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Incontri di aggiornamento del Dipartimento Oncologico

Responsabile Scientifico:
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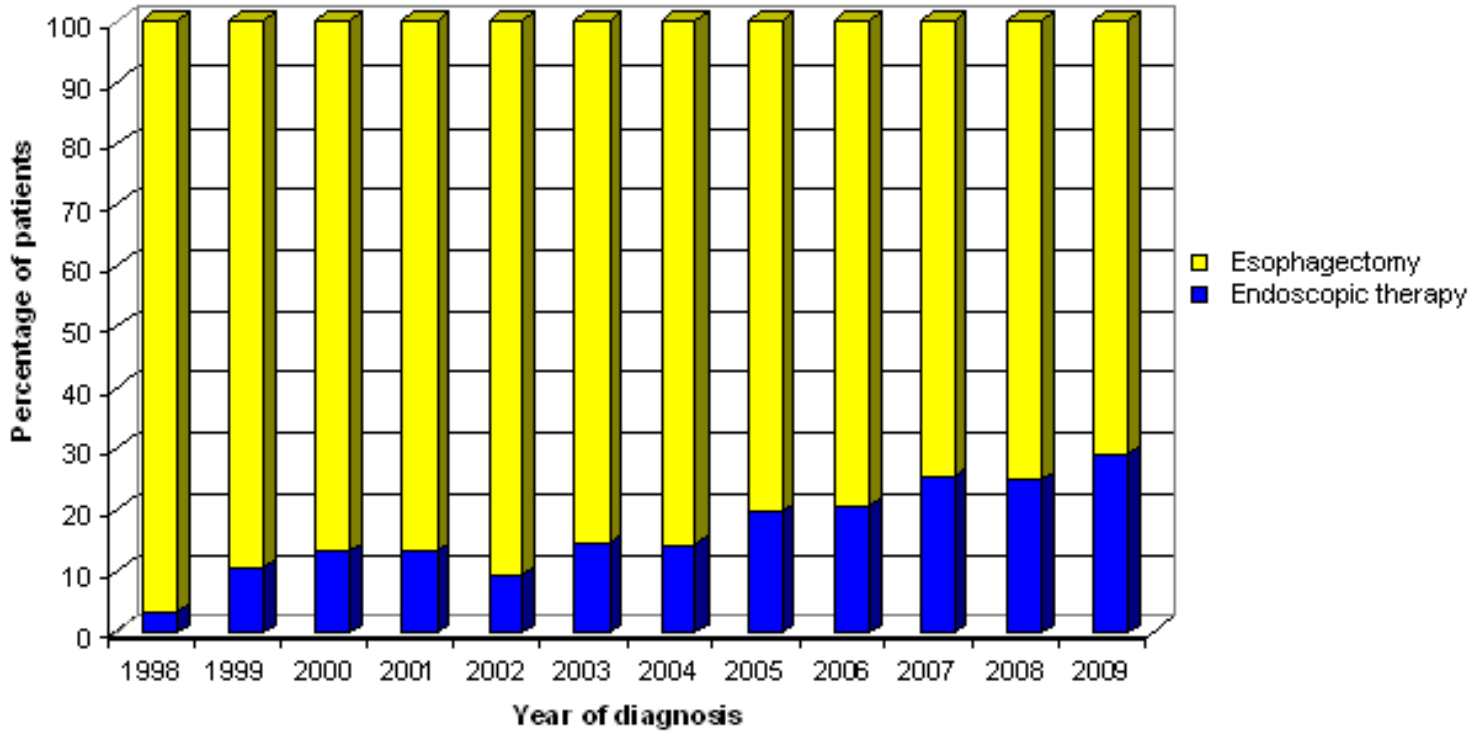
Trattamento endoscopico

13 Dicembre 2016

Survival of Patients with Superficial Esophageal Adenocarcinoma Following Endoscopic Treatment vs Surgery



Ngamruengphong S, Wolfsen HC, Wallace MB. Clin Gastro Hep 2013

Chi trattare? Con quale metodica? Quando? Perché?

ACG Clinical Guideline: Diagnosis and Management of Barrett's Esophagus

Nicholas J. Shaheen, MD, MPH, FACG[1], Gary W. Falk, MD, MS, FACG[2], Prasad G. Iyer, MD, MSc, FACG[3] and Lauren B. Gerson, MD, MSc, FACG[4]

Barrett's esophagus (BE) is among the most common conditions encountered by the gastroenterologist. In this document, the American College of Gastroenterology updates its guidance for the best practices in caring for these patients. These guidelines continue to endorse screening of high-risk patients for BE; however, routine screening is limited to men with reflux symptoms and multiple other risk factors. Acknowledging recent data on the low risk of malignant progression in patients with nondysplastic BE, endoscopic surveillance intervals are attenuated in this population; patients with nondysplastic BE should undergo endoscopic surveillance no more frequently than every 3–5 years. Neither routine use of biomarker panels nor advanced endoscopic imaging techniques (beyond high-definition endoscopy) is recommended at this time. Endoscopic ablative therapy is recommended for patients with BE and high-grade dysplasia, as well as T1a esophageal adenocarcinoma. Based on recent level 1 evidence, endoscopic ablative therapy is also recommended for patients with BE and low-grade dysplasia, although endoscopic surveillance continues to be an acceptable alternative. Given the relatively common recurrence of BE after ablation, we suggest postablation endoscopic surveillance intervals. Although many of the recommendations provided are based on weak evidence or expert opinion, this document provides a pragmatic framework for the care of the patient with BE.

SUPPLEMENTARY MATERIAL is linked to the online version of the paper at http://www.nature.com/ajg

Am J Gastroenterol advance online publication, 3 November 2015; doi:10.1038/ajg.2015.322

Recent population studies suggest that gastroesophageal reflux disease (GERD) is increasing in prevalence, both in the United States and worldwide (1,2). The diagnosis of GERD is associated with a 10–15% risk of Barrett's esophagus (BE), a change of the normal squamous epithelium of the distal esophagus to a columnar-lined intestinal metaplasia (IM). Risk factors associated with the development of BE include long-standing GERD, male gender, central obesity (3), and age over 50 years (4,5). The goal of a screening and surveillance program for BE is to identify individuals at risk for progression to esophageal adenocarcinoma (EAC), a malignancy that has been increasing in incidence since the 1970s (6,7).

The purpose of this guideline is to review the definition and epidemiology of BE, available screening modalities for BE detection, rationale and methods for surveillance, and available treatment modalities including medical, endoscopic, and surgical techniques. In order to evaluate the level of evidence and strength of recommendations, we used the GRADE (Grading of Recommendations Assessment, Development and Evaluation) system (8). The level of evidence ranged from "high" (implying that further research was unlikely to change the authors' confidence in the estimate of the effect) to "moderate" (further research would be likely to have an impact on the confidence in the estimate of effect) to "low" (further research would be expected to have an important impact on the confidence in the estimate of the effect and would be likely to change the estimate) or "very low" (any estimate of effect is very uncertain). The strength of a recommendation was graded as "strong" when the desirable effects of an intervention clearly outweighed the undesirable effects and as "conditional" when there was uncertainty about the tradeoffs. We used meta-analyses or systematic reviews when available, followed by clinical trials and cohort and case–control studies. In order to determine the level

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Communication from the ASGE Standards of Practice Committee

GUIDELINE

The role of endoscopy in Barrett's esophagus and other premalignant conditions of the esophagus

This is one of a series of statements discussing the use of GI endoscopy in common clinical situations. The Standards of Practice Committee of the American Society for Gastrointestinal Endoscopy prepared this text. In preparing this guideline, a search of the medical literature was performed using PubMed. Additional references were obtained from the bibliographies of the identified articles and from recommendations of expert consultants. When limited or no data exist from well-designed prospective trials, emphasis is given to results of large series and reports from recognized experts. Guidelines for appropriate use of endoscopy are based on a critical review of the available data and expert consensus at the time the guidelines are drafted. Further controlled clinical studies may be needed to clarify aspects of this guideline. This guideline may be revised as necessary to account for changes in technology, new data, or other aspects of clinical practice. The recommendations were based on reviewed studies and were graded on the strength of the supporting evidence (Table 1).[1] The strength of individual recommendations is based on both the aggregate evidence quality and an assessment of the anticipated benefits and harms. Weaker recommendations are indicated by phrases such as "we suggest," whereas stronger recommendations are typically stated as "we recommend."

This guideline is intended to be an educational device to provide information that may assist endoscopists in providing care to patients. This guideline is not a rule and should not be construed as establishing a legal standard of care or as encouraging, advocating, requiring, or discouraging any particular treatment. Clinical decisions in any particular case involve a complex analysis of the patient's condition and available courses of action. Therefore, clinical considerations may lead an endoscopist to take a course of action that varies from these guidelines.

Endoscopy plays an important role in the diagnosis and management of premalignant conditions of the esophagus. Early recognition of premalignant conditions provides an opportunity to prevent esophageal cancer or to diagnose it at an early stage. This guideline discusses the role of endoscopy in the management of premalignant conditions of the esophagus. The primary condition addressed will be Barrett's esophagus (BE), the only known precursor of adenocarcinoma of the esophagus, but the guideline also covers the role of endoscopy as it applies to the neoplastic potential of achalasia, aerodigestive cancers, tylosis, and caustic injuries, which have been suggested to be risk factors for squamous cell carcinoma. Discussion of other rare conditions such as esophageal GI stromal cell tumors, granular cell tumors, adenomatous polyps, and papillomas is outside the scope of this guideline.

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BARRETT'S ESOPHAGUS

Diagnosis of BE

BE has been defined in the United States by the presence of specialized intestinal metaplasia of the tubular esophagus and is recognized as a precursor lesion to esophageal adenocarcinoma (EAC). The development of BE is believed to be a reparative response to reflux-induced damage to the native squamous epithelium, with subsequent replacement with a metaplastic intestinalized epithelium, BE. Metaplastic BE is associated with increased cellular proliferation and turnover that may result in progression to dysplasia. Early studies reported up a 30- to 40-fold increased risk of the development of EAC,[2] but estimates of the risk of EAC associated with BE have been steadily decreasing in more recent, better controlled trials. In a recent population-based cohort study, the presence of BE conferred a relative risk of EAC of 11.3 over that of the general population (95% CI, 8.8-14.4).[3] Although some caution should be exercised in the interpretation of this analysis because of its retrospective nature and relatively short mean follow-up period of 5 years, these findings are consistent with the trend of decreasing risk estimates observed in multiple other studies over the past 5 to 10 years,[4-9] although the optimal prospective study has not been conducted.

BE is histologically graded as nondysplastic (NDBE), indeterminate-grade dysplasia (IGD), low-grade dysplasia (LGD), high-grade dysplasia (HGD), intramucosal carcinoma (IMC), or invasive EAC.[10] Management recommendations for BE typically do not include the approach to or management of IGD. IGD is considered by pathology experts to be an interim diagnosis, typically encountered in the presence of significant inflammation or ulceration or

TECHNOLOGY STATUS EVALUATION REPORT

Endoscopic mucosal resection

Prepared by: ASGE TECHNOLOGY COMMITTEE

Joo Ha Hwang, MD, PhD, FASGE, Vani Konda, MD, Barham K. Abu Dayyeh, MD, MPH, Shailendra S. Chauhan, MD, FASGE, Brintha K. Enestvedt, MD, MBA, Larissa L. Fujii-Lau, MD, Sri Komanduri, MD, John T. Maple, DO, FASGE, Faris M. Murad, MD, Rahul Pannala, MD, MPH, Nirav C. Thosani, MD, Subhas Banerjee, MD, FASGE, Chair

This document was reviewed and approved by the Governing Board of the American Society for Gastrointestinal Endoscopy.

The ASGE Technology Committee provides reviews of existing, new, or emerging endoscopic technologies that have an impact on the practice of GI endoscopy. Evidence-based methodology is used, by using a MEDLINE literature search to identify pertinent clinical studies on the topic and a MAUDE (U.S. Food and Drug Administration Center for Devices and Radiological Health) database search to identify the reported adverse events of a given technology. Both are supplemented by accessing the "related articles" feature of PubMed and by scrutinizing pertinent references cited by the identified studies. Controlled clinical trials are emphasized, but in many cases, data from randomized, controlled trials are lacking. In such cases, large case series, preliminary clinical studies, and expert opinions are used. Technical data are gathered from traditional and Web-based publications, proprietary publications, and informal communications with pertinent vendors. For this review, the MEDLINE database was searched for publications in English through September 2014 by using the keywords "endoscopic lesion removal," "endoscopic resection," "endoscopic mucosal resection," and "EMR."

Technology Status Evaluation Reports are drafted by 1 or 2 members of the ASGE Technology Committee, reviewed and edited by the committee as a whole, and approved by the Governing Board of the ASGE. When financial guidance is indicated, the most recent coding data and list prices at the time of publication are provided. Technology Status Evaluation Reports are scientific reviews provided solely for educational and informational purposes. Technology Status Evaluation Reports are not rules and should not be construed as establishing a legal standard of care or as encouraging, advocating, requiring, or discouraging any particular treatment or payment for such treatment.

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http://dx.doi.org/10.1016/j.gie.2015.05.001

BACKGROUND

EMR was developed for minimally invasive, organ-sparing endoscopic removal of benign and early malignant lesions in the GI tract. This report focuses on instruments, injection solutions, and techniques currently used for EMR. This report is an update of a previous Technology Status Evaluation Report titled "Endoscopic Mucosal Resection and Endoscopic Submucosal Dissection."[1] The topic of endoscopic submucosal dissection (ESD) is now discussed in a separate Technology Status Report.[2]

TECHNOLOGY UNDER REVIEW: EMR

EMR is an endoscopic technique developed for the removal of sessile or flat neoplasms confined to the superficial layers (mucosa and submucosa) of the GI tract. The commonly used techniques can be categorized as injection-, cap-, and ligation-assisted EMR. Underwater EMR is a newer technique that is useful, particularly for salvage EMR.

Proper patient and lesion selection for EMR with endoscopic and/or endosonographic evaluations is essential. Before the start of any EMR procedure, close visual inspection to delineate the margins, particularly of flat lesions, is imperative because manipulation of the lesion may obscure landmarks. It may be helpful to mark the margins of the targeted lesion with superficial cautery marks with the tip of a snare or with argon plasma coagulation (APC). Electrosurgical unit settings for polypectomy and EMR are discussed in a previous Technology committee document.[3] A retrieval device may then be used to retrieve EMR specimens.

Injection-assisted EMR

Injection-assisted EMR is also often called saline solution lift–assisted polypectomy. This technique was introduced in 1955 for rigid sigmoidoscopy and then in 1973 for flexible colonoscopy.[4,5] The procedure starts with injection of

Annals of Gastroenterology (2014) **27,** 1-8

Magnification endoscopy in esophageal squamous cell carcinoma: a review of the intrapapillary capillary loop classification

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Abstract

Recent developments in image-enhancement technology have enabled clear visualization of the microvascular structure of the esophageal mucosa. In particular, intrapapillary capillary loops (IPCLs) are observed as brown loops on magnification endoscopy with narrow-band imaging (NBI). IPCLs demonstrate characteristic morphological changes according to the structural irregularity of esophageal epithelium and cancer infiltration, summarized in the IPCL classification. In this review, the process from the first endoscopic description of IPCLs to the eventual development of the IPCL classification is described and discussed, particularly focusing on early stage squamous cell carcinoma of the esophagus.

Keywords intrapapillary capillary loop classification, narrow-band imaging, magnification endoscopy, endoscopic mucosal resection, endoscopic submucosal dissection

Ann Gastroenterol 2014; 27 (5): 1-8

Introduction

Early detection of esophageal squamous cell carcinoma is directly related to improved prognosis [1,2]. Lesions confined to the mucosal layer can be treated by local endoscopic resection (endoscopic mucosal resection [EMR]/ endoscopic submucosal dissection [ESD]) [3-6] and/or endoscopic ablation [7] instead of surgery [8,9], because there is usually no risk of lymph node metastasis [1,2,10,11]. Therefore, a major target of endoscopic screening is to pick up these early, endoscopically resectable lesions [12-14]. A submucosally invasive cancer often demonstrates considerable morphological changes: elevated (0-I) and/ or excavation (0-IIc/III) on standard non-magnified imaging [15]. This surface change is accompanied by a destruction of the original mucosal structure [11,15]. By contrast, an intramucosal cancer generally has a flat appearance with minimal impact on the contour of the mucosal surface (0-IIa, IIb, IIc). However, the relationship of these appearances with the depth of invasion is not always quantitative and clear. An endoscopic diagnosis based solely on this gross, macroscopic appearance of a tumor is therefore of limited value. It definitely needs to be stated that deciding whether a lesion is intramucosal or submucosally invasive (SM) has profound implications of the treatment modality chosen. It is essential, therefore, to have an additional - more accurate - method of determining the depth of invasion. In addition, the differential diagnosis of high- from low-grade intraepithelial neoplasia is also important, because high-grade intraepithelial neoplasia should be treated by endoscopic resection. When Lugol staining is employed, among Lugol-voiding areas a useful endoscopic criterion to detect high-grade intraepithelial neoplasia or intramucosal cancer is the "pink-color" sign [16,17](Fig. 1A). This is readily identified as the "metallic silver" sign when it is seen with narrow-band imaging (NBI) enhancement [18](Fig. 1B). However, flat unstained areas smaller than 5 mm are usually not high-grade dysplasia. These can be disregarded during endoscopy in order to save procedural time [19]. While the diagnostic accuracy of these criteria is acceptable, there still remains considerable room for improvement, particularly in the diagnosis of border-line lesions. In this situation, an accurate endoscopic diagnosis with magnification endoscopy is practically more important, considering the inter- and intra-observer variation for histologic assessment and the uncertainty that this generates [20].

NBI is in use as a novel image enhancement technology [21] employing light filters to allow penetration at peak wavelengths of 415 (390-445) nm and 540 (530-550) nm. Light in these "narrow bands" is readily absorbed by hemoglobin, such that blood vessels on the mucosal surface are highlighted brown

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Conflict of Interest: Haruhiro Inoue is an advisor for Olympus

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The Society of Thoracic Surgeons Guidelines on the Diagnosis and Staging of Patients With Esophageal Cancer

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Executive Summary

Diagnosis of Esophageal Cancer

Flexible endoscopy with biopsy is the primary method for the diagnosis of esophageal carcinoma (Class I recommendation: level of evidence B)

For related article, see page 7

Staging of Esophageal Cancer

1. For early stage esophageal cancer, computed tomography of the chest and abdomen is an optional test for staging. (Class I recommendation: level of evidence B)
2. For locoregionalized esophageal cancer, computed tomography of the chest and abdomen is a recommended test for staging. (Class I recommendation: level of evidence B)
3. For early stage esophageal cancer, positron emission tomography is an optional test for staging. (Class IIB recommendation: level of evidence B)
4. For locoregionalized esophageal cancer, positron emission tomography is a recommended test for staging. (Class I recommendation: level of evidence B)
5. In the absence of metastatic disease, endoscopic ultrasonography is recommended to improve the accuracy of clinical staging. (Class IIA recommendation: level of evidence B)
6. Endoscopic mucosal resection should be considered as a diagnostic/staging tool for small, discrete nodules or areas of dysplasia when the disease appears limited to the mucosa or submucosa as assessed by endoscopic ultrasonography. (Class IIA recommendation: level of evidence B)
7. For locally advanced (T3/T4) adenocarcinoma of the esophagogastric junction infiltrating the anatomic cardia, or Siewart type III esophagogastric tumors, laparoscopy is recommended to improve the accuracy of staging. (Class IIB recommendation: level of evidence C)

Introduction

Esophageal cancer is among the 10 most frequent cancers in the world, and is the seventh leading cause of cancer death. In 2010, the American Cancer Society estimated 16,640 adults (13,130 men and 3,510 women) in the United States would be diagnosed with esophageal cancer, and there would be 14,500 deaths (11,650 men and 2,850 women) [1]. For the past 4 decades, the incidence of esophageal cancer in the United States has increased at the fastest rate of any solid tumor [2–4].

Despite advances in treatment regimens, esophageal cancer remains one of the most lethal of all cancers with a dismal overall 5-year survival rate of less than 15%. The optimal treatment for localized esophageal cancer remains one of the most widely debated topics in oncology. Esophagectomy is considered the gold standard for localized disease. Although patients with early

Drs Varghese, Hofstetter, Rizk, Low, Darling, Watson, Mitchell, and Krasna have no conflicts of interest to declare regarding this work.

Report from STS Workforces on Evidence Based Surgery and General Thoracic Surgery.

The Society of Thoracic Surgeons Clinical Practice Guidelines are intended to assist physicians and other health care providers in clinical decision making by describing a range of generally acceptable approaches for the diagnosis, management, or prevention of specific diseases or conditions. These guidelines should not be considered inclusive of all proper methods of care or exclusive of other methods of care reasonably directed at obtaining the same results. Moreover, these guidelines are subject to change over time, without notice. The ultimate judgment regarding the care of a particular patient must be made by the physician in light of the individual circumstances presented by the patient.

For the full text of this and other STS Practice Guidelines, visit http://www.sts.org/resources-publications on the official STS website (www.sts.org).

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http://dx.doi.org/10.1016/j.athoracsur.2013.02.069

Endoscopic submucosal dissection: European Society of Gastrointestinal Endoscopy (ESGE) Guideline

Authors Pedro Pimentel-Nunes[1], Mário Dinis-Ribeiro[1], Thierry Ponchon[2], Alessandro Repici[3], Michael Vieth[4], Antonella De Ceglie[5], Arnaldo Amato[6], Frieder Berr[7], Pradeep Bhandari[8], Andrzej Bialek[9], Massimo Conio[10], Jelle Haringsma[11], Cord Langner[12], Søren Meisner[13], Helmut Messmann[14], Mario Morino[15], Horst Neuhaus[16], Hubert Piessevaux[17], Massimo Rugge[18], Brian P. Saunders[19], Michel Robaszkiewicz[20], Stefan Seewald[21], Sergey Kashin[22], Jean-Marc Dumonceau[23], Cesare Hassan[24], Pierre H. Deprez[17]

Institutions Institutions listed at end of article

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This Guideline is an official statement of the European Society of Gastrointestinal Endoscopy (ESGE). The Grading of Recommendations Assessment, Development, and Evaluation (GRADE) system [1, 2] was adopted to define the strength of recommendations and the quality of evidence.

Main recommendations

1 ESGE recommends endoscopic en bloc resection for superficial esophageal squamous cell cancers (SCCs), excluding those with obvious submucosal involvement (strong recommendation, moderate quality evidence). Endoscopic mucosal resection (EMR) may be considered in such lesions when they are smaller than 10 mm if en bloc resection can be assured. However, ESGE recommends endoscopic submucosal dissection (ESD) as the first option, mainly to provide an en bloc resection with accurate pathology staging and to avoid missing important histological features (strong recommendation, moderate quality evidence).

2 ESGE recommends endoscopic resection with a curative intent for visible lesions in Barrett's esophagus (strong recommendation, moderate quality evidence). ESD has not been shown to be superior to EMR for excision of mucosal cancer, and for that reason EMR should be preferred. ESD may be considered in selected cases, such as lesions larger than 15 mm, poorly lifting tumors, and lesions at risk for submucosal invasion (strong recommendation, moderate quality evidence).

3 ESGE recommends endoscopic resection for the treatment of gastric superficial neoplastic lesions that possess a very low risk of lymph node metastasis (strong recommendation, high quality evidence). EMR is an acceptable option for lesions smaller than 10–15 mm with a very low probability of advanced histology (Paris 0-IIa). However, ESGE recommends ESD as treatment of choice for most gastric superficial neoplastic lesions (strong recommendation, moderate quality evidence).

4 ESGE states that the majority of colonic and rectal superficial lesions can be effectively removed in a curative way by standard polypectomy and/or by EMR (strong recommendation, moderate quality evidence). ESD can be considered for removal of colonic and rectal lesions with high suspicion of limited submucosal invasion that is based on two main criteria of depressed morphology and irregular or nongranular surface pattern, particularly if the lesions are larger than 20 mm; or ESD can be considered for colorectal lesions that otherwise cannot be optimally and radically removed by snare-based techniques (strong recommendation, moderate quality evidence).

