



Barret's Oesophagus & Oesophageal cancer

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Introduction- BE



- Barrett's esophagus (BE) pre-malignant condition- inflammatory milieu in esophagus leads to progressive metaplastic transformation with conversion of the normal type of squamous epithelium into the columnar type of epithelium.
- Intestinal metaplasia as the columnar epithelium is a specialized type since it contains goblet cells.
- Most commonly known predisposing factor is gastroesophageal reflux disease (GERD) which is present in about 20% of adults in developed countries.
- Given the risk for progression to malignancy, surveillance programs exist in order to monitor and capture dysplastic changes in high-risk groups.

Barrett NR. Chronic peptic ulcer of the oesophagus and 'oesophagitis'. Br J Surg 1950; 38: 175-182 [RCA] [PMID: 14791960 DOI: 10.1002/bjs.18003815005]



Definition- BE



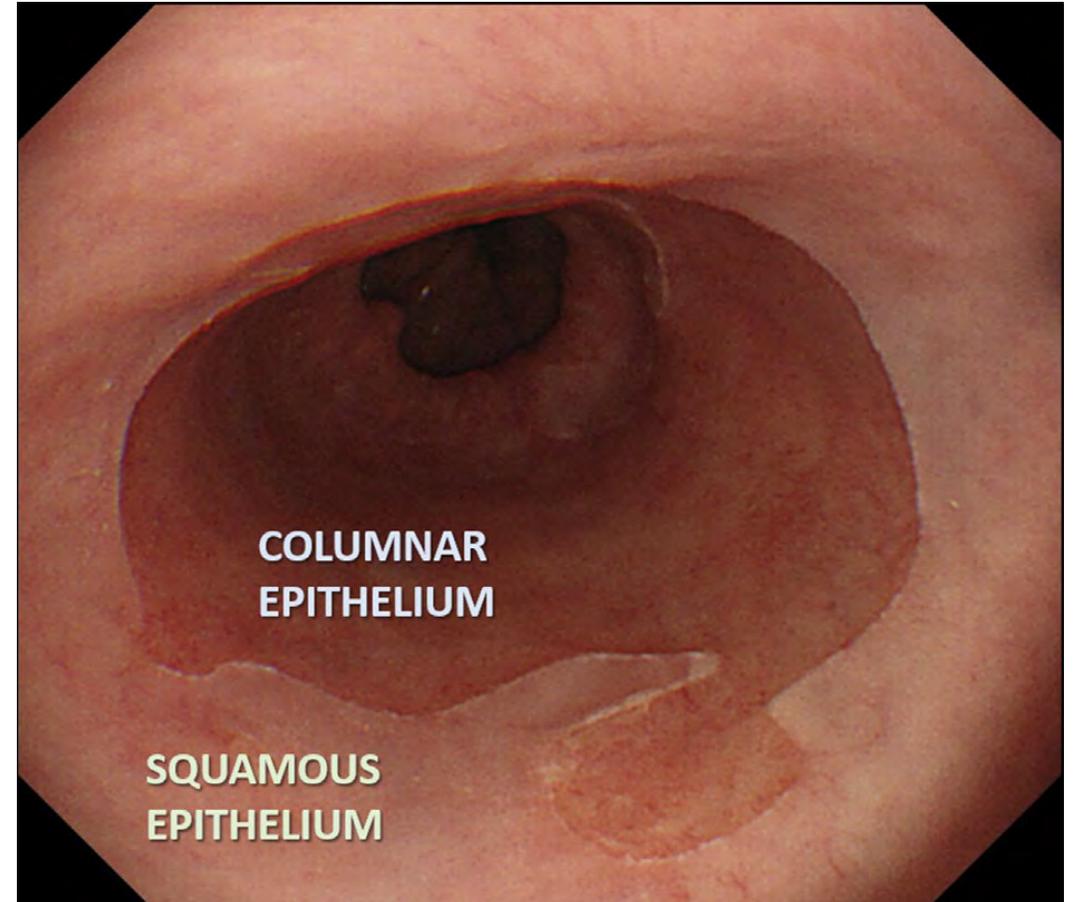
- US guidelines- BE is described as a metaplastic process resulting in a change of at least 1 cm of the distal esophagus from the normal squamous epithelium to a columnar-lined epithelium containing goblet cells.
- Segments less than 1 cm in length are categorized as specialized intestinal metaplasia (IM) of the esophagogastric junction.
- British Society of Gastroenterology states that the presence of cardiac or oxyntocardiac mucosae (which lack goblet cells) as sufficient for establishing the presence of Barrett's esophagus.
- Japan was the first nation to propose that intestinal metaplasia and goblet cells were not necessary for the diagnosis of BE. They frequently use the distal margin of the palisade vessels in the lower esophagus to define the columnar-lined esophagus, which is equivalent to BE.

Shaheen NJ, Falk GW, Iyer PG, Souza RF, Yadlapati RH, Sauer BG, Wani S. Diagnosis and Management of Barrett's Esophagus: An Updated ACG Guideline. Am J Gastroenterol 2022; 117: 559-587 [RCA] [PMID: 35354777 DOI: 10.14309/ajg.0000000000001680.

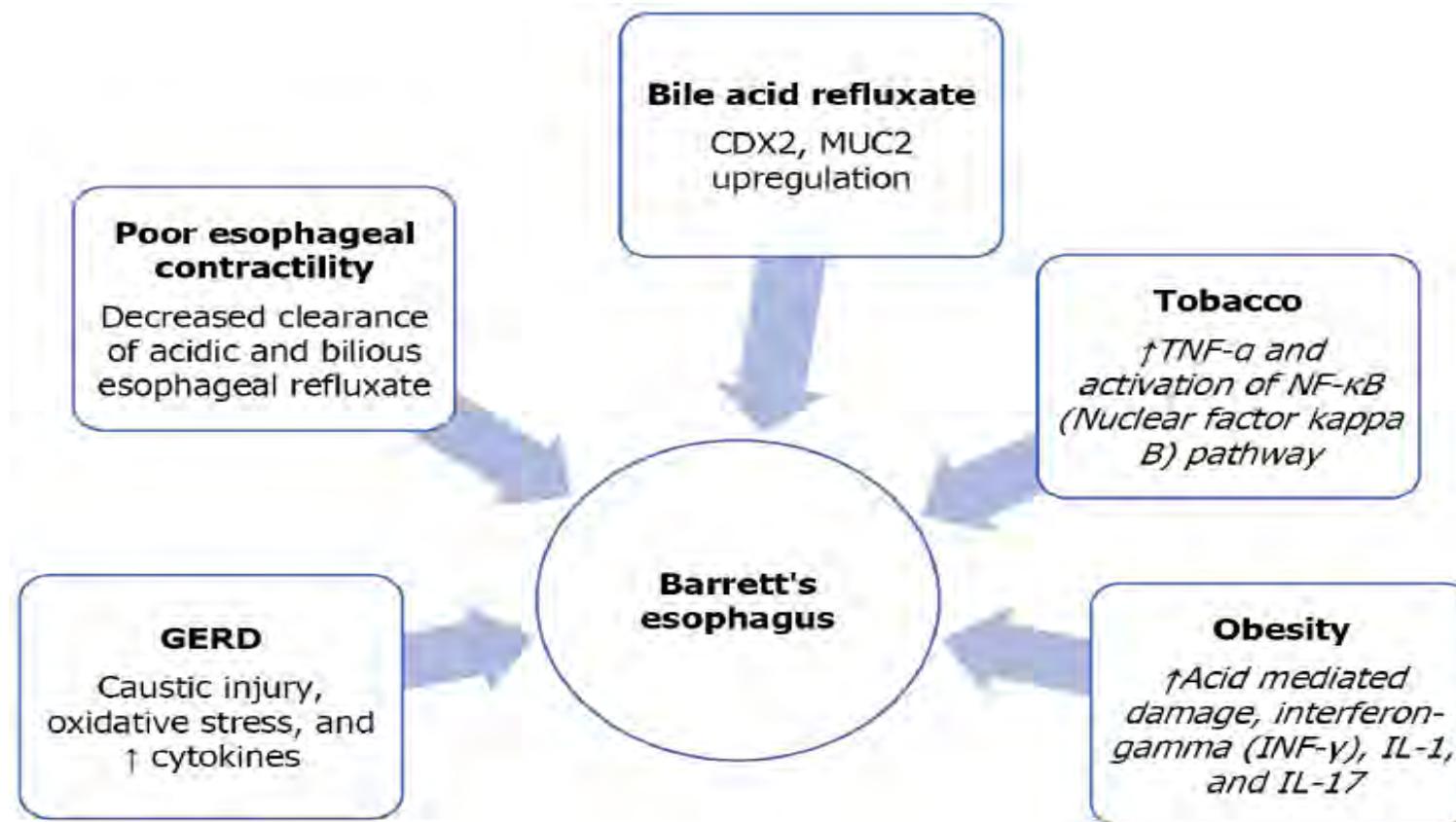
Riddell RH, Odze RD. Definition of Barrett's esophagus: time for a rethink--is intestinal metaplasia dead? Am J Gastroenterol 2009; 104: 2588-2594 [RCA] [PMID: 19623166 DOI: 10.1038/ajg.2009.390 2026/03/02

Epidemiology- BE

- Found during upper endoscopy of middle-age to older adults, for GERD symptoms.
- Average age – 55 years.
- Long segment (LSBE) 3-5% Short segment (SSBE) 10-20%
- Western countries - prevalence of Barrett's esophagus 1.6 - 6.8%
- Risk of cancer in the general population of patients with Barrett's esophagus - approx 0.5% per year.



