OESOPHAGEAL MALIGNANCIES

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14th March 2022

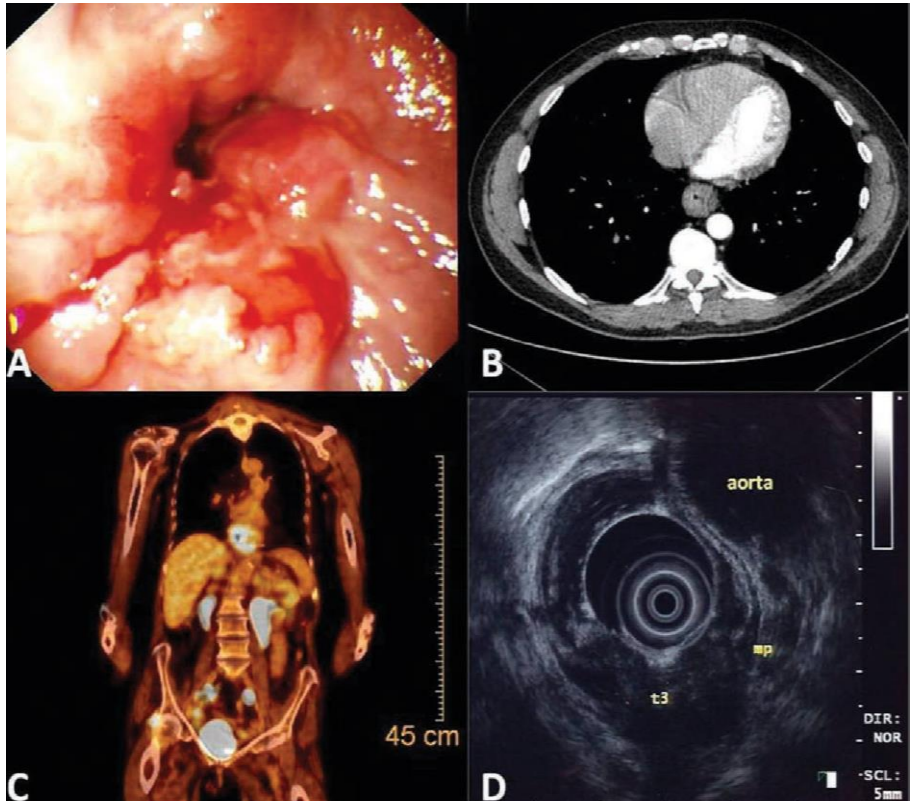
-8th most common cancer worldwide

-456000 incident cases diagnosed annually

-6th leading cause of cancer mortality worldwide

- South Africa : 8th and 11th most common in men and women; highest in Transkei

-2 main subtypes : Squamous Cell Ca (SCC) & AdenoCa (EAC)



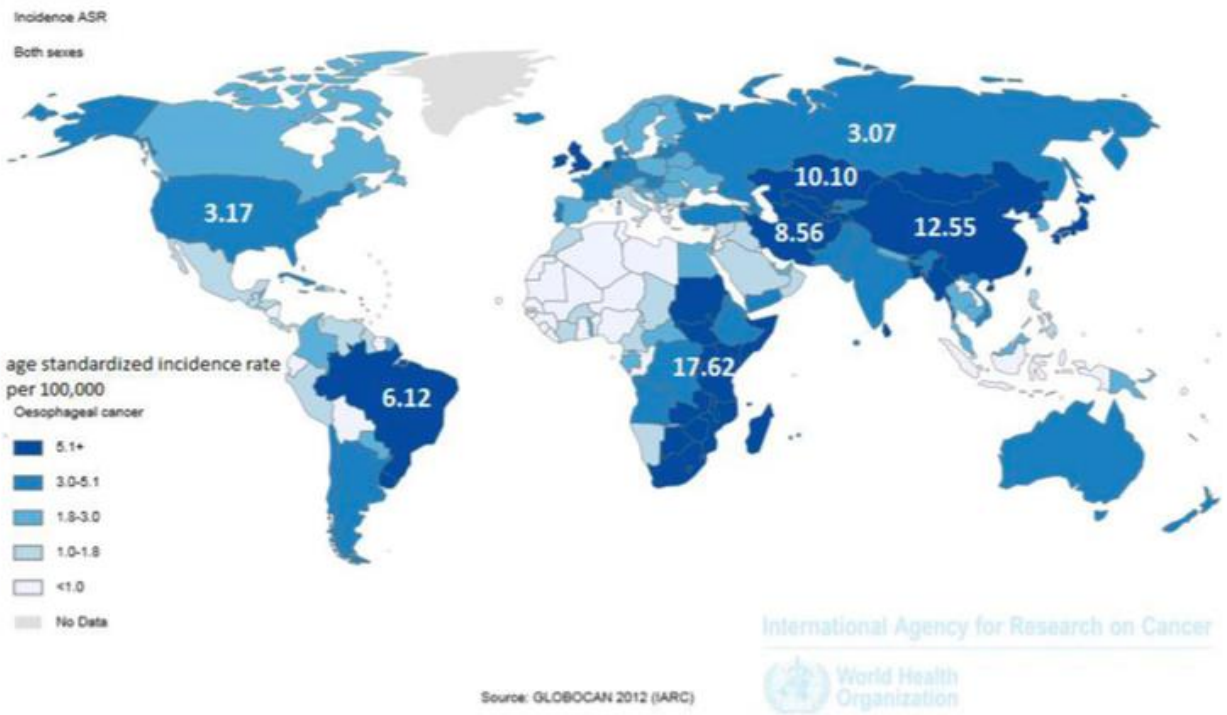


Figure 1:
The Asian and African esophageal cancer belts (in dark blue), where over 90% of cases are esophageal squamous cell carcinoma.
(Reprinted with permission from Ferlay J SI, et al. GLOBOCAN 2012 v1.0, [Internet]. Lyon, France: International Agency for Research on Cancer, 2013.)

