LEE KONG CHIAN SCHOOL OF MEDICINE

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Laryngeal carcinoma

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REDEFINING MEDICINE, TRANSFORMING HEALTHCARE

What are the risk factors for laryngeal cancer

- RR of laryngeal ca between smokers and non-smokers is 15.5 in men, 12.4 in women
- Drinking 100g alcohol per day (7 standard drinks) confers an RR of 15
- Using an additive risk model, combined use increases risk by 50%

Raitiola HS, Pukander JS. Etiological factors of laryngeal cancer. Acta Otolaryngol Suppl (Stockh) 1997;529:215–7
Maier H, Sennewald E, Heller GF, Weidauer H. Chronic alcohol consumption—the key risk factor for pharyngeal cancer. Otolaryngol Head Neck Surg 1994;110:168–73

HPV and laryngeal cancer?

- Retrospective study in Detroit
- Up to 27%
- Appears to have no effect on survival

Otolaryngol Head Neck Surg. 2012 Jan 20. [Epub ahead of print] Human Papillomavirus Outcomes in an Access-to-Care Laryngeal Cancer Cohort. Stephen JK et. al.

Describe the subsites of the larynx

- Supraglottis
  - 5 parts: suprahyoid and infrahyoid epiglottis, false cords, aryepiglottic folds, arytenoids
- Glottis
  - True vocal cords, floor of ventricle and region 5 mm below true vocal cords or 1 cm below lateral border of ventricle
  - 3 parts: true cords, anterior commissure and ventricle
- Subglottis
  - Region beyond 5 mm below true vocal cords or 1 cm below lateral border of ventricle to lower border of cricoid ring

What is the T staging of GLOTTIC carcinoma?

Glottis	
T1	Tumour limited to vocal cord(s) (may involve anterior or posterior commissure) with normal mobility
	T1a. Tumour limited to one vocal cord
	T1b. Tumour involves both vocal cords
T2	T2a. Tumour extends to supraglottis and/or subglottis with normal vocal cord mobility
	T2b. Tumour extends to supraglottis and/or subglottis with impaired vocal cord mobility
T3	Tumour limited to larynx with vocal cord fixation and/or invades paraglottic space, and/or with minor thyroid cartilage erosion (e.g. inner cortex)
T4a	Tumour invades through the thyroid cartilage, or invades tissues beyond the larynx, e.g., trachea, soft tissues of neck including deep/extrinsic muscle of tongue (genioglossus, hyoglossus, palatoglossus, and styloglossus), strap muscles, thyroid, oesophagus
T4b	Tumour invades prevertebral space, mediastinal structures, or encases carotid artery

What is the T staging of SUPRAGLOTTIC carcinoma?

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

What is the PRE- and PARAGLOTTIC SPACE? What is its significance?

