Review of Esophageal Cancer

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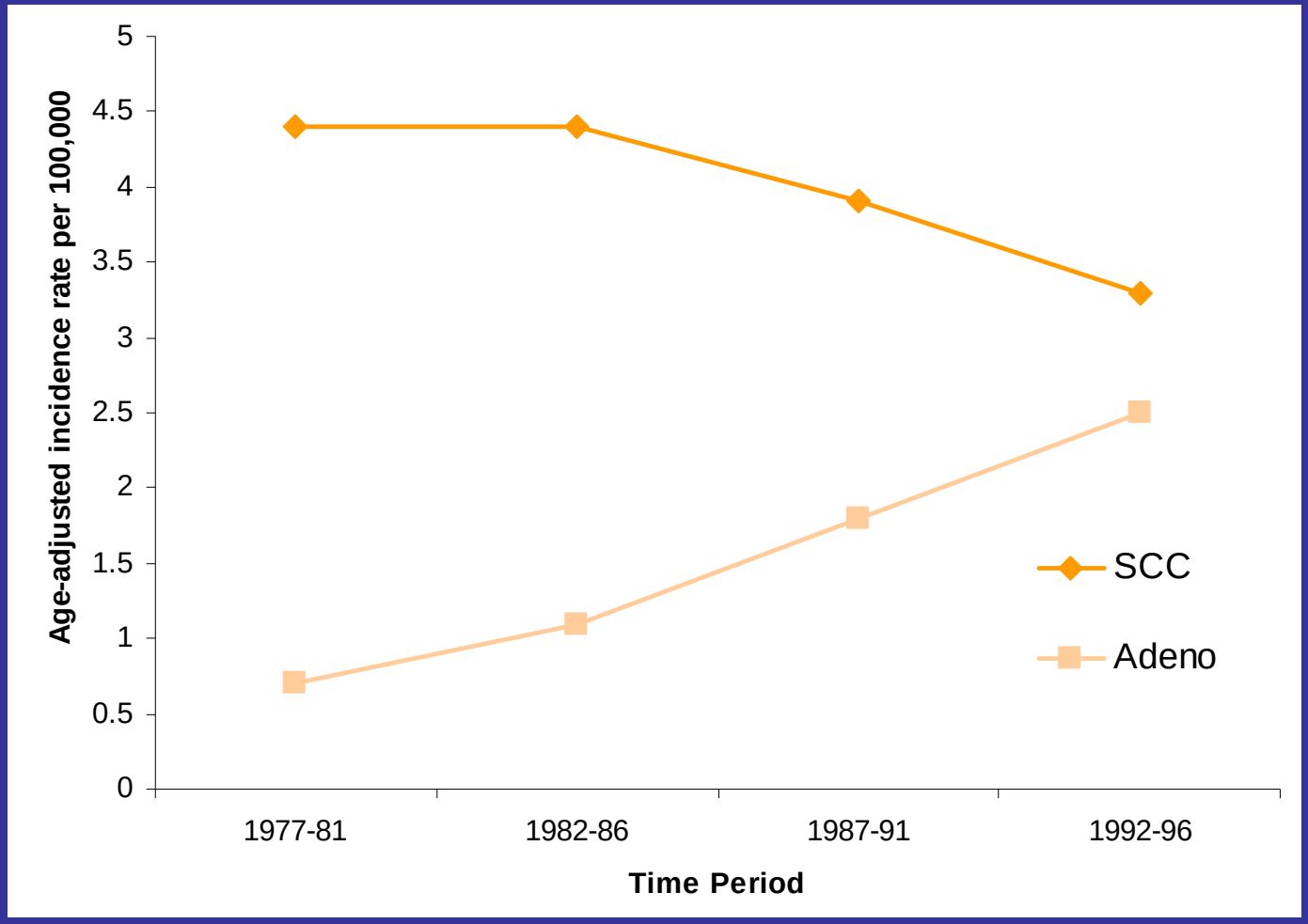
Esophageal Cancer

- Epidemiology and Risk Factors
- Diagnosis — signs, symptoms, and tests
- Work-up
- Treatment Overview
- Future Directions

Epidemiology

- Over 15,000 patients per year in the United States and 7th leading cause of cancer death in men.
- 8th most common cancer worldwide.
- Most cases are squamous cell, related to tobacco and alcohol exposure.
- In Western countries, adenocarcinoma increasing thought due to Barrett's esophagus.
- Approximately 50% present with advanced disease, which is incurable.

Incidence of Esophageal Cancer

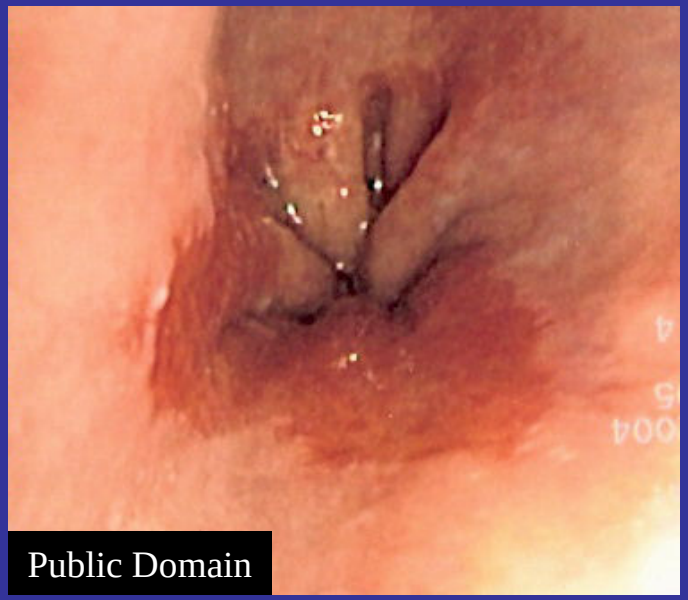


Adapted from El Serag HB. The epidemic of esophageal adenocarcinoma. Gastroenterol Clin North Am. 2002;31:421-440