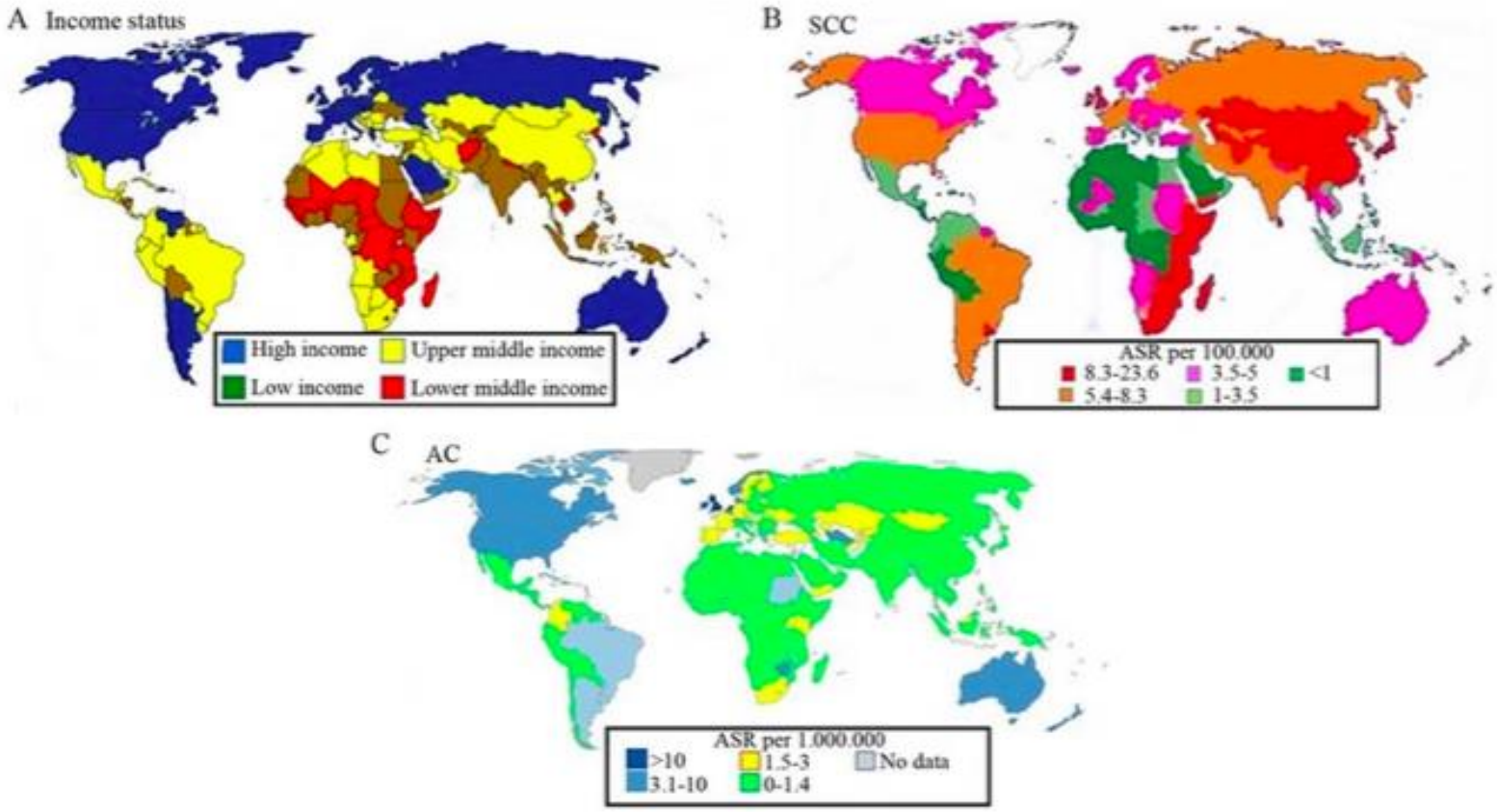


Figure 2. Oesophageal cancer incidence and income status of countries. (A) Countries divided into high, high middle, low middle and low income based on their GDP (145). (B) ASR per 100,000 for SCC. (C) Age-standardised incidence rate (ASR) per 100,000 for Adenocarcinoma (AC) (37,146). SCC, Squamous cell carcinoma; ASR, Age-standardised incidence rate.

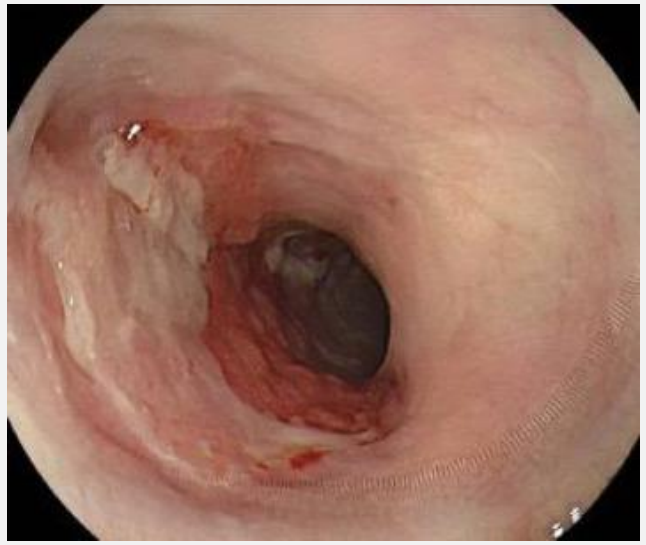
Table III. The incidence rates of oesophageal cancer by World area and sex (Torre, 2016 #264).

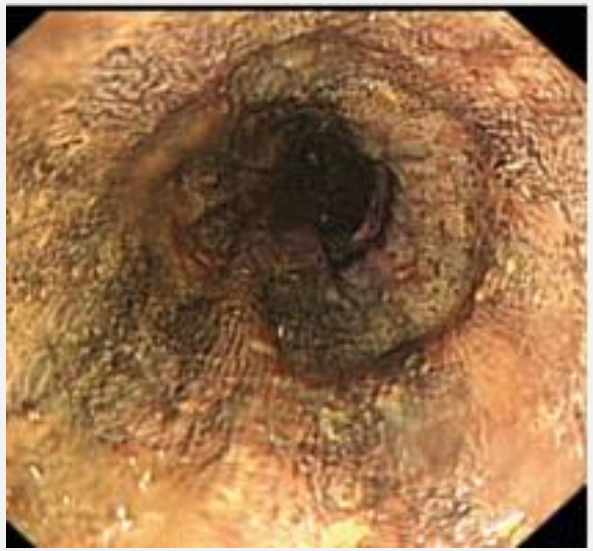
Country	Male (ASR of 100,000)	Female (ASR of 100,000)
Eastern Asia	16.9	5.4
Southern Africa	17.7	6.7
Eastern Africa	11.9	7.8
Northern Europe	8.1	2.7
South America	7.0	2.0
Western Europe	6.8	1.6
South-Central Asia	6.5	3.9
Central and Eastern Europe	5.6	0.8
Northern America	5.4	1.1
Australia/New-Zealand	5.4	1.7
Caribbean	4.6	1.2
Middle Africa	4.2	2.0
Melanesia	3.6	1.4
South-Eastern Asia	3.6	1.0
Southern Europe	3.2	0.6
Western Asia	2.9	2.1
Northern Africa	2.4	1.5
Central America	1.7	0.6
Western Africa	0.8	0.4

AGR, age standardized rate.