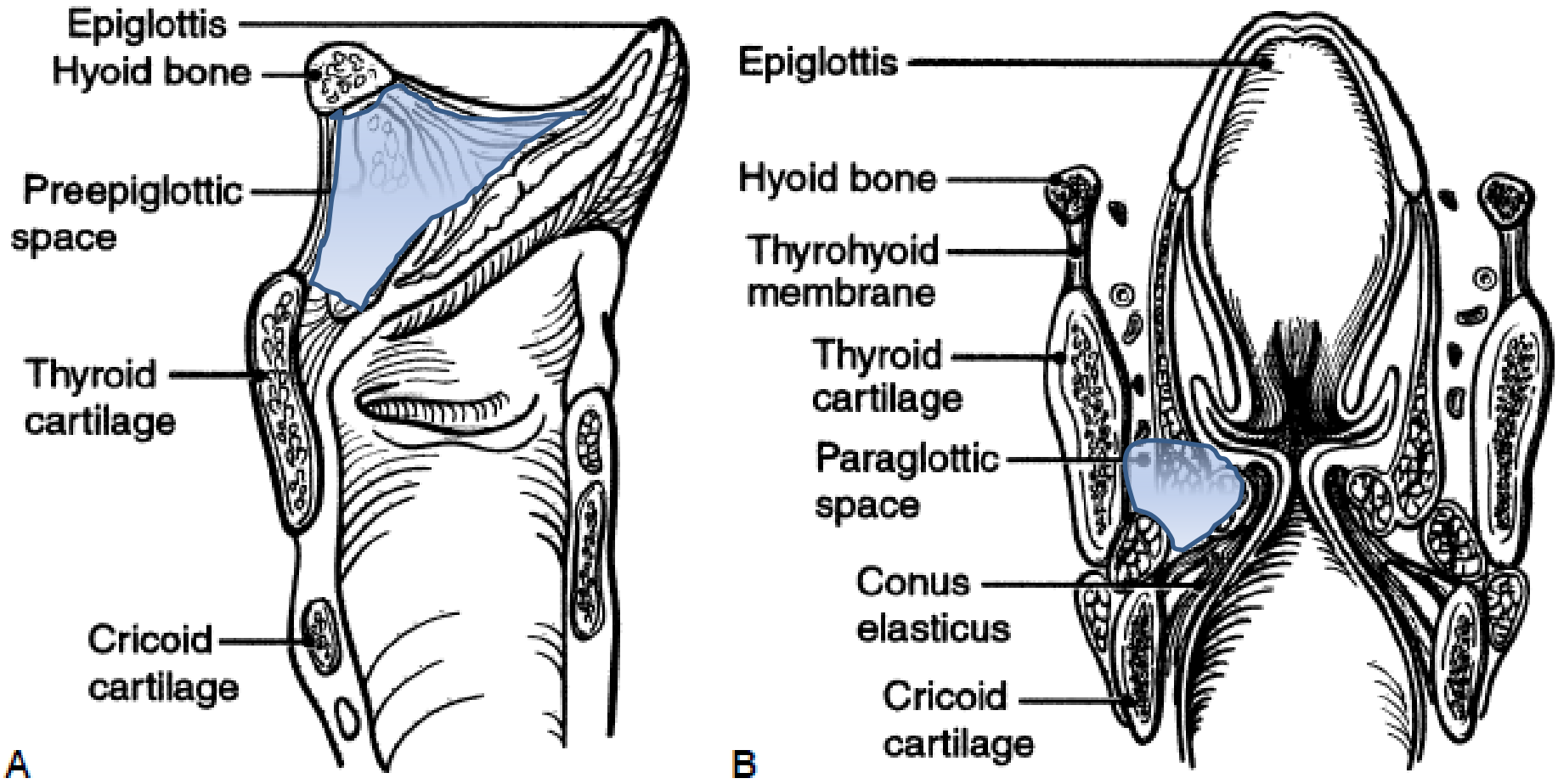
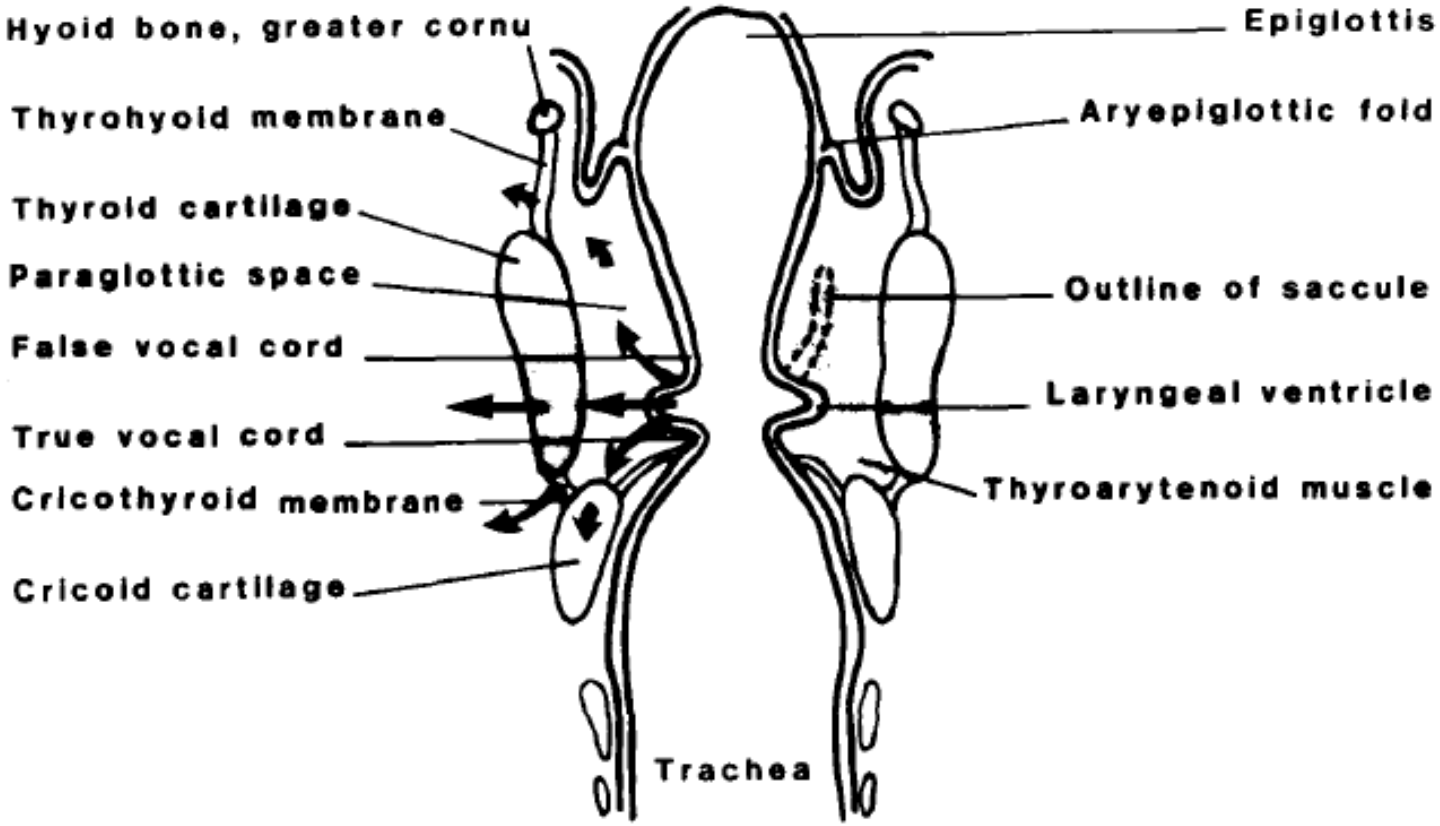


Figure 8–2. *A*, Sagittal section of larynx demonstrating the preepiglottic and *B*, coronal section of larynx demonstrating the paraglottic space.

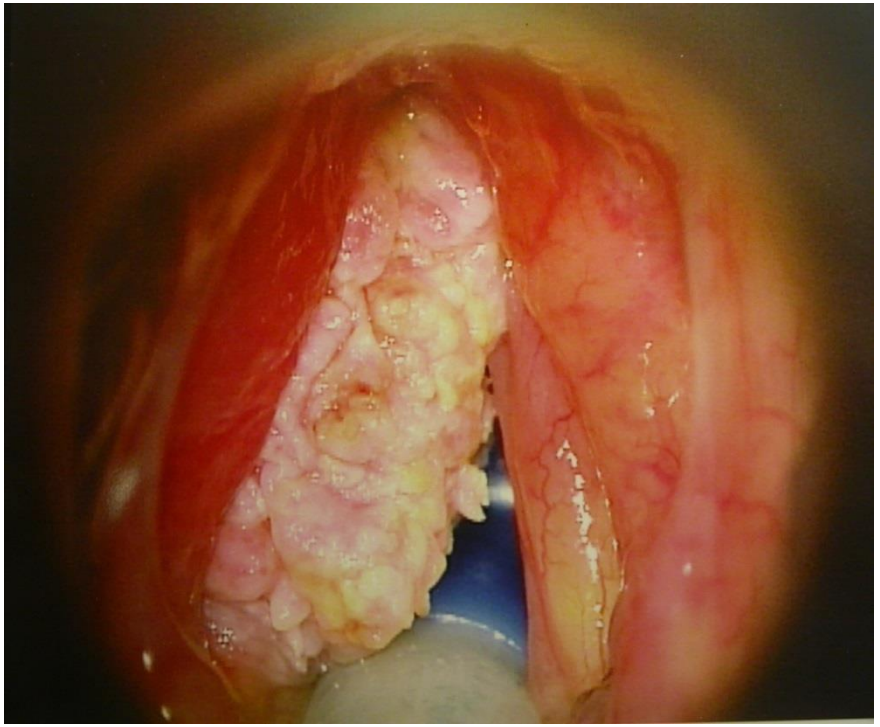
What is a TRANSGLOTTIC CARCINOMA?