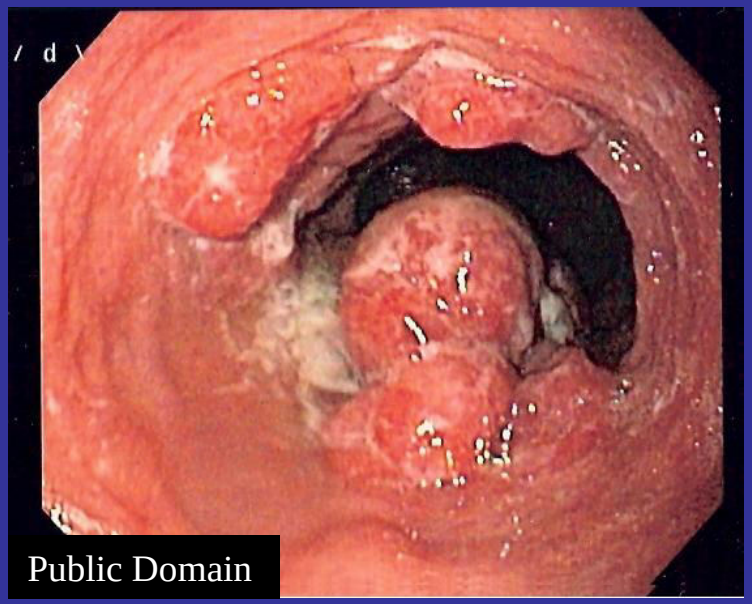
Adenocarcinoma: Barrett's Esophagus

- Likely related to chronic GERD, obesity.
- Pathway of malignant progression.
- 40 to 125 times relative risk of adenocarcinoma.
- Incidence of cancer is approximately 0.5% per year in patients with BE.
- No known effective screening tool.
- Usually Lower esophagus/GE junction.

Barrett's Esophagus and Esophageal Cancer

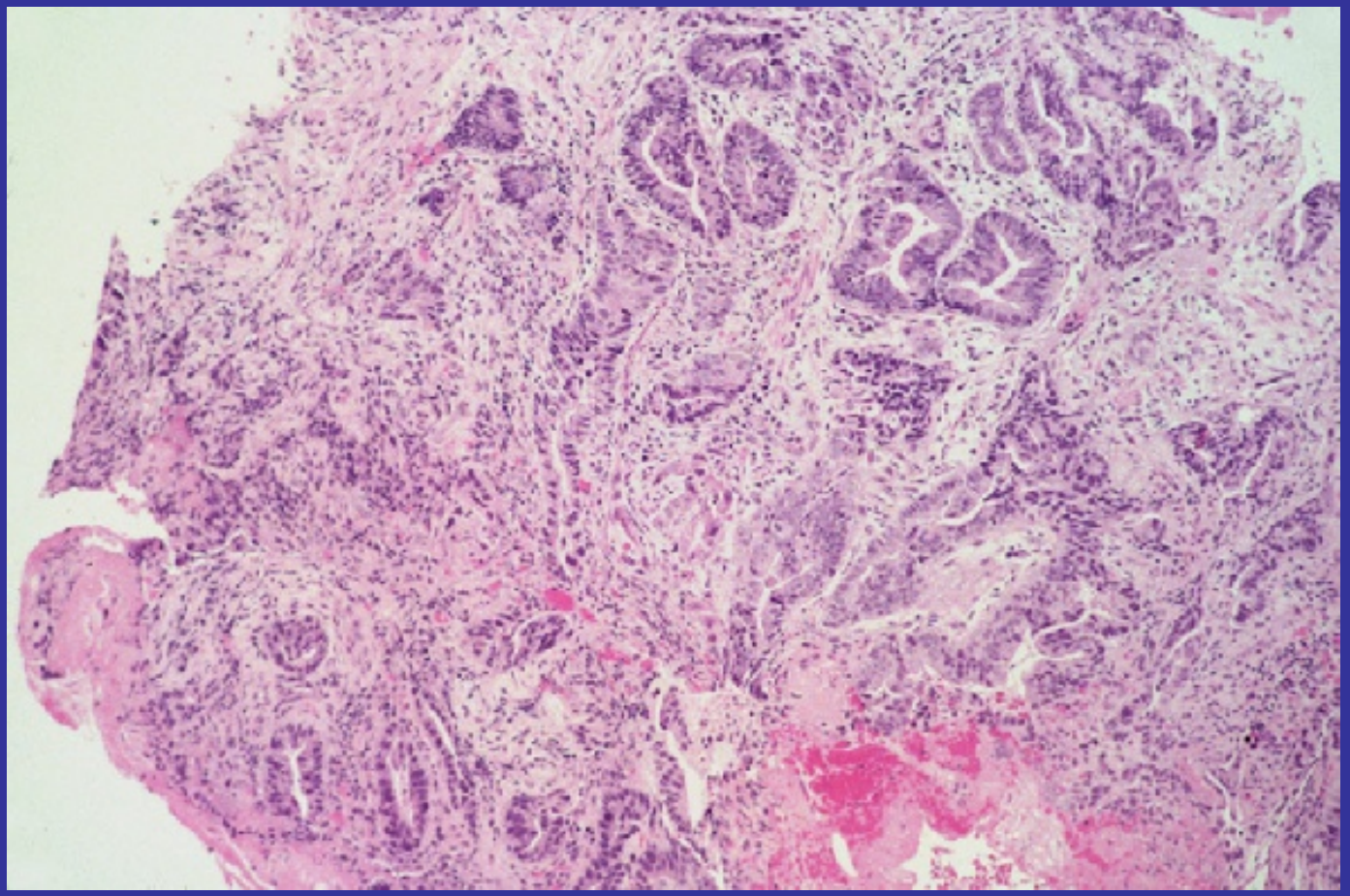


Endoscopic image of Barrett's esophagus with permission to place in public domain taken from patient