Pathogenesis- BE



Shaheen NJ, Falk GW, Iyer PG, Souza RF, Yadlapati RH, Sauer BG, Wani S. Diagnosis and Management of Barrett's Esophagus: An Updated ACG Guideline. Am J Gastroenterol 2022; 117: 559-587 [RCA] [PMID: 35354777 DOI: 10.14309/ajg.0000000000001680.



Risk factors- BE



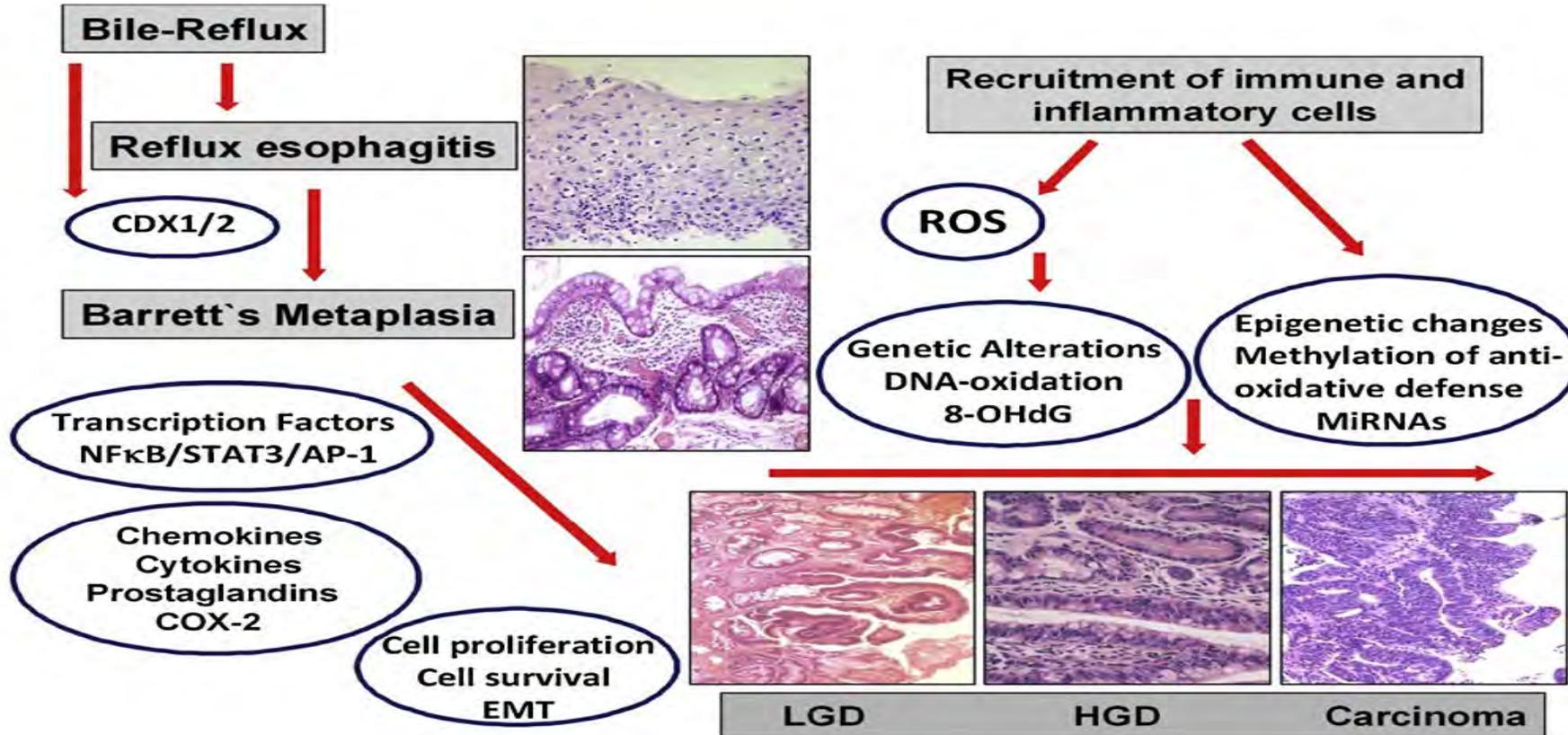
Modifiable

- Smoking(Tobacco)
- Chronic GERD(> 5 years symptoms)
- Central obesity(waist circ>102 cm or waist-hip ratio > 0.9)
- Alcohol consumption
- History of DM and oral non-metformin
- Anti-diabetic medications

Non modifiable

- Male sex
-
- White race(Caucasian)
-
- Family history of BE/EAC
-
- Age > 50 years

Progression to EAC

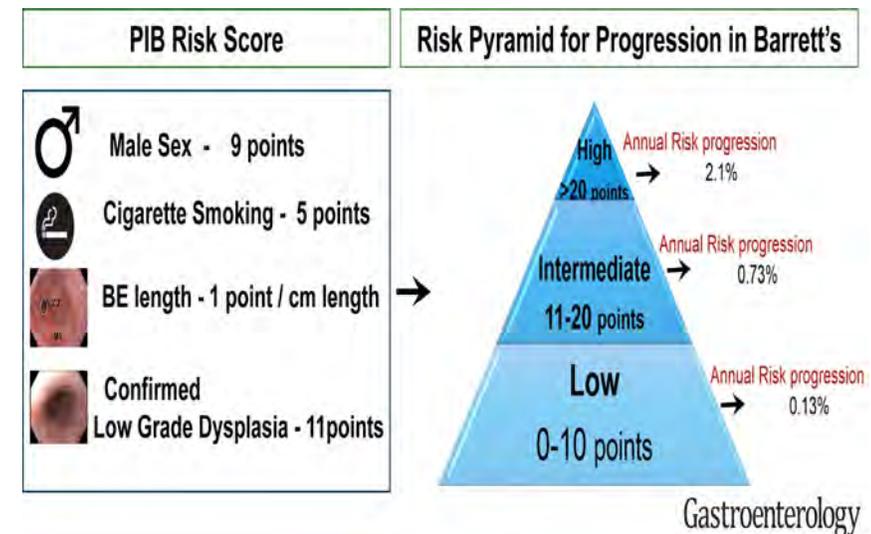


Malfertheiner P et al. Upper gastrointestinal tract inflammation and Barrett's carcinogenesis (2012)

Risk factors

- Male gender
- Older age
- Smoking history
- Low-grade dysplasia(low-grade intraepithelial neoplasia)
- Longer length of BE segment
- Lack of PPI, NSAID & statin use

Point progression in BE(PIB score)

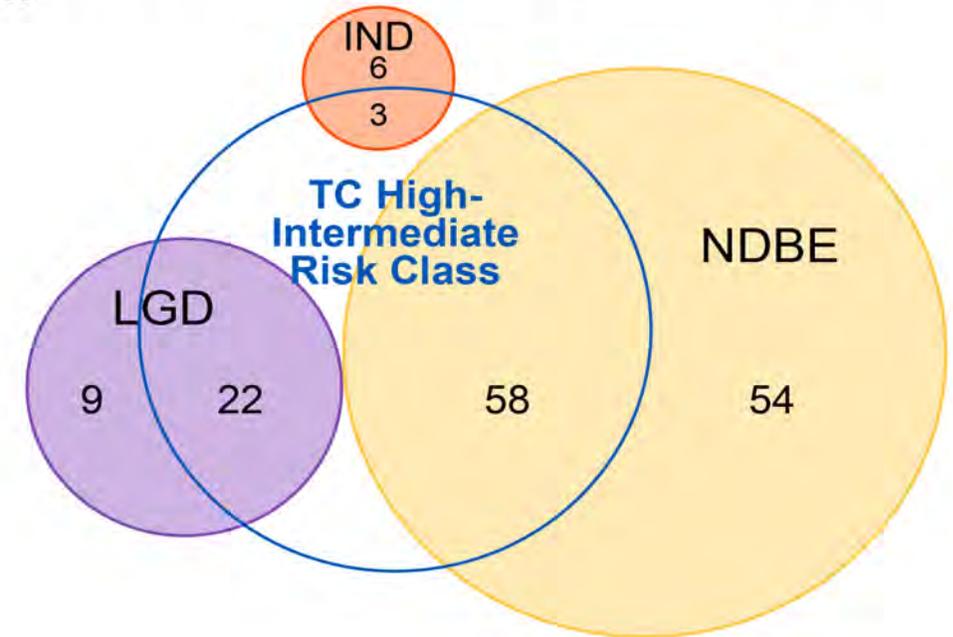


Biomarkers:

- Loss of tumour suppressor genes, **p53** and **p16**
- Lipid metabolism alteration, **AMACR**
- Oncogene amplification, **HER-2**
- Immune infiltration markers, **CD68** and **COX2**
- Angiogenesis markers, **HIF1 alpha** and **CD45RO**

B

N=152 Incident Progressors
 112 of 152 were NDBE
 9 of 152 were IND
 31 of 152 were LGD
 83 of 152 Incident Progressors had TC High/Intermediate risk class





Screening for BE



- Recommended in high- risk individuals.