term to describe the growth pattern of tumours that cross the laryngeal ventricle to involve both true and false vocal cords. Site of origin is uncertain

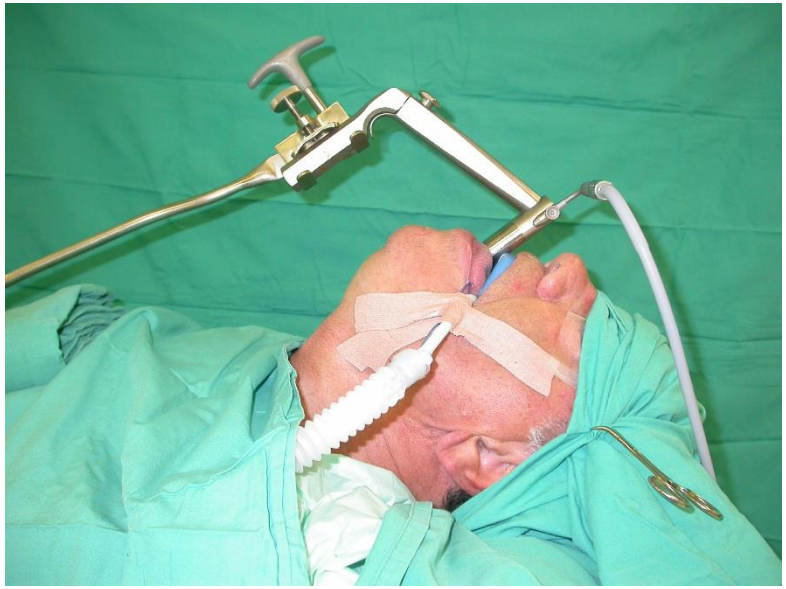


How would you assess a suspected laryngeal cancer?

- History, focus on symptoms of dysphonia, dyspnoea, stridor, dysphagia, aspiration, pain
- Office examination
  - Larynx / Pharynx
  - Neck
- Panendoscopy & ELMs
- Imaging



How do you perform a PANENDOSCOPY



- Neck and oral palpation. Assess tongue base
- Rigid oesophagoscopy
  - Turn scope to allow for examination of pyriform fossae
- ELMs
  - 0, and angled 30 and 70 degree telescopes
  - Subglottic extension
  - Photos

What about the ‘asphyxiating’ patient?

- Should you attempt intubation?
  - Discuss with anaethetist
  - Awake fibreoptic intubation is safest approach if you wish to attempt intubation
- Should you debulk a tumour?
  - Debulk all tumours that may obstruct
  - Laryngeal microdebriders better than laser
  - Ensure good haemostasis
- Should you do a tracheostomy?
  - ‘Do one when you first think of it!’
  - Effect on prognosis is a ‘secondary’ consideration

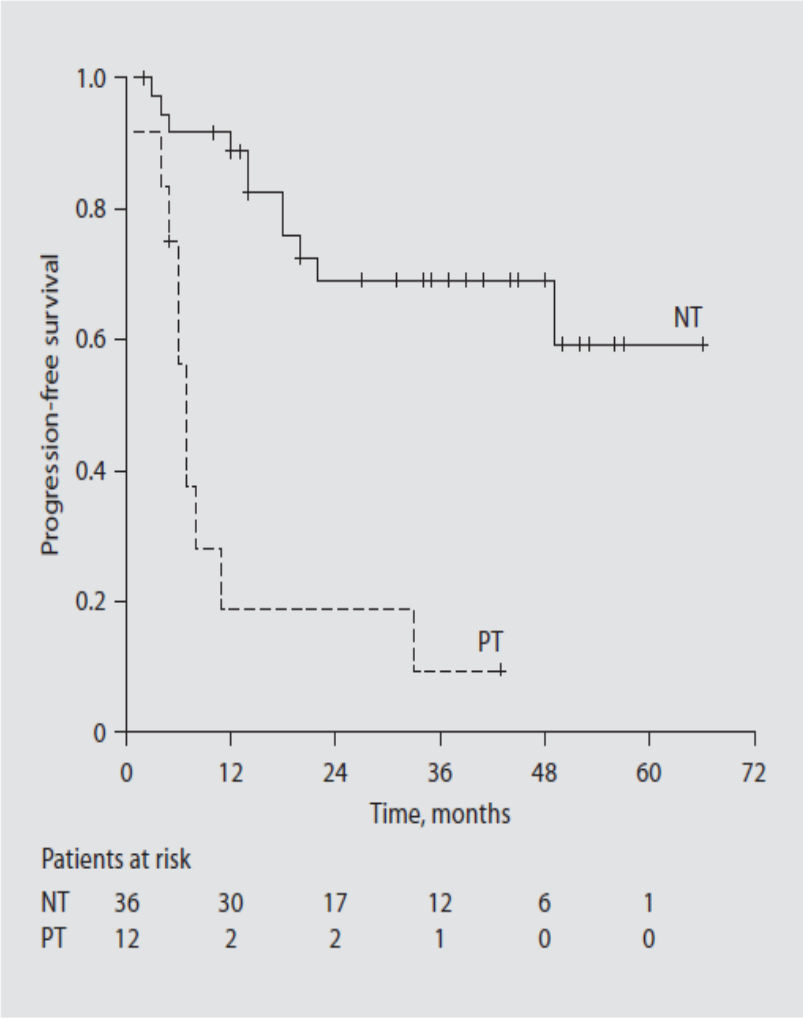


Fig. 1. Progression-free survival according to the presence of previous tracheotomy. PT = Previous tracheotomy; NT = no tracheotomy. HR 2.83; 95% CI 1.607–4.889; $p < 0.001$.