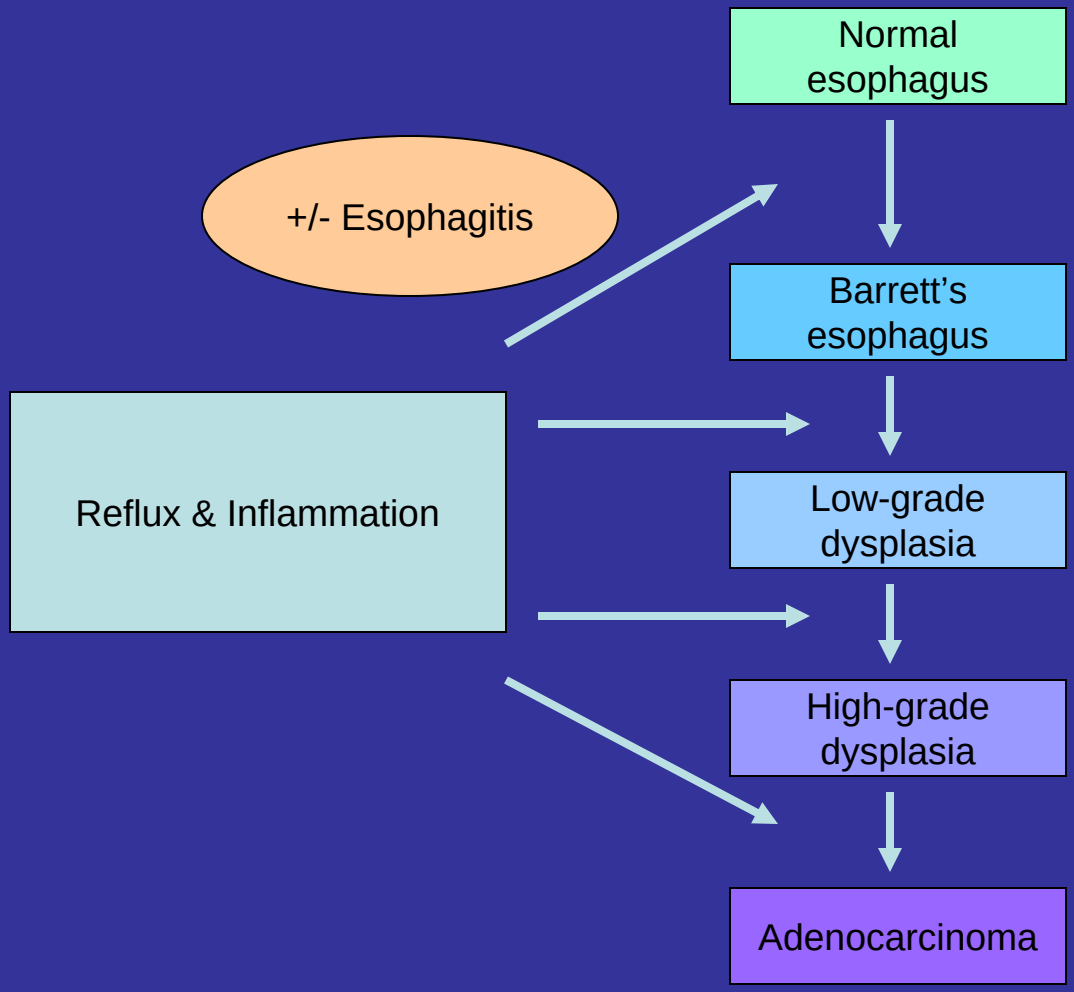
Endoscopic image of patient with esophageal adenocarcinoma seen at gastro-esophageal junction. Released into public domain on permission of patient

Adenocarcinoma



From Grading Dysplasia in Barrett's Esophagus. Used with permission. Available at: http://pathology2.jhu.edu/beweb/study.cfm.

Malignant Progression

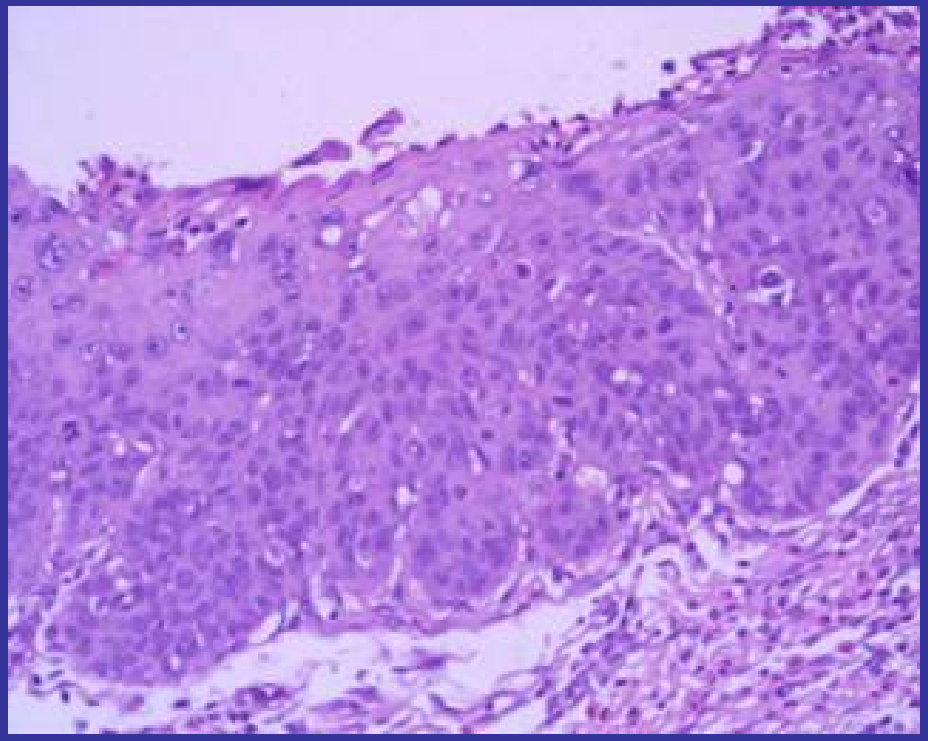


Adapted from Wild CP, Hardie LJ. Reflux, Barrett's oesophagus and adenocarcinoma: burning questions. *Nat Rev Cancer.* 2003;3:676-684

