Gy/ 35fr/7wks or eq.

• Postoperative
  - Dose – 60Gy/ 30fr/6wks. 3 field technique
  - Anterior shield not used
Conformal RT

- Advantageous as they effectively treat horse shoe shaped target volume
- GTV-grossly visible/palpable extent of primary tumor with metaststic l. node
- CTV- GTV +regions of potential microscopic disease ie; upper middle and lower jugular l. nodes, SA and RP lymph nodes ,RP space ,thyroid and criciod cartilage,SC L. node +/- upper mediastinal l. nodes
- PTV- CTV +1.5 cm margin
Cancer Hypopharynx - Results

- Overall cure rates for hypopharyngeal tumours – 55%
- Local disease – 80%
- Regional disease – 43%
- Distant disease – 20%
- 5 - year disease free survival rates
  - A-E fold - 66%
  - PFF - 55%
  - Post.pharyngeal wall - 49%
Sequalae

- **Acute effects**
  - Mucositis (major limitation) - sore throat, dysphagia, hoarseness
  - Dysguesia and xerostomia
  - Laryngeal edema

- **Late**
  - Late laryngeal chondronecrosis – 2-4%
  - Severe laryngeal edema requiring tracheostomy – 6%
  - Subcutaneous fibrosis

- Mortality 1-3% with RT alone, 5-6% with surgery + RT
  - Aspiration, pharyngeal stricture causing cachexia, asphyxia d/t laryngeal edema, carotid blow out
Thank you