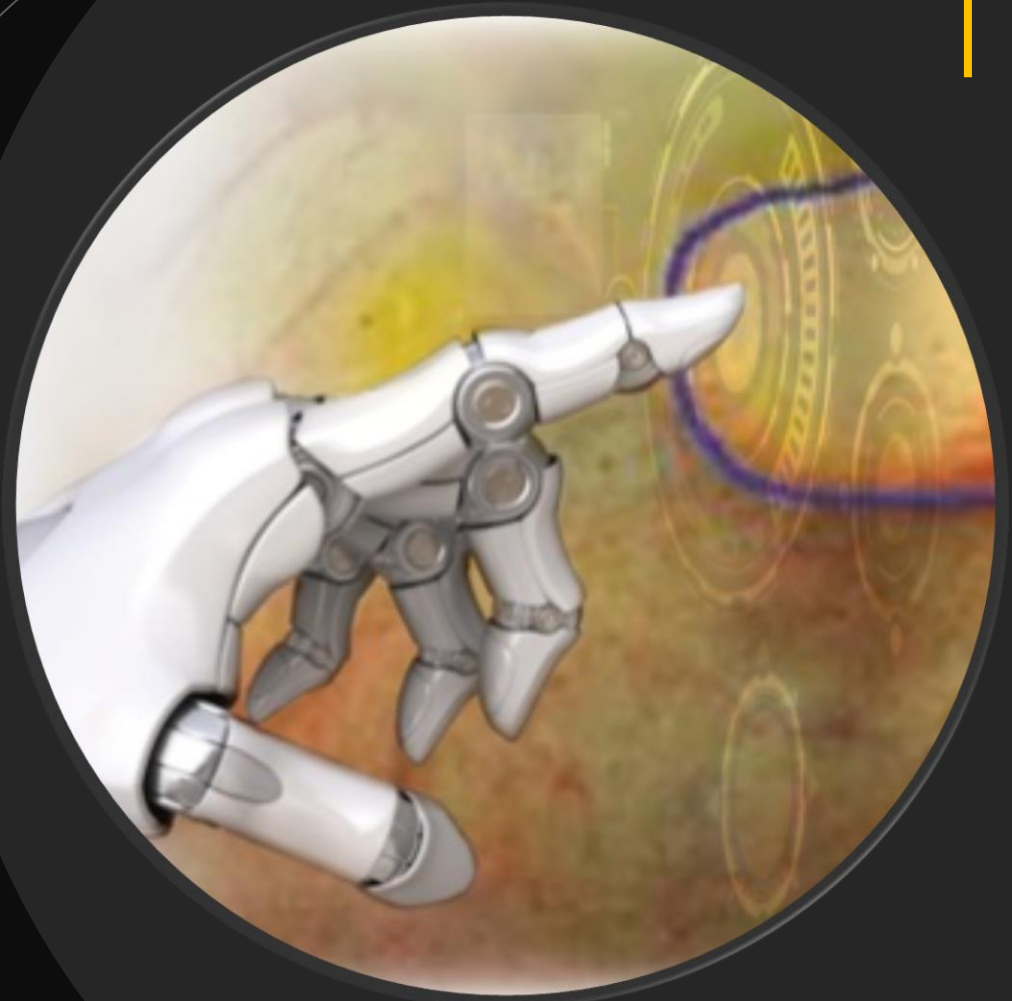
Gastric cancer



Dr Sadeghi , MD

Associate Professor of Gastroenterology and Hepatology

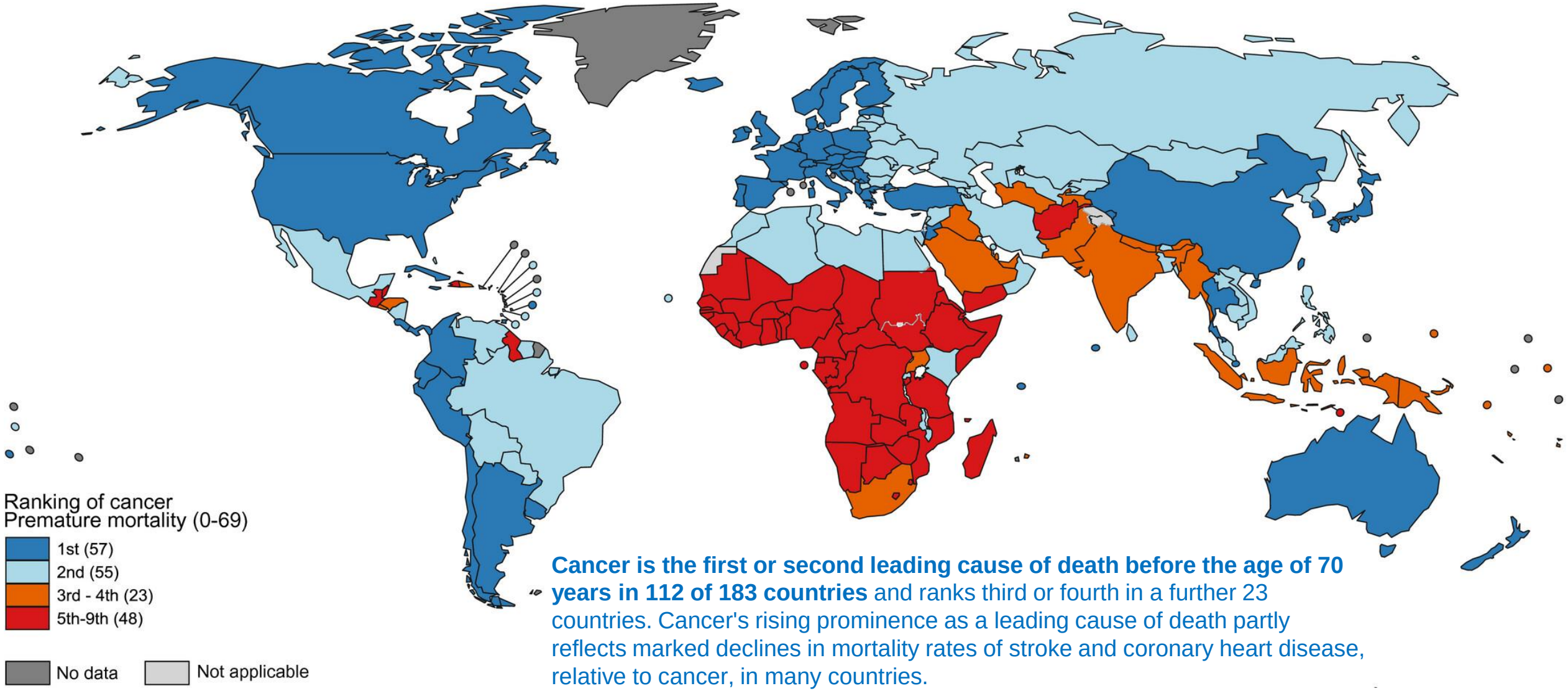
- **Epidemiology and**
- **Risk factors**



Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries

National Ranking of Cancer as a Cause of Death at Ages <70 Years in 2019.

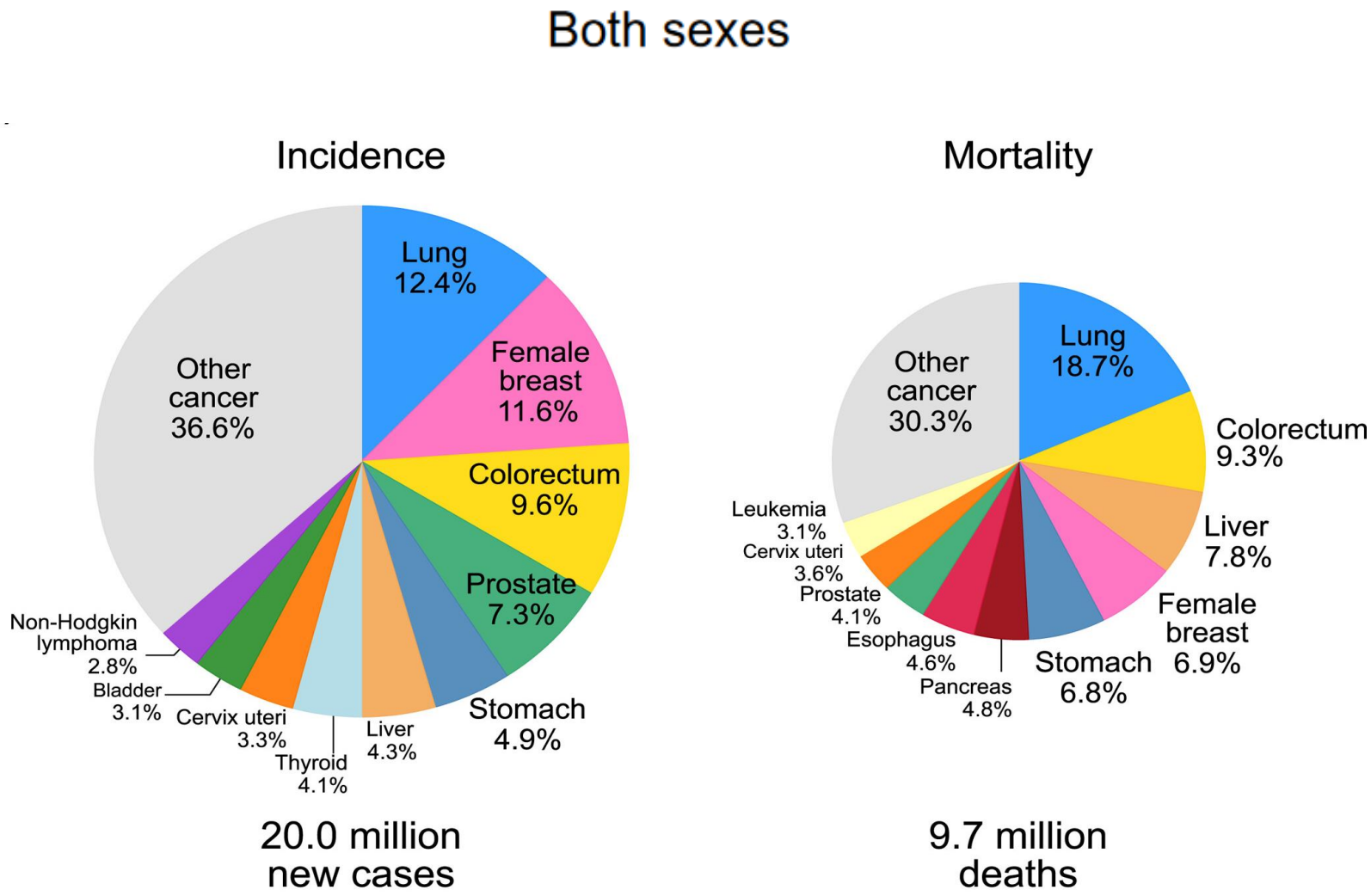
World Health Organization



Cancer is the first or second leading cause of death before the age of 70 years in 112 of 183 countries and ranks third or fourth in a further 23 countries. Cancer's rising prominence as a leading cause of death partly reflects marked declines in mortality rates of stroke and coronary heart disease, relative to cancer, in many countries.

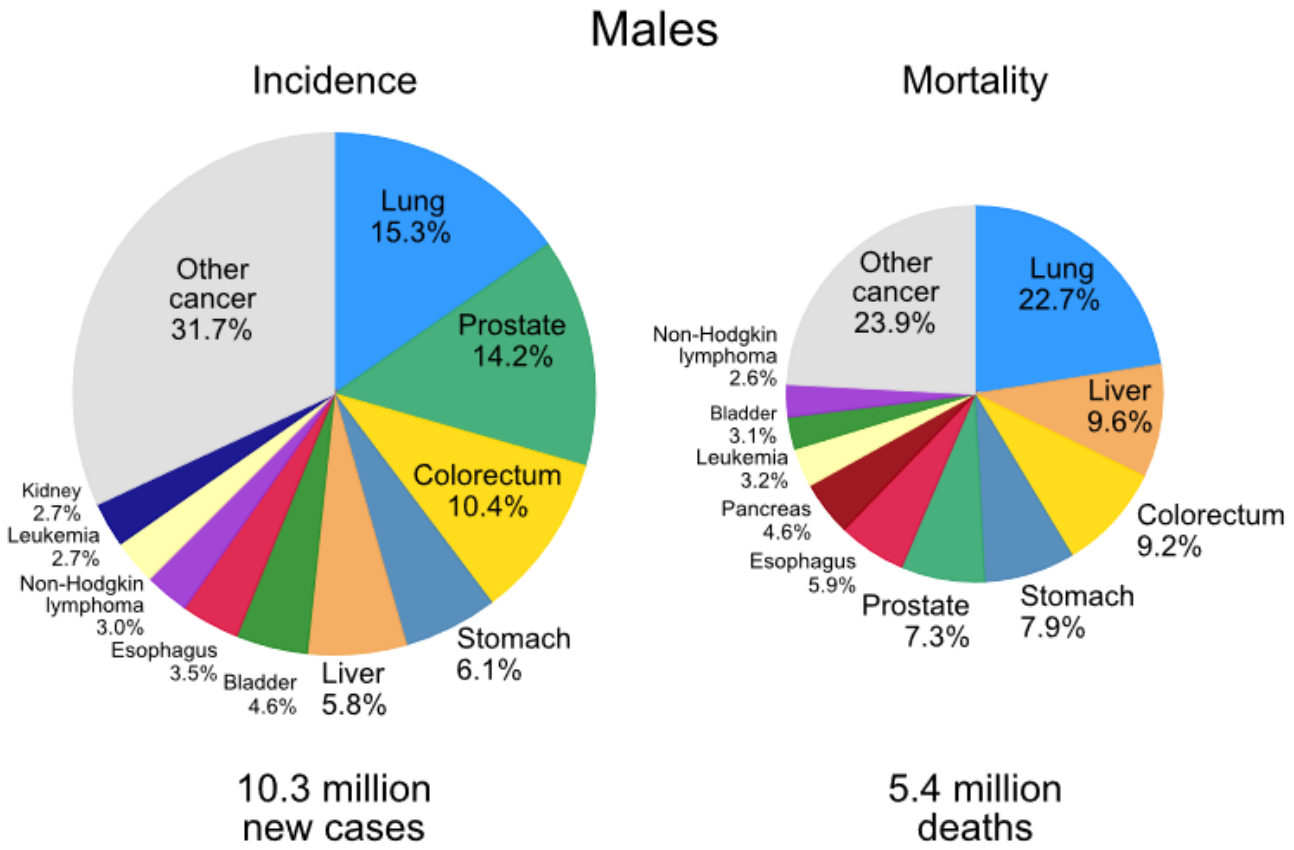
CA A Cancer J Clinicians, Volume: 71, Issue: 3, Pages: 209-249.

Distribution of Cases and Deaths for the Top 10 Most Common Cancers in 2022.



World Health Organization

Distribution of Cases and Deaths for the Top 10 Most Common Cancers in 2022.



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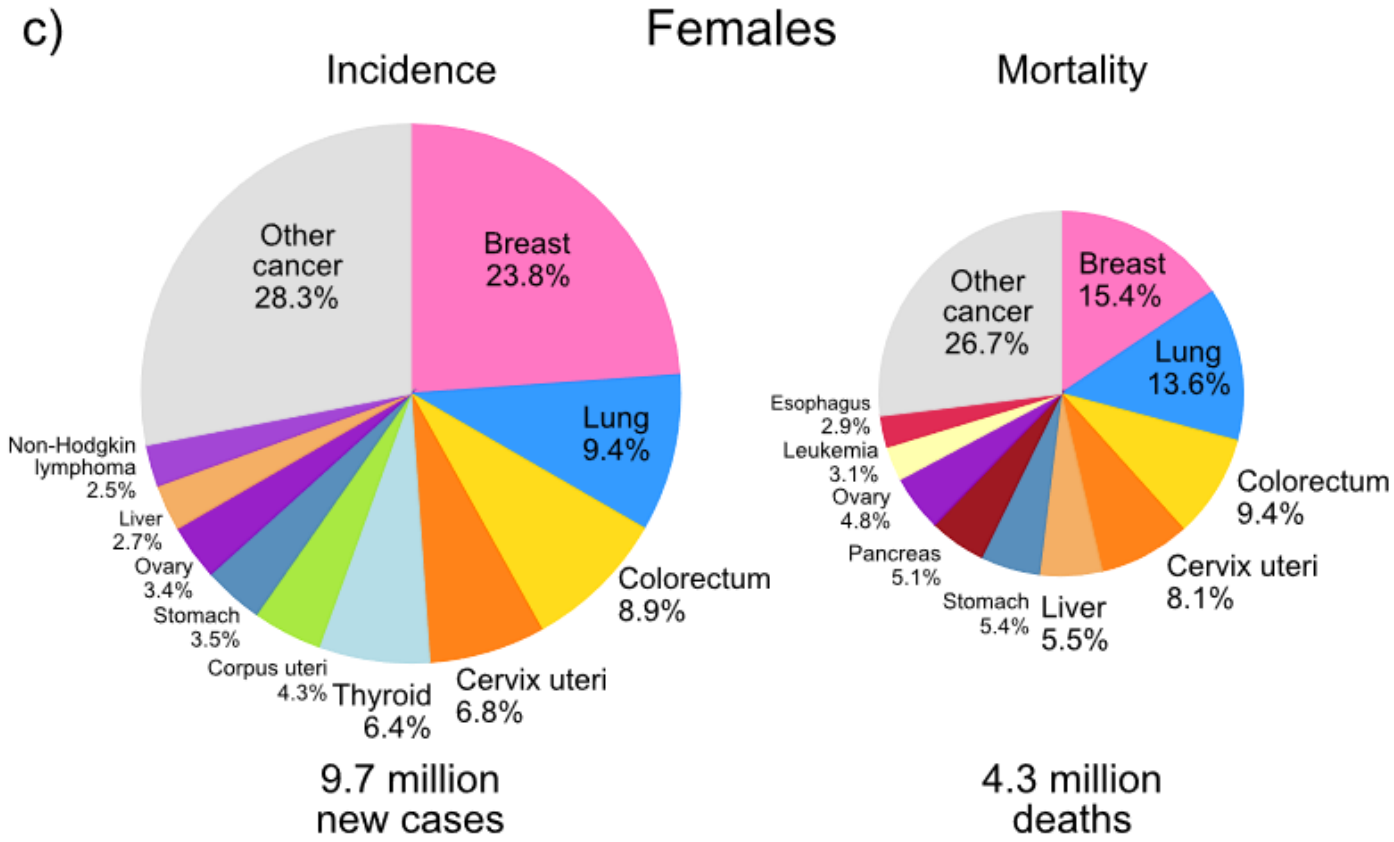
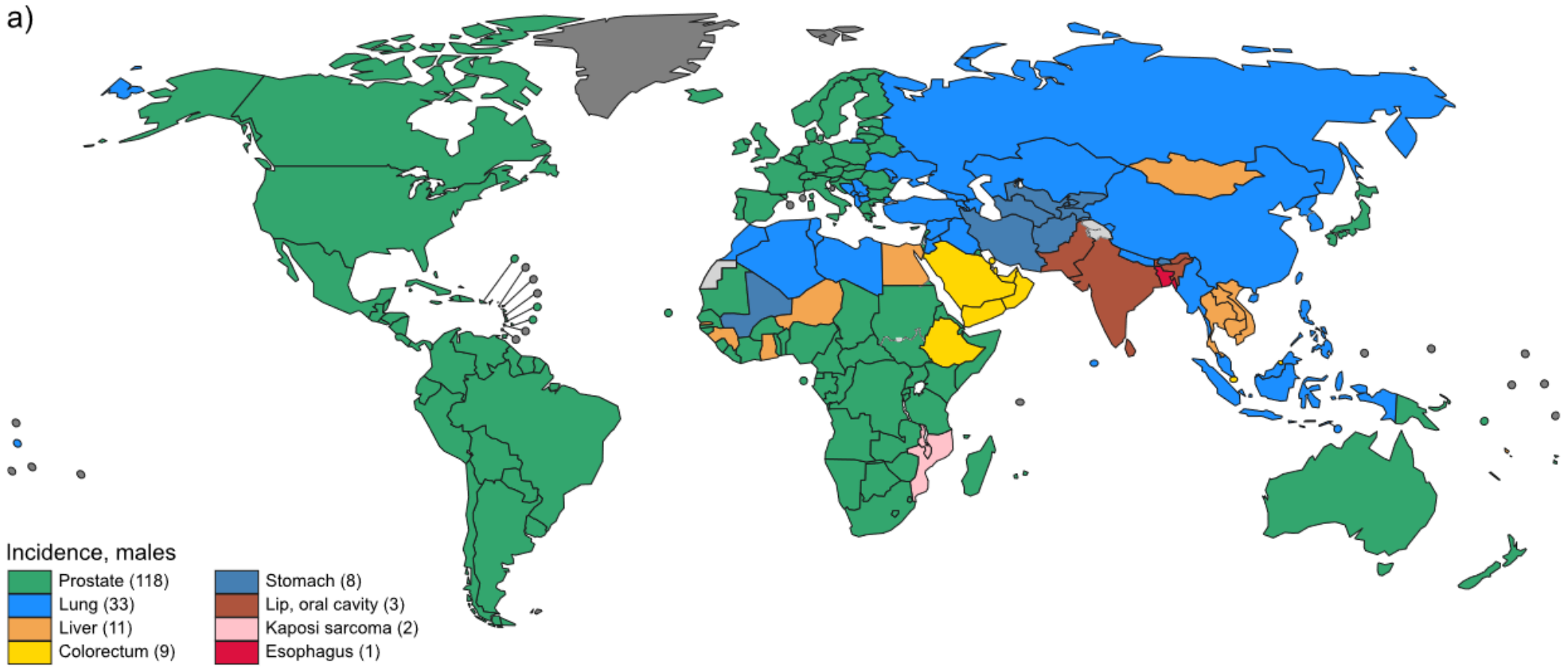


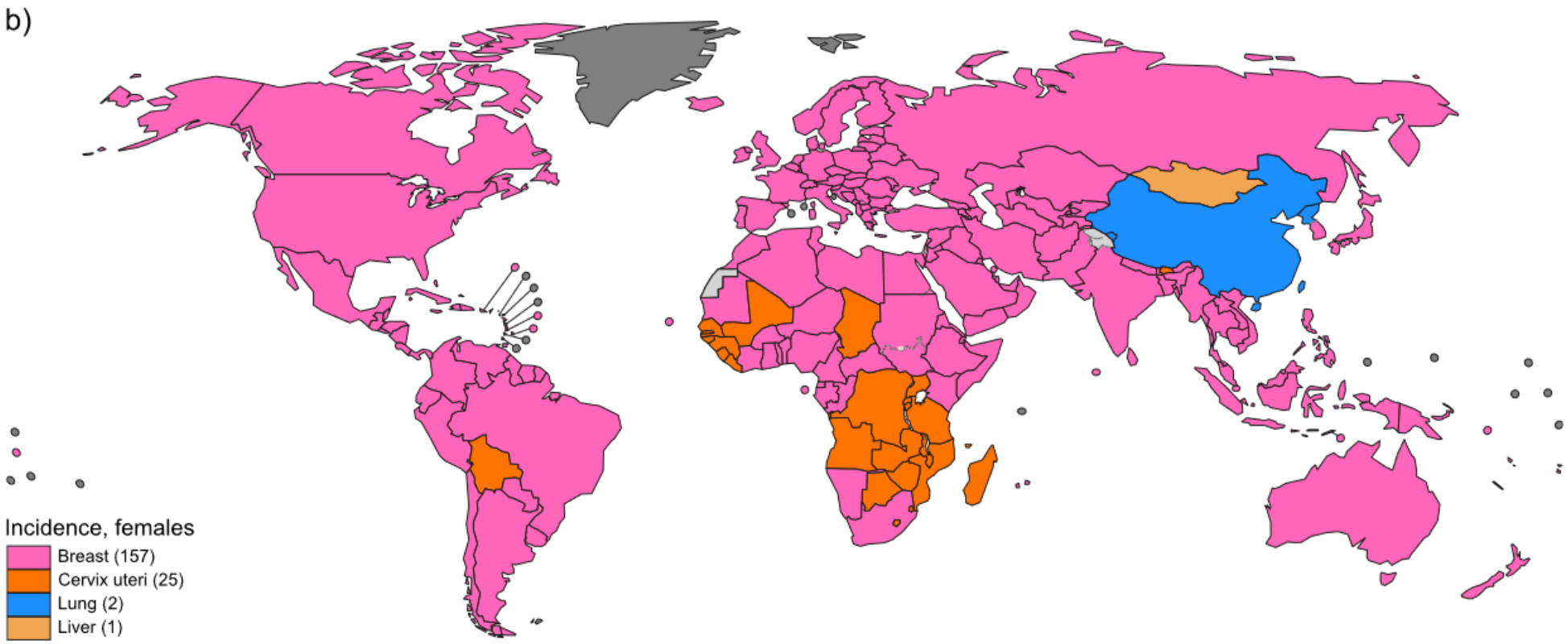
World Health Organization

Most Common Type of Cancer Incidence in 2022 in Each Country.



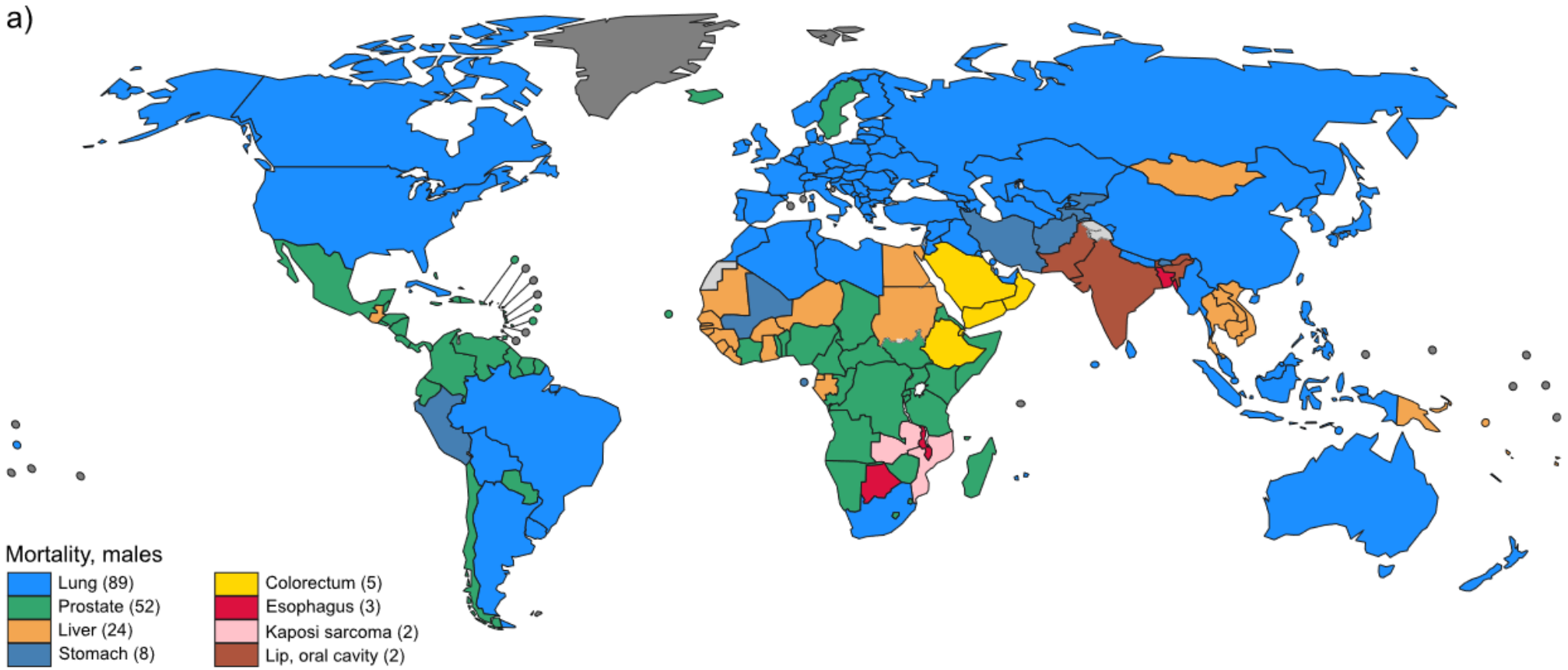
World Health Organization

Most Common Type of Cancer Incidence in 2022 in Each Country.



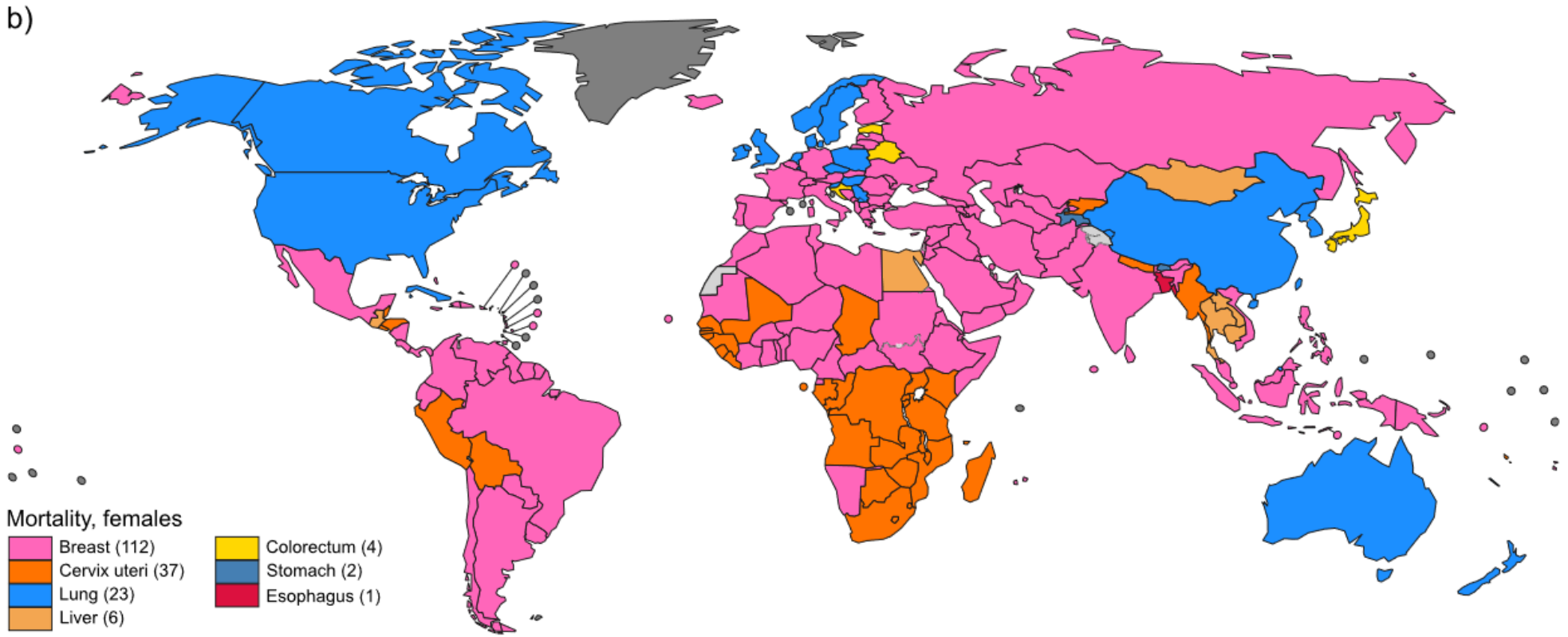
World Health Organization

Most Common Type of Cancer Mortality by Country in 2022.



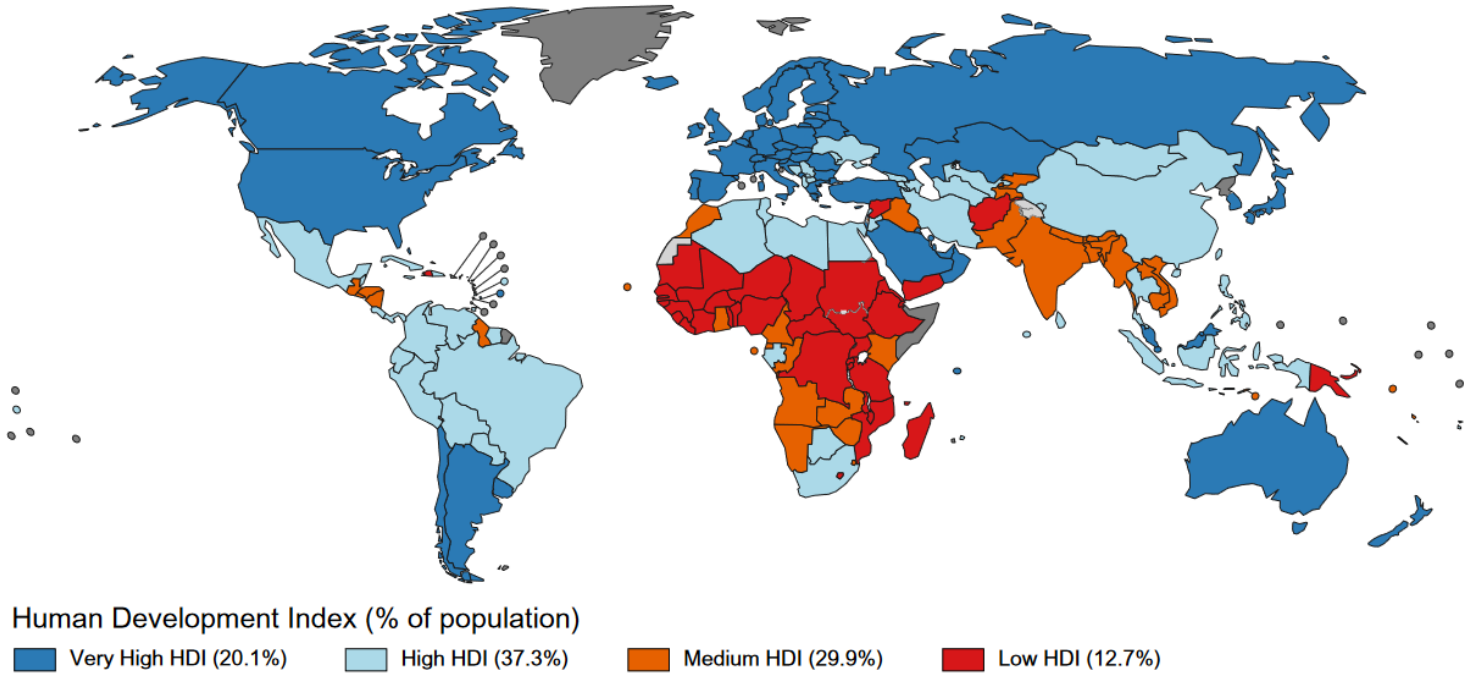
World Health Organization

Most Common Type of Cancer Mortality by Country in 2022.