SQUAMOUS CELL CARCINOMA

- Most common worldwide
- 2 geographic belts : Central Asia, Eastern coast Africa (from Ethiopia to SA)
- Men > Women (this can vary)
- Highest incidence in age >65yo
- Protective : Obesity, NSAIDs, aspirin
- Also HPV and radiation





ESCC risk factors

Tobacco
Alcoholic beverages
Low consumption of fruits and vegetables
Low socioeconomic status
Micronutrient deficiencies
High-temperature foods
Achalasia
Lye ingestionw
Rare disorders (Plummer-Vinson syndrome, Fanconi anemia, and tylosis)

OESOPHAGEAL ADENOCARCINOMA

- 2nd most common form
- Predominant type in the West
- 8X more common in men than women
- Increased incidence though to be due to increase in GORD and obesity
- Risk factors:

EAC
Tobacco
GERD
Obesity

- Protective : H pylori, PPI, statins, fruit &veg

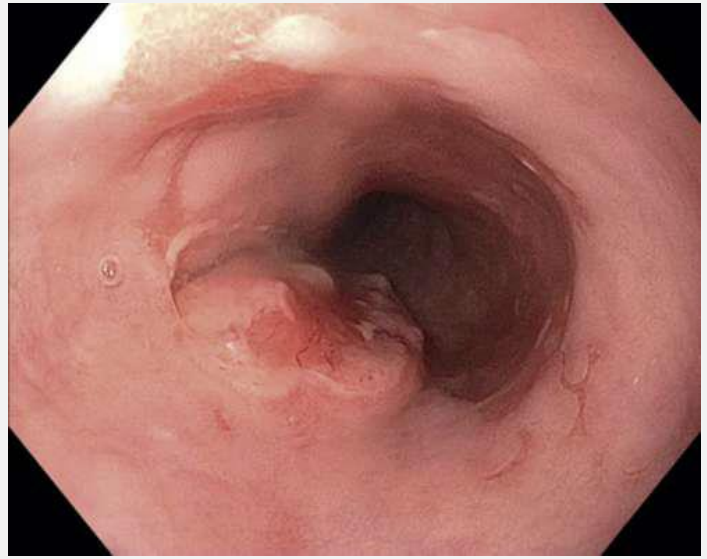


Table II. Relative risk factors for oesophageal cancer (13).

Risk factor	Squamous cell carcinoma	Adenocarcinoma
First or second hand smoke	+++	+
Alcohol consumption	+++	-
Red meat consumption	+	+
Barrett's oesophagus	-	++++
Reflux symptoms	-	+++
Overweight	-	++
Poverty	++	-
Caustic injury to the oesophagus	++++	-
History of head and neck cancer	++++	-
History of radiotherapy	+++	+++
Frequent consumption of hot drinks	+	-

-, no effect; +, suspicious effect; ++, positive effect; +++ and ++++, strong positive effect.

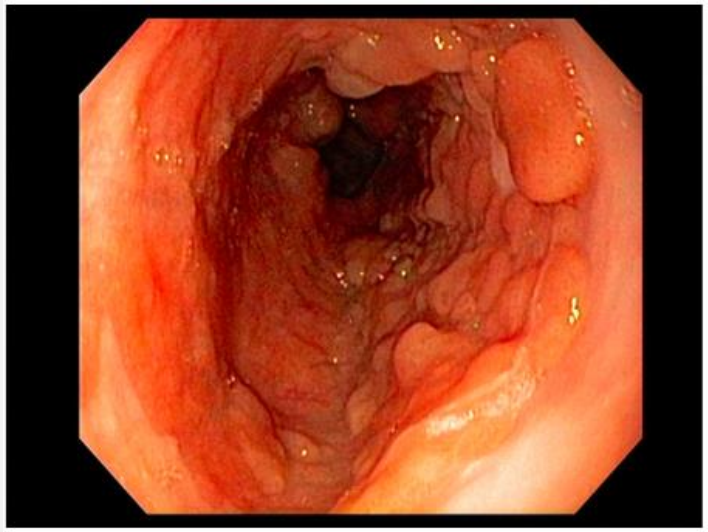
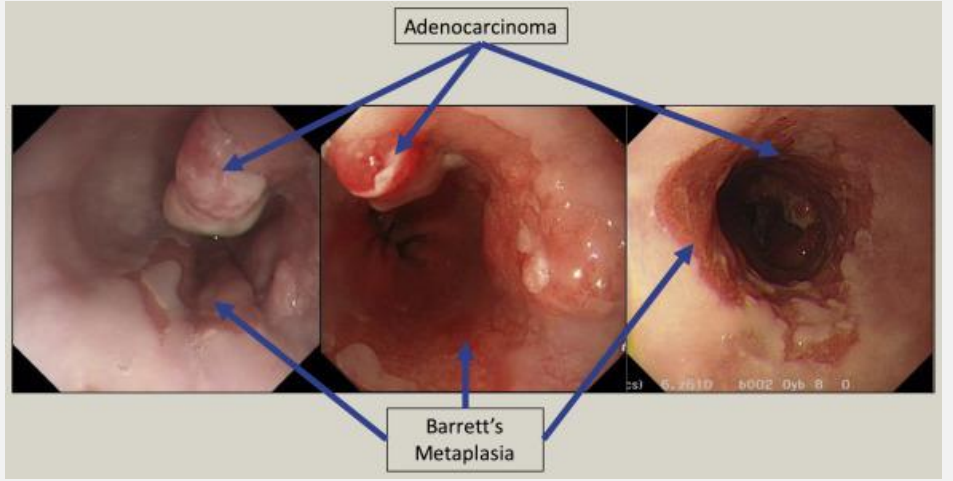


Figure 1. Barrett's esophagus with Nodules White Light Endoscopy.

PATHOGENESIS

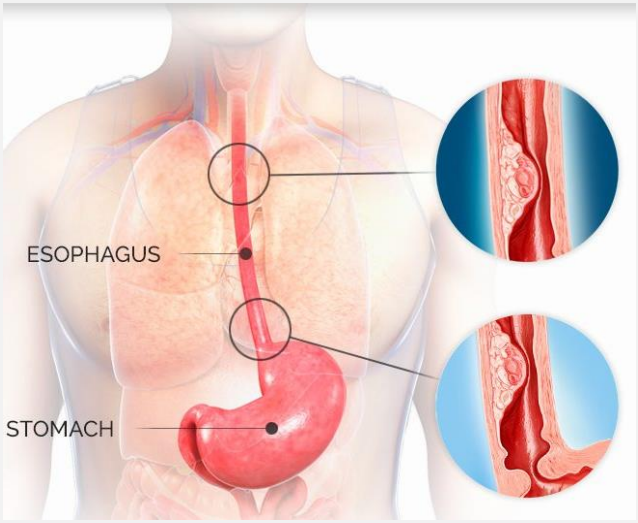
- Epigenetic & genetic alterations
- Environmental factors, hereditary factors, acquired genetic alterations
- Metaplasia-dysplasia-carcinoma sequence
- Hyperproliferative epithelium ⟶ low-, intermediate-, and high-grade ⟶ dysplasia ⟶ invasive cancer
- HER2, TP53, apoptosis regulators



CLINICAL

- EAC and SCC have similar presentations
- Early stages : asymptomatic
- Progressive dysphagia (initially solids) and LOW most common Sx
- Often delayed diagnosis
- Odynophagia > ulcerated lesion
- Less commonly : IDA, palpable cervical LAD, chest pain
- Oesophago-respiratory and -aortic fistulae
- Hoarseness (rare)
- Metastases : nodes, lungs, liver, brain, bone

DIAGNOSIS



- Lab test are non-specific : IDA, low albumin, hyperCa
- Endoscopy with biopsies
- Majority of EAC in distal oesophagus
- Majority of SCC in proximal-middle oesophagus
- Mass, raised nodule, ulceration, depression, stricture, subtle mucosal irregularity
- Other modalities : CXR, Barium oesophagogram, CT scan
- Imaging modalities : High resolution endoscopy, NBI, autofluorescene imaging (AFI), confocal laser endomicroscopy (CLE)