Abbreviations

AJCC/UICC	American Joint Committee on Cancer/Union for International Cancer Control
APC	argon plasma coagulation
CI	confidence interval
CT	computed tomography
EMR	endoscopic mucosal resection
EMRc	endoscopic mucosal resection with cap
ESD	endoscopic submucosal dissection
EUS	endoscopic ultrasonography
HGD	high grade dysplasia
HGIN	high grade intraepithelial neoplasia
LST	laterally spreading tumor
MRI	magnetic resonance imaging
NBI	narrow band imaging
OR	odds ratio
PET	positron emission tomography
RFA	radiofrequency ablation
SCC	squamous cell cancer
WHO	World Health Organization

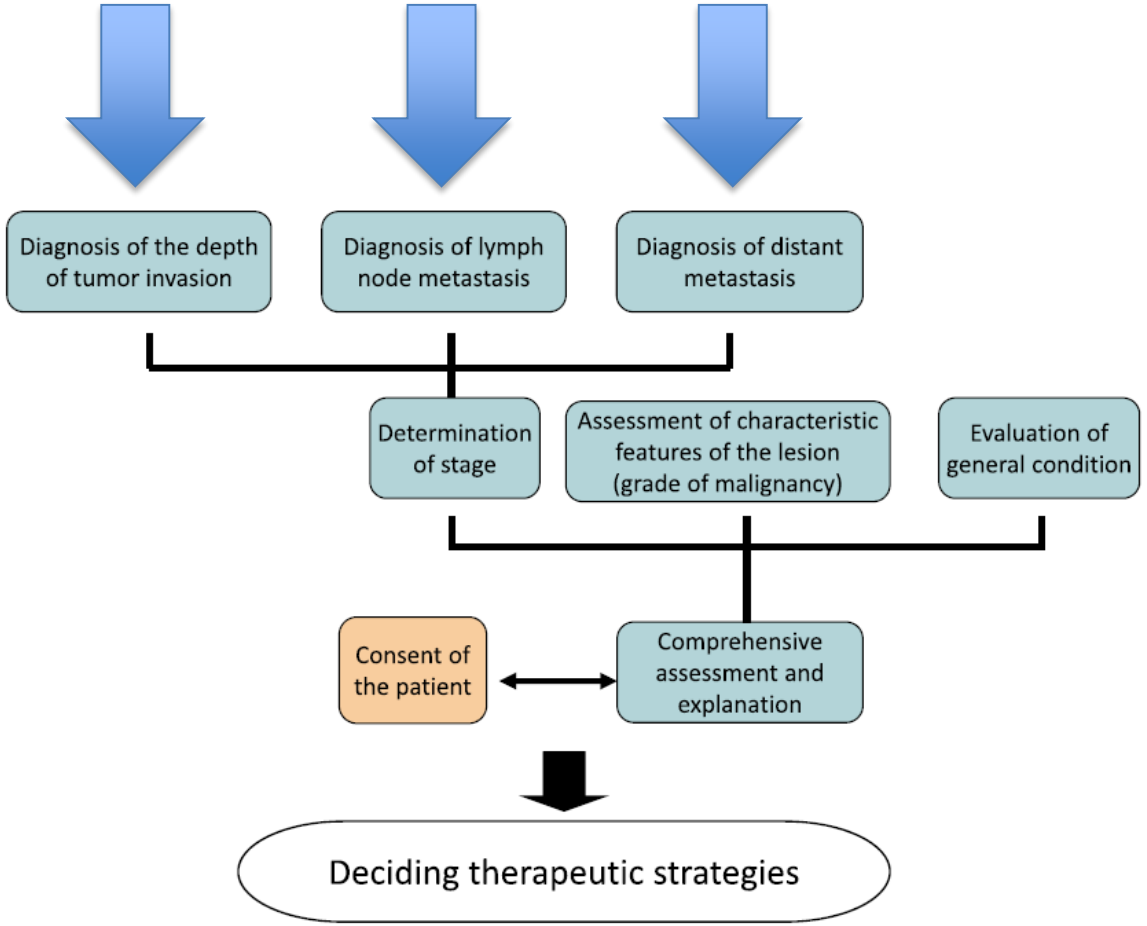
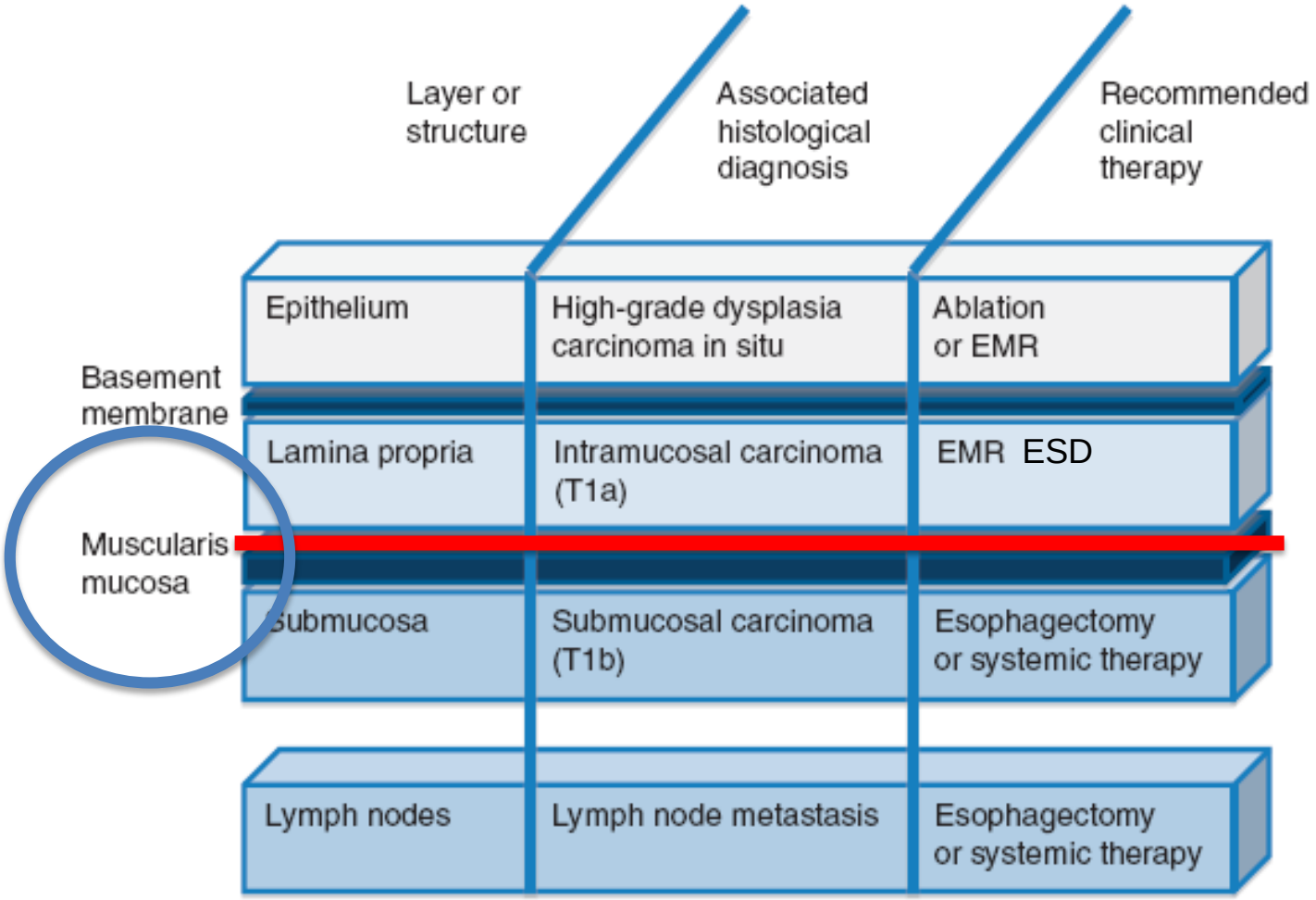


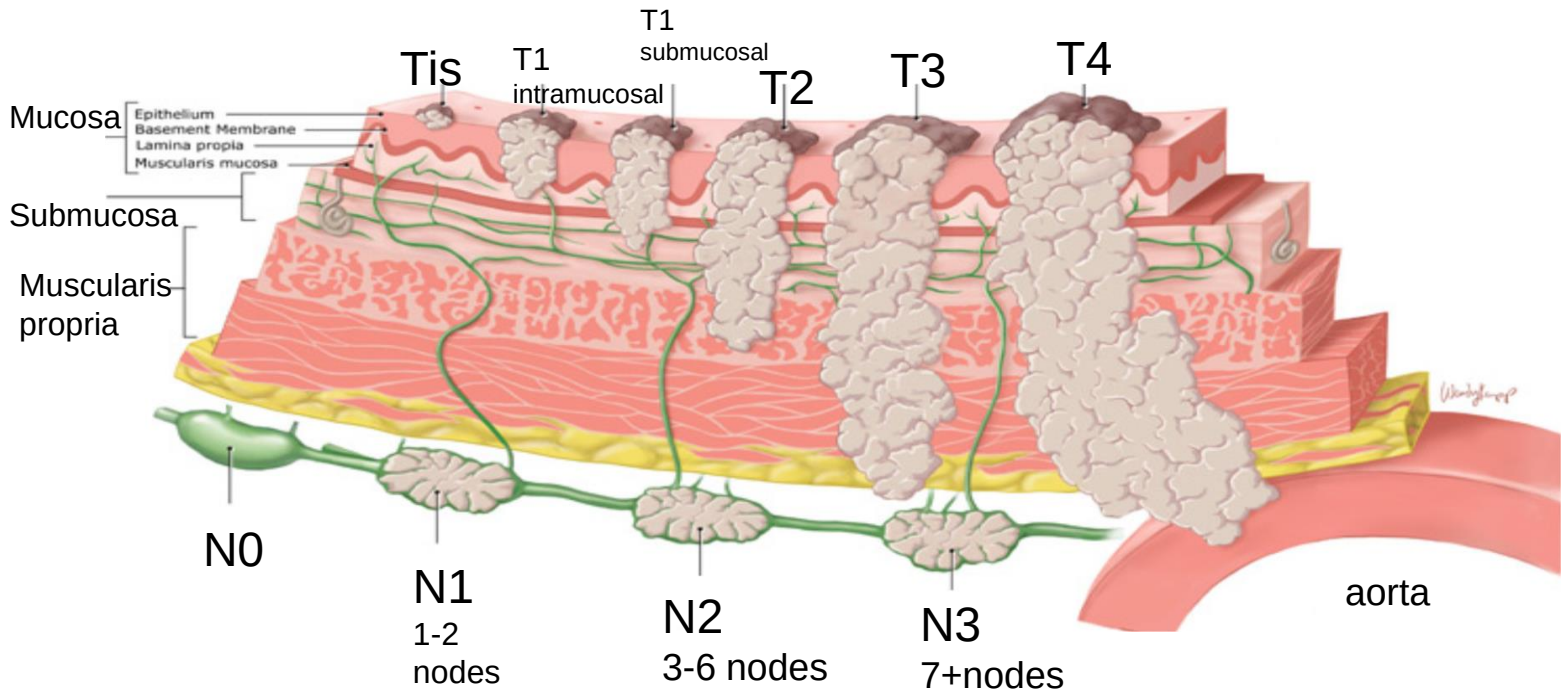
Fig. 2 Algorithm for deciding the therapeutic strategies for esophageal carcinoma

Impact of Staging on Esophageal Cancer



Konda, V.J. Am J Gastroenterol 2012; 107: 827-833

GOALS


Mucosa
Epithelium
Basement Membrane
Lamina propia
Muscularis mucosa
Submucosa
Muscularis propria
Tis
T1 intramucosal
T1 submucosal
T2
T3
T4
N0
N1
1-2 nodes
N2
3-6 nodes
N3
7+nodes
aorta

GOALS

L'incidenza di metastasi linfonodali è strettamente legata a:

- profondità di invasione
- al tipo istologico
- grado di differenziazione
- invasione linfatica e vascolare

I fattori che influenzano la profondità di invasione includono:

- pattern endoscopico
- le dimensioni della lesione
- caratteri istologici (l'invasione profonda, grado di differenziazione (G1–2, vs. G3) invasione linfovascolare).

Questi parametri possono essere valutati meglio con **resezioni en bloc**

Definition and Staging of Early Esophageal, Gastric and Colorectal Cancer

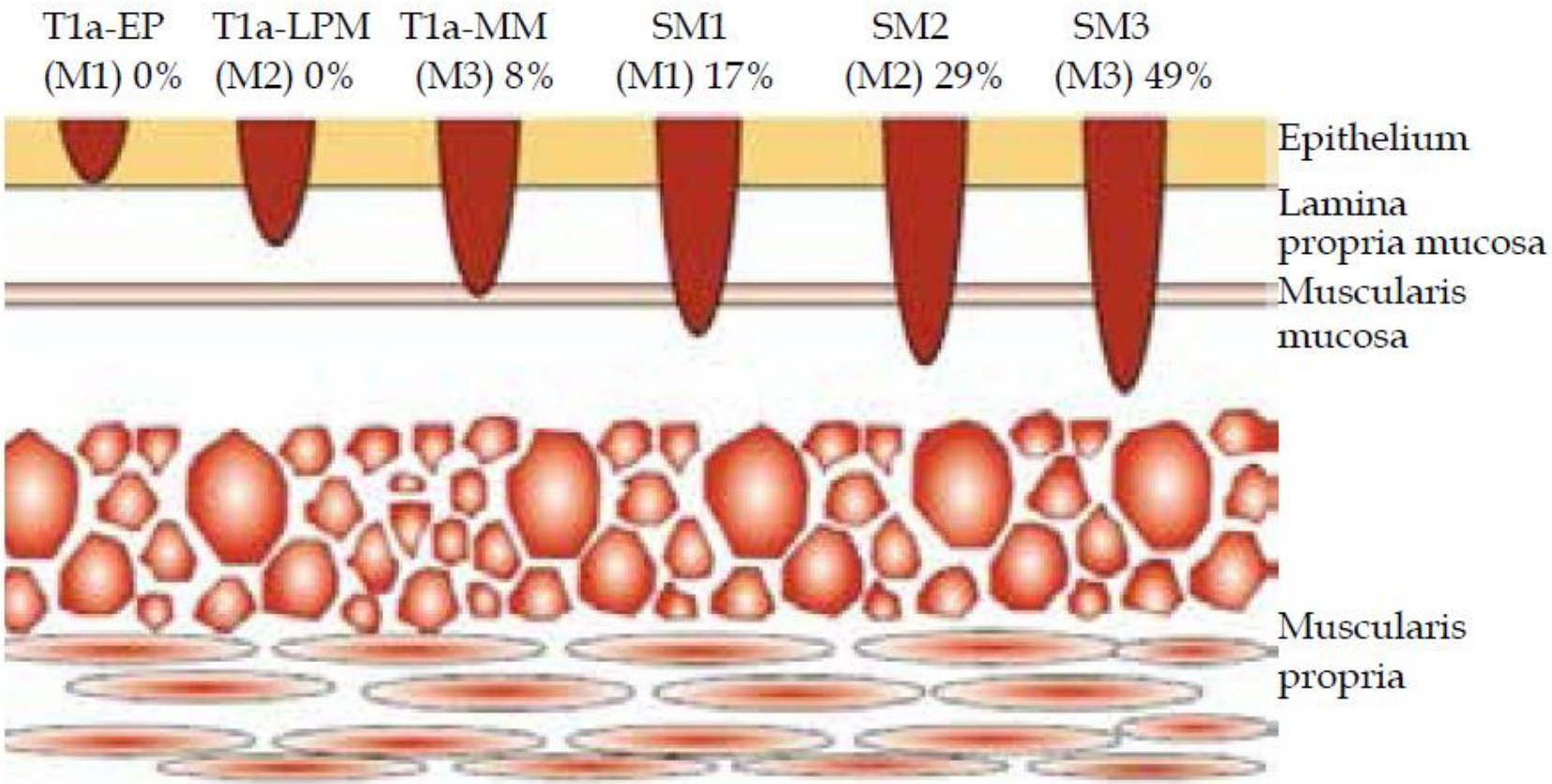


Figure 2 A Subclassification for superficial **esophageal** cancer and rate of lymph node metastases according to depth of invasion. (modified from the Guidelines for Esophageal Cancer Treatment).

Eleftheriadis N et al, Journal of Tumor 2014 July 18 2(7): 161-178

ESGE Main recommendations

1 ESGE recommends endoscopic en bloc resection for superficial esophageal squamous cell cancers (SCCs), excluding those with obvious submucosal involvement (strong recommendation, moderate quality evidence). Endoscopic mucosal resection (EMR) may be considered in such lesions when they are smaller than 10 mm if en bloc resection can be assured. However, ESGE recommends endoscopic submucosal dissection (ESD) as the first option, mainly to provide an en bloc resection with accurate pathology staging and to avoid missing important histological features (strong recommendation, moderate quality evidence).

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SCC

ESD en bloc preferibile

EMR se < 10 mm (en bloc)

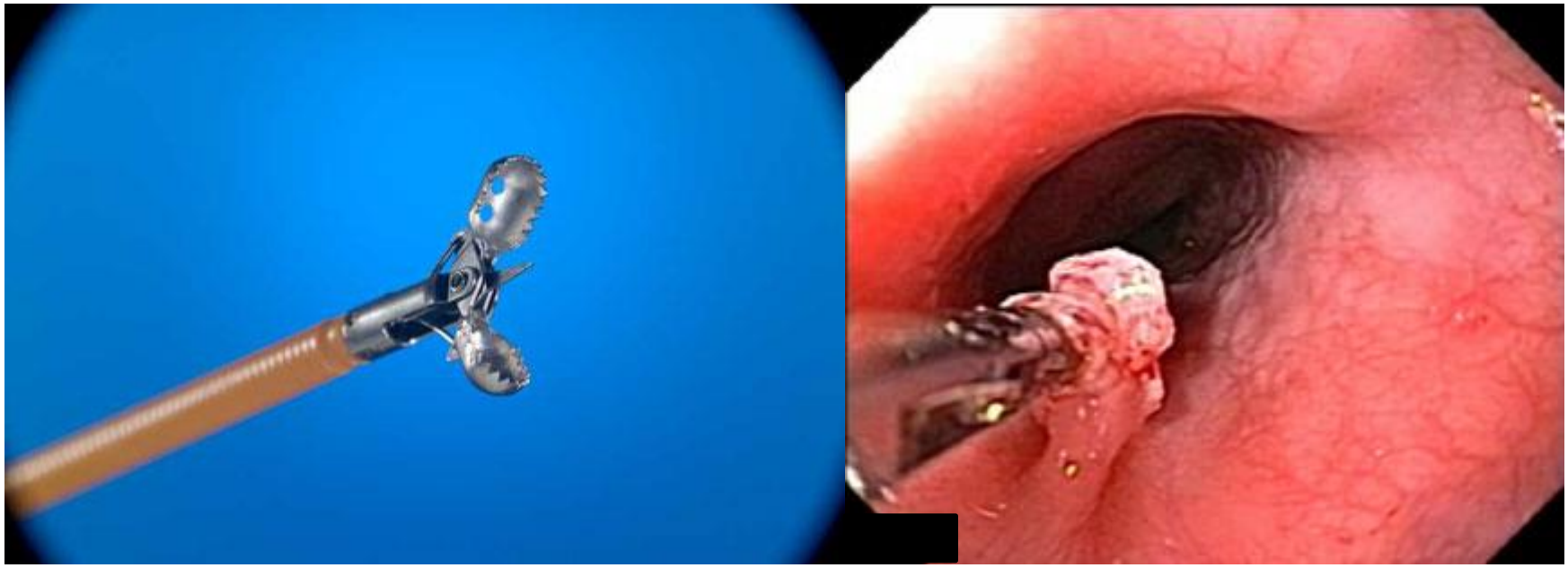
No piecemeal

Barrett + HGD o ADK

EMR

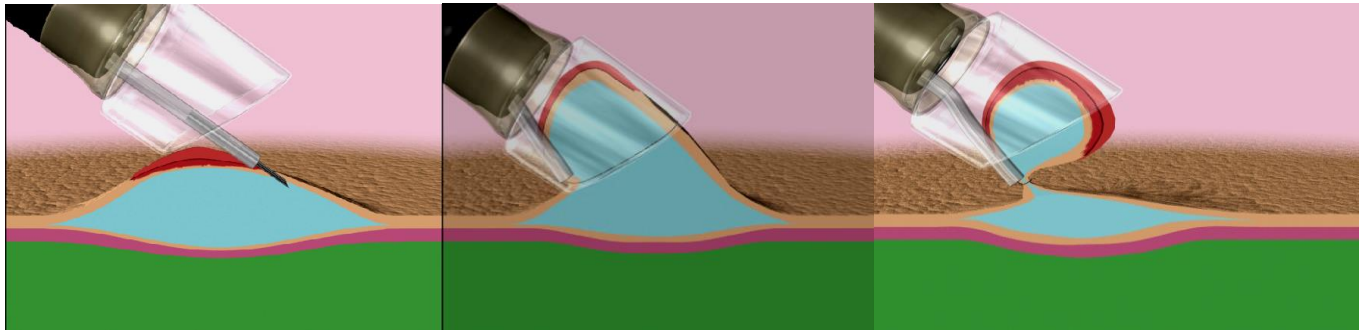
ESD > 15 mm e/o alto rischio di invasione profonda, scarso lift sign

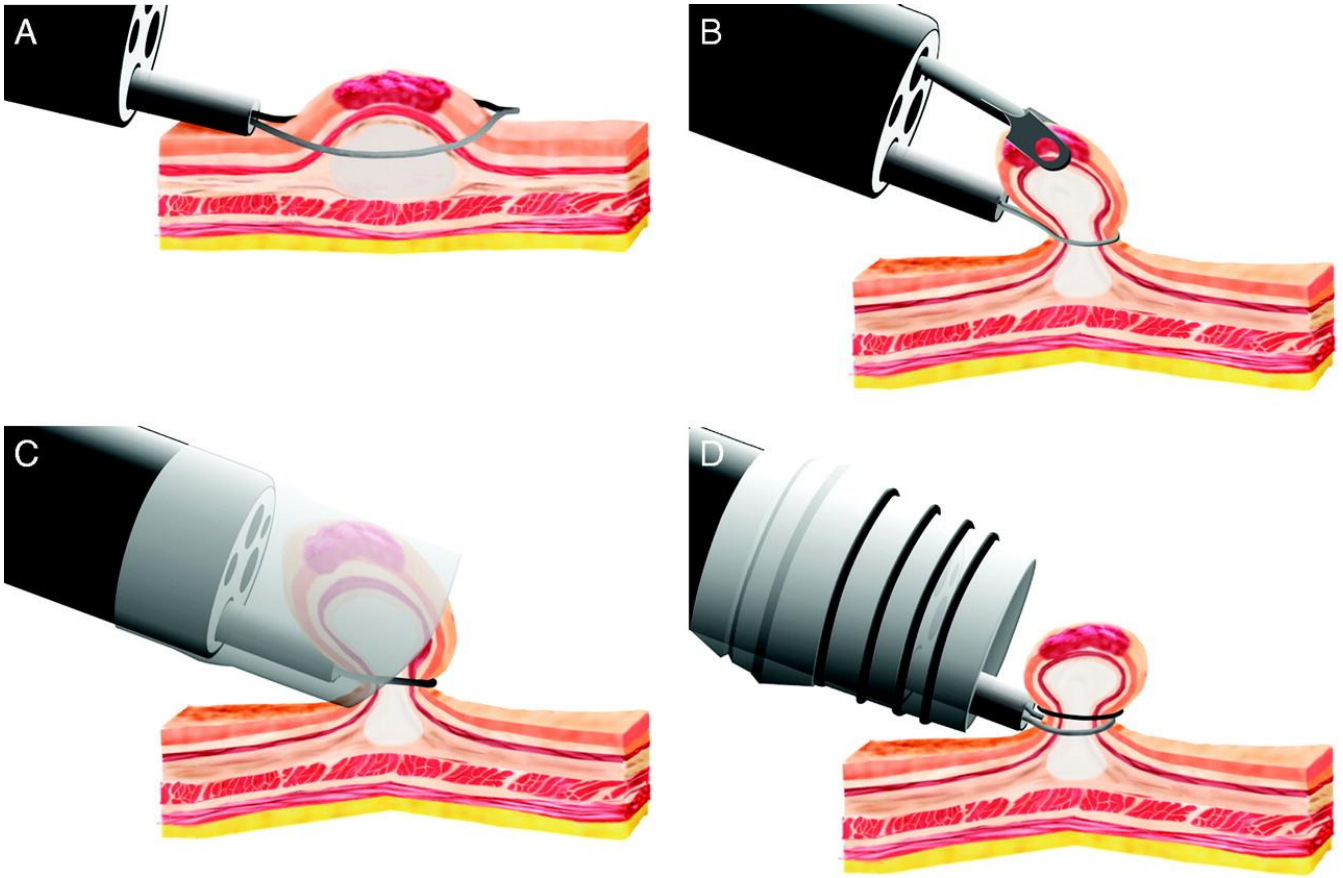
Biopsy of the lesion before EMR may result in a false-positive result due to fibrosis at the biopsy site. Because the result of mucosal biopsies is unlikely to alter treatment algorithms, biopsy prior to referral for EMR should be avoided. If biopsy is undertaken, minimization of the time interval between biopsy and EMR may help reduce false-positive results.