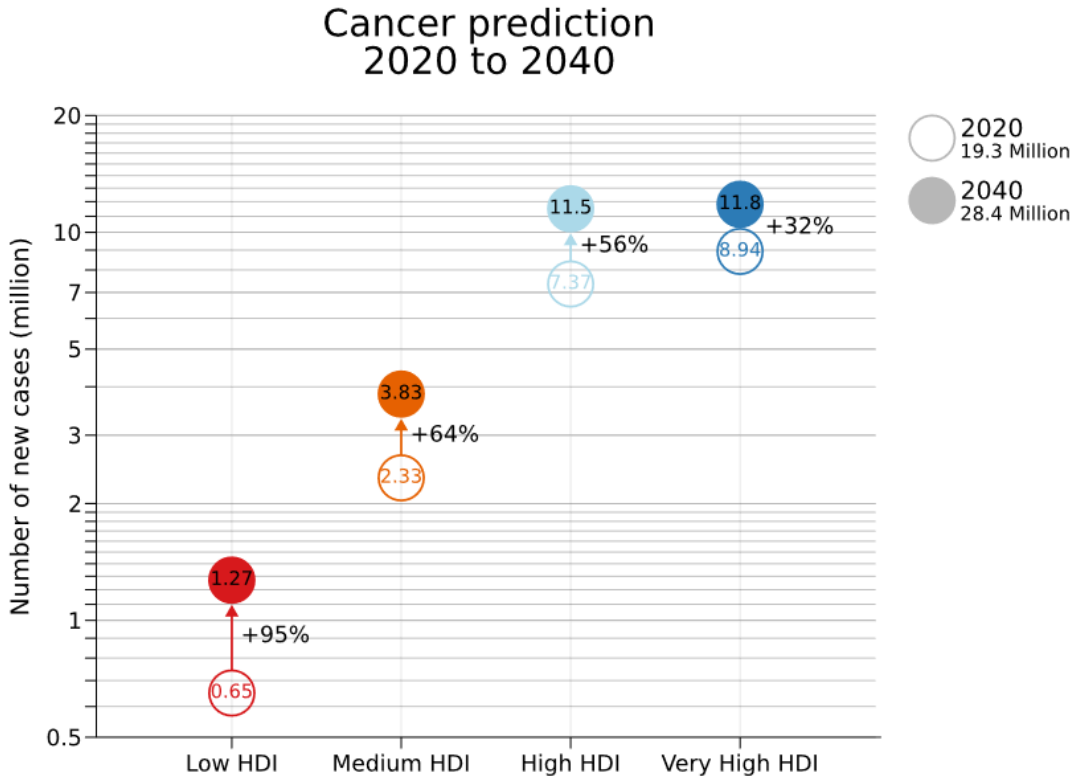


World Health Organization

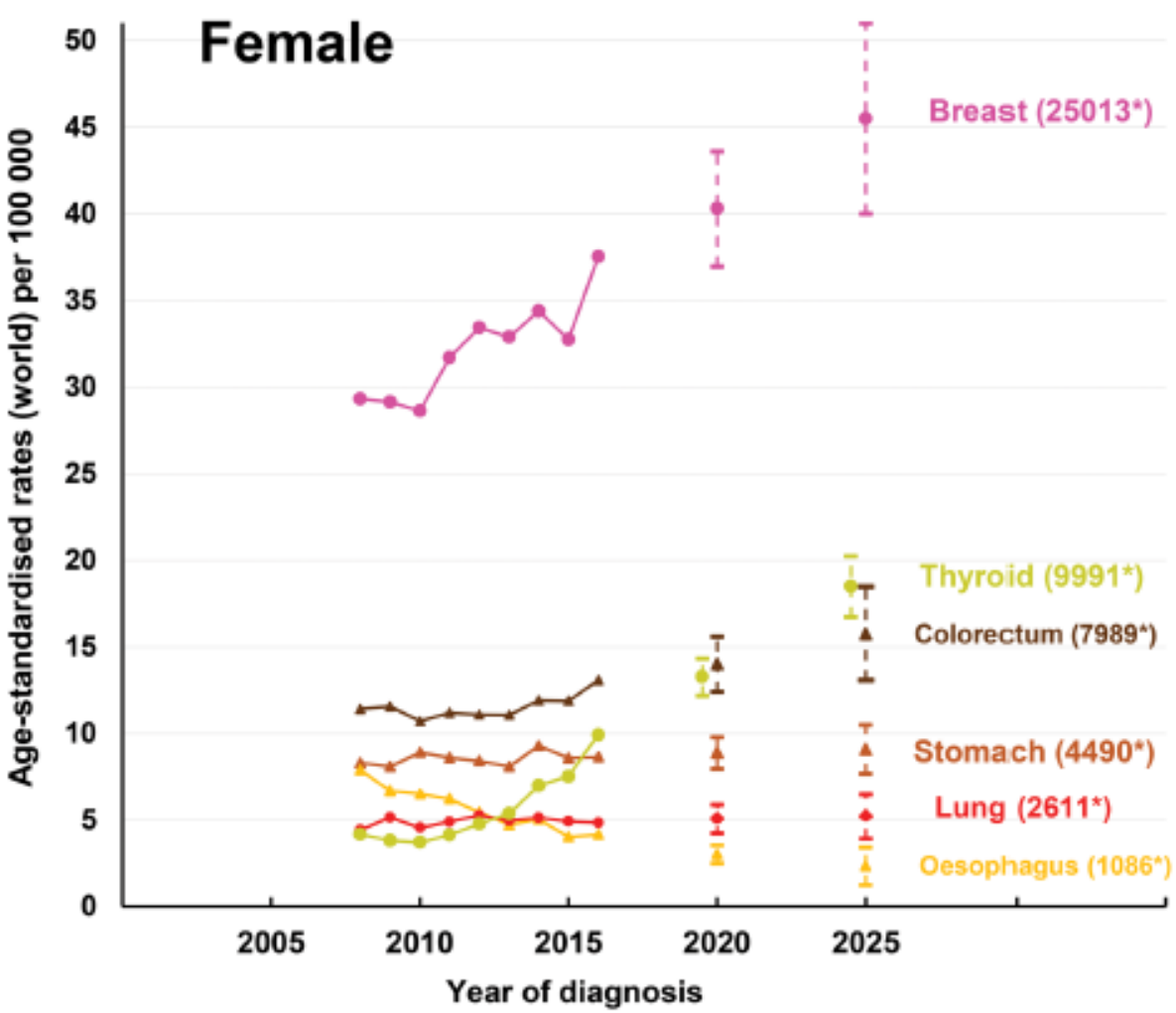
World Health Organization

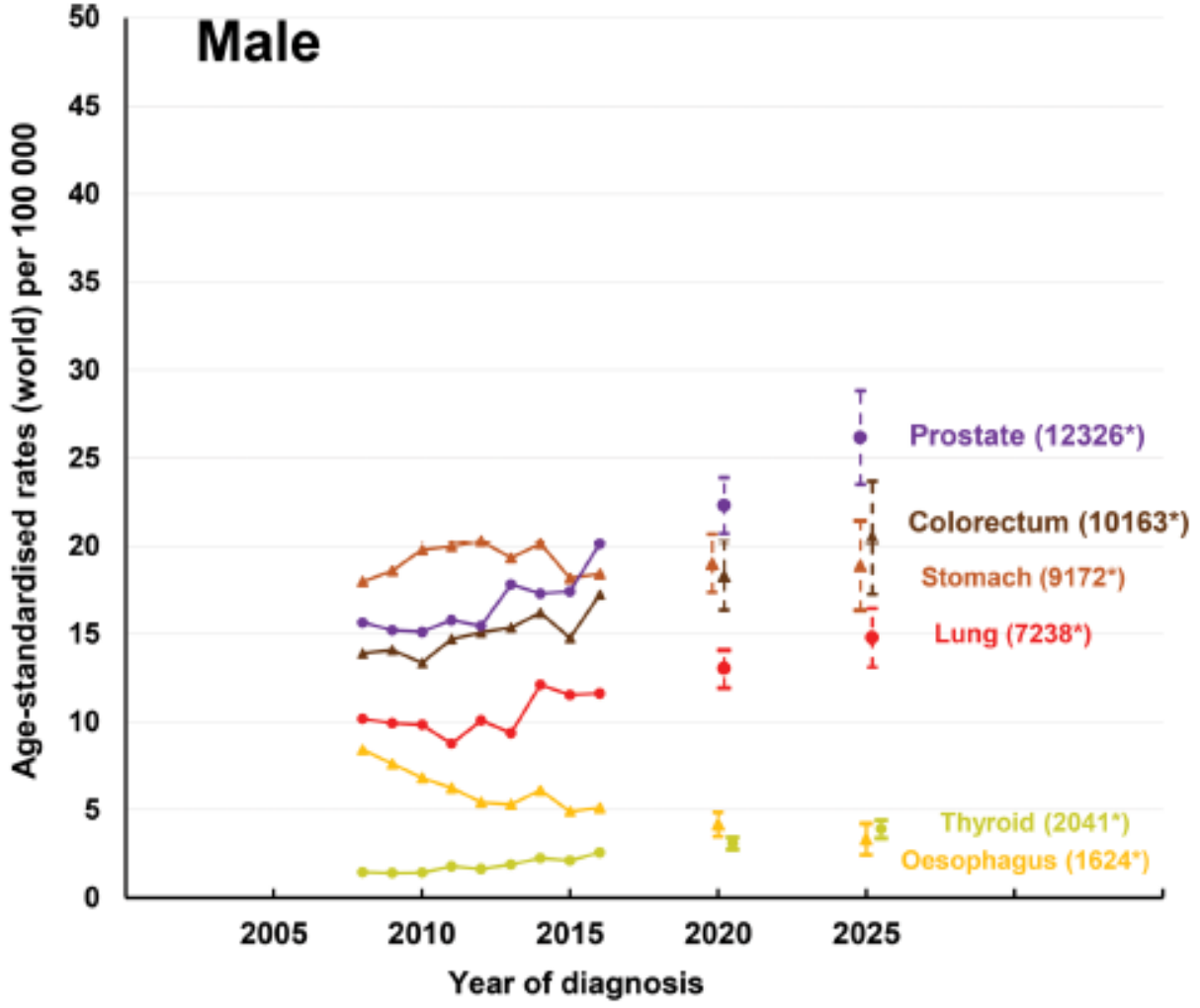


Projected Number of New Cases for All Cancers Combined in 2040 According to the 4-Tier Human Development Index (HDI).



Recorded and predicted rate of most common cancers in Iran





Int. J. Cancer. 2021

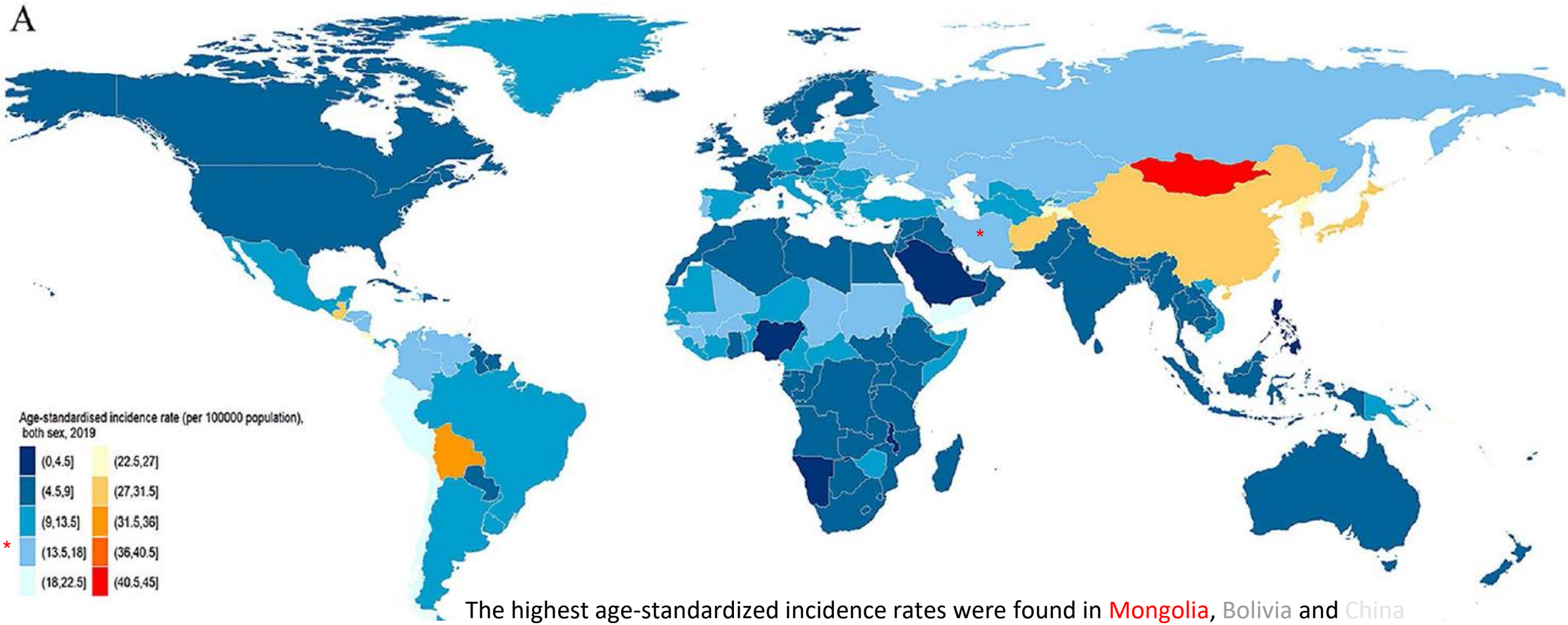
TABLE 2 Recorded (2008, 2016) and predicted (2025) number of cases, age-standardized (World standard) rates per 100 000 persons-year and percentage of change of most common cancers, Iran

	Recorded (2008, 2016)				Predicted (2025)				
	Number of cases		ASR				Percentage change in number of cases (2025 vs 2016)	Change due to, %	
Site	2008	2016	2008	2016	Number of cases	ASR		Risk	Population
Esophagus	4824	3554	8.2	4.6	2931	3.1	−17.5	−41.7	24.1
Stomach	7757	10 388	13.2	13.5	13 509	13.9	30.0	2.2	27.8
Colorectum	7774	11 558	12.7	15.1	17 812	17.7	54.1	20.5	33.6
Lung	4298	6217	7.3	8.2	9269	9.5	49.1	17.6	31.5
Breast (female)	9247	15 350	29.3	37.5	25 013	45.5	63.0	27.0	35.9
Ovary	1286	1917	4.1	4.8	2897	5.6	51.1	20.2	30.9
Prostate	4746	7394	15.7	20.1	12 326	26.2	66.7	35.3	31.4
Bladder	4821	6560	8.2	8.6	8278	8.5	26.2	−3.1	29.2
Brain & CNS	3536	4476	5.1	5.7	6266	6.4	40.0	16.2	23.8
Thyroid	1927	5576	2.8	6.2	11 921	11.2	113.8	88.3	25.5
NHL	2568	3519	4.0	4.5	5123	5.2	45.6	19.5	26.1
Leukemia	4333	5453	6.7	7.2	6768	7.6	24.1	6.2	18.0
Other but NMSC	23 453	30 511	38.1	39.2	38 268	39.8	25.4	−0.7	26.2
All cancers but NMSC	80 570	112 473	130.8	144.0	160 381	161.1	42.6	13.9	28.7

1st
4th
3rd
2nd
1st

Int. J. Cancer. 2021

The global, regional and national burden of stomach cancer

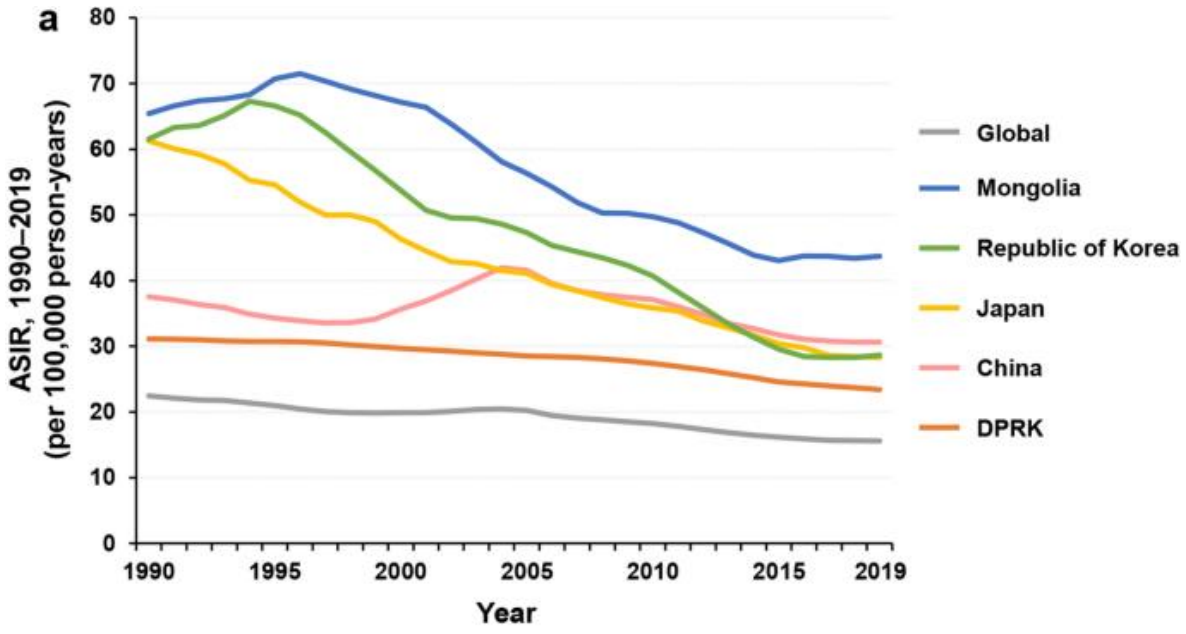


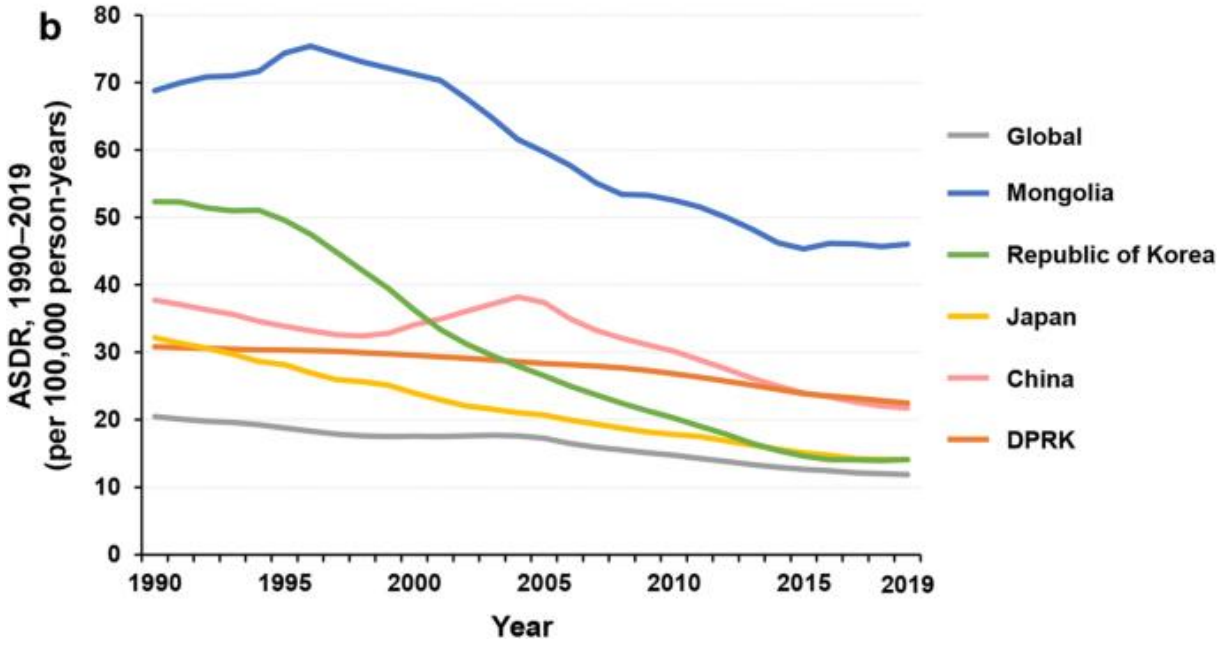
The highest age-standardized incidence rates were found in Mongolia, Bolivia and China

Age-standardized **incidence rates** of stomach cancer per 100,000 population both sex, **2019.**

Scientific Reports 2022; 12:11542

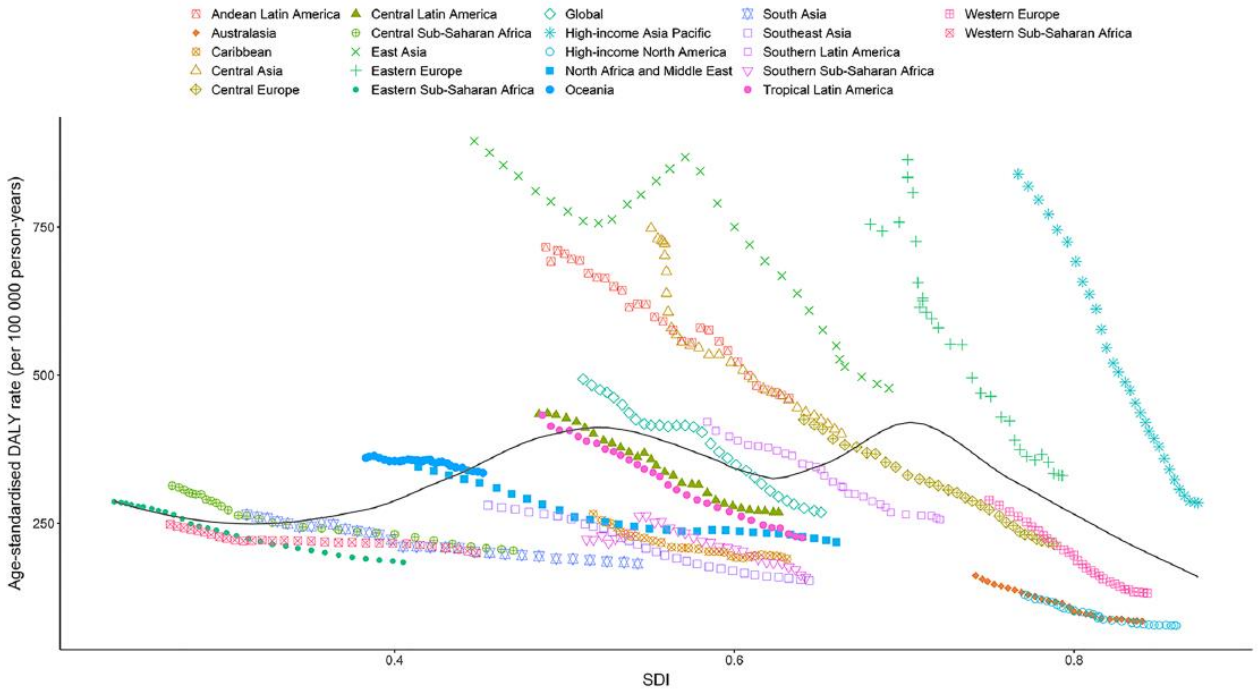
The burden and trend of gastric cancer in five Asian countries from 1990 to 2019

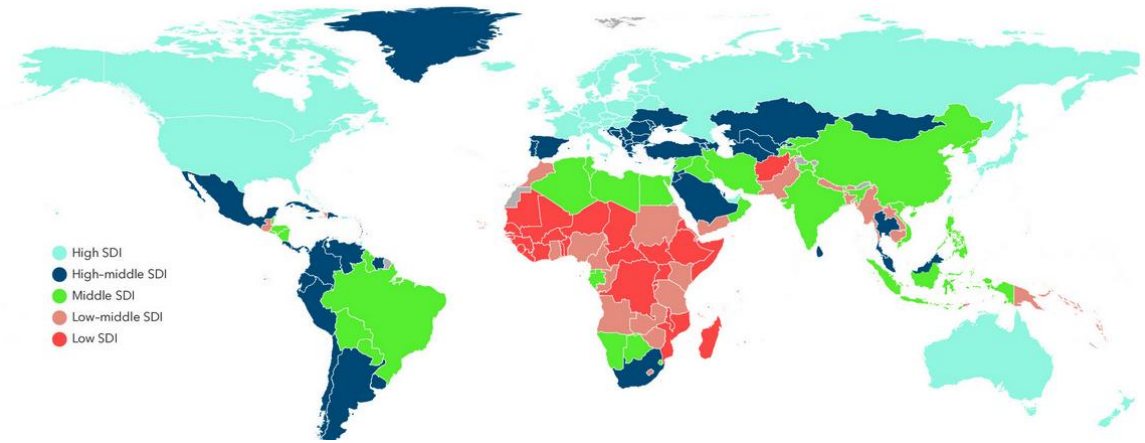




Scientific Reports 2022; 12:5980

The global, regional and national burden of stomach cancer



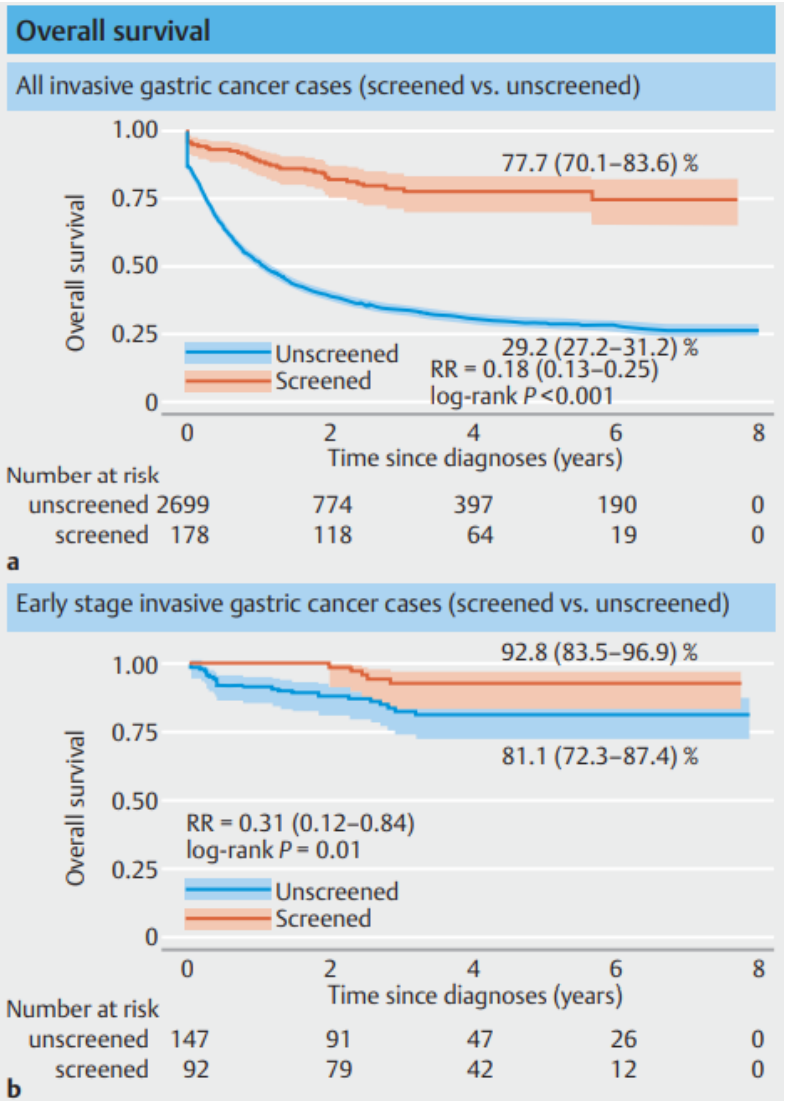


For each region, points from the left to right depict estimates from each year from **1990 to 2019**

SDI: Sociodemographic Index; DALY: disability adjusted life years.

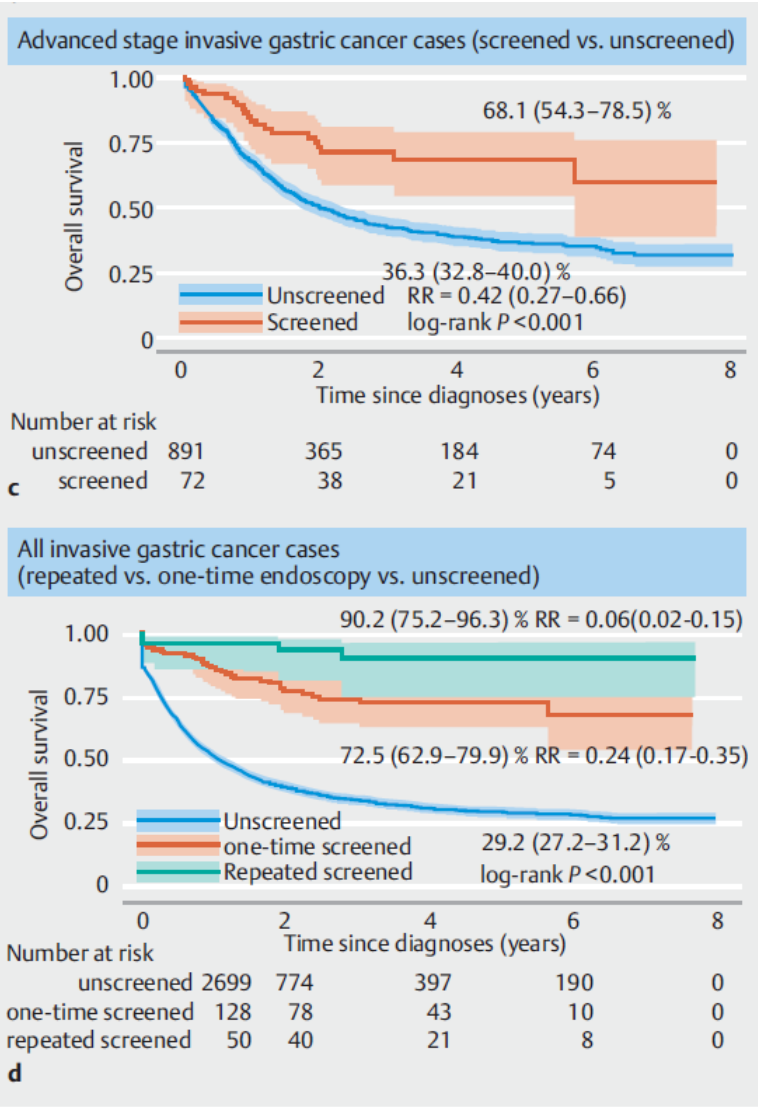
Scientific Reports 2022; 12:11542

Beneficial effects of endoscopic screening on gastric cancer and optimal screening interval: a population-based study



Results Ever receiving endoscopic screening significantly decreased the risk of invasive gastric cancer (age- and sex-adjusted relative risk [RR] 0.69, 95 % confidence interval [CI] 0.52–0.92) and gastric cancer-specific mortality (RR 0.33, 95 %CI 0.20–0.56), particularly for noncardia gastric cancer. Repeated screening strengthened the beneficial effect on invasive gastric cancer-specific mortality of one-time screening. Among invasive gastric cancers, screening-detected individuals had significantly better overall survival (RR 0.18, 95 %CI 0.13–0.25) and disease-specific survival (RR 0.18, 95 %CI 0.13–0.25) than unscreened individuals, particularly for those receiving repeated endoscopy. For individuals with intestinal metaplasia or low grade intraepithelial neoplasia, repeated endoscopy at an interval of < 2 years, particularly within 1 year, significantly enhanced the detection of early gastric cancer, compared with repeated screening after 2 years (*P*-trend = 0.02).

Conclusion Endoscopic screening prevented gastric cancer occurrence and death, and improved its prognosis in a population-based study. Repeated endoscopy enhanced the effectiveness. Screening interval should be based on gastric lesion severity.



Screening of high risk population

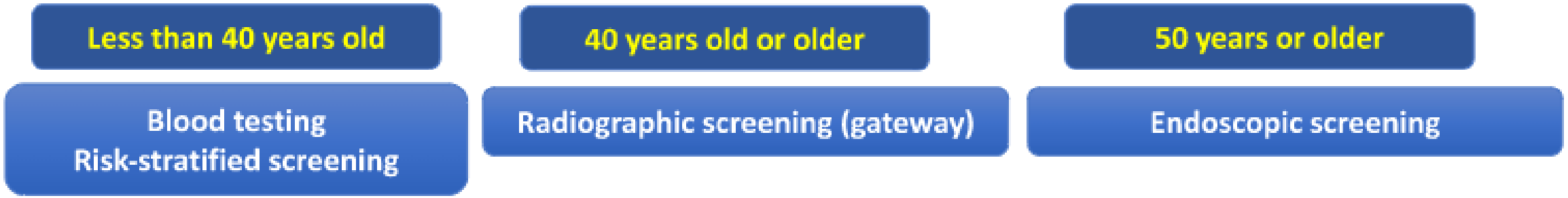
Statement 14: Asymptomatic individuals at age above 50 years are considered vulnerable and at increased risk of gastric cancer compared with younger individuals.

The incidence of gastric cancer was higher than 20/100 000 at the age of 40 years in high incidence countries, such as Korea, Japan and China. Therefore, **asymptomatic individuals aged 50 years or greater are at higher risk of gastric cancer and should be listed as higher priority for gastric cancer screening and prevention.**

Statement 13: Endoscopy with biopsies is recommended in asymptomatic individuals with a family history of gastric cancer (does not refer to hereditary gastric cancer) at age 45 and above.

Update version of the Japanese Guidelines for Gastric Cancer Screening

CancerScreening



Recommendations: Radiographic and endoscopic screenings for gastric cancer are recommended for population-based and opportunistic screenings. The *H. pylori* antibody and serum pepsinogen tests are not recommended for population-based screening because of insufficient evidence.

The Korean guideline for gastric cancer screening

CancerScreening

Recommendations: We recommend that asymptomatic adults from 40 to 75 years of age undergo biannual gastric cancer screening using gastric endoscopy (recommendation B). Gastric cancer screening using UGI series in asymptomatic adults aged between 40 to 74 years may be recommended based on clinicians' judgment regarding the patient's risk and the patient's preference (recommendation C). There is insufficient evidence to assess the benefits and harms of gastric cancer screening for adults aged between 75 to 84 years (recommendation I). We recommend against gastric cancer screening for adults older than 85 years (recommendation D).

The updated guidelines recommended that **endoscopic or radiographic (Barium studies: UGI series) screening be conducted in individuals 40-50 or older every 2 years in high risk populations (but no in areas with relatively low incidence of gastric cancer)**.

Screening of low to moderate risk population

Statement 9: *H. pylori* eradication offers the chance for gastric cancer prevention at any age in adulthood. The magnitude of the benefit decreases with age.