Men with chronic(> 5 years) and/ or frequent(weekly or more) GERD symptoms and three or more risk factors for BE or EAC:

- ✓ Age > 50
- ✓ Caucasian race
- ✓ Central Obesity
- ✓ History of tobacco smoking
- ✓ Family history(first- degree relative) of BE or EAC

BE Screening criteria

Association	Criteria	Risk Factors
AGA [13]	≥3 risk factors	<ul style="list-style-type: none"> - age >50 years - male sex - non-Hispanic white - history of smoking - chronic GERD - obesity - family history of BE or esophageal adenocarcinoma.
ACG [91]	Chronic GERD and ≥3 risk factors	<ul style="list-style-type: none"> - age >50 years - male sex - white race - tobacco smoking - obesity - family history of BE or EAC in a first-degree relative.
BSG [33]	Chronic GERD and ≥3 risk factors (the threshold of multiple risk factors should be lowered in the presence at least one first-degree relative with BE or EAC)	<ul style="list-style-type: none"> - age ≥ 50 years - white race - male sex - obesity
ESGE [52]	Screening for BE is not advised but can be considered in patients with GERD >5 years and multiple risk factors	<ul style="list-style-type: none"> - age ≥ 50 years - white race - male sex - obesity - first-degree relative with BE or EAC.

Limitations of screening for BE

- Risk based screening may miss a considerable proportion of BE.
- At least 40 % of patients who are ultimately diagnosed with EAC reported no history of typical GERD symptoms.
- Systematic review of 12 studies published between 1988 and 1999 showed only 4.7% of patients undergoing surgery for EAC carried prior diagnosis of BE.



Advanced Imaging



- Seattle protocol(systematic 4 quadrant biopsies) is relatively inefficient.
- Has low diagnostic yield for neoplasia.
- Much interest in studying the use of endoscopic advanced imaging techniques.
- Better diagnostic yield and value for BE surveillance.
- Goal is to move from random biopsies to image- directed targeted biopsies.



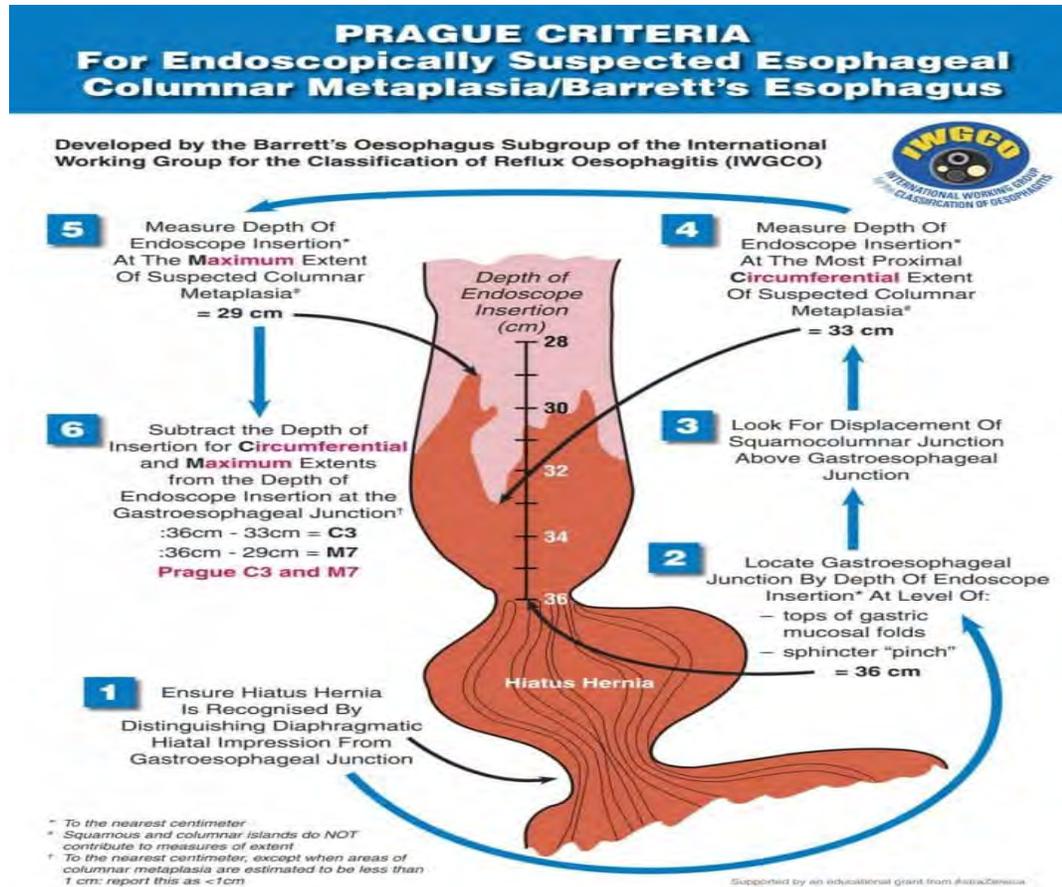
Advanced Imaging



Criteria: Sensitivity > 90% Specificity > 80% NPV > 98%

Advanced imaging modality	Sensitivity (%)	NPV (%)	Specificity (%)
Acetic acid chromoendoscopy*	96.6	98.3	84.6
Methylene blue chromoendoscopy	64.2	69.8	95.9
Indigo carmine chromoendoscopy	67.0	96.0	99.0
NBI*	94.2	97.5	94.4
eCLE*	90.4	98.3	92.7
pCLE	90.3	95.1	77.3

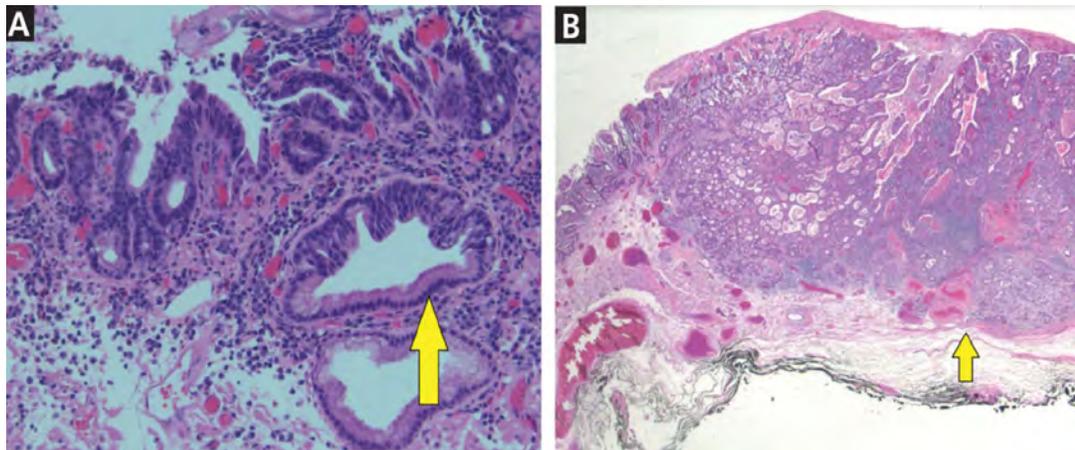
Diagnosis-Prague criteria



- Histopathological confirmation of intestinal metaplasia (IM), defined by the presence of columnar epithelium containing the goblet cells.
- Circumferential length is measured as the distance between the GEJ and the proximal margin of the circumferential BE extent. Maximum length is the distance between the GEJ and the proximal margin of the longest tongue