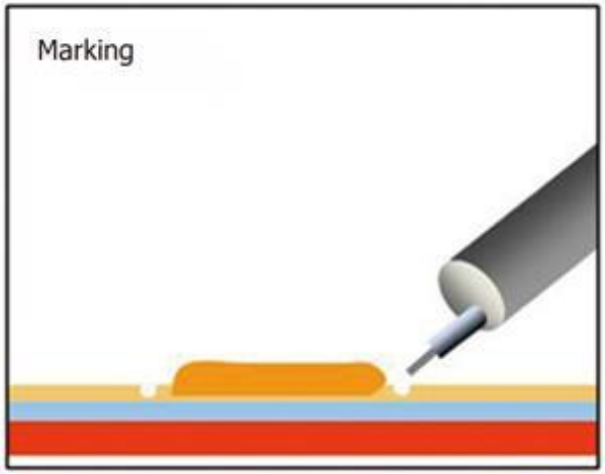
Han KS et al. Prolongation of the period between biopsy and EMR can influence the nonlifting sign in endoscopically resectable colorectal cancers. Gastrointest Endosc. 2008 Jan. 67(1):97-102

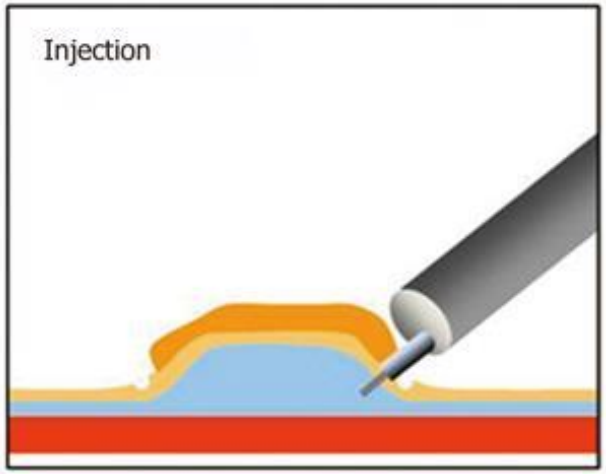
EMR (Endoscopic Mucosal Resection)

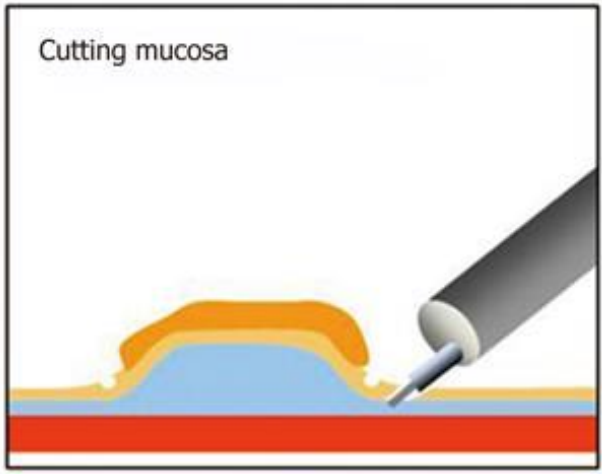


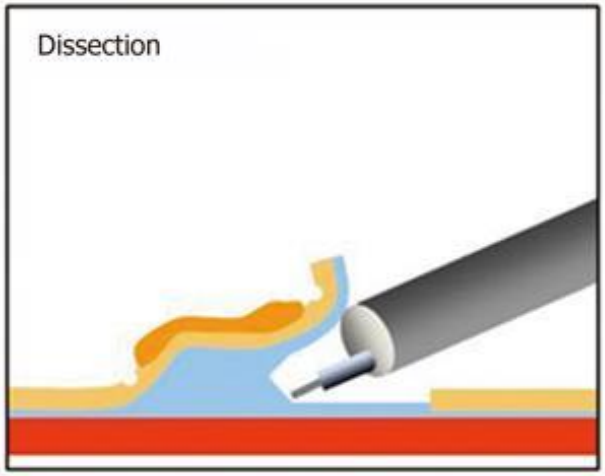


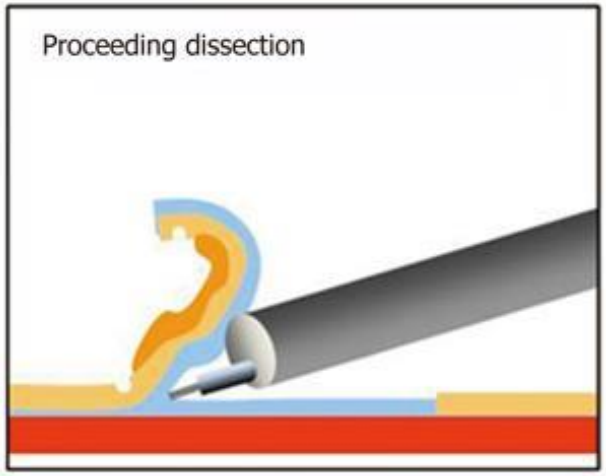
ESD (Endoscopic Submucosal Dissection)

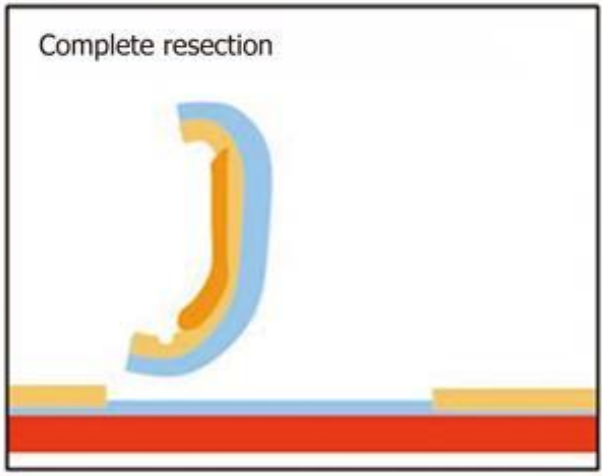




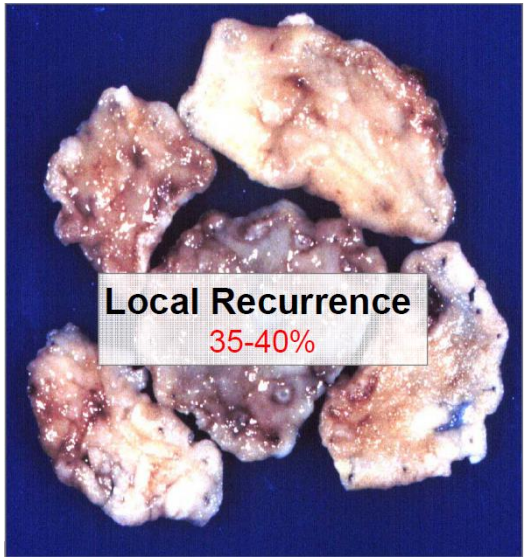






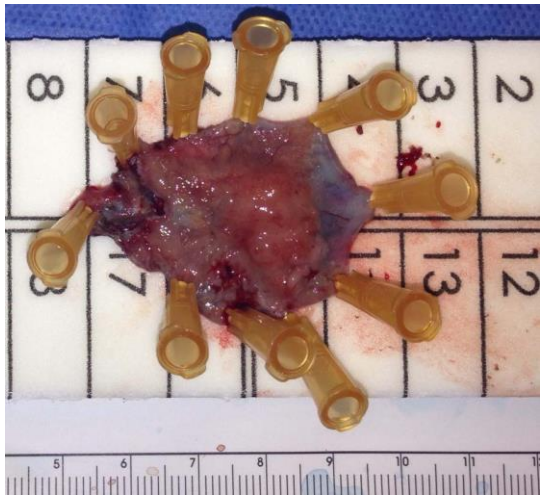


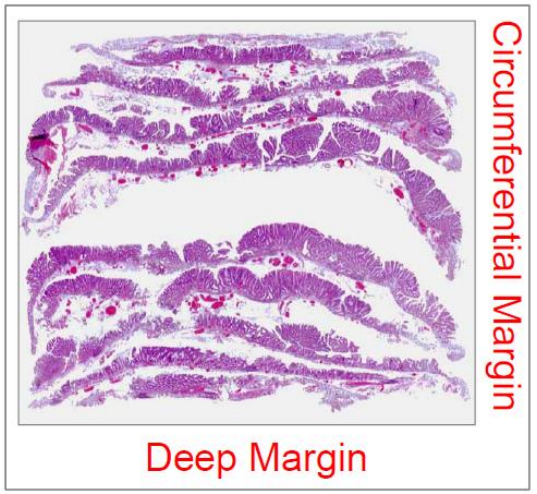
EMR (piecemeals)



Margini?

ESD (en bloc)



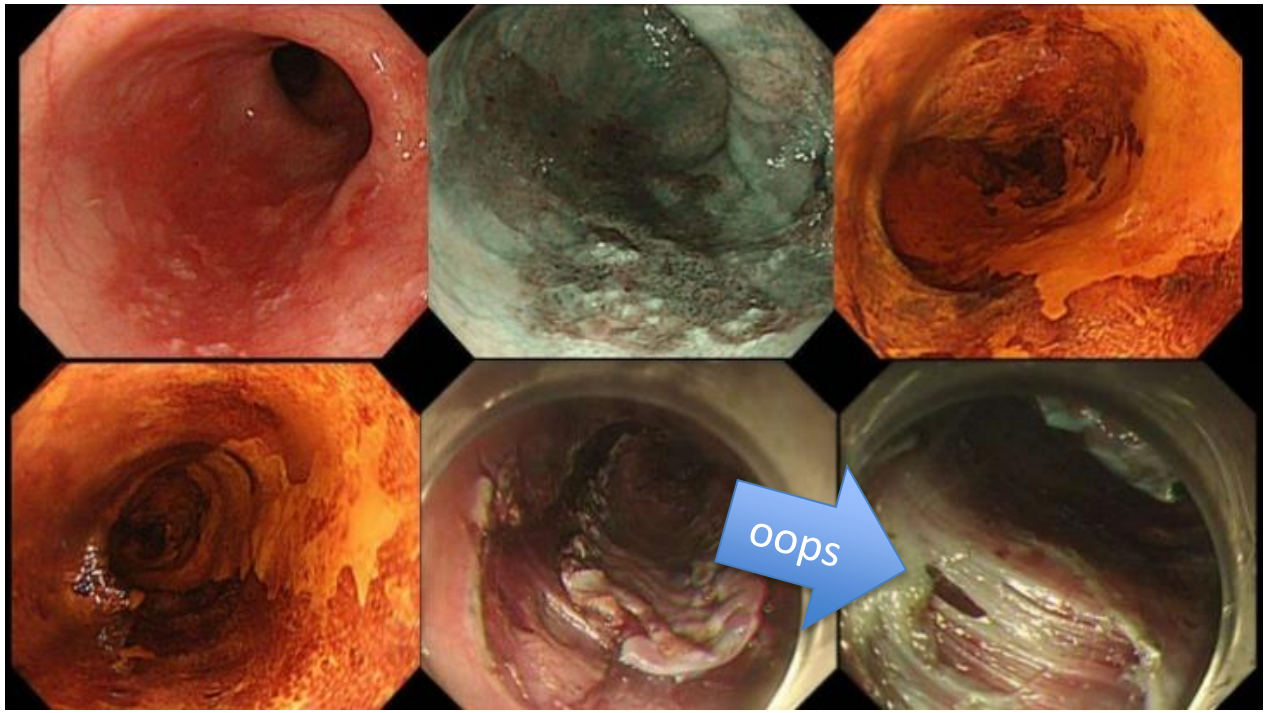


Carcinoma squamoso superficiale

La terapia endoscopica rappresenta il trattamento di riferimento per il carcinoma squamoso superficiale m1 (intraepiteliale) o m2 (invade la lamina propria), con un rischio linfonodale pressoché nullo.

Il rischio aumenta:

8%–18%	lesioni che invadono la muscolaris mucosae (m3)
11%–53%	lesioni che invadono la sottomucosa fino a 200 µm o meno (sm1)
30%–54%	lesioni più profonde (sm2).

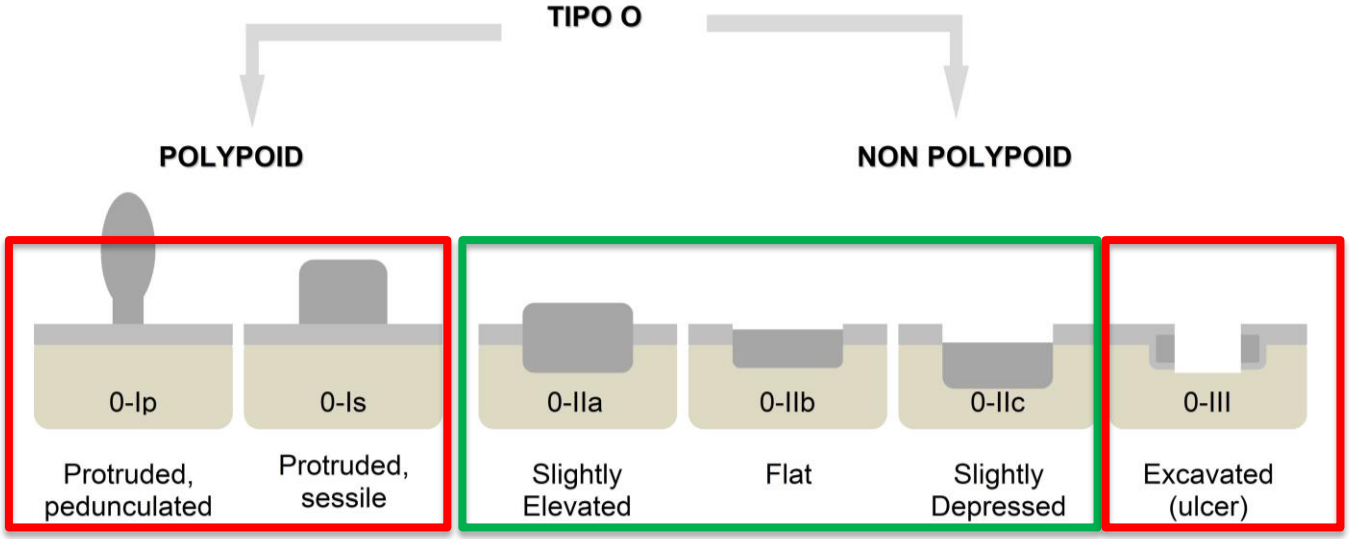


- Le lesioni tipo 0–I e 0–III della class. di Parigi presentano molto spesso infiltrazione sottomucosa e quindi non sono l'indicazione corretta al trattamento endoscopico
- I tipi 0–IIa, 0–IIb, e 0–IIc presentano lesioni intramucose

- In accordo con le "GL for treatment of esophageal cancer" della Japan Esophageal Society, la indicazione **assoluta** alla terapia endoscopica è:

  lesioni piatte (Parigi 0–II), con interessamento m1–m2, ed estensione circonferenziale ≤2/3

  Le indicazioni **relative** sono definite come lesioni m3–sm1 con una estensione circonferenziale ≥3/4



Definition and Staging of Early Esophageal, Gastric and Colorectal Cancer

Table 6 Absolute (+relative) indications for endoscopic resection of neoplastic lesions.

Factor	Esophagus	Stomach, Barrett's esophagus, colorectum
Histology	High-grade (+low-grade) dysplasia, squamous cell carcinoma	High-grade (+ low-grade) adenoma/dysplasia well- or moderately (+ poorly) differentiated adenocarcinoma
Depth	m1, m2 (+m3, sm1) [1]	m (+sm1) [1]
Type	IIa, IIb, IIc, but not I or III	IIa, IIb, IIc without scar, I, but not III
Size	<3 cm (+larger lesions), <three-quarters of circumference (+whole circumference)	IIa, I: <2 cm (+larger lesions), IIc: <1 cm (+1 ~ 3cm) (+poorly differentiated carcinoma ,< 1 cm)

[1] m: Mucosa; m1, intraepithelial extension; m2: invasion into the lamina propria but not reaching the muscularis mucosae; m3: intramucosal invasion reaching the muscularis mucosae; sm1: invasion into the superficial portion of the submucosal.

Eleftheriadis N et al, Journal of Tumor 2014 July 18 2(7): 161-178

Con la ESD, questi criteri sono stati **allargati** includendo trattamenti endoscopici di lesioni **maggiori di 3** cm occupanti anche **l'intera circonferenza** dell'esofago (sempre che siano ristrette alla sola mucosa).

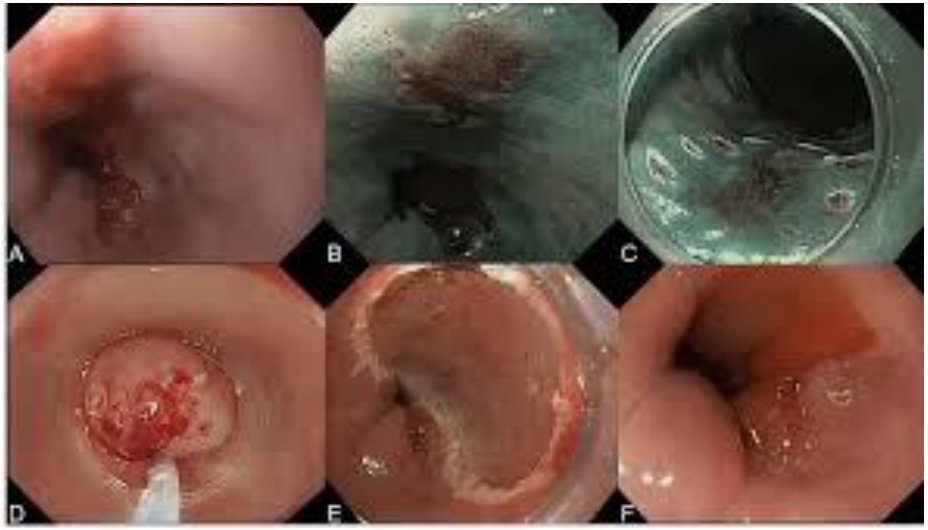
L'ESD allargata può essere presa in considerazione come metodica curativa in pazienti particolarmente anziani o che non desiderino o che non possano per comorbità essere sottoposti ad intervento chirurgico anche fino ad un interessamento m3 o sm1, in tumori ben differenziati, senza infiltrazione vascolare e/o linfatica e con margini negativi.

Esofago di Barrett

- ESGE raccomanda la resezione endoscopica con intento curativo di tutte le lesioni visibili nell'esofago di Barrett.
- La ESD in questo campo **non** si è dimostrata superiore alla EMR per la cura dei tumori mucosi, e per tale ragione dovrebbe essere preferita quest'ultima.

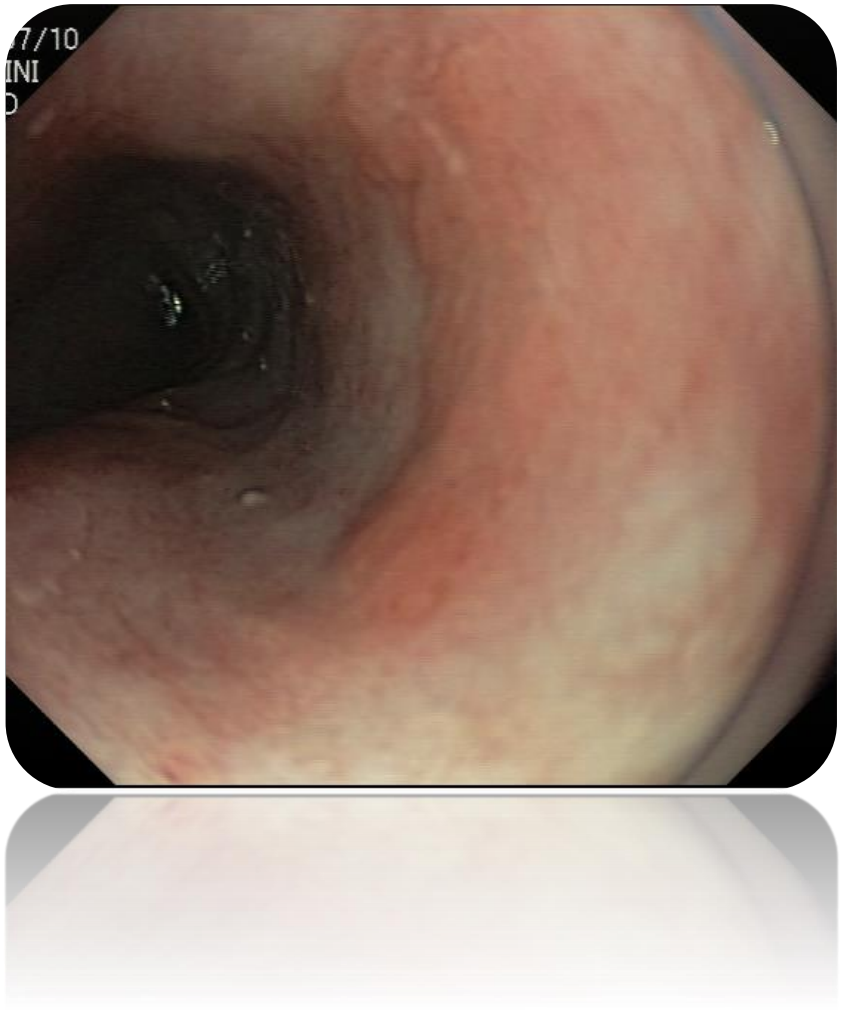
- La ESD dovrebbe essere preferita per lesioni superiori ai 15 mm, con scarso segno del lifting, e per lesioni a forte rischio di interessamento sottomucoso.
- Pochissimi dati in letteratura di ESD in Barrett.
- EMR è il gold standard nella pratica clinica corrente per l'eradicazione delle lesioni visibili nel Barrett.

- I pazienti con esofago di Barrett e displasia di alto grado (HGD) senza lesioni visibili o con cancro intramucoso (flat HGD/cancro intramucoso) dovrebbero venire trattati con ablazione con radiofrequenza (RFA).

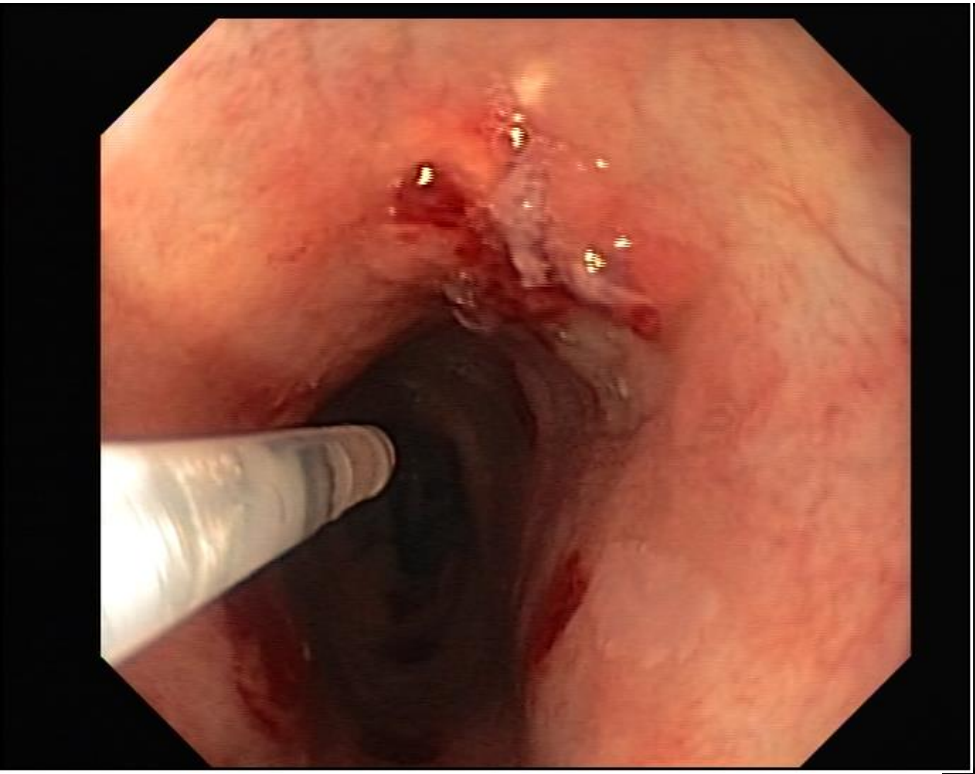


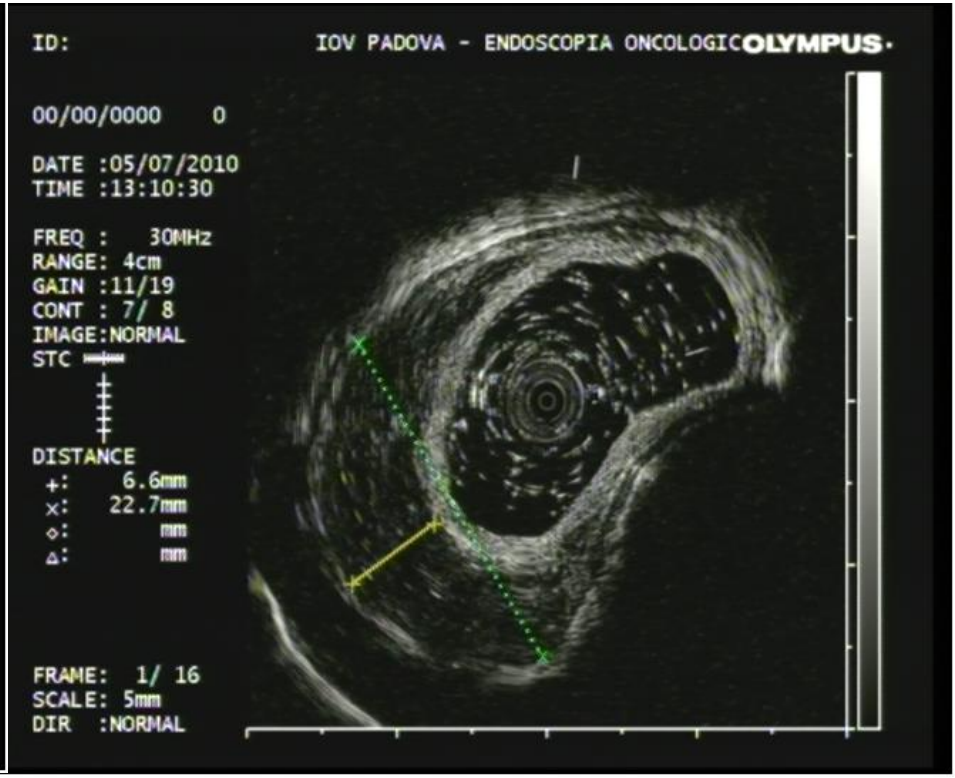
Adenocarcinoma in Barrett

Barrett “lungo” e bx con HGD su area rilevata Parigi IIa a 27 cm

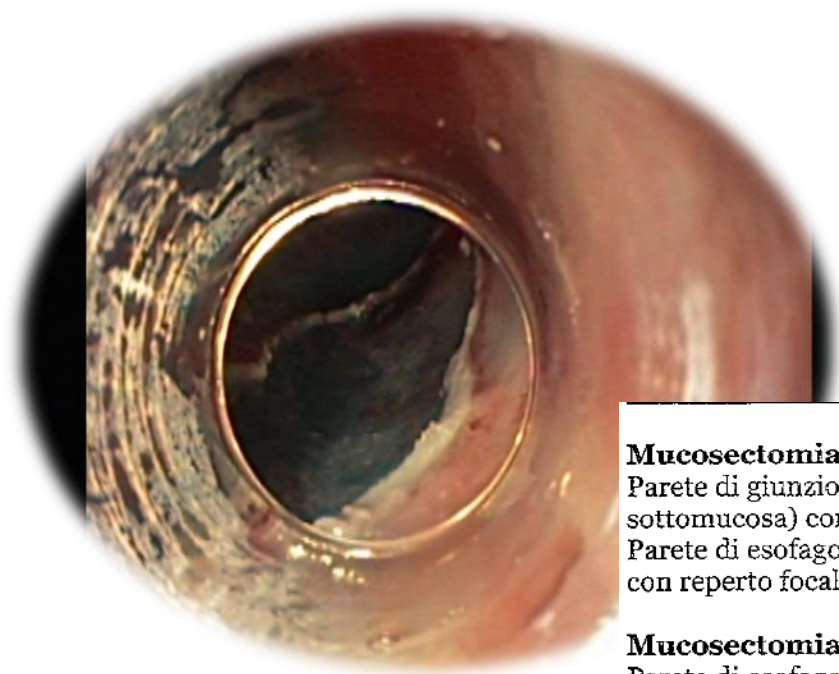


Mappattura+EUS





EMR



Mucosectomia "b"
Parete di giunzione squamo-colonnare (comprendente *muscularis mucosae* [anche duplicata] e sottomucosa) con erosione e metaplasia intestinale delle ghiandole (MI++-) (11).
Parete di esofago con focale erosione e iperparacheratosi dell'epitelio pavimentoso (7,8,9,10,12,13) e con reperto focale di metaplasia intestinale delle ghiandole (MI +--) (8,9,10,12).