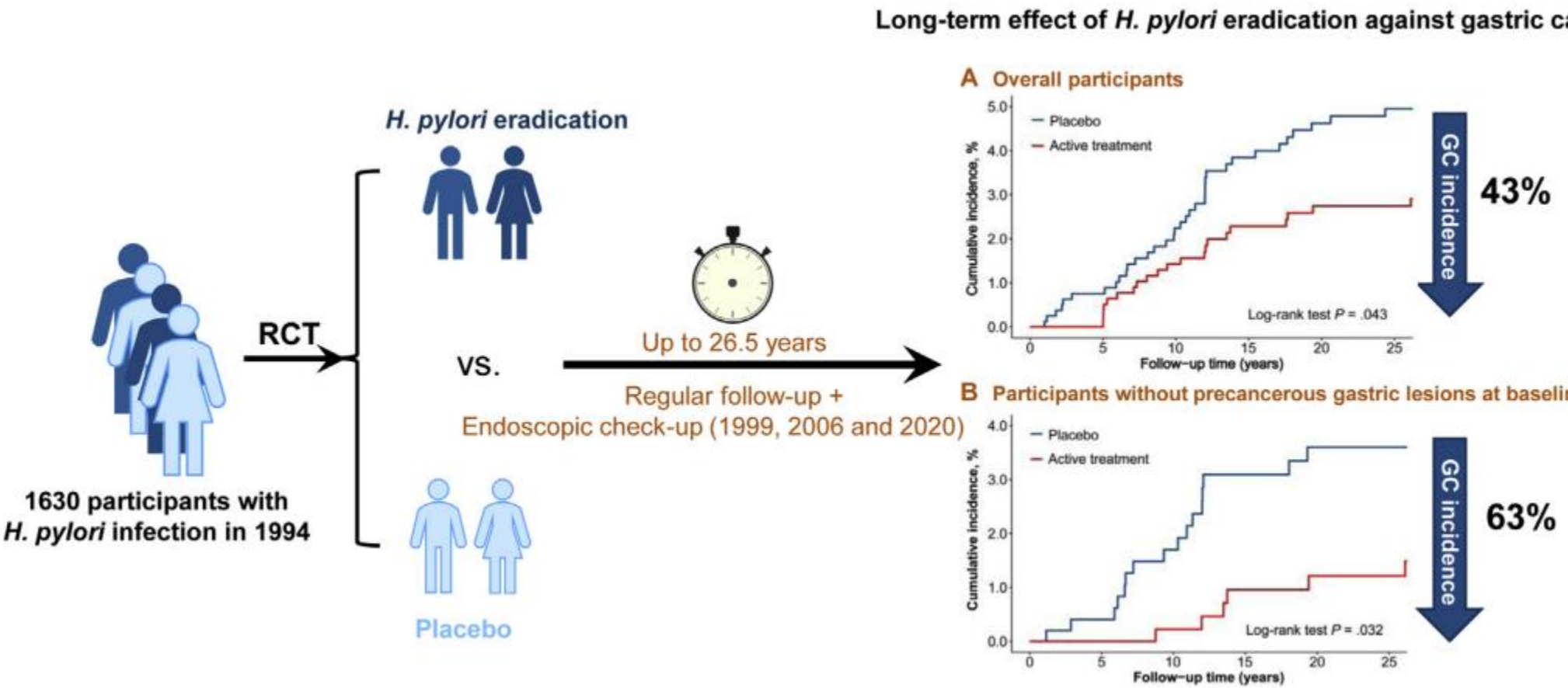
Eradication of H. pylori at a younger age is most cost-effective in gastric cancer prevention. There are additional benefits with the reduction of other H. pylori-related disease manifestations and complications that may increase during the prolonged course of disease (ie, dyspepsia and peptic ulcer disease). Furthermore curing the infection in young adults, especially in young females before their motherhood, can contribute to reducing the major risk of intra-familial H. pylori transmission to children. **It is never too late to eradicate H.pylori for the purpose of gastric cancer prevention and older age is not a limiting factor.**

Statement 11: Diagnostic tests used to screen *H. pylori* infection for the purpose of gastric cancer prevention should preferably be non-invasive.

Statement 12: If a serological method is used for *H. pylori* detection a further test (UBT, SAT) confirming current infection is required before initiating therapy

Effect of *Helicobacter pylori* Eradication on Gastric Cancer Prevention: Updated Report From a Randomized Controlled Trial With 26.5 Years of Follow-up

Lingjun Yan,[1,2,*] **Ying Chen**,[3,4,*] Fa Chen,[1,2] Tao Tao,[1,2] Zhijian Hu,[1,2] Junzhuo Wang,[1,2] Jianwang You,[4] Benjamin C. Y. Wong,[5] Jianshun Chen,[3,4] and Weimin Ye[1,2,6]



Gastroenterology 2022;163:154–162

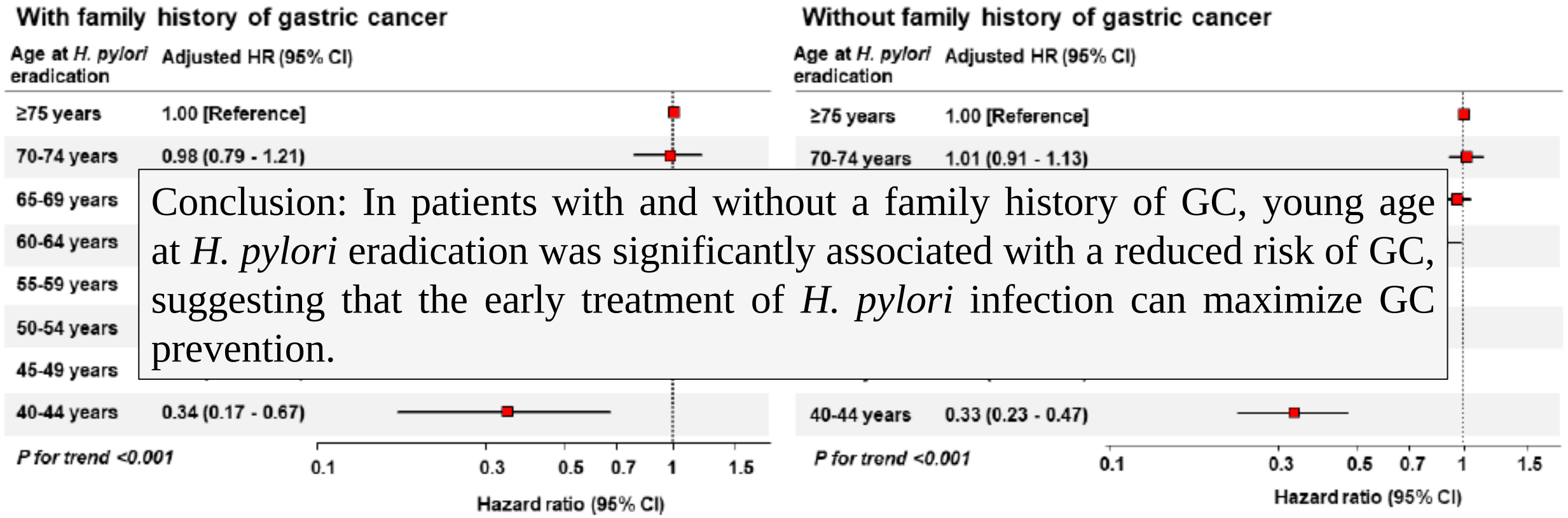
cancers

Association between Age at *Helicobacter pylori* Eradication and the Risk of Gastric Cancer Stratified by Family History of Gastric Cancer: A Nationwide Population-Based Study

by Yoon Suk Jung [1,†], Mai Thi Xuan Tran [2,†], Huiyeon Song [3], Boyoung Park [2,*] and Chang Mo Moon [4,5,*]

Cancers **2023**, *15*(5), 1604

Introduction: This study compares the risk of GC according to age at *H. pylori* eradication, stratified based on the presence of family history of GC using a population-based large cohort. Method: We analyzed individuals who underwent GC screening between 2013 and 2014 and received *H. pylori* eradication therapy before screening. Results: Among 1,888,815 *H. pylori*-treated patients, 2610/294,706 and 9332/1,594,109 patients with and without a family history of GC, respectively, developed GC. After adjusting for confounders, including age at screening, the adjusted hazard ratios (95% confidence intervals) for GC comparison, 70–74, 65–69, 60–64, 55–59, 50–54, 45–49, and <45 years with ≥75 years at *H. pylori* eradication were 0.98 (0.79–1.21), 0.88 (0.74–1.05), 0.76 (0.59–0.99), 0.62 (0.44–0.88), 0.57 (0.36–0.90), 0.38 (0.22–0.66), and 0.34 (0.17–0.67), respectively, among patients with a family history of GC ($p < 0.001$) and 1.01 (0.91–1.13), 0.95 (0.86–1.04), 0.86 (0.75–0.98), 0.67 (0.56–0.81), 0.56 (0.44–0.71), 0.51 (0.38–0.68), and 0.33 (0.23–0.47), respectively, among patients without a family history of GC ($p < 0.001$). Conclusion: In patients with and without a family history of GC, young age at *H. pylori* eradication was significantly associated with a reduced risk of GC, suggesting that the early treatment of *H. pylori* infection can maximize GC prevention.



Conclusion: In patients with and without a family history of GC, young age at *H. pylori* eradication was significantly associated with a reduced risk of GC, suggesting that the early treatment of *H. pylori* infection can maximize GC prevention.

Helicobacter pylori eradication therapy to prevent gastric cancer: systematic review and meta-analysis.

Results from 10 RCTs, seven recruited 8323 healthy individuals.

Our findings support screening for, and treatment of, H. pylori in both healthy individuals and patients with gastric neoplasia, as a means of reducing future incidence of gastric cancer.

Over 8 million disability-adjusted life-years (DALYS) would be gained globally if population screening and treatment for *H. pylori* were to be introduced.

Once H. pylori has been eradicated successfully it is unlikely to be acquired again, so unlike other cancer prevention programmes, it is likely that **screening would only need to occur once during an individual's life.**

Screening for and treatment of H. pylori is cost-effective in Western countries (where gastric cancer incidence is declining)?

There may be other benefits from eradicating H.pylori in these populations, such as a reduction in the prevalence of peptic ulcer disease or the incidence of dyspepsia

There could be approximately 0.5 million DALYs gained in relatively affluent populations, such as Western Europe.

Population screening and treatment may even be appropriate in some continents that are considered "low risk".

Gut 2020. 69 (12): 2113-2121.

Helicobacter pylori eradication therapy to prevent gastric cancer: systematic review and meta-analysis.

The vast majority of *H. pylori* infection is acquired in childhood (between the ages of 6 and 15) → **screening would be either in adolescence or young adulthood** → give the greatest chance of interrupting progression of the pre-cancerous cascade towards gastric cancer.

Concern : prescribing eradication therapy in younger people will promote antibiotic resistance or lead to substantial alterations of the microbiome; recent evidence suggests that **the gastric microbial dysbiosis seen with *H. pylori* infection is reversed by eradication, and there also appear to be beneficial effects on the intestinal microbiota.**

A *Helicobacter pylor*i screening and treatment program to eliminate gastric cancer among junior high school students in Saga Prefecture: a preliminary report

Japanese Society of Gastroenterology 2019

Methods A screening and treatment program to eradicate *H. pylori* from third-grade junior high students was started in Saga Prefecture in 2016,

In total, 501 students positive for *H. pylori* received eradication therapy (85.1% success) and adverse events occurred in 20 of these (4.0%). However, no serious complications occurred.

Conclusions The *H. pylori* screening and eradication project for school students in Saga Prefecture has started successfully and we have seen both a steady increase in the participation rate and a steady decrease in the infection rate, without major safety concerns.

Gut 2020. 69 (12): 2113-2121.

Diagnosis

Quality Standards in Endoscopy



It is suggested that the Inspection time during a diagnostic OGD should be recorded for surveillance procedures, such as Barrett's oesophagus and gastric atrophy/intestinal metaplasia surveillance.

Level of agreement: 90% Beg S, *et al. Gut* 2017;**66**:1886–1899.

Grade of evidence: weak

Strength of recommendation: weak

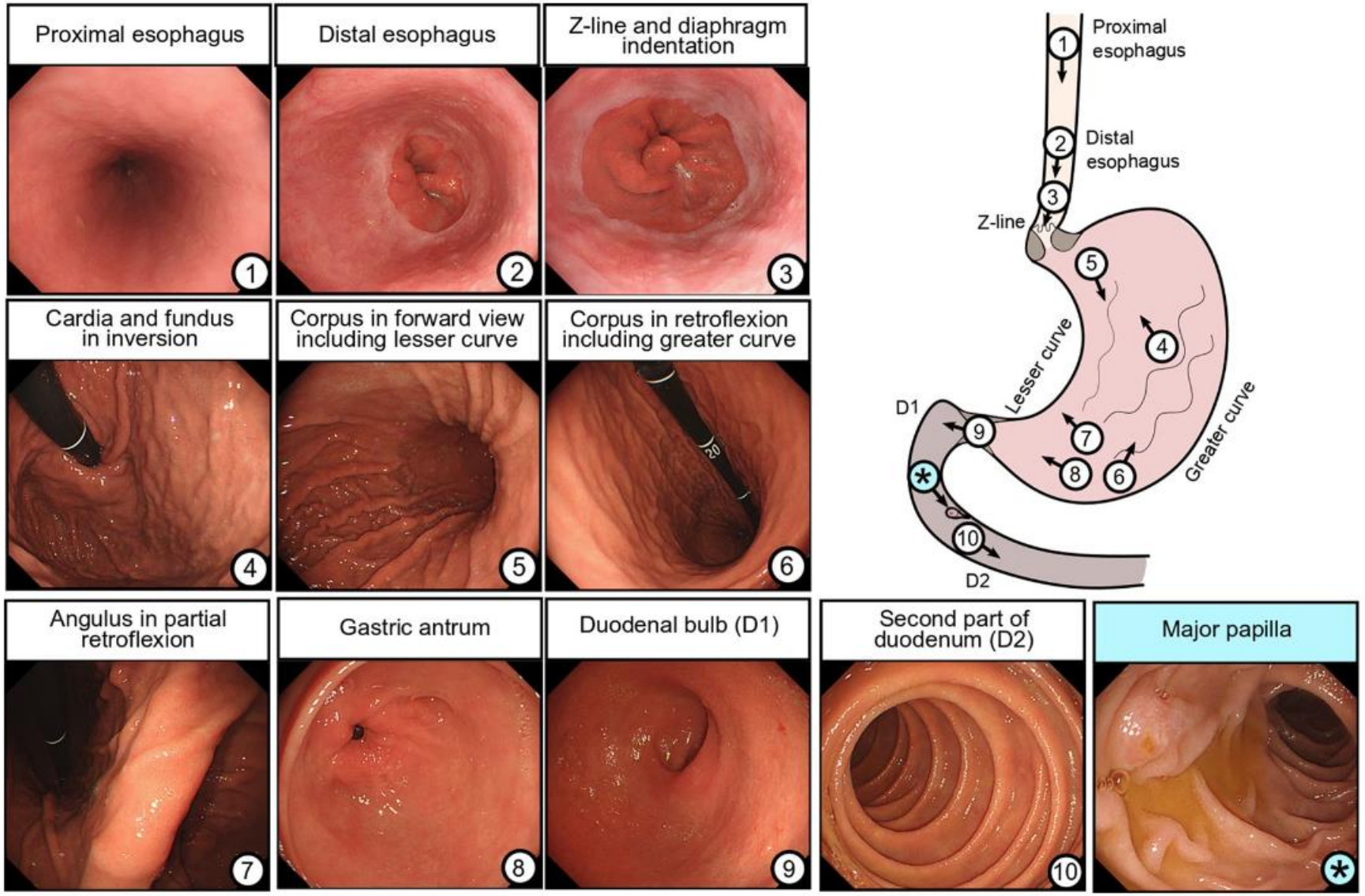
Despite the various tasks that require completion during an allocated endoscopy time slot, the time taken to perform the procedure itself should not be compromised. A high-quality examination, which includes mucosal cleansing and inspection, requires time. It is our opinion that a complete OGD begins after intubation of the upper oesophageal sphincter, then progresses to reach the distal duodenum before a careful withdrawal and inspection starts. The whole procedure should take on average 7 min. A single study has demonstrated that endoscopists taking on average of >7 min for an OGD had a threefold increase in the diagnosis of gastric cancer and dysplasia compared with those taking an average of <7 min to complete the procedure.[24] Given the heterogeneity of patients presenting for OGD it is recognised that procedure times will vary. In order to move towards an optimally timed examination, an endoscopist should first be aware of the time spent on the examination. It is therefore our recommendation that the total inspection time for high-risk and surveillance procedures such as Barrett's oesophagus or gastric atrophy surveillance is recorded and documented as part of the report.



A rounded cut-off time of 7 min was used to show that "slow" endoscopists (>7 min procedure time) were more likely to detect high-risk lesions (AG/GIM, dysplasia and cancers) and neoplasia (cancer or dysplasia) as compared with "fast" endoscopists [odds Ratios (OR) of 2.50; 95% confidence interval(CI), 1.52–4.12 and 3.42; 95%CI, 1.25–10.38, respectively].

Clin Gastroenterol Hepatol 2015

European requirements defined by ESGE, similarly to BSG, include a minimal number of 10 pictures for a normal endoscopic examination



Quality standards in upper gastrointestinal endoscopy: a position statement of the British Society of Gastroenterology (BSG) and Association of Upper Gastrointestinal Surgeons of Great Britain and Ireland (AUGIS)

Beg S, *et al*. *Gut* 2017;**66**:1886–1899.

UGI endoscopy should be performed with high-definition video endoscopy systems, with the ability to capture images and take biopsies.

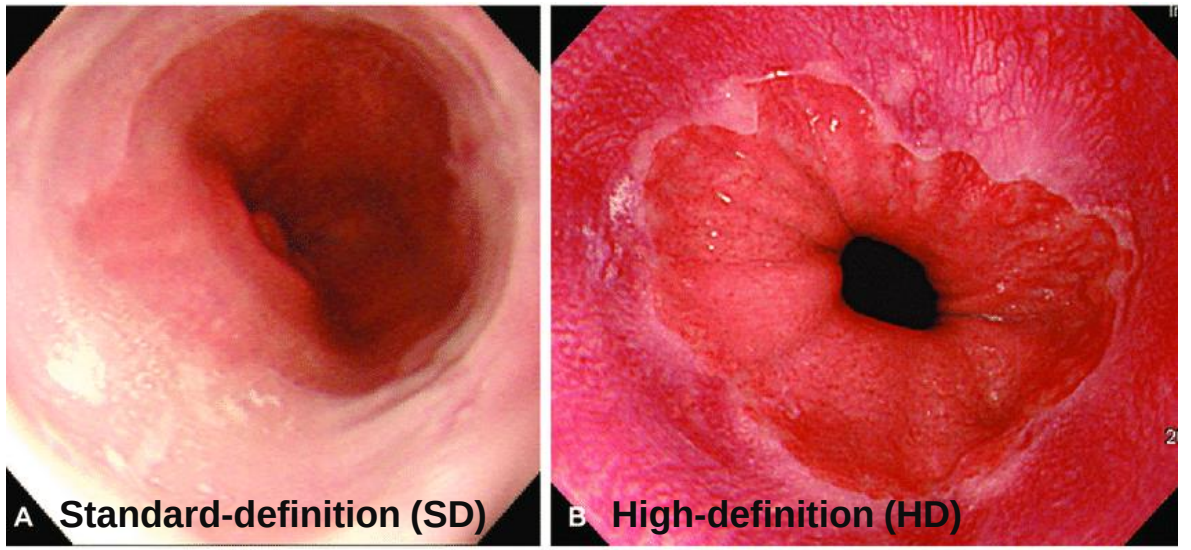
Level of agreement: 90%

Grade of evidence: weak

Strength of recommendation: strong

All diagnostic OGDs should be performed with equipment capable of achieving the intended purpose. As a minimum, endoscopes with the capacity to produce high-definition images should be used. Equipment for obtaining adequate mucosal views and acquisition of histological samples should be available

High-definition (HD) endoscopes **produce signal images with resolutions that range from 850,000 pixels to more than 1 million pixels.**



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Beg S, *et al*. *Gut* 2017;**66**:1886–1899.

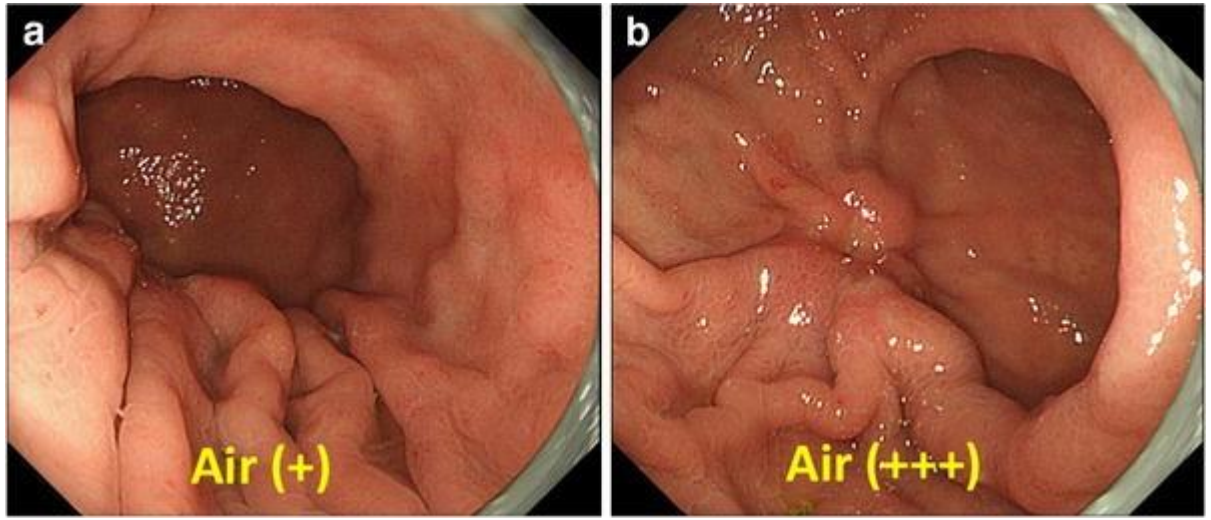
Adequate mucosal visualisation should be achieved by a combination of adequate air insufflation, aspiration and the use of mucosal cleansing techniques.

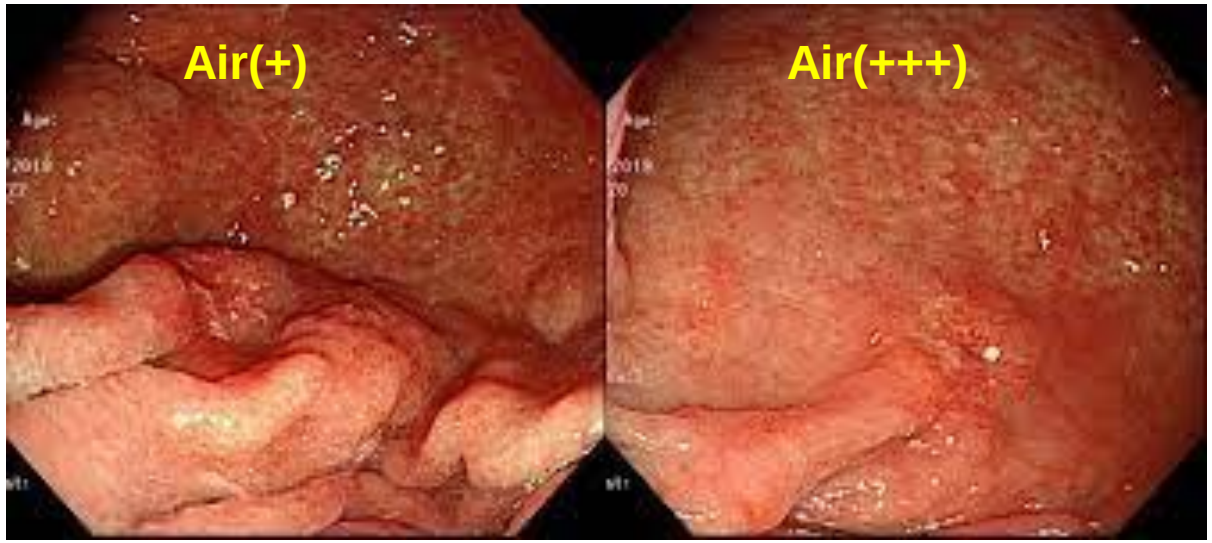
Level of agreement: 100%

Grade of evidence: moderate

Strength of recommendation: strong

Clear mucosal views can be attained by aspirating debris and washing the mucosal surface by flushing water through the accessory channel of the endoscope. Mucosal cleansing can be made more convenient with the use of a pump-controlled water jet, which allows for the simultaneous use of accessories through the working channel. The addition of mucolytic and defoaming agents such as simethicone, N-acetylcysteine or pronase enables the dispersion of bubbles and mucous. Premedication with a swallowed mucolytic has been shown to reduce the need for washing between procedures and consequently procedure time, as well as appearing to offer superior mucosal views.[50 52–59] The optimal timing for preprocedure consumption of these agents appears to be 10–30 min before and so could be incorporated into the admission process.[58]





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Beg S, *et al*. *Gut* 2017;**66**:1886–1899.



A malignant looking lesion should be photo-documented and a minimum of six biopsies taken.

Level of agreement: 100%

Grade of evidence: weak

Strength of recommendation: strong

A standardised approach to reporting malignant lesions enables the planning of potential endoscopic therapy and, where this is not possible, this may guide surgical or palliative measures. As a minimum, a report should describe the anatomical location, including the distance from a fixed landmark, (eg, from the incisors), number, size and morphology of any lesions as well as any abnormalities of the background mucosa.

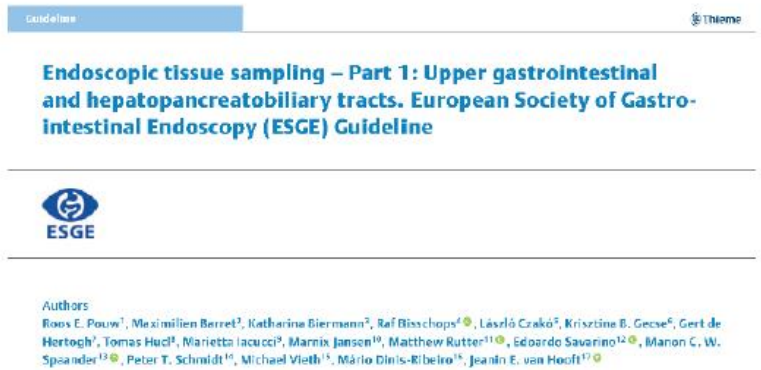
There is little evidence for the optimal number of biopsies required to ensure a diagnosis where malignancy is present.[186 187] Accepted convention is to obtain at least six representative biopsies of the lesion in question. This would appear to be an appropriate number given the biopsy protocols used for other pathologies of the gastrointestinal tract and in view of the importance of establishing a prompt diagnosis of malignancy without the need for repeated examinations. In addition to confirming a diagnosis, it may be necessary to obtain sufficient tissue to perform additional techniques, which may influence treatment options, such as HER2 testing.[188–190] Acquisition of fewer biopsies may need to be considered in individual patients—for example, those who are being anticoagulated, those with bleeding diathesis, or on the basis of lesion characteristics.

DIAGNOSIS/STAGING

Characterization of superficial lesions to define the best management approach

Recommendations

- Diagnosis should be made from multiple (5-8) endoscopic biopsies to guarantee an adequate representation of the tumour [IV, B].
- The histological diagnosis should be reported according to WHO criteria [V, B].
- HER2 expression by IHC and/or amplification by *in situ* hybridisation [I, A; ESCAT score: I-A], PD-L1 by IHC according to CPS [I, A] and MSI-H/dMMR [II, A; ESCAT score: I-B] are validated predictive biomarkers for drug therapy.


Guideline

Thieme

Endoscopic tissue sampling – Part 1: Upper gastrointestinal and hepatopancreatobiliary tracts. European Society of Gastrointestinal Endoscopy (ESGE) Guideline

ESGE

Authors

Roos E. Pouw[1], Maximilien Barret[2], Katharina Biermann[3], Raf Bisschops[4], László Czakó[5], Krisztina B. Gecse[6], Gert de Hertogh[7], Tomas Hucl[8], Marietta Iacucci[9], Marnix Jansen[10], Matthew Rutter[11], Edoardo Savarino[12], Manon C. W. Spaander[13], Peter T. Schmidt[14], Michael Vieth[15], Mário Dinis-Ribeiro[16], Jeanin E. van Hooft[17]

At least six biopsies in cases of suspected advanced cancer
Only one to two targeted biopsies for lesions that are potentially amenable to endoscopic resection
For suspected linitis plastica, at least 10 bite-on-bite biopsies, targeting mucosal abnormalities

DETECTION

High-quality endoscopy to determine presence of lesions and pre-malignant stomach

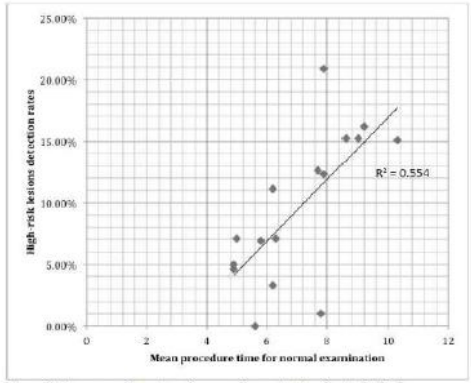
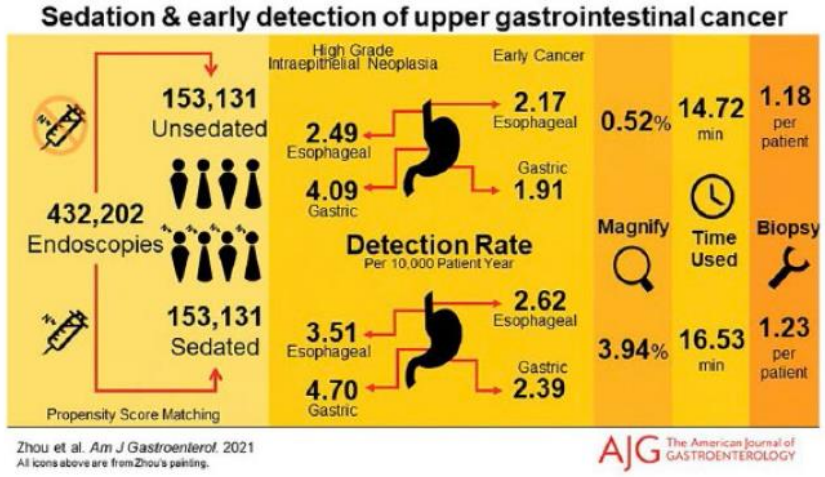


Figure 2: Mean procedure time for normal examinations by individual endoscopists against detection rates of high risk gastric lesions

The et al. CGH 2014

Influence of Sedation on the Detection Rate of Early Cancer and Precancerous Lesions During Diagnostic Upper Gastrointestinal Endoscopies: A Multicenter Retrospective Study

Jiawei Zhou, MD[1,2,3], Zhen Li, MD[1,2,3], Rui Ji, MD[1], Peizhu Wang, MS[1,2,3], Aijun Zhang, BS[4], Kangkang Wu, MS[4], Chengxia Liu, PhD[5], Qiong Niu, BS[5], Yanliu Chu, MD[6], Xiufeng Su, MD[6], Xiuli Zuo, MD[1,2,3] and Yanqing Li, MD[1,2,3]



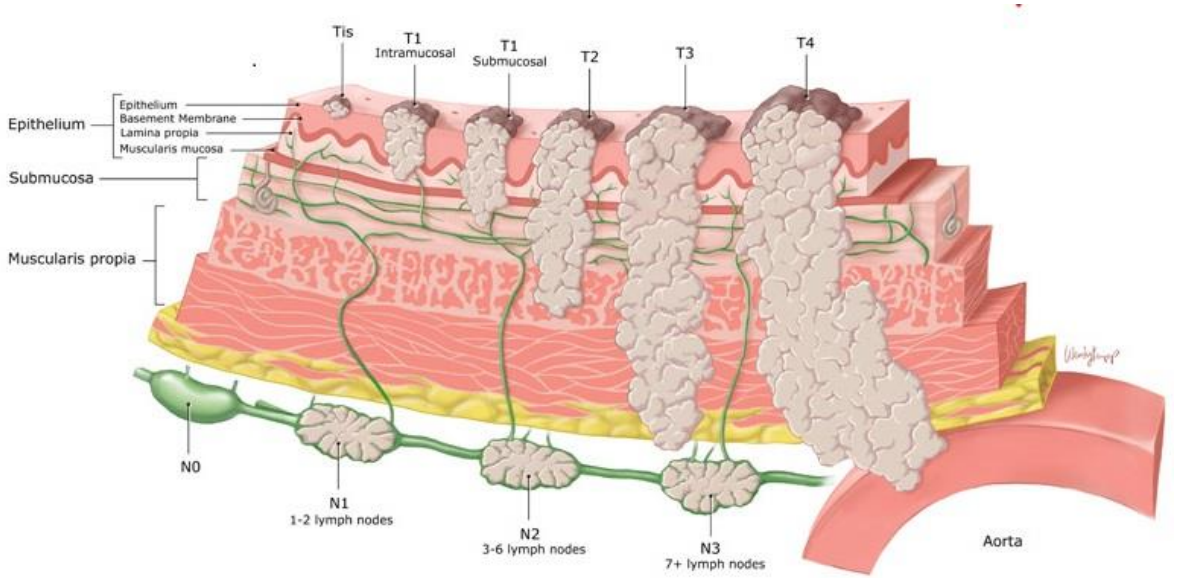
More gastric HGIN and EC were detected at gastric body in the sedation group (*P* = 0.001).
Sedation may improve the endoscopic detection rate of EC and HGIN in the UGI tract probably through enhancing the use of accessary endoscopic techniques, prolonging observation time, and taking more biopsies in different locations.