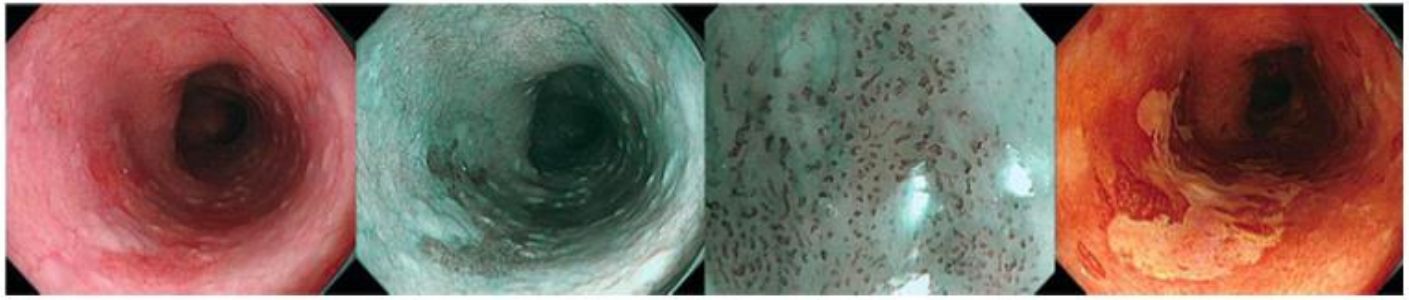


Figure 3:
Endoscopic images of the same lesion of esophageal squamous dysplasia, with WLE, NBI, Magnifying NBI, and Lugol's chromoendoscopy.

SCREENING & SURVEILLANCE

- EAC: as per Barrett's screening
- SCC: Endoscopic and Non-endosopic

Recommended Screening Guidelines for High Risk Populations

Risk factor	Screening method and duration	Outcome	Level of evidence[^20]
Head and neck cancer	Endoscopy with Lugol's or NBI every 6 months to 1 year after completion of therapy for HNSCC, for 10 years	• Detects earlier stage disease • Improved survival • No evidence for cost-effectiveness,	II-III (moderate)
Tylosis	4 quadrant biopsies from proximal, middle, and distal esophagus starting at age 30; repeat every 1–3 years	• Effective for early diagnosis • Only beneficial for Type A (late onset) Tylosis	III-IV (low)
Achalasia	Yearly EGD 10–15 years after disease onset +/– Lugol's solution	• No evidence for cost effectiveness • Need to screen many patients to detect one cancer	III (low)
Asian or African high-risk populations	One time Lugol's chromoendoscopy beginning at the age of 40	• Screened groups have lower ESCC incidence and mortality rates	II-III (moderate)
History of caustic esophageal injury	Endoscopy every 2–3 years 10–20 years following the injury	• No evidence for effectiveness	IV (low)

[^20] Levels of evidence: Level I evidence: presence of at least one prospective, randomized, controlled trial, level II evidence: well-designed cohort or case-controlled studies; level III evidence: case series or flawed clinical trials; level IV evidence: opinions of respected authorities or expert committees; level V evidence: insufficient evidence to form any opinions

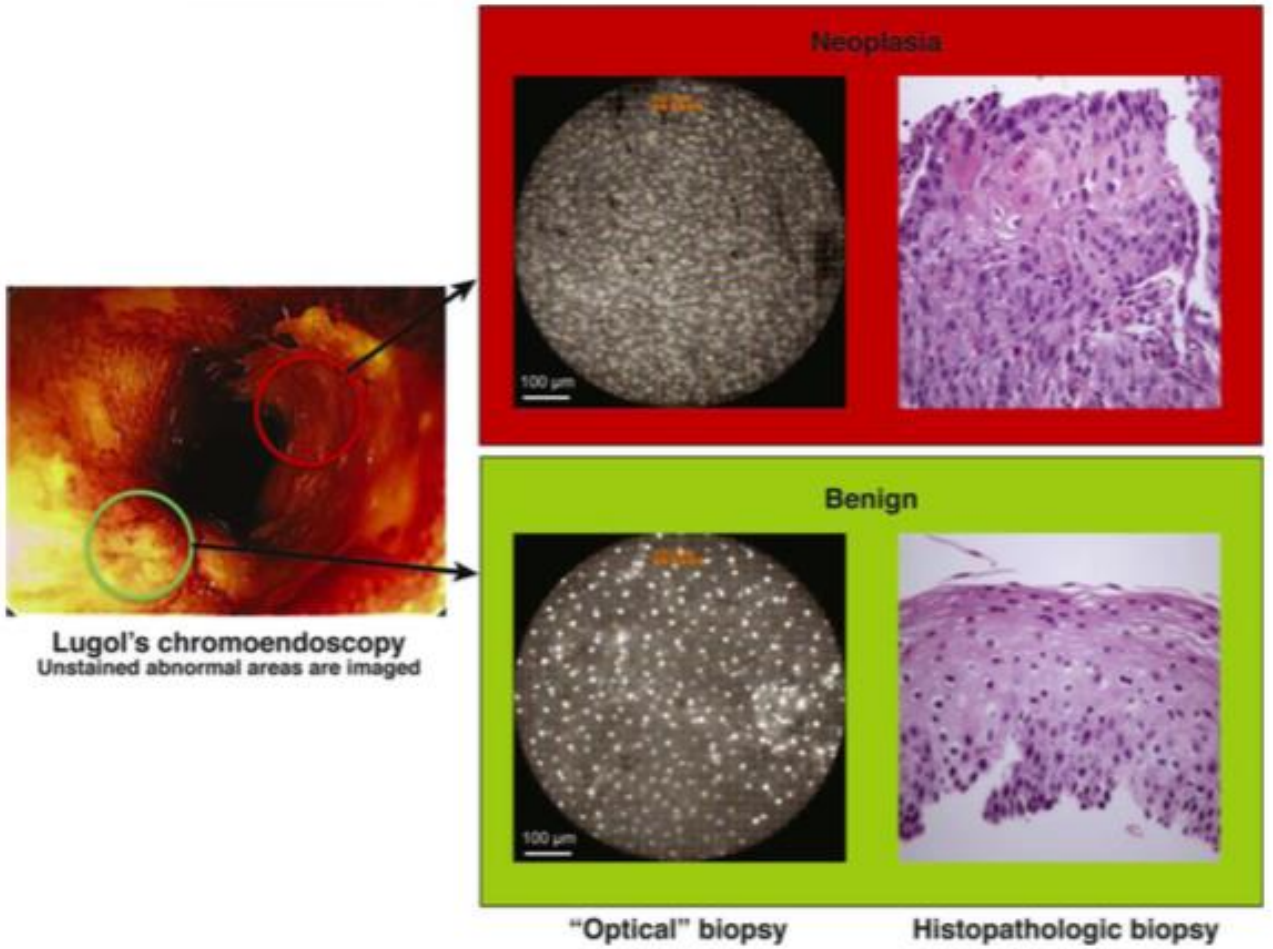


Figure 5:
High-resolution microendoscope[92]

STAGING

- American Joint Committee on Cancer (AJCC) staging system
- Using several methods: endoscopy and biopsies, endoscopic resection, MDCT, PET, EUS with FNA cytology