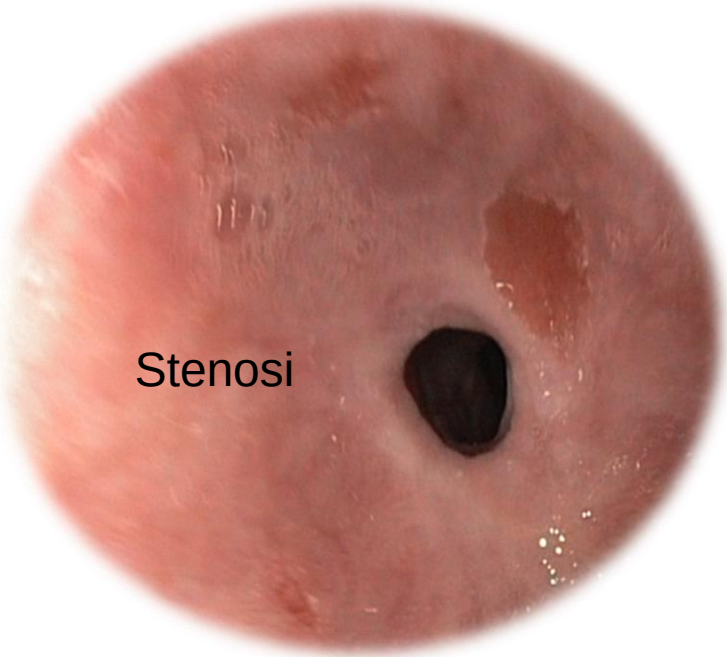
Mucosectomia "c"
Parete di esofago (comprendente *muscularis mucosae* [anche duplicata] e sottomucosa) con iperparacheratosi dell'epitelio pavimentoso (15), erosione e con metaplasia intestinale delle ghiandole (14,15,16).
Parete di esofago (comprendente *muscularis mucosae* e sottomucosa) con erosione dell'epitelio di superficie (17).

Mucosectomia "d"
Parete di esofago (comprendente *muscularis mucosae* [anche duplicata] e sottomucosa) con adenocarcinoma microinfiltrante la lamina propria e con adiacente neoplasia non-invasiva di alto grado, insorta in mucosa intestinalizzata (22,23,26).
Parete di esofago (comprendente *muscularis mucosae*) con neoplasia non-invasiva di alto grado delle ghiandole (20,24).
Parete di esofago (comprendente *muscularis mucosae*) con erosione e con neoplasia non-invasiva di basso grado insorta in mucosa ghiandolare intestinalizzata (MI++-) (18,19).
Parete di esofago (comprendente *muscularis mucosae* e sottomucosa) con erosione dell'epitelio mucoso (21,25).

L'esaminatore: Prof. M. Rugge /PP : MM

(Prof. M.Rugge)

RFA 360°



Termine

Conclusione: da esofagectomia a …..

DESCRIZIONE MACROSCOPICA

Materiale inviato in esame come:
1) n. 3 campioni bioptici della mucosa dell'esofago (prelievo operato a cm 36 dall'arcata dentaria)
2) n. 2 campioni bioptici della mucosa dell'esofago (prelievo operato a cm 35 dall'arcata dentaria)
3) n. 3 campioni bioptici della mucosa dell'esofago (prelievo operato a cm 34 dall'arcata dentaria)
4) n. 3 campioni bioptici della mucosa dell'esofago (prelievo operato a cm 33 dall'arcata dentaria)
5) n. 4 campioni bioptici della mucosa dell'esofago (prelievo operato a cm 32 dall'arcata dentaria)
6) n. 3 campioni bioptici della mucosa dell'esofago (prelievo operato a cm 31 dall'arcata dentaria)
7) n. 4 campioni bioptici della mucosa dell'esofago (prelievo operato a cm 30 dall'arcata dentaria)
8) n. 3 campioni bioptici della mucosa dell'esofago (prelievo operato a cm 29 dall'arcata dentaria).

Informazioni cliniche (come segnalate in richiesta):
- *Follow-up* di Barrx per *Barrett* con HGD.
- Reperto endoscopico: Esiti stabilizzati di Barrx. Ernia iatale.

DIAGNOSI

Campioni di mucosa gastrica dell'antro con minima flogosi linfomonocitaria della lamina propria (1).
Campioni di mucosa della giunzione esofago-gastrica con iperparacheratosi, iperplasia del compartimento proliferativo, esocitosi leucocitaria (+--) dell'epitelio squamoso e con angiectasie della lamina propria interpapillare (2).
Campioni di mucosa esofagea con iperparacheratosi, iperplasia del compartimento proliferativo, esocitosi leucocitaria (+--) dell'epitelio squamoso e con angiectsie della lamina propria interpapillare (3,4,5,6,7,8).

In considerazione delle informazioni clinico/endoscopiche che riferiscono:
- localizzazione dell'impronta dei pilastri diaframmatici a cm 38 dall'arcata dentaria
- localizzazione della giunzione esofago-gastrica a cm 35 dall'arcata dentaria
il reperto morfologico è coerente con:
- ernia iatale.

L'esaminatore: Dott. G. Pennelli /LAL : MM

- Numerosi studi hanno dimostrato che la EMR di lesioni visibili diagnosticate come HGD con precedenti biopsie porta ad un upgrading a cancro nel 25%–40% dei casi.
- Le lesioni di tipo I di Parigi sono più frequentemente cancri infiltranti (sm) così come le lesioni IIa+c.

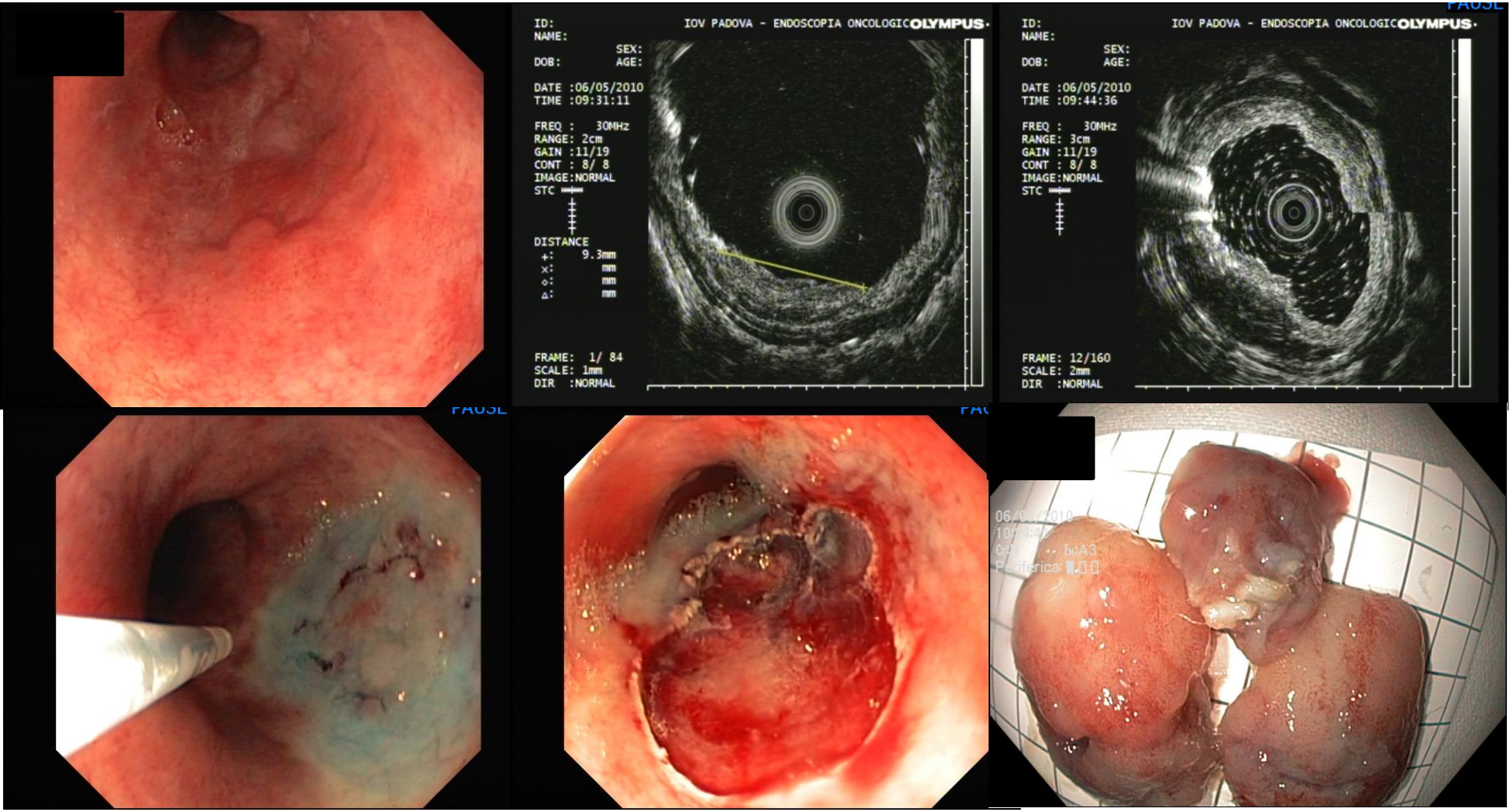
- In una serie chirurgica di esofagectomie eseguite per diagnosi di HGD la prevalenza di cancro coesistente è stata del 45% (14/31).
- Cancro è stato trovato:
- In 7 su 9 pazienti (78 %) con lesione visibile
- 7 su 22 pazienti (32 %) senza lesione visibile (P=0.019).

- **Le lesioni ad alto rischio di contenere cancro devono essere rimosse en bloc per assicurare un accurato staging anatomopatologico.**

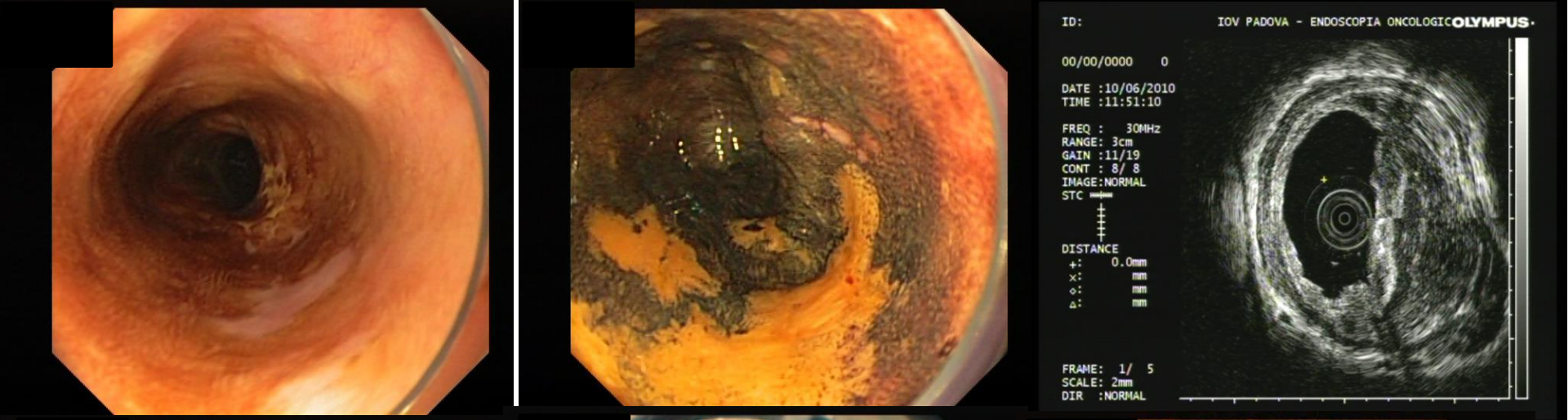
- Pech O, May A, Manner H et al. Long-term efficacy and safety of endoscopic resection for patients with mucosal adenocarcinoma of the esophagus. Gastroenterology 2014; 146: 652–660 (e651)
- Peters FP, Brakenhoff KP, Curvers WL et al. Histologic evaluation of resection specimens obtained at 293 endoscopic resections in Barrett's esophagus. Gastrointest Endosc 2008; 67: 604–609
- Pech O, Gossner L, Manner H et al. Prospective evaluation of the macroscopic types and location of early Barrett's neoplasia in 380 lesions. Endoscopy 2007; 39: 588–593