Squamous Cell Carcinoma

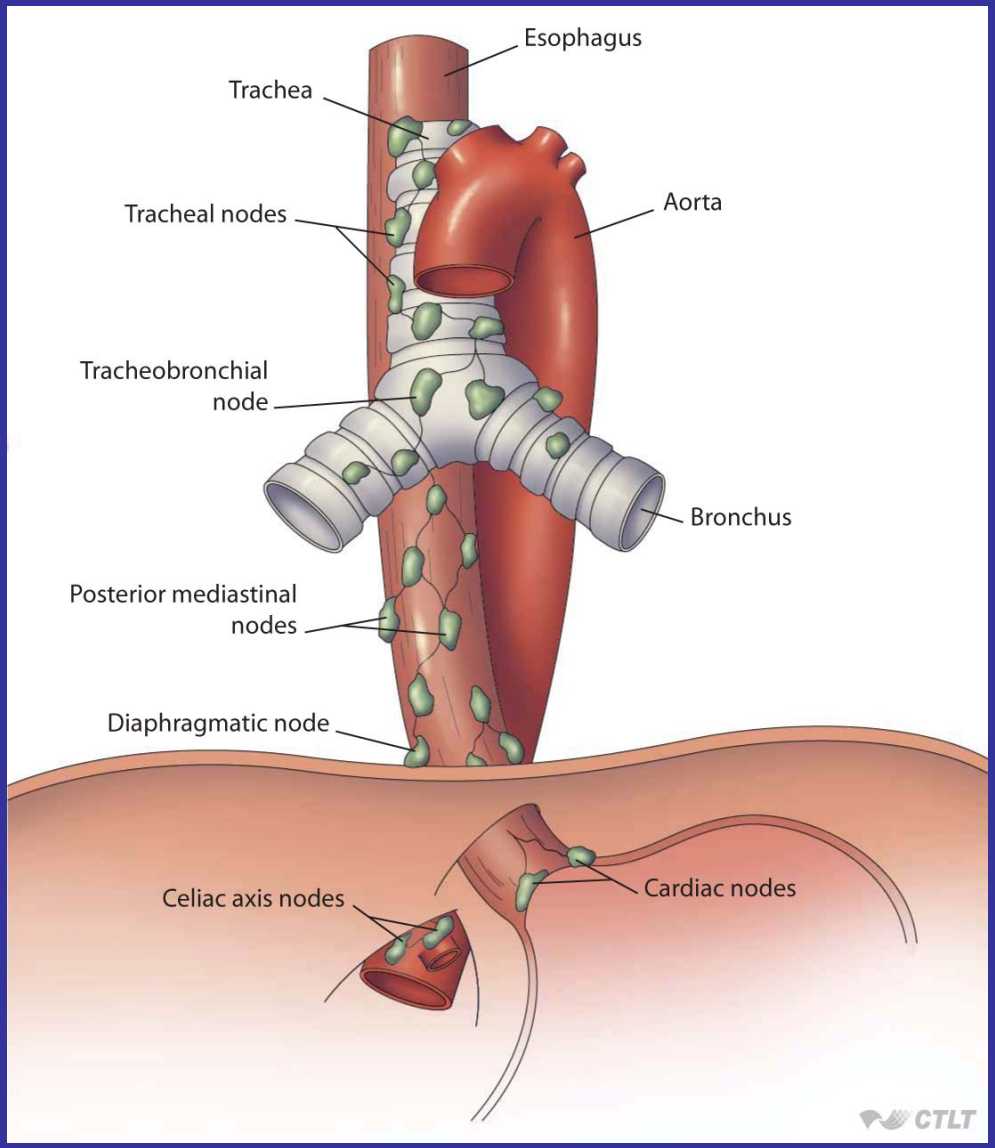
- Usually upper and middle esophagus.
- Tends to be a local problem—less metastases.
- Most common worldwide histology.
- Carcinogens present in tobacco and alcohol.

Squamous Cell Carcinoma



From Dionigi G, et al. Ten year survival after excision of Zenker's diverticulum: report of a case. World J Surg Oncol. 2006;4:17. Creative Commons BY

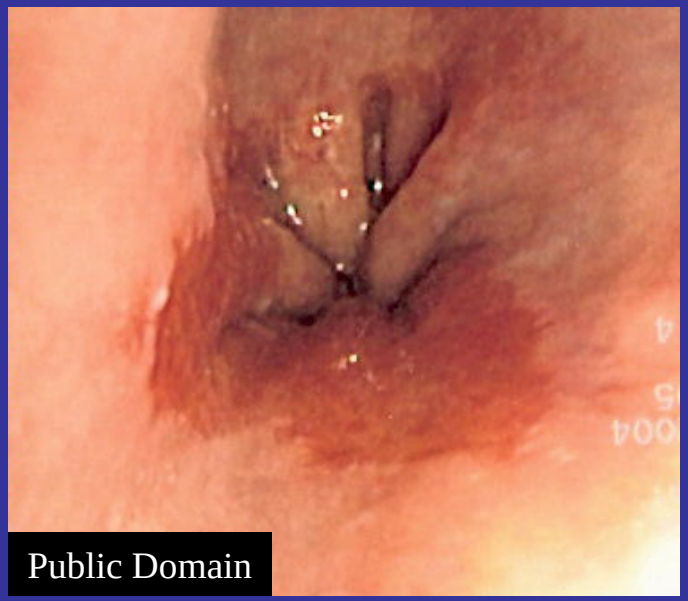
Anatomy


Esophagus
Trachea
Tracheal nodes
Aorta
Tracheobronchial node
Bronchus
Posterior mediastinal nodes
Diaphragmatic node
Celiac axis nodes
Cardiac nodes
CTLT