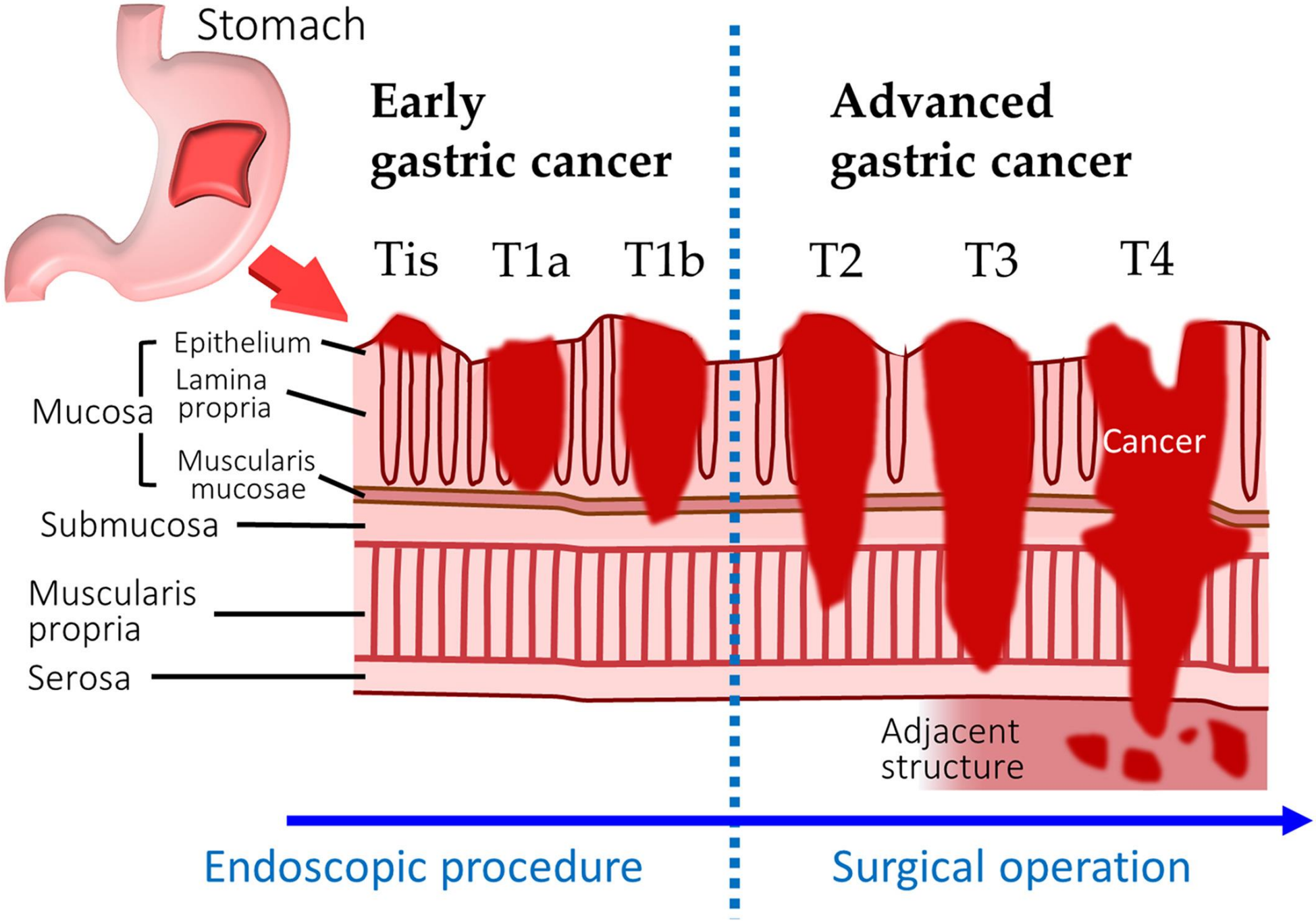
- **Staging of GC**



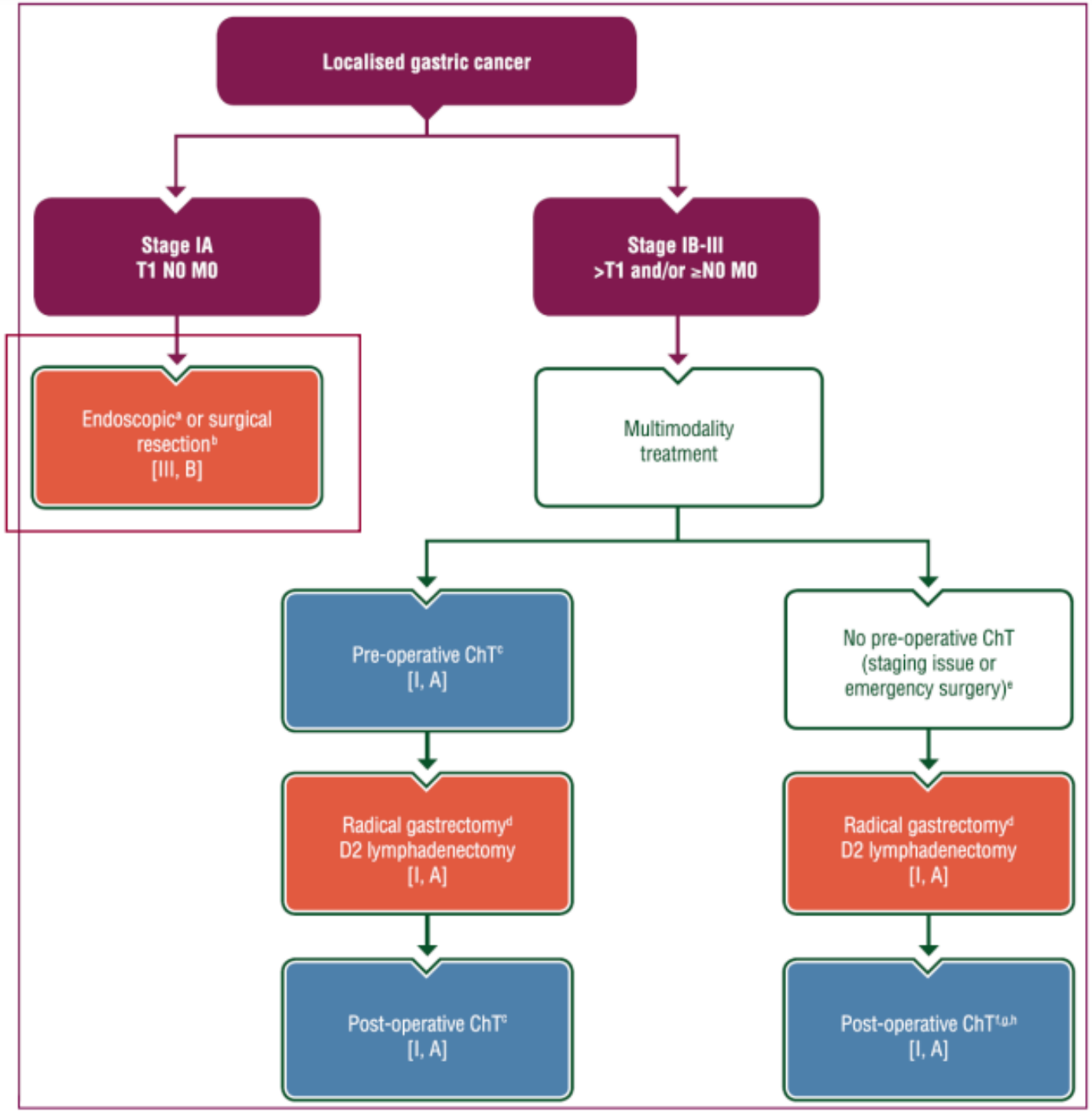
TNM staging for gastric cancer

	Primary tumor (T)
TX	primary tumor cannot be assessed
T0	no evidence of primary tumor
Tis	carcinoma in situ: intraepithelial tumor without invasion of the lamina propria
T1	tumor invades the lamina propria, the muscularis mucosa, or the submucosa
T1a	tumor invades the lamina propria or muscularis mucosa
T1b	tumor invades the submucosa
T2	tumor invades the muscularis propria layer
T3	tumor invades the subserosa layer without invasion of the serosa and adjacent structures
T4	tumor penetrates the serosa (visceral peritoneum) or adjacent structures
T4a	tumor penetrates the serosa (visceral peritoneum)
T4b	tumor invades adjacent structures
	Regional lymph nodes (N)
NX	regional lymph node(s) cannot be assessed
N0	no regional lymph node metastasis
N1	metastasis in 1 to 2 regional lymph nodes
N2	metastasis in 3 to 6 regional lymph nodes
N3	metastasis in more than 7 regional lymph nodes
N3a	metastasis in 7 to 15 regional lymph nodes
N3b	pmetastasis in more than 16 regional lymph nodes
	Distant metastasis (M)
M0	no distant metastasis
M1	distant metastasis




Stomach
Early gastric cancer
Advanced gastric cancer
Tis
T1a
T1b
T2
T3
T4
Epithelium
Lamina propria
Mucosa
Muscularis mucosae
Submucosa
Muscularis propria
Serosa
Cancer
Adjacent structure
Endoscopic procedure
Surgical operation

MANAGEMENT



2nd standard option

Postop Chemoradiation is no longer recommended after D2 surgery

Ann Oncol 2022

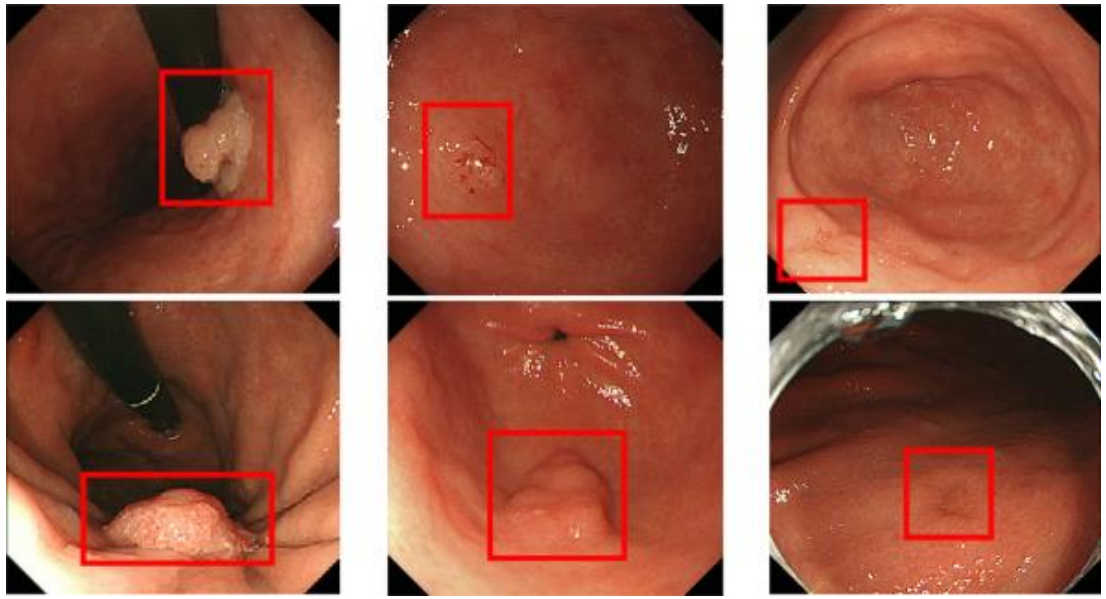
Endoscopy in early stage GC



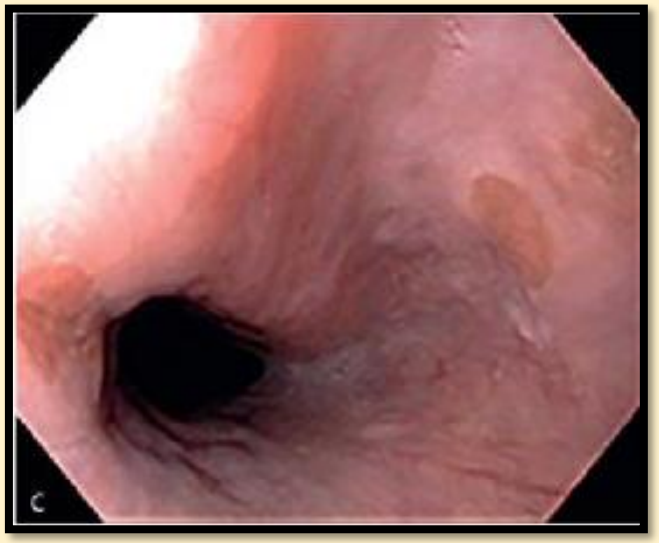
I. White Light Imaging (WLI)
II. Chromoendoscopy (CE)
III. Narrow Band Imaging (NBI)
IV. Magnified Narrow Band Imaging (MNBI)
V. Endocytoscopy
VI. AI-supported endoscopy

Early Gastric Cancer (EGC)

Superficial or early gastric cancer (EGC) is defined as invasive gastric cancer that invades no more deeply than the submucosa, irrespective of lymph node metastasis.



White Light Endoscopy (WLI)

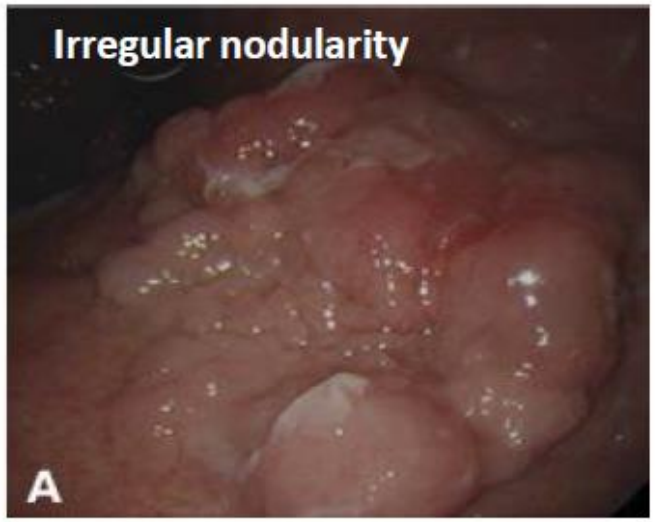


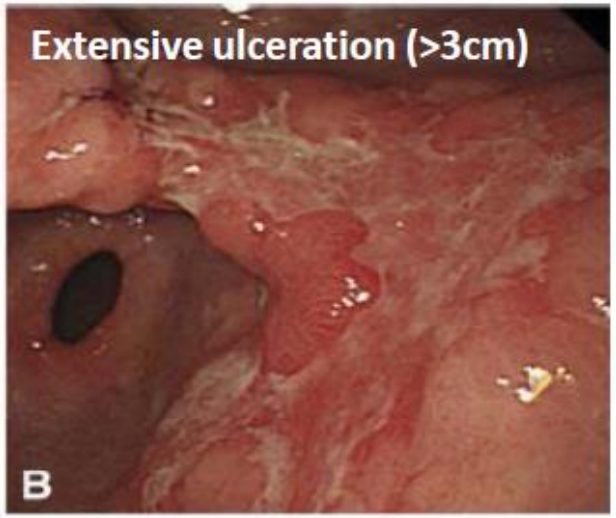
Use of all colors of the visible spectrum, is the standard method for all indications of upper endoscopy.

The most common indications for endoscopy

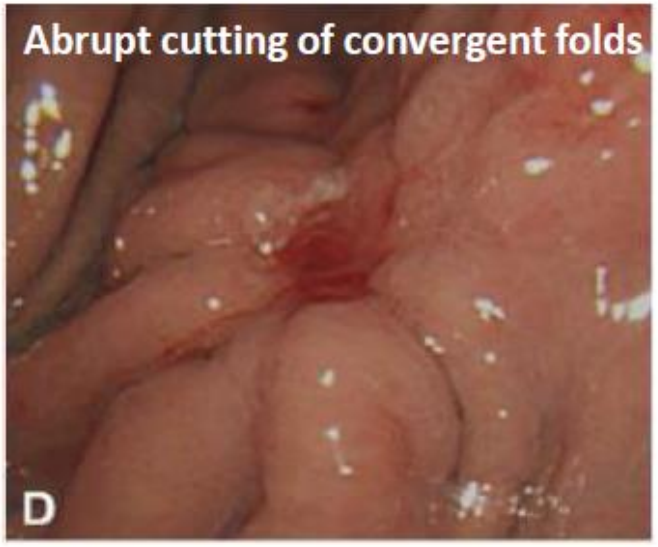
It is limited by the endoscope’s resolution as well as its weak ability to produce contrast between normal and abnormal tissues.

Endoscopic features of EGC

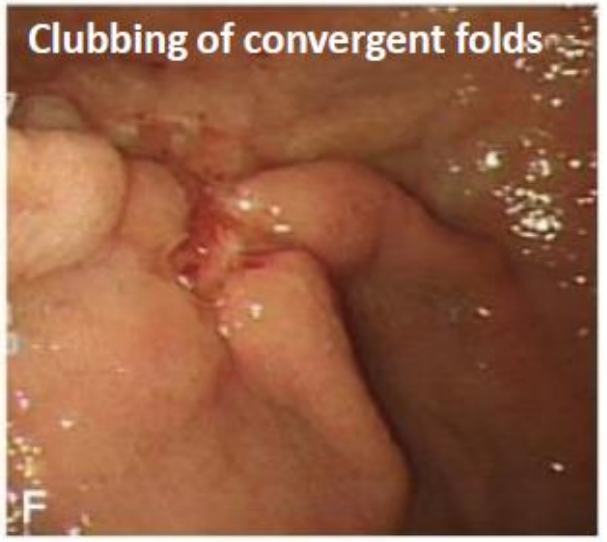










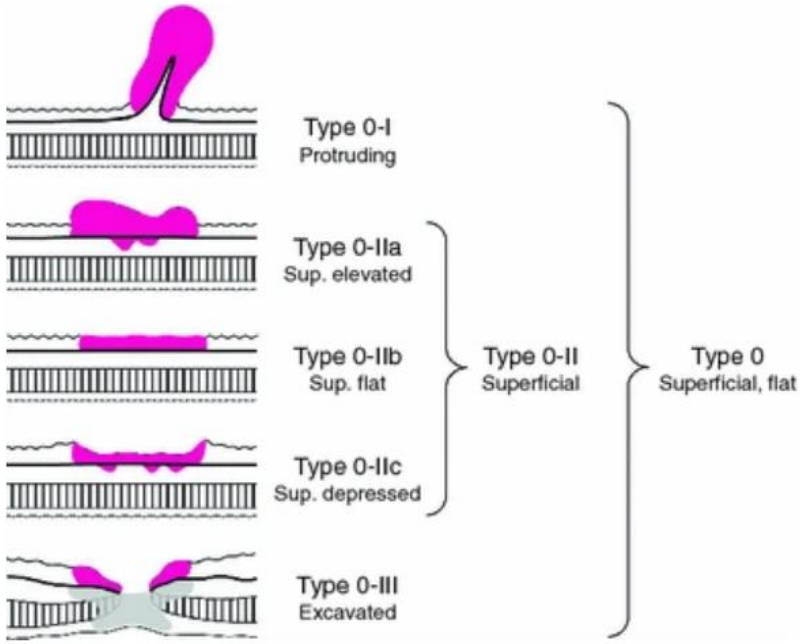


Gastrointest Endosc, 2011

White Light Endoscopy and Macroscopic Assessment

Japanese classification of gastric carcinoma

Type 0 (superficial)	Typical of T1 tumors.
Type 1 (mass)	Polypoid tumors, sharply demarcated from the surrounding mucosa.
Type 2 (ulcerative)	Ulcerated tumors with raised margins surrounded by a thickened gastric wall with clear margins.
Type 3 (infiltrative ulcerative)	Ulcerated tumors with raised margins, surrounded by a thickened gastric wall without clear margins.
Type 4 (diffuse infiltrative)	Tumors without marked ulceration or raised margins, the gastric wall is thickened and indurated and the margin is unclear.
Type 5 (unclassifiable)	Tumors that cannot be classified into any of the above types.



Subclassification of Type 0

Type 0–I (protruding)[a]	Polypoid tumors.
Type 0–II (superficial)	Tumors with or without minimal elevation or depression relative to the surrounding mucosa.
Type 0–IIa (superficial elevated)[a]	Slightly elevated tumors.
Type 0–IIb (superficial flat)	Tumors without elevation or depression.
Type 0–IIc (superficial depressed)	Slightly depressed tumors.
Type 0–III (excavated)	Tumors with deep depression.

White Long Endoscopy and Macroscopic Assessment

Where a lesion is identified, this should be described using the Paris classification.

0-I EGC are not very common since polypoid lesions have the lowest risk of progressing into carcinoma; however, 0-I EGCs are difficult to distinguish from hyperplastic polyps. Among these, 0-IIb lesions are the most challenging to detect and may be mistaken as atrophic gastritis.



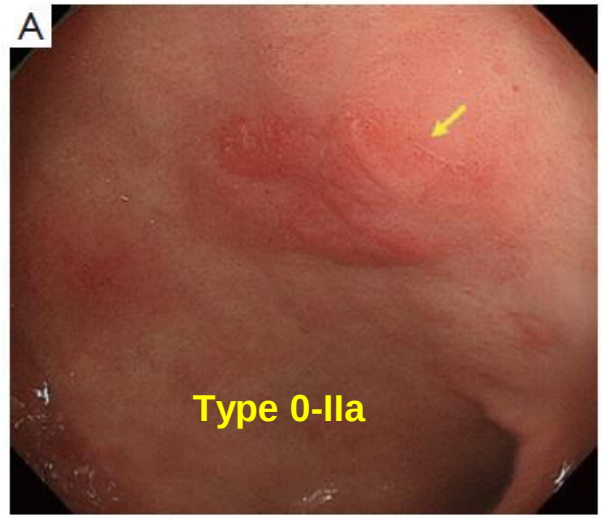
White Long Endoscopy and Macroscopic Assessment

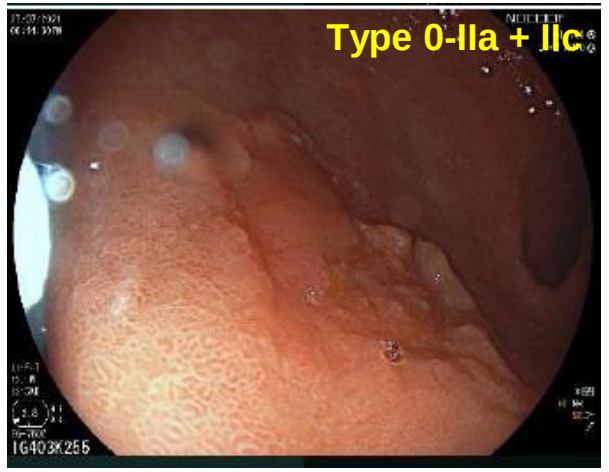
Paris classification

Most of of EGCs are 0-IIc lesions. The Paris classification is useful in screening neoplastic from non-neoplastic lesions, with **Type 0-IIc being a more specific indication for endoscopic resection, whereas for majority of Type 0-III lesions, surgical resection may be necessary.**

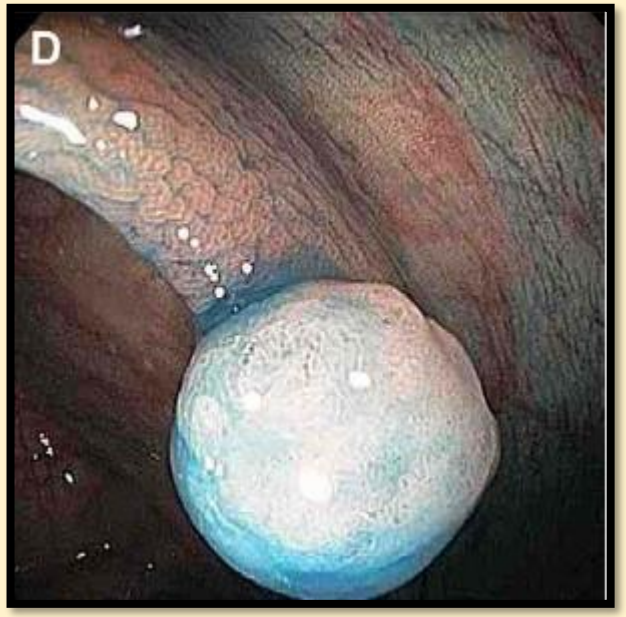
Another advantage of this classification is that it allows classification of lesions with mixed findings, such a elevated lesion with a central depression (0-IIa + IIc).

These mixed type lesions, especially 0-IIa + IIc, generally have a poorer prognosis and a higher risk of a large invasion into the submucosal layer.





Chromoendoscopy (CE)

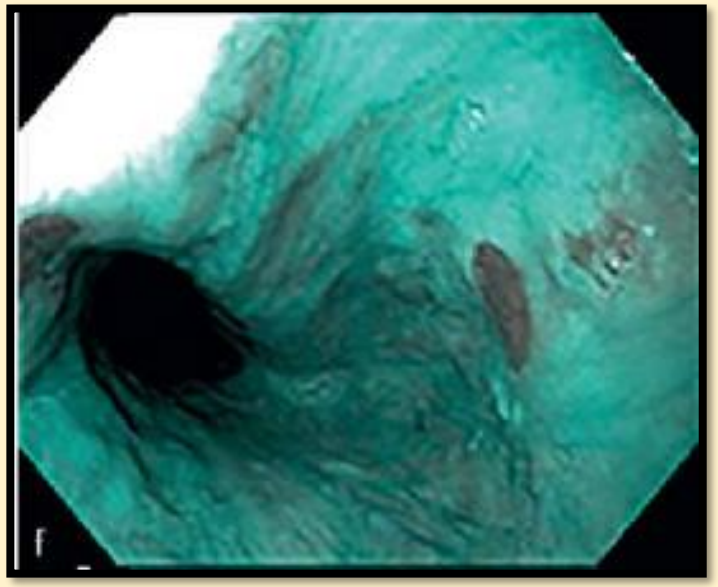


Uses stains, pigments or dyes to locate cancerous spots in the lining (mucosa) of digestive tract.

Cancer cells react differently to these dyes than normal cells

Some limitations are: lack of standardized classification systems for chromoendoscopic findings, poor reproducibility

Narrow Band Imaging (NBI)

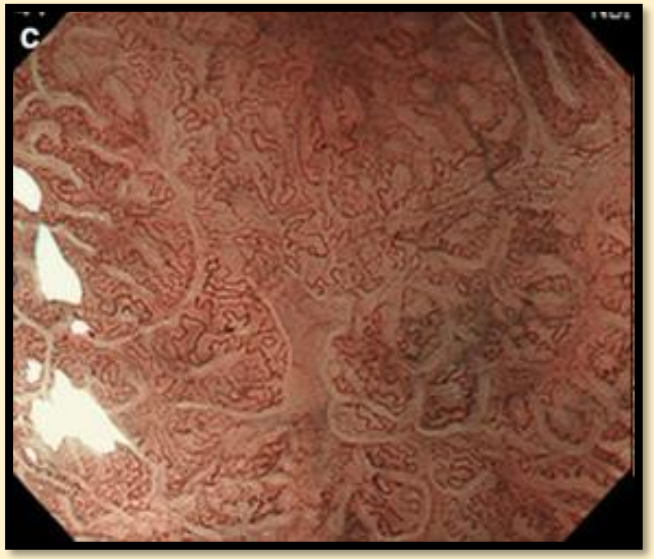


Light of specific blue (415 nm) and green (540 nm) wavelengths is used to enhance the detail of certain aspects of the surface of the mucosa.

Indication for Barrett's esophagus, colorectal polyps and tumors.

The current limitation of NBI is the high frequency of false positives and subsequent negative biopsies.

Magnified Narrow Band Imaging (MNBI)



Conventional white-light endoscopy for the diagnosis of EGCs has its limitations. There have been difficulties in diagnosing minute (≤5 mm) and superficial flat (0-IIb) types of EGCs using conventional endoscopy alone.

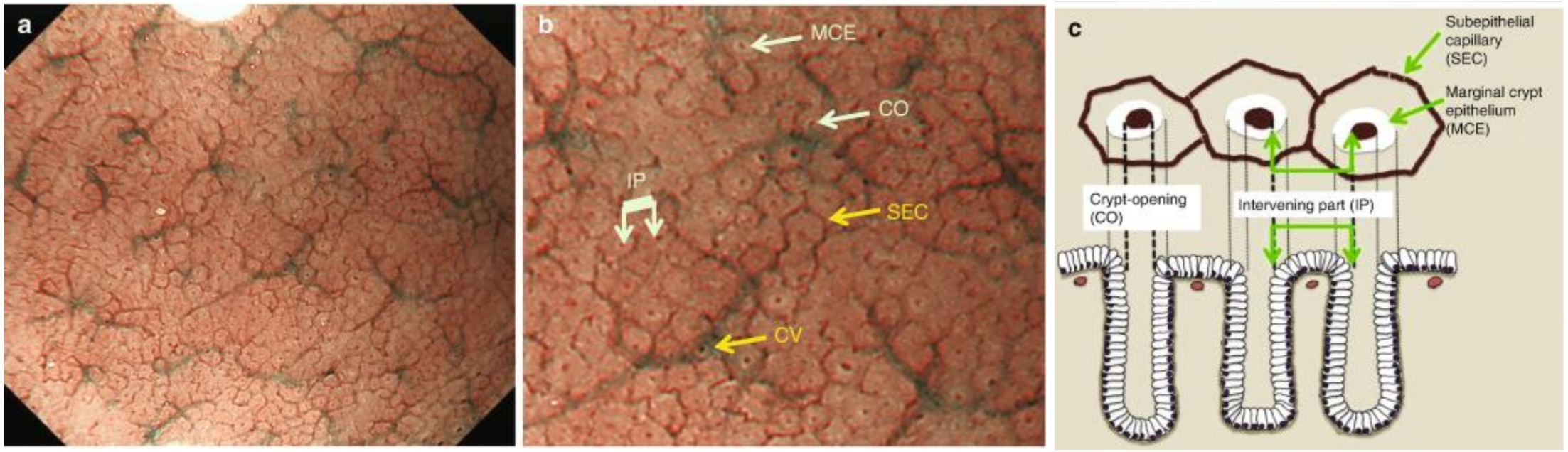
Magnifying endoscopy used widely in Early Gastric Cancer Detection.

M-NBI in conjunction with conventional endoscopy with white light imaging identified small depressed gastric mucosal cancers with 96.6% accuracy, 95.0% sensitivity, and 96.8% specificity.

Magnified Narrow Band Imaging (MNBI)

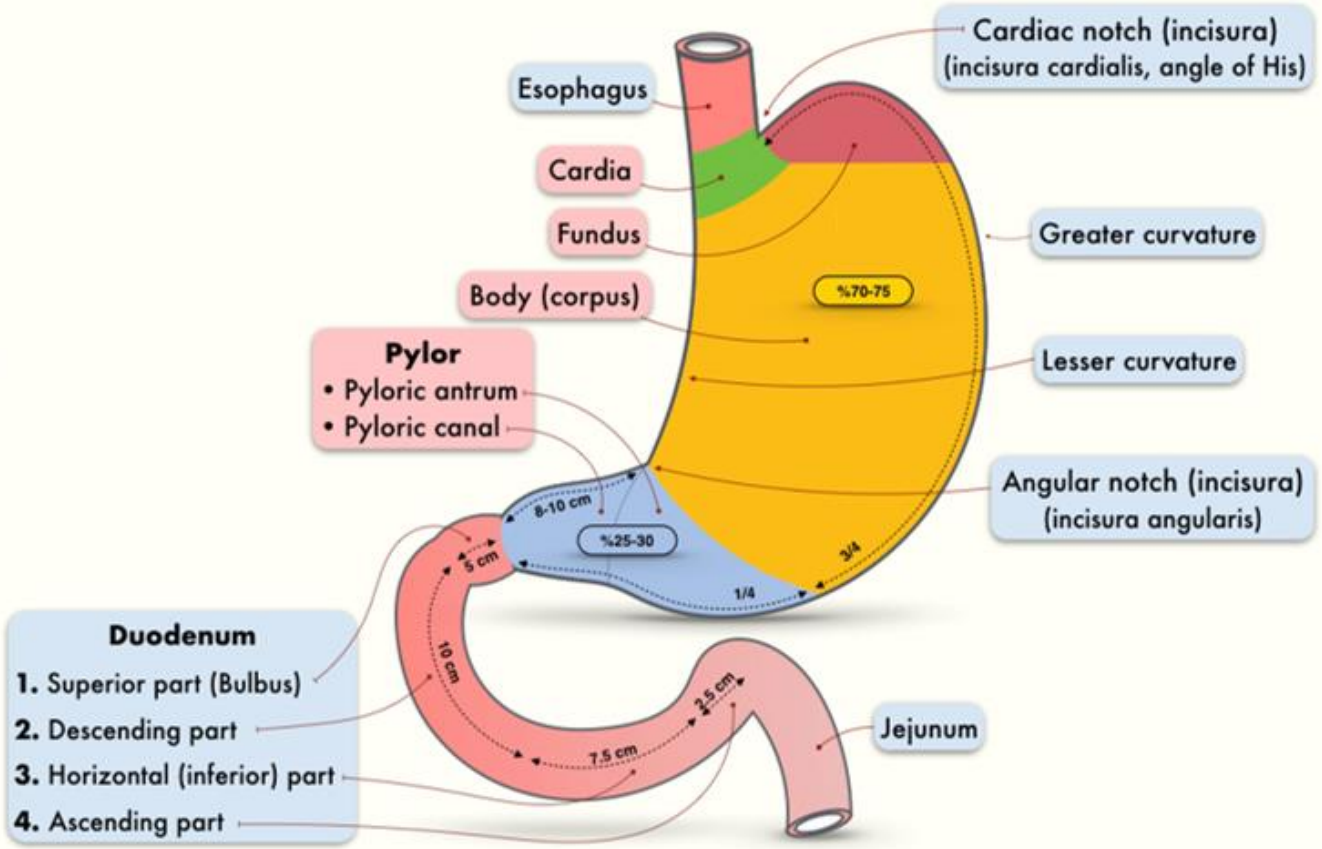
VS classification system

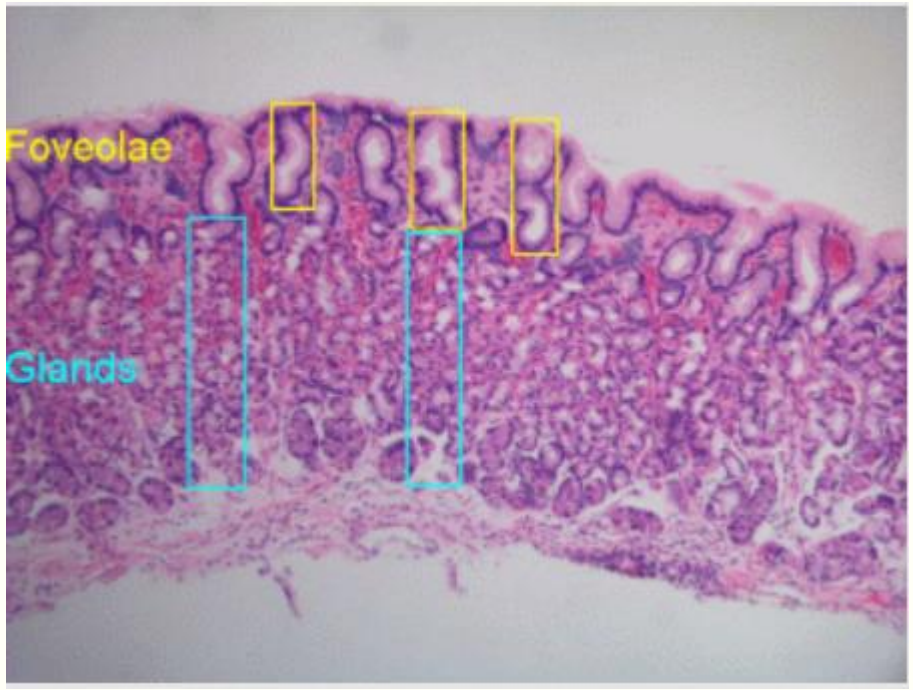
vessel plus surface (VS) classification system



The stomach is composed of several anatomic zones. Moving proximal to distal, you pass:
1) the gastroesophageal junction, 2) the cardia, 3) the fundus and body, 4) the antrum and 5) the pylorus.

