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Gastroenterology & Hepatology
Advanced Practice Providers

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Esophageal Cancer

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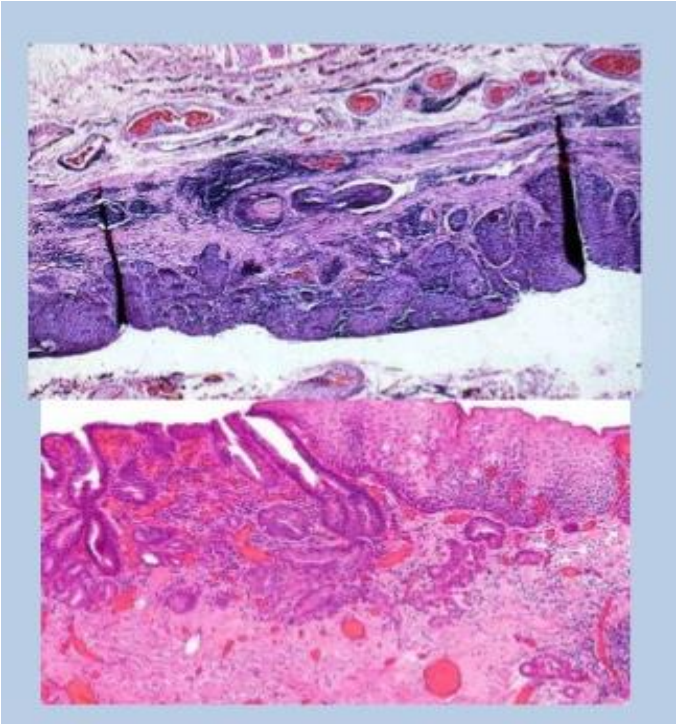
Disclosures

Gwen M. Cassidy, MSN, APN

- No financial relationships to disclose

Esophageal Cancer

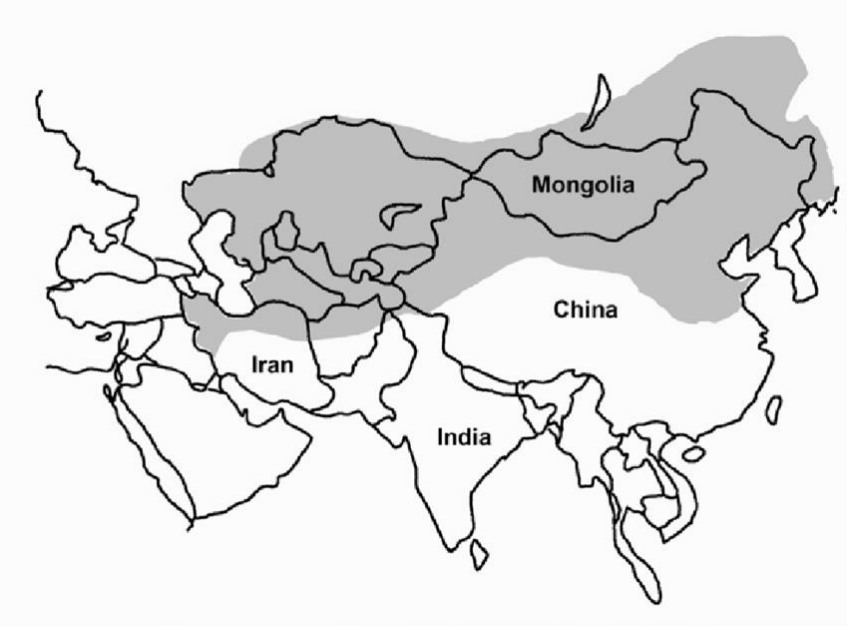


- Eighth most-common CA worldwide
- Sixth most common cause of death worldwide
- 18,440 cases will be dx in US each year
- Highly lethal
  - 16,170 deaths from disease

1. Napier KJ et al. *World J Gastrointest Oncol*. 2014;6(5):112. 2. Siegel RL et al. *CA Cancer J Clin*. 2020;70(1):7.

Esophageal Cancer Belt

- Southern/Eastern Africa, Eastern Asia
  - Worst in Northern Iran to North-Central China
- 90% of cases are squamous cell
- RF not well understood



