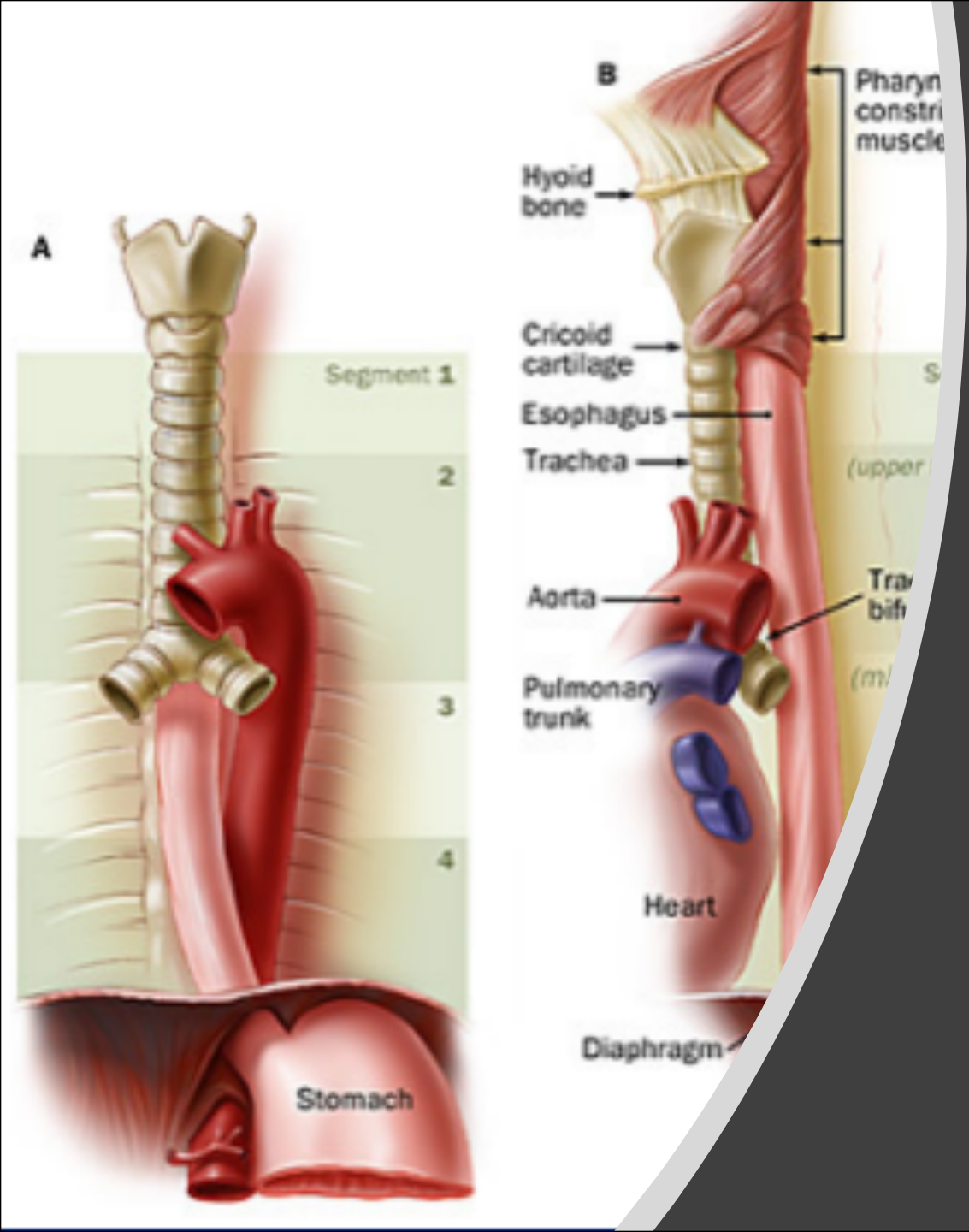


Esophageal Cancer

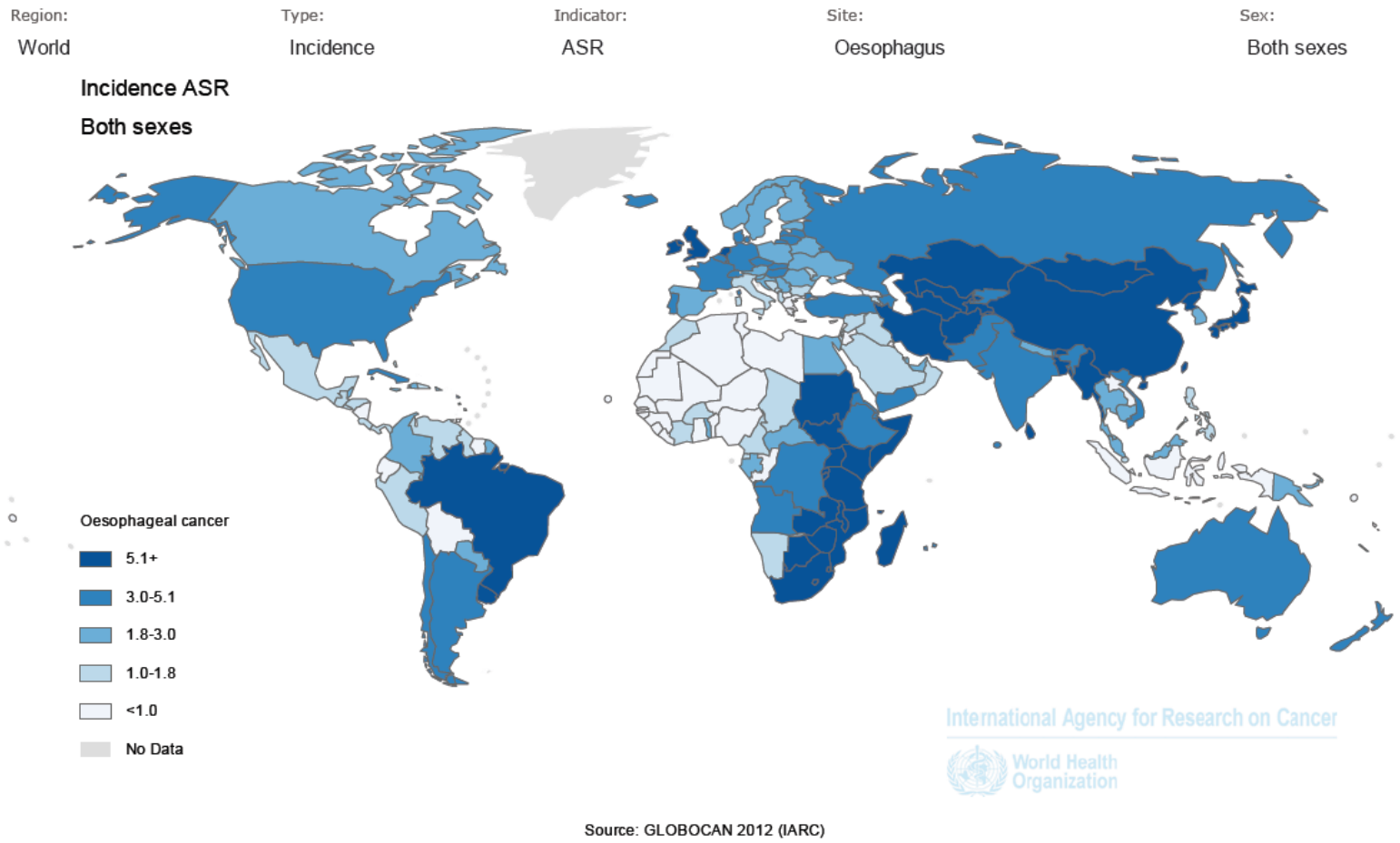
Epidemiology

Worldwide, an estimated 455,800 new esophageal cancer cases and 400,200 deaths

Incidence rates vary internationally by nearly 16-fold, with the highest rates found in Southern and Eastern Africa and Eastern Asia, and the lowest rates in Western and Middle Africa and Central America in both males and females .

In the highest-risk area, stretching from Northern Iran through the central Asian republics to North-Central China (often referred to as the "esophageal cancer belt"), 90 percent of cases are squamous cell carcinomas (SCC) .