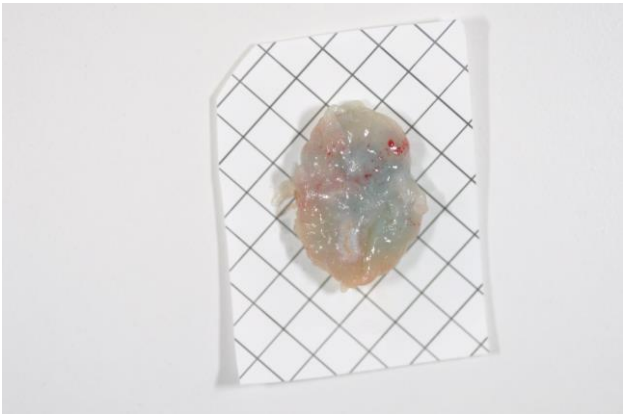
Esofago di Barrett con adenocarcinoma

Piecemeal



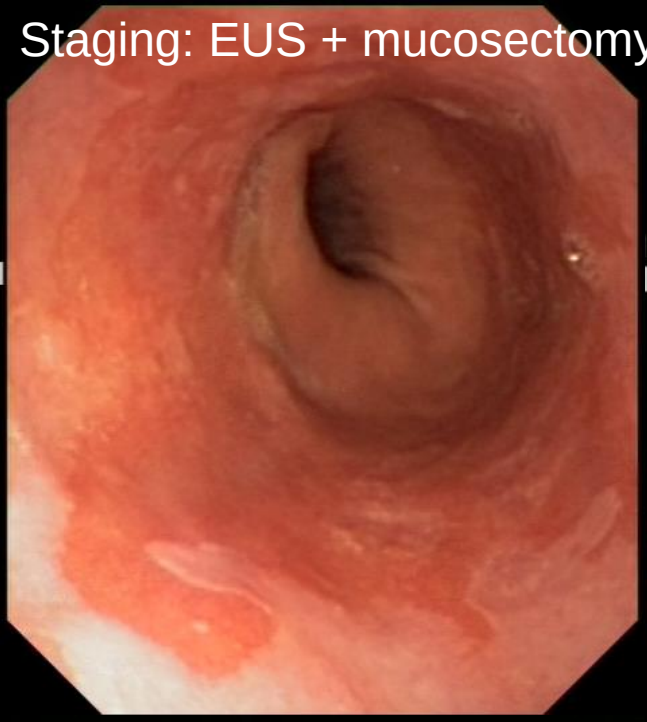
Corretta terapia: ESD en bloc

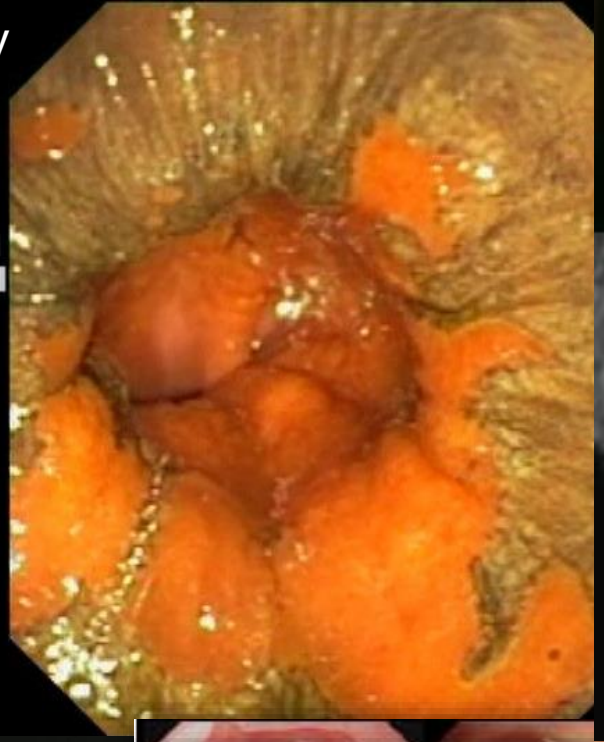


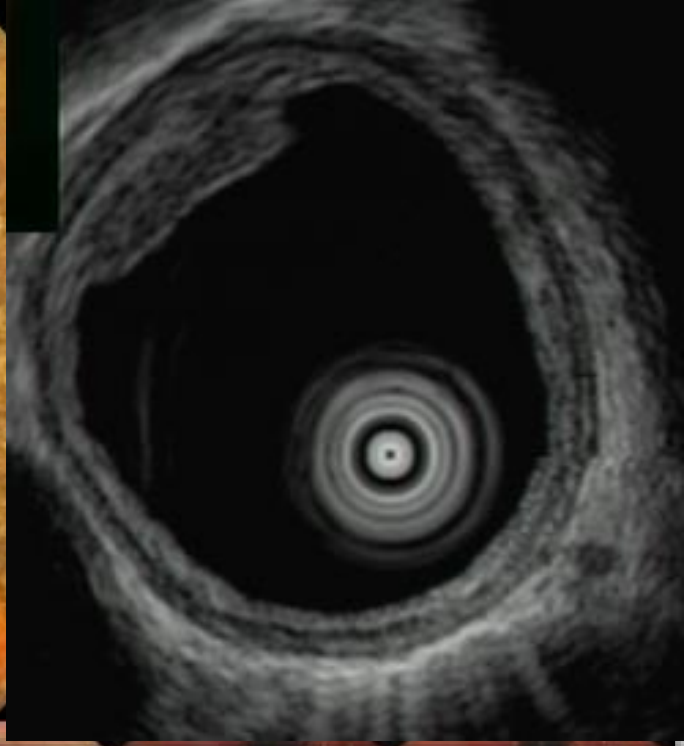


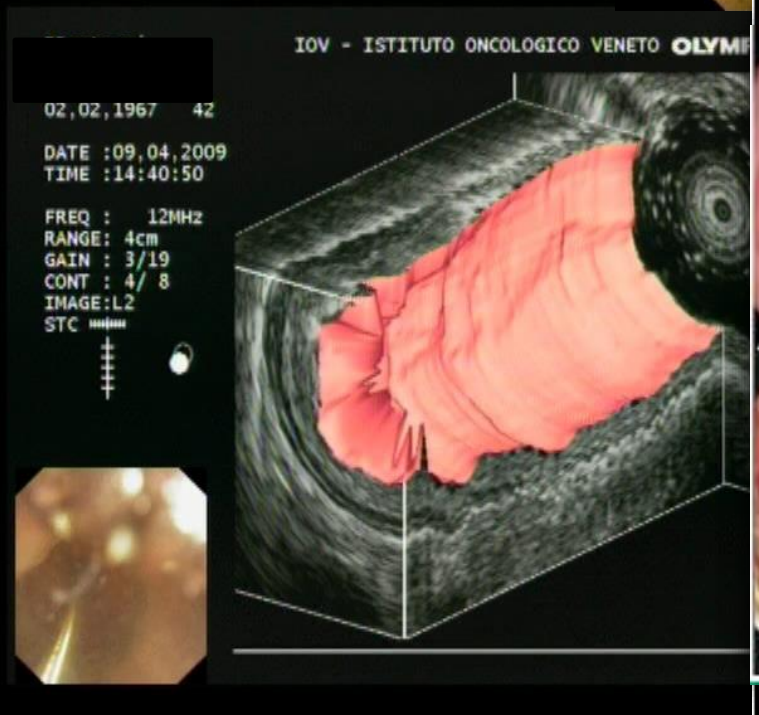
Recidiva di SCC già RT

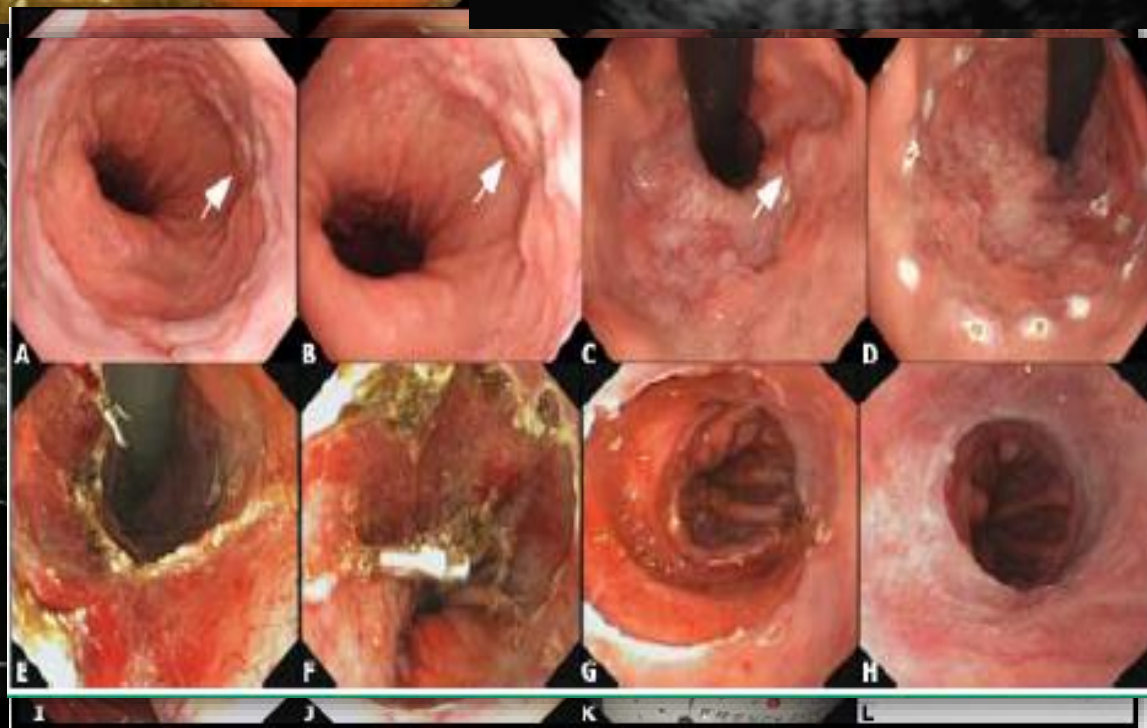
Staging: EUS + mucosectomy



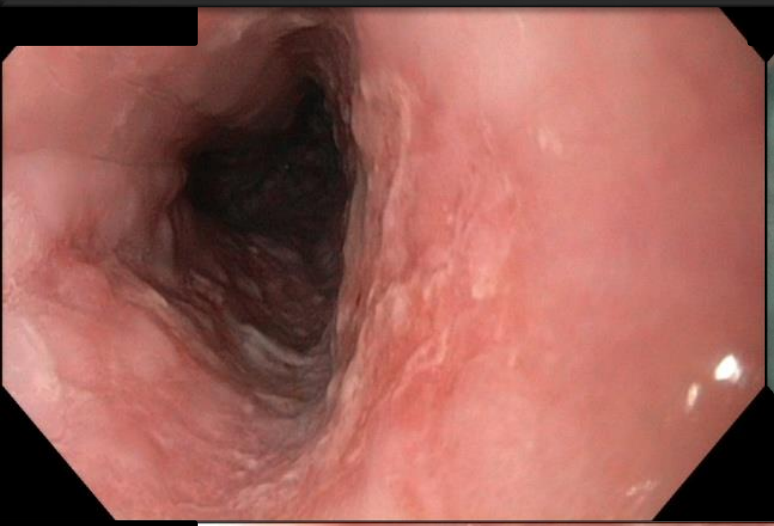


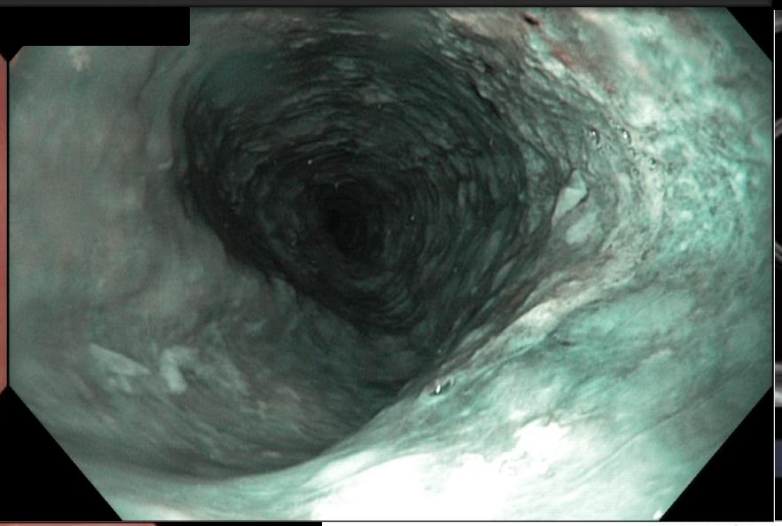


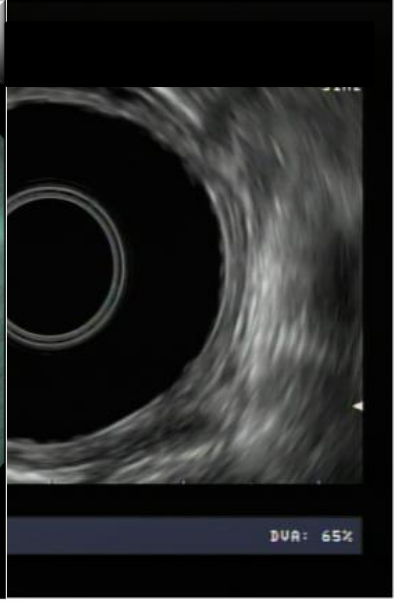


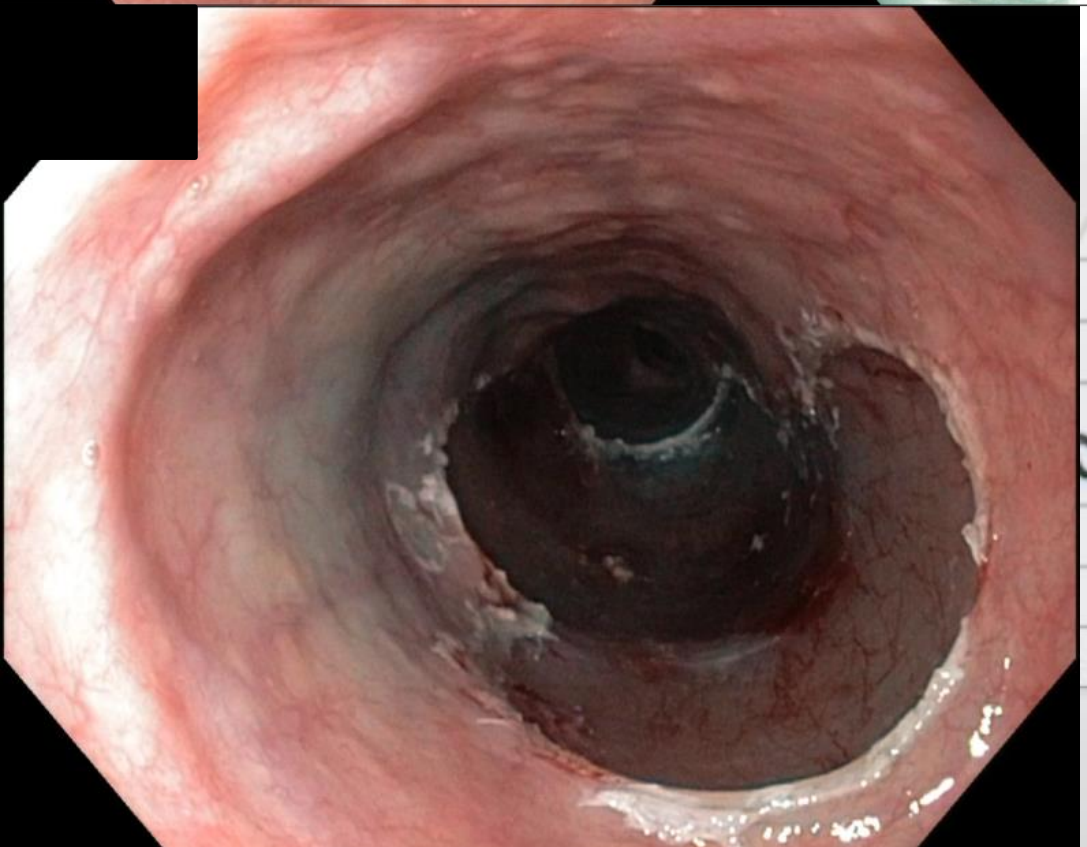


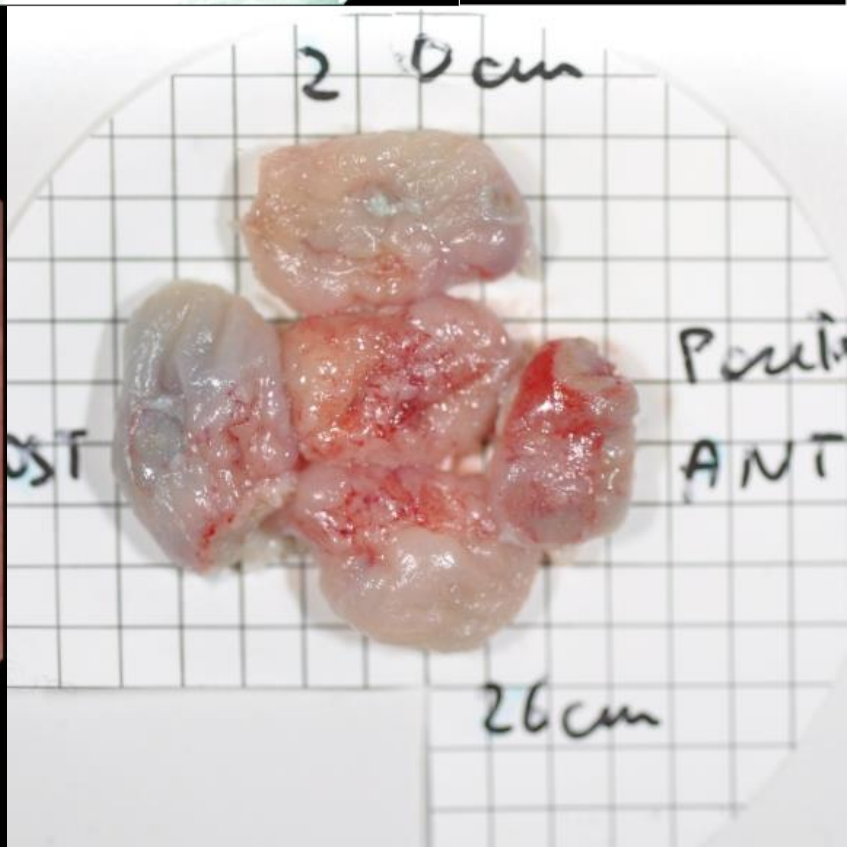
Staging: EUS + mucosectomy in squamous carcinoma

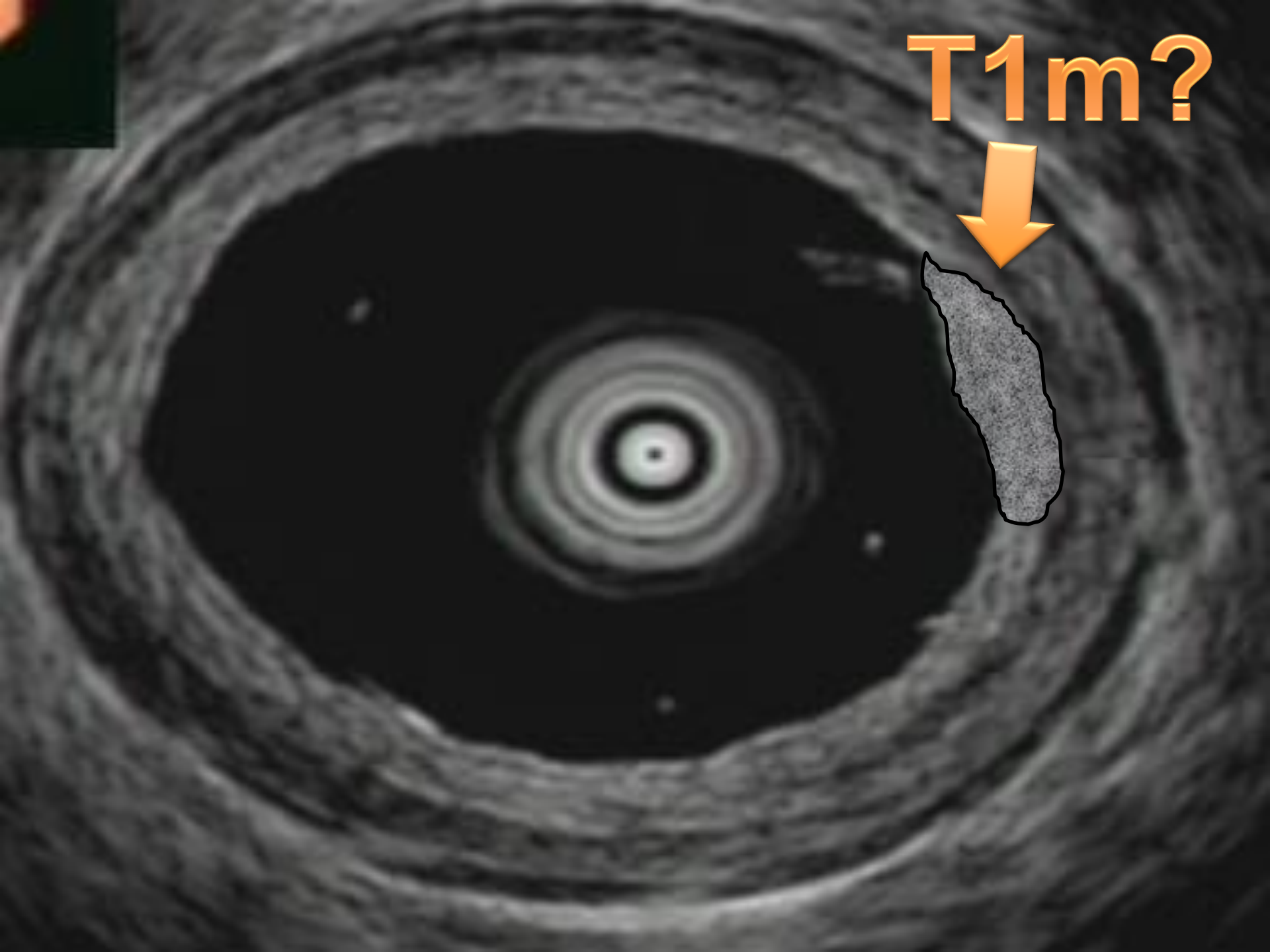


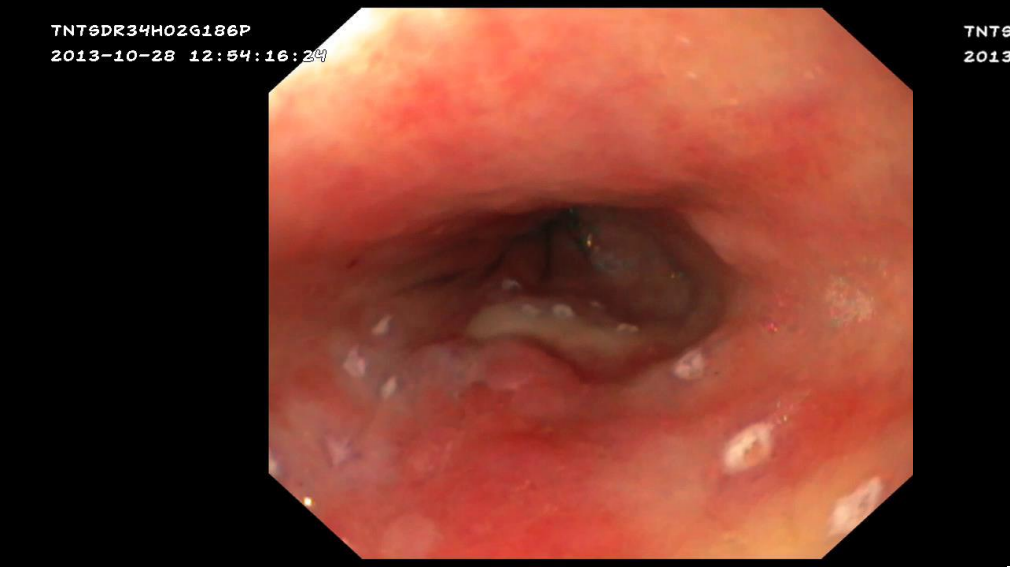









T1m?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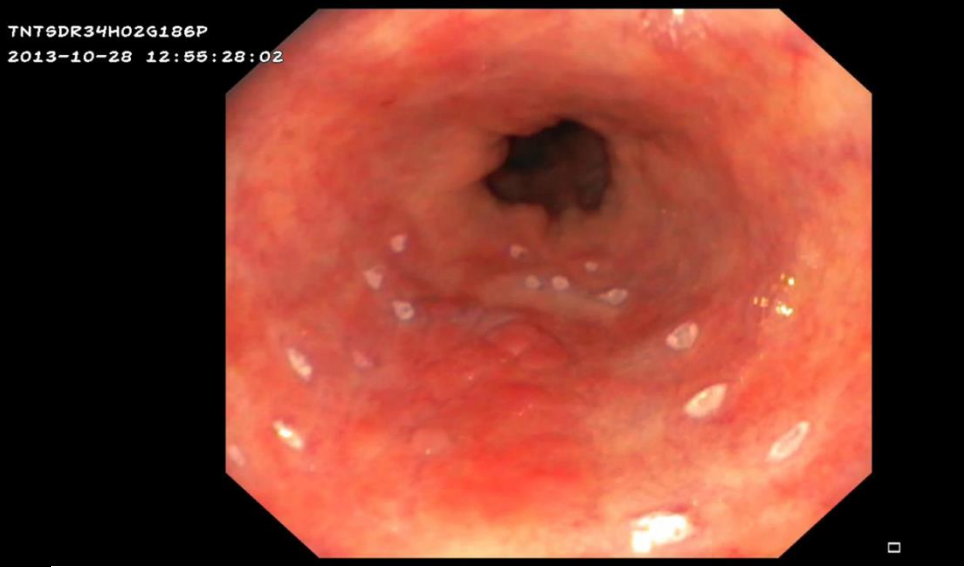
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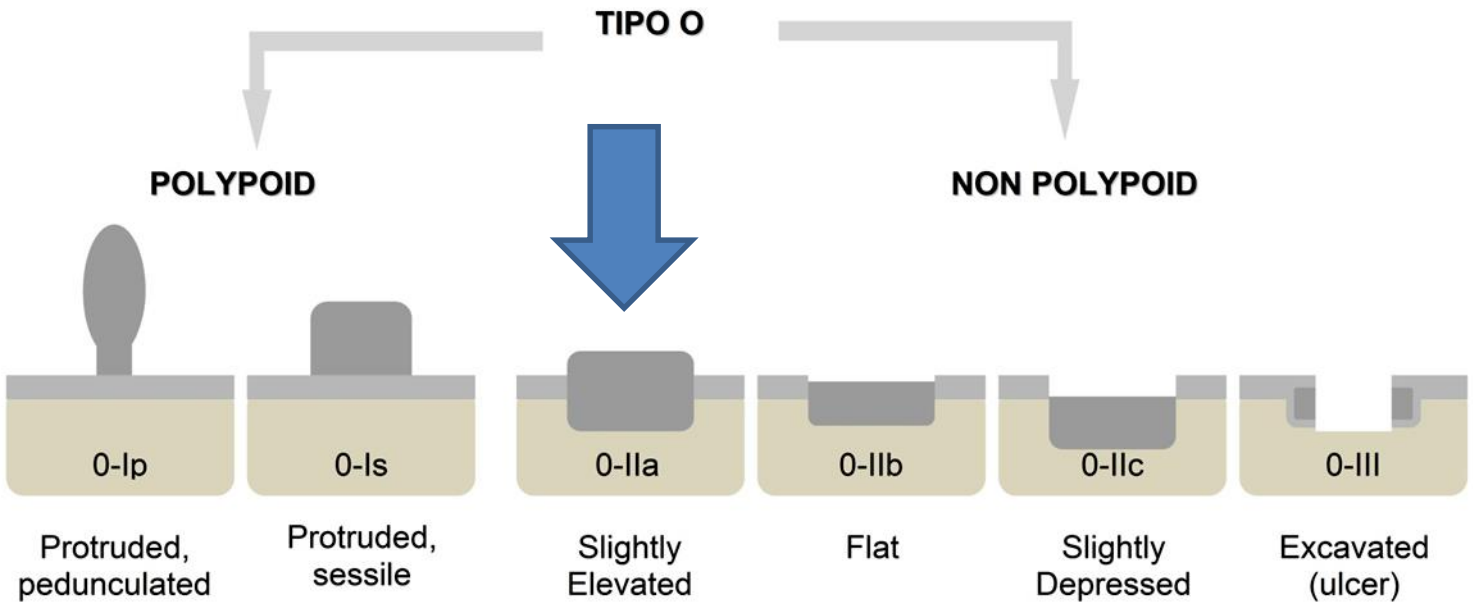
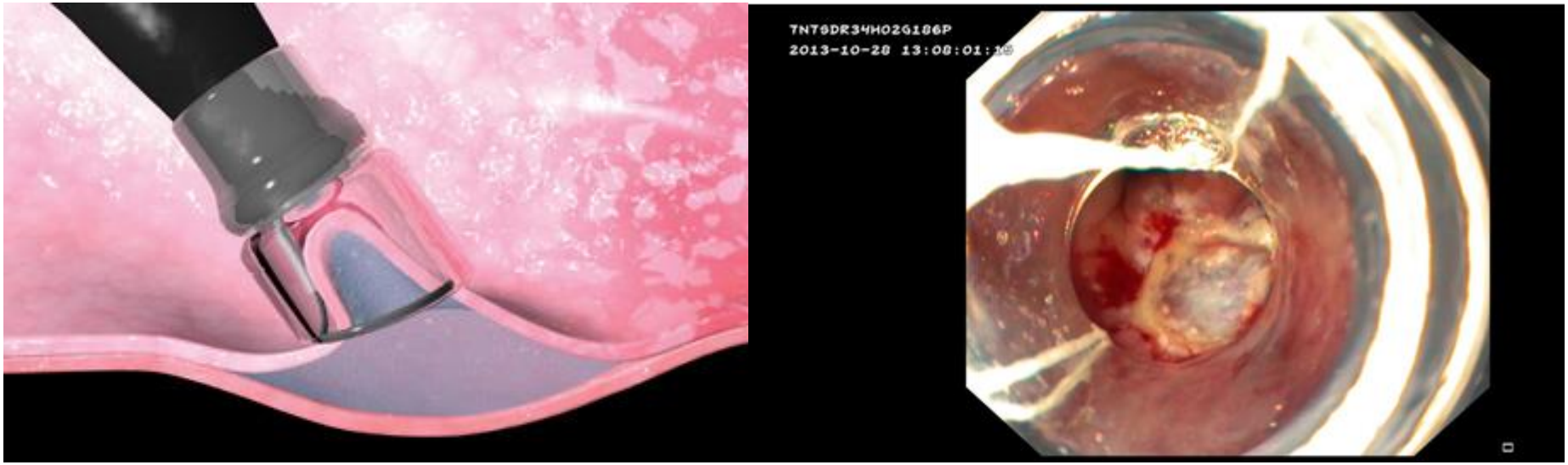
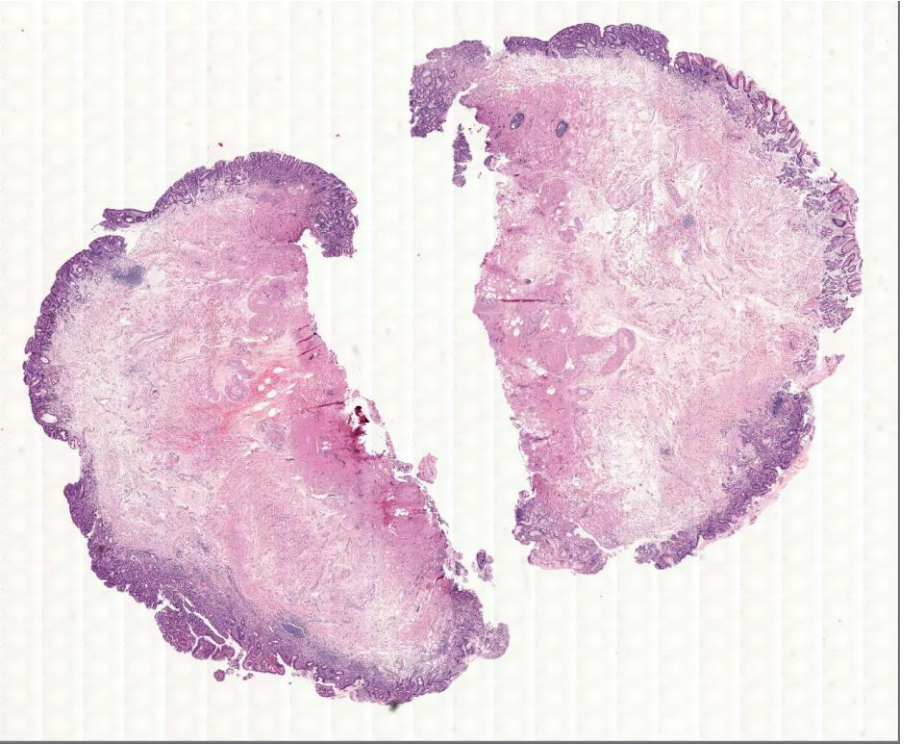
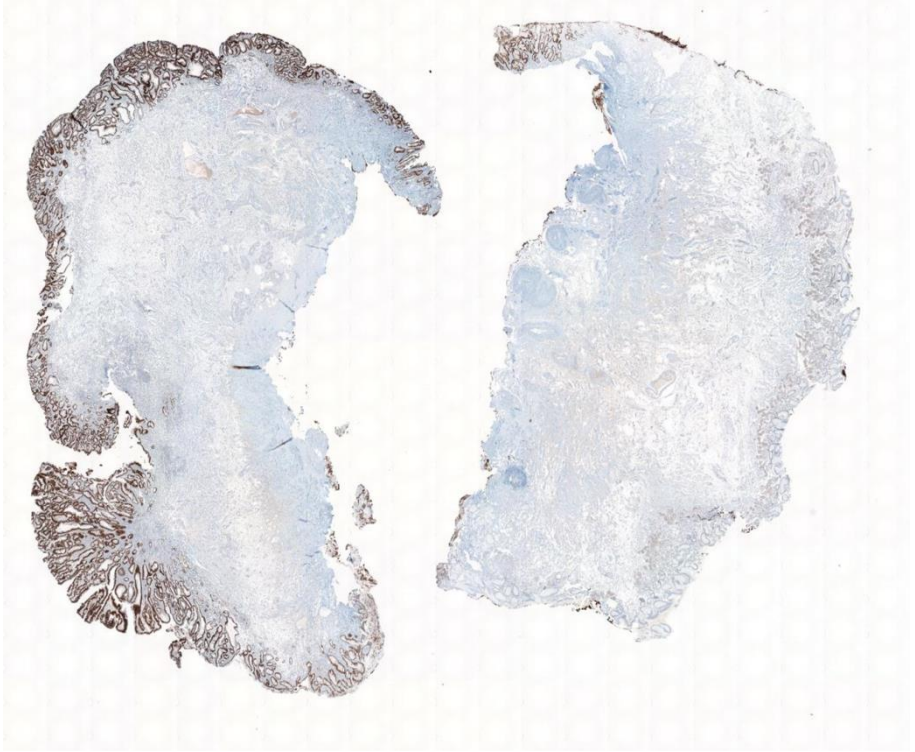

TIPO O
POLYPOID
NON POLYPOID
0-Ip
0-Is
0-IIa
0-IIb
0-IIc
0-III
Protruded, pedunculated
Protruded, sessile
Slightly Elevated
Flat
Slightly Depressed
Excavated (ulcer)

EMR





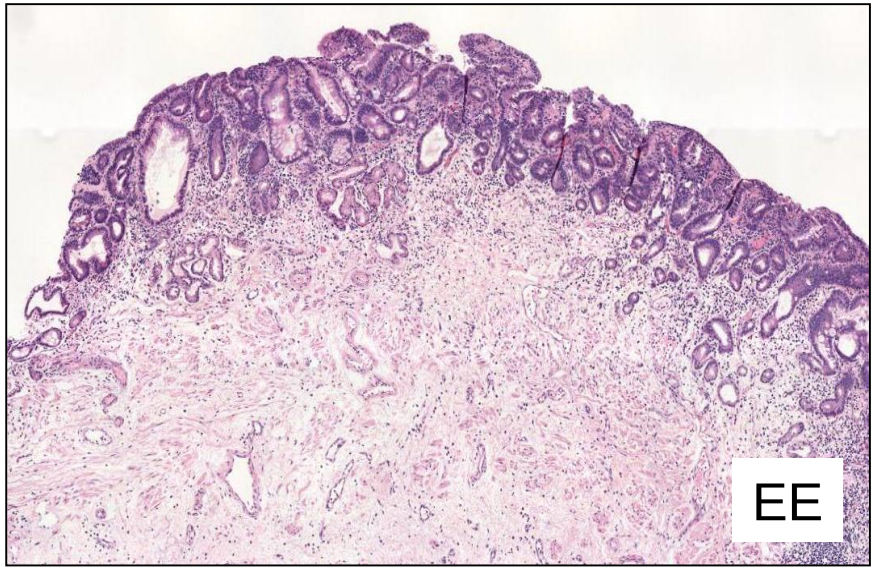


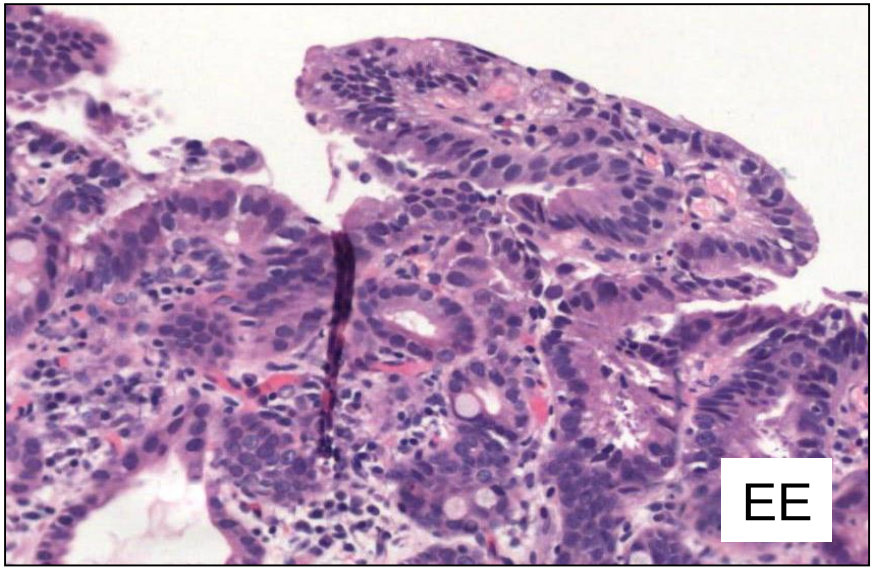
Paolo, queste sono le diapo con il caso di Barrett con displasia di alto grado, sia in bio (EE, p53) che sulle tue resezioni, con EE (presenza di mucosa, sottomucosa e qualche tralcetto di muscolare propria), p53 (diffusa positività) e incremento significativo della proliferazione (ki-67 arriva fino in superfice).