Histopathology

Vienna histological classification



Category

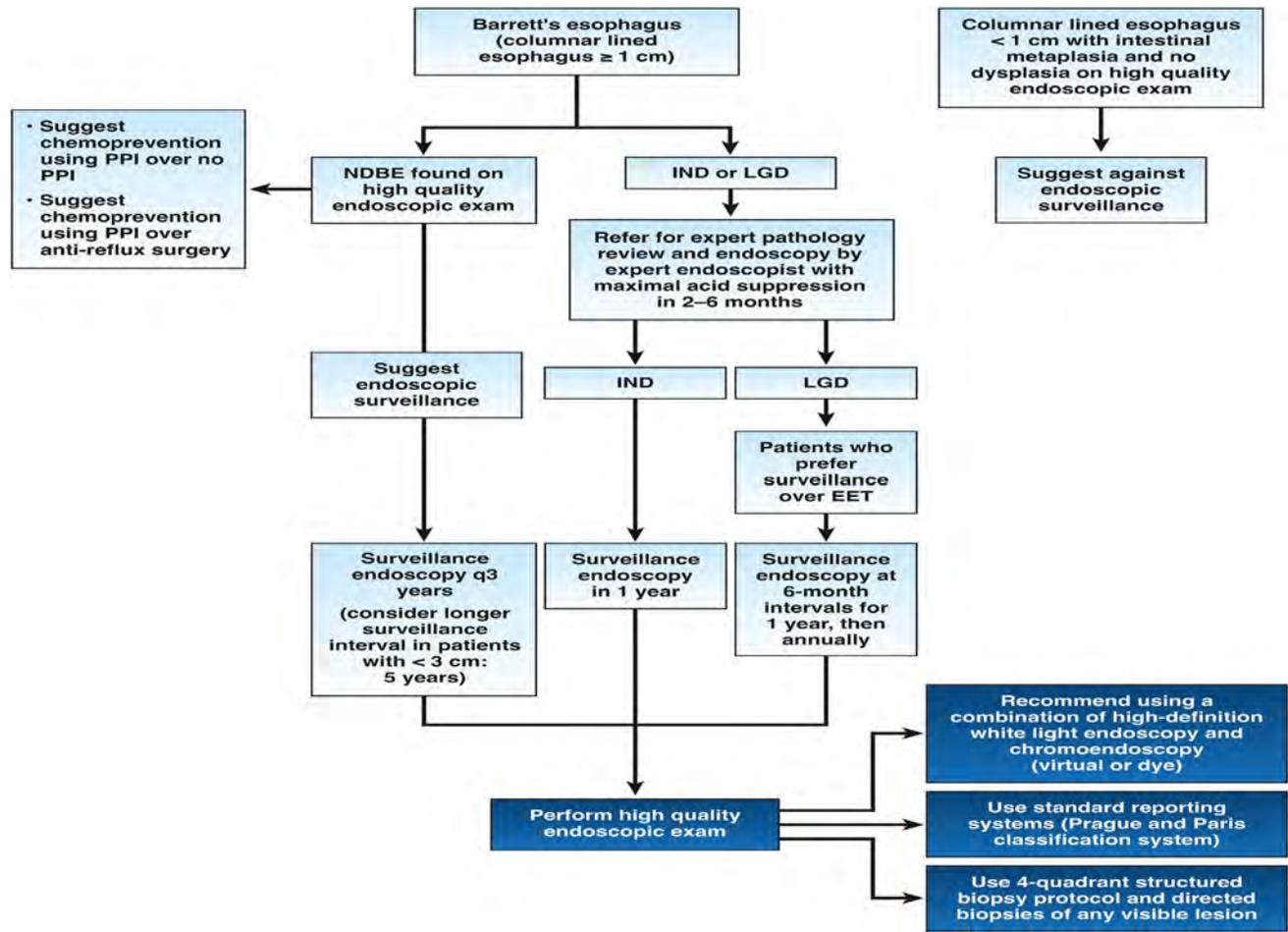
Classification

1	Negative for dysplasia
2	Indefinite for dysplasia
3	Low-grade dysplasia
4a	High-grade dysplasia
4b	Intramucosal carcinoma
5	Submucosal invasion by adenocarcinoma

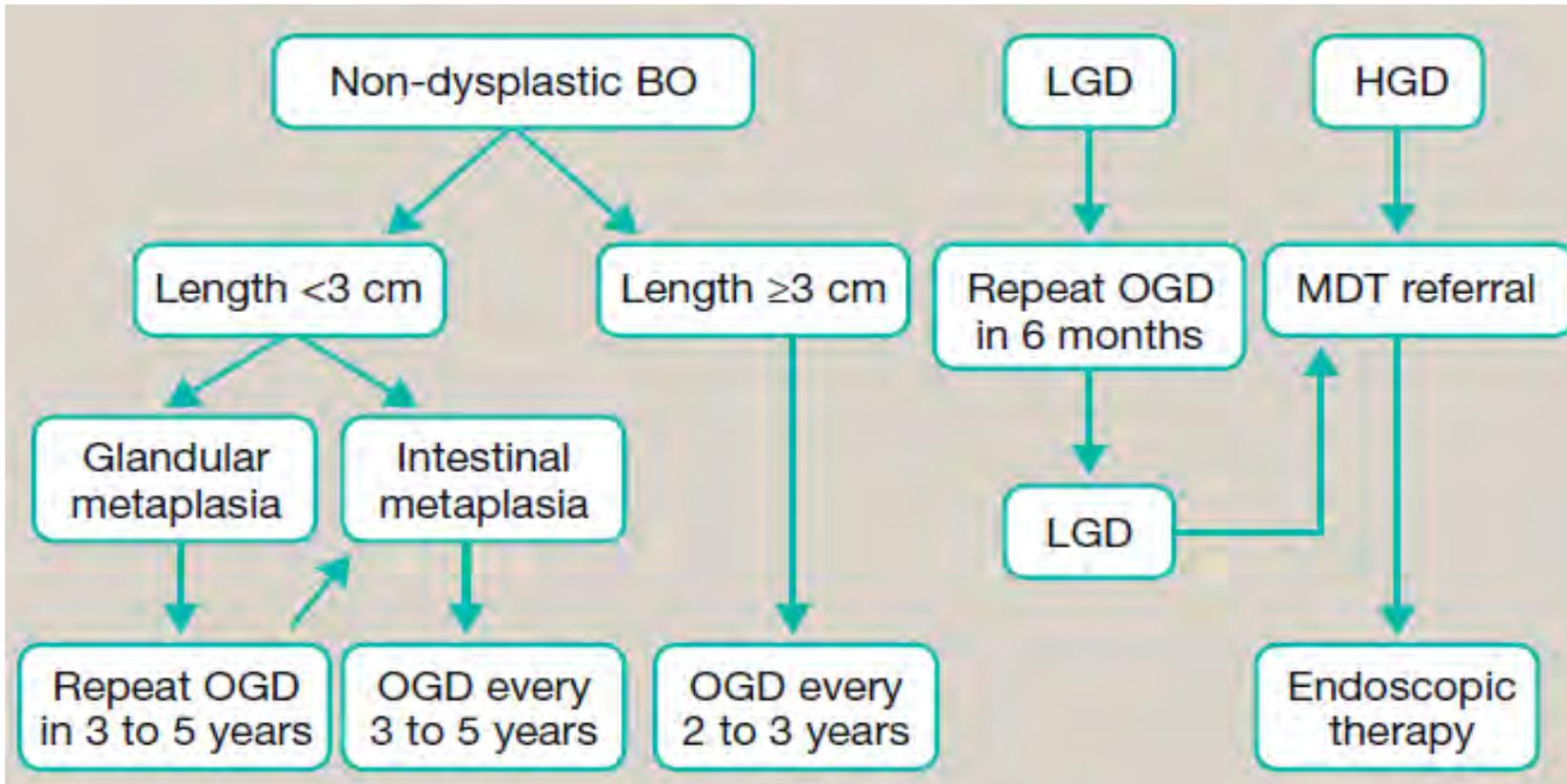
Surveillance in BE

- Goal is to detect dysplasia or early cancer so that curative treatment can be offered prior to the development of advanced EAC.
- Observational studies: Improved outcomes in patients with EAC who had been undergoing surveillance for BE as opposed to those without Barretts surveillance.

Surveillance of BE



BSG guidelines for BO surveillance



British Society of Gastroenterology Guideline on Surveillance of Barrett's Esophagus.



Chemoprevention



- Given the poor prognosis of EAC after diagnosis, there is great interest in preventive strategies.
- Goal of chemoprevention in BE is to avoid the initiation or progression of dysplasia/ inhibit invasion of dysplastic epithelial cells across basement membrane.
- Most widely studied classes of drugs are Acid suppressive agents, NSAIDS and statins.



Proton pump inhibitors(PPIs)



- Mixed results but most studies(prospective and retrospective cohorts) concluded PPIs may be protective in patients with BE.
- Systematic review and metanalysis of 7 observational studies showed PPI use was associated with 71% risk reduction of EAC or HGD with trend towards a dose-response relationship.



NSAIDS



- Pooled analysis of 6 population based studies showed that use of NSAIDS(including aspirin) significantly reduced risk of development of EAC.
- However, a randomised trial studying celecoxib in chemoprevention showed no benefit.
- Population-based case control study of low dose aspirin or NSAIDS in 2025 was also unable to show a reduction in risk of HGD and EAC in patient with BE.
- Hence use of NSAIDS exclusively for chemoprevention is not recommended.

Liao LM, Vaughan TL, Corley DA, et al. Nonsteroidal anti-inflammatory drug use reduces risk of adenocarcinomas of the esophagus and Esophagogastric junction in a pooled analysis. *Gastroenterology* 2012;142:442-452.e5; quiz e22-3.

Statins

- A meta- analyses of 13 observational studies reported a significant reduction(41%) in the risk of EAC in patients with BE.
- A nested case- control study of patients with BE showed an inverse association between statin use and development of EAC, with greater effect for higher doses and longer duration of use.
- Despite the results observed, use of statin for the sole purpose of chemoprevention in BE is not routinely recommended.

Singh S, Singh AG, Singh PP, et al. Statins are associated with reduced risk of esophageal cancer, particularly in patients with Barrett's esophagus: a systematic review and meta-analysis. Clin Gastroenterol Hepatol 2013;11:620-9.