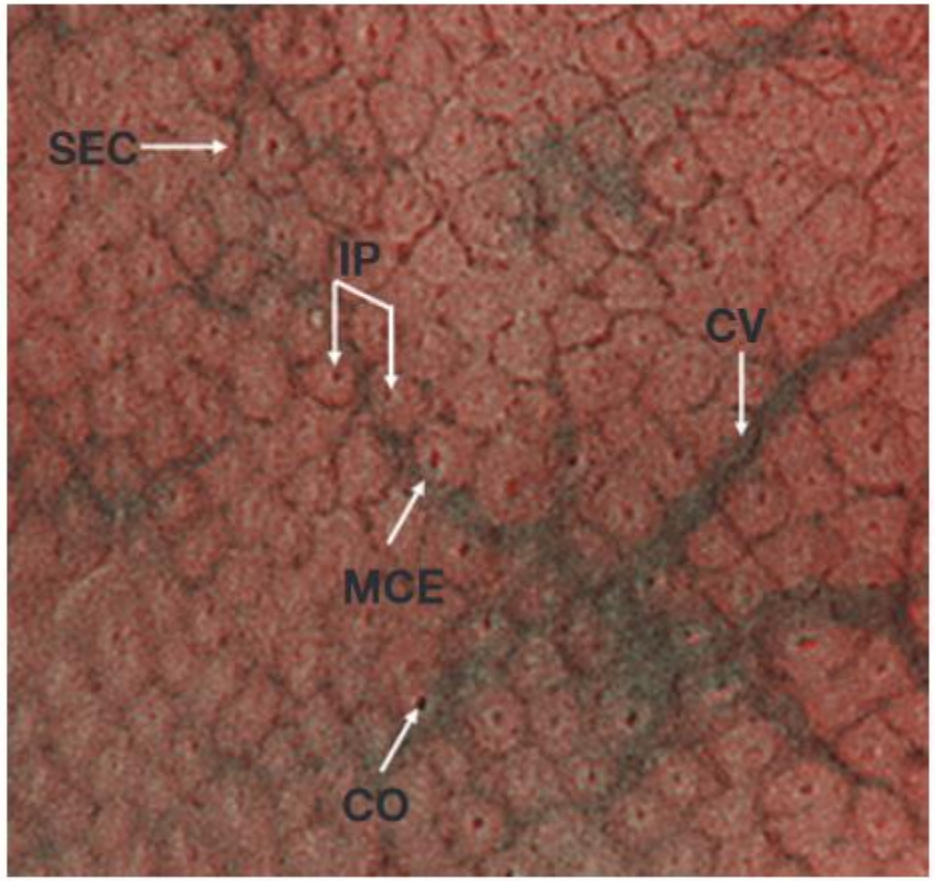
Histologically, the entire stomach is made up of simple tubular glands and foveolae (gastric pits) and there are essentially only 2 types of mucosa:
•**Antral** (cardia, antrum and pylorus)
•**Oxyntic** (fundus and body).

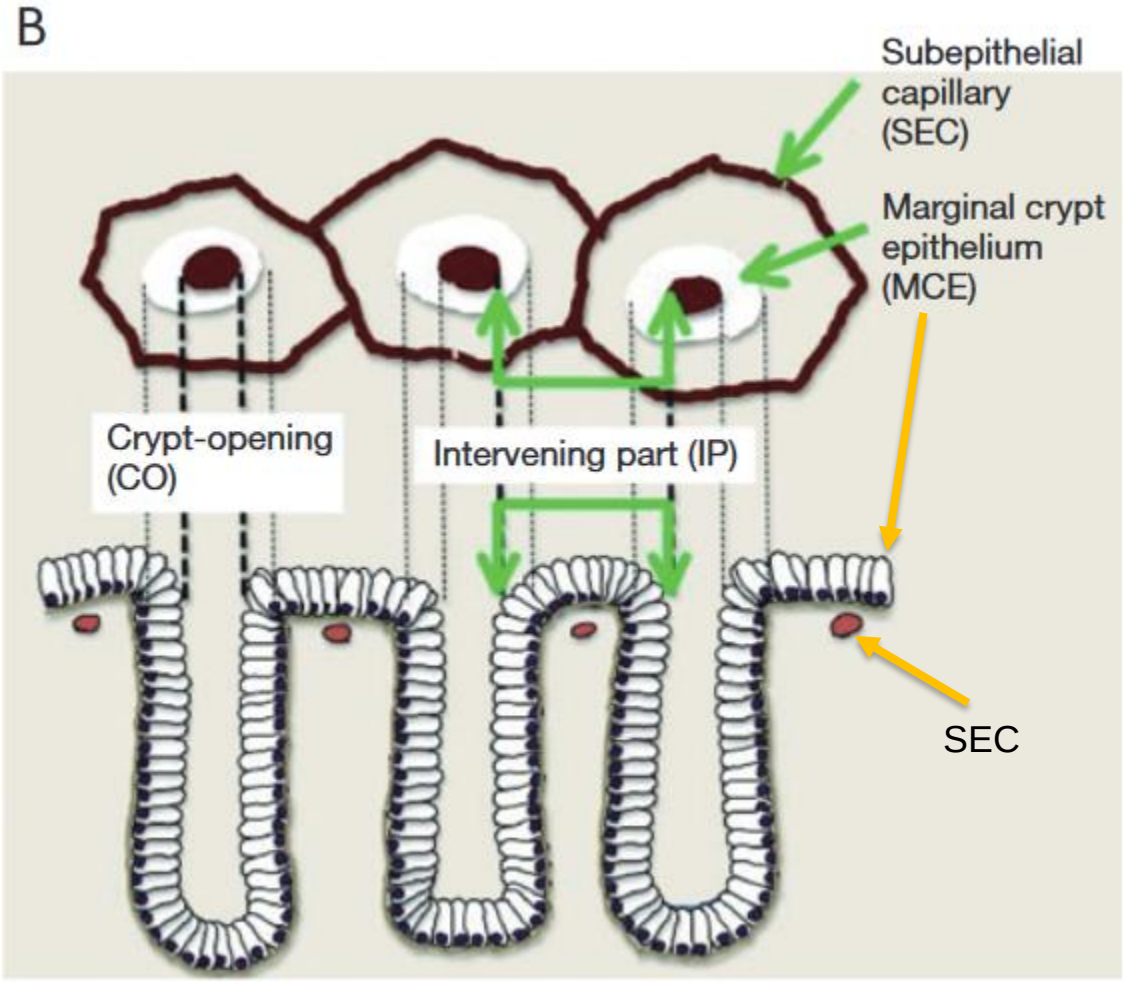




Magnified Narrow Band Imaging (MNBI)

Fundus and body

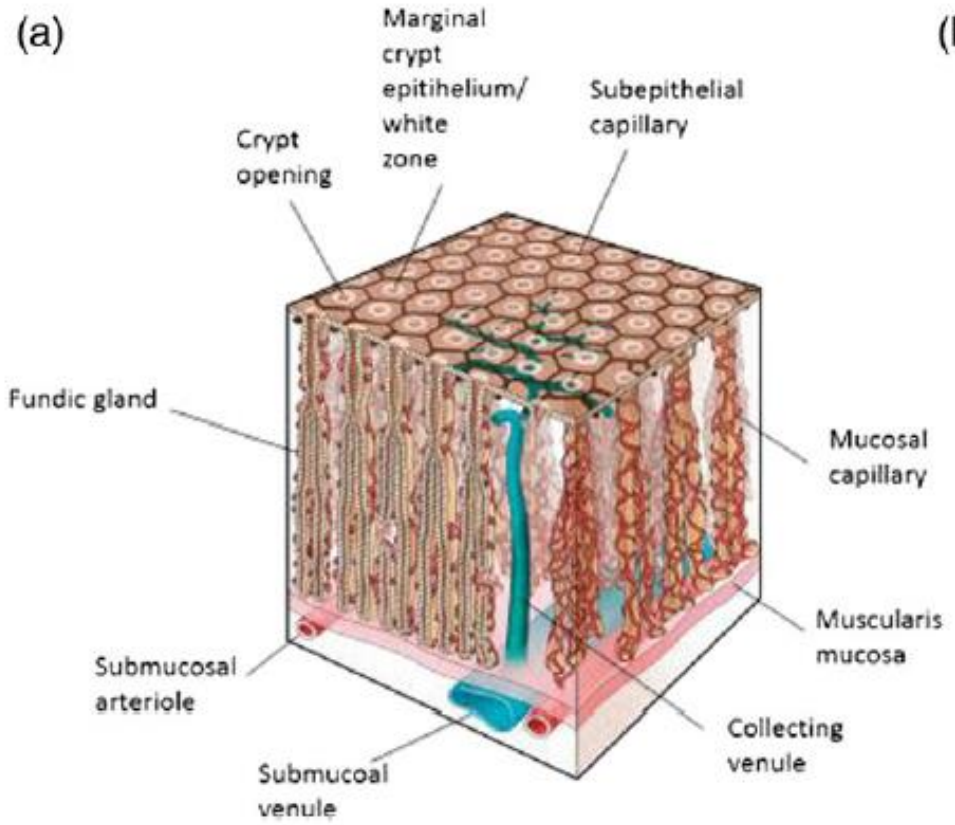




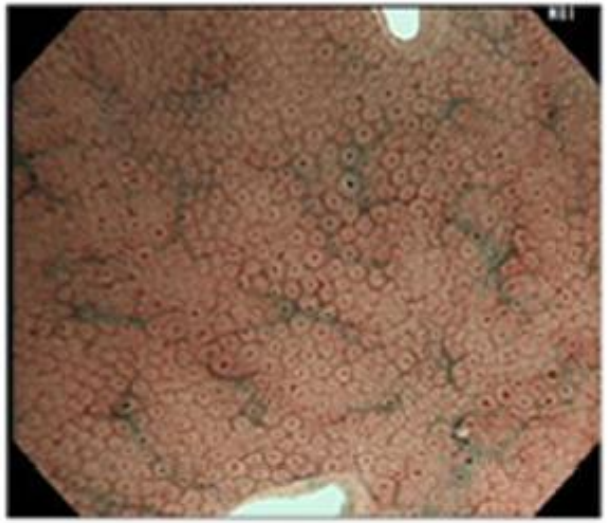
(A) Magnifying endoscopic image with NBI of **normal gastric fundic gland mucosa.** (B) Correspondence between the magnifying endoscopic image with NBI and histological findings of normal gastric fundic gland mucosa. CV, collecting venule

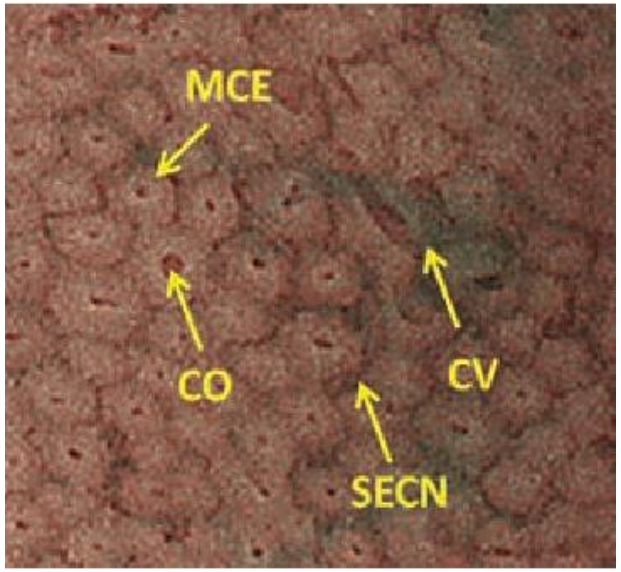
Magnified Narrow Band Imaging (MNBI)





(b)



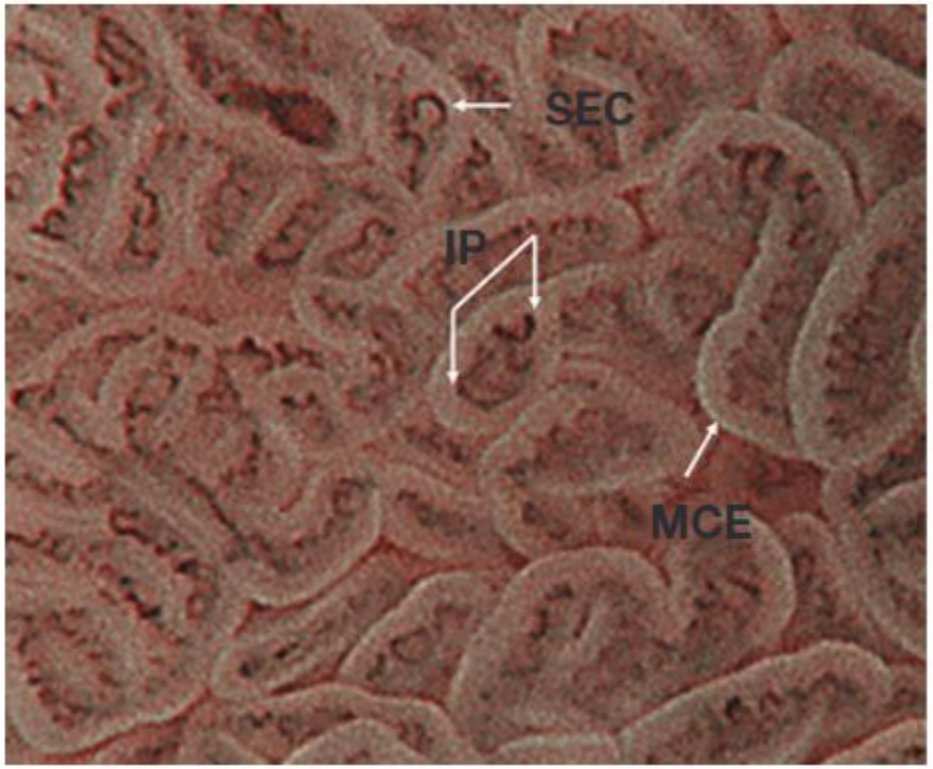


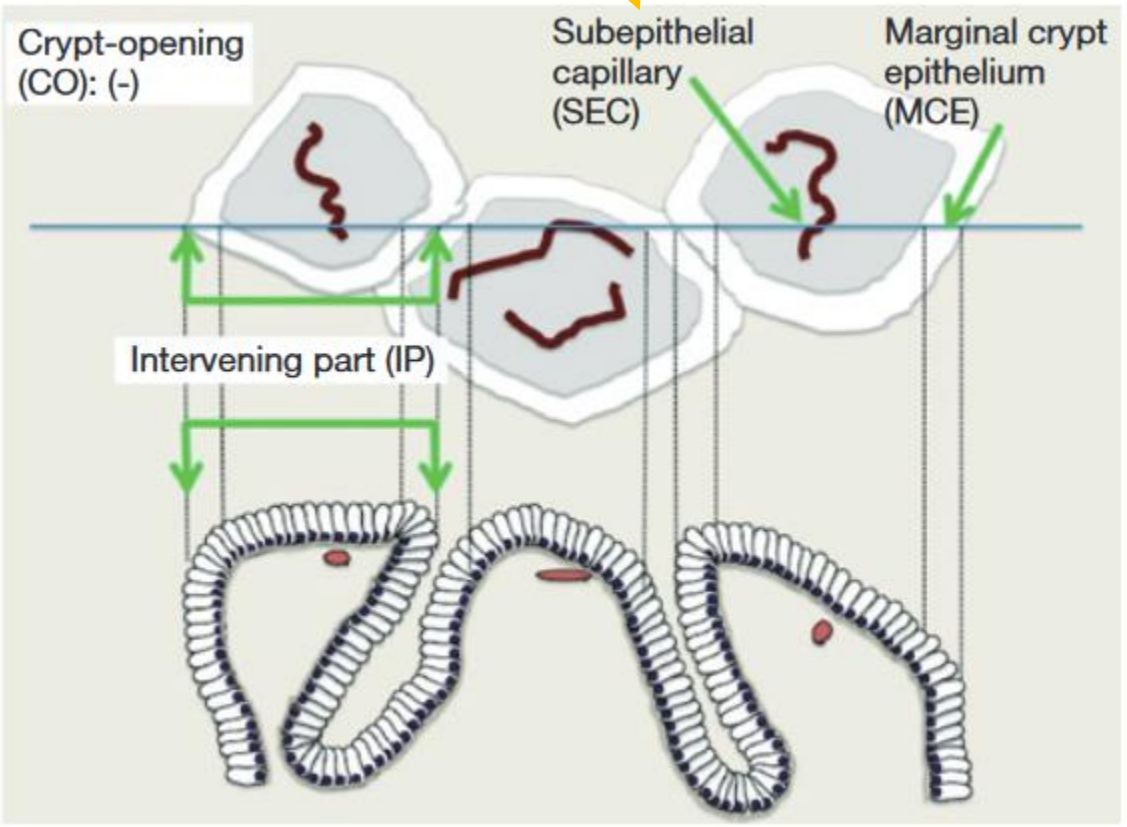
Normal gastric fundic gland mucosa. The morphology of each capillary is that of a polygonal closed loop. These loops anastomose repeatedly with each other, forming **a regular honeycomb-like subepithelial capillary network pattern.** The microsurface structure is made up of the marginal crypt epithelium/white zone (MCE/WZ), and the intervening part in between.

Magnified Narrow Band Imaging (MNBI)

Antrum

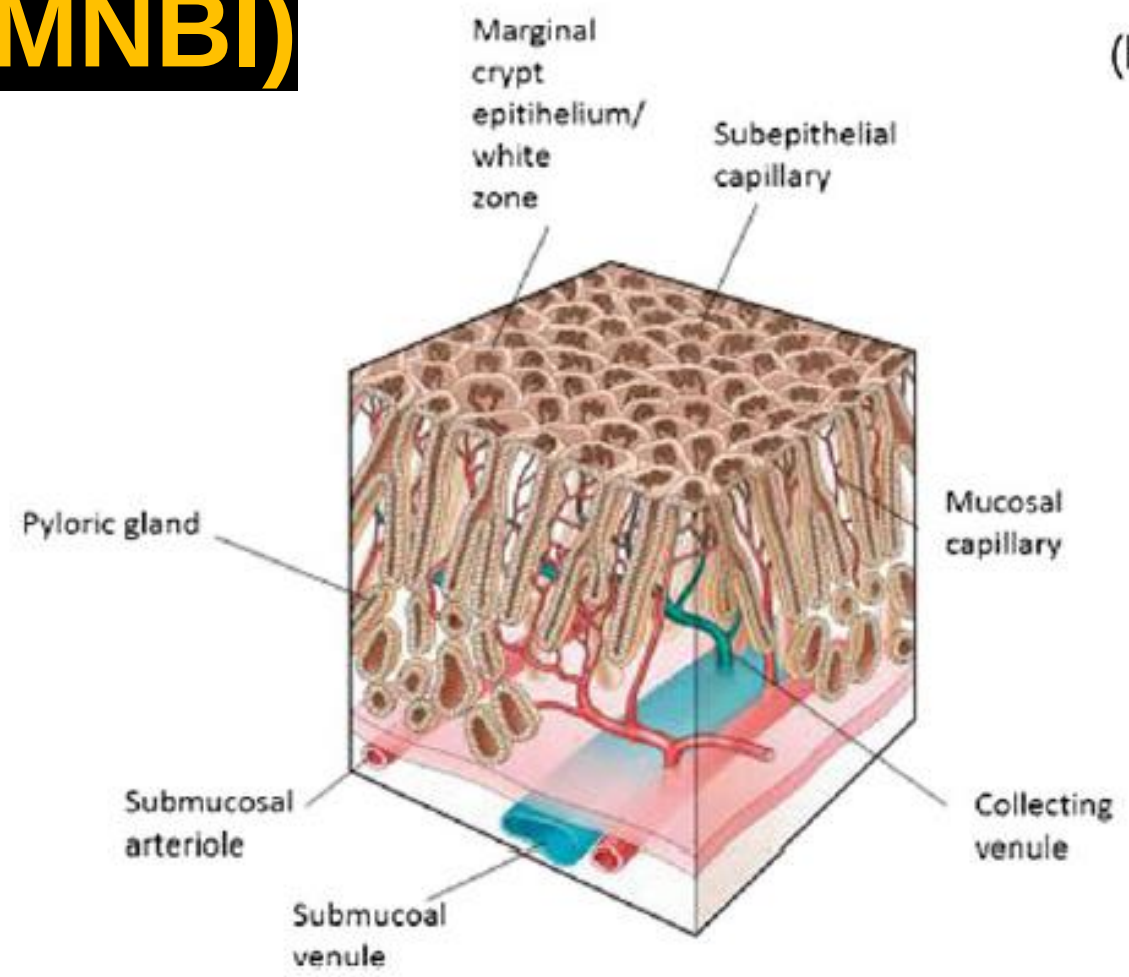
Coil-shaped





(C) Magnifying endoscopic image with NBI of **normal gastric pyloric gland mucosa.** (D) Correspondence between the NBI-combined magnifying endoscopic image and histological findings of normal gastric pyloric gland mucosa.

Magnified Narrow Band Imaging (MNBI)



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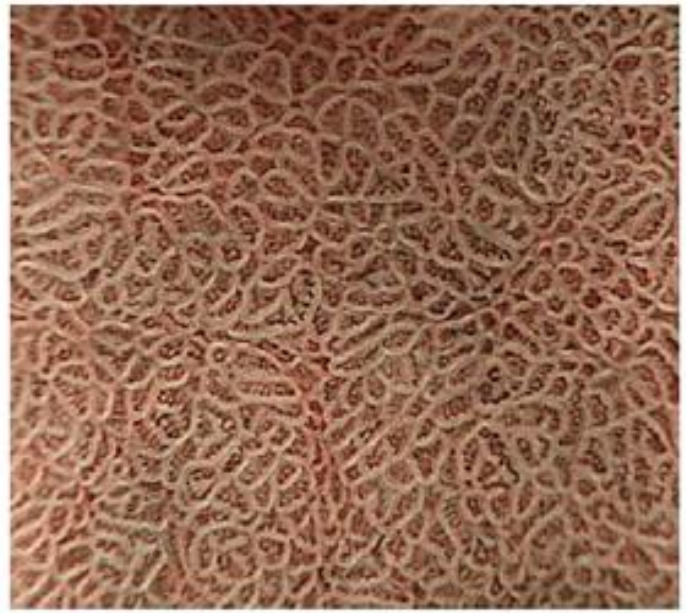


The microvascular architecture is formed by capillaries and collecting venules, but the latter are rarely observed from the mucosal surface. **The morphology of each capillary is that of coil-shaped open loops. The mucosal surface structure is made up of the marginal crypt epithelium/white zone (MCE/WZ)** and the intervening parts surrounded by MCE/WZ.

Magnified Narrow Band Imaging (MNBI)

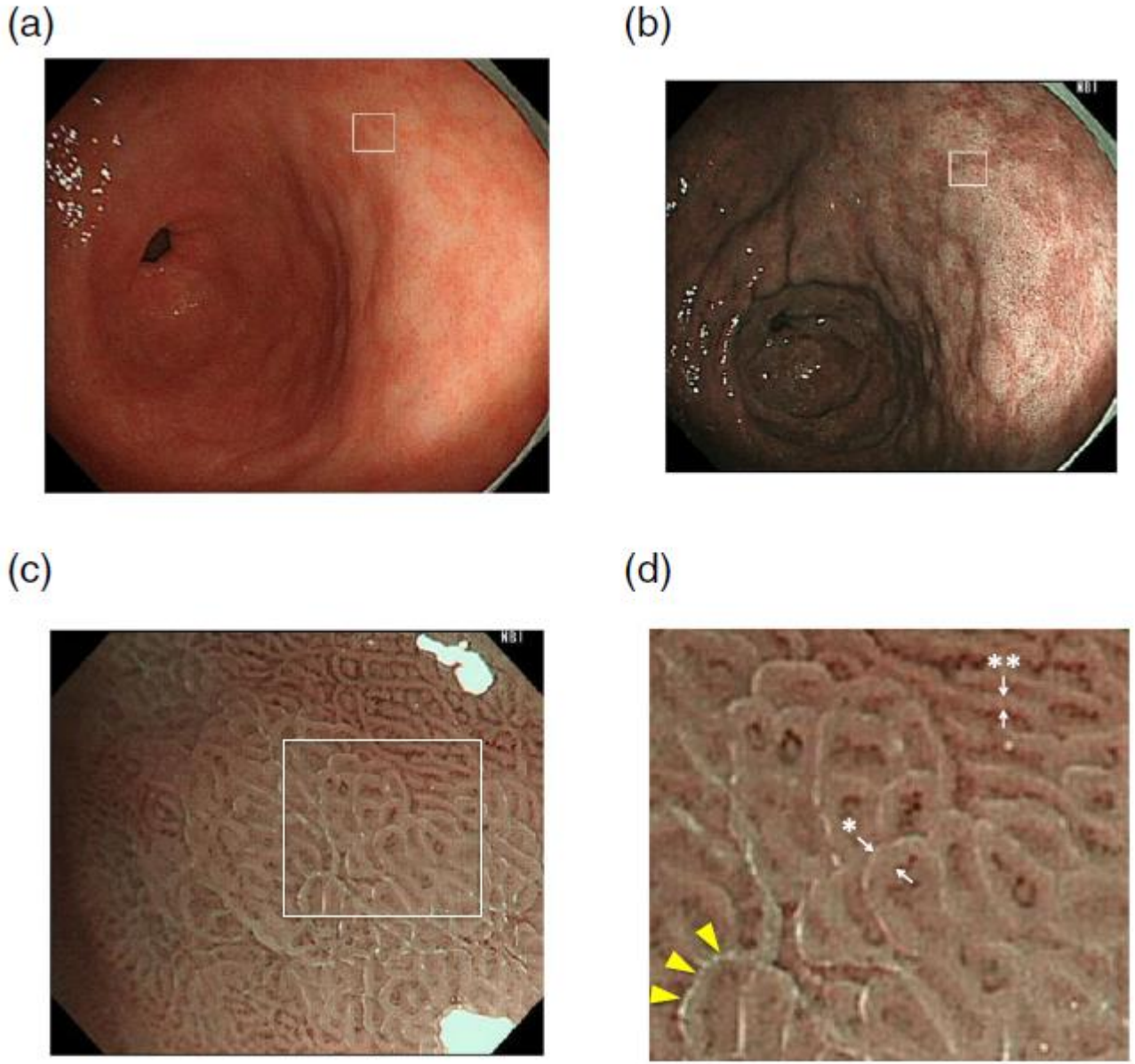


Figure 6 (a) Gastric intestinal metaplasia in the antrum looks like a whitish, slightly elevated area. (b) Narrow-band imaging (NBI) enhances the whitish color of the intestinal metaplasia. (c) In magnifying endoscopy (ME) with NBI, the metaplastic mucosa shows a groove-type mucosa (also see white box in (b)). (d) Magnifying view of white box in (c). On the crests of the mucosal surface/gyri, a light blue crest (yellow arrowheads) is seen (also see white box in (c)). Note that the marginal crypt epithelium in the metaplastic mucosa (white arrow, single asterisk) is wider and cloudier than that of the non-metaplastic mucosa (white arrow, double asterisk).

Magnified Narrow Band Imaging (MNBI)

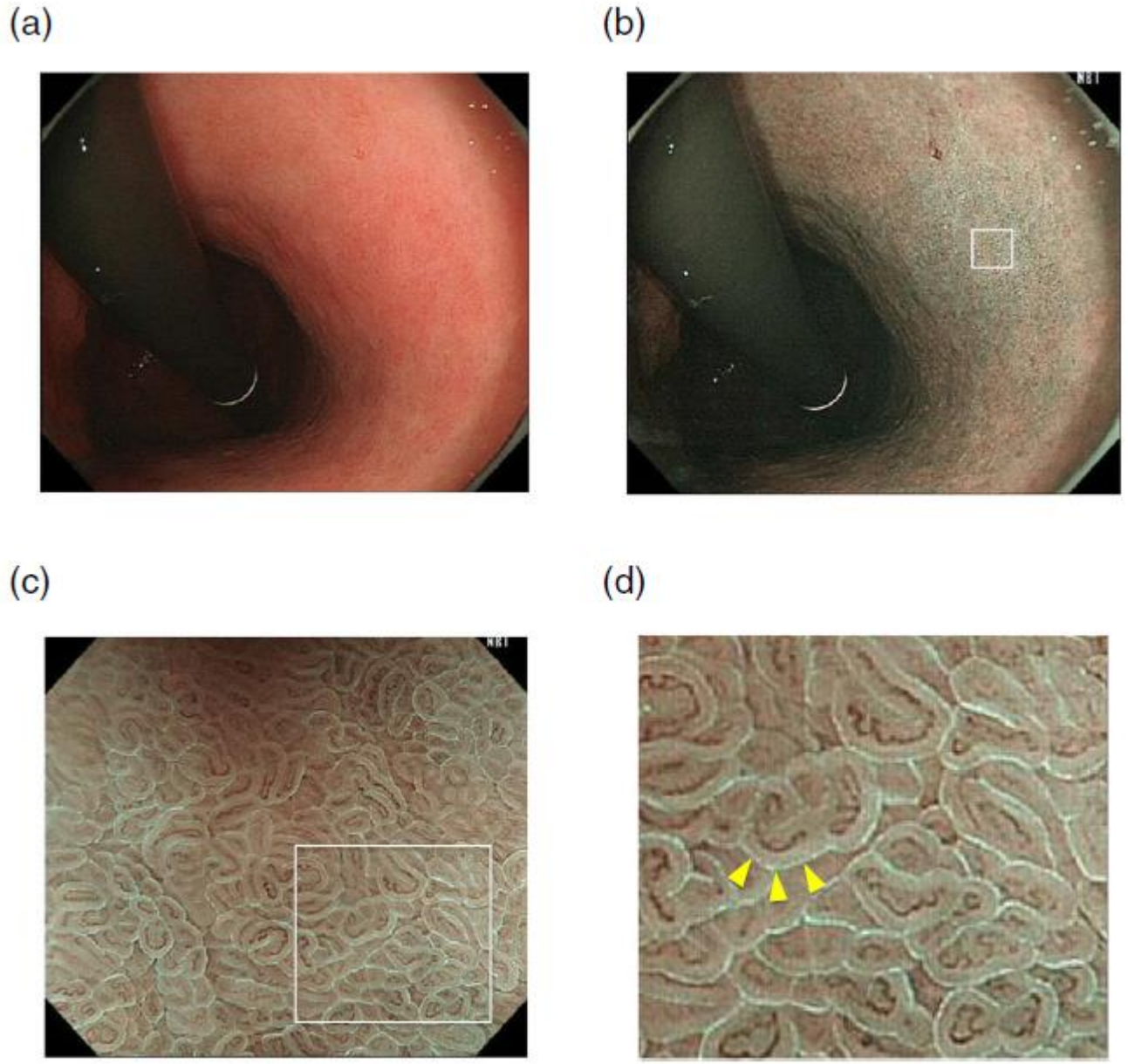
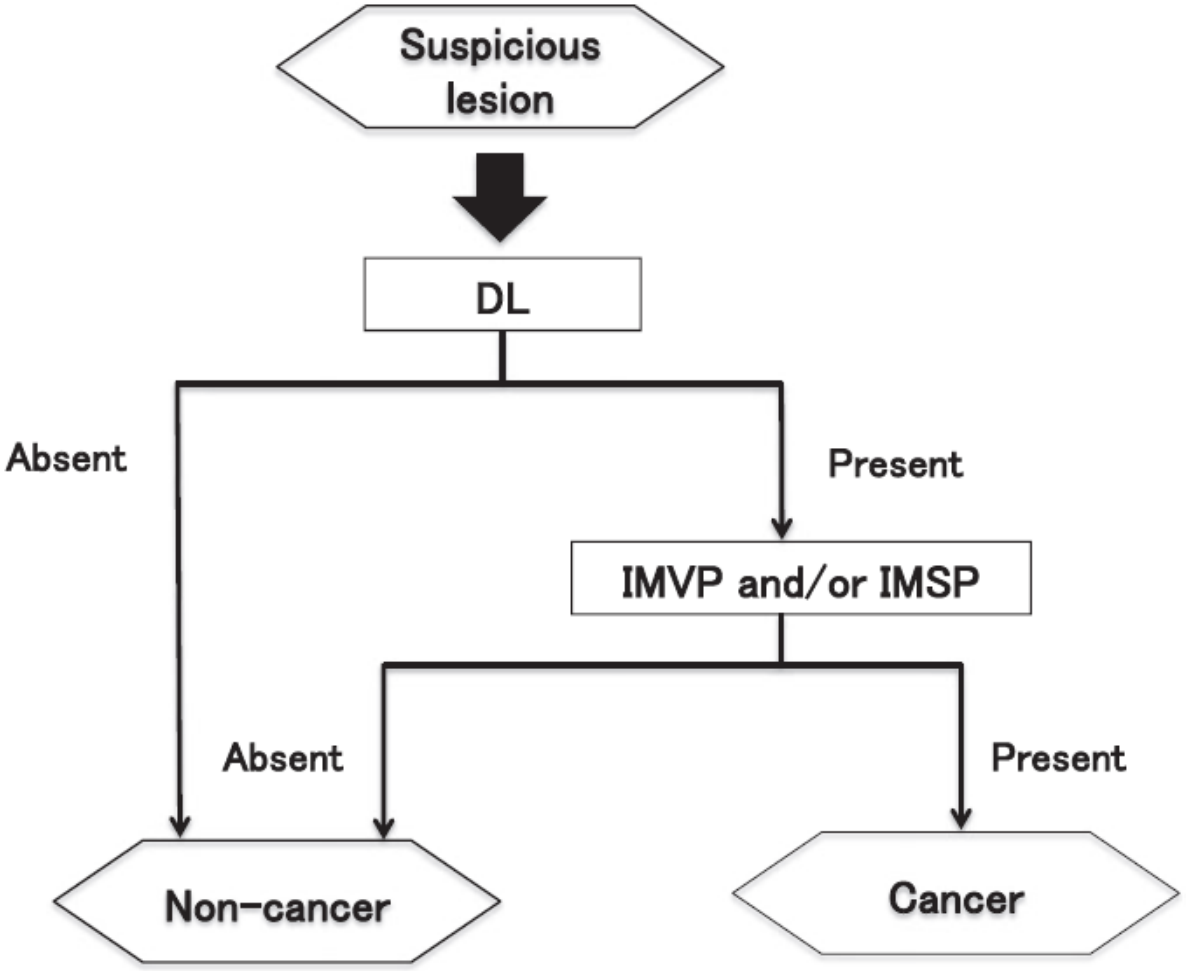


Figure 7 Gastric intestinal metaplasia in the corpus appears as a flat mucosa without any particular finding in (a) white light imaging and (b) narrow-band imaging (NBI). (c) In magnifying endoscopy (ME) with NBI, the mucosa shows a villiform microsurface structure (also see white box in (b)). (d) A light blue crest (yellow arrowheads) is observed on the surface of the villiform epithelium (also see white box in (c)).

Magnified Narrow Band Imaging (MNBI)



VS classification system

vessel plus surface (VS) classification system

The identification of a demarcation line (DL) between the lesion and the background mucosa is the first step in distinguishing EGC from non-cancerous lesions.

If a DL is absent, a benign lesion **may be** diagnosed. If a DL is present, the subsequent presence of an irregular microvascular pattern (IMVP) and an irregular microsurface (IMSP) pattern should be determined.

If IMVP and/or IMSP are present within the demarcation line, EGC can be diagnosed.