Clinical Presentation

- Signs: weight loss, palpable lymph nodes, usually non-specific.
- Symptoms: dysphagia, loss of appetite, pain with swallowing, fatigue, cough, retrosternal and abdominal pain.
- Lab Data: no tumor markers.

Endoscopy



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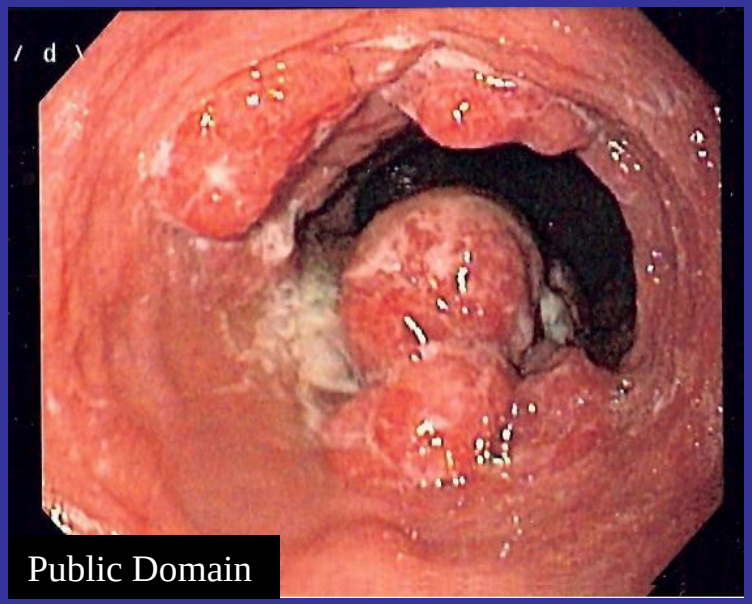

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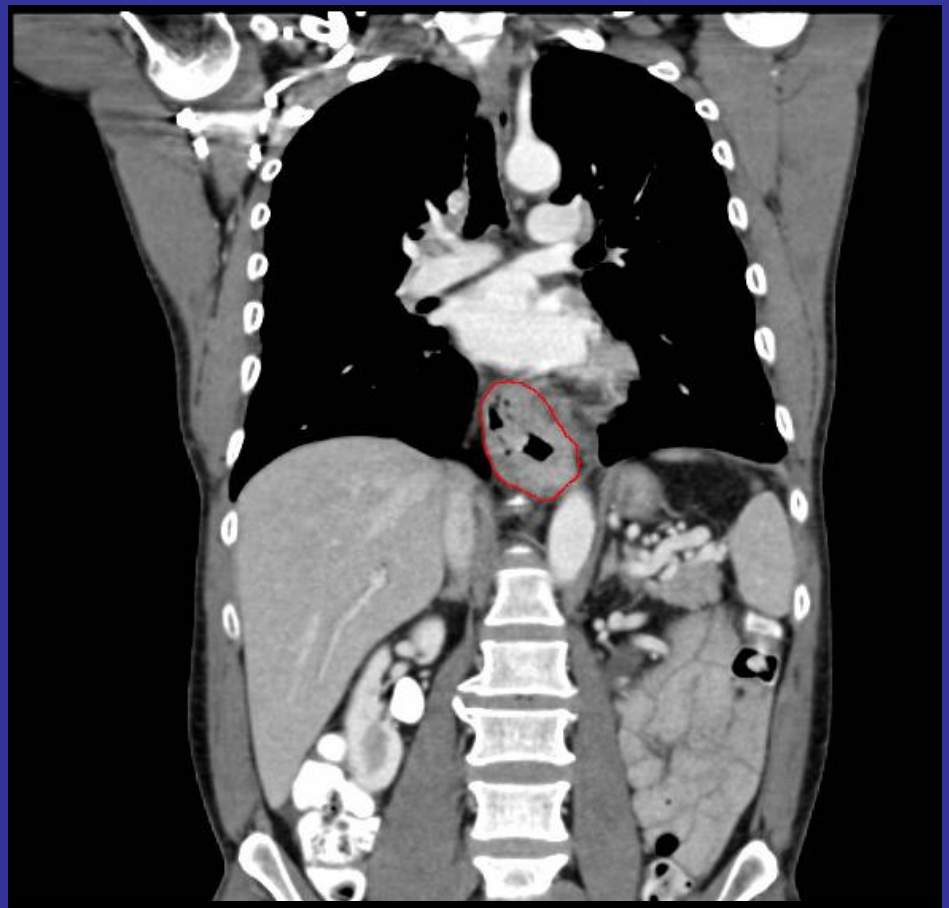
Endoscopic Ultrasound

Tomographic Imaging (CT)



Positron Emission Tomography

From Kelly J, et al. Primary malignant melanoma of the oesophagus: a case report *Journal of Medical Case Reports* 2007;1:50. Creative Commons BY.