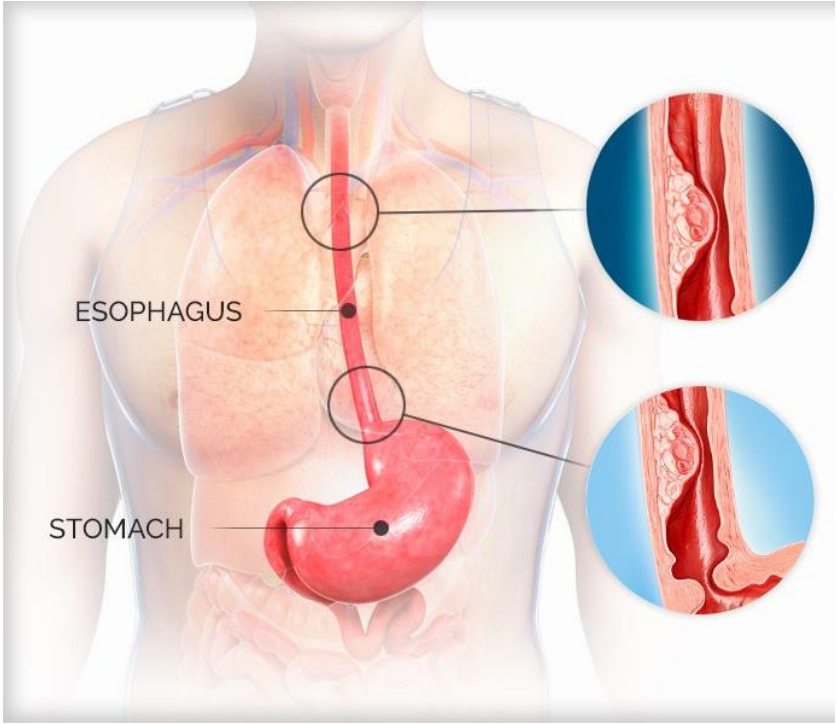
1. Jemal A et al. *CA Cancer J Clin*. 2011;61(2):69. 2. Gholipour C et al. *Dis Esophagus*. 2008;21(4):322. 3. Tran GD et al. *Int J Cancer*. 2005;113(3):456.

Esophageal Malignant Tumors

- Squamous cell
  - Was predominant form of tumor in most of 20th century
  - Accounting for 90% of tumors
  - Still the most predominant worldwide
- Adenocarcinoma
  - Increasing in prevalence in Western countries
  - Now > 60% of tumors in US
  - Predominantly in distal esophagus and EGJ

1. Thrift AP. *Cancer Epidemiol.* 2016;41:88. 2. Baquet CR et al. *J Natl Med Assoc*. 2005;97(11):1471.

GI Workup and Assessment



Esophageal Malignant Tumors

- Squamous cell
  - Precursor is epithelial dysplasia
  - Leads to carcinoma in situ and eventually invasive carcinoma
  - Generally arises 10 years prior to adenocarcinoma
  - Perioperative mortality higher
- Adenocarcinoma
  - Precursor is intestinal metaplasia
  - Metaplastic cells hyperproliferate
  - As they acquire DNA damage, becomes dysplastic and eventually malignant
  - Many (but not all) data support better prognosis

Lieberman MD et al. *J Thorac Cardiovasc Surg*. 1995;109(1):130.

Most Common RF

- Squamous cell
  - Male gender (2.5:1)
    - In low-instance areas
  - AA ethnicity (4:1)
  - Middle esophagus
  - Smoking
  - Alcohol
- Adenocarcinoma
  - Male gender (2.5:1)
  - Caucasian ethnicity (4:1)
  - Distal esophagus
  - GERD/Barrett's esophagus
  - Obesity
  - Smoking

1. Thrift AP. *Cancer Epidemiol*. 2016;41:88. 2. Engel LS et al. *J Natl Cancer Inst*. 2003;95(18):1404. 3. Wang L et al. *Int J Cancer.* 1997;71(5):719.

Case Study

James R.