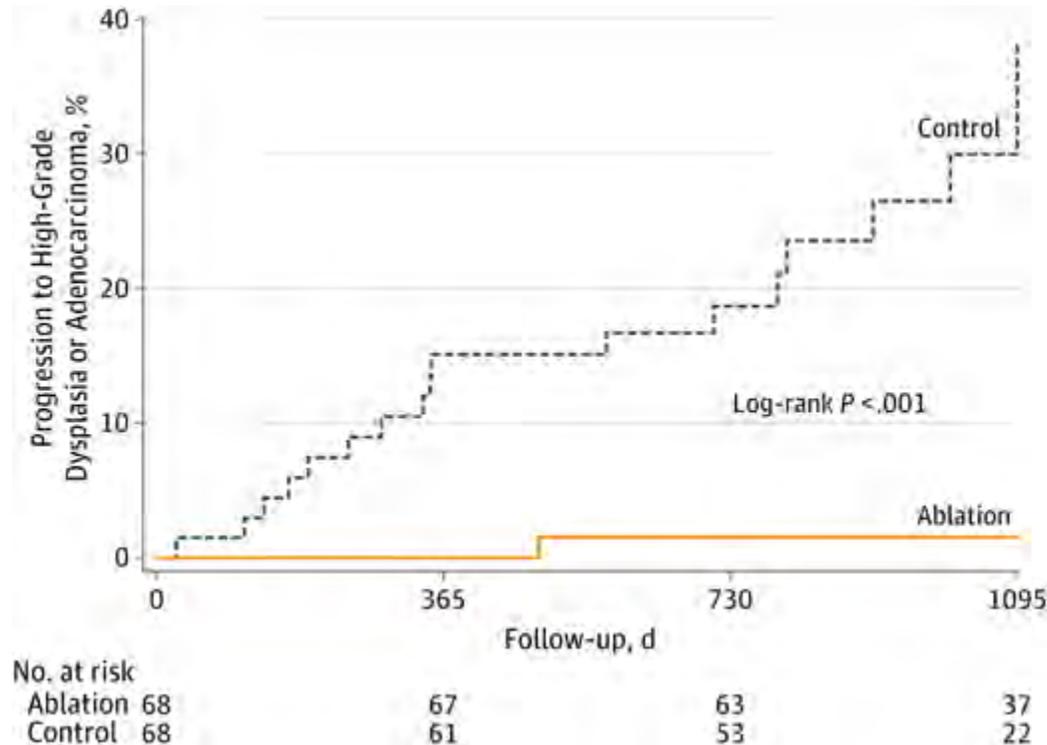


Endoscopic Therapy for BE



- Endoscopic eradication therapy(EET) has transformed the management of dysplastic BE and early(T1a) EAC.
- It has virtually eliminated the need for surgery in the majority of these patients.
- EET recommended in patients with:
 - ✓T1a(intramucosal) EAC
 - ✓BE with confirmed HGD
 - ✓BE with confirmed LGD
- Not recommended in patients with NDBE(surveillance alone sufficient)

AIM Dysplasia Trial



- Ablation group less likely progress to HGD (1.5% [n = 1] vs 26.5% control group [n = 18], $P < .001$).
- Ablation group less likely to progress to EAC(1.5% [n = 1] vs 8.8% [n = 6], $P = .03$)
- Risk reduction: HGD- 25% (NNT 4)
EAC- 7.4% (NNT-13.6)

Barrett's esophagus - ACG Guidelines Update 2022/ESGE Guidelines 2023 – Diagnosis/ Surveillance

- Offering endoscopic ablation therapy for BE and low grade dysplasia on at least two separate endoscopies, both confirmed by a second experienced pathologist
- Ablative therapy for BE with confirmed high grade dysplasia
- Endoscopic resection – T1a Barrett's cancer with well/moderate differentiation and no signs of lympho-vascular invasion
- Ablation for complete eradication of residual Barrett's epithelium following endoscopic resection

Recommended management- LGD vs HGD

	LGD	HGD
BSG [33,104]	Endoscopic ablation therapy (preferably with RFA), surveillance after 6 months if ablation was not undertaken (recommendation grade A for ablation and C for surveillance)	Endoscopic therapy (options ought to be discussed by an upper GI multidisciplinary team beforehand)
ESGE [52]	Endoscopic ablation therapy (with RFA)	Endoscopic resection is recommended for all the visible lesions. If no lesions suspicious for dysplasia are visible, endoscopist ought to take 4-quadrant biopsies. In case of histopathological conformation of the HGD, endoscopic ablation (with RFA) is recommended. Otherwise, endoscopy should be repeated after 3 months.
AGA [110]	Surveillance or EET (endoscopic eradication therapy)	EET (removal of visible lesions with EMR)
Australian [111]	Surveillance every 6 months, however, reverting to a less frequent follow-up schedule should be considered if two consecutive endoscopies show no dysplasia or Endoscopic ablation may be considered—especially if LGD is definite, multifocal and present on more than one occasion	Endoscopic resection of visible/nodular lesions and RFA within the flat segments
ACG [91]	Surveillance (6 and 12 months after diagnosis, and annually thereafter) or EET (resection of all visible lesions, followed by ablation) and then surveillance endoscopy after 1 years, 3 years and afterwards continued every 2 years)	EET (resection of visible lesions followed by ablation and surveillance 3, 6 and 12 months after complete eradication of remaining metaplastic epithelium and then continued annually)
Asia-Pacific consensus [25]	Surveillance endoscopy after 6 months or Endoscopic resection of focal lesions and if there is the absence of such lesions consider RFA	Endoscopic resection followed by RFA



Post Treatment Surveillance



- Recurrence of BE following CE-IM is not uncommon.
- Meta analysis of 41 studies published in 2016 reported a pooled incidence of BE recurrence of 9.5% per patient-year with rates in individual studies ranging from 0.9% to 28.8%.
- Most often occurs as non-dysplastic BE.
- Vast majority of recurrences(95.4%) were successfully treated endoscopically.
- Predicators of recurrence- Increasing age and length of BE.



Post- Treatment surveillance



- Continued endoscopic surveillance after treatment is essential.
- HGD: q3 months for the first year following CE-IM, q6 months in the second year, then annually.
- LGD: q6 months in the first year following CE-IM and annually thereafter.
- Targeted biopsies of any visible abnormalities should be obtained in addition to random 4 quadrant biopsies from the entire length of prior BE segment.



Subsquamous Intestinal Metaplasia(SSIM)

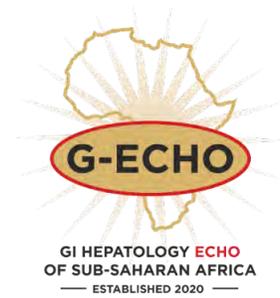


- “Buried Barret's” or “Buried glands”
- Presence of Barret's metaplasia beneath an intact layer of squamous epithelium.
- Development of EAC from SSIM after RFA has been described in case reports.
- Fears that SSIM may be caused by ablation and increase risk of EAC not corroborated.
- Cohort studies have shown SSIM often present prior to ablation in upto 38% of patients.
- Appears that SSIM may actually decrease following ablation of BE.

Wolf WA, Pasricha S, Cotton C, et al. Incidence of Esophageal Adenocarcinoma and Causes of Mortality After Radiofrequency Ablation of Barrett's Esophagus. Gastroenterology 2015;149:1752-1761.e1.



Subsquamous Intestinal metaplasia(SSIM)



- A randomised, sham controlled trial of RFA in BE; presence of SSIM in 25% of cases prior to ablation which decreases to 5% 12 months after ablation.
- 2015 study from the U.S RFA registry:
 - SSIM associated with increased risk of EAC but all subsquamous cancers occurred prior to CE-IM.
 - After CE-IM, SSIM was much less common suggesting that RFA may eradicate SSIM and prevent subsquamous cancers.

Wolf WA, Pasricha S, Cotton C, et al. Incidence of Esophageal Adenocarcinoma and Causes of Mortality After Radiofrequency Ablation of Barrett's Esophagus. *Gastroenterology* 2015;149:1752-1761.e1.

Esophageal cancer

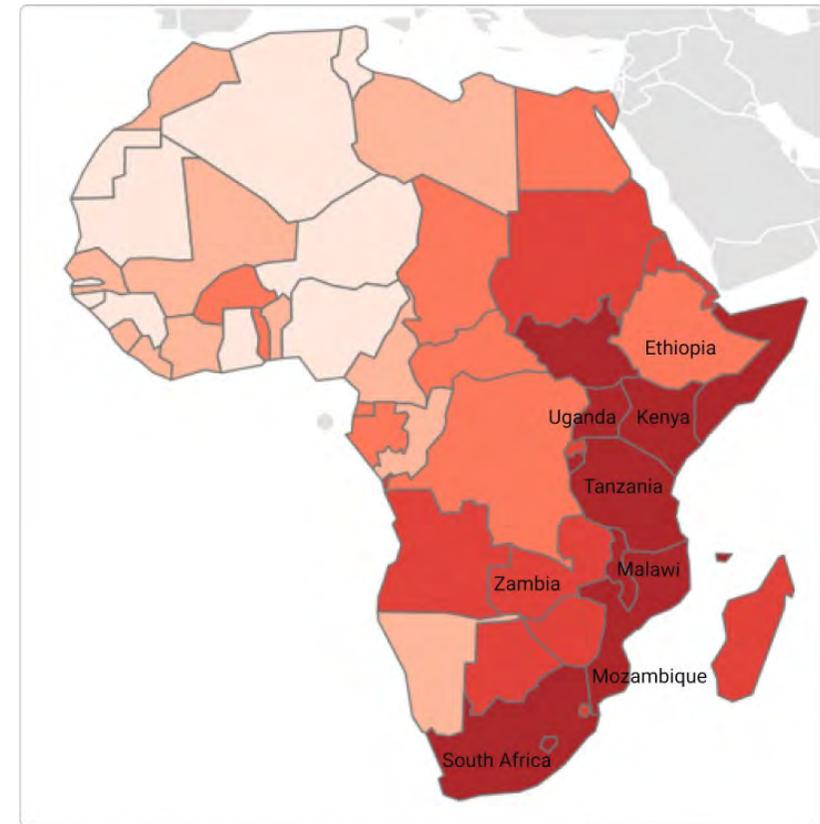
Introduction

- “Esophageal cancer(EC) is one of the most unknown and deadliest cancers worldwide.
- Extremely aggressive nature and poor survival rate.
- EC is the the 11th prevalent cancer and 7th leading cause of death(GLOBOCAN, 2022)
- Presents in 6th and 7th decade. Lifetime risk is 0.5% both men and women.5-year survival 15%-25%.
- SCC- Asia & Africa. EAC- North Europe and North America
- Differences between the risk factors of both histological types that affect their incidence and distribution worldwide.