Epidemiology



Source: GLOBOCAN 2012 (IARC)

Epidemiology

- Major risk factors in these areas are not well understood, but are thought to include
  - poor nutritional status,
  - low intake of fruits and vegetables,
  - drinking beverages at high temperatures.
- Low-risk areas:
  - smoking
  - excessive alcohol consumption in 90% of SCC
- The male to female ratio is 3:2 for SCC and 10:1 for ACA.

Epidemiology

Table (3) Number and percentage of cancer by primary site & gender- Jordan, 2015

Primary Site	Male		Female		Total	
	N	%	N	%	N	%
All Sites	2668	100.0	2888	100.0	5556	100.0
Lip	7	0.3	3	0.1	10	0.2
Tongue	12	0.4	9	0.3	21	0.4
Mouth	11	0.4	6	0.2	17	0.3
Salivary glands	6	0.2	10	0.3	16	0.3
Pharynx	32	1.2	9	0.3	41	0.7
Esophagus	20	0.7	5	0.2	25	0.4
Stomach	101	3.8	56	1.9	157	2.8
Small intestine	13	0.5	15	0.5	28	0.5
Colon	250	9.4	196	6.8	446	8.0
Rectum	138	5.2	84	2.9	222	4.0
Liver, Biliary Passages	74	2.8	43	1.5	117	2.1
Pancreas	57	2.1	42	1.5	99	1.8
Other & Unspecified Digestive	4	0.1	11	0.4	15	0.3
Larynx	76	2.8	16	0.6	92	1.7

ETIOLOGIC FACTORS:

- **Hereditary factors**

  Familial aggregation

  Uncertain

- **Squamous cell carcinoma**

  Smoking and alcohol

  Dietary factors

  N-nitrous compounds

  Certain types of pickled vegetables.

  Toxin-producing fungi (eg, aflatoxin)

ETIOLOGIC FACTORS

- High temperature beverages and foods
- Red meat intake
- Zinc deficiency
- low intake of dietary folate

ETIOLOGIC FACTORS

- Underlying esophageal disease:
  - Achalasia
  - Caustic strictures
- Prior gastrectomy
- Atrophic gastritis
- Tylosis
- Upper aerodigestive tract cancer
- Poor oral hygiene

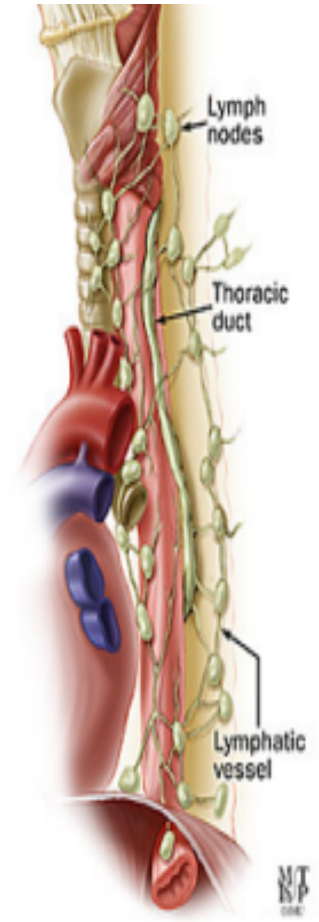
ETIOLOGIC FACTORS

Adenocarcinoma:

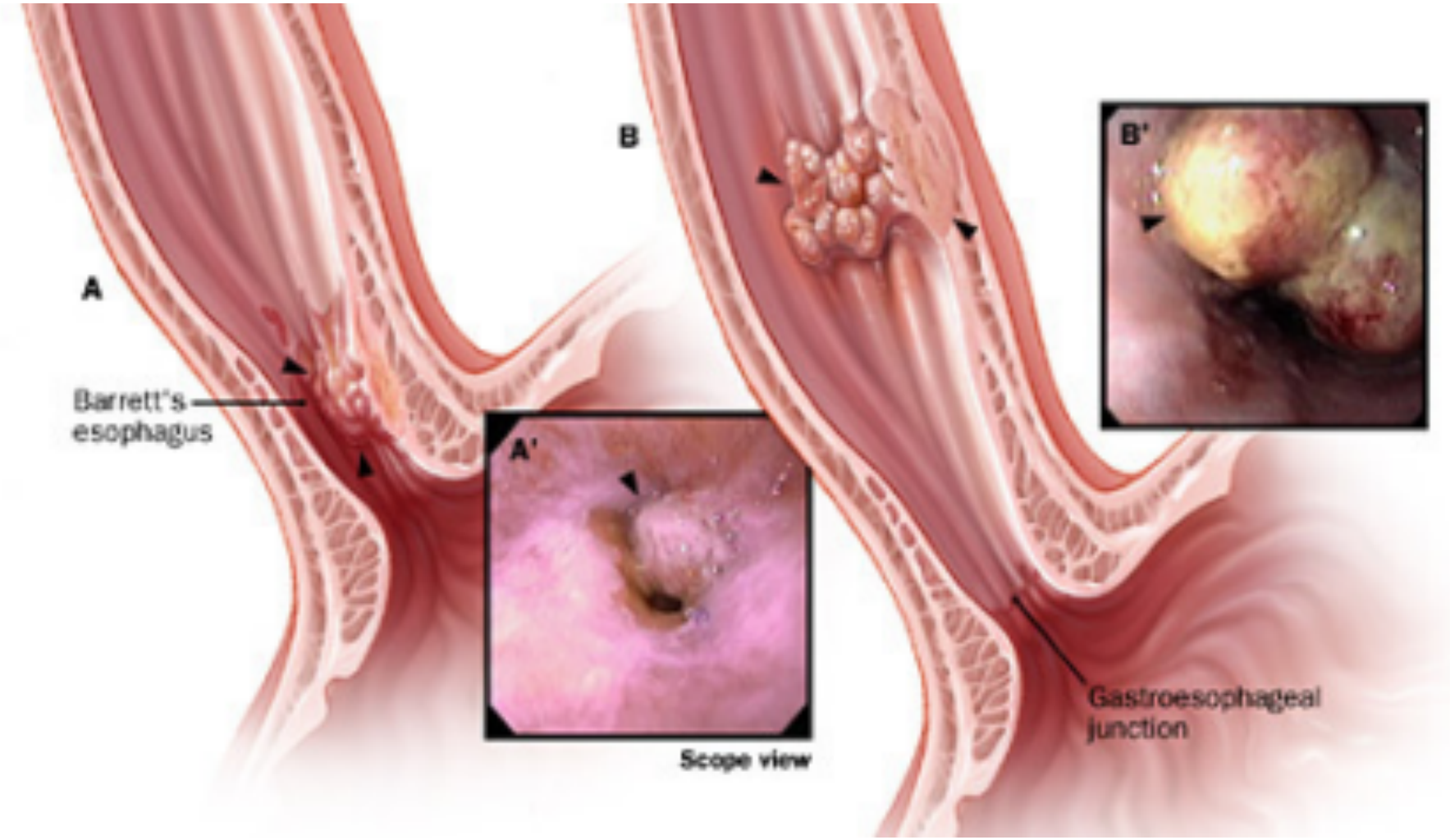
- Gastroesophageal reflux disease
- Barrett's metaplasia
- Smoking
- Alcohol
- Obesity
- Helicobacter pylori infection

Lymphatic Drainage:

- Local lymph node invasion occurs early and quickly because the lymphatics in the esophagus are located in the lamina propria, in contrast to the rest of the gastrointestinal tract, in which they are located beneath the muscularis mucosa.
- The tumor spreads to regional lymph nodes along the esophagus, the celiac area, and adjacent to the aorta.