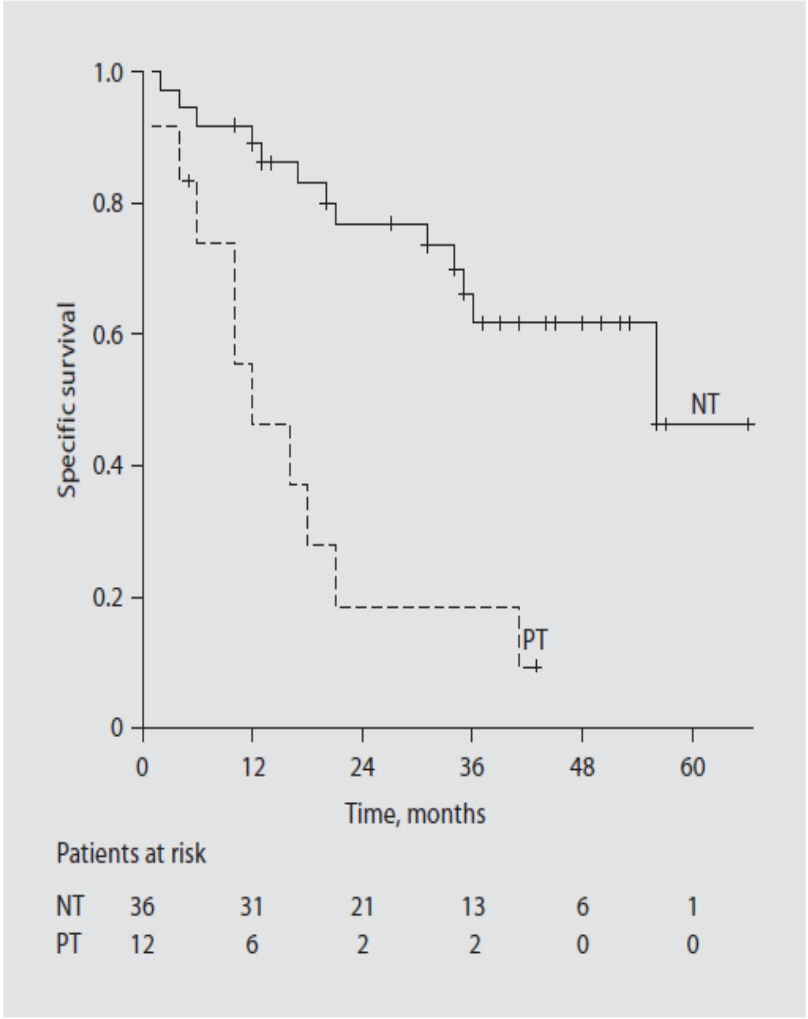


Fig. 2. Overall survival according to the presence of previous tracheotomy. PT = Previous tracheotomy; NT = no tracheotomy. HR 2.37; 95% CI 1.430–3.933; $p < 0.001$.

What imaging would you do?

- Contrast-enhanced CT of the larynx and thorax for all patients. CXR may be sufficient for stage I disease
- No need for bone scans / liver ultrasound
- MRI is fast becoming modality of choice and accuracy of staging is 10% more than CT
- But problems with
  - Movement artefact
  - Cost

Treatment

In the last 2 decades, 5-year survival of patients with laryngeal cancer has not changed dramatically…due to the lack of improvement in survival, significant efforts have been made to improve the quality of life in these patients. Paramount to this is preservation of a functional larynx

Pioneering work on patient preferences showed that approximately 25% of healthy individuals interviewed were willing to trade a 20% absolute difference in survival for the opportunity to save their voice

Anatomic preservation is not functional preservation!

Treatment

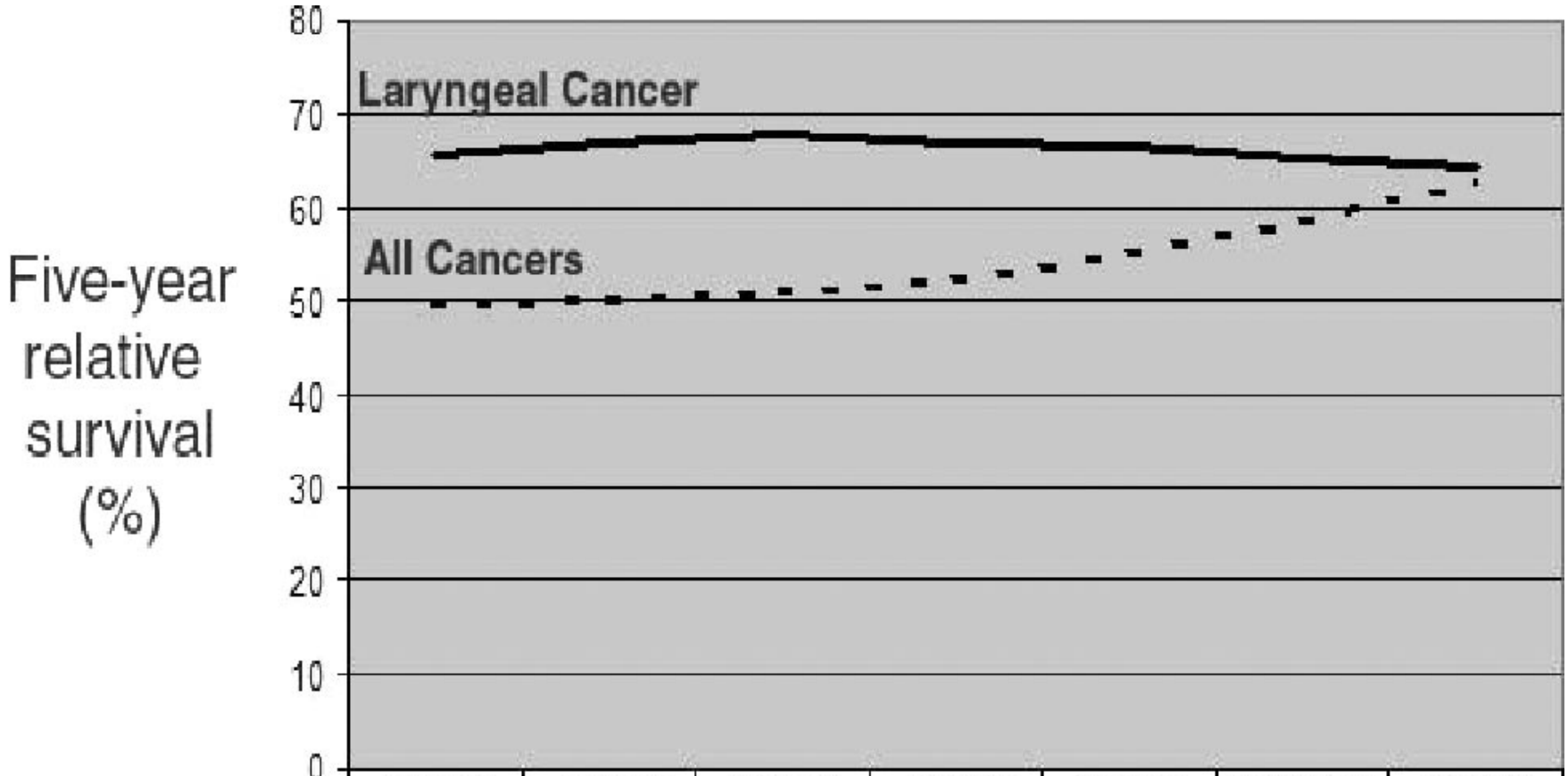
The Laryngoscope
Lippincott Williams & Wilkins, Inc.

