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Laryngeal Cancer

David M. Cognetti, MD
Associate Professor
Vice Chair, Department of Otolaryngology –Head and Neck Surgery
Thomas Jefferson University

September 14, 2019

AMERICAN ACADEMY OF OTOLARYNGOLOGY– HEAD AND NECK SURGERY

AHNS/AAO
Head and Neck Surgery Course for Residents and Fellows

AMERICAN HEAD & NECK SOCIETY

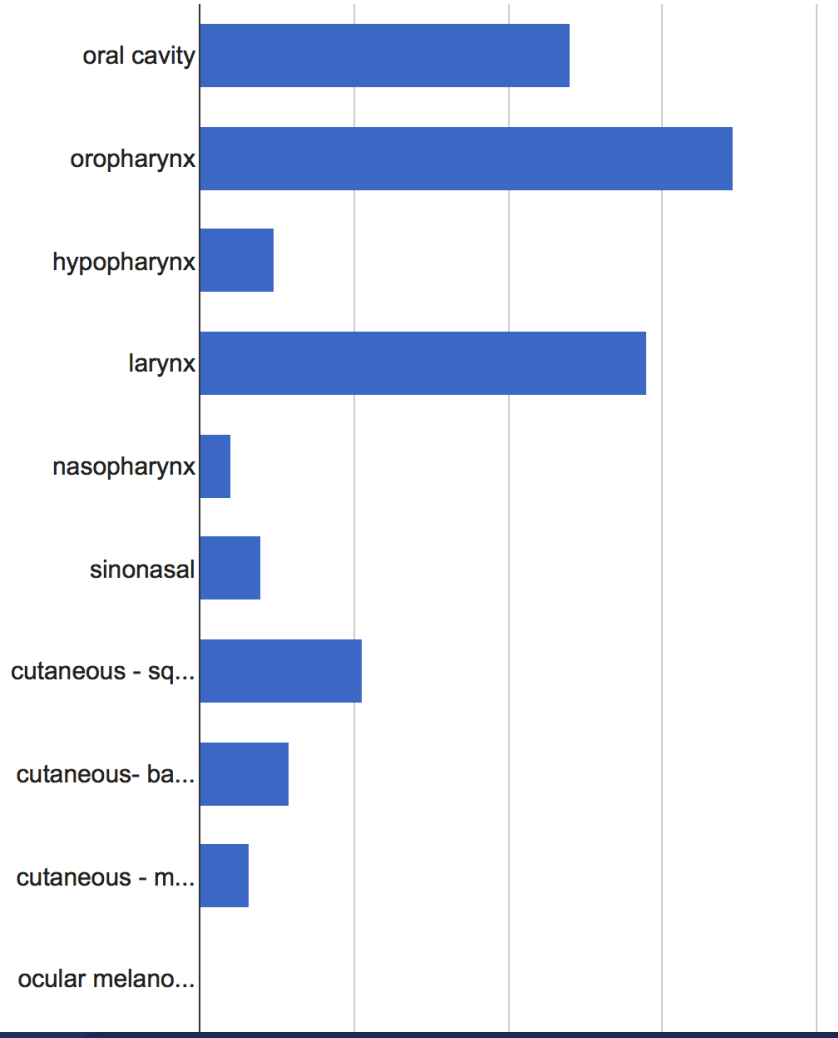
Epidemiology

- 12,630 new cases
- 3,610 estimated deaths
- 50% with advanced stage
- 62.9% 5-year relative survival
- 4:1 male:female

1. R. Siegel, J. Ma, Z. Zou, et al. Cancer statistics, 2014 CA Cancer J Clin, 64 (2014), pp. 9–29

2. Ries LAG, Harkins D, Krapcho M, Mariotto A, Miller BA, Feuer EJ, Clegg L, Eisner MP, Horner MJ, Howlader N, Hayat M, Hankey BF, Edwards BK (eds). SEER Cancer Statistics Review, 1975-2004, National Cancer Institute. Bethesda, MD, http://seer.cancer.gov/csr/1975_2004/, based on November 2006 SEER data submission, posted to the SEER web site 2007

Counts/frequency: oral cavity (120, 16.3%), oropharynx (173, 23.5%), hypopharynx (24, 3.3%), larynx (145, 19.7%), nasopharynx (10, 1.4%), sinonasal (20, 2.7%), cutaneous - squamous cell ca (53, 7.2%), cutaneous- basal cell ca (29, 3.9%), cutaneous - melanoma (16, 2.2%), ocular melanoma (conjunctival) (0, 0.0%), lacrimal (3, 0.4%), salivary - parotid (71, 9.7%), salivary - submandibular (3, 0.4%), salivary - minor salivary (0, 0.0%), thyroid (poorly differentiated, anaplastic, medullary) (6, 0.8%), lymphoma (0, 0.0%), unknown primary (24, 3.3%), other (38, 5.2%)



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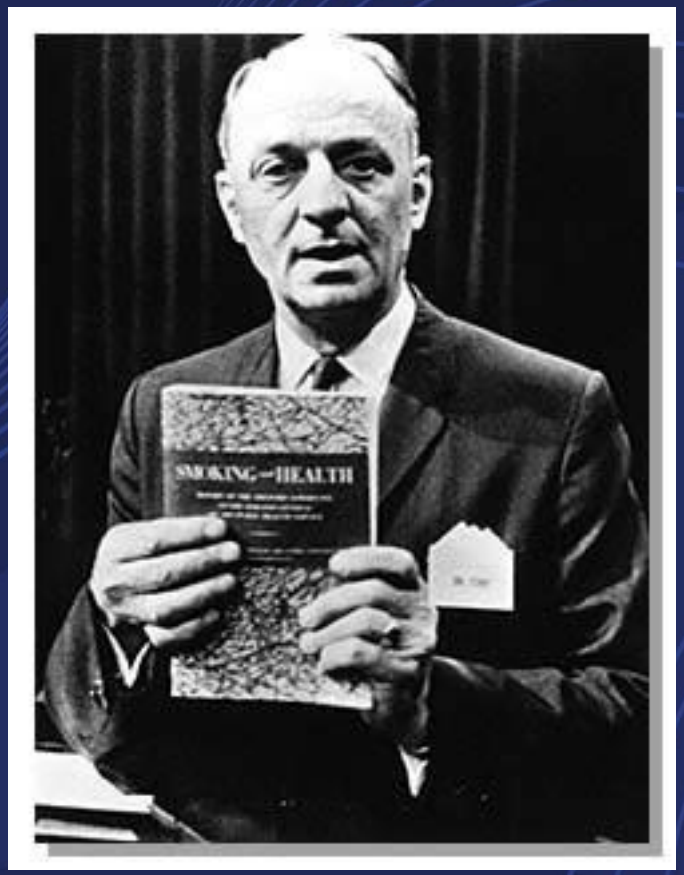
Smoking Causes Cancer



http://tobacco.health.usyd.edu.au

Surgeon General Luther Terry, MD
January 11, 1964

Surgeon General's Report 1964

- First widely publicized, official recognition of the dangers of smoking
- Findings based on animal studies, clinical and autopsy observations, retrospective reviews, and seven prospective trials with a total of 1,123,00 subjects
- Documented causal relationship between smoking and cancer of the lung and larynx
- Association between smoking and heart disease was suggested

http://profiles.nlm.nih.gov

Surgeon General's Report 1964

TABLE 2.[1]—*Expected and observed deaths for smokers of cigarettes only and mortality ratios in seven prospective studies*

Underlying cause of death	Expected deaths	Observed deaths	Mortality ratio
Cancer of lung (162-3) [2]	170.3	1,833	10.8
Bronchitis and emphysema (502, 521.1)	89.5	546	6.1
Cancer of larynx (161)	14.0	75	5.4
Oral cancer (140-8)	37.0	152	4.1
Cancer of esophagus (150)	33.7	113	3.4
Stomach and duodenal ulcers (540, 541)	105.1	294	2.8
Other circulatory diseases (451-68)	254.0	649	2.6
Cirrhosis of liver (581)	169.2	379	2.2
Cancer of bladder (181)	111.6	216	1.9
Coronary artery disease (420)	6,430.7	11,177	1.7
Other heart diseases (421-2, 430-4)	526.0	868	1.7
Hypertensive heart (440-3)	409.2	631	1.5
General arteriosclerosis (450)	210.7	310	1.5
Cancer of kidney (180)	79.0	120	1.5
All causes [3]	15,653.9	23,223	1.68

[1] Abridged from Table 26, Chapter 8, Mortality.
[2] International Statistical Classification numbers in parentheses.
[3] Includes all other causes of death as well as those listed above.

Surgeon General's Report 1964

THE COMMITTEE'S JUDGMENT IN BRIEF

On the basis of prolonged study and evaluation of many lines of converging evidence, the Committee makes the following judgment:

Cigarette smoking is a health hazard of sufficient importance in the United States to warrant appropriate remedial action.