Types:


A
Barrett's esophagus
A'
Scope view
B
B'
Gastroesophageal junction

A- Squamous cell carcinoma

- Midportion of the esophagus.
- SCC arises from small polypoid , denuded epithelium, or plaques .
- These early lesions are usually subtle, and can easily be missed on endoscopy.
- More advanced lesions are characterized by infiltrating and ulcerated masses, which may be circumferential
- SCC invades the submucosa at an early stage, and extends along the wall of the esophagus usually in a cephalad direction
- Invasion of local structures may result in fistula formation (such as to the trachea).
- Erosion into the aorta can be associated with massive upper gastrointestinal hemorrhage.
- Distant metastases to the liver, bone, and lung are seen in nearly 30% of patients

B- Adenocarcinoma

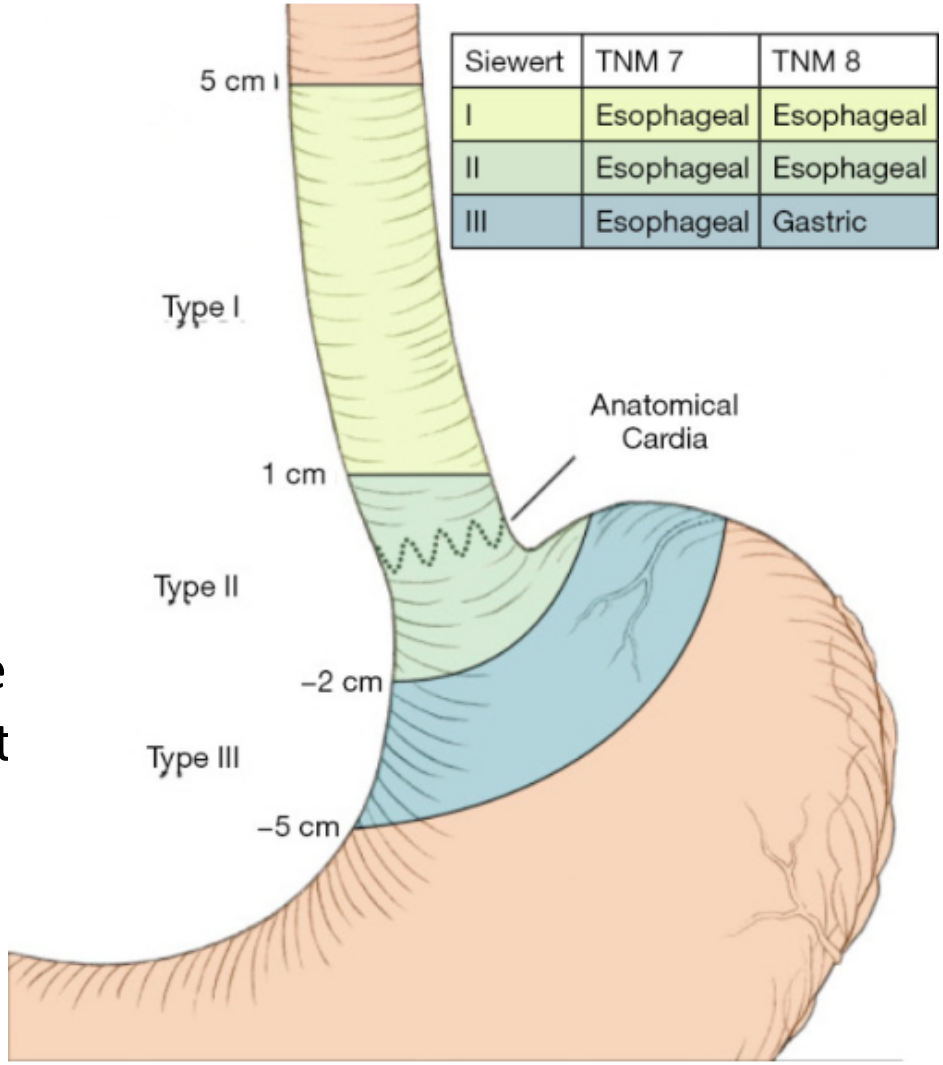
The majority of cases are located near the **gastroesophageal junction** and are associated with endoscopic evidence of **Barrett's esophagus**.

- Adenocarcinoma arising in Barrett's esophagus may present as an ulcer, a nodule, an altered mucosal pattern, or no visible endoscopic abnormality
- Early adenocarcinoma not associated with Barrett's esophagus arises from an ulcer, plaque, or nodule near the gastroesophageal junction

Siewert I: spread to mediastinal and celiac nodes: esophagectomy only required, with negative gastric margins.

Siewert II: generally esophagectomy only is required, with negative gastric margins. Spread is to abdominal lymph node

Siewert III: best treated wit total gastrectomy, with possible esophagectomy. Spread is to abdominal lymph nodes.



Siewert	TNM 7	TNM 8
I	Esophageal	Esophageal
II	Esophageal	Esophageal
III	Esophageal	Gastric

Adenocarcinoma:

- Similar to SCC, lymph node metastases occur early to adjacent or regional lymph nodes.
- Involvement of celiac and perihepatic nodes is more common with adenocarcinoma because of the location of the tumor at the gastroesophageal junction

CLINICAL MANIFESTATIONS:

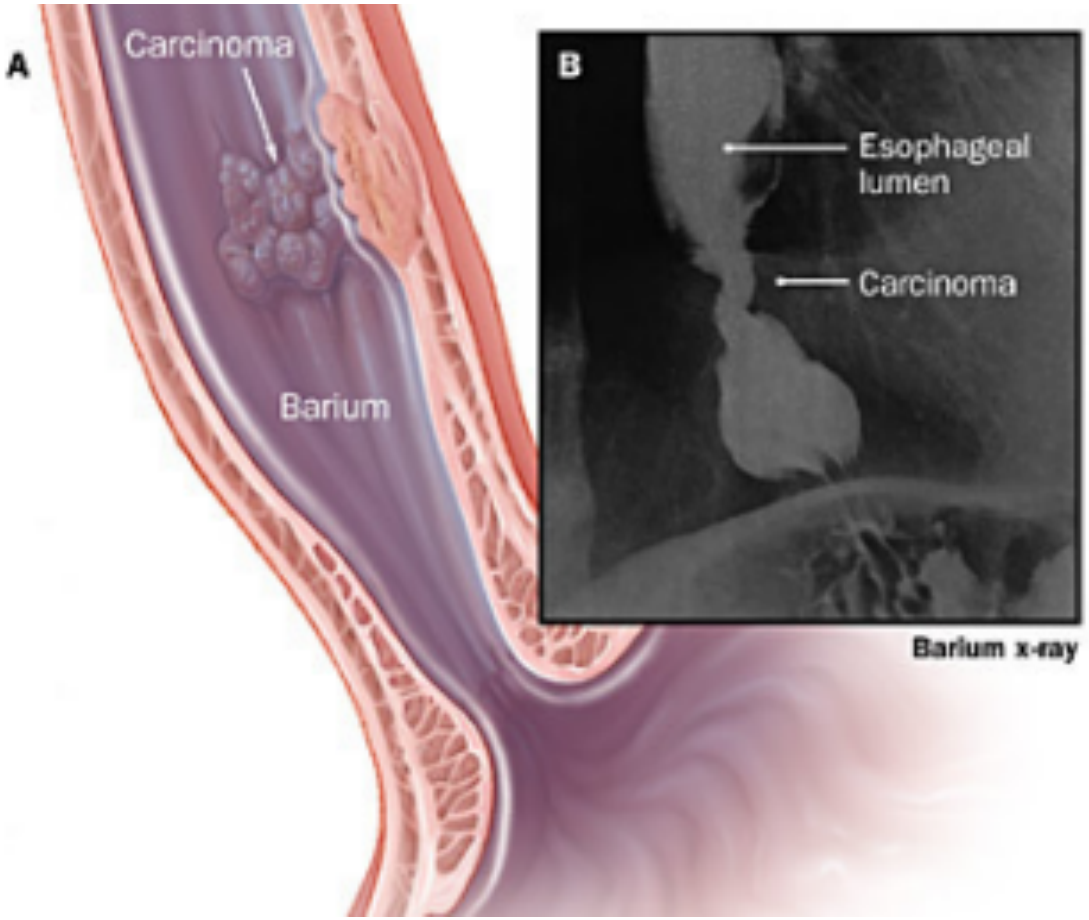
- Early intramucosal cancers are not specifically symptomatic
- Early symptoms of esophageal cancer are subtle and nonspecific.
  Transient "sticking" of apples, meat, hard-boiled eggs, or bread
  Retrosternal discomfort or burning sensation.
- Progressive solid food dysphagia
- weight loss:
  dysphagia
  changes in diet
  tumor-related anorexia.
- Regurgitation of saliva or food uncontaminated by gastric secretions
- Aspiration pneumonia
- Hoarseness
- Chronic gastrointestinal blood loss.
- Tracheobronchial fistulas Life expectancy is less than four weeks following the development of this complication.