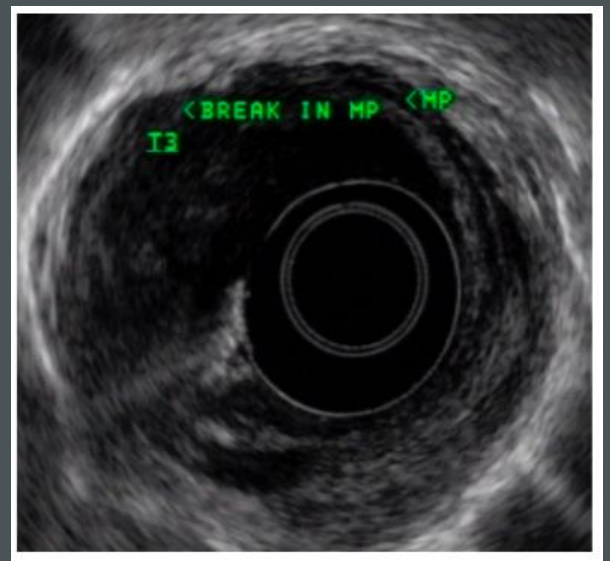
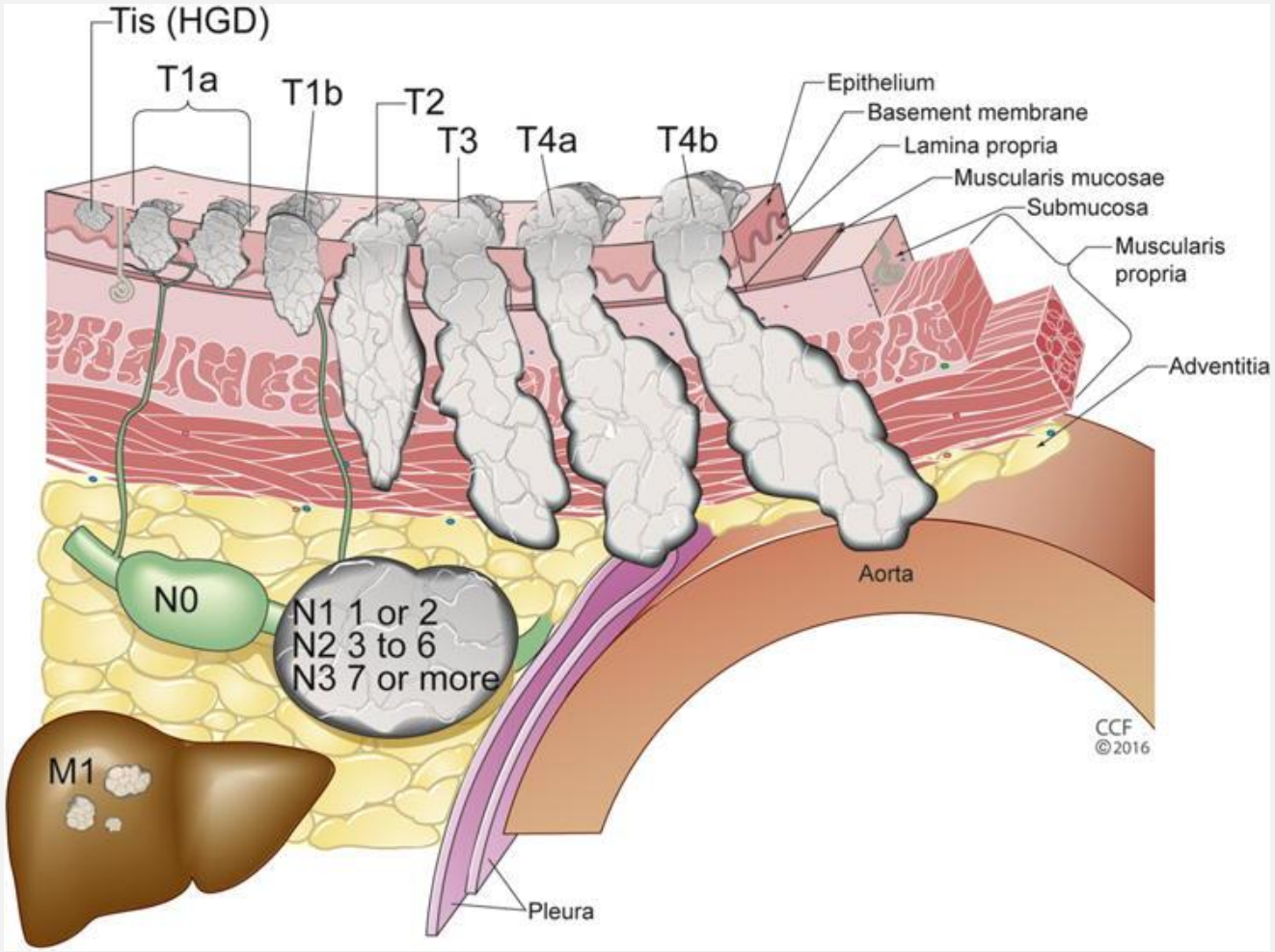


Figure 4. Esophageal cancer endoscopic ultrasound (EUS) image T3.