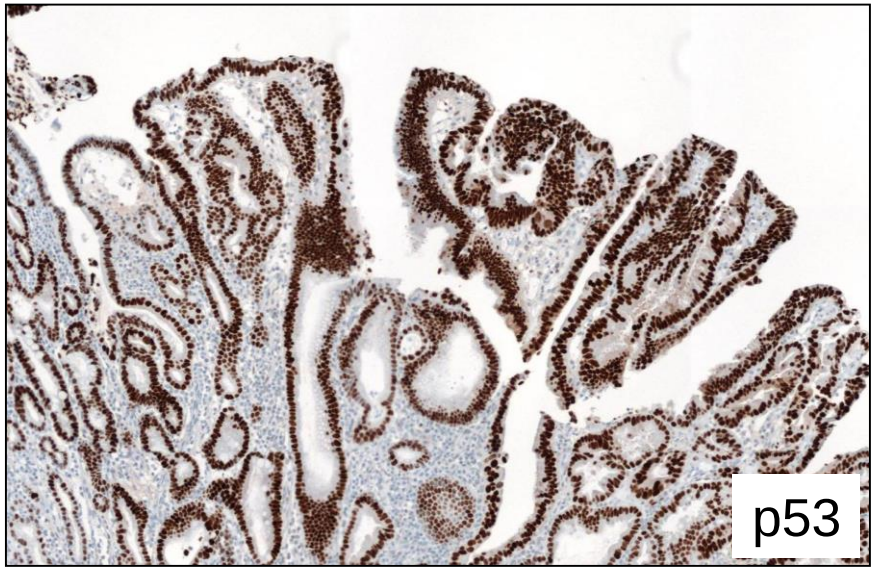
A disposizione

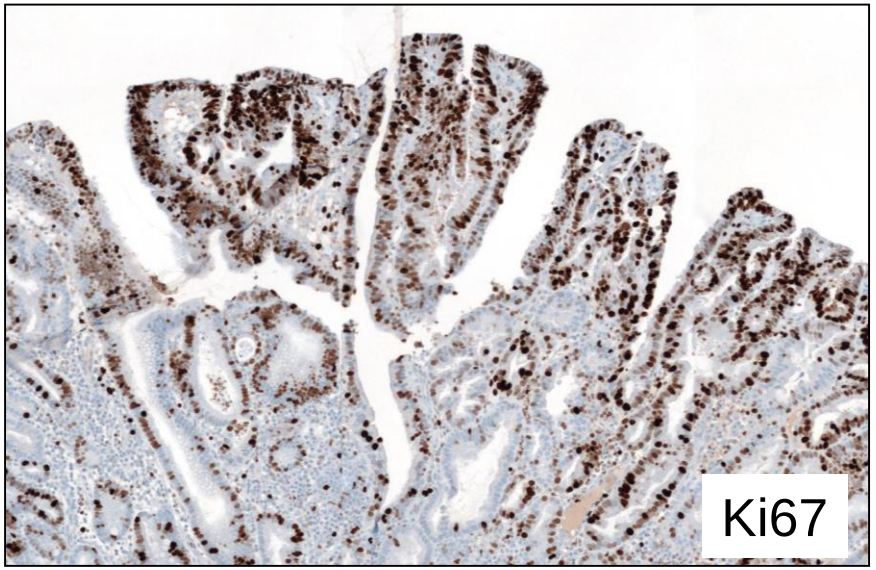
Giuseppe

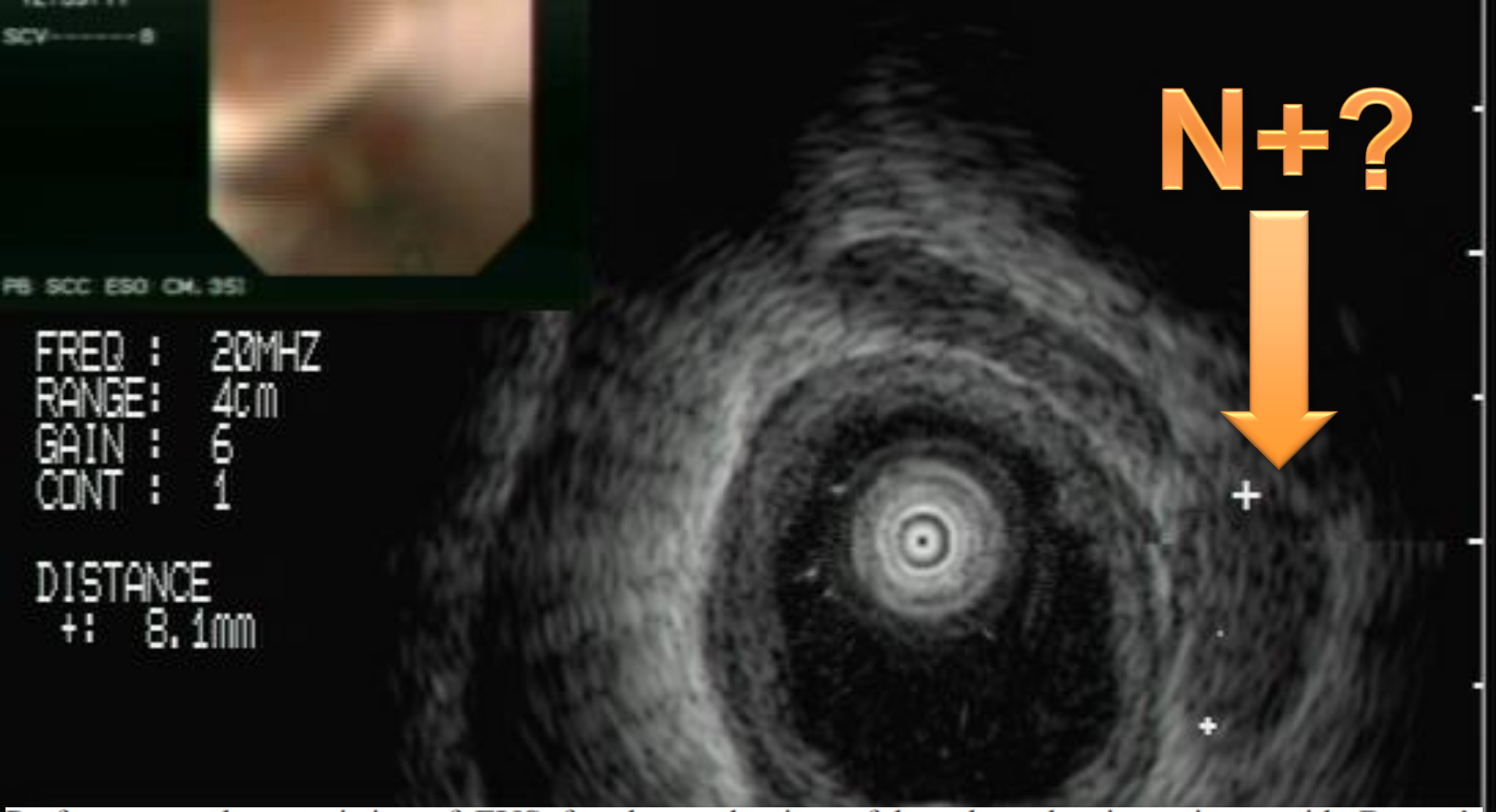
Barrett-Displasia Alto Grado





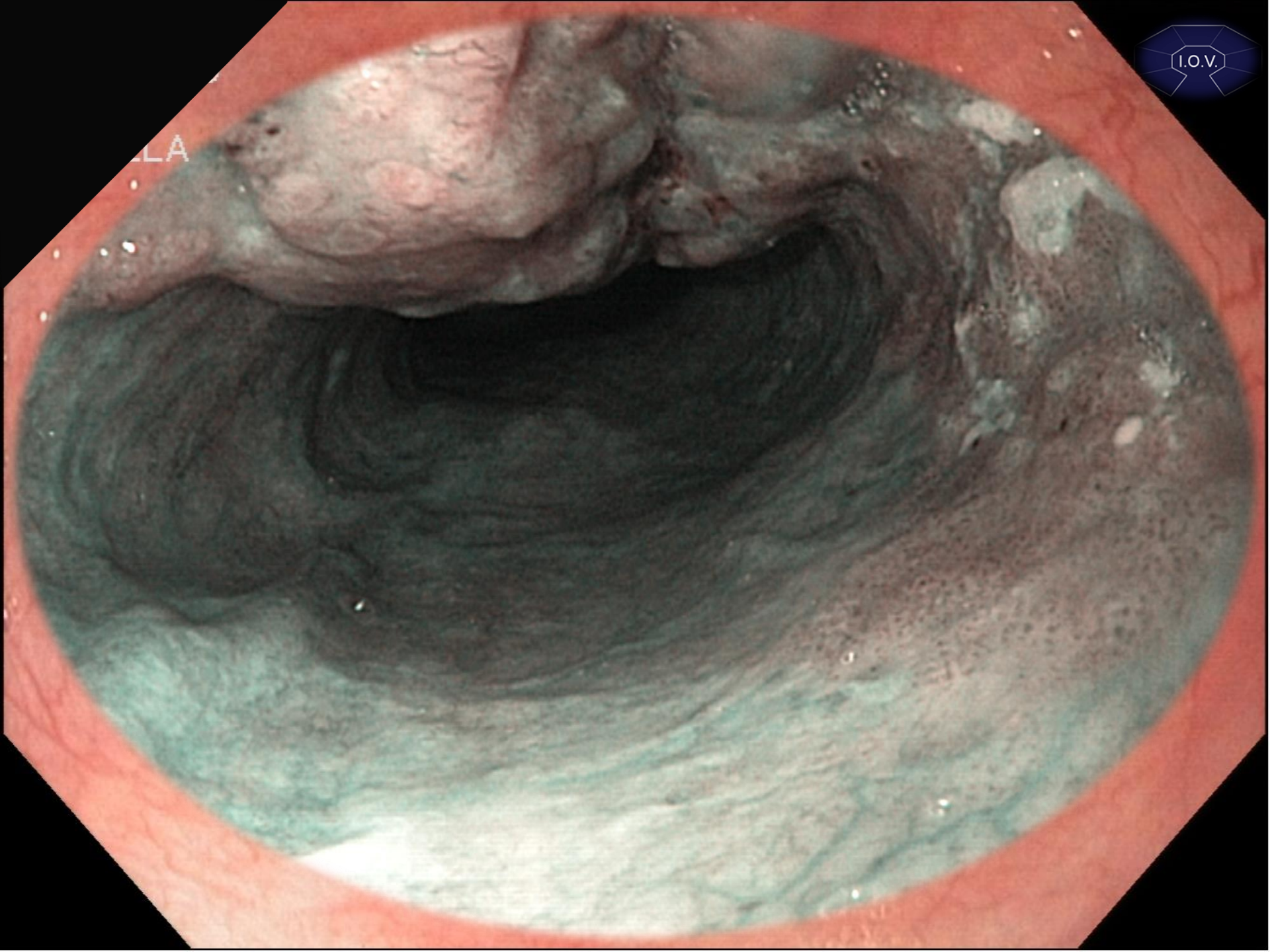






Performance characteristics of EUS for the evaluation of lymph nodes in patients with Barrett's esophagus with high-grade dysplasia or early adenocarcinoma

Study	*n*	Accuracy	Sensitivity	Specificity	PPV	NPV
Buttar et al [12]	84	88%				
Canto et al [19]	27	89%	100%	89%	25%	100%
Scotiniotis et al [15]	22	82%	100%	81%	20%	100%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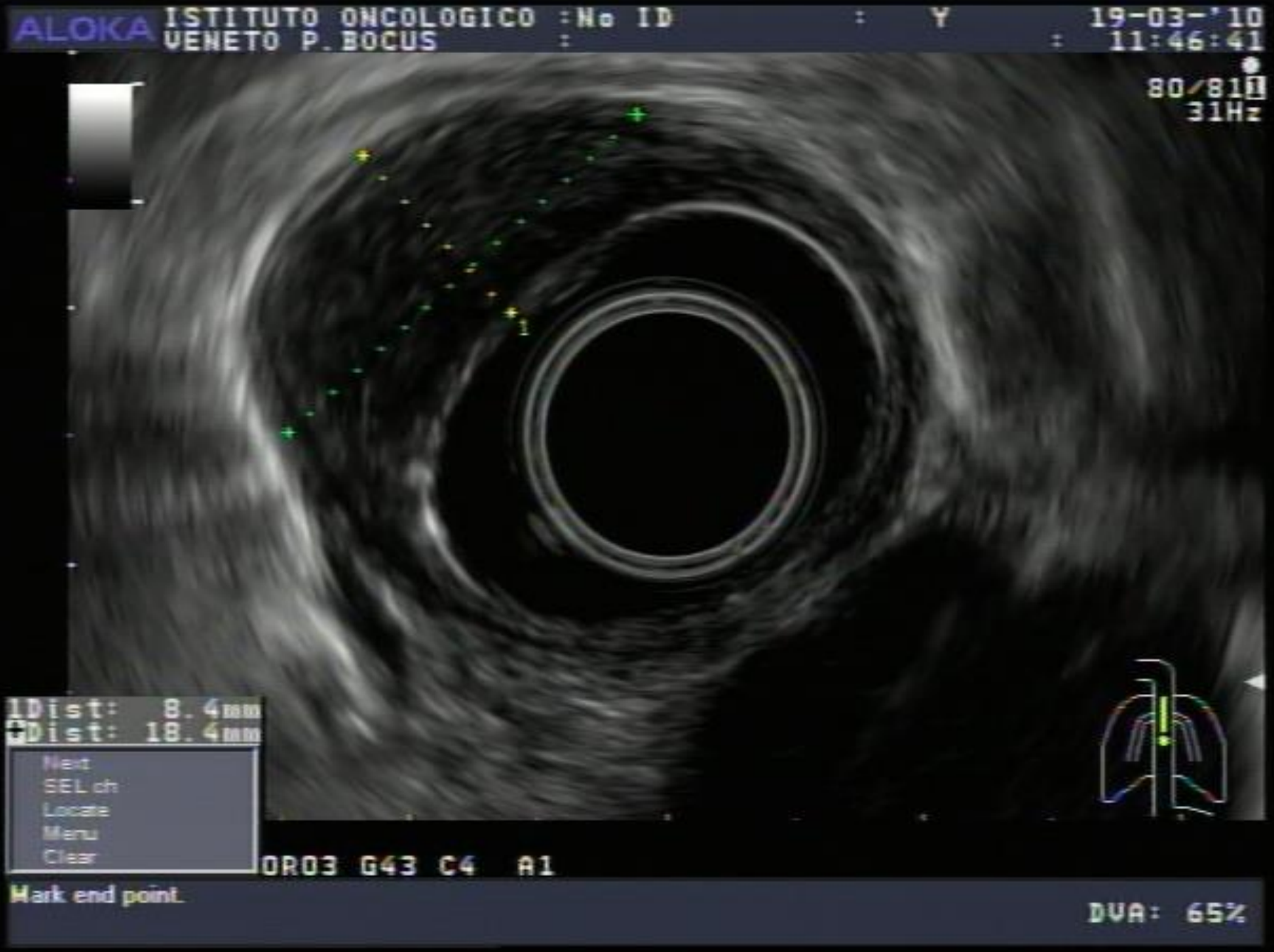
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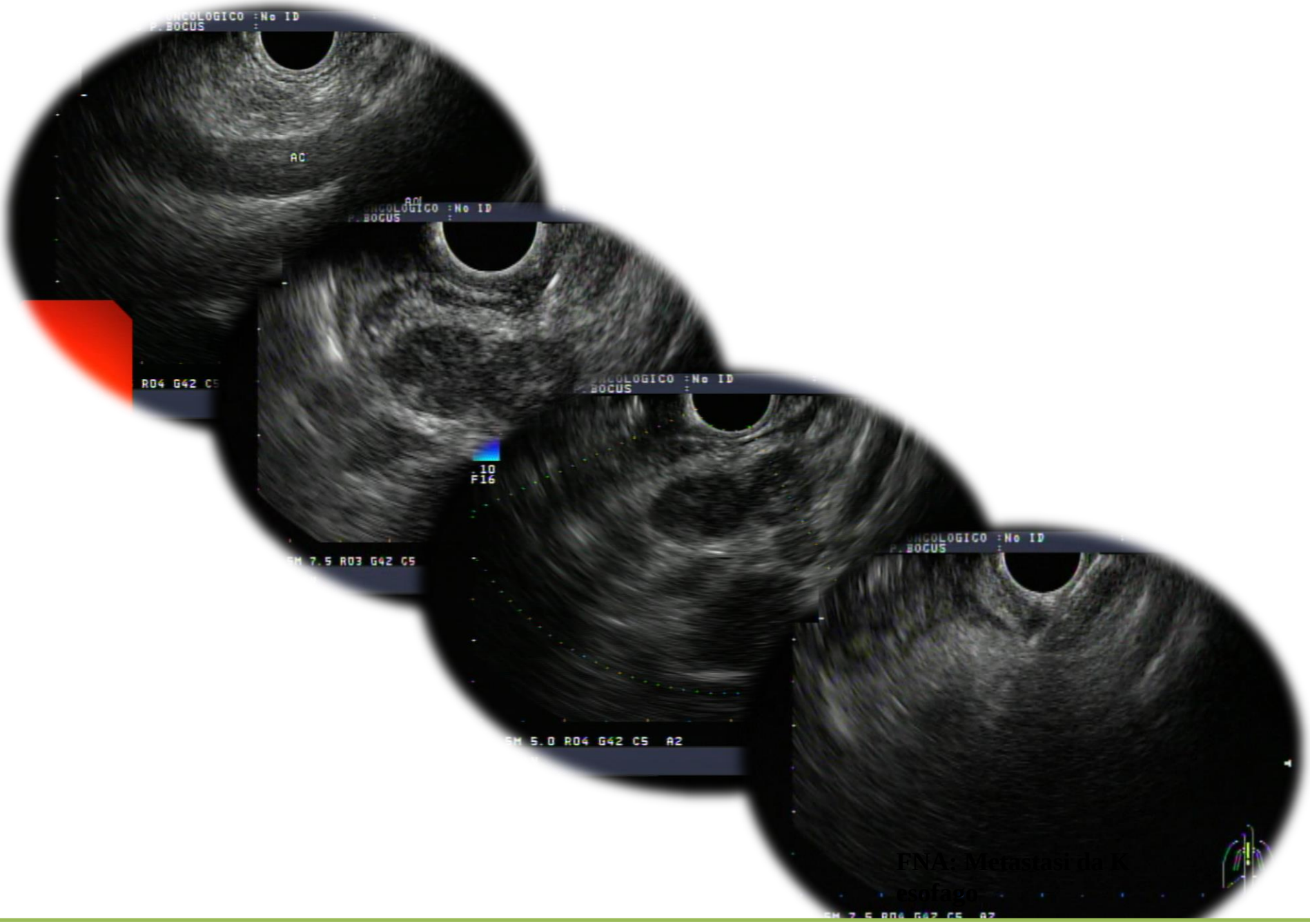


FNA: Metastasi da K esofago

Eloubeidi Ma. Predictors of survival for esophageal cancer patients with and without celiac axis lymphadenopathy: impact of staging endosonography. Ann Thorac Surg 2001

Techniques for Mucosal Ablation

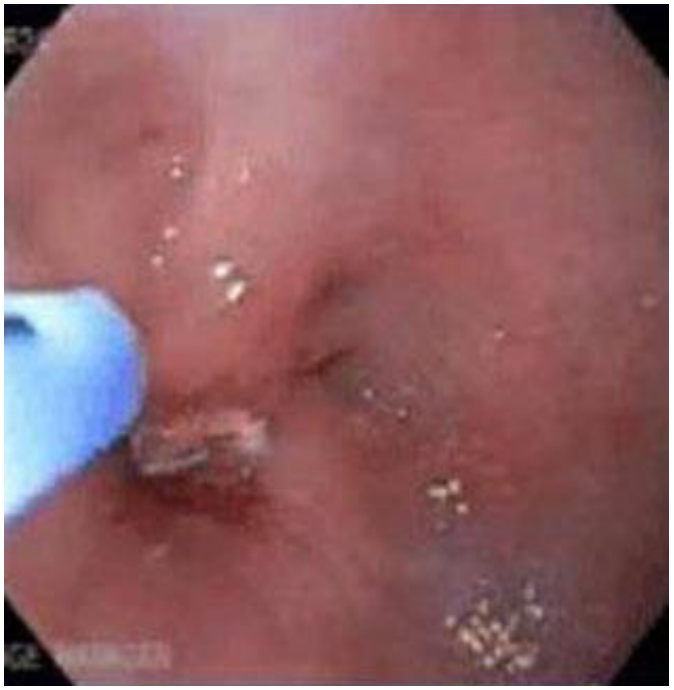
- Mechanical
  - Endoscopic mucosal resection (EMR)
  - Endoscopic submucosal resection (EMR)

- Thermal
  - Argon plasma coagulation (APC)
  - Multi-polar coagulation
  - Bipolar energy
  - Lasers: Argon, Nd: YAG, KTP-YAG
  - RFA

- Photochemical
  - Photodynamic Therapy

Argon Plasma Coagulation

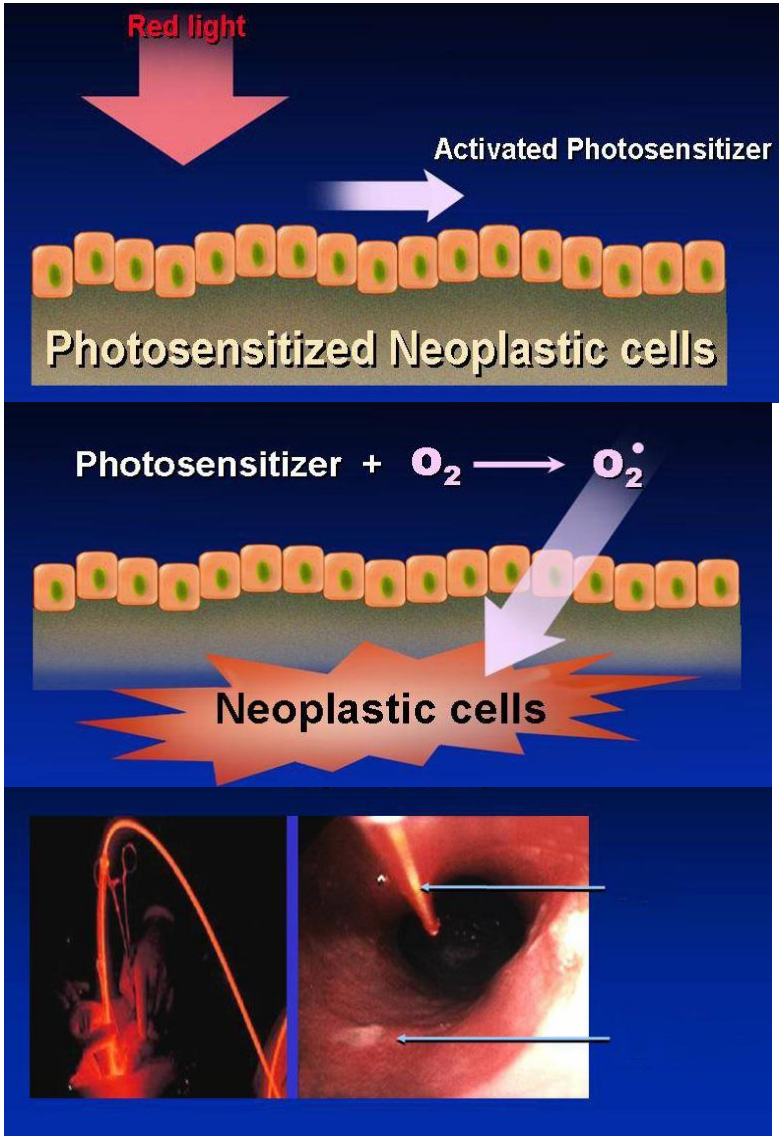
- Most commonly used for non-dysplastic IM
- Technically difficult to get all IM, multiple treatments required
- Buried glands and residual disease remains an issue



Pereira-Lima JC, Am J Gastroenterol 2000; 95:1661-8
Kahaleh M, Endoscopy 2002; 34:950-5.