- James R is a 63 yo M with PMH of obesity, remote smoking, HLD, HTN and long-standing GERD
  - Currently on omeprazole 20 mg that PCP placed him on 6 weeks ago
  - He still reports breakthrough symptoms with trigger foods
  - Reports he took OTC antacids for many years prior to starting PPI
- Main complaint is dysphagia to meats and breads, but reports that it is worsening to soft foods as well
  - Liquids are still okay and he has been supplementing with boost
  - 12-lb weight loss

Differential Diagnosis

- Benign stricture
- Achalasia
- Other motility disorders
- EOE
- Esophagitis
- Web and rings

Common Clinical Manifestations
Thoracic Tumor

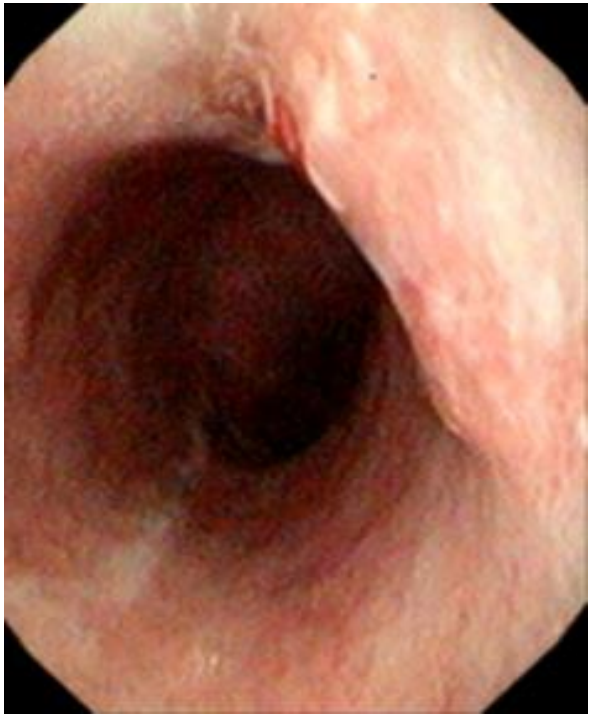
- Both types have similar presentation
- Early CA can be found on BE screening (6-10%)
- Odynophagia (20%)
- Dysphagia
  - Progressive
  - Frequently occurs when lumen is < 13 mm
  - Weight loss

Less Common Clinical Manifestations

- Regurgitation (saliva or food)
- Iron deficiency anemia
- TE fistula (late complication)
- S/S of metastatic dz

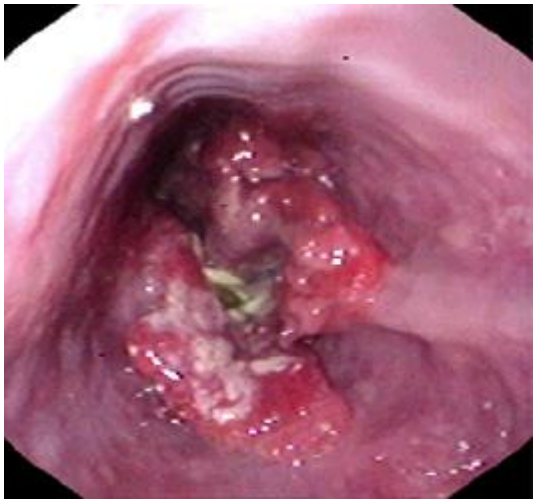
Meltzer CC et al. *Clin Nucl Med*. 2000;25(11):882.