Laryngeal Cancer in the United States: Changes in Demographics, Patterns of Care, and Survival

Henry T. Hoffman, MD, MS, FACS; Kimberly Porter, MPH; Lucy H. Karnell, PhD; Jay S. Cooper, MD; Randall S. Weber, MD; Corey J. Langer, MD; Kie-Kian Ang, MD, PhD; Greer Gay, PhD; Andrew Stewart, MA; Robert A. Robinson, MD, PhD

Background: **Survival has decreased among patients with laryngeal cancer during the past 2 decades in the United States. During this same period, there has been an increase in the nonsurgical treatment of laryngeal cancer.** ***Objective:*** **The objectives of this study were to identify trends in the demographics, management, and outcome of laryngeal cancer in the United States and to analyze factors contributing to the decreased survival.** ***Study Design:*** **The authors conducted a retrospective, longitudinal study of laryngeal cancer cases.** ***Methods:*** **Review of the National Cancer Data Base (NCDB) revealed 158,426 cases of glottic cancers classified as T3N0M0. Initial treatment of T3N0M0 laryngeal cancer (all sites) in the 1994 to 1996 period resulted in poor 5-year relative survival for those receiving either chemoradiation (59.2%) or irradiation alone (42.7%) when compared with that of patients after surgery with irradiation (65.2%) and surgery alone (63.3%). In contrast, identical 5-year relative survival (65.6%) rates were observed during this same period for the subset of T3N0M0 glottic cancers initially treated with either chemoradiation or surgery with irradiation.** ***Conclusions:*** **The decreased survival recorded for patients with laryngeal cancer**

Are we losing the battle…



	1974-76	1977-79	1980-82	1983-85	1986-88	1989-1991	1992-99
Laryngeal Cancer	65.7	67	68.1	67.1	66.7	65.5	64.7
All Cancers	49.6	50.1	51	52.5	55.3	58.8	63

Treatment

- Glottic
- Supraglottic
- Subglottic

Glottic - early stage (T1 -2a)

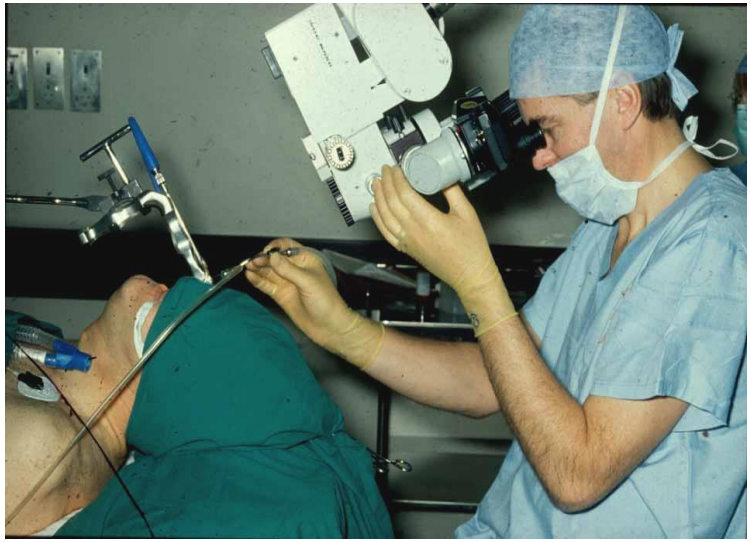
- T1-T2 disease should be treated with either radiation or larynx preserving surgery (transoral laser or open partial laryngeal surgery)
- Surgery should be with the aim of achieving clear margins
- Avoid combined modality therapy

- Usual RT is 50-52 Gy in 16# or 53-55 Gy in 20#
- No need for elective treatment of nodes
- Local control rates for T1a (90-93%) and T1b (85-89%) at 5 years

What are the types of laryngeal preservation surgery?

- Transoral Laser Micorsurgery (TLM)
- Vertical Partial Hemilarygectomy
- Fronto-lateral Partial Hemilaryngectomy
- Supraglottic Laryngectomy
- Supracricoid Laryngectomy + CHP / CHEP

Transoral Laser Surgery



- Utilises Carbon Dioxide laser beam to resect tumour
- Offers a quick alternative to radiotherapy
- Is organ sparing
- Useful in managing laryngeal recurrence