Staging

- Two basic groups
  - Locally Advanced (primary tumor and regional lymph nodes): potentially curable
  - Metastatic (distant spread)
    - Incurable
    - survival increased with chemotherapy

Locally Advanced Stage

- “Best” treatment approach is controversial and continually evolving.
- Concepts to consider:
  - Local control (primary tumor)
  - Distant disease (“micrometastases”)
- Modes of treatment include surgery, radiation and chemotherapy in various sequences and combinations

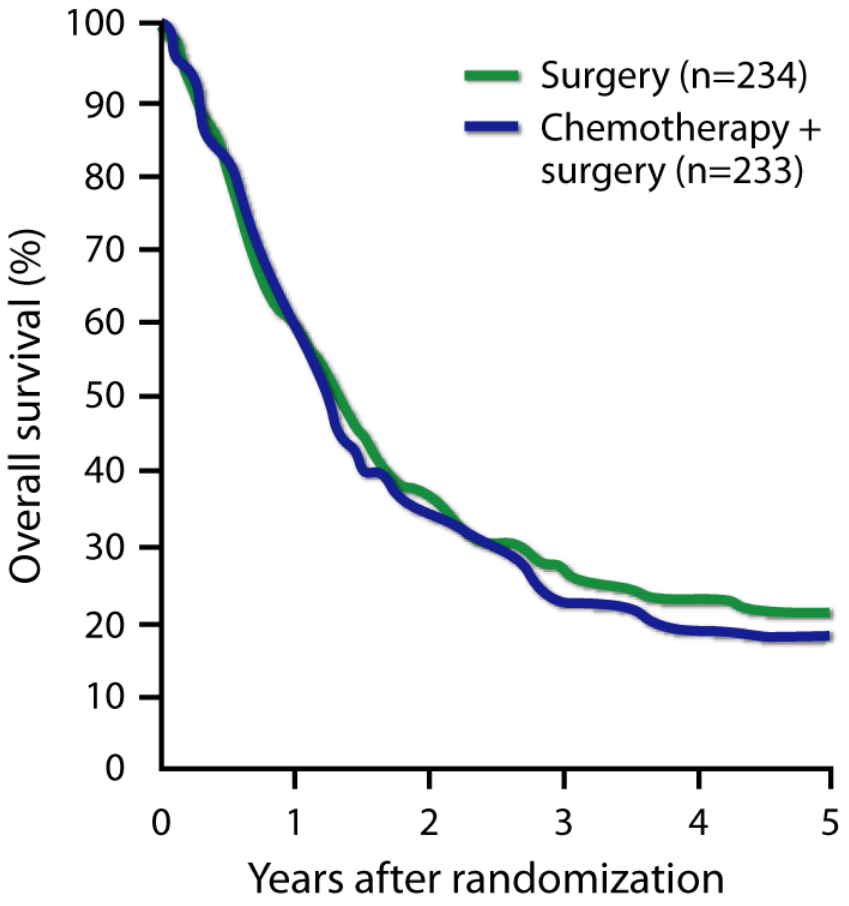
Surgery Alone

Stage-dependent Kaplan-Meier actuarial survival curves in patients undergoing transhiatal esophagectomy for carcinoma of the intrathoracic esophagus and cardia. From Orringer MB. Transhiatal Esophagectomy: Clinical Experience and Refinements. Ann Surg. 1999;230:392

This image has been deleted because JHSPH OpenCourseWare was unable to secure permission for its use.

Chemotherapy plus Surgery

Overall Survival of All Registered Patients



Adapted by CTLT from Kelsen et al. NEJM 1998;339:1979.

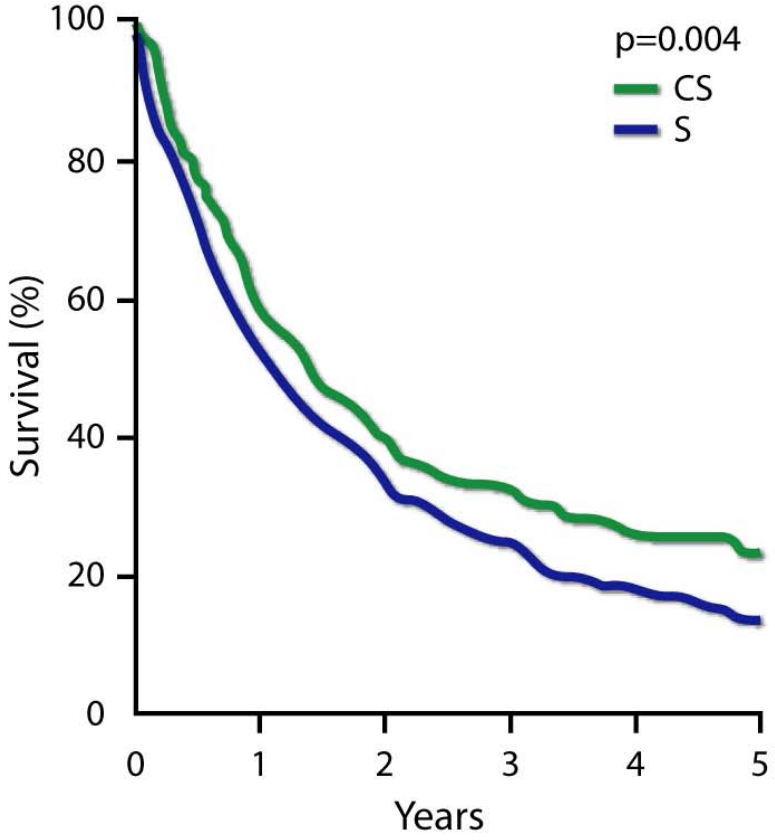
Number of Patients at Risk

Years after randomization	1	2	3	4	5
Surgery	138	81	45	27	16
Chemotherapy + surgery	136	73	42	28	15

The distribution curves represent the results of an intention-to-treat survival analysis involving all registered patients. Patients who received chemotherapy before surgery had a median survival of 14.9 months; in comparison, patients who had only surgery had a median survival of 16.1 months (P=0.53 by the log-rank test). Of the 233 patients receiving preoperative chemotherapy, 180 died; of the 234 not receiving it, 173 died.