Epidemiology in Africa

- In 2022 alone, Africa saw 30,000 new cases and 28,000 deaths.
- High prevalence in Eastern Africa.
- Over 90% of EC in the high-risk areas is SCC.
- Majority of EC patients present with advanced cancer with 3-6 months survival.

Distribution of AfrECC sites in Africa



* Darker color correlates with higher frequency of the disease

Introduction

- SCC arises from the cells that line the upper part of the oesophagus.
- Adenocarcinoma arises from glandular cells that are present at the GEJ and stomach.
- EC is the most prevalent type with an incidence of 46.7/100,00(males) and 19.2/100,000(females).
- Second highest number of cancer-related deaths in SA.



Paucity of data in South Africa



SA Journal of Oncology
ISSN: (Online) 2523-0646, (Print) 2518-8704



Page 1 of 9  Review Article

Oesophageal cancer in South Africa: A scoping review



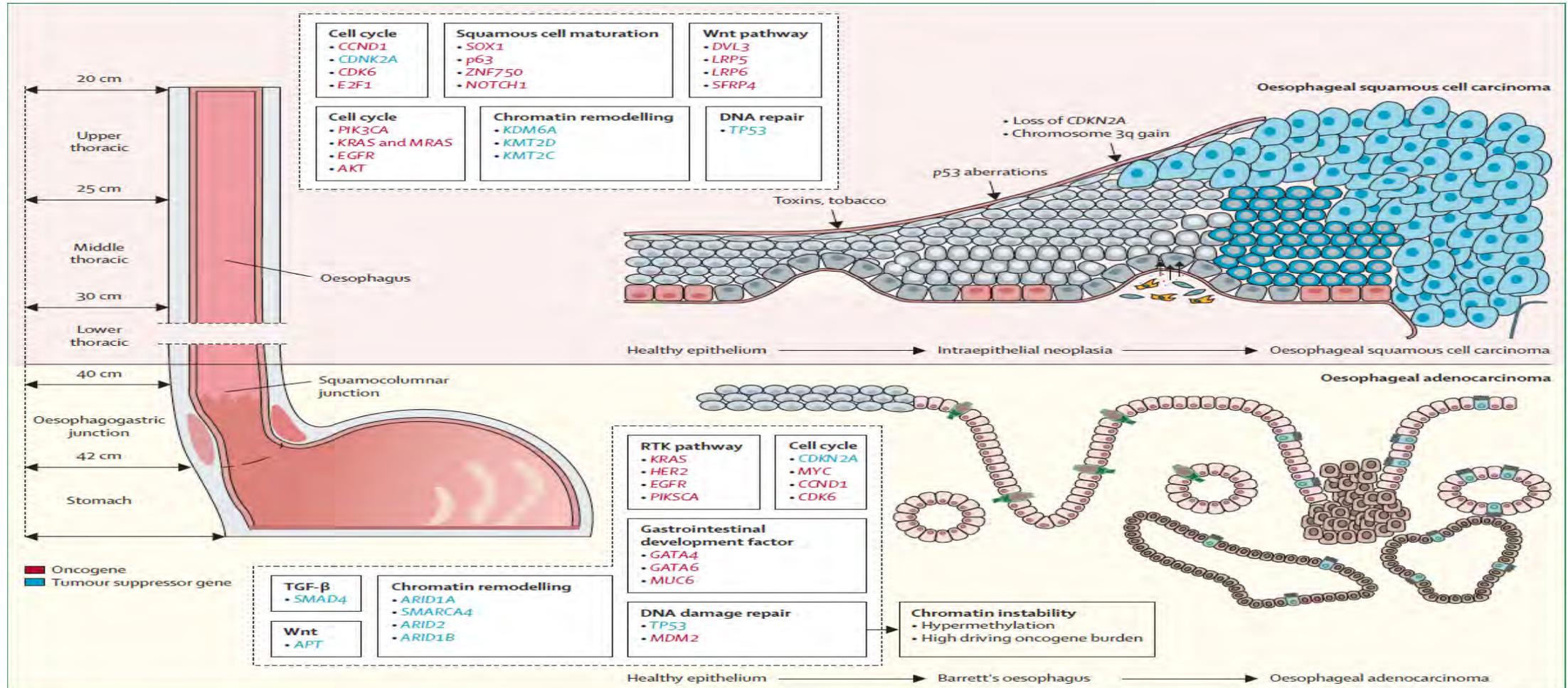
Study highlight

- **Study Aim:** To assess the body of literature on clinical and epidemiological research on esophageal cancer from South Africa and identify key research gaps.
- **Methods:** search of databases and manual searches after cross-referencing selected appropriate articles published up to the end of 2020. Genetic and laboratory-based studies without clinical components excluded.
- **Results:** 81 articles identified published from 1957 to 2020.
 - ✓ Significant decrease in the number of publications after the year 2000.
 - ✓ Inconsistencies in data on incidence of EC in South Africa.
 - ✓ Late presentation is huge factor in South Africa hence poor prognosis.
- **Conclusion:** Strong drive towards research on EC to assess the burden of disease in South Africa.

Risk factors for SCC

- A- Achalasia & alcohol
- B- Bad diet(high fat, high temperature)
- C-Caustic stricture(lye ingestion)
- C- Cigarette smoking x9 risk
- D- Dysplasia/diverticuli
- E- Esophageal webs(PVS)
- F- Familial/ genetic
- Cancers of the head, neck, or lungs
- Human papillomavirus (HPV) infection
- Tylosis- excess skin growth on the palms of the hands and the soles of the feet.
- Race - SCC common among blacks.
- Vitamin Deficiencies-beta carotene, vitamin E, selenium, and iron
- Radiation treatment- chest or upper abdomen

Pathogenesis



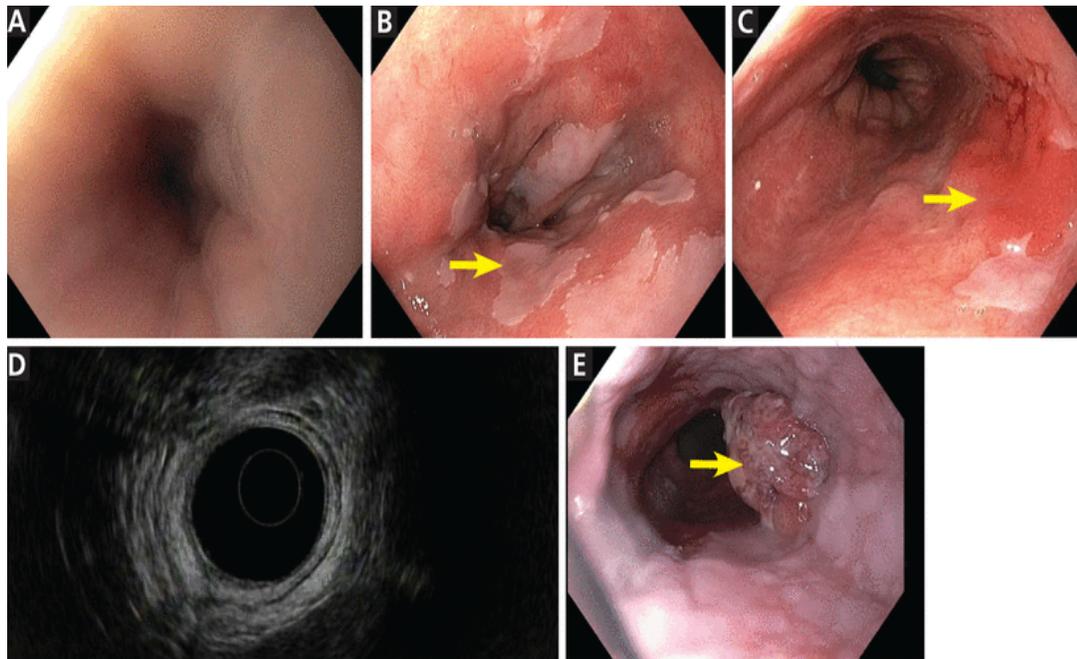
Pathology and molecular typing

- SCC and EAC have different molecular hallmarks.
- Molecular biomarkers- favourable responses to immunotherapy.
 - ✓ Microsatellite instability-high
 - ✓ Mismatch repair deficiency- GEJ adenocarcinomas
 - ✓ Human epidermal growth factor receptor 2 (*HER2*)- Anti-HER2 therapy.
 - ✓ Programmed death-ligand 1 (*PD-L1*)-Immunotherapy in SCC.