Smoking Trends

1964

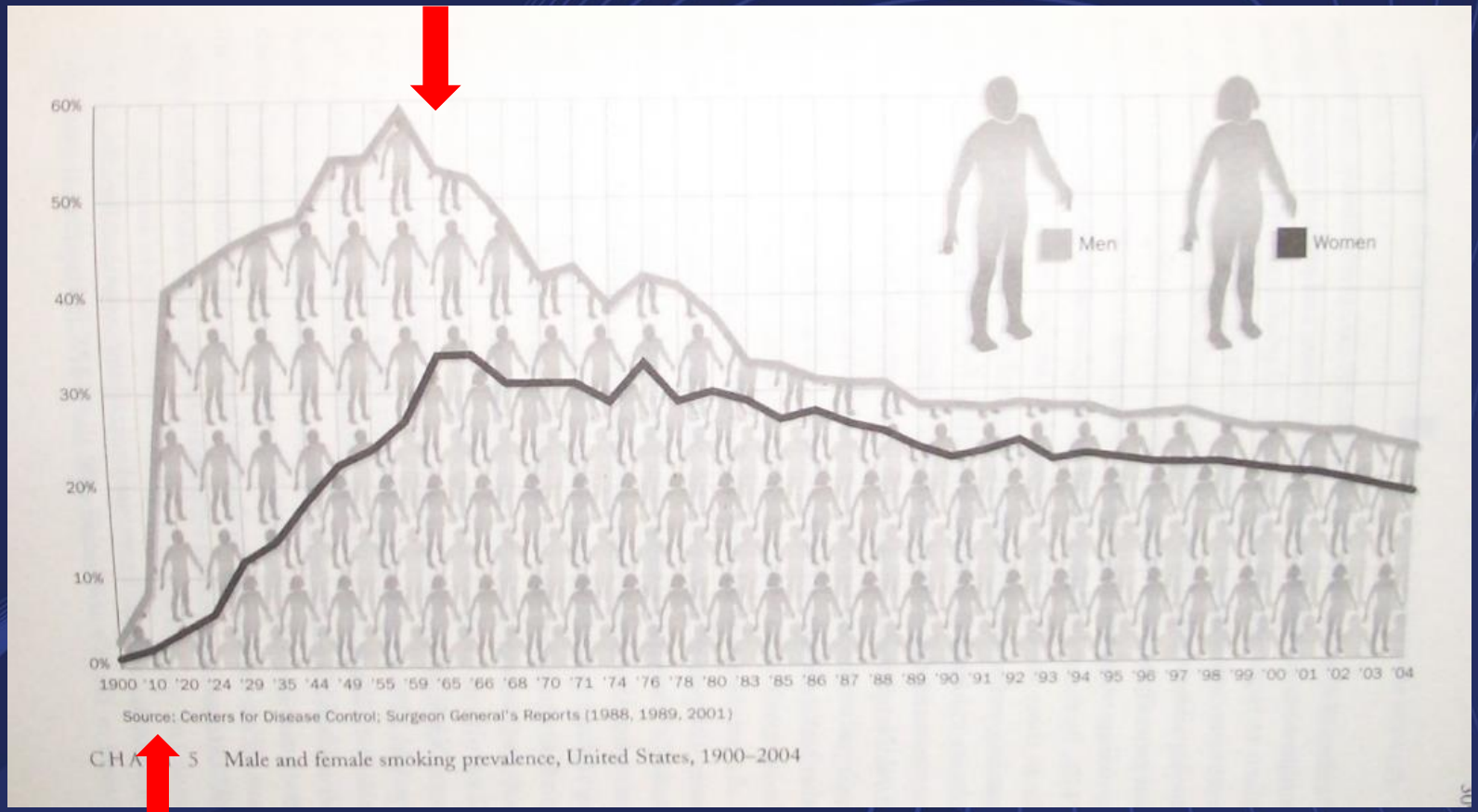


CHART 5 Male and female smoking prevalence, United States, 1900–2004

1910

Brandt, Alan M. (2007.) *The Cigarette Century: The rise, fall, and deadly persistance of the product that defined America.* New York: Basic Books

Categories
U.S. news
World news
Politics
Business
Entertainment
Sports
Tech & science
Health
Diet and nutrition
Cold and flu
Women's health
Men's health
Kids and parenting
Sexual health
Pet health
Fitness

U.S. smoking rate under 20 percent for 1st time

Cigarettes still kill nearly half a million people a year, CDC report reveals

Video

Launch

More Americans butting out

Nov. 13: Public health officials reported Thursday that for the first time on record, the smoking rate in the U.S. country has dropped below 20 percent of the total adult population. NBC's Brian Williams reports.

Nightly News

Trends in Head and Neck Cancer Incidence in Relation to Smoking Prevalence

An Emerging Epidemic of Human Papillomavirus-Associated Cancers?

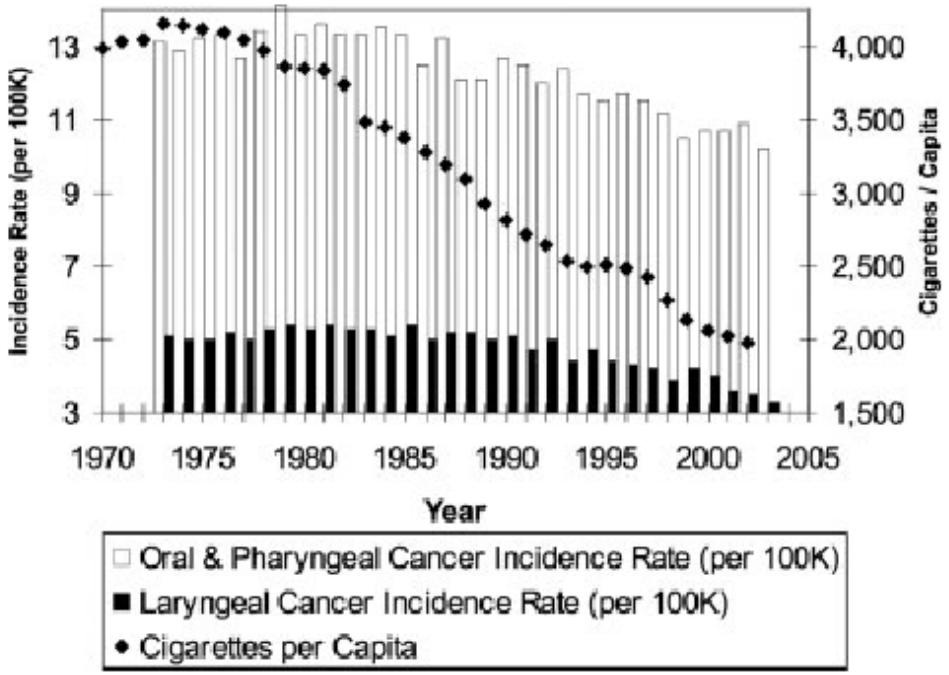
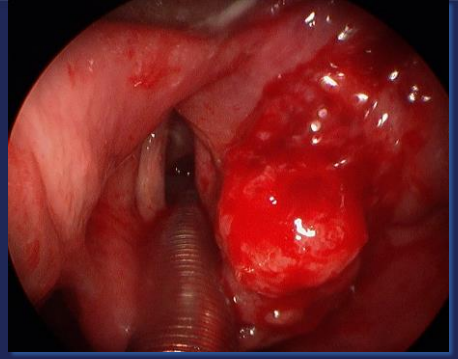


FIGURE 4. Per capita yearly consumption of cigarettes and annual age-adjusted (to U.S. 2000 standard) incidence rates of oral/pharyngeal and laryngeal cancers per 100 thousand persons in the U.S.[6,25]



Staging

Table 3

2002 American Joint Committee on Cancer (AJCC)
TNM Staging System for the Larynx

Primary Tumor (T)

TX Primary tumor cannot be assessed
T0 No evidence of primary tumor
Tis Carcinoma *in situ*

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 glottis or region outside the supraglottis (eg, 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, pre-epiglottic tissues, paraglottic space, and/or minor thyroid cartilage erosion (eg, inner cortex)
T4a Tumor invades through the thyroid cartilage and/or invades tissues beyond the larynx (eg, trachea, soft tissues of neck including deep extrinsic muscle 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 the vocal cord(s) (may involve anterior or posterior commissure) with normal mobility
T1a Tumor limited to one vocal cord
T1b Tumor involves both vocal cords
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 (eg, inner cortex)
T4a Tumor invades through the thyroid cartilage and/or invades tissues beyond the larynx (eg, trachea, soft tissues of neck including deep extrinsic muscle 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 invades tissues beyond the larynx (eg, trachea, soft tissues of neck including deep extrinsic muscle of the tongue, strap muscles, thyroid, or esophagus)
T4b Tumor invades prevertebral space, encases carotid artery, or invades mediastinal structures

Regional Lymph Nodes (N)

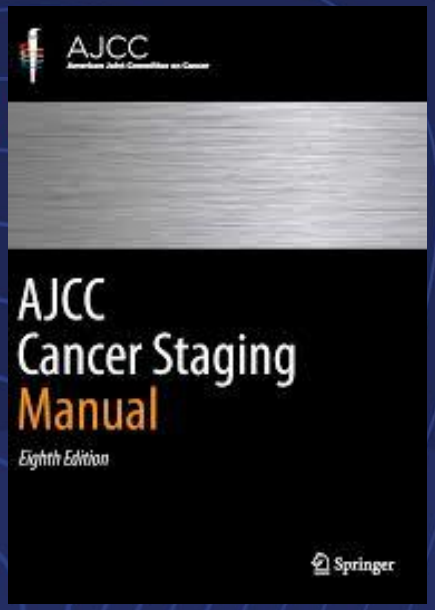
NX Regional lymph nodes cannot be assessed
N0 No regional lymph node metastasis
N1 Metastasis in a single ipsilateral lymph node, 3 cm or less in greatest dimension
N2 Metastasis in a single ipsilateral lymph node, more than 3 cm but not more than 6 cm in greatest dimension; or in multiple ipsilateral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

MX Distant metastasis cannot be assessed
M0 No distant metastasis
M1 Distant metastasis

Continued...

Staging



Supraglottis

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

Glottis

T1	Tumor limited to the vocal fold(s) (may involve anterior or posterior commissure) with normal mobility
T1a	Tumor limited to one vocal fold
T1b	Tumor involves both vocal folds
T2	Tumor extends to the supraglottis and/or subglottis, and/or with impaired vocal fold mobility
T3	Tumor limited to the larynx with vocal fold fixation and/or invasion of paraglottic space, and/or inner cortex of the thyroid cartilage
T4a	Moderately advanced local disease Tumor invades the outer cortex of the thyroid cartilage and/or invades tissues beyond the larynx (e.g., trachea, soft tissues of the neck, including deep extrinsic muscle of the tongue, strap muscles, thyroid, or esophagus)
T4b	Very advanced local disease Tumor invades prevertebral space, encases carotid artery, or invades mediastinal structures

Subglottis

T1	Tumor limited to the subglottis
T2	Tumor extends to the vocal cord(s) with normal or impaired mobility.
T3	Tumor imited to the larynx with vocal fold fixation.
T4a	Moderately advanced local disease Tumor invades cricoid or 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)
T4b	Very advanced local disease Tumor invades prevertebral space, encases carotid artery, or invades mediastinal structures

8th edition HPV negative neck staging

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TABLE 10. Regional Lymph Nodes Pathologic Category Criteria (pN)[a]

N CATEGORY	N CRITERIA[b]
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 and ENE-negative
N2	Metastasis in a single ipsilateral lymph node, 3 cm or less in greatest dimension and ENE-positive; *or* more than 3 cm but not more than 6 cm in greatest dimension and ENE-negative; or metastases in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension and ENE-negative; *or* metastasis in bilateral or contralateral lymph nodes, none more than 6 cm in greatest dimension, ENE-negative
N2a	Metastasis in a single ipsilateral or contralateral lymph node 3 cm or less in greatest dimension and ENE-positive; *or* metastasis in a single ipsilateral lymph node more than 3 cm but not more than 6 cm in greatest dimension and ENE-negative
N2b	Metastasis in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension and ENE-negative
N2c	Metastasis in bilateral or contralateral lymph nodes, none more than 6 cm in greatest dimension and ENE-negative
N3	Metastasis in a lymph node more than 6 cm in greatest dimension and ENE-negative, or metastasis in a single ipsilateral lymph node more than 3 cm in greatest dimension and ENE-positive; *or* metastasis in multiple ipsilateral, contralateral, or bilateral lymph nodes, with any ENE-positive
N3a	Metastasis in a lymph node more than 6 cm in greatest dimension and ENE-negative
N3b	Metastasis in a single ipsilateral node more than 3 cm in greatest dimension and ENE-positive; *or* metastasis in multiple ipsilateral, contralateral, or bilateral lymph nodes, with any ENE-positive

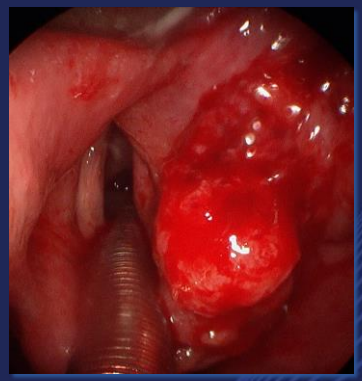
Abbreviations: ENE, extranodal extension. [a]Table 10 is used with the permission of the American Joint Committee on Cancer (AJCC), Chicago, Illinois. The original source for this material is the AJCC Cancer Staging Manual, Eighth Edition (2017) published by Springer Science and Business Media LLC (springer.com) (Amin MB, Edge SB, Greene FL, et al, eds. AJCC Cancer Staging Manual. 8th ed. New York: Springer; 2017, with permission[2]). [b]Note that a designation of "U" or "L" may be used for any N stage to indicate metastasis above the lower border of the cricoid (U) or below the lower border of the cricoid (L). Similarly, clinical and pathologic ENE should be recorded as ENE-negative or ENE-positive.