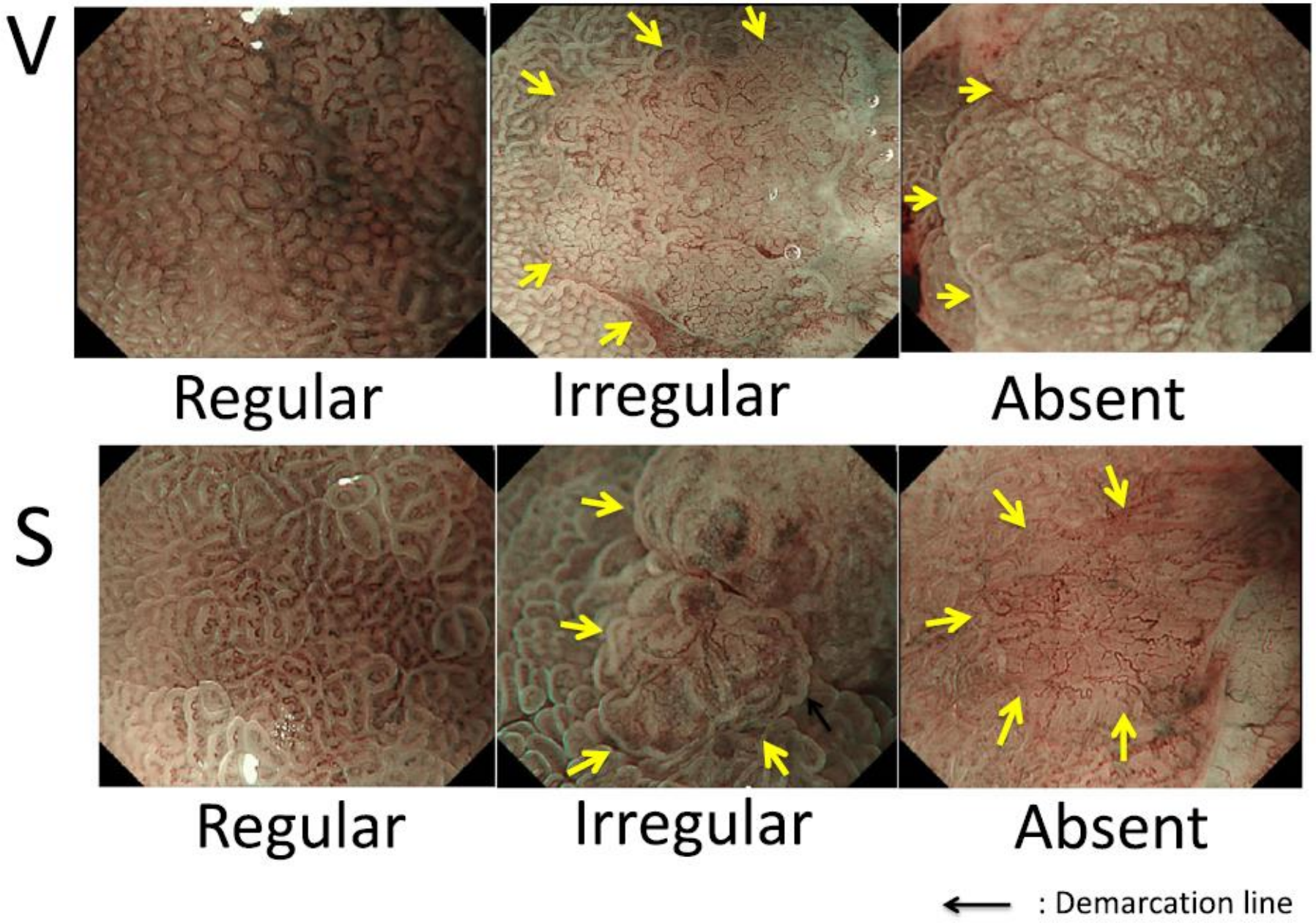
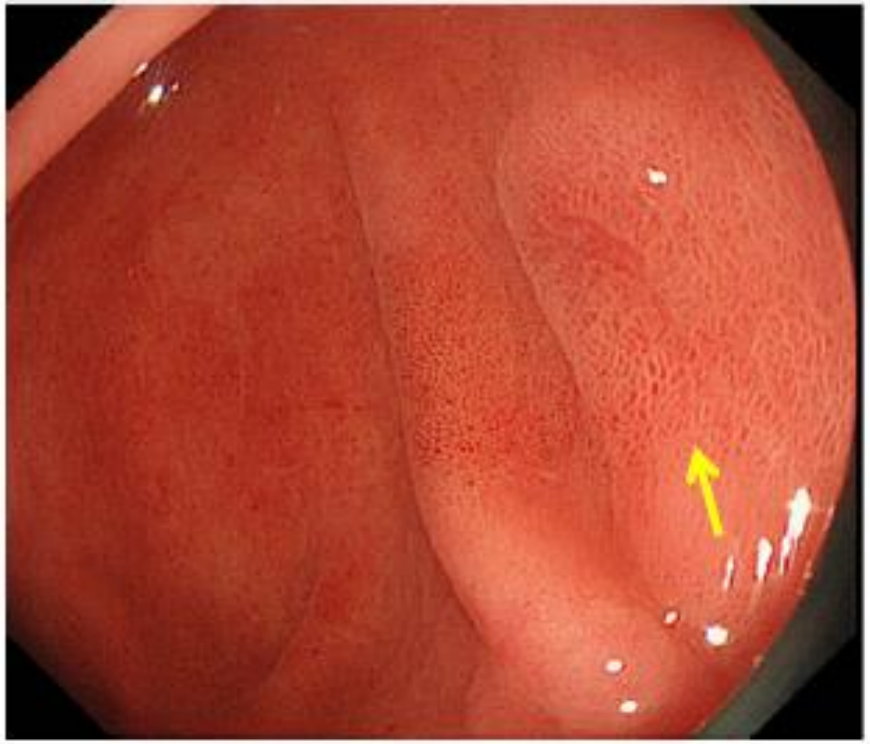
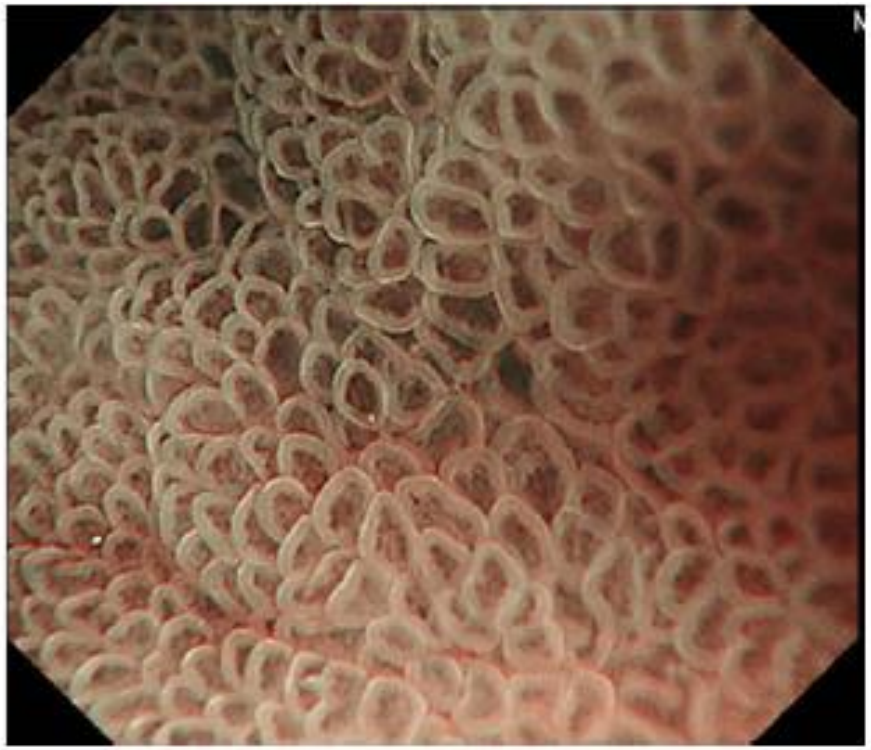


Figure 13 Vessels plus surface (VS) classification: The microvascular pattern (V) is classified as regular, irregular, or absent; the microsurface pattern (S) is also classified as regular, irregular, or absent. Arrows indicate the demarcation line in each panel.

Slightly reddened, depressed lesion; DL absent; Regular MS/MV pattern

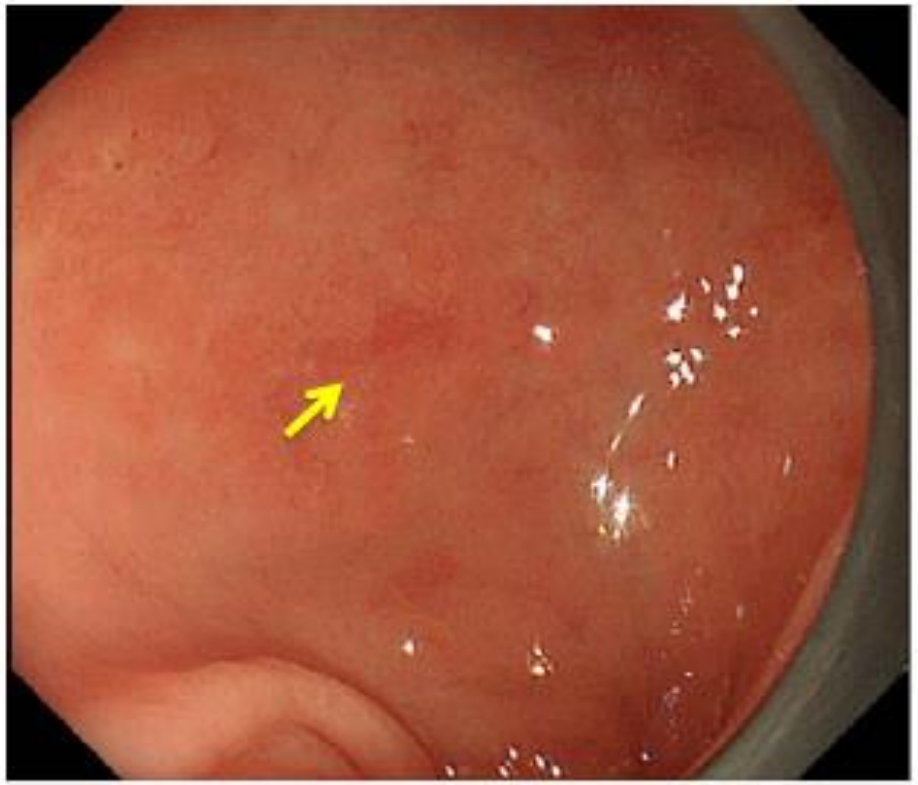
Non-cancerous

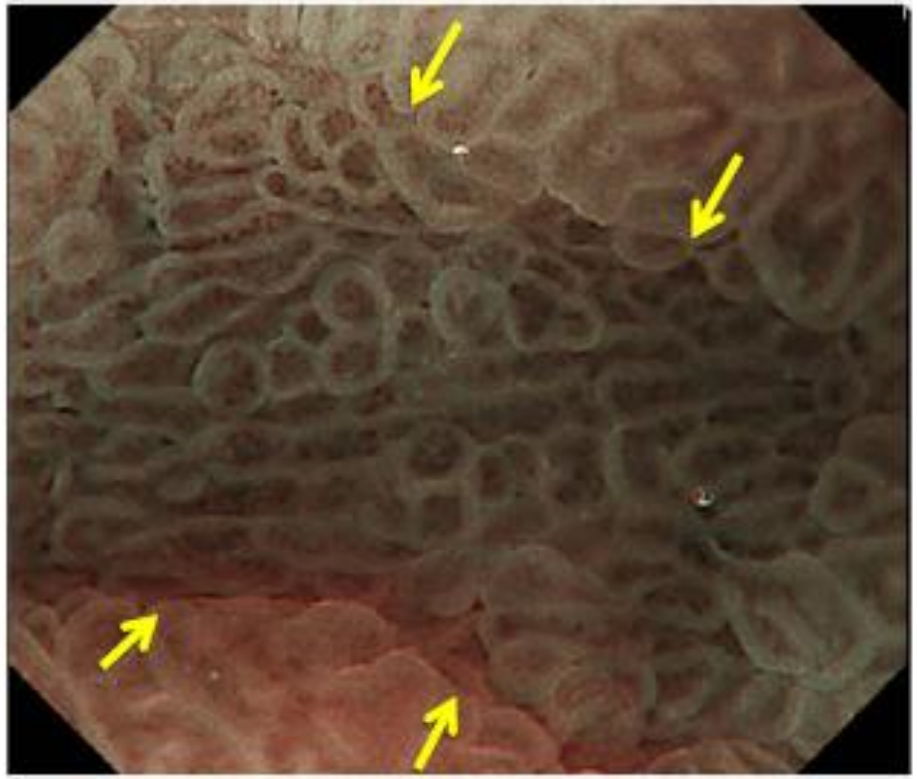




Depressed reddened lesion; DL present; Regular MS/MV pattern

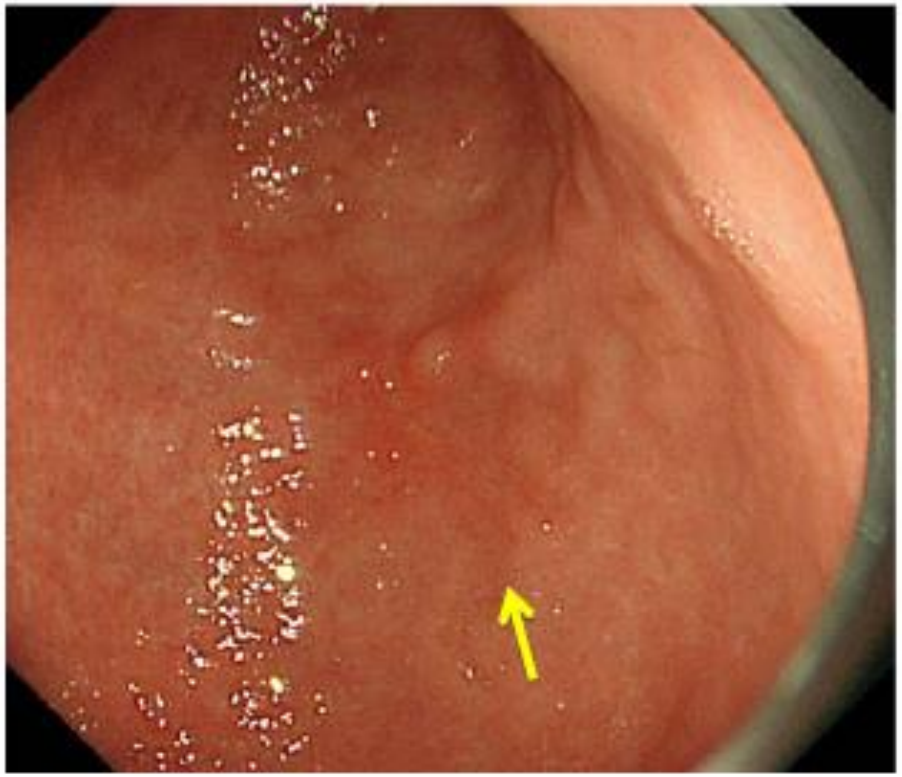
Non-cancerous

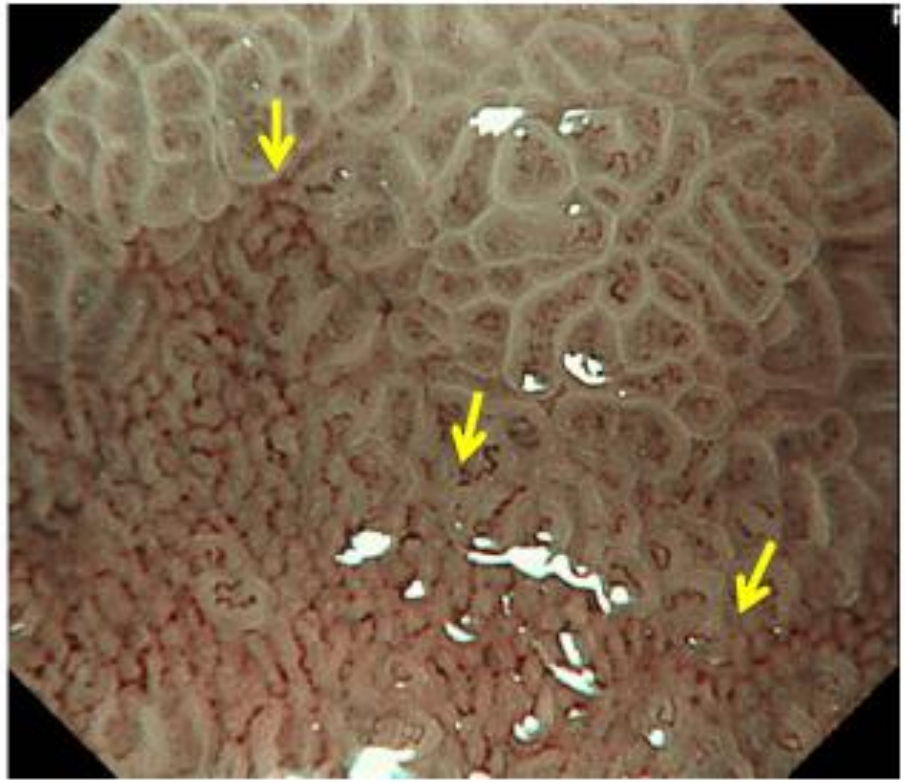




Reddened depressed lesion; DL present; Regular MS/MV pattern

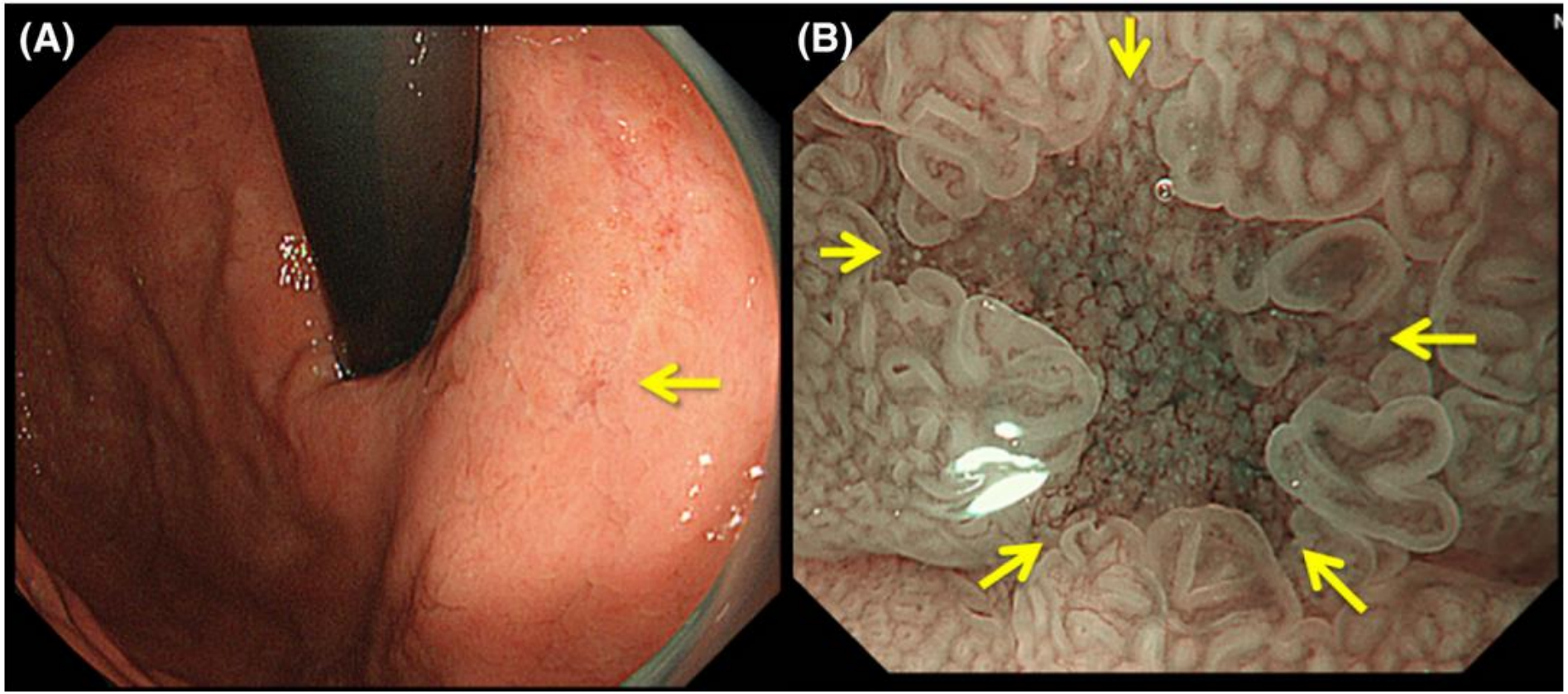
Non-cancerous





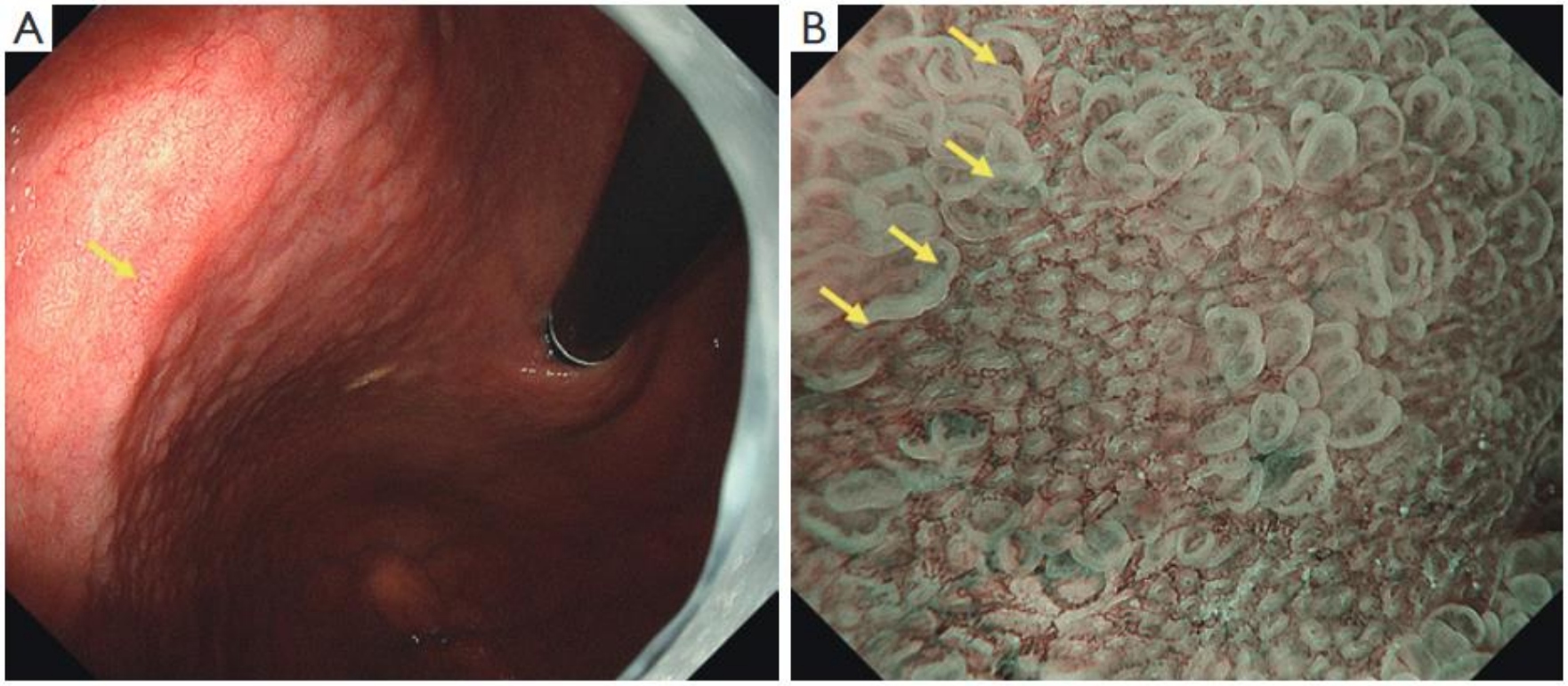
Slightly depressed lesion; DL present; Regular MV/MS pattern

Non-cancerous



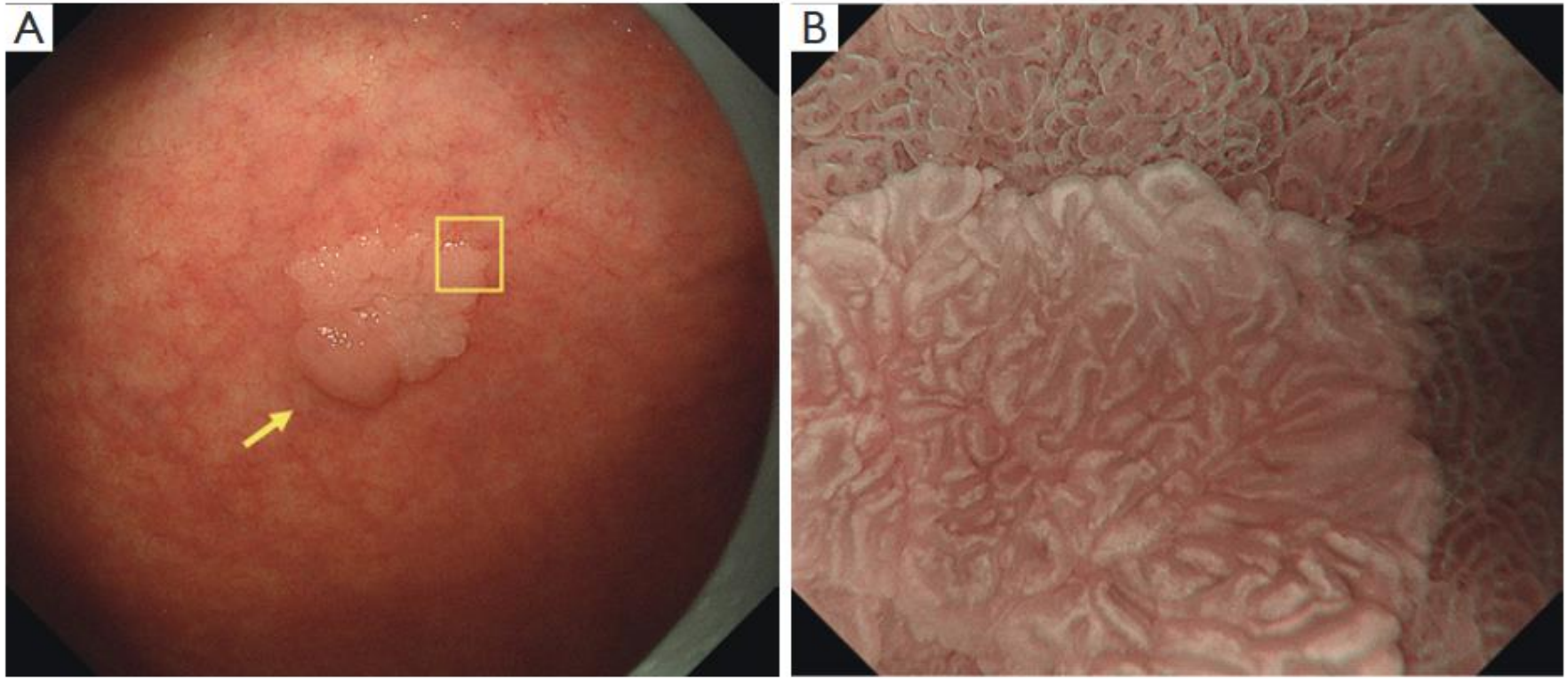
Same colored depressed lesion; DL present; Regular MS/MV pattern

Non-cancerous



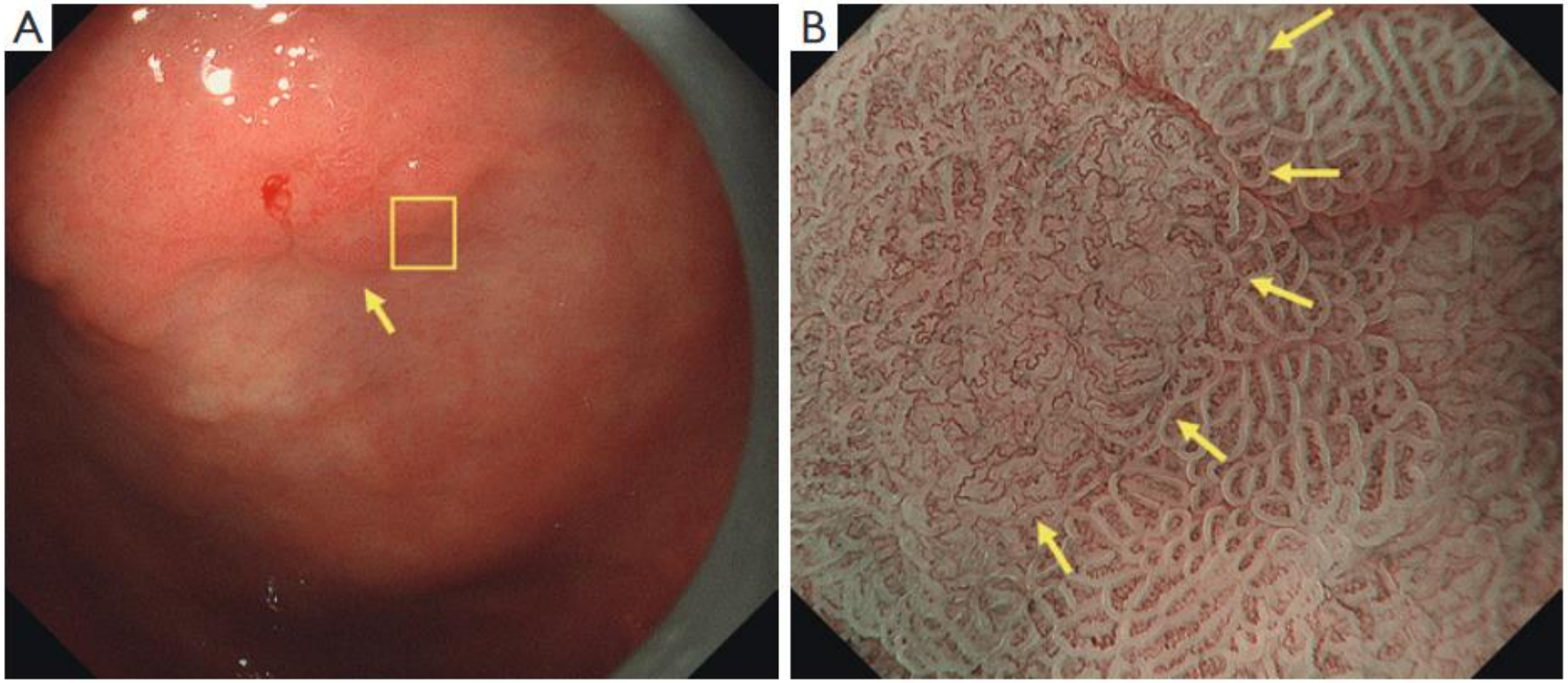
Dicolored, flat elevated lesion; DL present; Regular MS pattern; Absent MV pattern

Non-cancerous; Tubular adenoma



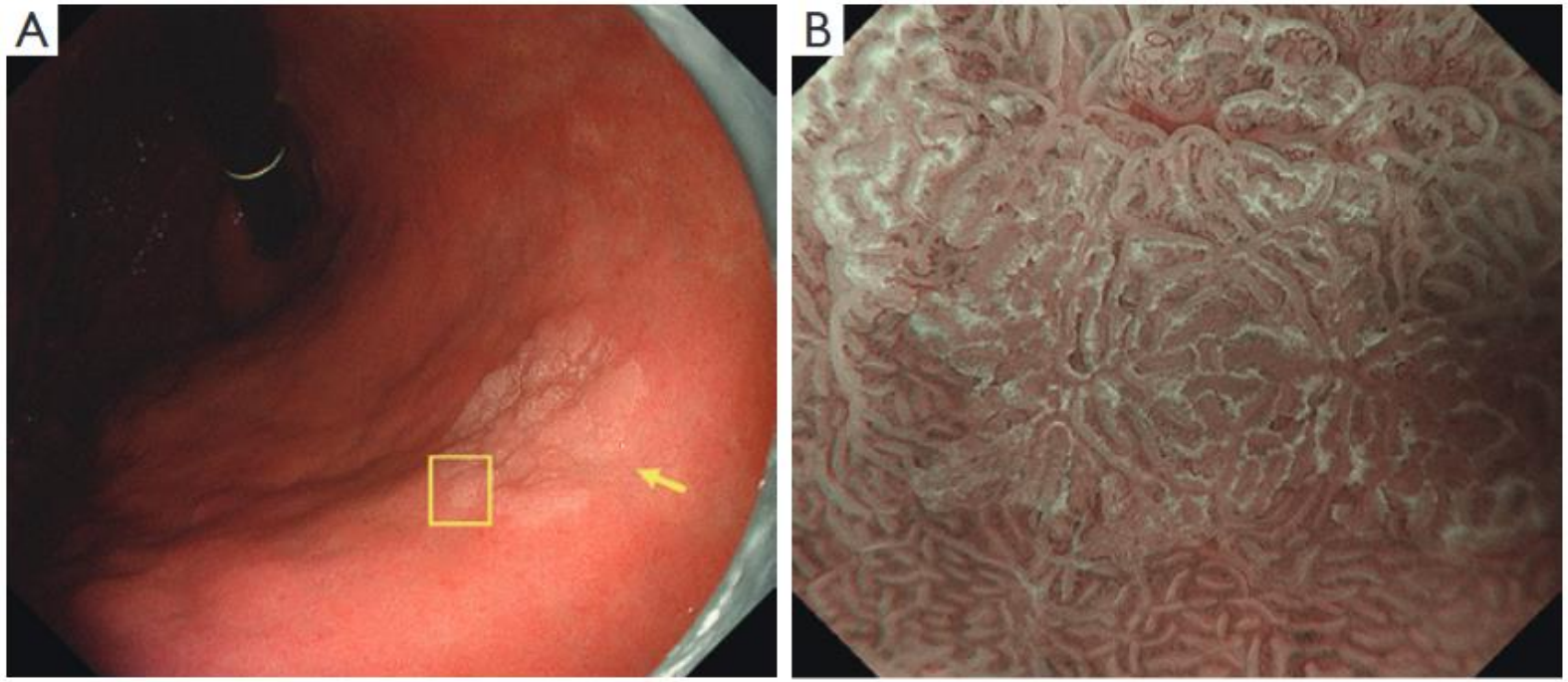
Same colored depressed lesion; DL present; Absent MS pattern; Irregular MV pattern