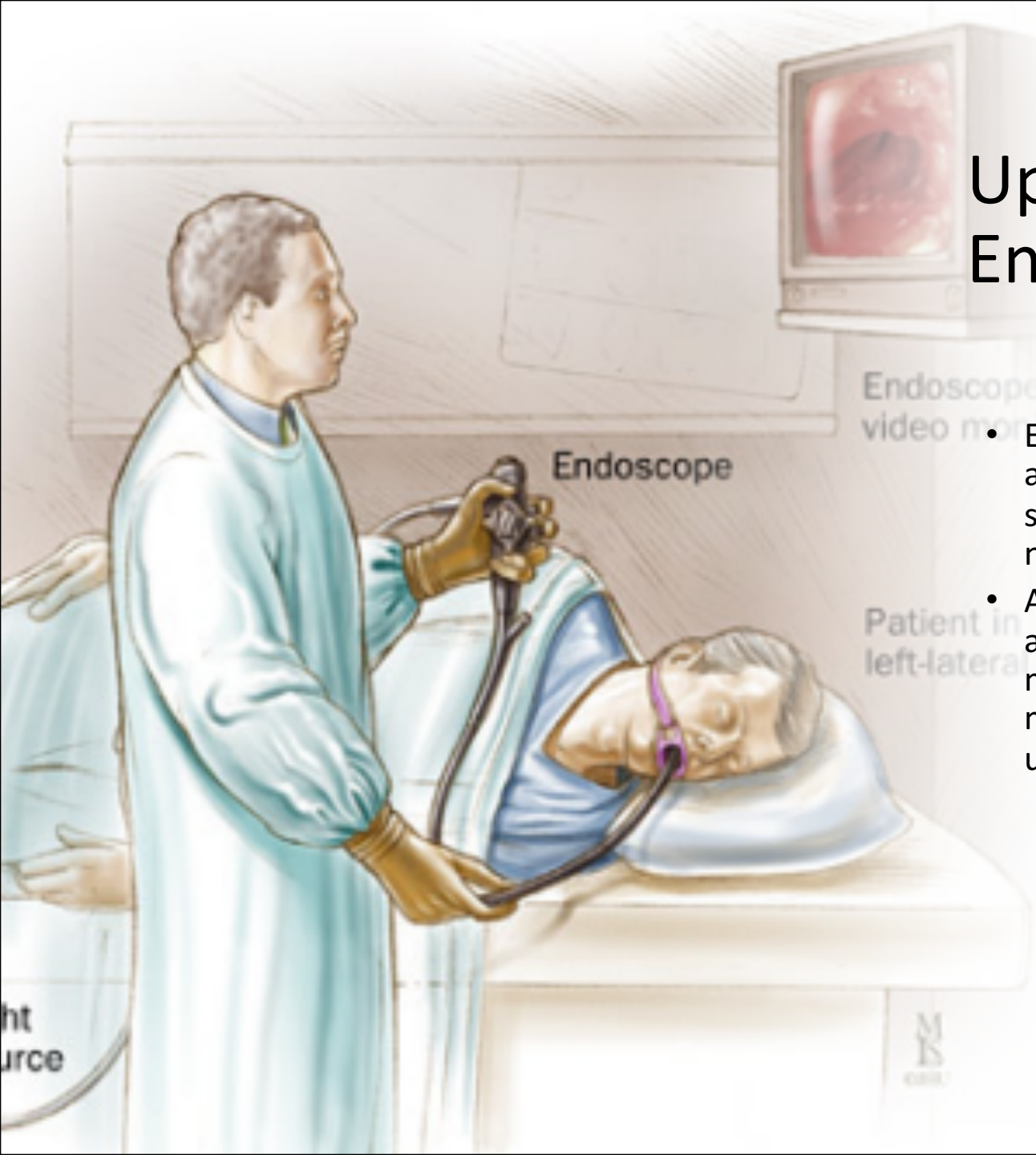
DIAGNOSTIC TESTING

- **Barium studies**
- **Endoscopic biopsy .**
- **Brush cytology**

17% of lesions thought to be benign endoscopically were subsequently proven to be malignant

Barium Study

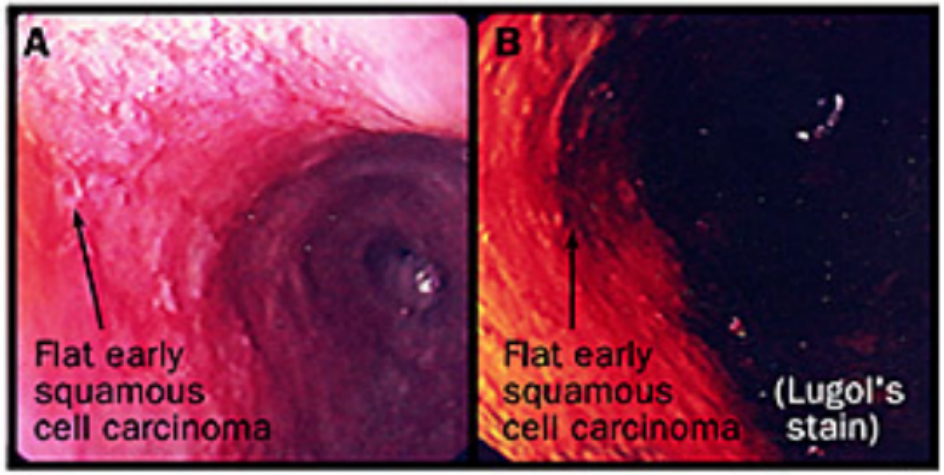


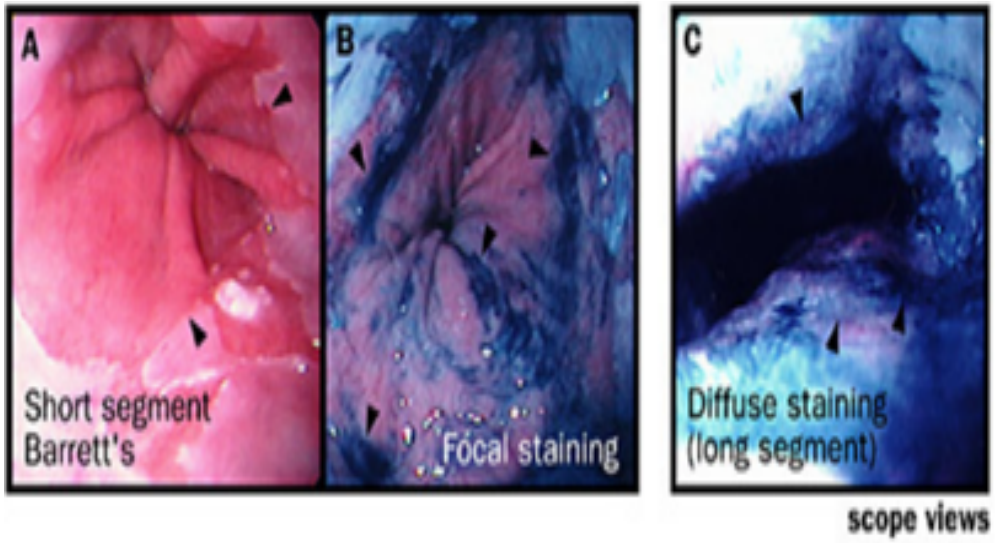


Upper Endoscopy:

- Early esophageal cancers appear endoscopically as superficial plaques, nodules, or ulcerations
- Advanced lesions appear as strictures , ulcerated masses, circumferential masses , or large ulcerations.