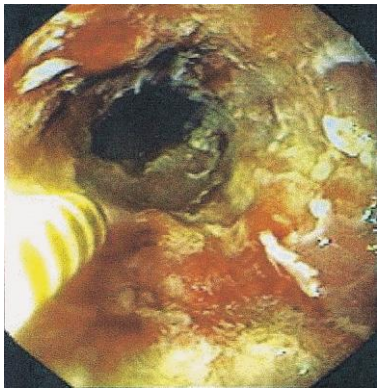
Photodynamic Therapy: Theory

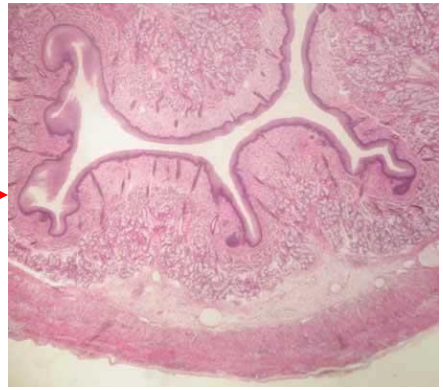
- Approved for HGD
- Photosensitizer given IV (sodium porfimer) or orally (5-ALA)
- Affected esophagus exposed to non-ablative laser light for ~12 minutes
- Oxygen free radicals induced in high light dose areas
- Free radicals induce cell death
- Strictures, chest pain, effusions remain issues



Ablation Technical Challenges

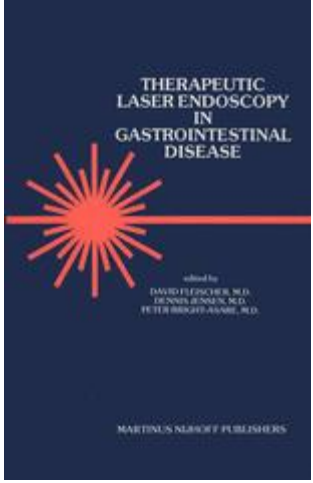
- Hand-held “Point and Shoot”
- Technically demanding to achieve proper effect
- Non-uniform ablation
- Uncontrolled power delivery
- Visual endpoint for completing session
- Anatomy of distal esophagus not considered, its not round
- Repeat therapy is the rule





1990

Laser



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World J Gastroentero, 2001;7(3):317 - 323
World Journal of Gastroenterology
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Lasers in gastroenterology

Laurence B. Lovat and Stephen G. Bown

Subject headings lasers/therapy use; lasers/diagnosis use; gastroenterology

Lovat LB, Bown SG. Lasers in gastroenterology. *World J Gastroenterol*, 2001;7(3):317-323

INTRODUCTION

Endoscopy has revolutionised our management of many gastrointestinal disorders over the past 30 years. We are increasingly able to diagnose gastrointestinal (GI) tumors at an early stage, and endoscopic therapy has made a difference to the outcome of GI haemorrhage. We still rely on surgery for cure of cancer but as diagnostic techniques improve the goal of minimally invasive diagnosis and therapy appears ever more attainable. As populations get older, it is also increasingly desirable. Laser light can be used for both diagnosis and therapy in the gut. This article reviews the value of lasers in these areas.

HOW LASERS WORK

Biological effects

Lasers are sophisticated sources of monochromatic light in the visible and near infrared part of the optical spectrum. The ones of most interest to gastroenterologists are those where the beam penetrates living tissue well and which can be transmitted via thin, flexible fibers, so they can be used with flexible endoscopes. These can be used to deliver light as heat to cause thermal contraction of soft tissue. The most important laser in this group has been the Neodymium yttrium aluminium garnet (NdYAG) laser with a near infrared beam at 1064nm. Short, sharp shots from this laser cause thermal contraction in soft tissues, which provides good haemostasis. Longer shots at high power can vaporise tissue and coagulate the underlying layers, which is effective for debulking advanced cancers. At much lower powers, it is possible to coagulate a larger volume of tissue without vaporisation.

The other main group of effects is *photodynamic* where there is no increase in tissue temperature, but laser light is used to activate a previously administered photosensitising drug. This causes the release of highly reactive singlet oxygen which causes cell death by necrosis and apoptosis over a prolonged period. This can be used to completely eradicate small tumours.

A minor application is to use pulsed lasers endoscopically to fragment gall stones. These effects are summarised in Table 1.

Table 1 Laser effects used in gastroenterology

Laser effect	Clinical use
High power thermal:	Haemostasis Cutting or debulking of tissue by vaporisation and coagulation
Low power thermal: (Interstitial laser photocoagulation,ILP)	Gentle coagulation of lesions within solid organs
Photochemical: (Photodynamic therapy, PDT)	Non-thermal destruction of tissue by activation of a previously administered photosensitising drug
Pulsed shock wave	Fragmentation of gall stones

Non-biological effects

All living tissue display a number of interactions with light, which are altered in areas of dysplasia. Intrinsic fluorescence may be detected at endoscopy by exciting the tissue with blue laser light and using special detector cameras on the endoscope. Elastic scattering depends on the different way light is scattered depending on the density of cellular and nuclear packing. These approaches may allow us to detect premalignant lesions of the GI tract that would otherwise beinvisible at conventional endoscopy.

THERAPEUTIC USES FOR LASER

Palliation of advanced cancers

The main role of high power, thermal lasers like the NdYAG in current practice is for palliation of advanced, inoperable cancers of the upper and lower gastrointestinal tract. Under direct vision, nodules of exophytic tumour can be vaporised and underlying tumour coagulated either to relieve obstruction or to reduce blood loss (Figure 1). The incidence of complications is low, although it often takes several treatments to achieve optimum recanalisation. These laser beams are dangerous if viewed directly, so safety filters must be fitted to fibreoptic scopes. There is no risk to operators with video scopes, although filters are required to protect the chips in the camera.

Most patients with cancers of the oesophagus or gastric cardia present when the disease is too

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Email. l.lovat@ucl.ac.uk
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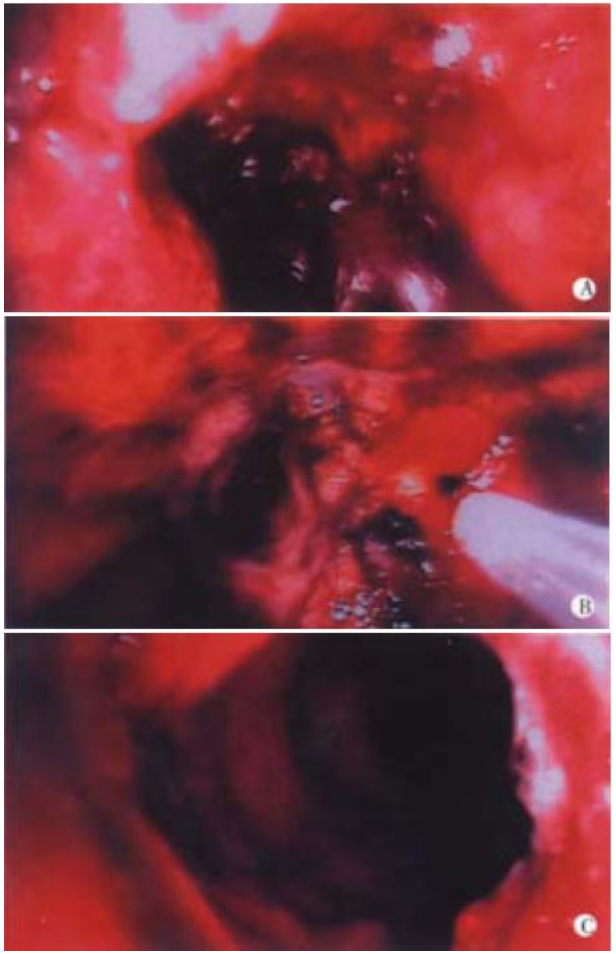
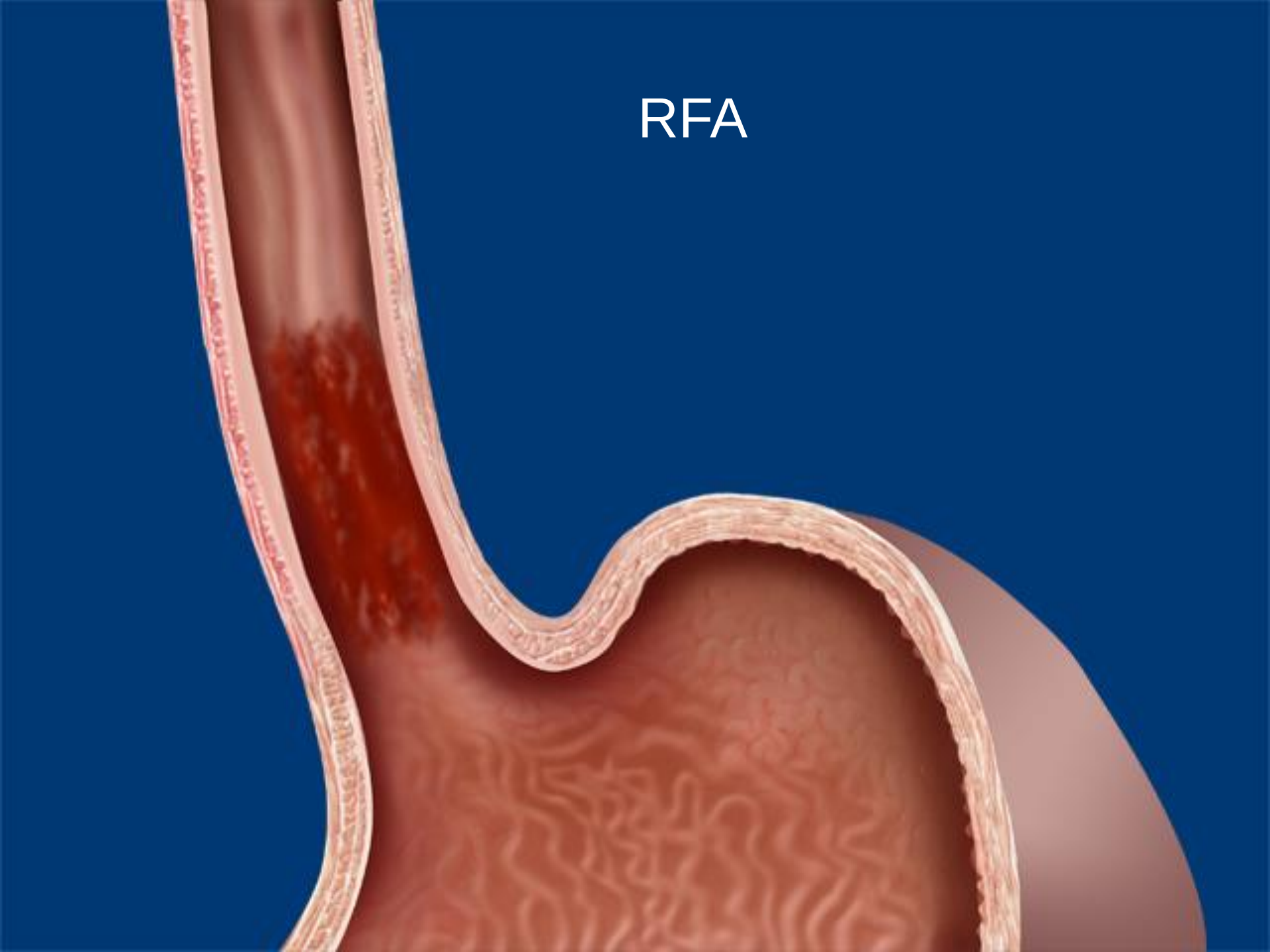


Norberto L, et al Endoscopic palliation of esophageal and cardial cancer: neodymium-yttrium aluminum garnet laser therapy. Dis Esophagus **1999**; 12(4):294-6.

Palliative therapy for esophageal cancer: laser therapy alone is associated with a better functional outcome. Pozza A, Erroi FR, Scarpa M, Polese L, Rampazzo L, Norberto L. Updates Surg. **2015** Mar;67(1):61-7. 28.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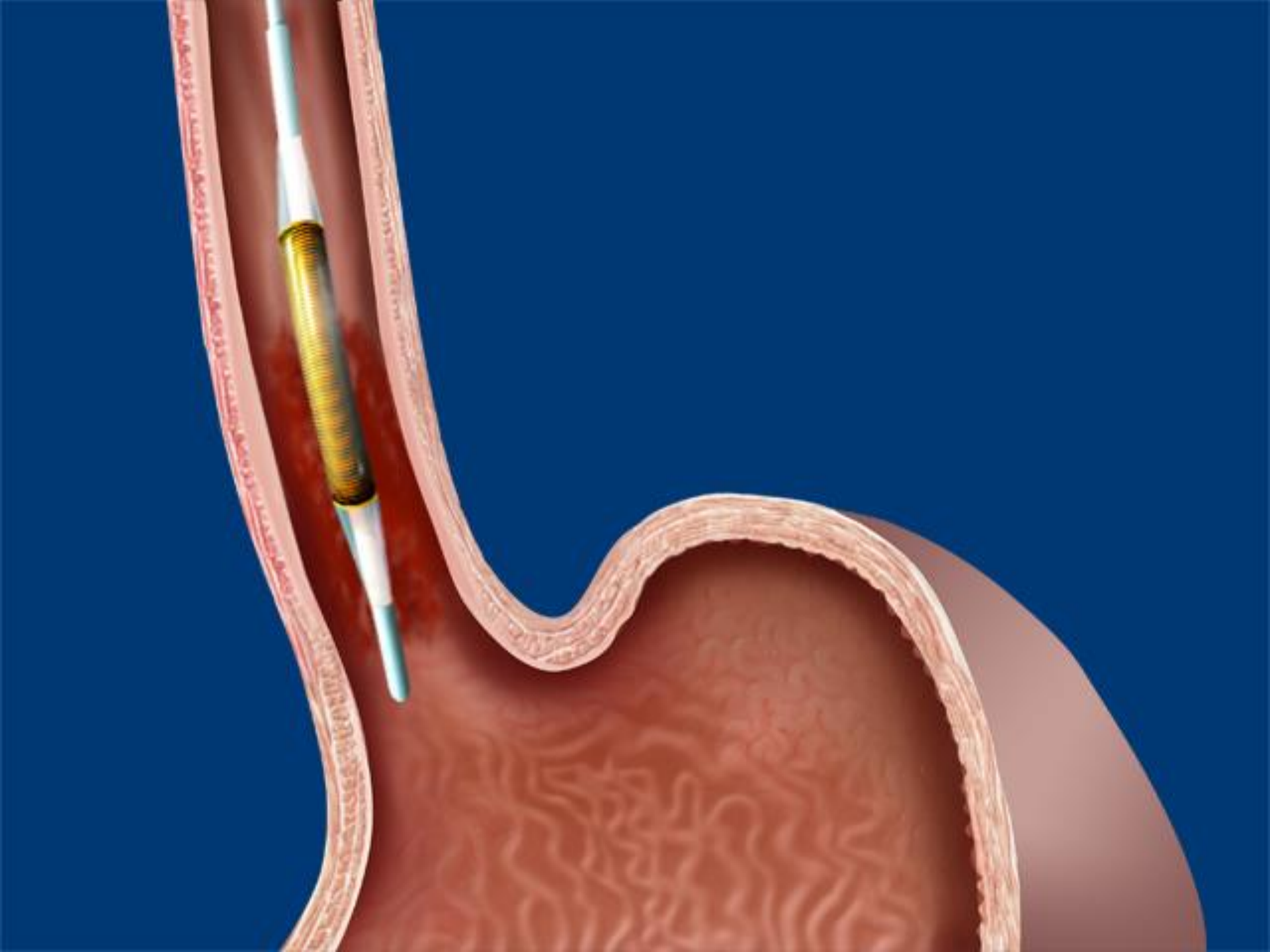
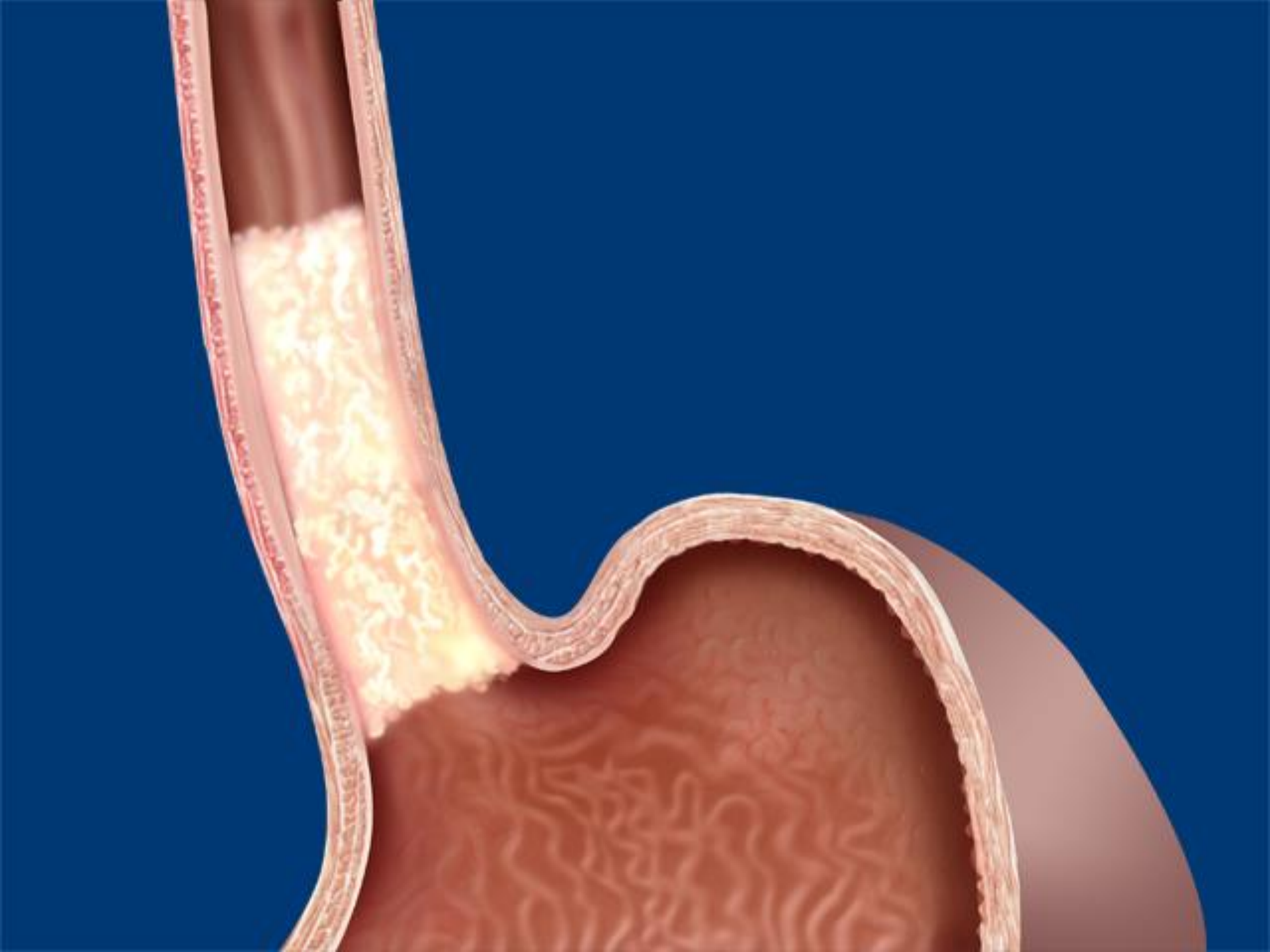
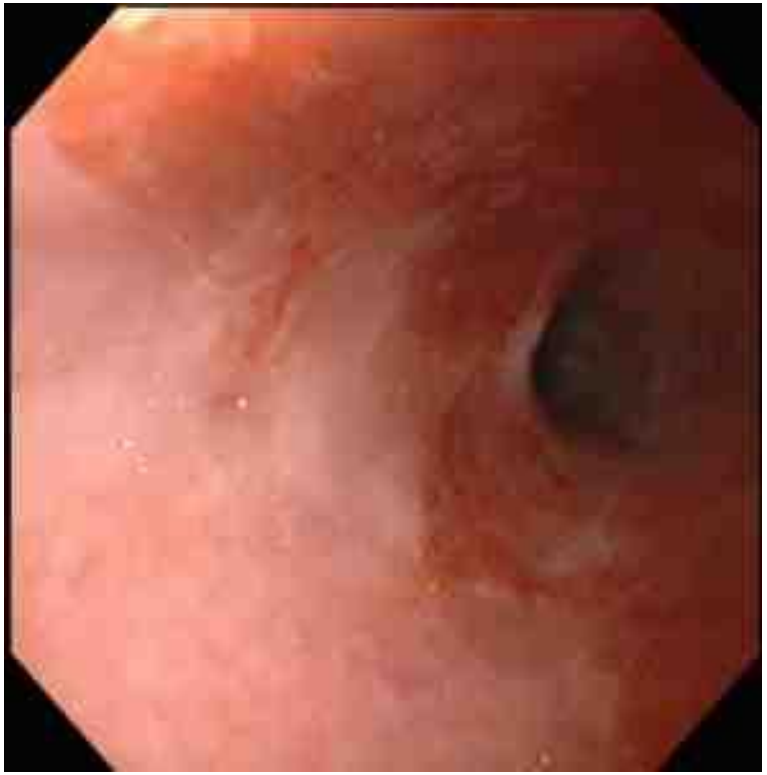
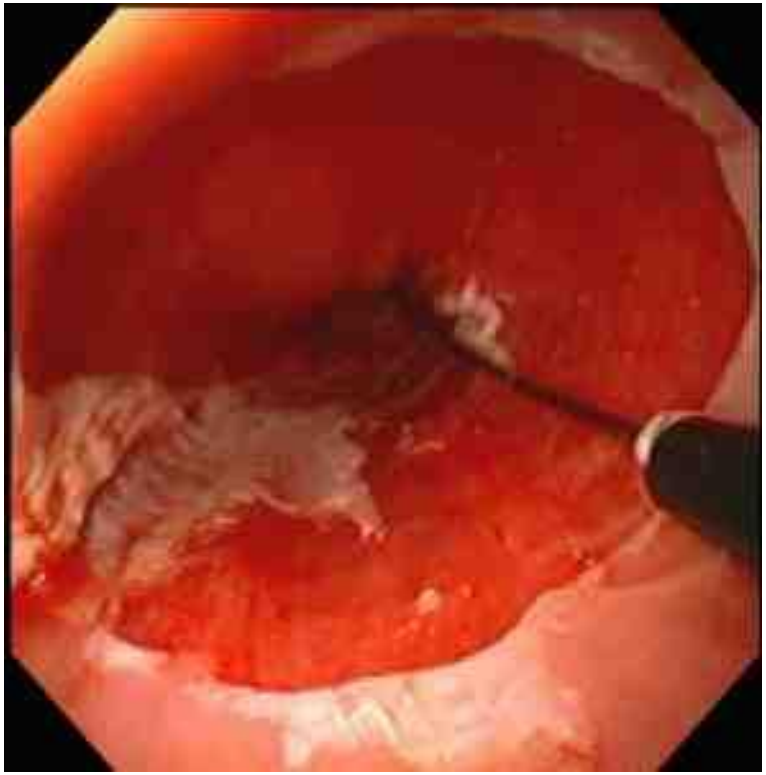