Chemotherapy plus Surgery

Survival from Date of Randomization



Patients at Risk (Events)

Years	0	1	2	3	4	5
CS	400 (164)	231 (73)	143 (26)	81 (13)	36 (2)	14
S	402 (185)	212 (76)	124 (32)	70 (18)	28 (5)	10

Kaplan-Meier curve showing survival from date of randomisation. Two CS patients died after 5 years. From Medical Research Council Oesophageal Cancer Working Party. Surgical resection with or without preoperative chemotherapy in oesophageal cancer: a randomised controlled trial.

Adapted by CTLT from Lancet 2002;359:1727-1733.

Chemotherapy & Radiation Without Surgery

Time	No. (%) alive after radiation therapy only (randomized)	No. (%) alive after combined modality therapy	
		Randomized	Nonrandomized
0 years	62 (100)	61 (100)	69 (100)
1 years	21 (34)	32 (52)	43 (62)
2 years	6 (10)	22 (36)	24 (35)
3 years	0 (0)	18 (30)	18 (26)
4 years	0 (0)	17 (30)	13 (19)
5 years	0 (0)	14 (26)	10 (14)
6 years	0 (0)	12 (22)	6 (10)[a]
7 years	0 (0)	12 (22)	2 (6)[a]
8 years	0 (0)	10 (22)	–
9 years	0 (0)	4 (20)[a]	–
10 years	0 (0)	3 (20)[a]	–
Total dead (median, mo)	62/62 (9.3)	48/61 (14.1)	65/69 (16.7)

[a]Percentages are unreliable because of the small number of people at risk.

Adapted by CTLT from Cooper JS, et al. JAMA 1999;281:1623-1627

Overall Survival With Surgery Followed by Adjuvant Paclitaxel and Cisplatin (E8296)