Subsites

Sites of the Larynx

Site	*Subsite*
Supraglottis	Suprahyoid epiglottis Infrahyoid epiglottis Aryepiglottic folds (laryngeal aspect) Arytenoids Ventricular bands (false vocal folds)
Glottis	True vocal folds, including anterior and posterior commissures; occupies a horizontal place 1 cm in thickness, extending inferiorly from the lateral margin of the ventricle
Subglottis	Region extending from the lower boundary of the glottis to the lower margin of the cricoid cartilage

Subsites



Supraglottic

- Often present advanced stage (dysphagia; otalgia; neck mass)
- High rate of neck metastases
- Radiation is often required

Glottic

- Often present early stage (hoarseness)
- Low rate of neck metastases
- Radiation can often be avoided

Evolution of Treatment

- 1900's - 1940's
  - high surgical complications
  - poor radiation results
- 1940's - 1970's
  - improved peri-operative care and surgical outcomes
  - improved radiation techniques and outcomes
- 1970's - 2000's
  - increased role of chemotherapy
  - increased focus on functional preservation
  - Improved reconstruction
- 2000s….
  - Targeted therapies
  - Intensity-modulated radiation therapy
  - Advanced surgical technologies (robotics, etc)
  - Immunotherapy

Evolution of Treatment

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Induction chemotherapy

- 1980 -1986
  - Several pilot studies showed high response rates and tolerable toxicities
- 1987
  - Head and Neck Contracts Program - randomized trial found no survival benefit

Head and Neck Contracts Program. Cancer 1987; 60:301-311

- 1988
  - Southwest Oncology Group (SWOG) - randomized trial found no survival benefit

Schuller DE, Wilson, et al. Laryngoscope 1988; 98:1205-1211

*No survival benefit but response to induction CT predicted response to further treatment

Evolution of Treatment

Laryngeal Preservation

- 1991- Department of Veterans Affairs Laryngeal Cancer Group Study
  - Randomized trial of Stage III and Stage IV laryngeal cancers
  - Induction CT followed by RT vs. surgery and post-operative RT
  - 2-year survival was 68% for both groups
  - Laryngeal preservation was achieved in 64% of induction CT group

INDUCTION CHEMOTHERAPY PLUS RADIATION COMPARED WITH SURGERY PLUS RADIATION IN PATIENTS WITH ADVANCED LARYNGEAL CANCER

THE DEPARTMENT OF VETERANS AFFAIRS LARYNGEAL CANCER STUDY GROUP*

(N Engl J Med 1991; 324:1685-90.)

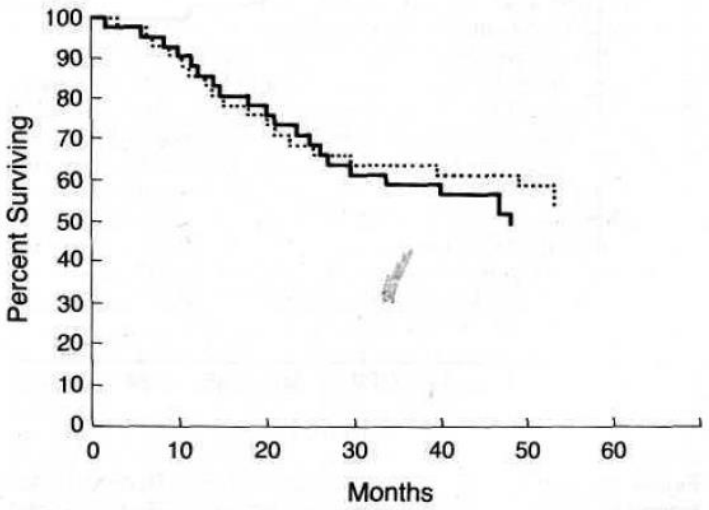


Figure 1. Overall Survival of 332 Patients Randomly Assigned to Induction Chemotherapy and Radiation Therapy (Solid Line) or Conventional Laryngectomy and Postoperative Radiation (Dotted Line).

Survival rates at two years were 68 percent for both groups (P = 0.9846). The median follow-up was 33 months.

Otolaryngology–Head and Neck Surgery (2006) 135, 831-837

Changes in treatment of advanced laryngeal cancer 1985-2001

Amy Y. Chen, MD, MPH, Nicole Schrag, MSPH, Yongping Hao, PhD, W. Dana Flanders, MD, DSc, James Kepner, PhD, Andrew Stewart, MS, and **Elizabeth Ward, PhD,** Atlanta, Georgia; and Chicago, Illinois

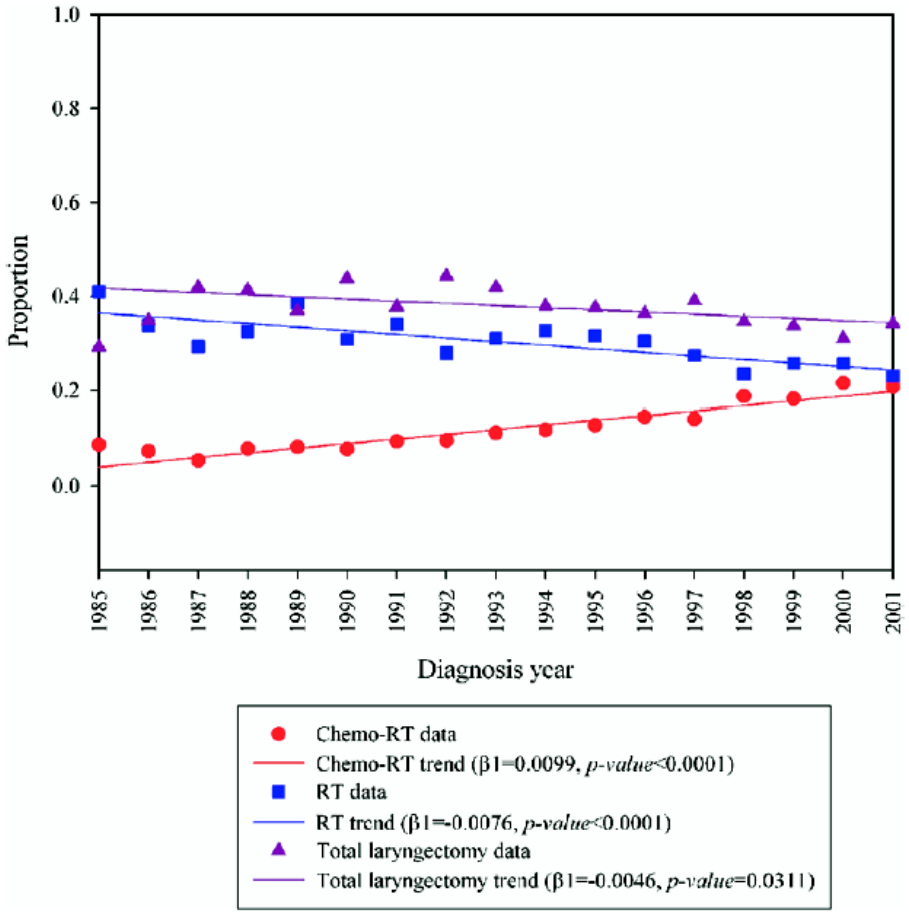


Figure 3 Trends in treatment for advanced-stage laryngeal cancer, 1985-2001, NCDB data, N = 35,921.

Evolution of Treatment

- Randomized trial of Stage III and IV laryngeal cancers
- Induction CT followed by RT vs. concurrent CRT vs. RT alone
- Laryngeal preservation and locoregional control

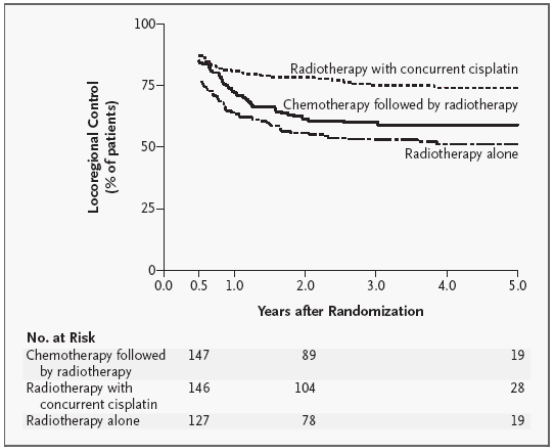
  CRT > CT then RT > RT alone
- Overall survival was similar in all 3 groups

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 NOVEMBER 27, 2003 VOL. 349 NO. 22

Concurrent Chemotherapy and Radiotherapy for Organ Preservation in Advanced Laryngeal Cancer

Arlene A. Forastiere, M.D., Helmuth Goepfert, M.D., Moshe Maor, M.D., Thomas F. Pajak, Ph.D., Randal Weber, M.D., William Morrison, M.D., Bonnie Glisson, M.D., Andy Trotti, M.D., John A. Ridge, M.D., Ph.D., Clifford Chao, M.D., Glen Peters, M.D., Ding-Jen Lee, M.D., Ph.D., Andrea Leaf, M.D., John Ensley, M.D., and Jay Cooper, M.D.



No. at Risk			
Chemotherapy followed by radiotherapy	147	89	19
Radiotherapy with concurrent cisplatin	146	104	28
Radiotherapy alone	127	78	19

Figure 2. Rates of Locoregional Control According to the Treatment Group.

At two years, the rates of locoregional control were as follows: 61 percent (95 percent confidence interval, 54 to 69 percent) among the patients who received induction cisplatin plus fluorouracil followed by radiotherapy, 78 percent (95 percent confidence interval, 72 to 85 percent) among those who received radiotherapy with concurrent cisplatin, and 56 percent (95 percent confidence interval, 48 to 63 percent) among those who received radiotherapy alone ($P=0.003$ for the comparison between induction cisplatin plus fluorouracil followed by radiotherapy and radiotherapy with concurrent cisplatin, $P=0.16$ for the comparison between induction cisplatin plus fluorouracil followed by radiotherapy and radiotherapy alone, and $P<0.001$ for the comparison between radiotherapy with concurrent cisplatin and radiotherapy alone).