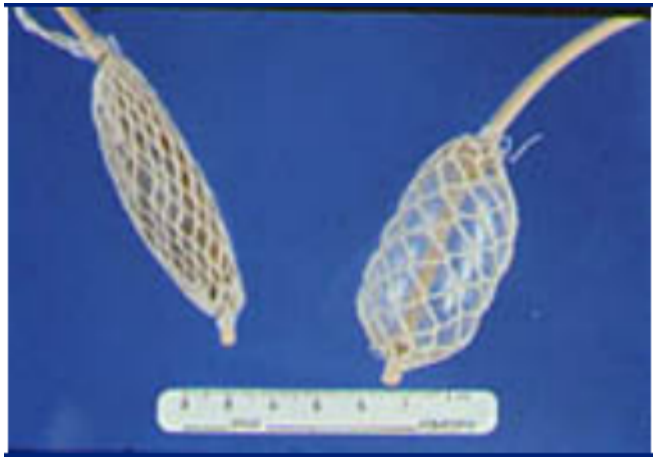
Chromoendoscopy:





Balloon Cytology

- screening



Imaging for diagnosis and staging

Accurate staging of esophageal cancer includes:

- Endoscopy
- Chest and abdominal CT
- PET
- EUS

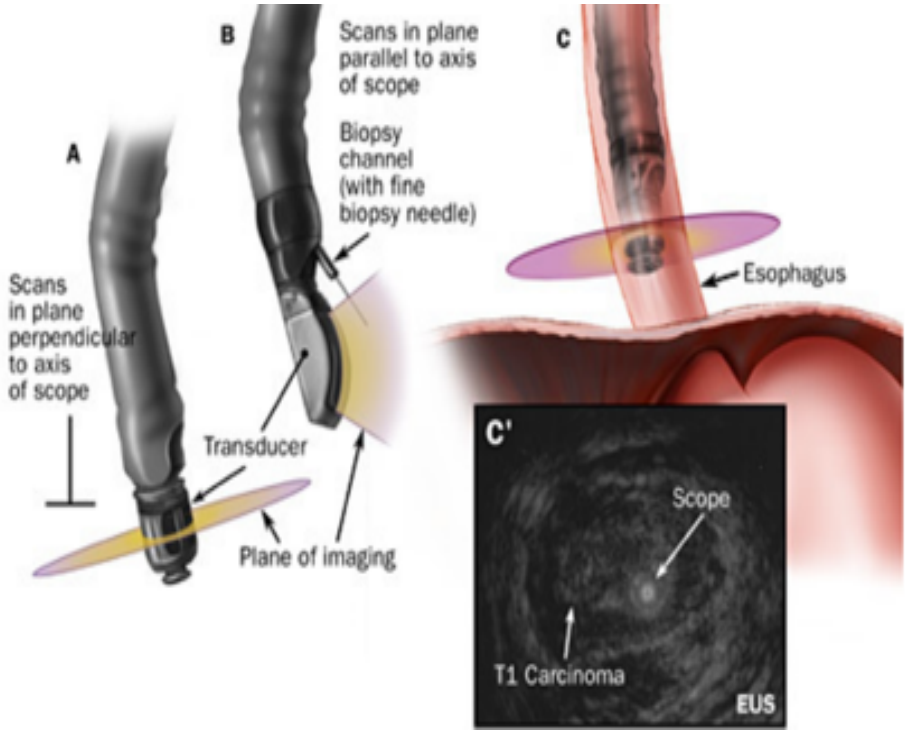
- EUS and CT together offer a 79% accuracy for T staging and 82% accuracy for N staging.

Endoscopic ultrasound

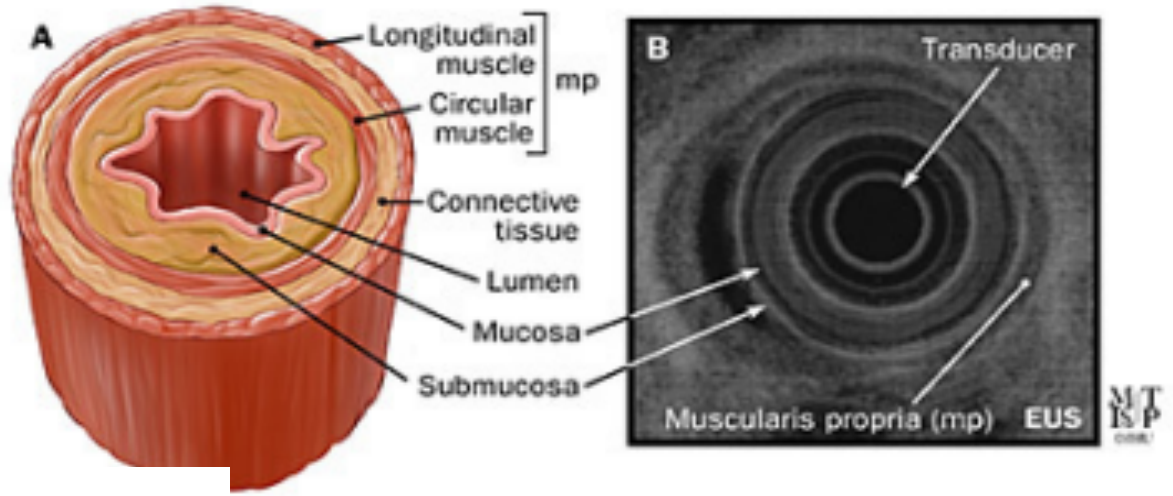
This is the gold standard for defining T stage: it allows detailed assessment of esophageal wall and surrounding structures.

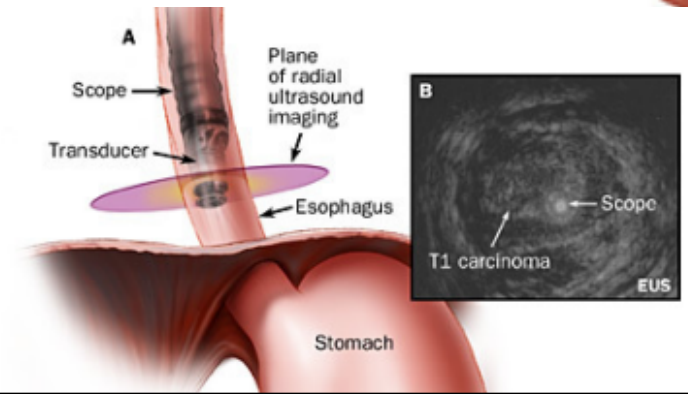
- Also allows fine needle aspiration (FNA) of suspicious lymph nodes.

- EUS has several limitations: it is poor at assessing tracheobronchial invasion, may be unable to pass through very tight stenoses, and cannot detect distant metastases.



EUS:

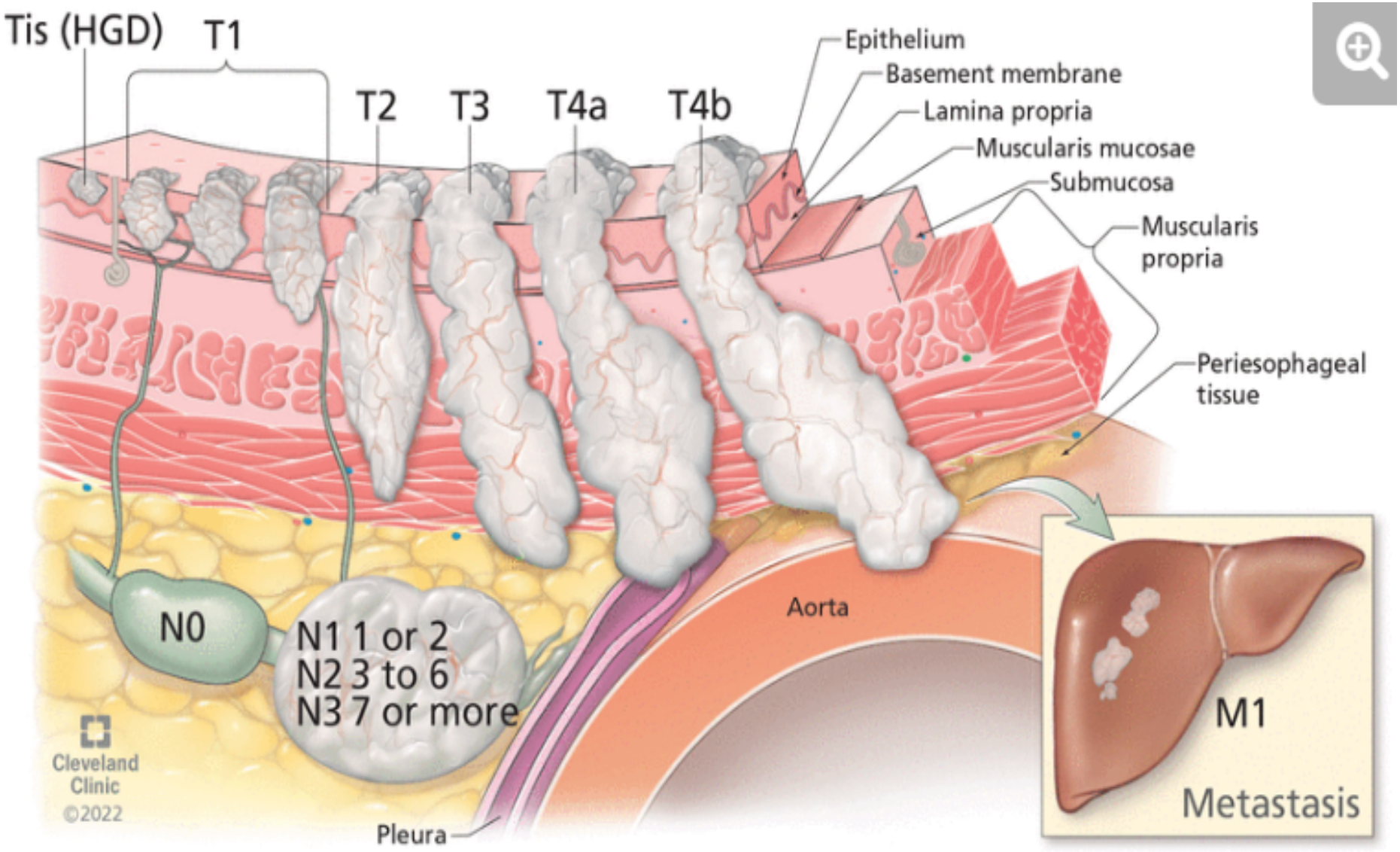

A
Longitudinal muscle
Circular muscle
mp
Connective tissue
Lumen
Mucosa
Submucosa
B
Transducer
Muscularis propria (mp)
EUS


A
Scope
Plane of radial ultrasound imaging
Transducer
Esophagus
Stomach
B
Scope
T1 carcinoma
EUS

PET scan

- PET is most useful as a combination PET/CT fusion where it has a 78% sensitivity for identifying nodal disease and distant metastasis.

TNM staging:


Tis (HGD)
T1
T2
T3
T4a
T4b
Epithelium
Basement membrane
Lamina propria
Muscularis mucosae
Submucosa
Muscularis propria
Periesophageal tissue
N0
N1 1 or 2
N2 3 to 6
N3 7 or more
Aorta
M1
Metastasis
Pleura
Cleveland Clinic
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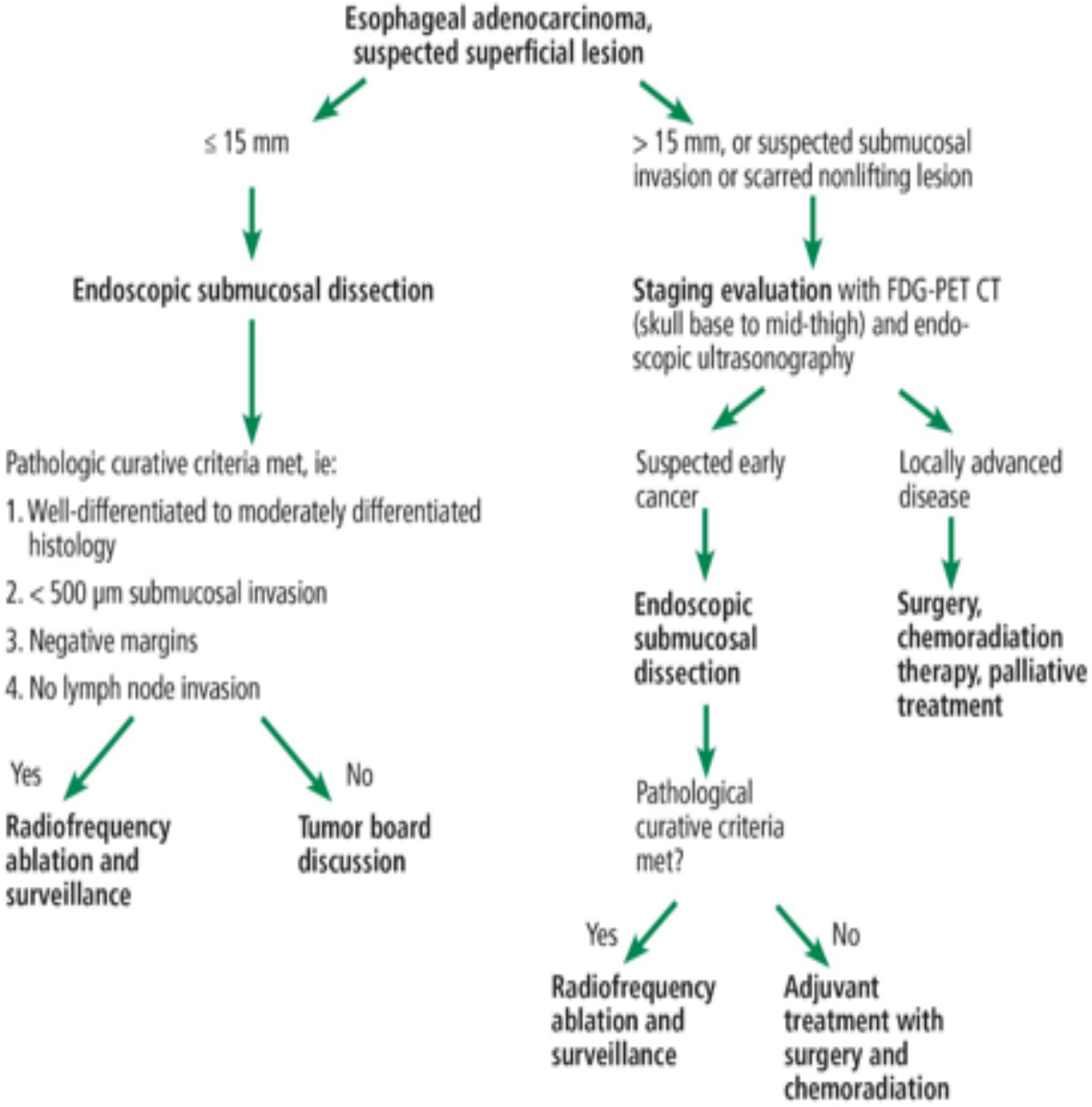
Treatment options include:

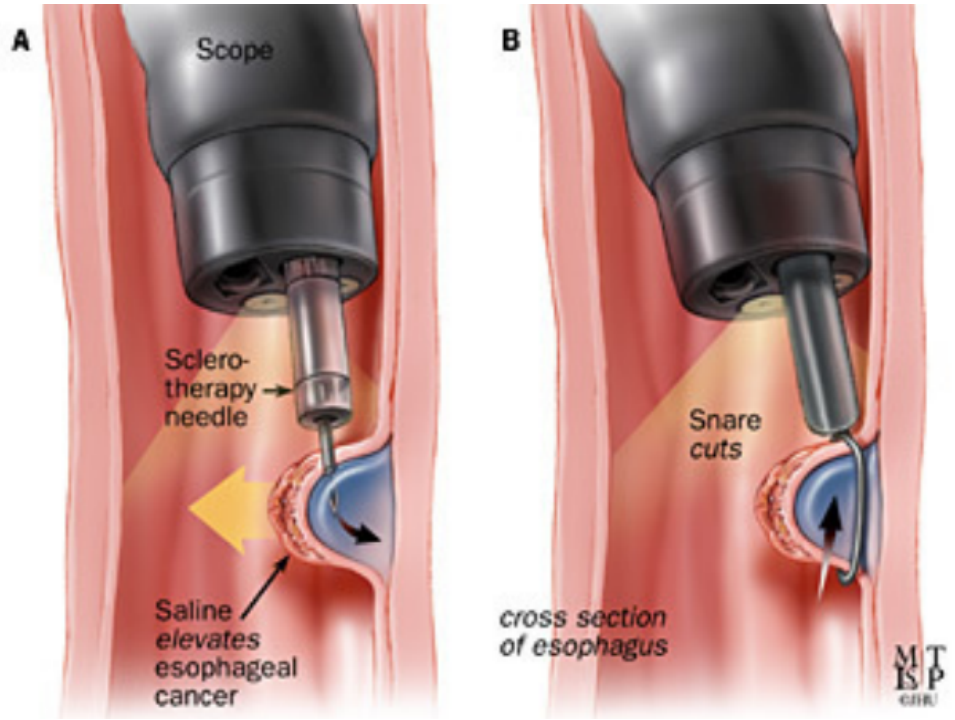
- Primary surgery
- Neoadjuvant chemoradiation followed by surgery
- Postoperative adjuvant chemoradiotherapy
- Definitive or primary chemoradiation
- Palliative chemotherapy and radiotherapy.

Treatment:


Esophageal adenocarcinoma, suspected superficial lesion
≤ 15 mm
> 15 mm, or suspected submucosal invasion or scarred nonlifting lesion
Endoscopic submucosal dissection
Staging evaluation with FDG-PET CT (skull base to mid-thigh) and endoscopic ultrasonography
Pathologic curative criteria met, ie:
1. Well-differentiated to moderately differentiated histology
2. < 500 µm submucosal invasion
3. Negative margins
4. No lymph node invasion
Suspected early cancer
Locally advanced disease
Endoscopic submucosal dissection
Surgery, chemoradiation therapy, palliative treatment
Yes
No
Radiofrequency ablation and surveillance
Tumor board discussion
Pathological curative criteria met?
Yes
No
Radiofrequency ablation and surveillance
Adjuvant treatment with surgery and chemoradiation

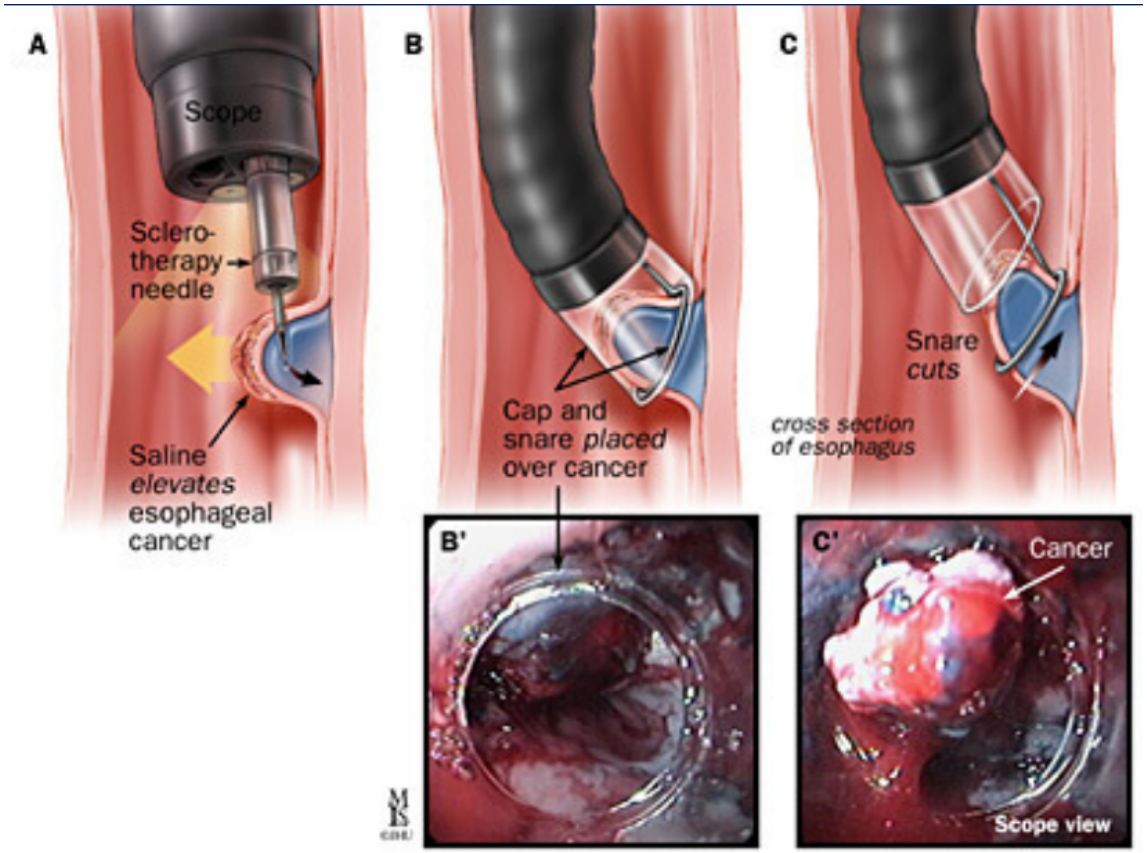
Endoscopic surgery

- **Endoscopic mucosal resection.**
- **Endoscopic submucosal dissection**



Technique of endoscopic mucosal resection using a clear cap.

Endoscopic surgery:



SELECTION OF OPERATIVE CANDIDATES

- A surgical resection was the standard treatment approach for patients with an early esophageal cancer, but its utility as a monotherapy has been challenged .
- **Criteria for resection**
- **Esophagectomy as first line of therapy**

  T1N0M0

  T2N0M0
- **Esophagectomy following neoadjuvant chemotherapy or chemoradiotherapy**

❑ Patients with thoracic or esophagogastric junction tumors and full-thickness (T3) involvement of the esophagus with/without nodal disease

❑ Selected patients with T4 disease with invasion of local structures (pericardium, pleura, and/or diaphragm only) that can be resected en bloc, and who are without evidence of metastatic disease to other organs (eg, liver, colon).

- **Relative contraindications**

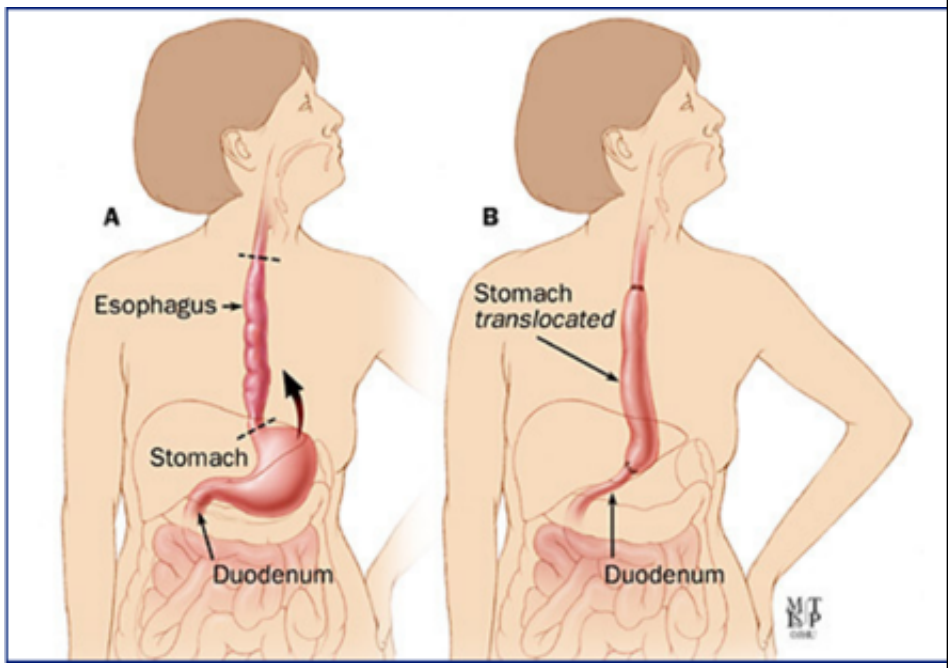
  Advanced age

  Comorbid illness

- **Indicators of unresectability** — The presence of **metastatic disease,** such as peritoneal, lung, bone, adrenal, brain, or liver metastases, or extraregional lymph node spread (eg, paraaortic or mesenteric lymphadenopathy), precludes an attempt at resection.