Assessment

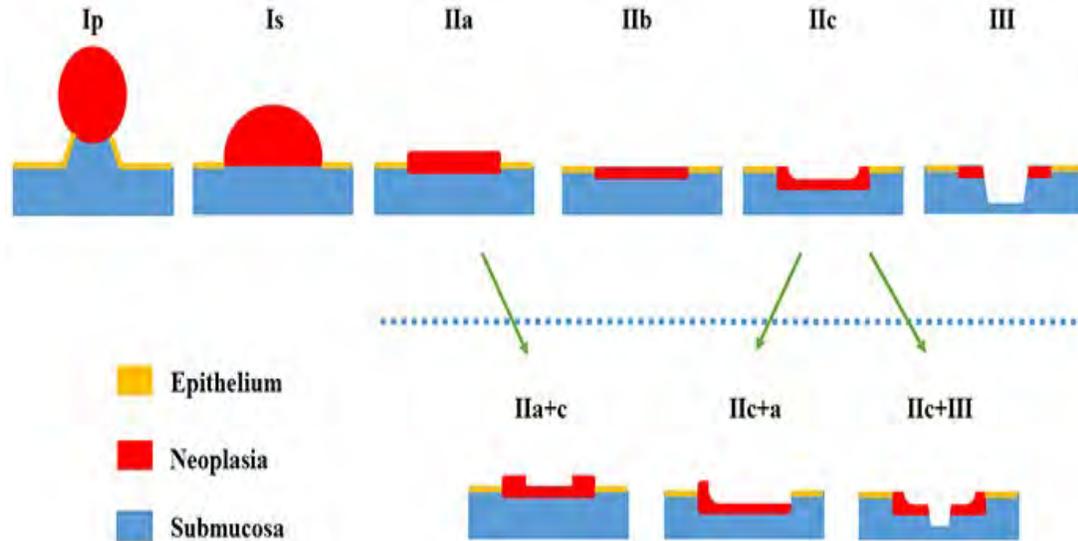
- All patients with new dysphagia, gastrointestinal bleeding, recurrent aspiration or emesis and weight loss and/or loss of appetite should undergo an upper endoscopy.
- Obtain $\geq 6-8$ representative biopsies of the lesion. The number of biopsies should be sufficient for pathological and molecular analysis.
- FBC- Assess for IDA.
- Renal and Liver function- Assess function to determine appropriate therapeutic options
- Brochoscopy with endobronchial Us- Tumor growth in central airways and TEF.
- CT CAP with Oral and IV Contrast- staging to detect local/distant LN .
- FDG PET-CT- systemic metastases.
- EUS- Node assessment and depth of invasion

BE- EAC progression



Endoscopic views of the esophagus. (A) Normal esophagus. (B) Barrett esophagus with islands of normal squamous mucosa (arrow). (C) Barrett esophagus with a discrete erythematous mass 4 × 2 cm (arrow) in the involved segment. (D) Barrett esophagus, endoscopic ultrasonographic view. (E) Esophageal adenocarcinoma (arrow).

Paris classification



- Polypoid (0-Ip–pedunculated 0-Is–sessile)
- Non-polypoid (0-IIa–slightly elevated, 0-IIb–flat, 0-IIc–slightly depressed, 0-III–excavated (ulcer))

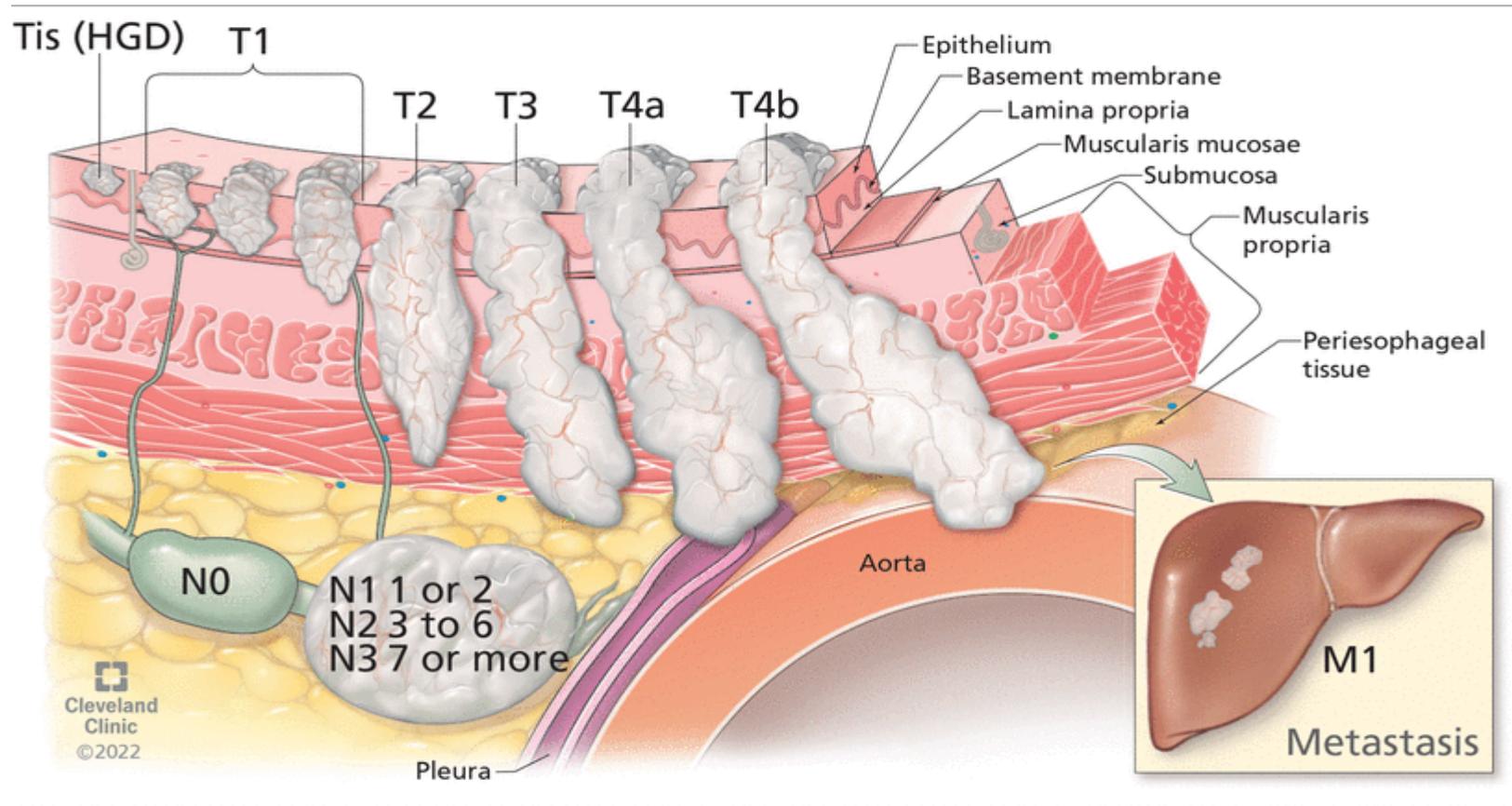
Recommendations- Assesment

- Patients with new dysphagia, gastrointestinal bleeding, recurrent aspiration or emesis and weight loss and/or loss of appetite should undergo an upper intestinal endoscopy [III, A].
- Diagnosis should be made by histopathological assessment of multiple (atleast 6) endoscopic biopsies to guarantee an adequate representation of the tumour and sufficient tissue for molecular analysis [I, B].
- Histological diagnosis should be reported according to the WHO criteria [IV, A].
- IHC staining is recommended in poorly differentiated and undifferentiated cancers when differentiation between SCC and EAC using morphological characteristics is not possible [V, B].
- For oesophageal SCC, PD-L1 expression by IHC according to the TPS or CPS is a validated predictive biomarker for ICI therapy [I-II, A].

Recommendations

- Initial staging and risk assessment should include physical examination, endoscopy and contrast-enhanced CT or FDG-PET-CT scan of the thorax, abdomen & pelvis.
- EUS can be used for T and N staging [III, A].
- FDG-PET should be carried out in candidates for oesophagectomy [III, B].
- In locally advanced (T3/T4) ACs of the OGJ which cross the diaphragm to infiltrate the anatomical cardia, laparoscopy should be carried out [IV, B].
- The TNM stage should be recorded according to the latest edition of the AJCC/UICC guidelines and staging manual [IV, A].
- Nutritional status and history of weight loss should be assessed [III, A] and nutritional support provided [II, A] according to ESPEN guidelines.