Temporal Trends in the Treatment of Early- and Advanced-Stage Laryngeal Cancer in the United States, 1985-2007

Amy Y. Chen, MD, MPH; Stacey Fedewa, MPH; Jason Zhu, BA

Arch Otolaryngol Head Neck Surg. 2011;137(10):1017-1024

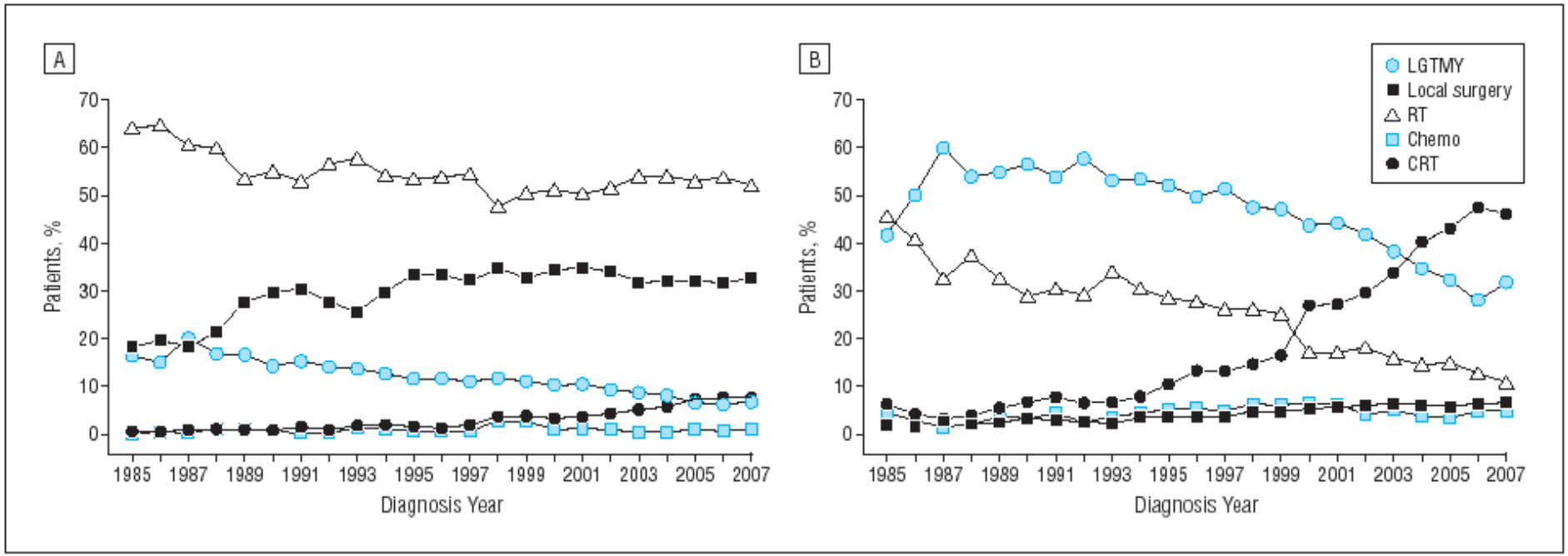


Figure 2. Treatment trends in patients with laryngeal cancer, National Cancer Database 1985-2007.[5] A, Patients with early-stage laryngeal cancer. B, Patients with advanced-stage laryngeal cancer. Chemo indicates chemotherapy; CRT, chemoradiation; LGTMY, laryngectomy; RT, radiation.

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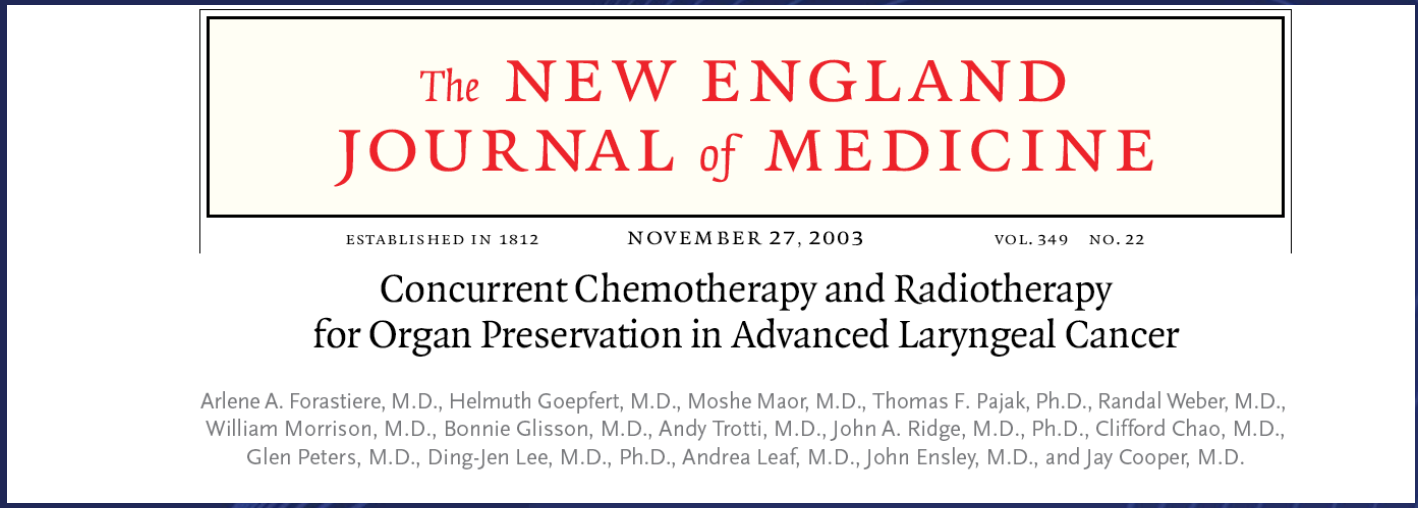
- "Radiotherapy with concurrent cisplatin should be considered standard care…and laryngectomy should be performed only as salvage therapy."

Forastiere AA, Goepfert H, et al. NEJM 2003; 349:2091-2098



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- Response by Weinstein, Myers, and Shapshay:

  "…the final sentence of the report…lacks balance and may be misleading to readers…By not mentioning options involving less-than-total laryngectomy, the authors leave the readers with the impression that total laryngectomy is the only surgical option for laryngeal cancer"

Weinstein GS, Myers EN, Shapshay SM. NEJM 2004; 350:1049

Treatment

- Goal is cure
- Focus is on functional preservation and reconstruction
- Both surgical and non-surgical approaches have evolved in an attempt to minimize treatment related morbidity

How Do Head and Neck Cancer Patients Prioritize Treatment Outcomes Before Initiating Treatment?

By Marcy A. List, John Stracks, Laura Colangelo, Pamela Butler, Natasha Ganzenko, Donna Lundy, Paula Sullivan, Daniel Haraf, Merrill Kies, William Goodwin, and Everett E. Vokes

J Clin Oncol 18:877-884.

Table 2. Rankings of Items

Item	Patients Ranking Item in Top 3 %	Patients Ranking Item in Top 3 No.	Patients Ranking Item First %	Patients Ranking Item First No.	Item Ranking (mean ± SD)
Being cured of my cancer	93	122	75	98	1.55 ± 1.3
Living as long as possible	56	73	8	11	4.93 ± 3.9
Having no pain	35	46	9	12	5.42 ± 3.2
Having normal amount of energy	24	31	1	1	5.92 ± 2.7
Returning to regular activities quickly	24	31	1	1	6.11 ± 3.1
Being able to swallow all foods/liquids	19	25	2	3	6.06 ± 2.6
Keeping my natural voice	18	23	1	1	6.96 ± 3.1
Keeping my appearance unchanged	10	13	1	1	8.43 ± 3.2
Being able to chew normally	8	11	1	1	7.89 ± 2.7
Being understood easily	9	12	1	1	7.84 ± 3.0
Keeping normal sense of taste & smell	4	5	1	1	7.93 ± 2.5
Having a comfortably moist mouth	1	1	0	0	8.96 ± 2.4

Functions of the larynx

- Phonation
- Respiration
- Prevention of Aspiration

Table 1. Summary of Recommended Strategies for Treatment of the Primary Site for Larynx Preservation

Type of Cancer	Organ-Preservation Strategy		Basis for Recommendation	Quality of Evidence
	Recommended	Other Options		
T1 cancer of the glottis: T1—tumor limited to the vocal cord(s) (may involve anterior or posterior commissure) with normal mobility T1a—tumor limited to one vocal cord T1b—tumor involves both vocal cords	Endoscopic resection (selected patients) OR radiation therapy	Open organ-preservation surgery	High local control rates and quality of voice after endoscopic resection compared with radiation therapy; possible cost savings; ability to reserve radiation for possible second primary cancers of the upper aerodigestive tract; however, not suitable for all patients	Comparison of outcomes from case series/ prospective single-arm studies
T2 cancer of the glottis, favorable*:T2—tumor extends to supraglottis and/or subglottis, or with impaired vocal cord mobility	Open organ-preservation surgery OR radiation therapy	Endoscopic resection (selected patients)	Open organ-preservation surgery is associated with highest local control rates; however, leads to permanent hoarseness; local control rates after radiation therapy are also high, and functional outcomes may be better	Comparison of outcomes from case series/ prospective single-arm studies
T2 cancer of the glottis, unfavorable*	Open organ-preservation surgery OR concurrent chemoradiation therapy (selected patients with node-positive disease)	Radiation therapy Endoscopic resection (selected patients)	Higher local control rates after surgery compared with radiation therapy alone; quality of voice after therapy of less concern if vocal cord function is irreversibly compromised by tumor invasion; endoscopic surgery requires careful patient selection For patients with T2 N+ disease, evidence from randomized trials supports concurrent chemoradiation therapy as an organ-preservation option	Comparison of outcomes from case series/ prospective single-arm studies; randomized controlled clinical trials comparing concurrent chemoradiation therapy, and/or induction chemotherapy followed by radiation, and/or radiation therapy alone, and/or surgery followed by radiation
T1-T2 cancer of the supraglottis, favorable*: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 glottis or region outside the supraglottis (eg, mucosa of base of tongue, vallecula, medial wall of pyriform sinus) without fixation of the larynx	Open organ-preservation surgery OR radiation therapy	Endoscopic resection (selected patients)	Open organ-preservation surgery associated with highest local control rates; however, requires temporary tracheostomy and may lead to increased risk of aspiration after therapy; local control rates after radiation therapy are also high, and functional outcomes may be better	Comparison of outcomes from case series/ prospective single-arm studies
T2 cancer of the supraglottis, unfavorable*	Open organ-preservation surgery OR concurrent chemoradiation therapy (selected patients with node-positive disease)	Radiation therapy Endoscopic resection (selected patients)	Open organ-preservation surgery is more likely to yield higher local control rates than radiation therapy; for patients with T2 N+ disease, evidence from randomized trials supports concurrent chemoradiation therapy as an organ-preservation option	Comparison of outcomes from case series/ prospective single-arm studies; randomized controlled clinical trials comparing concurrent chemoradiation therapy, and/or induction chemo-therapy followed by radiation, and/or radiation therapy alone, and/or surgery followed by radiation

VOLUME 24 · NUMBER 22 · AUGUST 1 2006

JOURNAL OF CLINICAL ONCOLOGY

ASCO SPECIAL ARTICLE

American Society of Clinical Oncology Clinical Practice Guideline for the Use of Larynx-Preservation Strategies in the Treatment of Laryngeal Cancer

David G. Pfister, Scott A. Laurie, Gregory S. Weinstein, William M. Mendenhall, David J. Adelstein, K. Kian Ang, Gary L. Clayman, Susan G. Fisher, Arlene A. Forastiere, Louis B. Harrison, Jean-Louis Lefebvre, Nancy Leupold, Marcy A. List, Bernard O. O'Malley, Snehal Patel, Marshall R. Posner, Michael A. Schwartz, and Gregory T. Wolf