-No pre-op therapy

-R0 resection

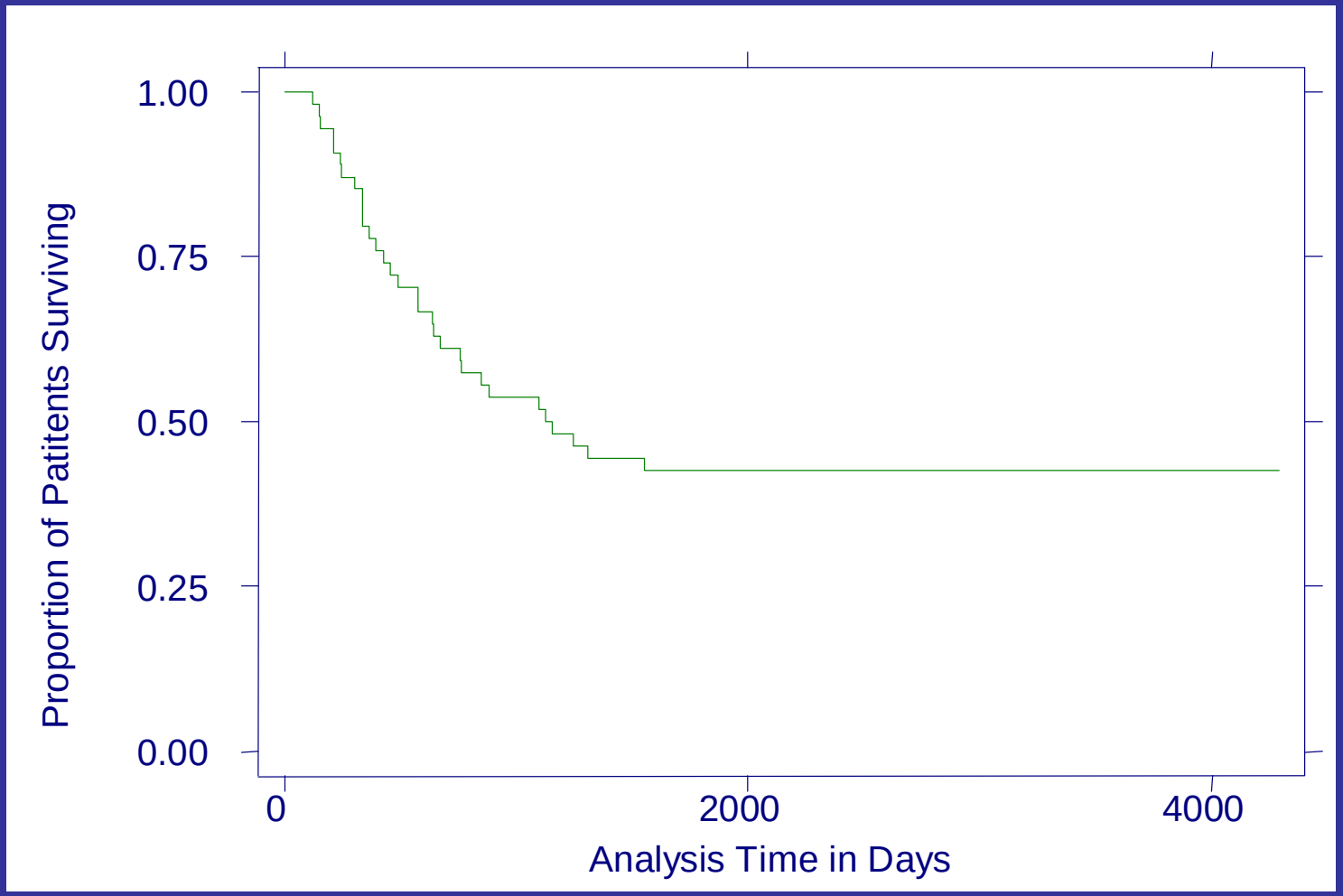
-T_2N_1 or greater/T_3Nx

-41% three yr survival

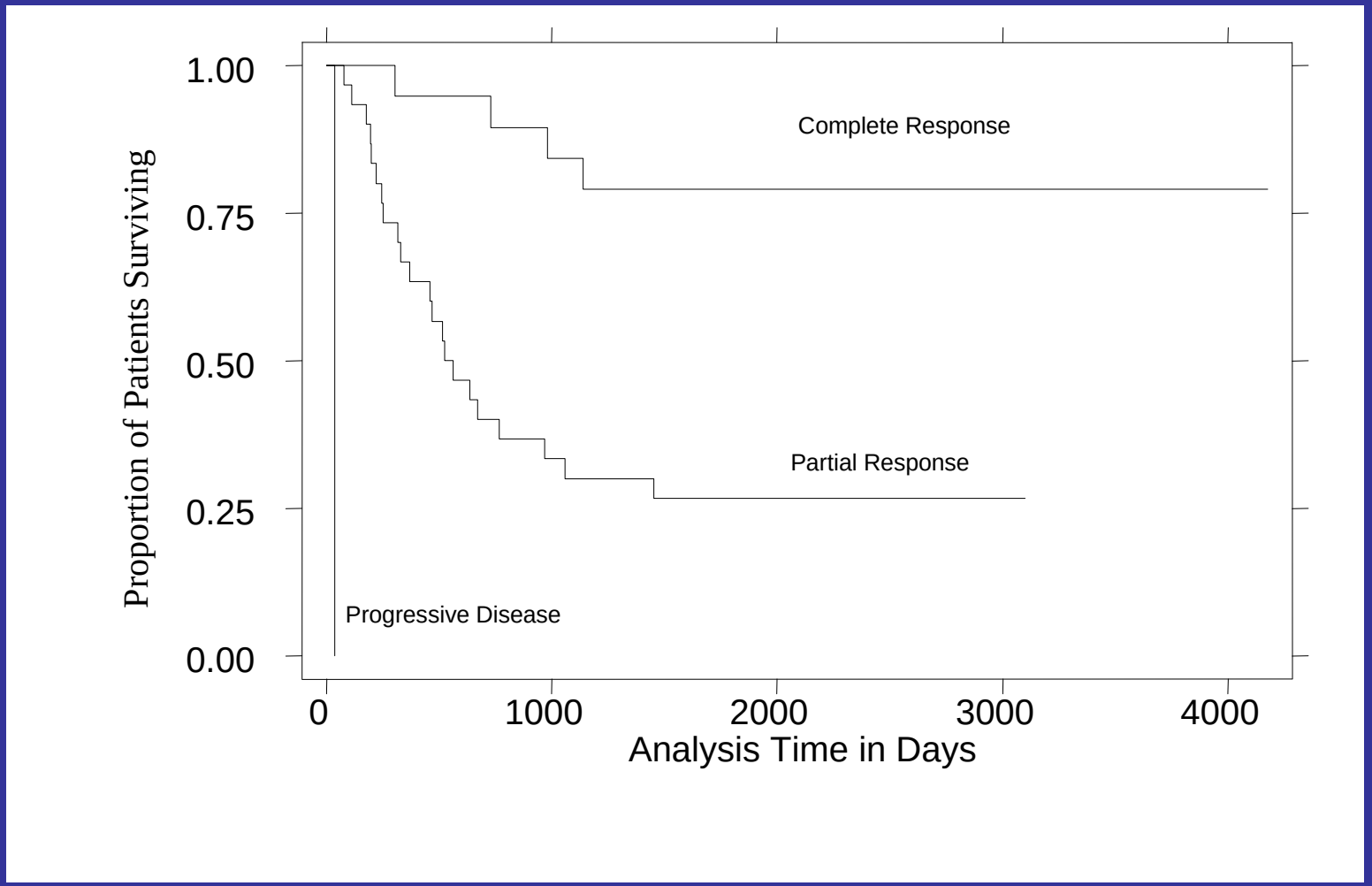
Concomitant Chemoradiotherapy Followed by Surgery

Study	RO Resection Surgery Only Arm	3 year Surv., Surg.	3 year Surv., CMT*	Median Follow-Up for Survivors	Histology	Schedule
Preoperative Chemoradiotherapy						
Le Prise	Not available (total n = 86)	47%+	47%+	Not available	Squamous	Sequential to 20 Gy
Bosset	69% (94/137)	34%	36%	55.2 months	Squamous	Sequential, Interrupted (no 5-FU) to 37 Gy
Urba	88% (44/50)	16%	30%	8.2 years	Both	Concurrent to 45 Gy
Walsh	Not available (total n = 113)	6%	32%	>5 years	Adeno	Concurrent to 40 Gy
Preoperative Chemotherapy						
Kelsen	59% (135/227)	26%	23%	46.5 months	Both	N/A
MRC	54% (215/402)	25%	32%	37.9 months	Both	N/A
Primary Chemoradiotherapy (CRT), 5-year Survival						
Herskovic	N/A	CRT 27%	R only 0 %	12.5 months	Both	CRT, 64 Gy R, 50 Gy

Overall Survival With Pre-operative Chemoradiotherapy Followed by Surgery



Survival by Pathologic Response



Pattern of Recurrence

- Almost always at a distant site.
- Approaches to this problem.
  - Adjuvant chemotherapy
  - Newer chemotherapy
  - Induction chemotherapy
  - Intensified chemotherapy

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  Result: nothing is much better…

Treatment of Metastatic Disease

- Palliative
- No standard chemotherapy approach
- Combination of two drugs based on 5-FU, platins, taxanes.
- Cisplatin/CPT-11, FOLFOX
- Median survival ~ 9 months
- Clinical trial

Palliation

- For swallowing trouble: stent most common
- For pain: narcotics, radiation
- For Cachexia: appetite stimulants, feeding tubes

Molecular Markers/Targets