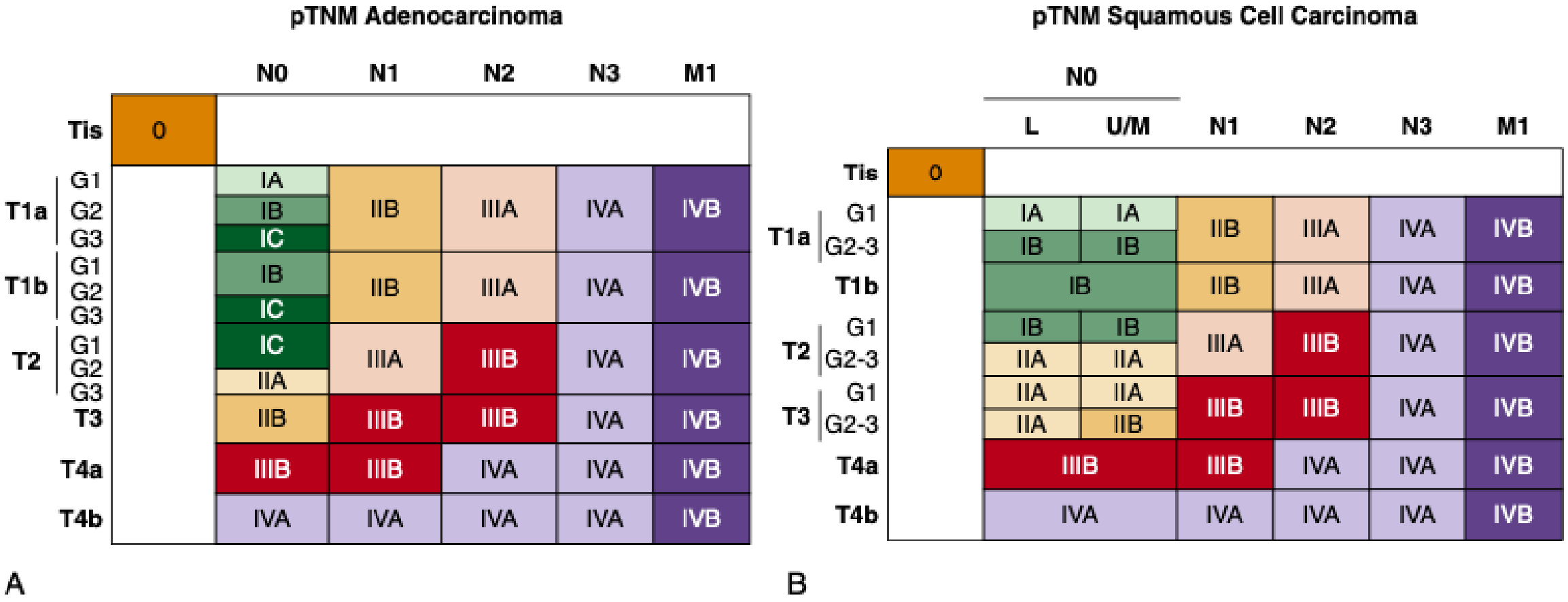
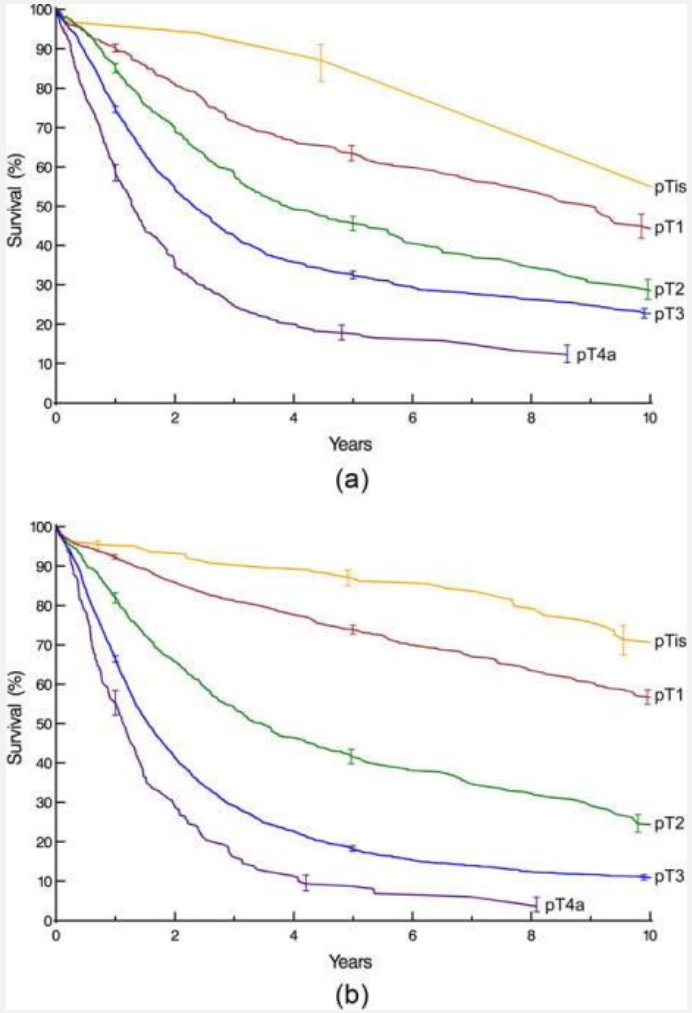
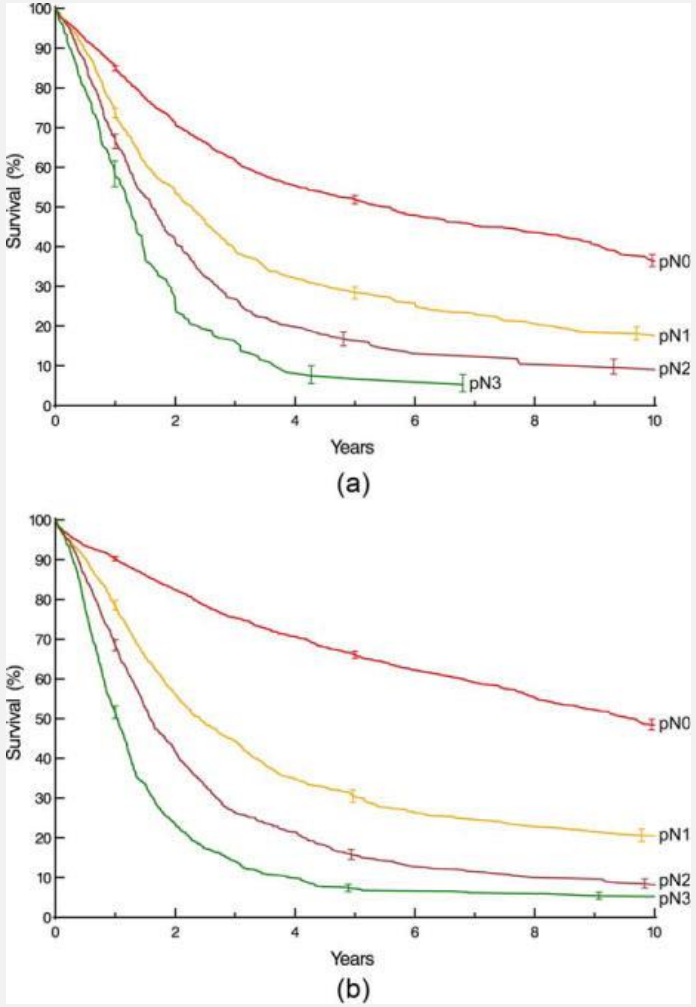
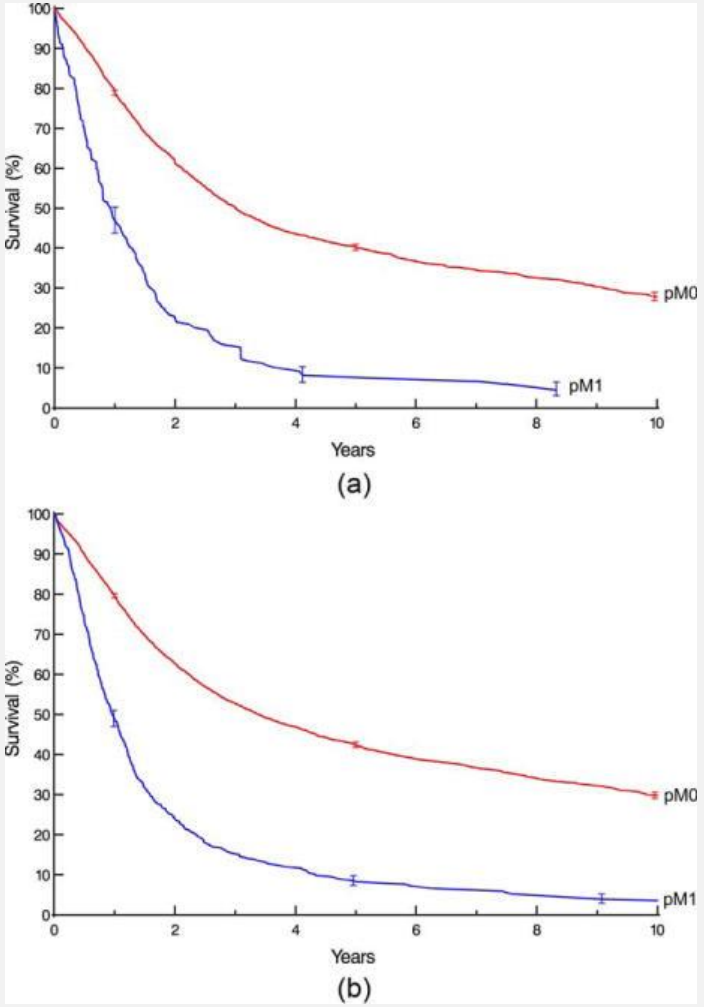


Fig. 48.8 Pathologic stage groups (pTNM) for esophageal adenocarcinoma (*A*) and squamous cell carcinoma (*B*). (Redrawn from Rice TW, Ishwaran H, Ferguson MK, Blackstone EH, Goldstraw P. Cancer of the esophagus and esophagogastric junction: an eighth edition staging primer. J Thorac Oncol 2017; 12[1]:36-42.)