Table 1. Summary of Recommended Strategies for Treatment of the Primary Site for Larynx Preservation

Type of Cancer	Organ-Preservation Strategy		Basis for Recommendation	Quality of Evidence
	Recommended	Other Options		
T3-T4 cancers of the glottis or supraglottis: T3 glottis—tumor limited to the larynx with vocal cord fixation, and/or invades paraglottic space, and/or minor thyroid cartilage erosion (eg, inner cortex) T3 supraglottis—tumor limited to larynx with vocal cord fixation and/or invades any of the following: postcricoid area, pre-epiglottic tissues, paraglottic space, and/or minor thyroid cartilage erosion (eg, inner cortex) T4a glottis or supraglottis—tumor invades through the thyroid cartilage and/or invades tissues beyond the larynx (eg, trachea, soft tissues of neck including deep extrinsic muscle of the tongue, strap muscles, thyroid, or esophagus) T4b glottis or supraglottis—tumor invades prevertebral space, encases carotid artery, or invades mediastinal structures	Concurrent chemoradiation therapy OR open organ-preservation surgery (in highly selected patients)	Radiation therapy	Highest rate of larynx preservation is associated with concurrent chemoradiation therapy compared with other radiation-based approaches, at the cost of higher acute toxicities but without more long-term difficulties in speech and swallowing; when salvage total laryngectomy incorporated, no difference in overall survival; organ preservation surgery is an option in highly selected patietns (eg, there are patients with T3 supraglottic cancers that have minimal or moderate pre-epiglottic invasion and are candidates for organ preserving surgery)	Randomized controlled clinical trials comparing concurrent chemoradiation therapy, and/or induction chemotherapy followed by radiation, and/or radiation therapy alone; and/or surgery followed by radiation; comparison of outcomes from case series/prospective single-arm studies

Survival

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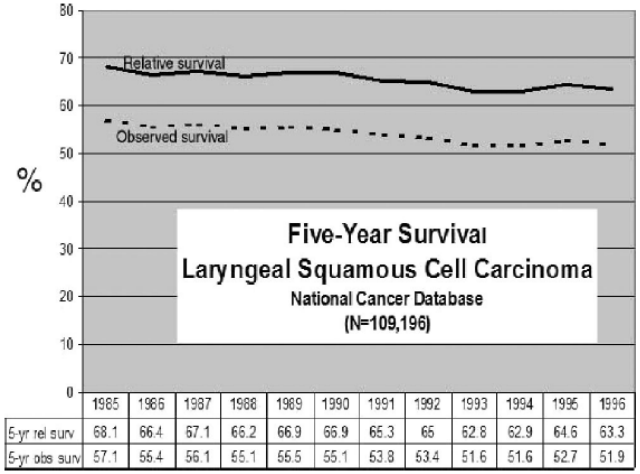
Laryngeal Cancer in the United States: Changes in Demographics, Patterns of Care, and Survival

Laryngoscope, 116(Suppl. 111):1–13, 2006

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

- NCDB review of 158,426 cases of laryngeal SCC
- Decrease in survival of patients with laryngeal cancer in the 1990's compared with the 1980's



	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996
5-yr rel surv	68.1	66.4	67.1	66.2	66.9	66.9	65.3	65	62.8	62.9	64.6	63.3
5-yr obs surv	57.1	55.4	56.1	55.1	55.5	55.1	53.8	53.4	51.6	51.6	52.7	51.9

Fig. 2. Survival for patients with laryngeal squamous cell carcinoma within the NCDB decreased progressively from the mid-1980s to the mid-1990s.

Survival

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HEALTH IS ALL WE DO

Factors Predictive of Survival in Advanced Laryngeal Cancer

Amy Y. Chen, MD, MPH; Michael Halpern, MD, PhD

Arch Otolaryngol Head Neck Surg. 2007;133(12):1270-1276

- NCDB review of 7019 patients
- TL associated with increased survival when compared to CRT, especially in patients with Stage IV disease

Temporal Trends in the Treatment of Early- and Advanced-Stage Laryngeal Cancer in the United States, 1985-2007

Amy Y. Chen, MD, MPH; Stacey Fedewa, MPH; Jason Zhu, BA

Arch Otolaryngol Head Neck Surg. 2011;137(10):1017-1024

Table 4. Hazard Ratio (HR) Model Predicting 4-Year Survival Among Patients With Early-Stage Cancer Receiving Local Surgery or Radiation Therapy, 1998-2002[a]

Category	HR (95% CI)
Race/ethnicity	
White	1 [Reference]
Hispanic	0.89 (0.72-1.10)
African American	**1.16 (1.03-1.30)**
Other	**0.69 (0.50-0.95)**
Missing	1.00 (0.87-1.14)
Treatment	
Radiation	1 [Reference]
Local surgery	**0.71 (0.65-0.76)**
Subsite	
Glottic	1 [Reference]
Supraglottic	**1.89 (1.74-2.05)**
No high school diploma, median, %	
<14.0	**0.86 (0.78-0.96)**
14.0-19.9	0.89 (0.80-1.00)
20.0-28.9	0.96 (0.87-1.06)
>29.0	1 [Reference]
Missing	**0.75 (0.63-0.91)**
Facility type	
Community facility	1 [Reference]
Community cancer center	**0.88 (0.80-0.97)**
Teaching research	**0.86 (0.78-0.96**

Table 5. Hazard Ratio (HR) Model Predicting 4-Year Survival Among Patients With Advanced-Stage Receiving Chemoradiation (CRT) or Laryngectomy, 1998-2002[a]

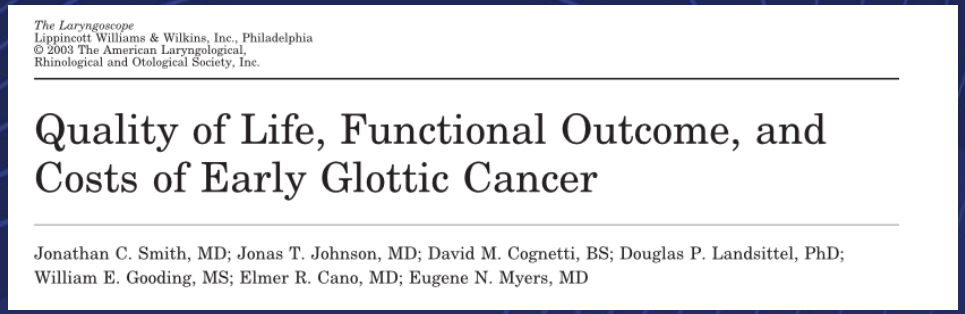
Category	HR (95% CI)
Race/ethnicity	
White	1 [Reference]
Hispanic	0.99 (0.83-1.18)
African American	**1.15 (1.05-1.25)**
Other	0.88 (0.68-1.15)
Missing	1.06 (0.91-1.23)
Treatment	
Laryngectomy	1 [Reference]
CRT	**1.13 (1.06-1.21)**
Subsite	
Glottic	1 [Reference]
Supraglottic	1.03 (0.97-1.10)
No high school diploma, median, %	
<14.0	0.91 (0.83-1.01)
14.0-19.9	0.92 (0.84-1.01)
20.0-28.9	0.99 (0.91-1.08)
>29.0	1 [Reference]
Missing	1.06 (0.91-1.23)
Facility type	
Community facility	1 [Reference]
Community cancer center	0.94 (0.86-1.04)
Teaching research	**0.88 (0.80-0.97)**

Management Options

- Surgical
  - Endoscopic resection
    - Laser
    - TORS
  - Open partial resection
    - Laryngofissure
    - Vertical hemilaryngectomy
    - Supraglottic laryngectomy
    - Supracricoid laryngectomy
  - Total Laryngectomy
- Non-surgical
  - Radiation
  - Chemoradiation

Management options

- Early Glottic
  - Endoscopic resection
  - ~~Definitive radiation~~
  - ~~Laryngofissure~~

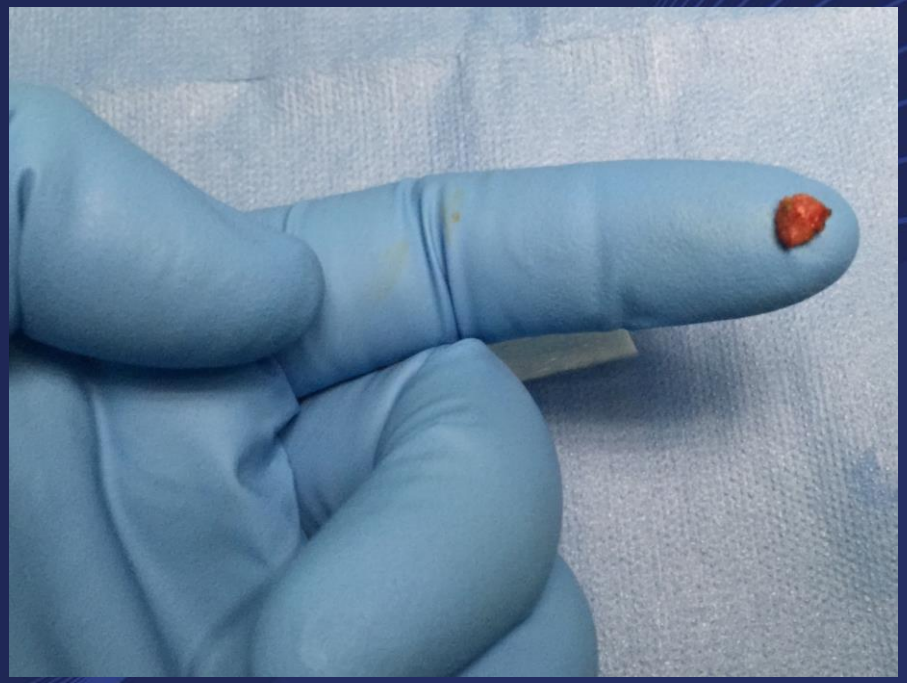


The Laryngoscope
Lippincott Williams & Wilkins, Inc., Philadelphia

Quality of Life, Functional Outcome, and Costs of Early Glottic Cancer

Jonathan C. Smith, MD; Jonas T. Johnson, MD; David M. Cognetti, BS; Douglas P. Landsittel, PhD; William E. Gooding, MS; Elmer R. Cano, MD; Eugene N. Myers, MD

Early glottic



Eur Arch Otorhinolaryngol (2000) 257:227–231

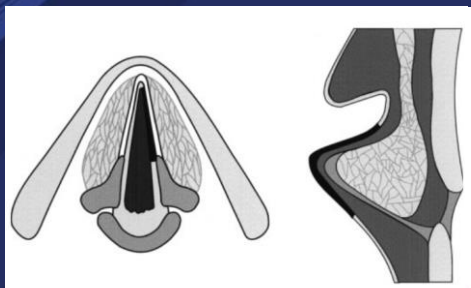


Fig. 1a, b Subepithelial cordectomy (type I)