Endoscopic Findings: Early Cancer



Appears as superficial plaques, nodules or ulcerations

Endoscopic Findings: Advanced Lesions



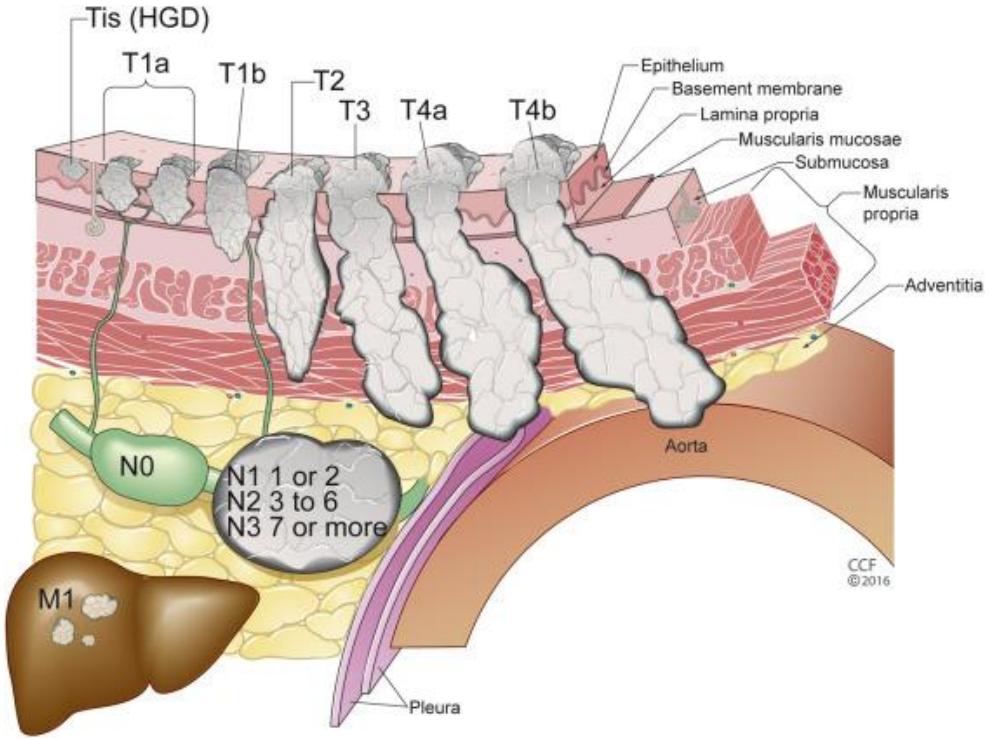
Appears as stricture, ulcerated masses,
circumferential masses or large ulcerations

Biopsy

- Confirms diagnosis in 90% of cases
- Greater number of bx increases accuracy
  - 98% accuracy for 7 bx
- Brush cytology increases bx accuracy to 100%

Graham DY et al. *Gastroenterology.* 1982;82(2):228.

Importance of Staging



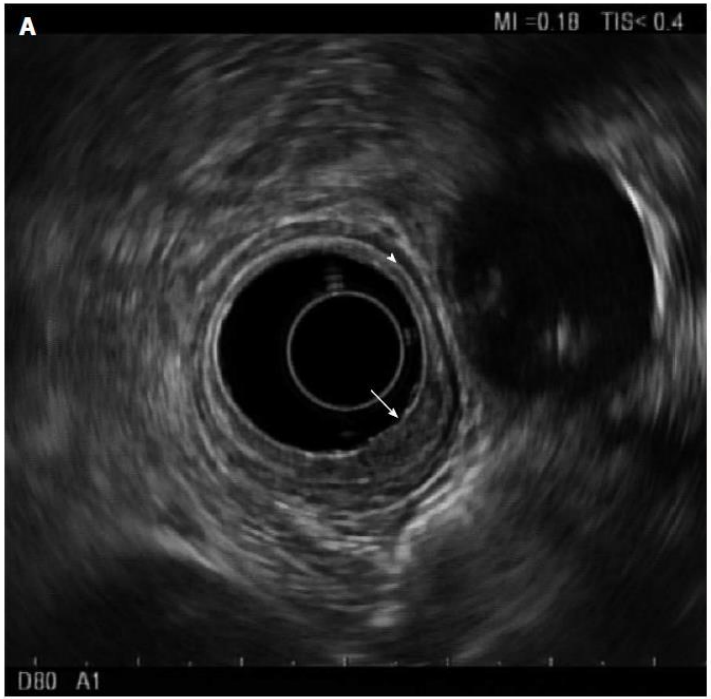
TNM staging system universally used

Directly impacts Tx decisions!

Pretreatment Staging Evaluation

- Locoregional staging
  - Endoscopic Ultrasound preferred
  - Bronchoscopy or laryngoscopy in certain cases
- Distant Metastases
  - CT neck, chest, abdomen
  - Whole-body integrated fluorodeoxyglucose (FDG)
  - Positron emission tomography (PET)/CT
  - Diagnostic laparoscopy (less common)

EUS for Superficial Tumors



- Controversial
  - Should it be used to determine who gets surgery?
- Argument that EGD with resection could be enough to determine