Fig. 1

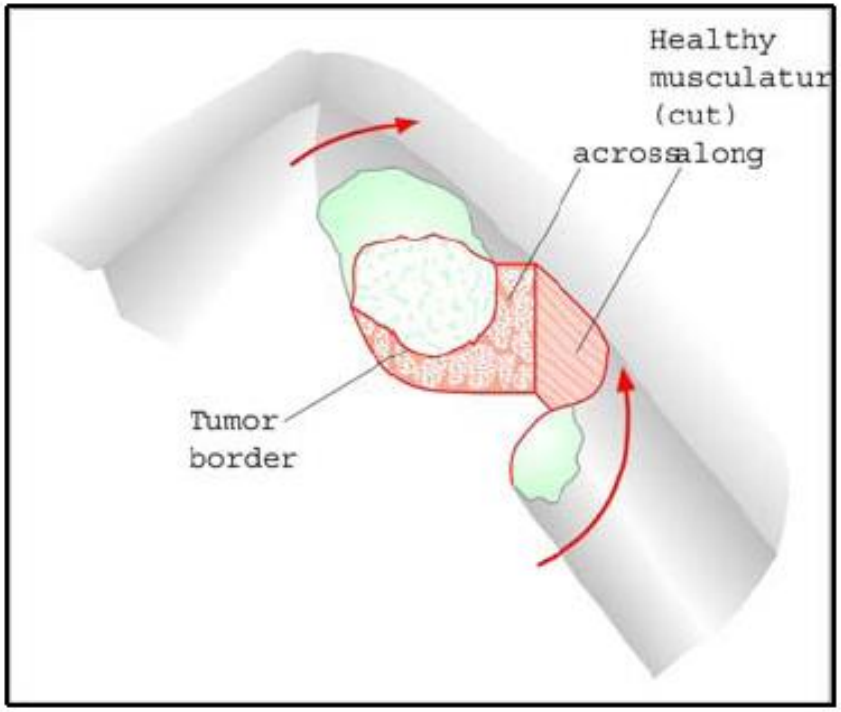
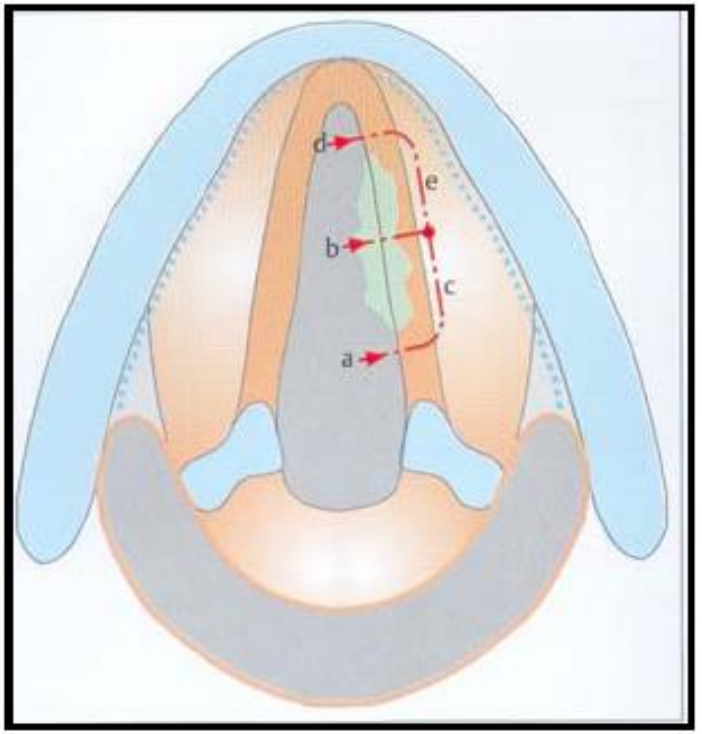


Fig. 2



Results of 333 cases of vocal cord carcinomas pT1a (1979 - 2001)

Tumor extent:	more than 1/3 of the vocal cord: 68%; anterior commissure involvement: 22%; only midcordal lesion: 14%.
Complication rate:	1.2% (postoperative hemorrhage 2, edema 2; no tracheostomy, no feeding tube
Median follow-up:	72 months

Table 1: Oncologic Results of Laser Microsurgery for pT1a vocal cord carcinomas (n=333)

5 yrs Kaplan-Meier local control rate	96.2%
Larynx preservation rate	97.6%
5 yrs Kaplan-Meier disease-specific survival rate	100%
5 yrs Kaplan-Meier overall survival rate	86.8%

Fig. 4

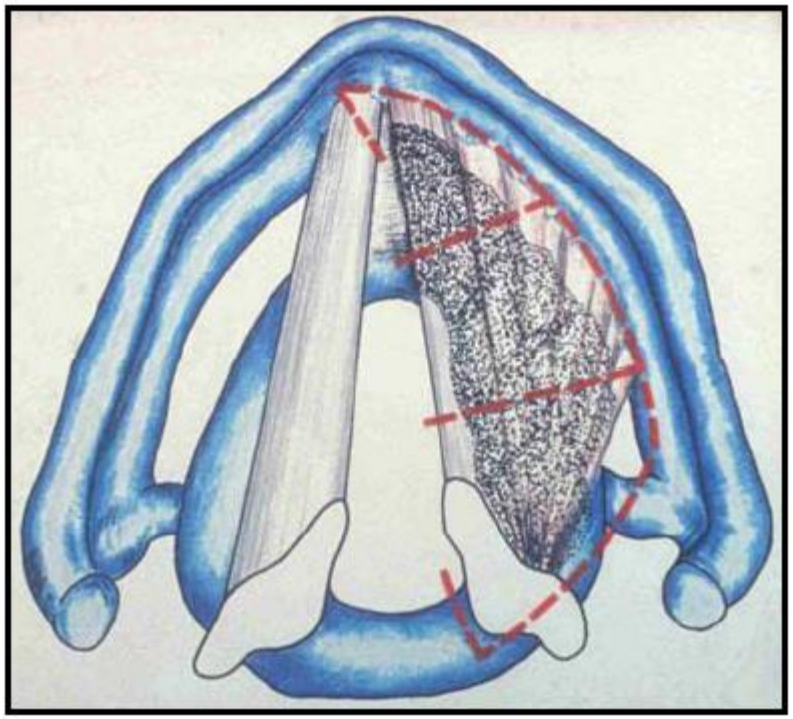
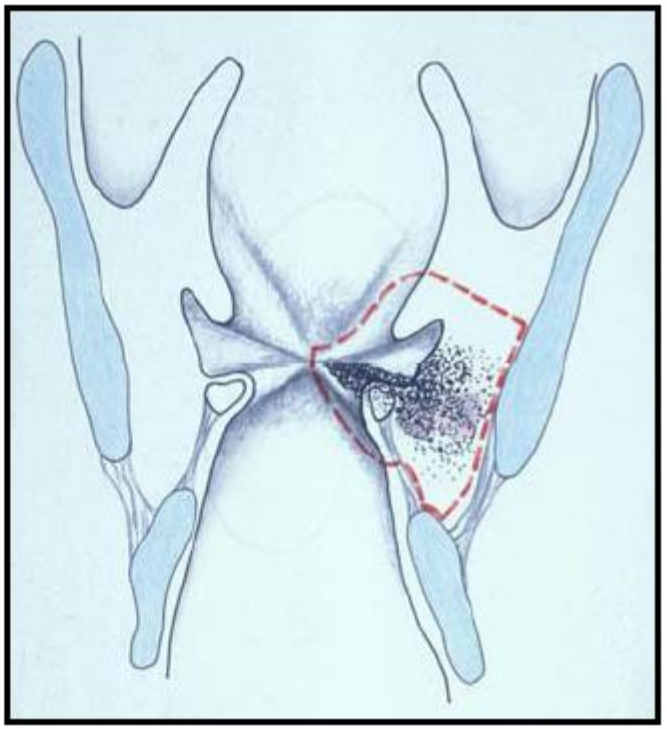