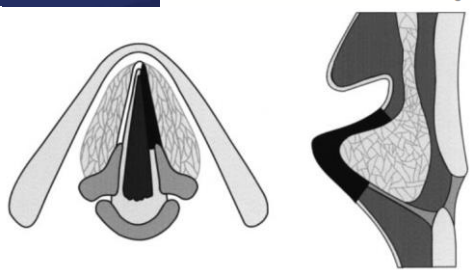


Fig. 2a, b Subligamental cordectomy (type II)

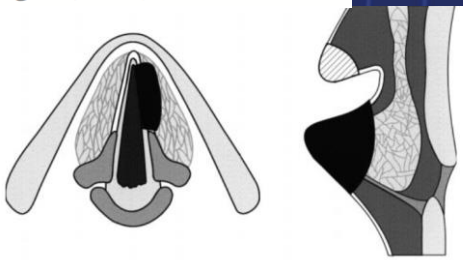


Fig. 3a, b Transmuscular cordectomy (type III). In order to expose the entire vocal fold, partial resection of the ventricular fold may be necessary (hatched area)

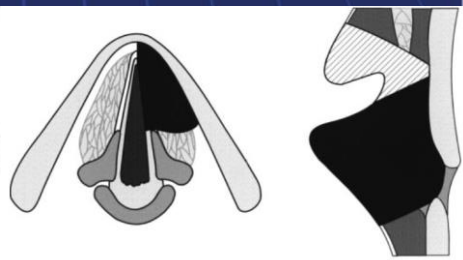


Fig. 4a, b Total or complete cordectomy (type IV). The ipsilateral ventricular fold can be removed partially or totally to ensure complete resection of the vocal fold (hatched area)

Early glottic

Original Research—Head and Neck Surgery

AMERICAN ACADEMY OF OTOLARYNGOLOGY–HEAD AND NECK SURGERY FOUNDATION

Otolaryngology–Head and Neck Surgery
2015, Vol. 152(5) 856–862

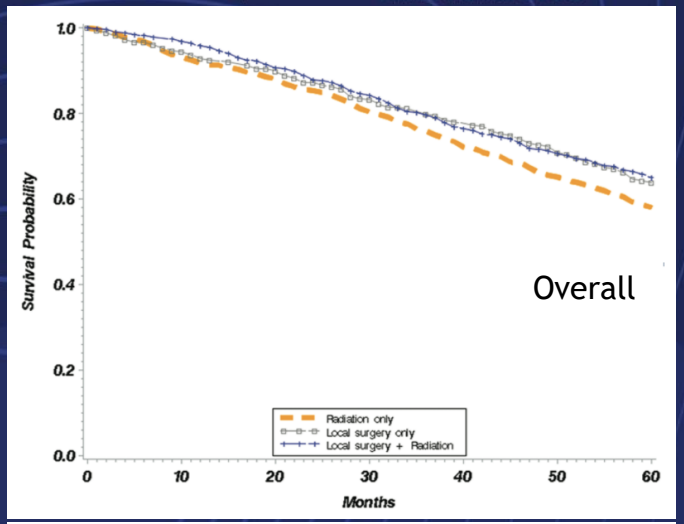
DOI: 10.1177/0194599815572112
http://otojournal.org
SAGE

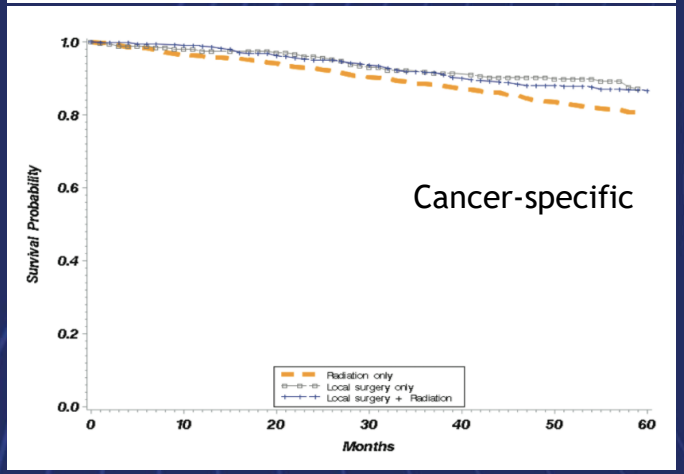
T1 Glottic Carcinoma: Do Comorbidities, Facility Characteristics, and Sociodemographics Explain Survival Differences across Treatment Types?

Stephanie Misono, MD, MPH[1], Schelomo Marmor, PhD[1,2], Bevan Yueh, MD, MPH[1], and Beth A. Virnig, PhD, MPH[3]

- SEER database, 1991-2009
- 2338 cases, 66 y/o and older
- 47% radiation alone
- 14% surgery alone

- Higher survival in patients who underwent local surgery





Original Research—Head and Neck Surgery

AMERICAN ACADEMY OF OTOLARYNGOLOGY–HEAD AND NECK SURGERY FOUNDATION

Otolaryngology–Head and Neck Surgery
2016, Vol. 155(2) 257–264

DOI: 10.1177/0194599816638085
http://otojournal.org
SAGE

Survival Impact of Initial Therapy in Patients with T1-T2 Glottic Squamous Cell Carcinoma

Jacob S. Brady[1], Emily Marchiano[1], David Kam[1], Soly Baredes, MD[1,2], Jean Anderson Eloy, MD[1,2,3], and Richard Chan Woo Park, MD[1]

- SEER database, 1998 – 2012
- 13,312 cases
- 52.5% radiation alone
- 15.9% surgery alone

- 5-year DSS survival higher for surgery alone for T1 tumors, but same for T2 tumors

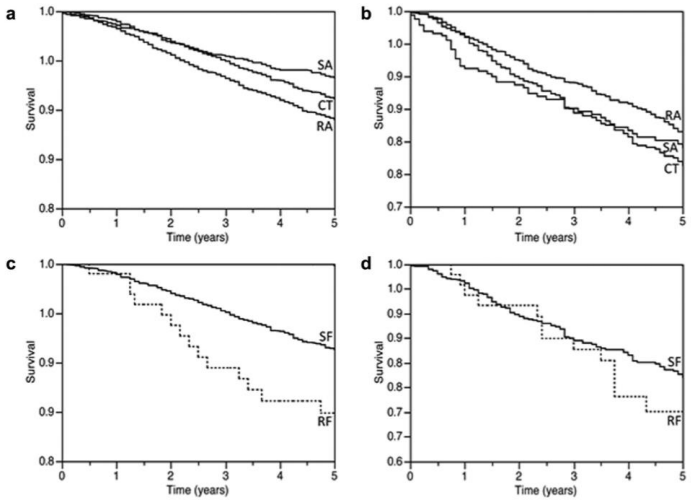


Figure 2. Kaplan-Meier analysis of 5-year disease-specific survival (DSS) for (a) T1N0M0 and (b) T2N0M0 glottic cancers by treatment modality. CT, combined therapy; RA, radiation alone; SA, surgery alone. Kaplan-Meier analysis of 5-year DSS for (c) T1N0M0 and (d) T2N0M0 glottic cancers by treatment sequence in combination therapy. RF, radiotherapy first; SF, surgery first.

AMERICAN ACADEMY OF OTOLARYNGOLOGY–HEAD AND NECK SURGERY FOUNDATION

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Jacob S. Brady[1], Emily Marchiano[1], David Kam[1], Soly Baredes, MD[1,2], Jean Anderson Eloy, MD[1,2,3], and Richard Chan Woo Park, MD[1]

Table 4. Disease-Specific Survival Analysis for T1N0 and T2N0 Glottic Cancer by Treatment Modality.[a]

	T1N0			T2N0			T1T2N0		
	n	Survival, %	*P* Value (Log-Rank)	n	Survival, %	*P* Value (Log-Rank)	n	Survival, %	*P* Value (Log-Rank)
Overall survival	10,455	90.4	—	2857	80.0	—	13,312	88.4	—
Treatment modality									
Combination therapy	3581	91.1	.0658	771	76.4		4352	88.4	.1056
Single-modality therapy	6874	90.1		2086	81.1	**.0255**	8960	88.1	
Surgery alone	1779	93.2	**<.0001**	331	79.1		2110	91.2	**<.0001**
Radiation alone	5095	89.0		1755	81.5	.1232	6850	87.1	

[a]Bold format indicates statistical significance ($P < .05$).

Management options

- Early Glottic
  - Endoscopic resection
  - Definitive radiation
  - Laryngofissure

Management options

- Early Supraglottic

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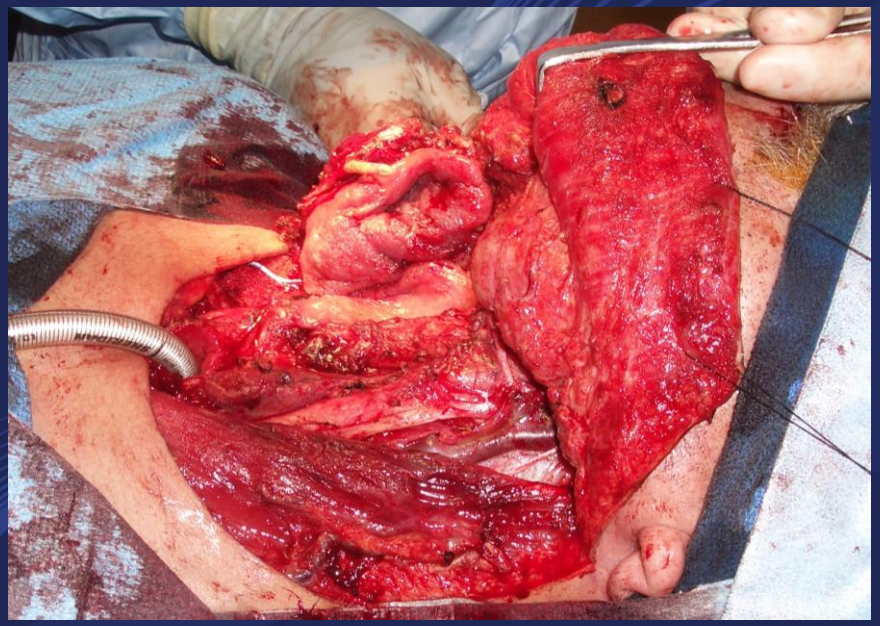
Management options

Management options

- Advanced Cancers



Disadvantages of Treatment

Laryngectomy

- Loss of natural voice
- Decrease sense of smell and taste
- Permanent stoma

Social stigma, disability, and decreased quality of life caused by separation of the aero-digestive tracts is drive for organ preserving treatments.