Staging of Esophageal cancer



Abel Joseph, Siva Raja, Suneel Kamath, Sunguk Jang, Daniela Allende, Mike McNamara, Gregory Videtic, Sudish Murthy, Amit Bhatt
Cleveland Clinic Journal of Medicine May 2022, 89 (5) 269-279; DOI: 10.3949/ccjm.89a.21053

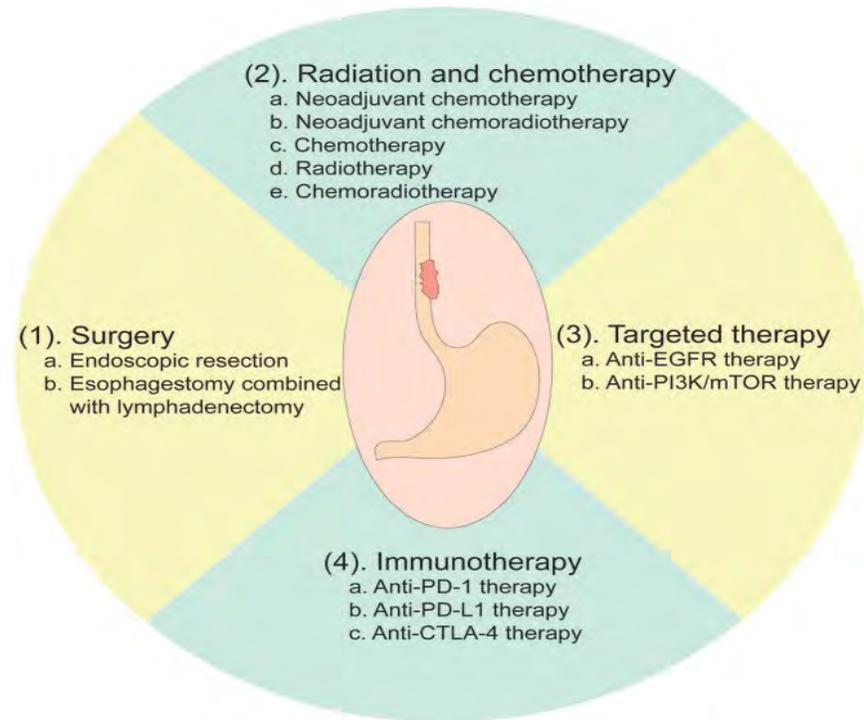


Treatment Principles

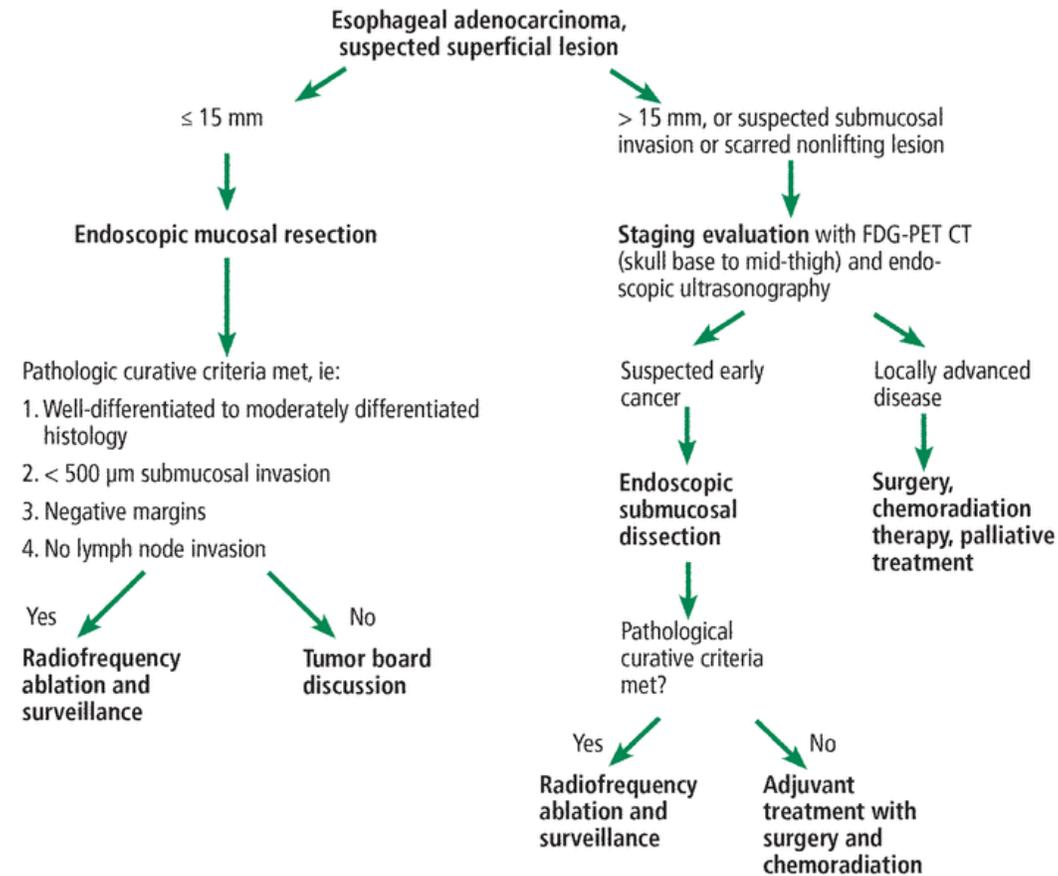


- Comprehensive assessments to determine
 - ✓ Pathological subtype
 - ✓ TNM stage.
 - ✓ Tumour location.
 - ✓ Performance status(CR fitness + treatment tolerability)
- Optimal therapeutic strategies vary by TNM stage.
- Stage-specific therapy recommendations essential for both SCC & EAC

Treatment options



Treatment Algorithm for EAC



Treatment recommendations

cTis-1aN0M0

Oesophageal squamous cell carcinoma	Endoscopic submucosal dissection or endoscopic mucosal resection or endoscopic radiofrequency ablation
Oesophageal adenocarcinoma	Endoscopic submucosal dissection or endoscopic mucosal resection or endoscopic radiofrequency ablation

cT1b-2N0M0

Oesophageal squamous cell carcinoma	Oesophagectomy options include two-field lymphadenectomy including recurrent laryngeal nerve lymph node, minimally invasive oesophagectomy, ⁴²⁻⁴⁴ or robot-assisted minimally invasive oesophagectomy, ⁴⁵ rather than open surgery; adjuvant chemotherapy if patients staged as pN1-3; ⁴⁶ postoperative radiation for patients without R0 resection
Oesophageal adenocarcinoma	Oesophagectomy options include two-field lymphadenectomy including recurrent laryngeal nerve lymph node, minimally invasive oesophagectomy, ⁴²⁻⁴⁴ or robot-assisted minimally invasive oesophagectomy, ⁴⁵ rather than open surgery; adjuvant chemotherapy if patients staged as pN1-3; ⁴⁶ postoperative radiation for patients without R0 resection

cT1-4aN1-3M0 or cT3-4aN0M0

Oesophageal squamous cell carcinoma	Neoadjuvant chemoradiotherapy and surgery (paclitaxel and platinum and 41.4 Gy radiation) ^{47,48} or neoadjuvant triplet chemotherapy (fluorouracil, platinum, and docetaxel); ⁴⁹ adjuvant single-agent immune checkpoint inhibitors for patients without pathological complete response after neoadjuvant therapy; ⁵⁰ postoperative radiation for patients without R0 resection
Oesophageal adenocarcinoma	Perioperative chemotherapy (fluorouracil, leucovorin, oxaliplatin, and docetaxel) ⁵¹ or neoadjuvant chemoradiotherapy and surgery (paclitaxel and platinum and 41.4 Gy radiation); ⁴⁸ adjuvant single-agent immune checkpoint inhibitors for patients without pathological complete response after neoadjuvant therapy; ⁵⁰ postoperative radiation for patients without R0 resection

Treatment recommendations

cT4bN0-3M0

Oesophageal squamous cell carcinoma	Definitive chemoradiotherapy (50-4 Gy radiation, FOLFOX or paclitaxel and platinum); ^{52,53} surgery for persistent and recurrent disease ^{54,55}
Oesophageal adenocarcinoma	Definitive chemoradiotherapy (50-4 Gy radiation, FOLFOX or paclitaxel and platinum); ^{52,53} surgery for persistent and recurrent disease ^{54,55}

cTanyNanyM1

Oesophageal squamous cell carcinoma	For patients with low PD-L1 expression, chemoimmunotherapy combining paclitaxel, platinum, and immune checkpoint inhibitors remains a recommended approach; ²⁸ however, the survival benefit in this group is less pronounced than individuals with high PD-L1 expression*
Oesophageal adenocarcinoma	If HER2-positive and PD-L1-high, anti-HER2 trastuzumab and chemoimmunotherapy (fluorouracil and cisplatin and immune checkpoint inhibitors); ⁵⁶ if HER2-negative and PD-L1-high, chemoimmunotherapy (fluorouracil and cisplatin and immune checkpoint inhibitors); if HER2-negative and PD-L1-low: chemotherapy (fluorouracil and cisplatin) and immune checkpoint inhibitors†

Conclusion

- Chronic gastro-oesophageal acid and bile reflux can lead to Barrett's oesophagus, a well-described precursor of oesophageal adenocarcinoma.
- The incidence of oesophageal adenocarcinoma has been dramatically increasing in developed countries.
- Regular endoscopic monitoring of Barrett's oesophagus is recommended to detect neoplastic changes at an early curative stage.
- Endoscopic diagnostic and therapeutic technologies to detect and treat early lesions are rapidly advancing.
- Surgery, increasingly combined with chemotherapy and radiotherapy, remains the main treatment modality for advanced EAC