Esophagectomy:

- **Approaches:**
  - esophagectomy *with thoracotomy*
  - esophagectomy *without thoracotomy*
  - no survival difference
- **Conduits:**
  - Stomach: right gastric and right gastric epiploic artery pedicles.
  - Left colon: ascending branch of left colic artery pedicle.
  - Right colon: middle colic artery pedicle.
  - Jejunal free graft: microsurgery implantation of mesenteric arcade.
  - Myocutaneous tube flaps: radial forearm, pectoralis major, TRAM.



Lymphadenectomy

- The optimal extent of lymph node dissection in esophageal cancer is **controversial.**
- The esophagus has an extensive lymphatic drainage, which is divided into three zones (fields): abdominal, intrathoracic, and cervical.
- Lymph node resection strategies at the time of esophagectomy range from standard regional and one-field lymphadenectomy, to radical approaches involving two- or three-field lymphadenectomy.

- **Neoadjuvant chemoradiotherapy followed by surgery** probably offers best survival in patients with locally advanced resectable tumor: cure rate is 50% due to a combination of inadequate pathologic response and distant metastases:
  - Stage 0, I, and IIa should be offered primary surgery.
  - Stage IIB and III tumors should be offered trimodality therapy.
  - Stage IV tumors are treated with primary chemoradiotherapy.

Nutritional status should be optimized before treatment, possibly requiring either NG or jejunal tube feeds.

PEG should be avoided, if possible, if the stomach is planned as a conduit. PEG may injure the right gastroepiploic artery which is a necessary vascular pedicle for a gastric conduit.

- Adjuvant therapy:

Patients with R1 or R2 resection or residual postoperative N1 disease should be considered for adjuvant chemotherapy & radiation, though there is no conclusive data that supports this regimen.

- Primary chemoradiation:

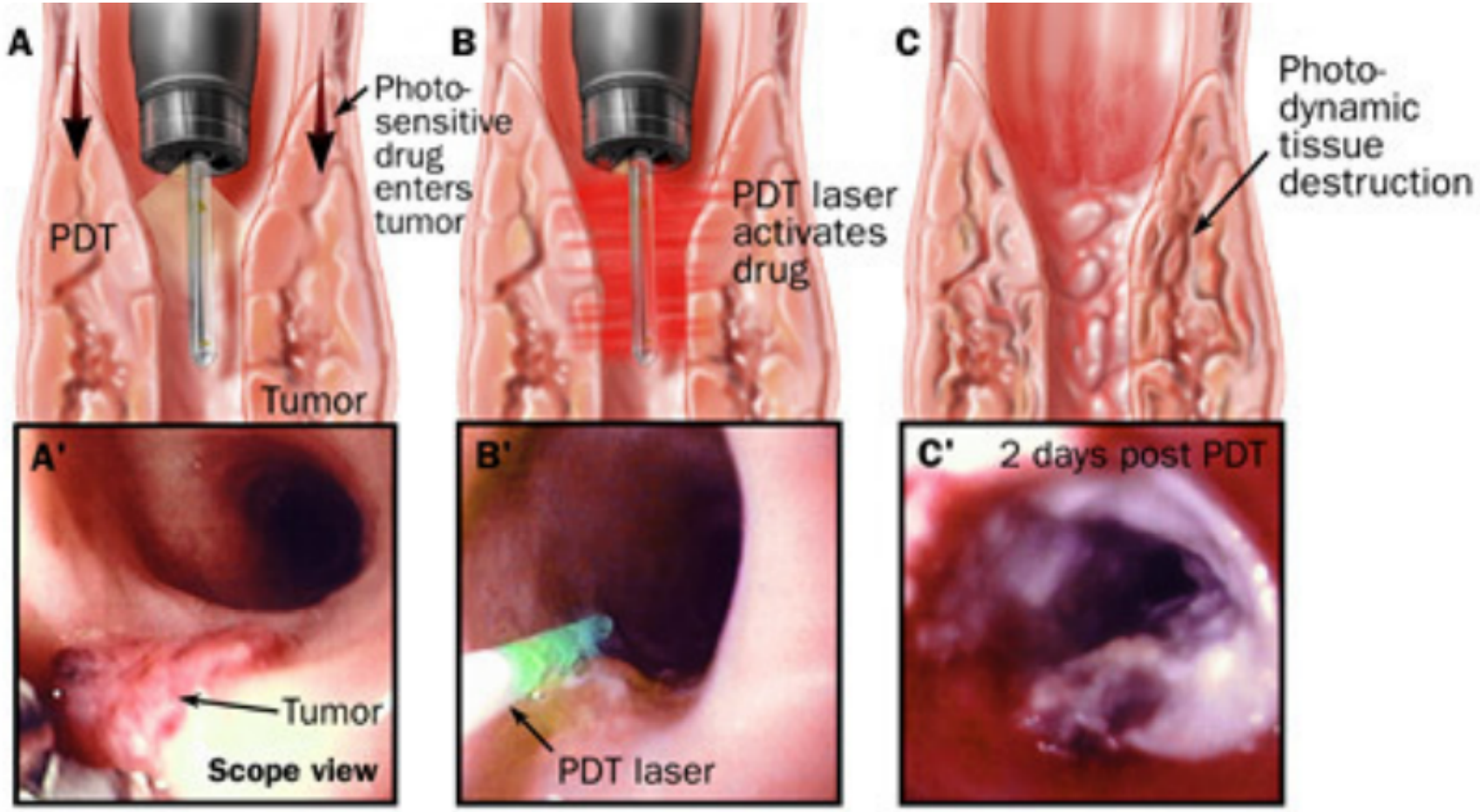
Poor surgical candidates, or who refuse surgery, and for stage IV tumors.

Endoscopic Therapy for Palliation:

Dilation	Passage of expandable balloon or wire-guided bougie
Sclerotherapy	Injection of a sclerosant like alcohol
Thermal Ablation	Coagulation of tumor using electrocautery
ND-YAG laser photoablation	Coagulation and vaporization of tumor using high energy laser
Stent	Placement of a hollow plastic tube or expandable metal stent
Photodynamic therapy	Injection of photosensitizing agent activated by low-power laser light, resulting in selective tumor necrosis

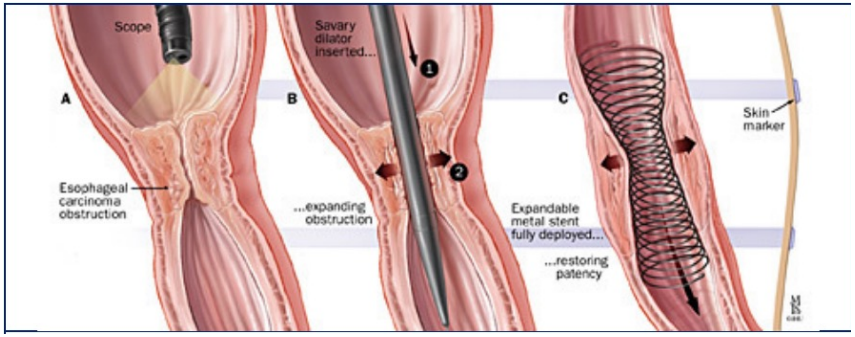
Endoscopic surgery

Photodynamic Therapy and mucosal ablation.



Esophageal stents:

- Endoscopy-directed plastic or self-expanding metal stents (SEMS).
- Plastic stents are easily removed, but frequently migrate.
- Nickel/titanium (nitinol) stents are common. Covered stents (silicone or polyurethane) are beneficial in temporarily sealing trachealesophageal fistulas. **95% effective in alleviating dysphagia.**



THANK YOU