Chemoradiation

- Acute toxicity of treatment
- Need for salvage
- Xerostomia
- Aspiration

Role of Total Laryngectomy

- VA Study - % of each tumor characteristic requiring salvage laryngectomy:

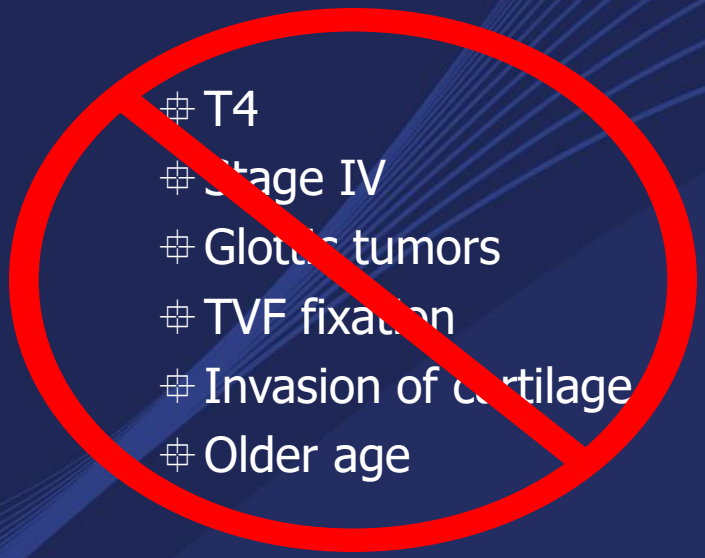
• Glottic	43%
• Supraglottic	31%
• Fixed TVF	41%
• Mobile TVF	29%
• Invasion of cartilage	41%
• No invasion of cartilage	35%
• Stage III	29%
• Stage IV	44%
• T4	56%
• < T4	29%

Predicting treatment outcomes

- Pre-operative tumor/patient characteristics
  - T4
  - Stage IV
  - Glottic tumors
  - TVF fixation
  - Invasion of cartilage

Predicting treatment outcomes

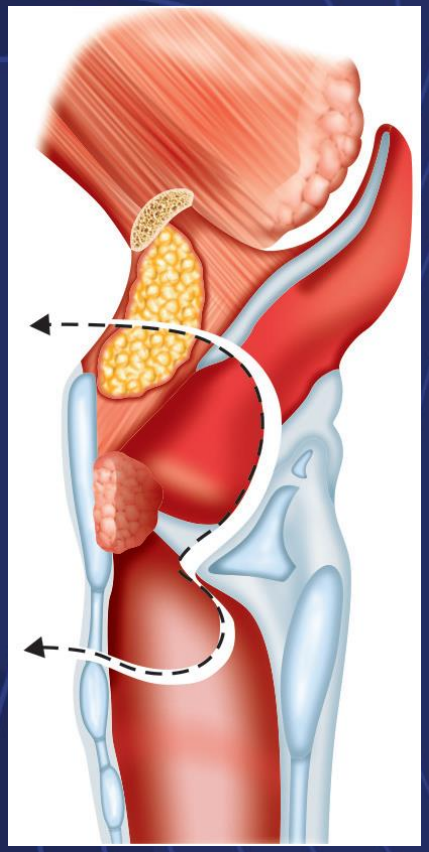
- Pre-operative tumor/patient characteristics



Patients who would be candidates for organ-preservation surgery

Open partial laryngectomy

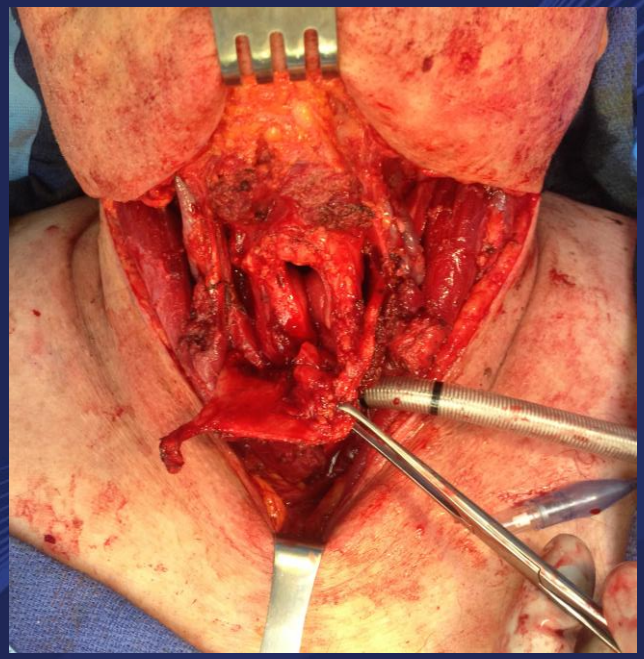
- Laryngofissure
- Vertical hemilaryngectomy
- Supraglottic laryngectomy
- Supracricoid laryngectomy

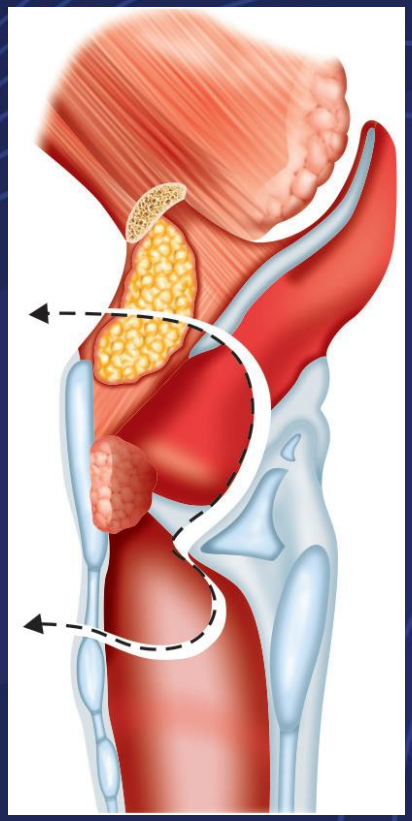


Supracricoid laryngectomy

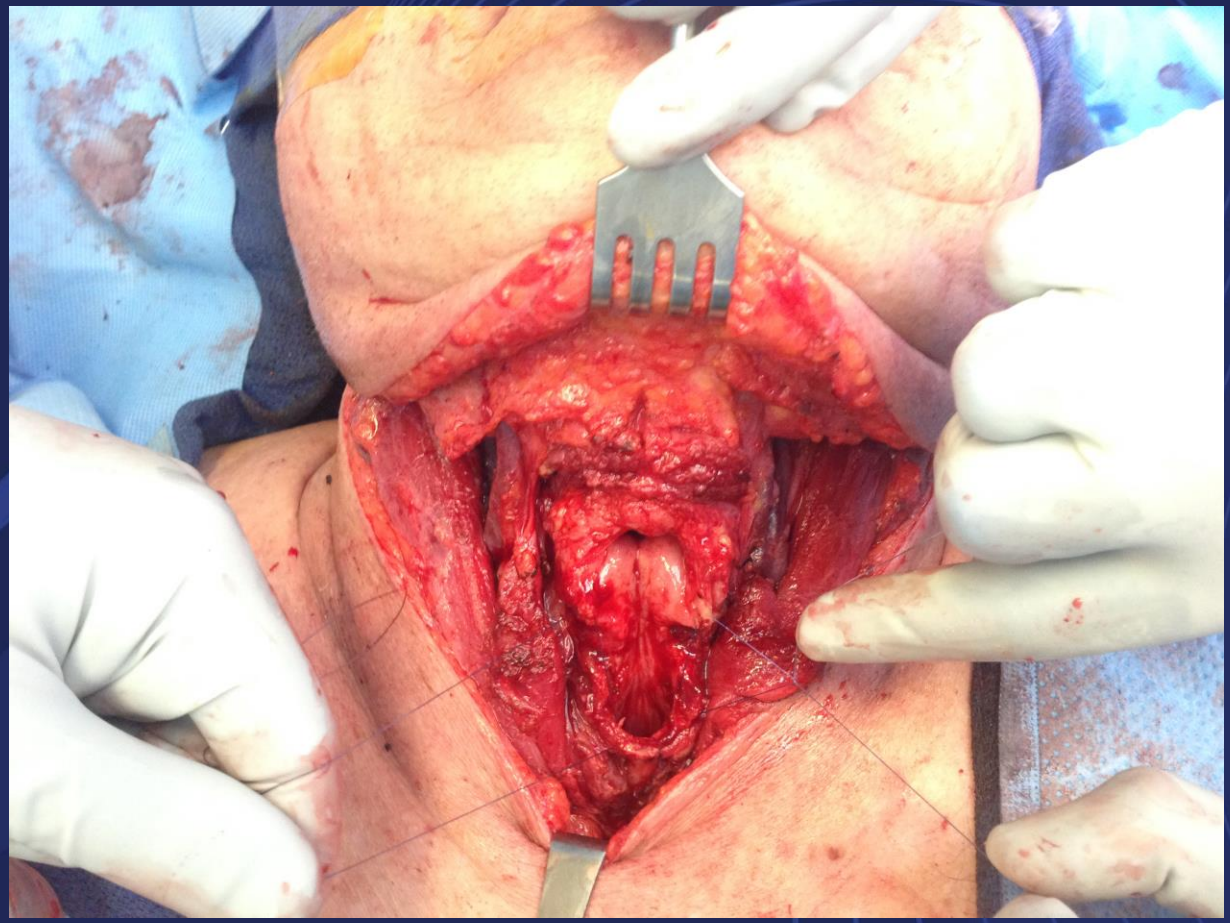
- 74 y/o
- T2N0 SCCA
- No COPD
- Quit smoking 20 years ago