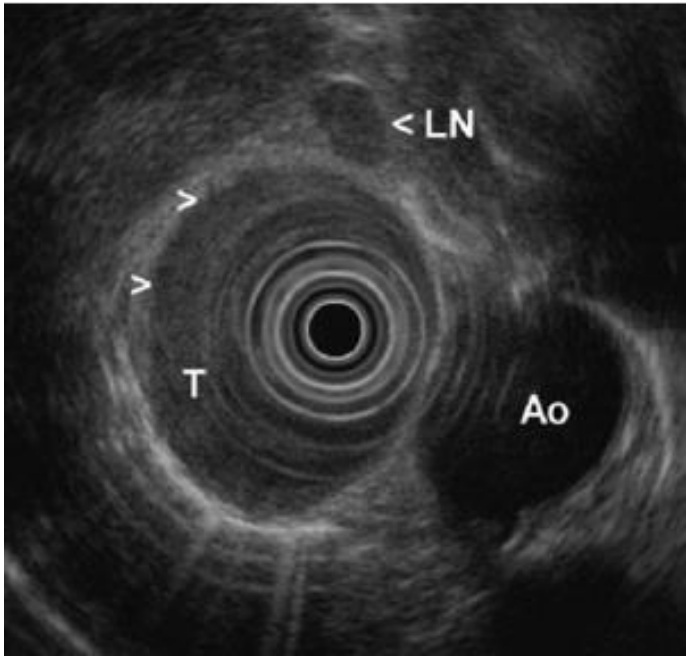
Pouw RE et al. *Gastrointest Endosc.* 2011;73(4):662.

EUS for Superficial Tumors

- Only Mucosal
  - Remove the tumor and determine invasion
  - Bx will guide if resection is enough or if surgery is needed
- Invades muscularis mucosa or lymph node involvement
  - Surgery recommended

EUS for Advanced Tumors

- Large caliber scope may preclude complete staging
- Accuracy much higher for transversable tumors
  - 81% vs 28% in one study



Catalano MF et al. *Gastrointest Endosc*. 1995;41(6):535.

Ways to Improve Accuracy

- Dilation with savary or balloon dilator
  - To 14-16 mm
  - **Perforation frequency 24%**
  - Newer scopes improve risk for perforation
  - Savary had 85-100% without complications
- US Catheters through the bx channel of the endoscope

1. Catalano MF et al. *Gastrointest Endosc.* 1995;41(6):535. 2. Kallimanis GE et al. *Gastrointest Endosc*. 1995;41(6):540.
3.Van Dam J et al. *Cancer.* 1993;71(10):2910. 4. Wallace MB et al. *Gastrointest Endosc*. 2000;51(3):309.

EUS in Node Staging

- High accuracy (80%) in the following areas
  - Cervical paraesophageal, right recurrent laryngeal, left paratracheal, upper and lower paraesophageal, infra-aortic, infracarinal, lower posterior mediastinal, and perigastric regions
- Fine-needle biopsies
  - 85% accuracy
  - Gold standard

Vazquez-Sequeiros E et al. *Gastrointest Endosc*. 2001;53(7):751.

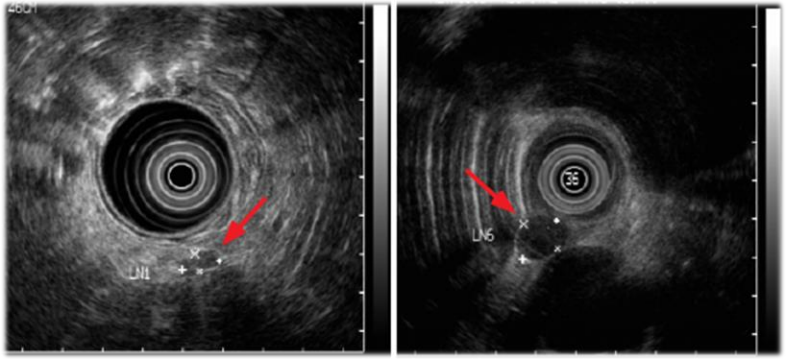
T Stage

T1	T2	T3	T4 resectable	T4 unrescectable
Mucosal	Involve the muscularis propria but do not have transmural invasion through the esophageal wall	Extra esophageal mass that extends into the into the adventitia	Extraesophageal mass that have invaded through the muscularis propria and adventitia to involve mediastinal structures such as the pleura, pericardium, azygos vein, diaphragm, or peritoneum	Extraesophageal mass that have invaded through the muscularis propria and adventitia to involve mediastinal structures such as the vertebral body, or airway