Survival stratified by pT, pN, pM respectively – (a) SCC (b) AdenoCa







TREATMENT

- MDT approach is essential
- Factors to consider : tumour location, staging, histologic type, medical comorbidities, patient preference
- General principles:
  - Surgery is standard care for medically optimized surgical candidate with a localized, non-superficial tumour
  - For pt with a localized tumour who is not a surgical candidate, definitive chemoradiation with curative intent may be considered
  - For all others (metastatic disease), palliation is recommended

TREATMENT ACCORDING TO STAGE

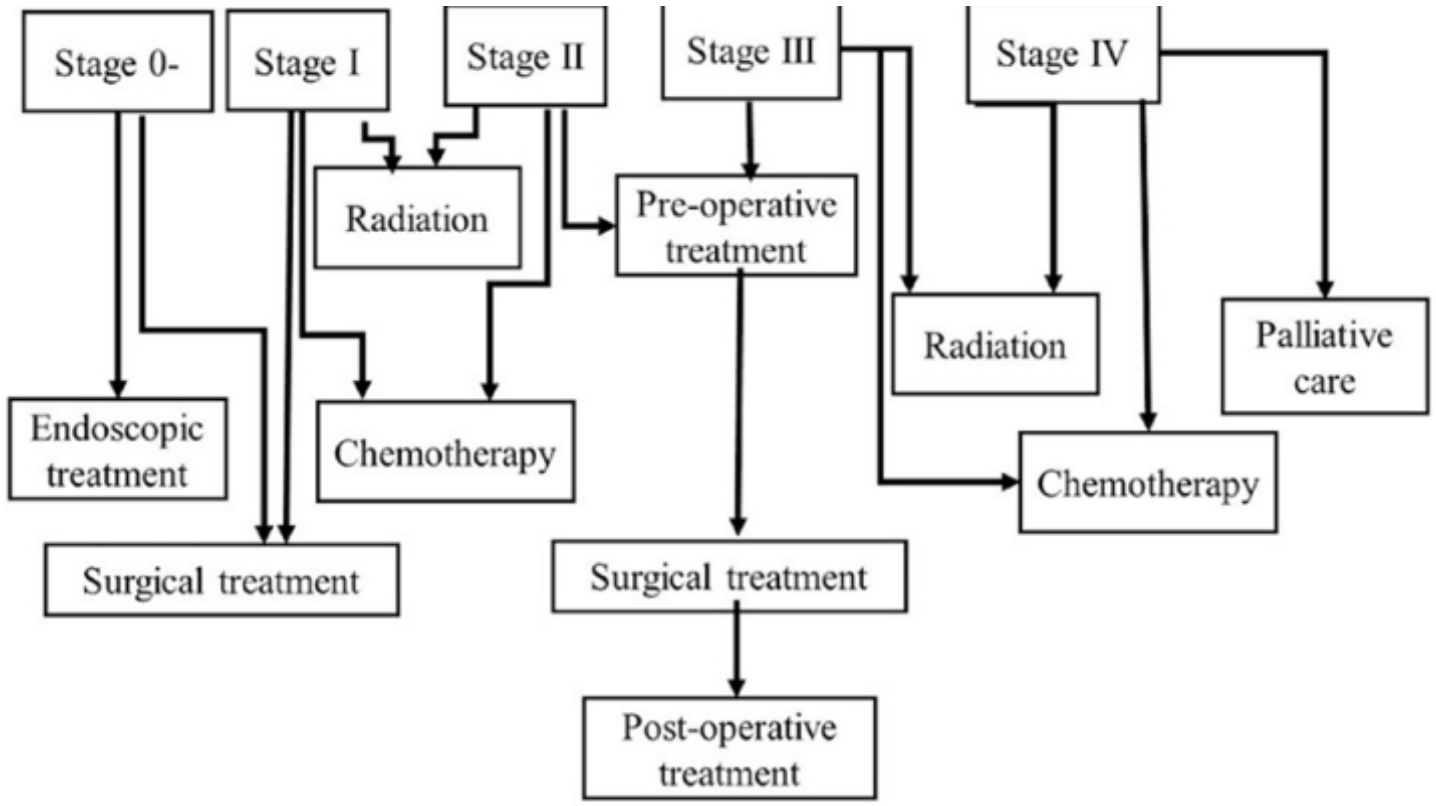


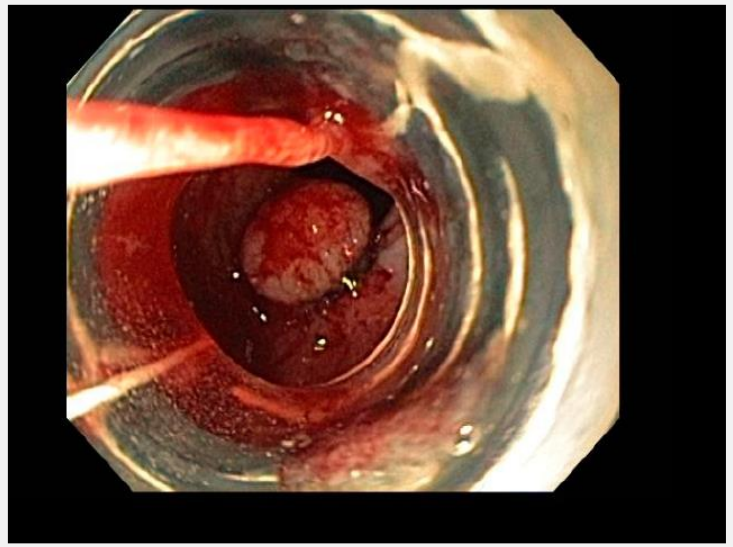
Figure 3. Treatment of oesophageal cancer at different stages (130).