Supracricoid laryngectomy



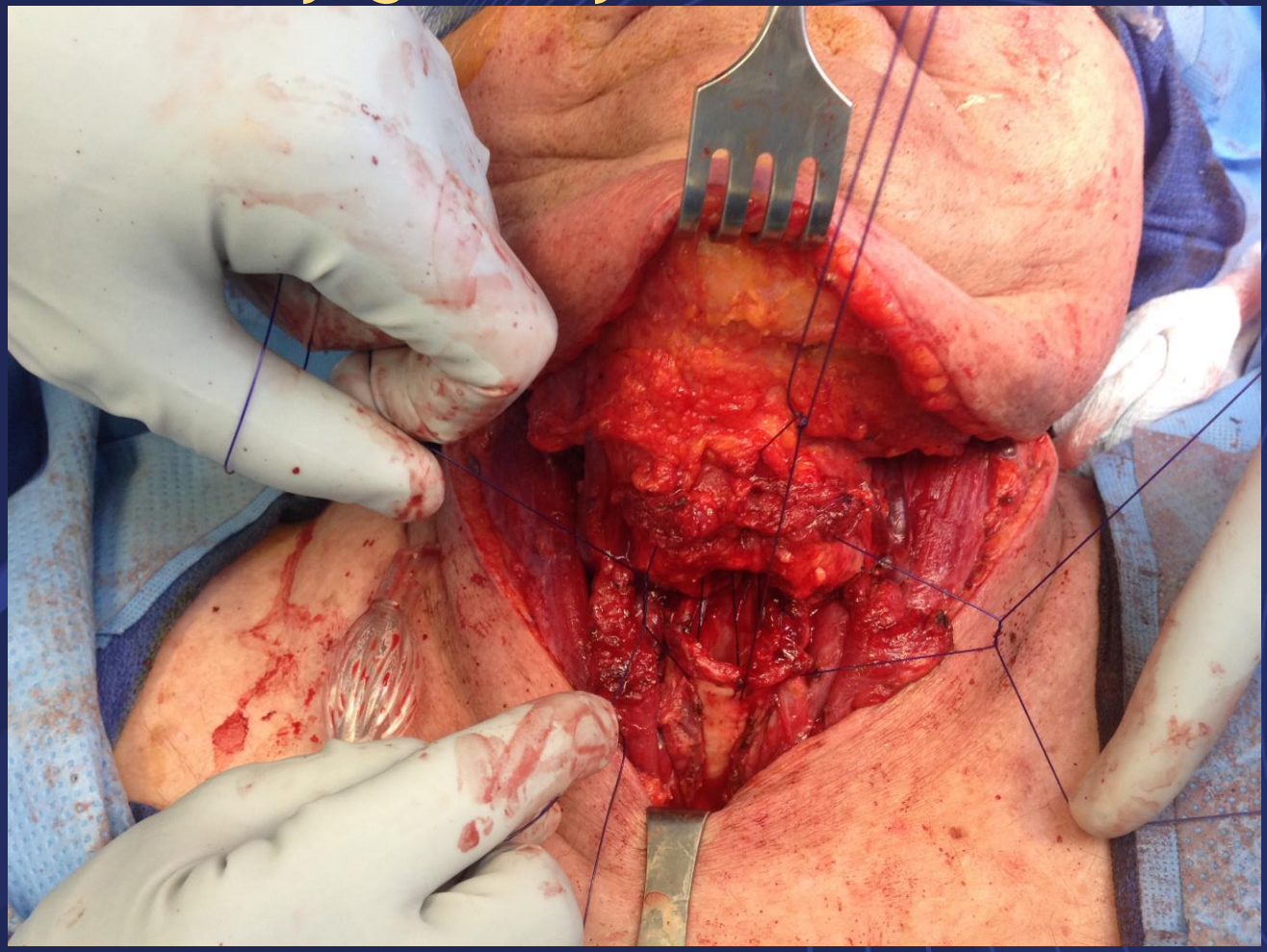


Supracricoid laryngectomy



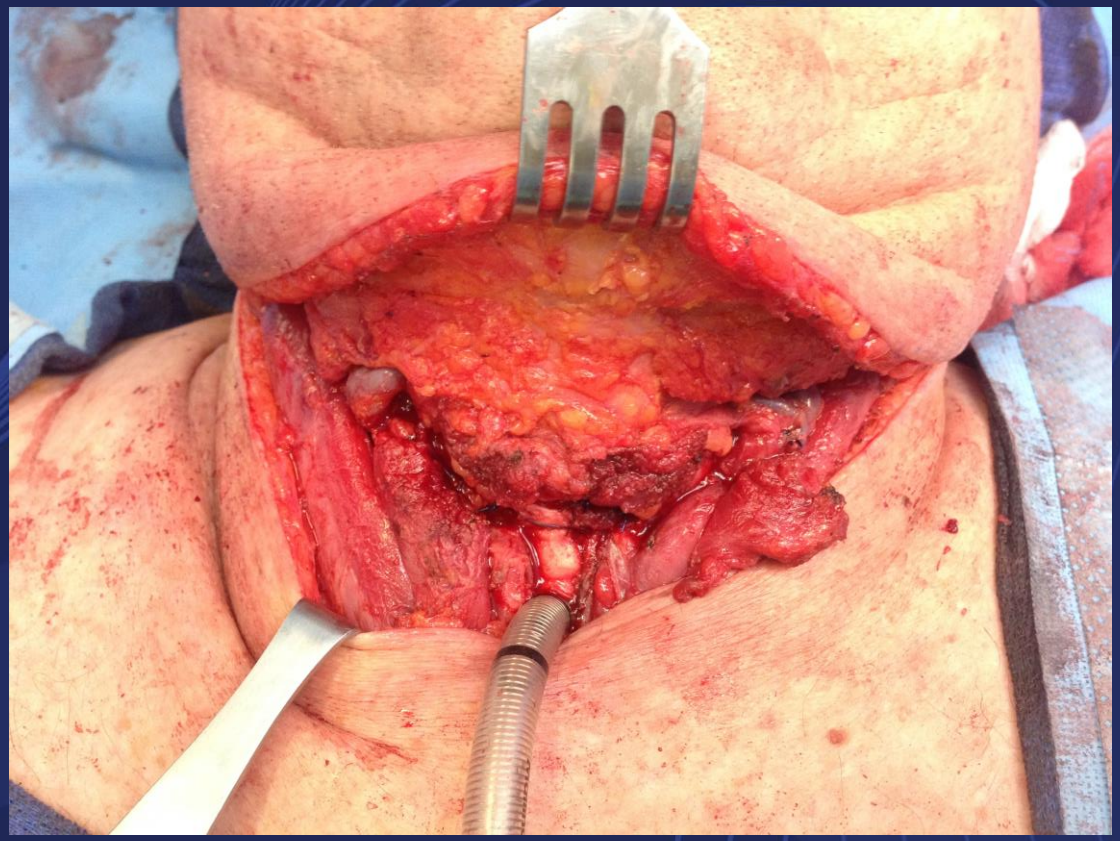
Arytenoid pexy

Supracricoid laryngectomy



Impaction suture

Supracricoid laryngectomy



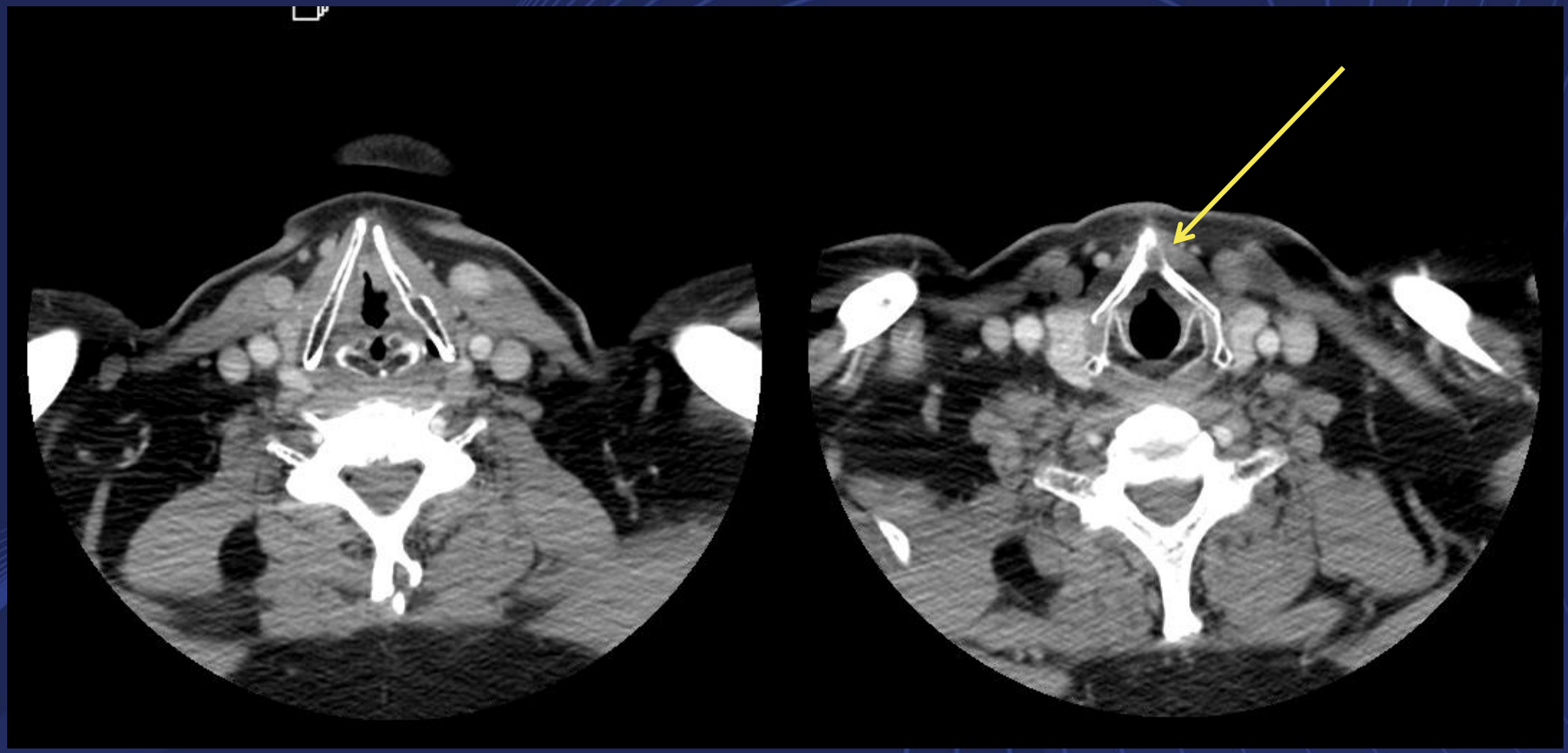
Impaction suture

Supracricoid laryngectomy

Supracricoid laryngectomy

- 59 y/o
- T2N0 SCCA s/p radiation
- Non-smoker

Supracricoid laryngectomy



Supracricoid laryngectomy

Supracricoid laryngectomy

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Conclusions

- Laryngeal cancer has declined with smoking rates
- Tobacco cessation is an important component of treatment
- Laryngeal cancer survival rates have worsened in the chemoradiation era
- There is database evidence of surgical survival advantage in both early and advanced stage glottic cancers
- Endoscopic and open partial laryngeal surgery are important tools in the armamentarium of the head and neck surgeon

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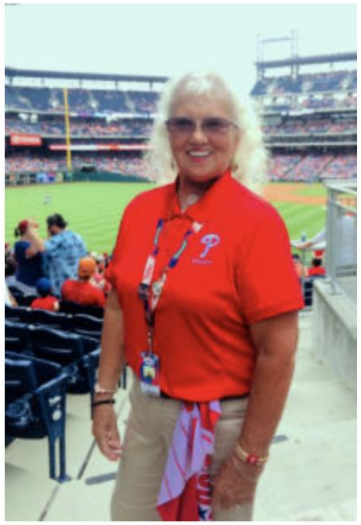
THIS THROAT CANCER SURVIVOR AND LARYNGECTOMY PATIENT CHEERS ON THE PHILLIES AS A HOSTESS

A laryngectomy to battle throat cancer didn't stop Barbara Kuhn from pursuing her dream retirement job – being a hostess for the Phillies.

By **Barbara Kuhn, Laryngectomy Patient, Lover of Life**
September 12, 2019

I will never be able to speak again. That's all I kept thinking to myself when I heard I had a cancerous mass on my throat, after already winning my fight against throat cancer several years before.

My surgeon told me I needed a laryngectomy, which meant I would need surgery to remove my larynx – my voice box. As a result, I would have an opening in my neck that would allow me to speak through a valve or "button."



Barbara Kuhn will greet fans for up to 81 baseball games at Citizens Bank Park, the home

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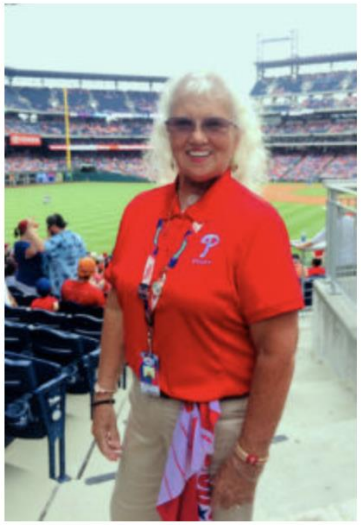

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Contact information

- david.cognetti@jefferson.edu
- Cell: 215-760-4590