Cancerous



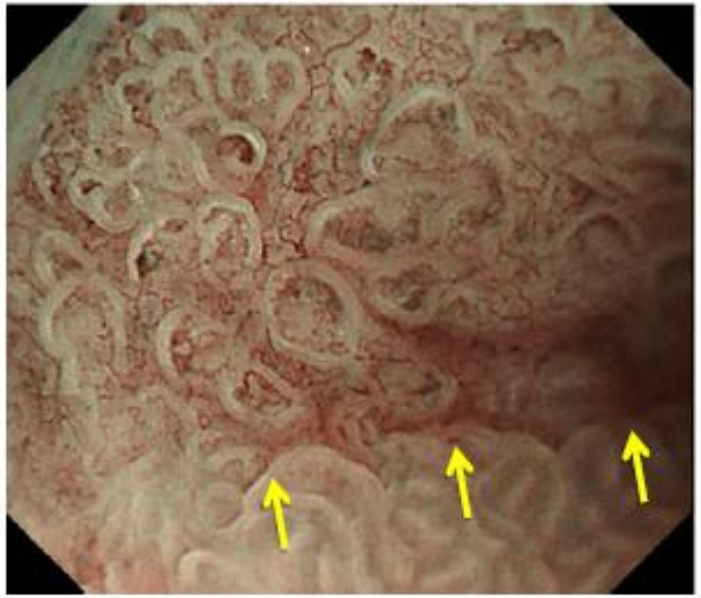
Dicolored elevated lesion; DL present; Irregular MS pattern; Absent MV pattern

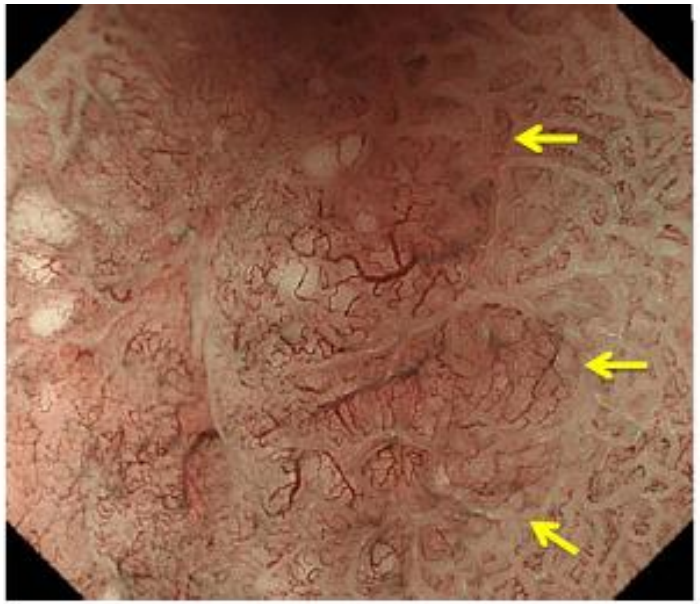
Cancerous

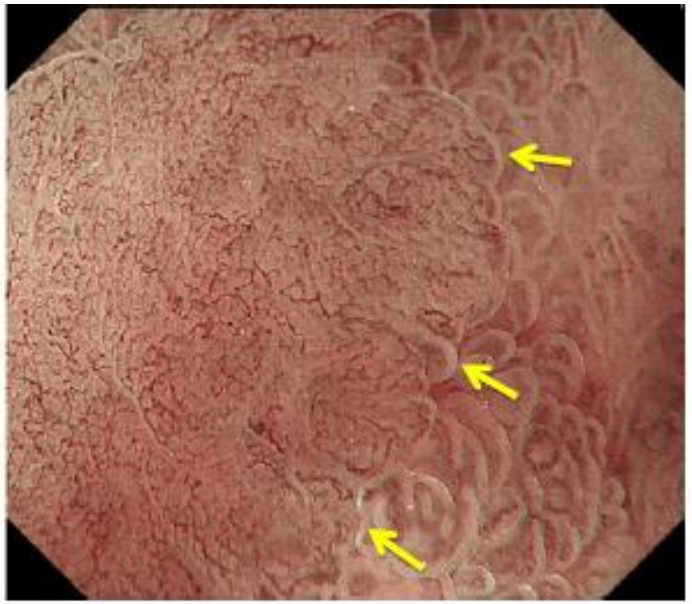


DL present ; Irregular MV pattern

Cancerous

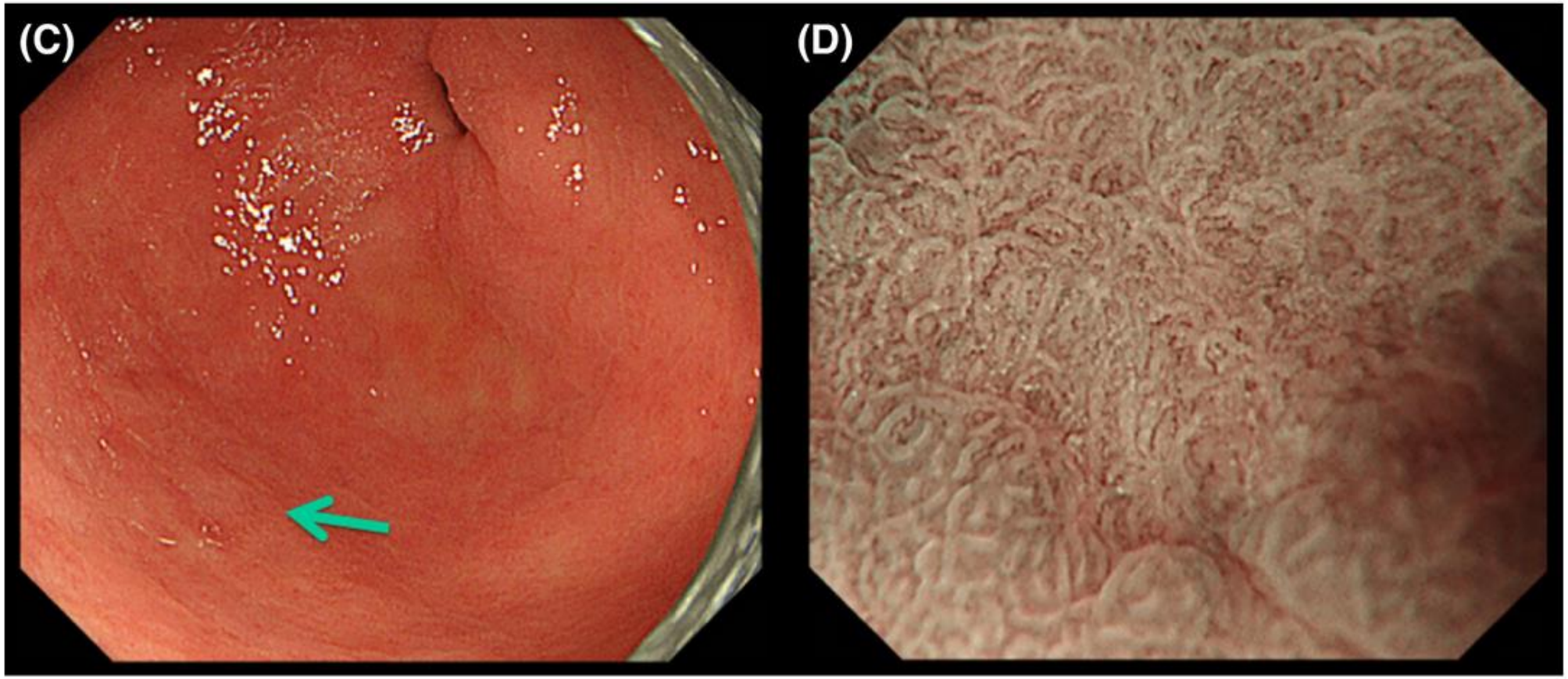






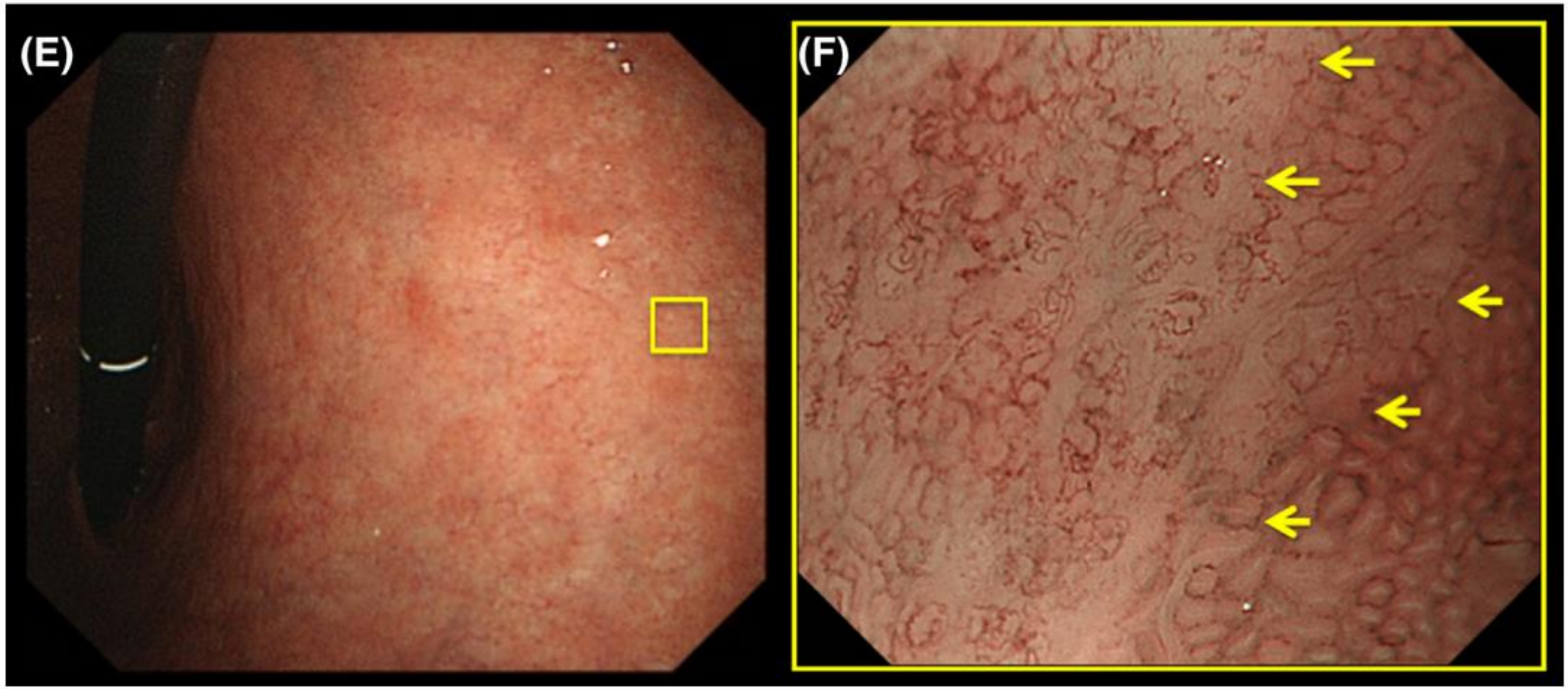
Flat pale mucosal lesion; DL present; Irregular MV/MS pattern

Cancerous

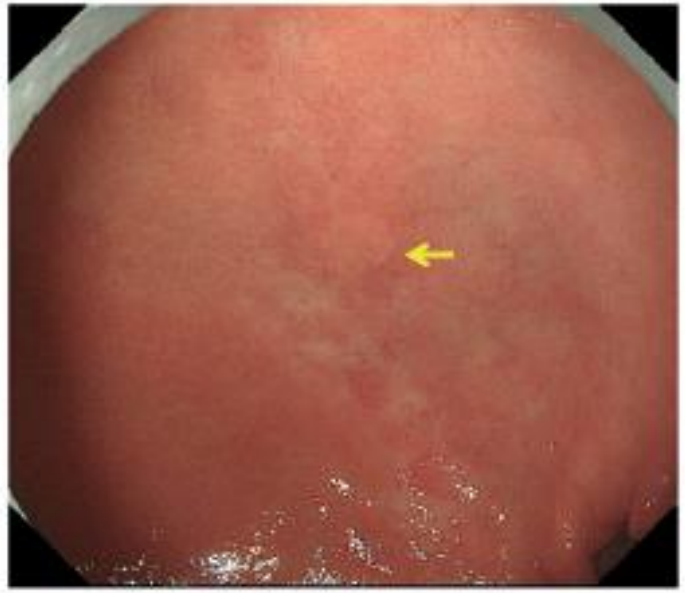


Pale flat lesion; DL present; Irregular MV pattern; Absent MS pattern

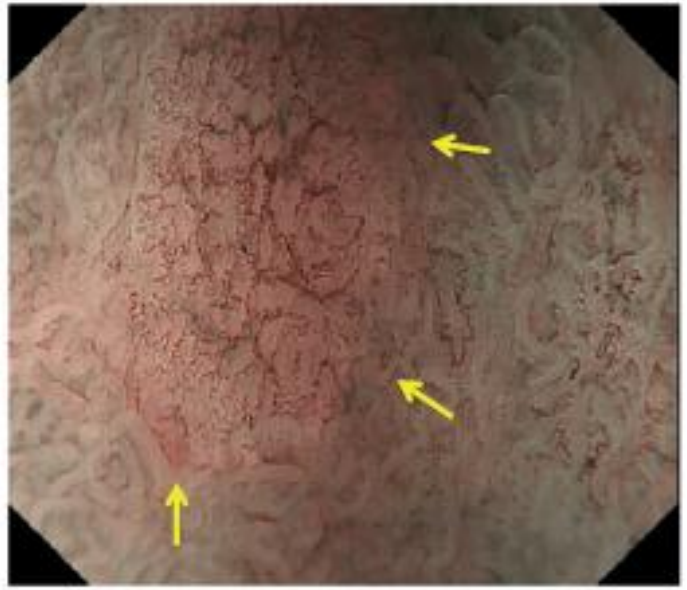
Cancerous



Pale mucosal lesion; DL present; Irregular MV pattern; Absent MS pattern

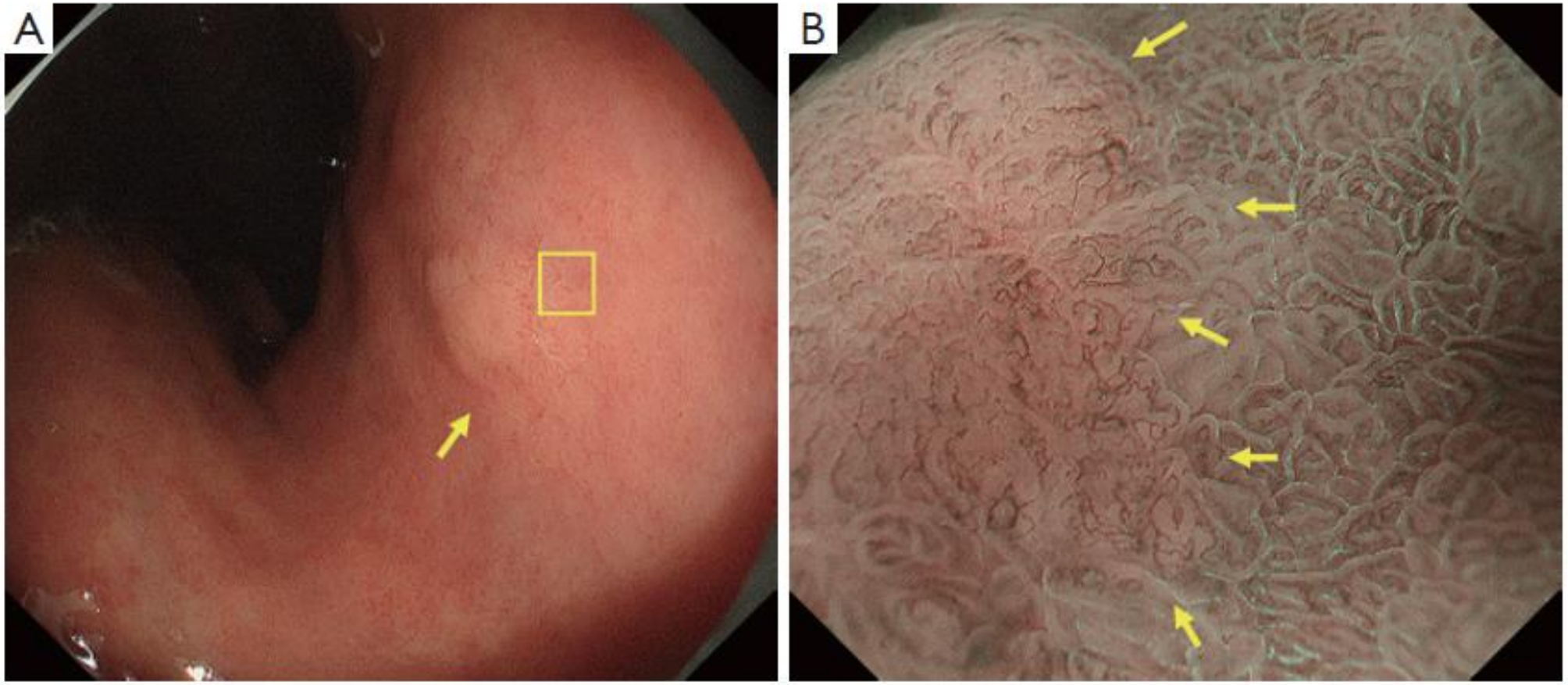


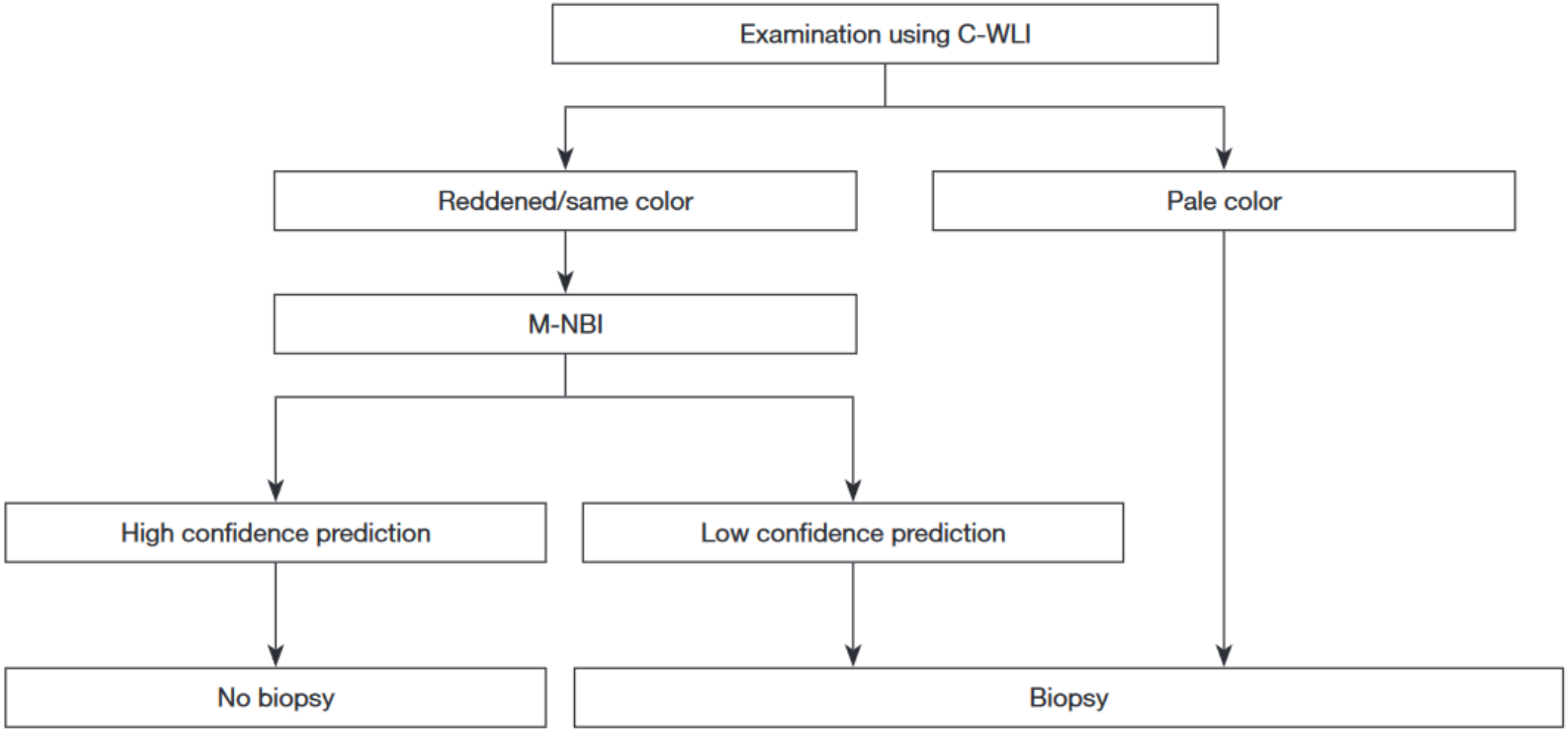
Cancerous



Flat pale lesion; DL present; Irregular MV/MS pattern

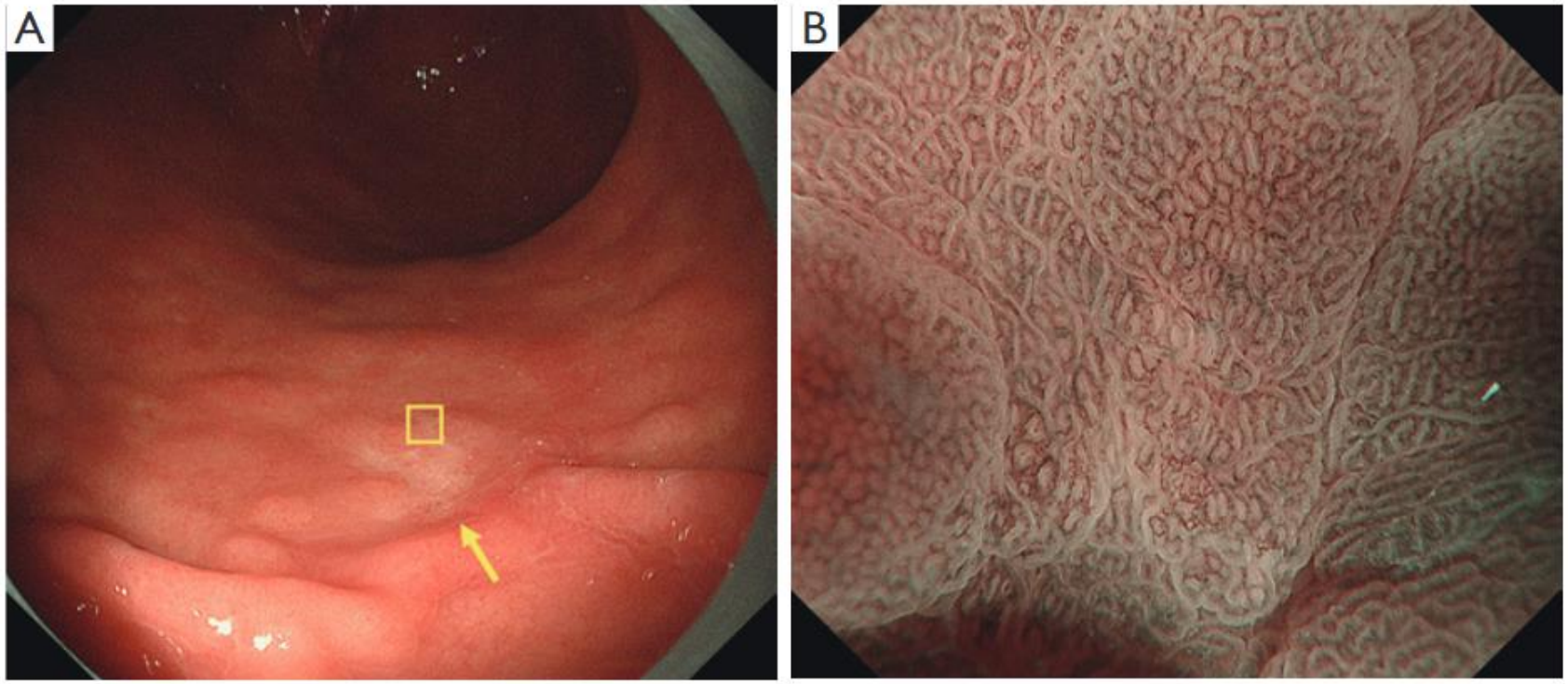
Cancerous



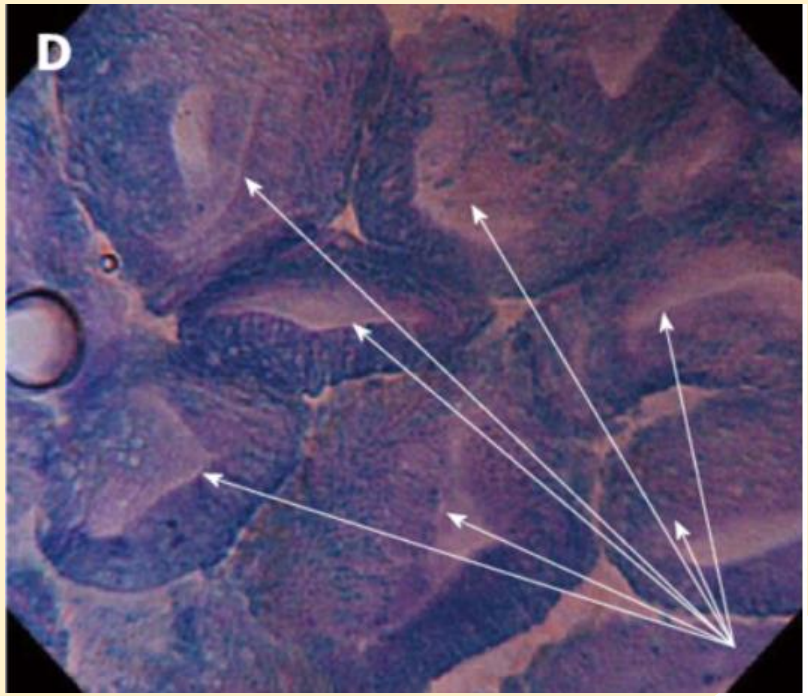

Examination using C-WLI
Reddened/same color
Pale color
M-NBI
High confidence prediction
Low confidence prediction
No biopsy
Biopsy

Flat pale lesion; DL present; Regular MV and MS pattern

Cancerous



Endocytoscopy

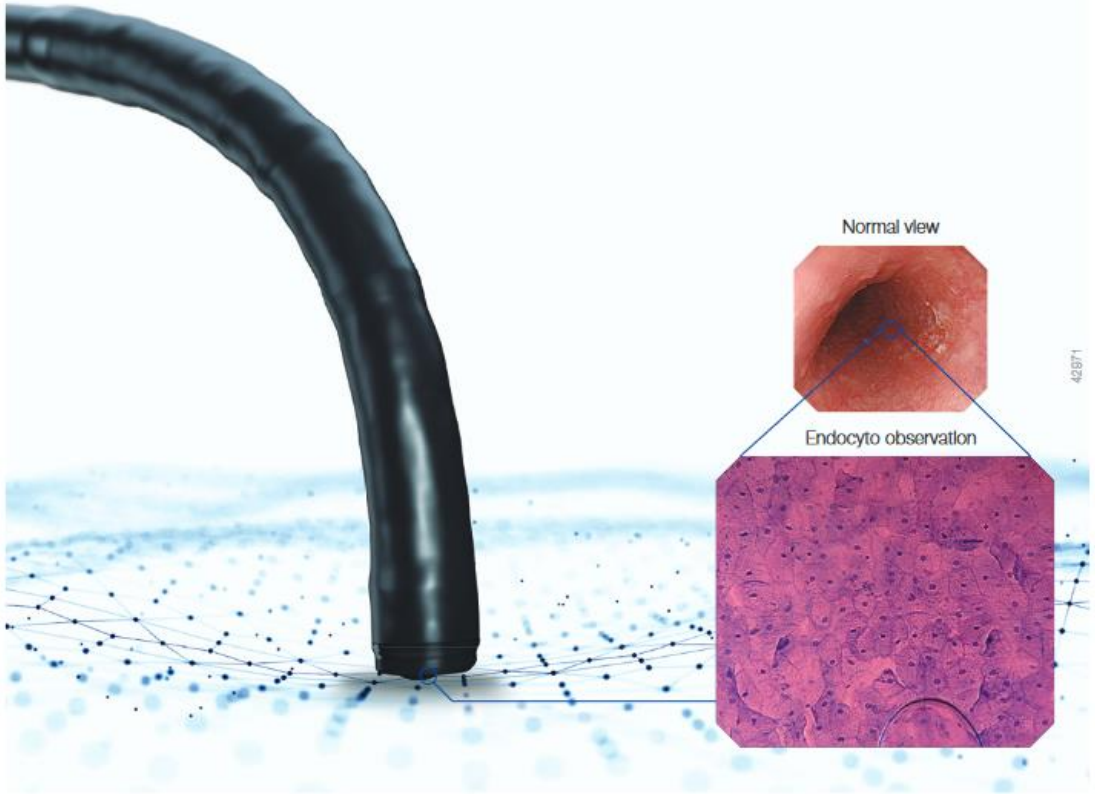


Cell nuclei are stained with an appropriate dye. The objective lens is then brought into contact with the mucosa to observe the cells of the superficial mucosal layer.

Light emitted by the light guide is sent into the cells and partially returned as scattered light, facilitating cytological observation of the superficial mucosal layer.

Endocytoscopy

Three dyes with varying concentrations have been accounted for as the most utilized ones: toluidine blue (TB), methylene blue (MB), and crystal violet(CV).



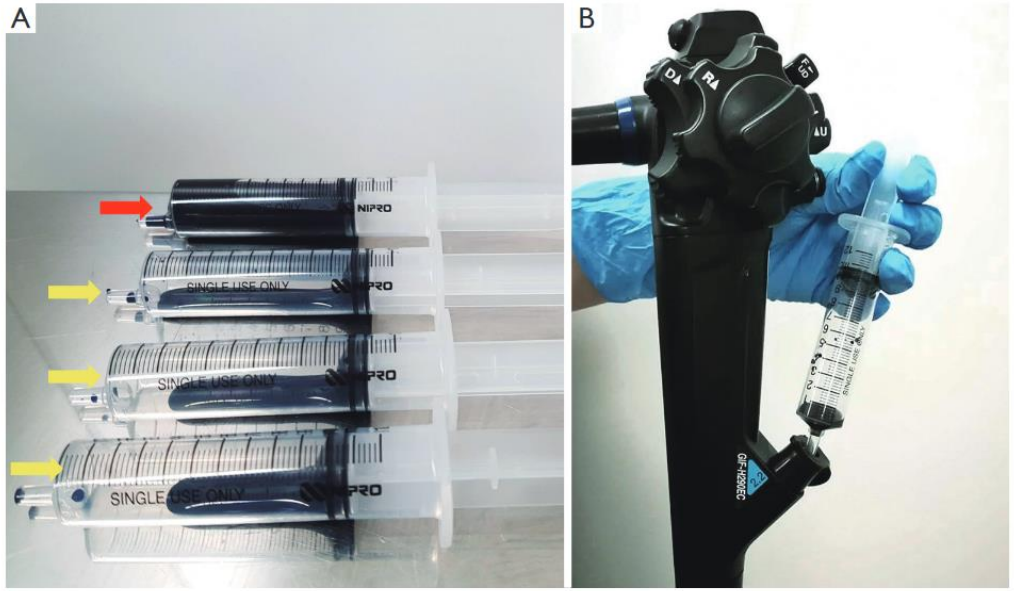
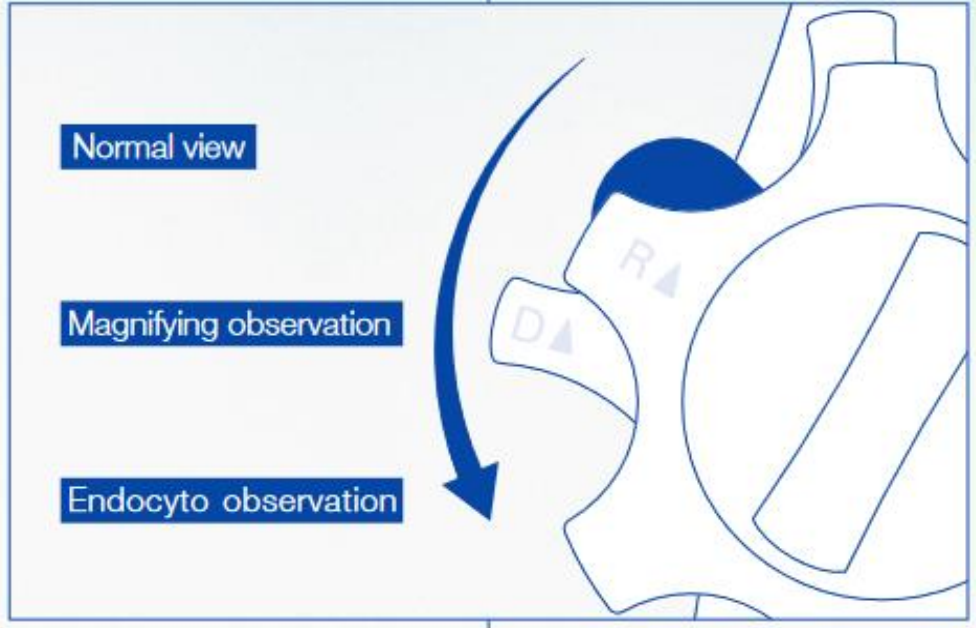
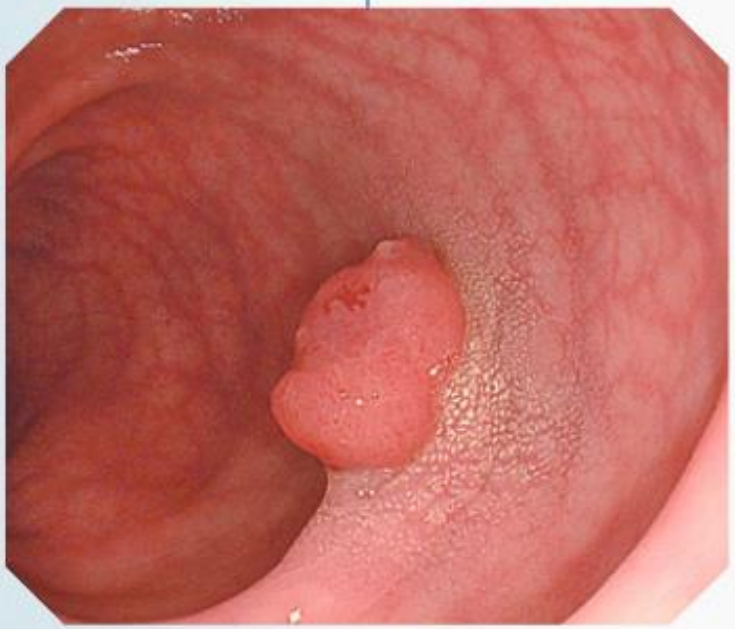
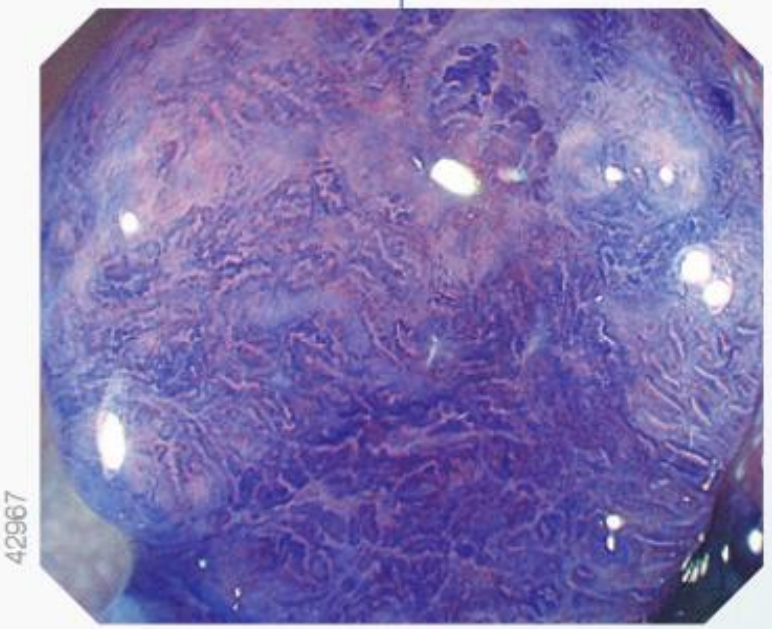


Figure 1 CM double staining: (A) 10 cc of 0.05% crystal violet and 1 cc of 1% methylene blue is mixed in a 10 cc syringe (red arrow), and 1 cc of this mixture is aspirated in several different 10 cc syringes with 9 cc of air (yellow arrows). (B) Spraying of the CM mixture is done several times through the scope channel with an interval of 15 to 30 seconds until a satisfactory staining is achieved.