N Stage

- Width > 10 mm
- Round shape
- Smooth border
- Echo-poor pattern

N0	N1	N2	N3
No regional lymph node mets	1-2 regional lymph node mets	3-6 regional lymph node mets	> 7 regional lymph node mets



1. Catalano MF et al. *Gastrointest Endosc.* 1994; 40:442. 2. Bhutani MS et al. *Gastrointest Endosc.*1997; 45:474.

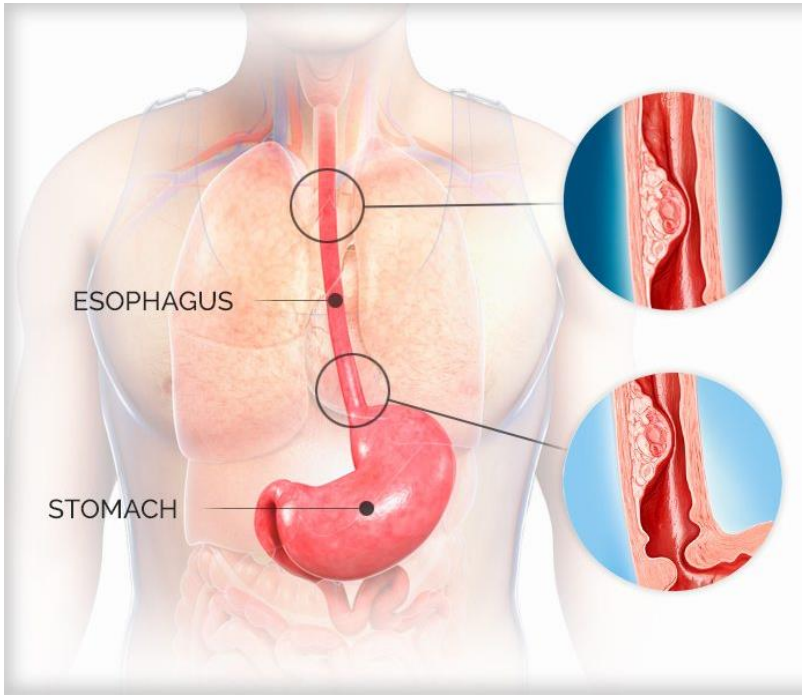
M Stage

- Common sites
  - Liver
  - Lungs
  - Bone
  - Adrenal glands
- Systemic imaging
  - CT
  - PET/CT
    - Can restage after initial therapy
- EUS
- Diagnostic Laparoscopy
  - Somewhat controversial
  - Reserved for potentially resectable cases
- Brain imaging not recommended

M0	N1
No distant mets	Distant mets

1. Meltzer CC et al. *Clin Nucl Med*. 2000;25(11):882. 2. National Comprehensive Cancer Network (NCCN). NCCN clinical practice guidelines in oncology. https://www.nccn.org/professionals/physician_gls. 3. Weinberg JS et al. *Cancer*. 2003;98(9):1925.

Treatment Overview



Endoscopic Resection of Small Lesions (T1N0)

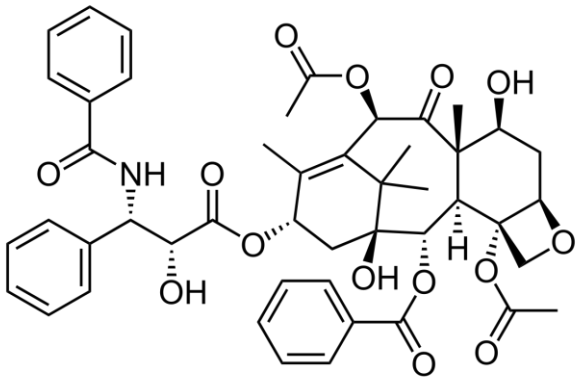
- May be suitable therapy under these conditions:
  - Diameter < 2 cm
  - Involves less than 1/3 of the esophageal wall
  - Limited to the mucosa of the esophagus