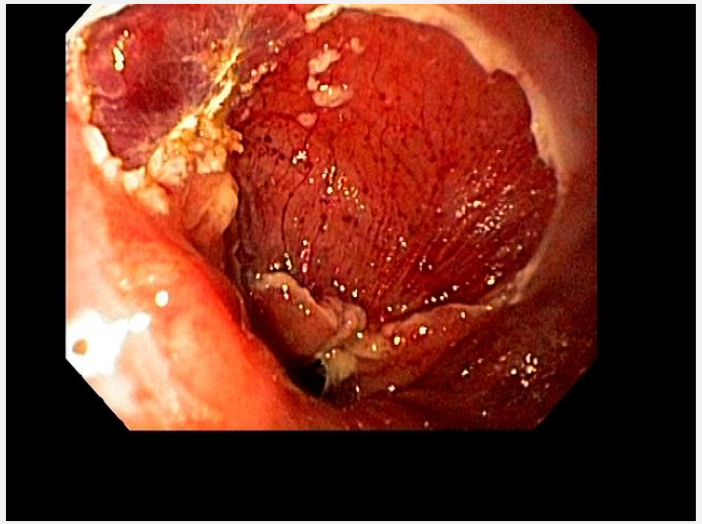
SURGERY

- Resection of oesophagus with en bloc lymphadenectomy
- T1b and T2 > surgery alone
- T1-T4a with LN mets > surgery + multimodal approach
- Outcome dependant on stage, comorbidities, performance status and NB surgical expertise and center volume
- Techniques: surgical access site (transthoracic vs transhiatal), extent of LAD, type of anastomosis, type & preparation of oesophageal conduit, pyloric drainage procedure, route of reconstruction
- Minimally invasive approaches being used increasingly ie MIE
- Most common complications: anastomotic leak, pneumonia
- Survival after surgery without neoadjuvant therapy : 30% at 5 years

1) ENDOSCOPIC TREATMENT

- Early-Stage T1a and T1b:
  - EMR & ESD
  - Cap-assisted EMR
  - Multiband Musectomy (MBM)
  - Ablation
  - Complications





2) MULTIMODALITY THERAPY FOR LOCALLY ADVANCED CANCER

- Locally advanced (T2 or with nodal involvement) > combination of neoadjuvant chemoradiation therapy and surgical therapy
- Systemic chemoTx reserved for metastatic disease (Stage IV); possible consolidation chemoradiation to sites of disease involvement if pt responds well
- Operable non-metastatic with T1b or greater primary lesions &/or any nodal disease > oesophagectomy
- Surgery alone for early-stage, low-risk adenoCa (<3cm and well differentiated) and early-stage SCC
- For more advanced disease > trimodality therapy with neoadjuvant chemoradiation followed by surgery is preferred > MDT essential
- Significant bleeding or dysphagia > palliative radioTx

3) NEOADJUVANT RADIATION THERAPY ALONE & ADJUVANT THERAPY

- ***

4) PREOPERATIVE CHEMORADIATION

5) DEFINITIVE RADIATION & CHEMORADIATION

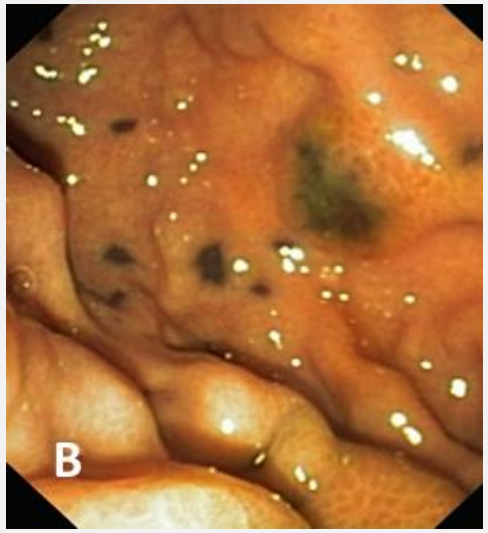
THERAPY FOR METASTATIC DISEASE

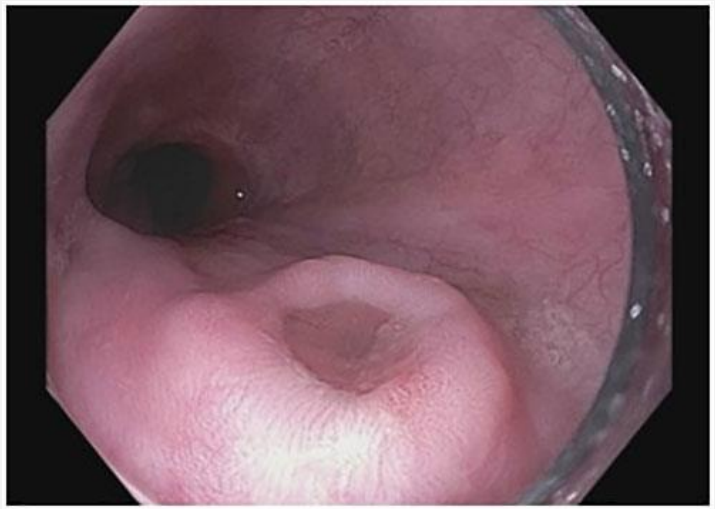
- RadioTx : obstruction, dysphagia, severe pain, chronic blood loss, nausea
- External beam or intraluminal brachytherapy
- SEMS : dysphagia
- ChemoTx : to improve QoL and survival
- 5-FU, Cisplatin, platinum agents, Docetaxel
- Targeted therapies eg Her-2 expressing tumors

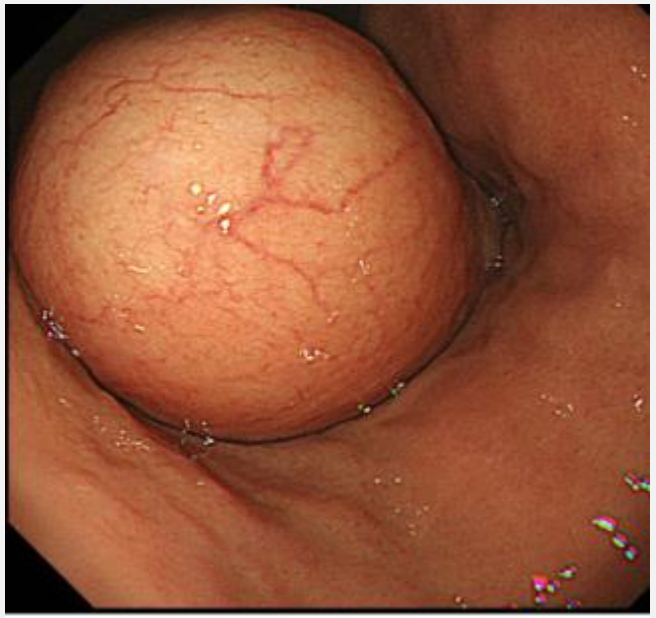
- Prognosis: best predictors of survival are depth of invasion and LN involvement
- 5-year survival for local, regional and distant disease : 41%, 23% and 5%
- This improves to 90% if HGD (cancer-in-situ) or T1a
- Histologic type, degree of differentiation, location also

OTHER TUMOURS

- Malignant Epithelial:
  - Small Cell Carcinoma
  - Malignant Melanoma
- Benign Epithelial:
  - Squamous papilloma
  - Adenoma
  - Inflammatory fibroid polyp
- Malignant non-epithelial
  - Lymphomas, Sarcomas, GISTs, Mets
- Benign non-epithelial
  - Leiomyoma, Granular Cell Tumour, Fibrovascular polyp, Hamartoma, Haemangioma, Lipoma







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