Fig. 5



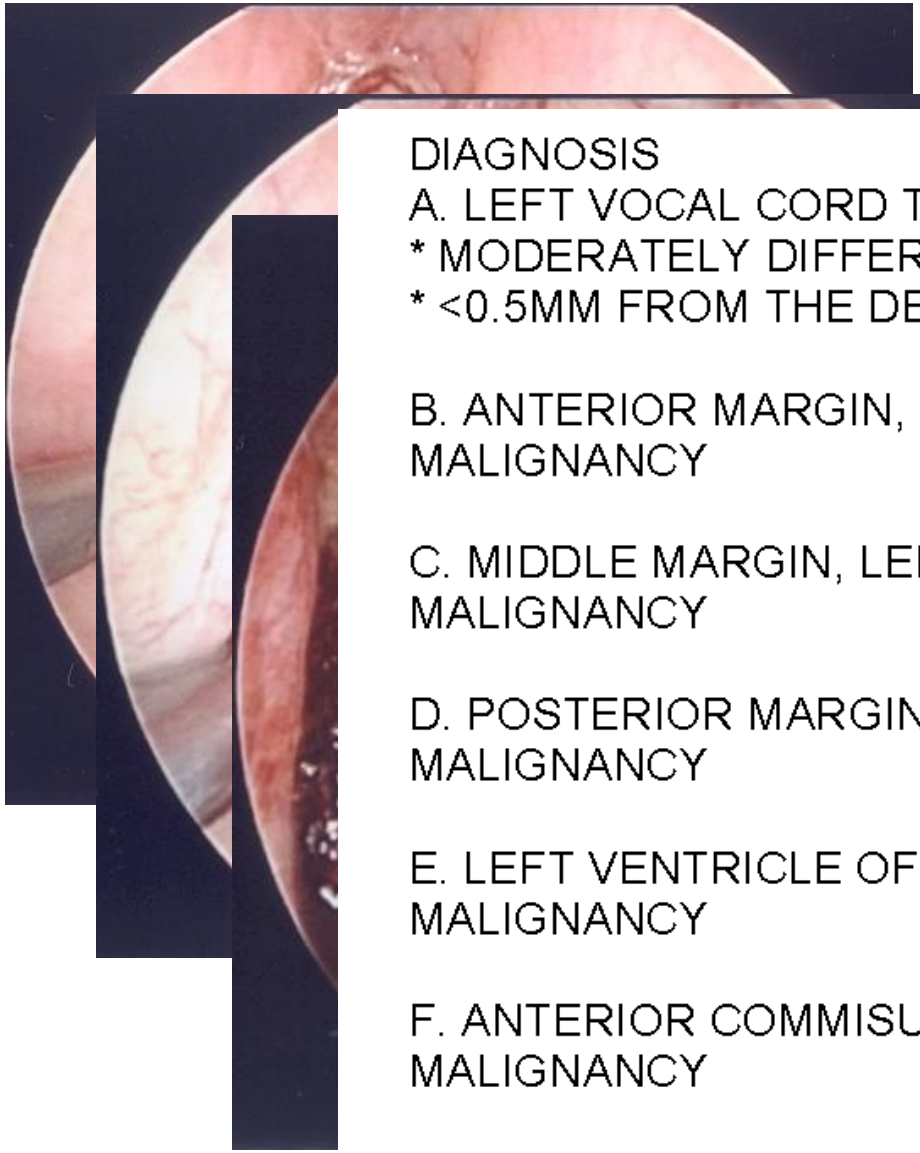
Results of 338 patients with pT2 and pT3 glottic cancer (1979 - 2001)

Stage Distribution: stage II 71%, stage III 27%, stage IV 2%
Median follow-up: 69 months

Table 3: Therapy of Glottic Carcinomas (n=338)

	pT2a (n=128)	**pT2b** (n=115)	**pT3** (n=95)
Laser	116 (91%)	87 (76%)	42 (44%)
Laser + ND	12	15	41
Laser + RT	-	11	3
Laser + ND + RT	-	2	9

	pT2a (n=128)	**pT2b** (n=115)	**pT3** (n=95)
5 yrs Kaplan-Meier local control rate	85%	65%	68%
5 yrs Kaplan-Meier larynx preservation rate	96%	84%	80%
5 yrs Kaplan-Meier recurrence-free survival rate	82%	61%	60%
5 yrs Kaplan-Meier overall survival rate	75%	65%	58%



DIAGNOSIS
A. LEFT VOCAL CORD TUMOUR:
* MODERATELY DIFFERENTIATED SQUAMOUS CELL CARCINOMA
* <0.5MM FROM THE DEEP MARGIN FOCALLY