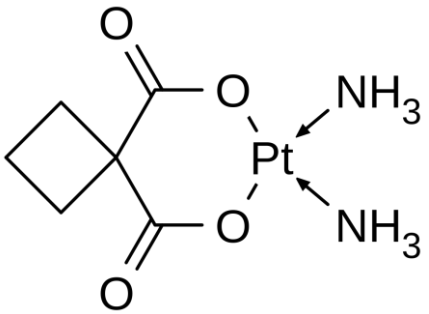
Treatment of Other Small Lesions (T2N0)

- Debated
- Upfront surgical intervention vs CRT
- Initial resection generally recommended for lesions < 2 cm and well-differentiated
- Role of neoadjuvant therapy is unknown
- Errors in staging can affect outcome

National Comprehensive Cancer Network (NCCN). NCCN clinical practice guidelines in oncology. https://www.nccn.org/professionals/physician_gls. Accessed September 14, 2020.

Approach to T3-T4 Lesions or N +





- Multimodality approach recommended
- Low-dose weekly carboplatin plus paclitaxel regimen
- Docetaxel, oxaliplatin, leucovorin, and fluorouracil (FLOT)

Shah MA et al. *J Clin Oncol*. 2020;38(23):2677.

Adenocarcinoma

- Chemoradiotherapy or chemotherapy
  - Can be used even if surgery is not recommended
  - Preoperative should be considered for pts who are not candidates for postoperative
  - Postoperative complications worse with CRT
  - FLOT regimen recommended
- RT
  - More beneficial in less optimal or extensive surgery

Shah MA et al. *J Clin Oncol.* 2020;38(23):2677.

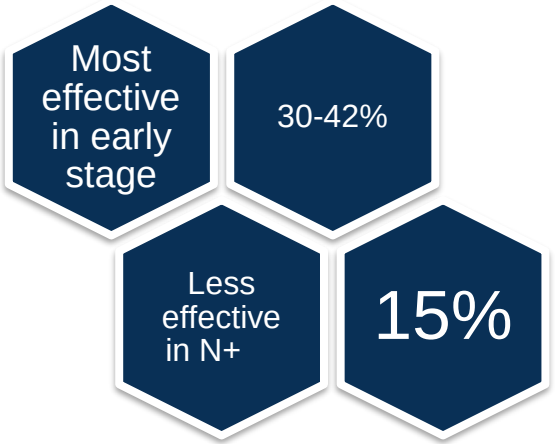
Squamous Cell Carcinoma

- Chemoradiotherapy or chemotherapy
- If responded completely to CRT, surgery has limited benefit
- CT can be used preoperatively when CRT is not an option
- Definitive CRT for CA in cervical esophagus
- Definitive CRT for non-surgical candidates

Shah MA et al. *J Clin Oncol.* 2020;38(23):2677.

Efficacy

Surgery alone



RT alone

- Similar outcome to surgery alone in SCC
  - 35-56%

1. Rice TW et al. *Dis Esophagus*. 2009;22(1):1. 2. Worni M et al. *J Am Coll Surg*. 2012;215(5):643. 3. Schreiber D et al. *J Thorac Oncol.* 2010;5(2):244. 4. Wong AT et al. *Ann Surg.* 2017;265(6):1146

Efficacy Concurrent Chemoradiotherapy

- VS RT alone
  - Statistically significant survival benefit
  - 58% vs 44%
- VS surgery alone
  - Mixed results
  - Half show statistically significant benefit
  - CROSS study showed 58 vs 44% at 3 years and 47 vs 33% 5 year survival rate

Sjoquist KM et al. *Lancet Oncol.* 2011;12(7):681.

Preopertive Therapy

CRT

- Response to preoperative therapy is an indicator of disease-free and overall survival
- 33-36% mean survival benefit
- 5-7 week interval in-between is preferred

CT

- Half of studies show benefit

Wang CC et al. *Radiother Oncol*. 2015 Apr;115(1):9-15.

Postoperative Adjuvant Therapy

CRT

- Adenocarcinoma, standard approach
- SCC
  - Potential benefit
- Improvement in outcome over RT

CT

- Not as strong of evidence

1. Bédard EL et al. *Cancer.* 2001;91(12):2423. 2. Adelstein DJ et al. *J Thorac Oncol.* 2009 Oct;4(10):1264-9. 3. Speicher PJ et al. *J Thorac Oncol*. 2015;10(1):181.