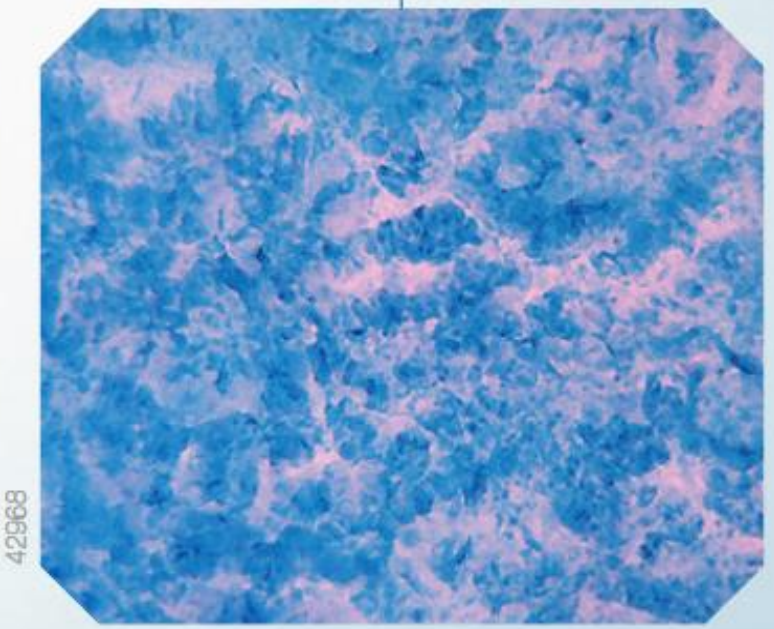




Normal view



Magnifying observation



Endocyto observation

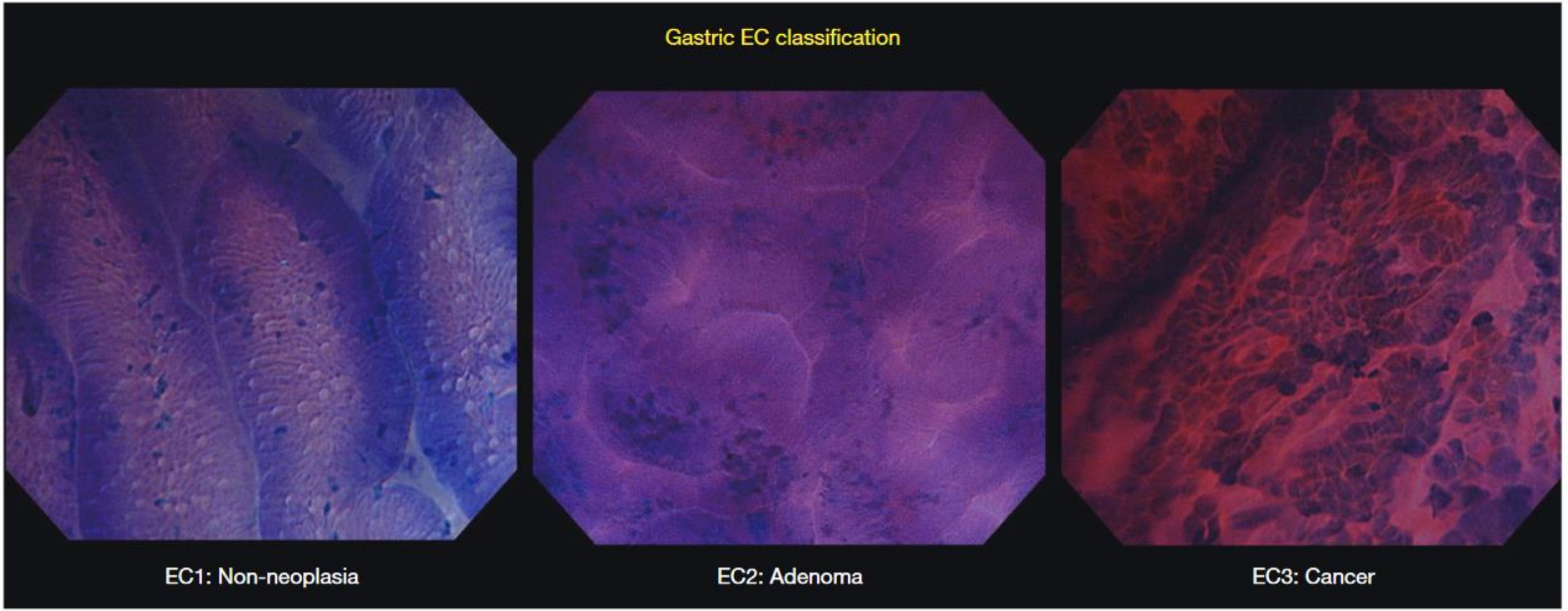
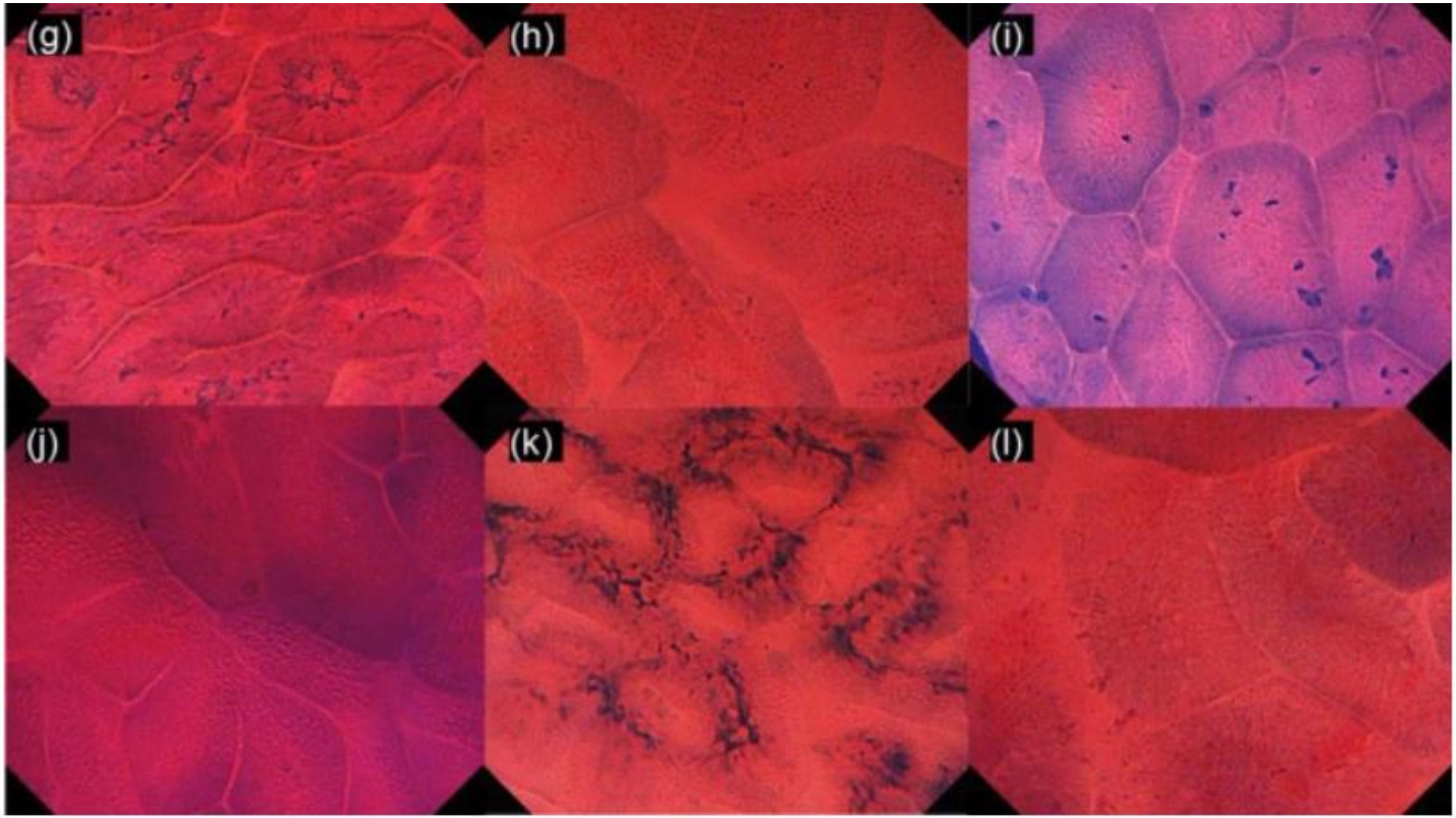
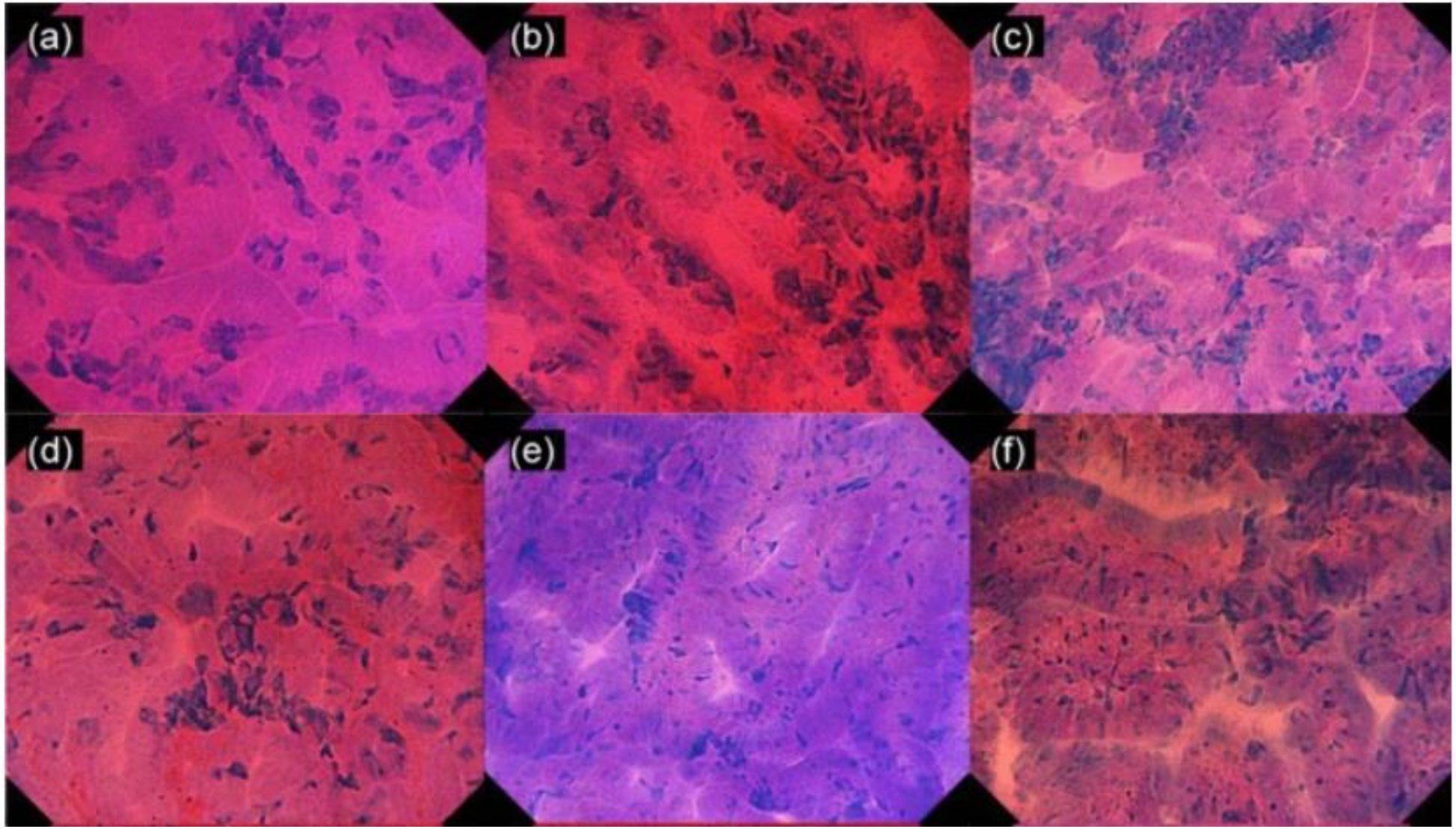


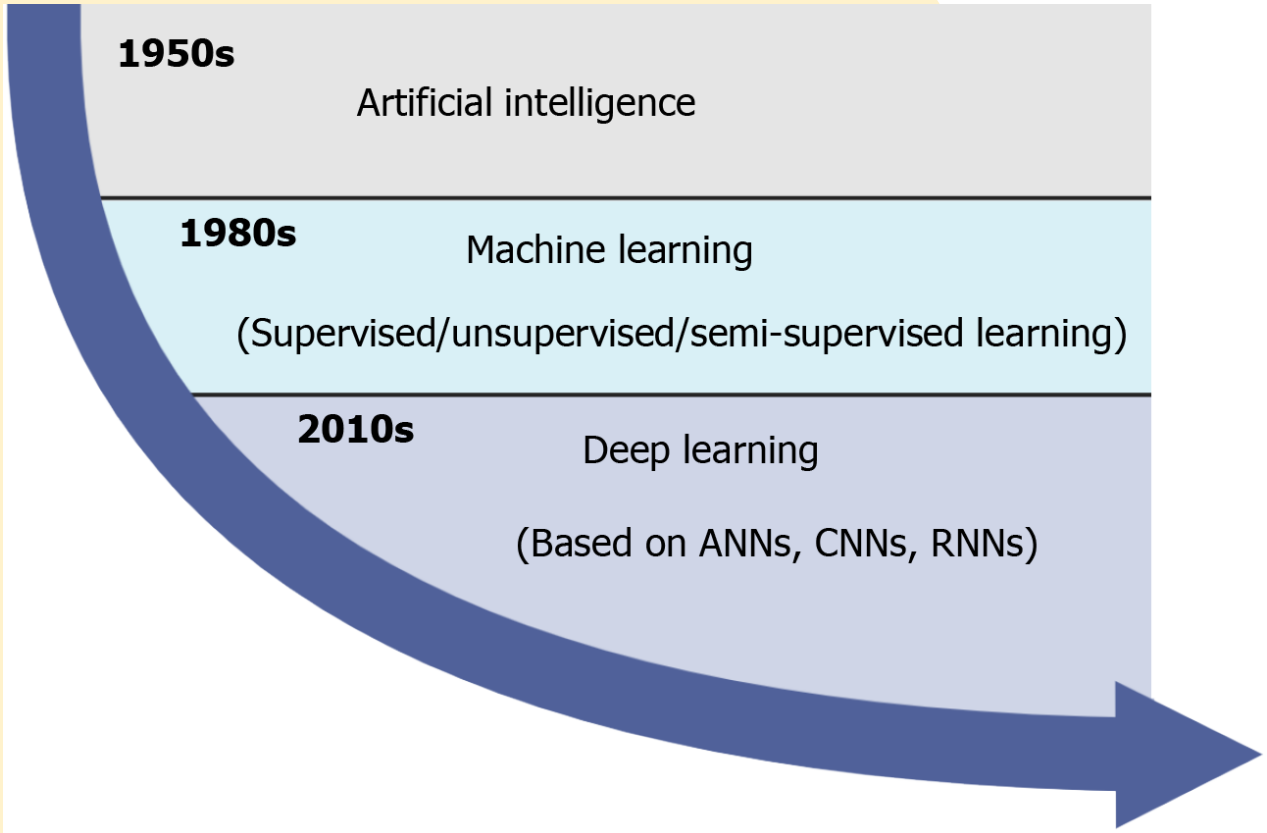
Figure 3 Gastric EC classification: representative pictures differentiating EC1 (non-neoplasia), EC2 (adenoma), and EC3 (cancer). EC1 shows regularly arranged glands with consistent pattern and preserved lumen. EC2 shows narrowing of the lumen and a more compact arrangement of glands. EC3 shows complete distortion of glandular structure and significant swelling of the nuclei (enlarged nuclear sign).



Cases of noncancerous gastric mucosa a, in which the gland lumen is well preserved and mucosal cells are regularly arranged



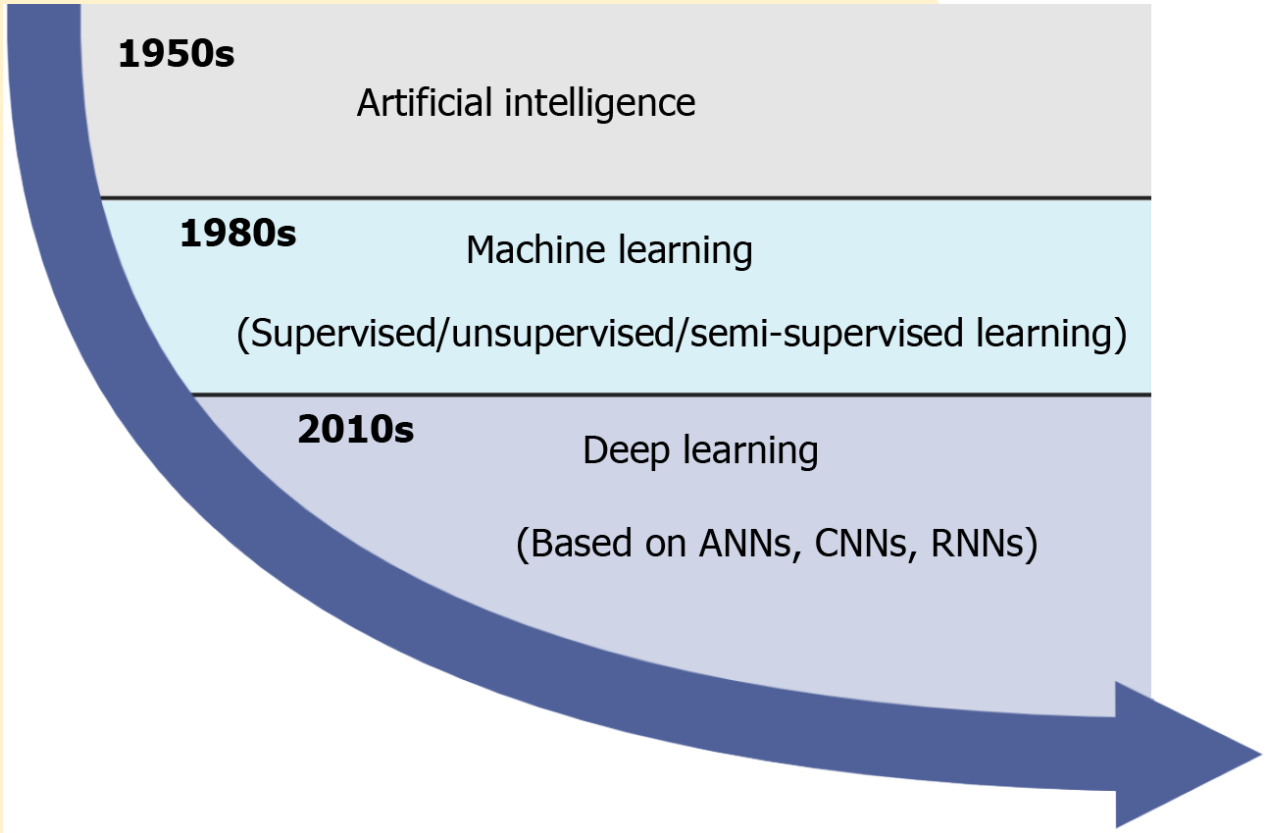
Cases of intestinal-type early gastric cancer showing specific irregularities in gland structure and cell nuclei.



Artifical intelligence (AI) consists of several overlapping technologies such as machine learning (ML), artificial neural networks (ANNs), deep learning (DL), **convolutional neural networks (CNNs)**, and recurrent neural networks (RNN).

Since the 1980s, ML has been performed to construct a mathematical model and predict outcomes based on input data.

ML is roughly divided into supervised (labeled data), unsupervised (unlabeled data), and semi-supervised (both labeled and unlabeled data) learning techniques.

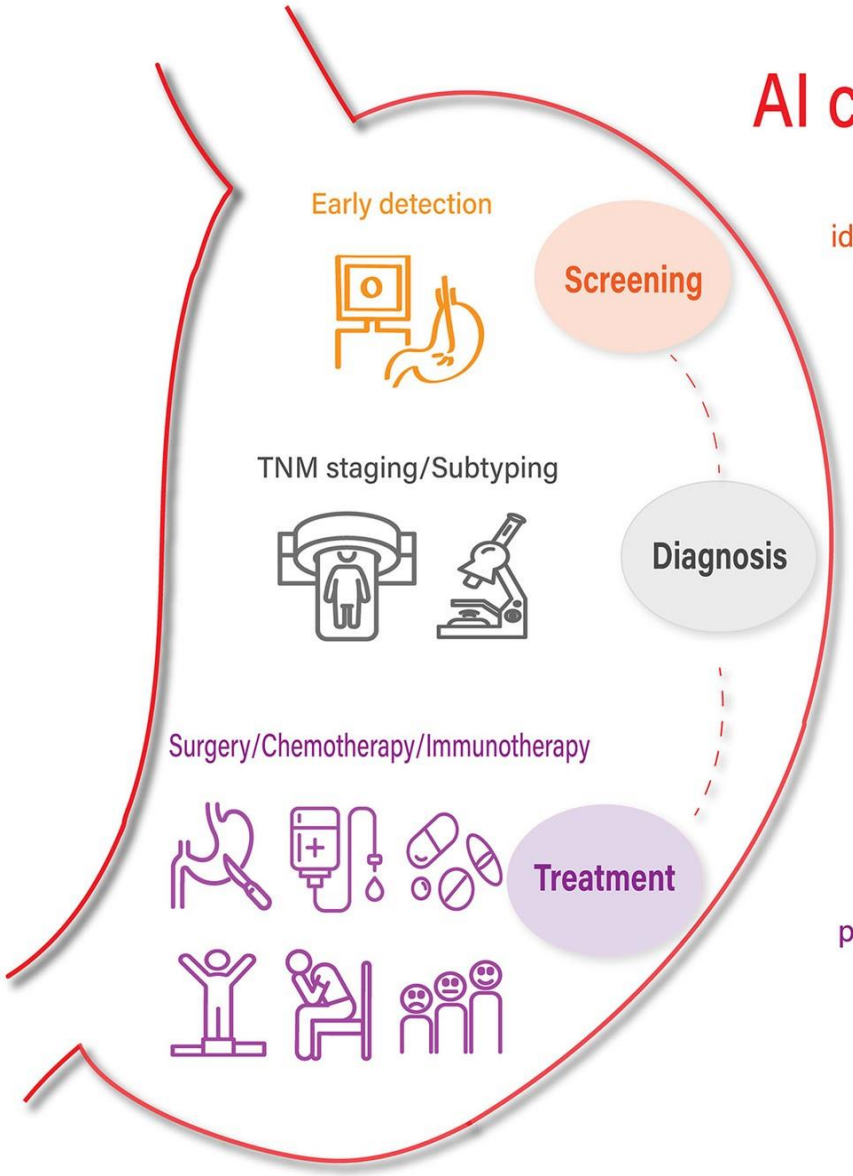


Recently, as a subset of ML, ANNs have received increased interest because they can identify and learn input data by themselves instead of being labeled by experts.

In the last decade, DL, a new model of ML, holds great promise in clinical medicine. DL is particularly suitable for enormous complex or highly dimensional medical image analysis.

CNNs have demonstrated excellent performance in image recognition such as endoscopy, radiology, and pathology.

Roadmap of artificial intelligence (AI)-supported applications in gastric cancer



AI can ...

identify precancerous disease

support early cancer detection

estimate invasion depth for early gastric cancer

determine TNM staging for advanced gastric cancer

help with hispathological and molecular subtyping

delineate tumor resection margins

predict treatment reponse and prognosis

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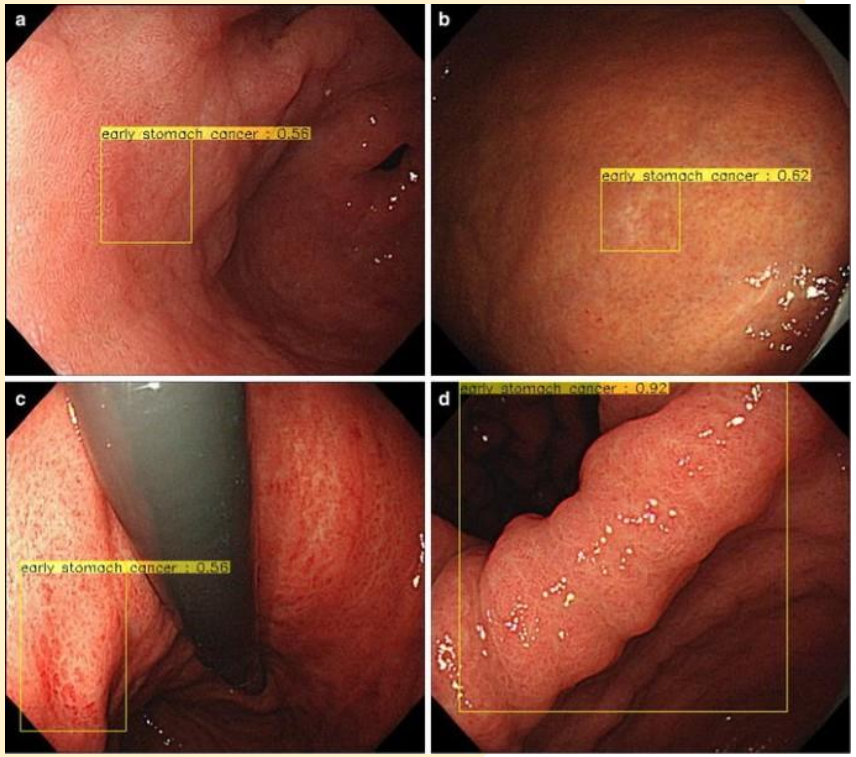
AI-supported screening and staging



GC screening is the most promising and popular research of AI in GC.

Miss rates of GC detection ranged from 4.6% to 25.8% by endoscopists.

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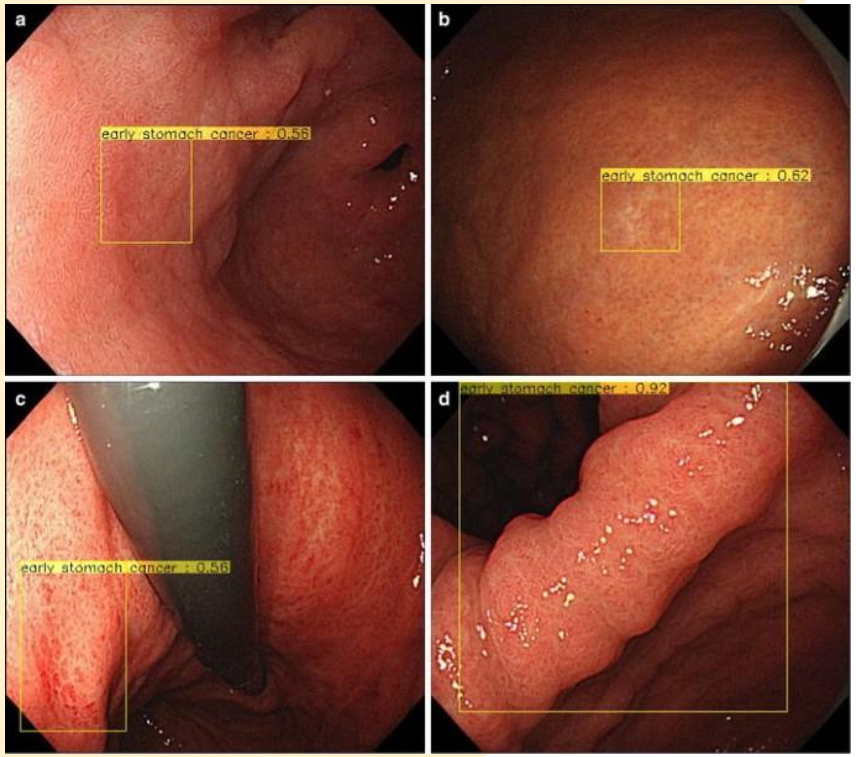
AI-supported screening and staging



Accurate estimation of invasion depth is difficult through visual examination. **AI could achieve a relatively high T-staging accuracy for EGC**, which might provide suggestions for endoscopic resection.

Overdiagnosis is more unacceptable than underdiagnosis for the irreversible consequences caused by over-treatment.

EUS was once considered a preferable technique; however, it was reported to be not superior to conventional endoscopy with ~70% overall accuracy.

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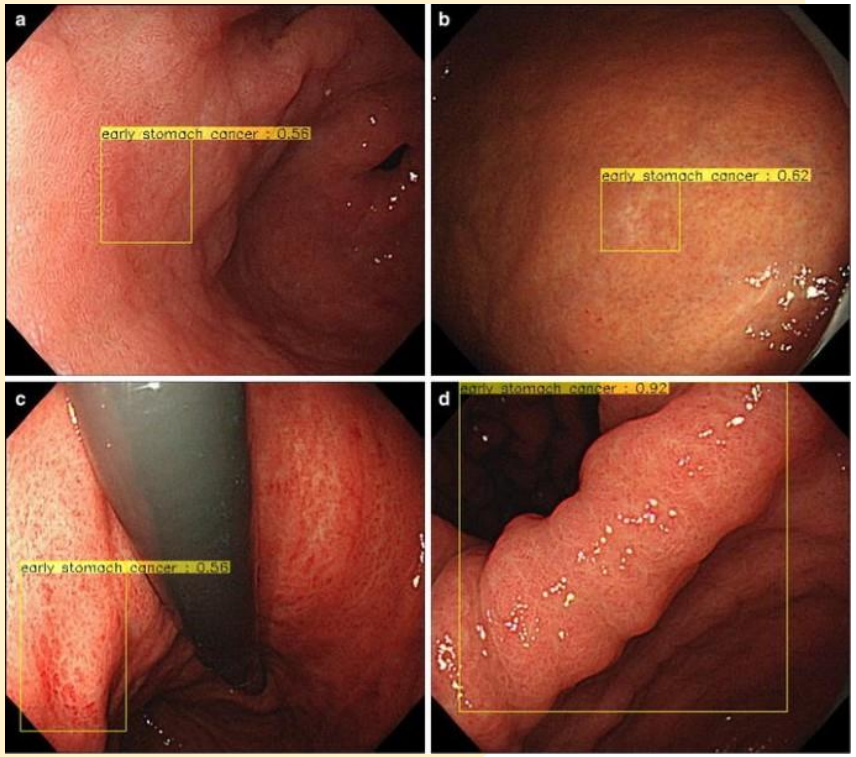
AI-supported screening and staging



To predict the invasion depth for EGC, ResNet was trained on 790 images and tested on 203 images, which achieved an **AUC of 94%** that had significantly higher sensitivity and specificity than endoscopists.

Three independent ResNet-50-based models were trained individually, reaching an **AUC of 94.5%, 94.3%, and 95.5% for WLI, NBI, and Indigo images**, respectively.

This work demonstrated that automatic invasion depth prediction for GC can be applied to endoscopic images of various modalities.

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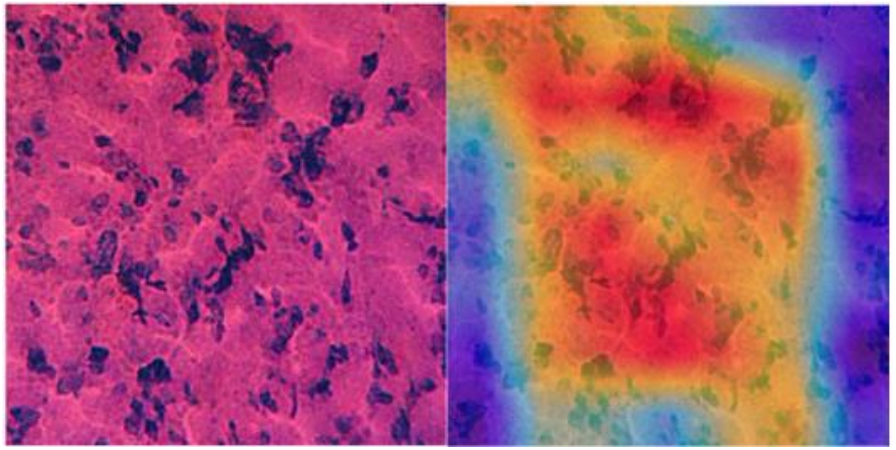
Noda *et al. BMC Gastroenterology* (2022) 22:237
https://doi.org/10.1186/s12876-022-02312-y

Convolutional neural network-based system for endocytoscopic diagnosis of early gastric cancer

		Per–image	Per–lesion
Accuracy, % (95% CI)	CNN	83.2 (79.8–86.2)	86.1 (75.9–93.1)
	Endoscopists	76.8 (74.6–78.8)	82.4 (76.7–87.2)
Sensitivity, % (95% CI)	CNN	76.4 (71.3–81.0)	82.1 (66.5–92.5)
	Endoscopists	73.4 (70.4–76.2)	79.5 (71.0–86.4)
Specificity, % (95% CI)	CNN	92.3 (88.2–95.4)	90.9 (75.7–98.1)
	Endoscopists	81.3 (78.2–84.1)	85.9 (77.4–92.0)
PPV, % (95% CI)	CNN	93.0 (89.2–95.8)	91.4 (76.9–98.2)
	Endoscopists	83.9 (81.2–86.4)	86.9 (79.0–92.7)
NPV, % (95% CI)	CNN	74.6 (69.2–79.5)	81.1 (64.8–92.0)
	Endoscopists	69.6 (66.4–72.8)	78.0 (69.0–85.4)



Conclusions: Using the CNN in ECS-based EGC diagnosis may improve the diagnostic performance of endoscopists.


THANK YOU