B. ANTERIOR MARGIN, LEFT VOCAL CORD: NEGATIVE FOR MALIGNANCY

C. MIDDLE MARGIN, LEFT VOCAL CORD: NEGATIVE FOR MALIGNANCY

D. POSTERIOR MARGIN, LEFT VOCAL CORD: NEGATIVE FOR MALIGNANCY

E. LEFT VENTRICLE OF LEFT VOCAL CORD: NEGATIVE FOR MALIGNANCY

F. ANTERIOR COMMISURE, LEFT VOCAL CORD: NEGATIVE FOR MALIGNANCY

End of Report

Glottic – advanced stage

- Surgery then RT or ChemoRT and salvage for residual or recurrent disease?
- No organ-preserving strategy offers a survival advantage over laryngectomy and adjuvant therapy
- Through and through cartilage involvement necessitates surgery
- Cord fixation is unlikely to be reversible with CRT
- Levels II-IV should be treated in N0 neck and II-V in N+ neck

- Functional larynx with advanced disease is suitable for chemoRT
- Selected T3 cases may be amenable to partial laryngeal surgery
- Neoadjuvant chemo currently unproven but should use TPF
- New agents e.g. Cetuximab useful when conventional chemo is contraindicated e.g. in the elderly

Table 8–2. RESULTS OF CONVENTIONAL TREATMENT OF ADVANCED CARCINOMA OF THE LARYNX

Author	Year	No.	Type of Therapy	Stage III/IV (%)	5 yr Survival (%)
Kirchner[12]	1977	308	S/RT	100	54–56*
Harwood[13]	1979	353	RT	54	70
Harwood[43]	1983	410	RT	66	57
Yuen[41]	1984	192	S	100	77
		50	S/RT	100	91
Mendenhall[42]	1992	100	RT	100	74
		65	S±RT	100	63
Nguyen[11]	1996	116	S/RT	100	68
Myers[10]	1996	65	S±RT	100	62†

Survival rates refer to disease-free survival when available, otherwise they refer to overall survival.

* study included both laryngeal and non-laryngeal sites.

S = Surgery; RT = Radiation therapy; † 2-year survival.

Table 2. Phase III Studies of Induction Chemotherapy Followed by Radiation for Larynx Preservation

Study and Patient Characteristics	Study Arms	Treatment of Disease in the Neck	Indications for Salvage Surgery After Chemoradiation Therapy	Overall Survival		Rate of Larynx Preservation	
				%	Timeframe	%	Timeframe
VA Laryngeal Cancer Study[78] (n = 332) Stage III/IV disease (%), 57/43 (2/3 primary lesions of the supraglottis); T3/T4 (%), 65/26; N0-N1 (%), 72	Chemoradiation Arm						
	Induction chemotherapy (3 cycles standard cisplatin and fluorouracil) followed by radiation therapy (66-76 Gy to primary site 50-75 Gy to nodes)	Lymph node dissection if residual disease after radiation therapy	Less than partial response to chemotherapy after 2 cycles; residual disease at biopsy 12 weeks after completion of radiation therapy	68	2 years	66	2 years
	Surgery Arm						
	Standard total laryngectomy followed by radiation therapy (50 Gy [no residual disease], up to 73 Gy [residual disease])	Lymph node dissection for all patients	—	68	2 years	—	
GETTEC Study[82] (n = 68) Stage III/IV (%), not provided; T3/T4 (%), 100/0; N0-N1 (%), 93	Chemoradiation Arm						
	Induction chemotherapy (3 cycles standard cisplatin and fluorouracil) followed by radiation therapy (65-70 Gy to primary site 50-70 Gy to nodes)	Lymph node dissection if salvage surgery only	Less than 80% regression of tumor after chemotherapy, lack of return of laryngeal mobility	69	2 years	42	Median, 8 years
	Surgery Arm						
	Standard total laryngectomy followed by radiation therapy (50 Gy [no residual disease], up to 70 Gy [residual disease])	Lymph node dissection for all patients	—	84	2 years		
				$P = .006$			

Intergroup Head and Neck Trial (RTOG 91-11)
(n 547) Stage III/IV (%), 65/35; T3/T4 (%),79/10

Table 3. Phase III Studies of Concurrent Chemoradiation Therapy for Larynx Preservation

Study Arms	Treatment of Disease in the Neck	Indications for Salvage Surgery	Overall Survival %	Overall Survival Timeframe	Larynx Preservation %	Larynx Preservation Timeframe	Toxicity
					Radiation therapy alone		
			75	2 years	70	2 years	Swallowing difficulties in 18% at 1 year and in 14% at 2 years
			56	5 years			
Primary radiation therapy: 70 Gy to primary site, 50-70 Gy to nodes Induction chemotherapy: cisplatin/fluorouracil (3 cycles) followed by radiation therapy for those who had a response (if salvage surgery, 50-70 Gy administered postoperatively) Concurrent chemoradiation: high-dose cisplatin (days 1, 22, 43) plus 70 Gy to primary site; 50-70 Gy to nodes	Lymph node dissection after completion of radiation therapy for all patients with clinical involvement of nodes before beginning of treatment	Less than partial response to induction chemotherapy; residual disease found at biopsy after completion of radiation therapy			Induction chemotherapy		
			76	2 years	75	2 years	Rate of grade 3 or 4 toxicity during radiation no different from that for radiation therapy–alone arm; swallowing difficulties in 9% at 1 year and 16% at 2 years
			55	5 years	$P = .27$ *v* radiation therapy–alone arm		
					Concurrent chemoradiation		
			74	2 years	88	2 years	Highest rate of grade 3 or 4 acute toxicity; no increase in late toxic effects; swallowing difficulties in 26% at 1 year and in 15% at 2 years
			54	5 years	$P < .001$ *v* radiation therapy–alone arm; $P = .005$ *v* induction-chemotherapy arm		

What about laryngeal dysplasia?

- What is the risk of dysplasia becoming carcinoma?
  - 16.7%
- What is the risk of severe dysplasia becoming carcinoma
  - 30.4%
- What is the difference between severe dysplasia and carcinoma in situ?
  - NONE!

- How do you manage mild-moderate dysplasia?
  - Excision
- What is wide spread?
  - Observe
  - Excise if there is change in appearance
- How do you manage severe dysplasia / carcinoma in situ?
  - Excise
  - Radiotherapy if persistent or widespread

THANK YOU!