Post-Treatment Surveillance

- Majority of recurrences in the 1st year
- Local recurrences more frequent after definitive CRT
  - Some percentages were amenable to salvage surgery
- Occurs more frequently with pts with neuroadjuvant therapy vs surgery alone
  - Although could be selection bias

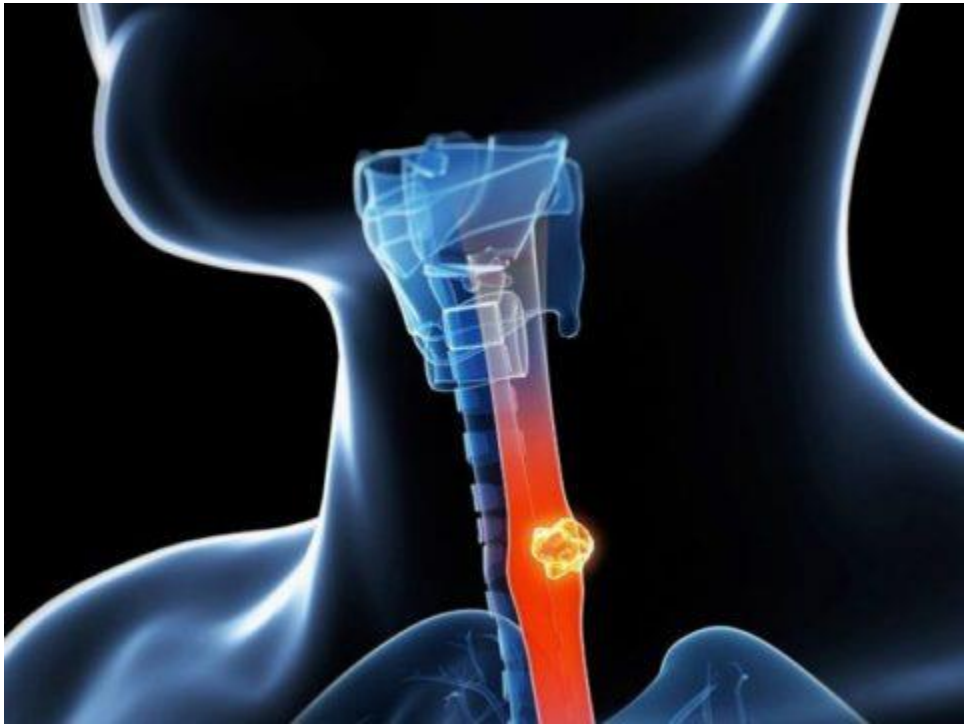
1. Sudo K et al. *J Clin Oncol.* 2014;32(30):3400. 2. Abate E et al. *J Am Coll Surg.* 2010;210(4):428.

Surveillance Strategy

H and P	CBC	Imaging
EGD	Dilation	Nutrition

National Comprehensive Cancer Network (NCCN). NCCN clinical practice guidelines in oncology. https://www.nccn.org/professionals/physician_gls. Accessed September 14, 2020.

Advanced and Inoperable Treatment



Thoracoabdominal Tumors

- RT with concurrent chemotherapy (if tolerated)
- Optimal regimen has not been established
- Most patients will not benefit from esophagectomy
- Inconsistent data of RT vs CRT, although favors CRT
- Salvage esophagectomy (rare cases)

RT Complications

- TE fistula
- Stricture

Endoscopic Palliation of Dysphagia

- Dilation
- Injection therapy
- Photodynamic therapy
- APC
- Ablation
- Stent

Brachytherapy

- Can be more durable palliation than stent
- Restricted to pts with < 6 months life expectancy, but stents preferred for > 3 months life expectancy
- Used with caution 2/2 risk for fistula formation

Gaspar LE et al. *Int J Radiat Oncol Biol Phys.* 1997;38(1):127.

Case Study

James R.

- T3N1M0 Tumor on EUS
- Was given preoperative CRT and esophagectomy and post-operative CT
- Doing well 1 year out, but will require lifelong follow-up as discussed

Conclusion

- An ounce of prevention is worth a pound of cure
  - Acid suppression in high-risk patients
  - Stressing smoking cessation
  - Screening for BE
  - Early detection is key

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Questions?