Endoscopic Appearance

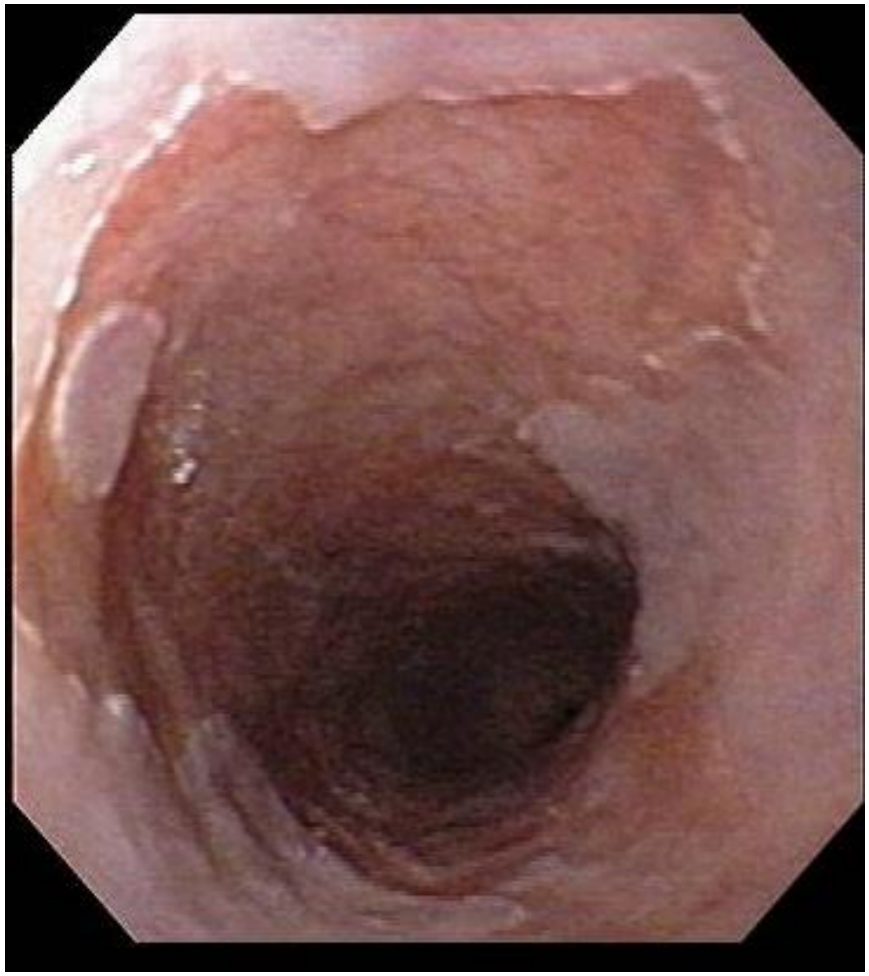


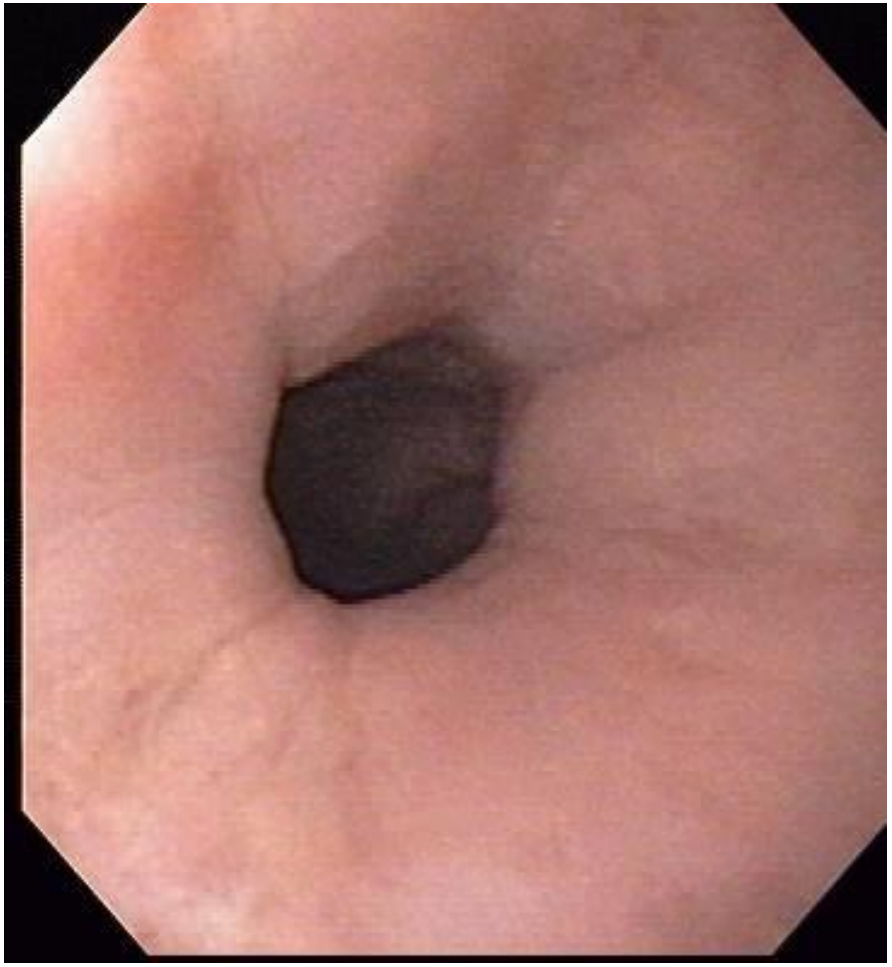
Baseline, 4 cm IM



Immediate Slough

Complete Response after HALO^{360}





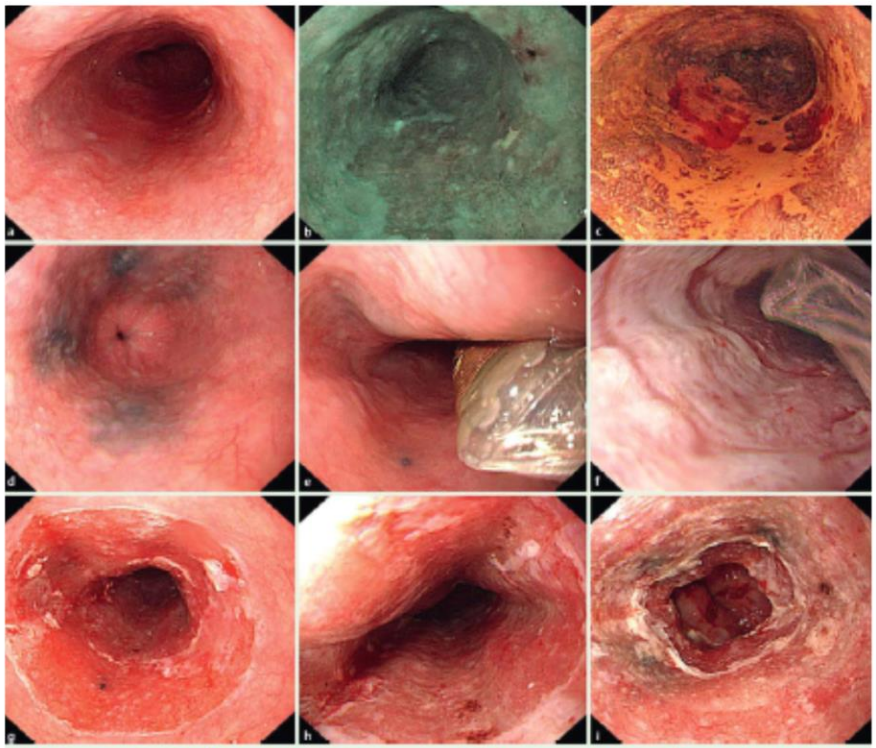


Fig. 1 Primary circumferential radiofrequency ablation (RFA) of a 4-cm-long flat type early esophageal squamous cell neoplasia with high-grade intraepithelial neoplasia. **a** Pretreatment white light endoscopy image showing minimal reddish discoloration; **b**, **c** Corresponding views with narrow-band imaging and after Lugol's chromoscopy; **d**, **e** The distal and proximal RFA balloon is positioned at the level of the proximal tattoo (visible at the 6 o'clock position); **f** Appearance of the mucosa after the initial ablation; **g** Appearance of the ablation zone after cleaning off the coagulum; **h**, **i** Appearance of the proximal (**h**) and distal (**i**) part of the ablation zone after the second ablation pass.

Radiofrequency ablation for early esophageal squamous cell neoplasia

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Institutions: Institutions are listed at the end of article.

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Introduction

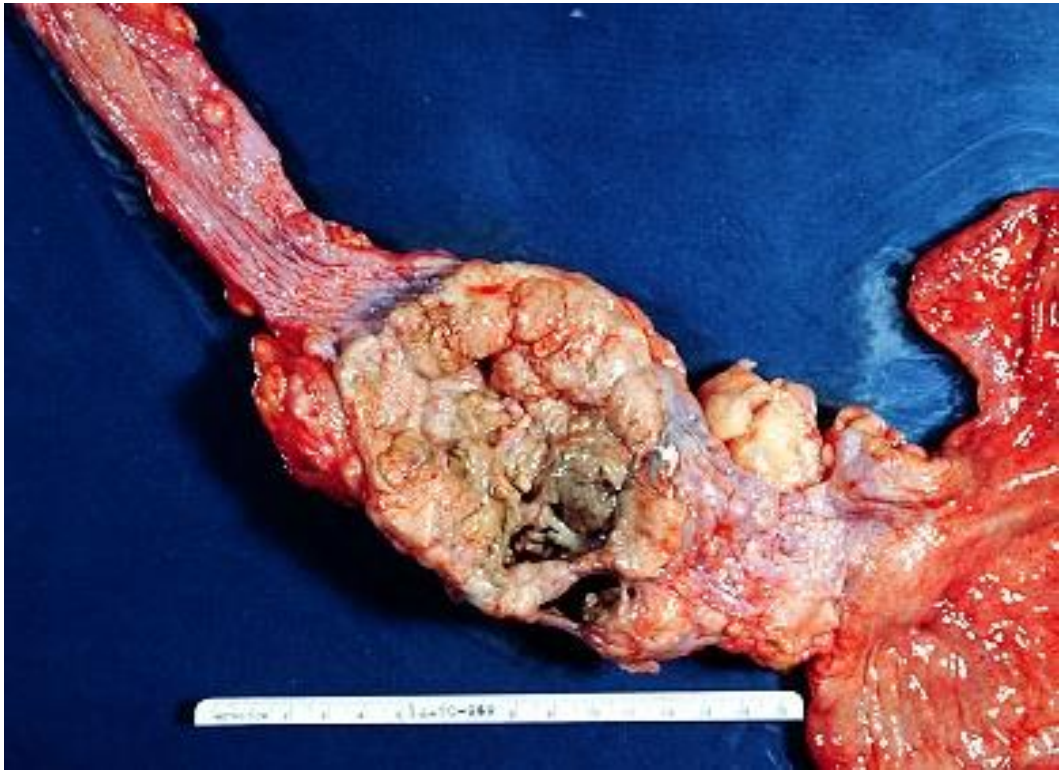
Esophageal cancer is the sixth most common cause of cancer death in the world [1]. Over 80% of esophageal cancers occur in developing countries [1], and in these areas, 90% of these cancers are esophageal squamous cell carcinoma (ESCC) [2]. The precursor lesion of ESCC is squamous intraepithelial neoplasia (squamous dysplasia), defined histologically as nuclear atypia (enlargement, pleomorphism, and hyperchromasia), loss of normal cellular polarity, and abnormal tissue maturation [3, 4]. The World Health Organization (WHO) subclassifies squamous intraepithelial neoplasia into low-grade intraepithelial neoplasia (LGIN) and high-grade intraepithelial neoplasia (HGIN), depending on the extent of the nuclear atypia and the involvement of the epithelium [4]. In China, where ESCC and its precursors are very common in some areas, a three-tier system is used, including LGIN (mild dysplasia, involving the lower third of the epithelium), medium-grade intraepithelial neoplasia (MGIN, moderate dysplasia, involving the lower two-thirds of the epithelium), and HGIN (severe dysplasia, involving the full thickness of the epithelium) [3]. Follow-up studies in China have shown that the rate of progression to ESCC differs significantly between LGIN (5.3% over 3.5 years), MGIN (26.7%), and HGIN (65.2%), and because of their significant risk of progression, MGIN and HGIN are targets for screening and therapy [5, 6].

Current treatment of esophageal squamous cell neoplasia (ESCN, including squamous intraepithelial neoplasia and invasive squamous cell carcinoma) involves surgery for lesions invading into the deep submucosa or beyond and endoscopic treatment for lesions restricted to the epithelial layer (intraepithelial neoplasia; *m1*) or the lamina propria (*m2*). Lesions invading into the muscularis mucosae (*m3*) or superficial submucosa (*sm1*) are considered the "grey zone" between endoscopic and surgical treatment.

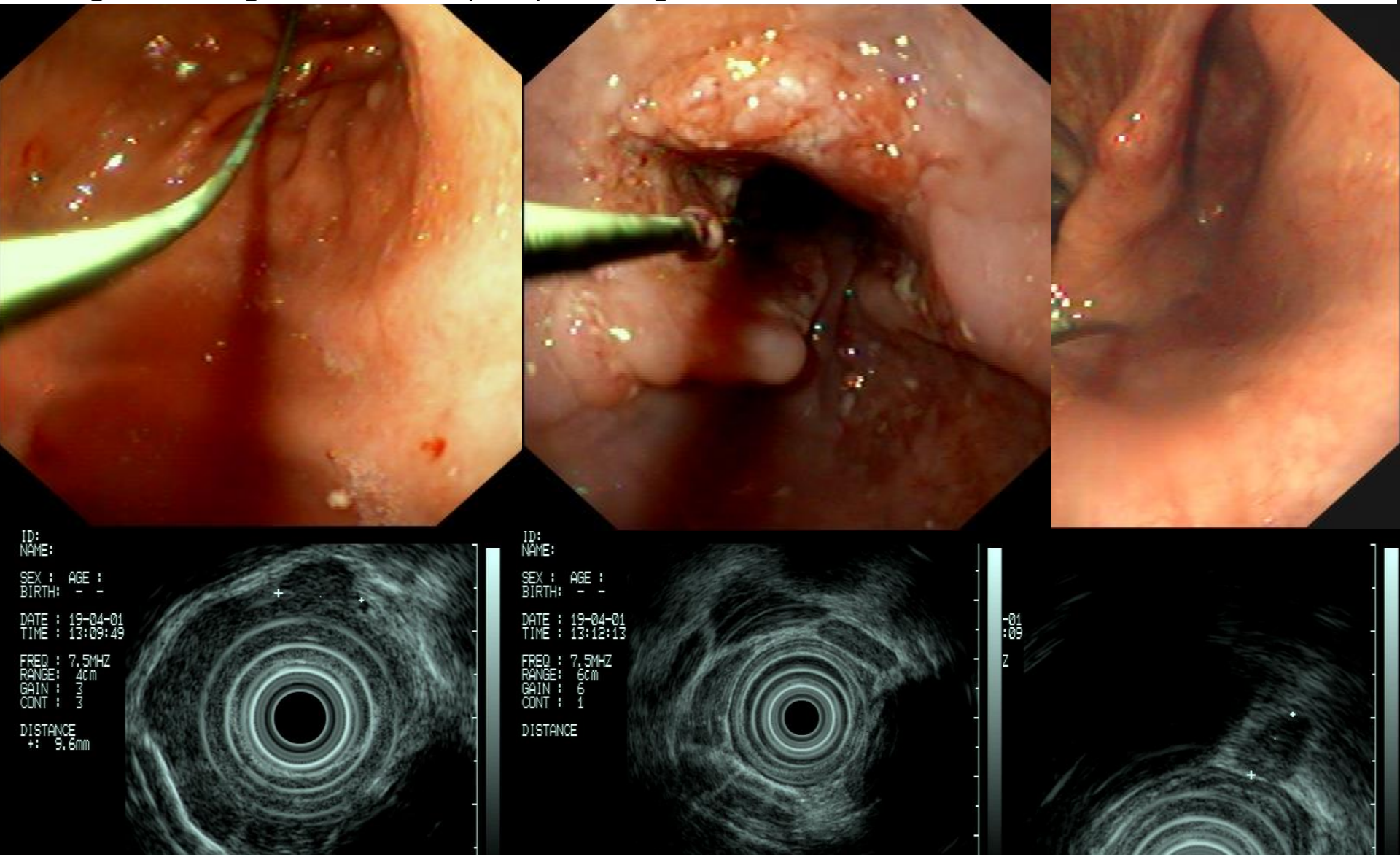
One option for endoscopic treatment of early ESCN involves endoscopic resection of unstained lesions (USLs) after Lugol's chromoscopy, as USLs are predictive for the presence of neoplasia. Endoscopic resection allows for histologic staging of infiltration depth, tumor differentiation, and lymph-vascular invasion, while completely removing the visible lesion. USLs larger than 15 mm require either piecemeal resection with the standard cap-based endoscopic resection techniques or endoscopic submucosal dissection (ESD) for complete resection. Widespread endoscopic resection/ESD, however, is technically demanding, with procedure times of many hours; it is also associated with severe esophageal stenosis for lesions that encompass > 75% of the circumference and a significant risk for esophageal perforation and bleeding. Complete endoscopic resection is also not necessarily the best approach for all patients with early ESCN. Large flat-type lesions (i.e. type 0-IIb), which carry a very low risk for deeper invasion, can be effectively treated by an endoscopic ablation technique that is much easier to apply and is associated with a very low rate of complications, such as esophageal stenosis. A safe, effective, and technically easy-to-administer ablation method is especially attractive for geographic areas where ESCN is endemic and most endoscopists have a lower level of expertise in endoscopic resection/ESD.

In China, there are many high-risk areas for ESCN, such as the Taihang mountain range in North-Central China and areas in Sichuan, Shandong, Jiangsu, and Fujian Provinces and the Xinjiang Uygur Autonomous Region [7]. These high-risk areas in China are estimated to include a total of over 100 million people, and invasive ESCN occurs here at rates approaching or surpassing 100/100 000 people per year [2], an incidence approximately 30-fold that of Barrett's-related

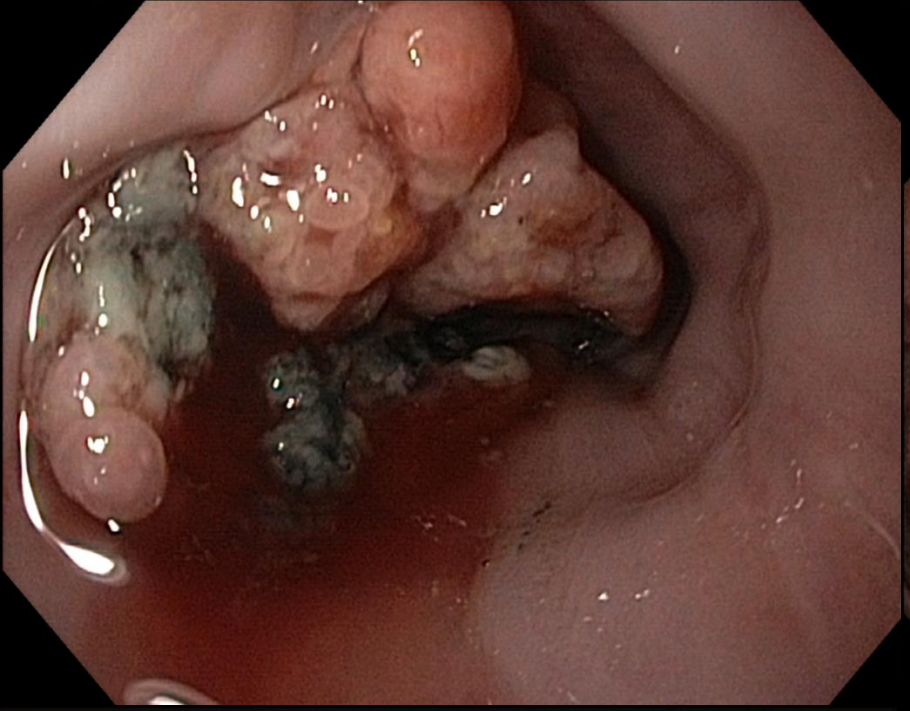
Neoplasie avanzate

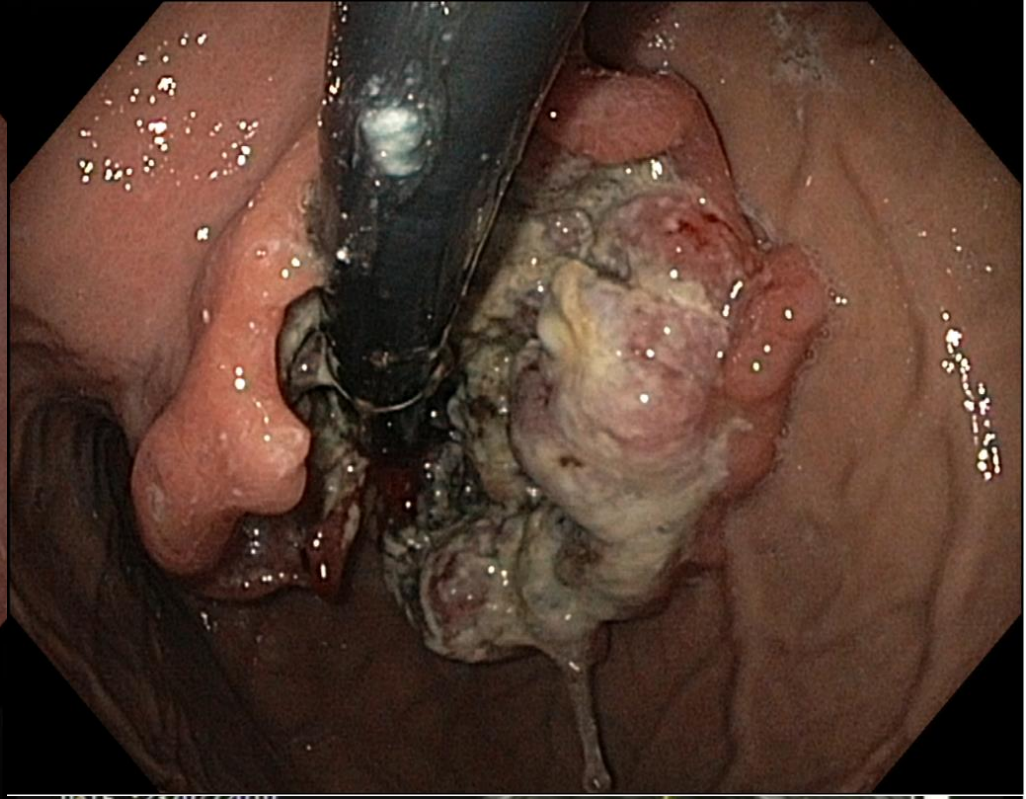


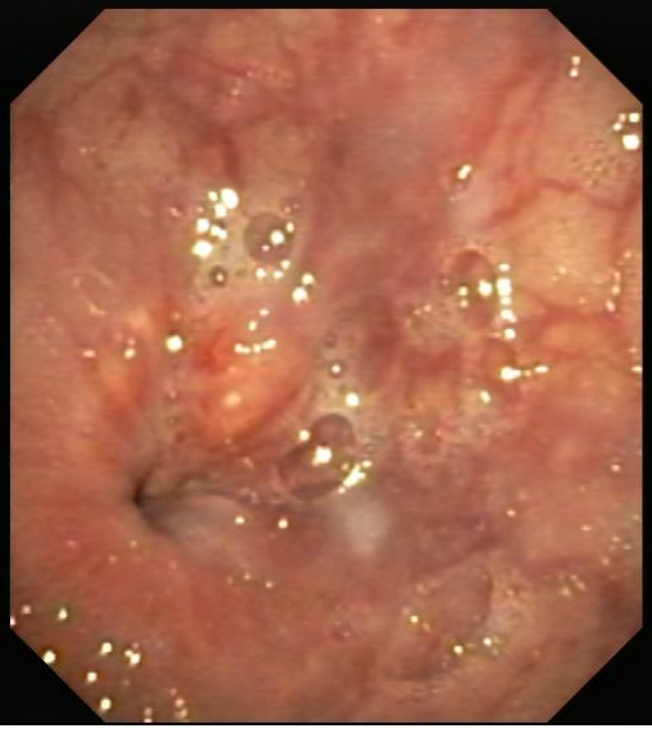
Esophageal cancers that are **> 5 cm in length**, or are sufficiently stenotic to prevent passage of an endoscope, are much more likely to be T3 or higher-stage lesions, while those that are < 5 cm in length have a greater chance (92%) of being T1 or T2.

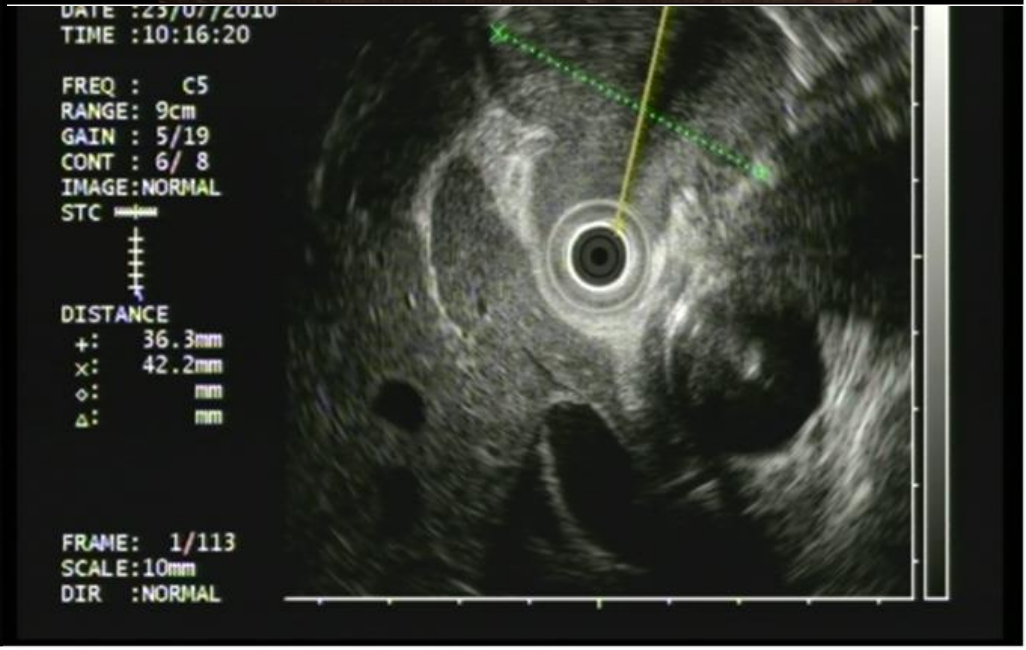


Bhutani MS et al. Length of esophageal cancer and degree of luminal stenosis during upper endoscopy predict T stage by endoscopic ultrasound. Endoscopy 2002





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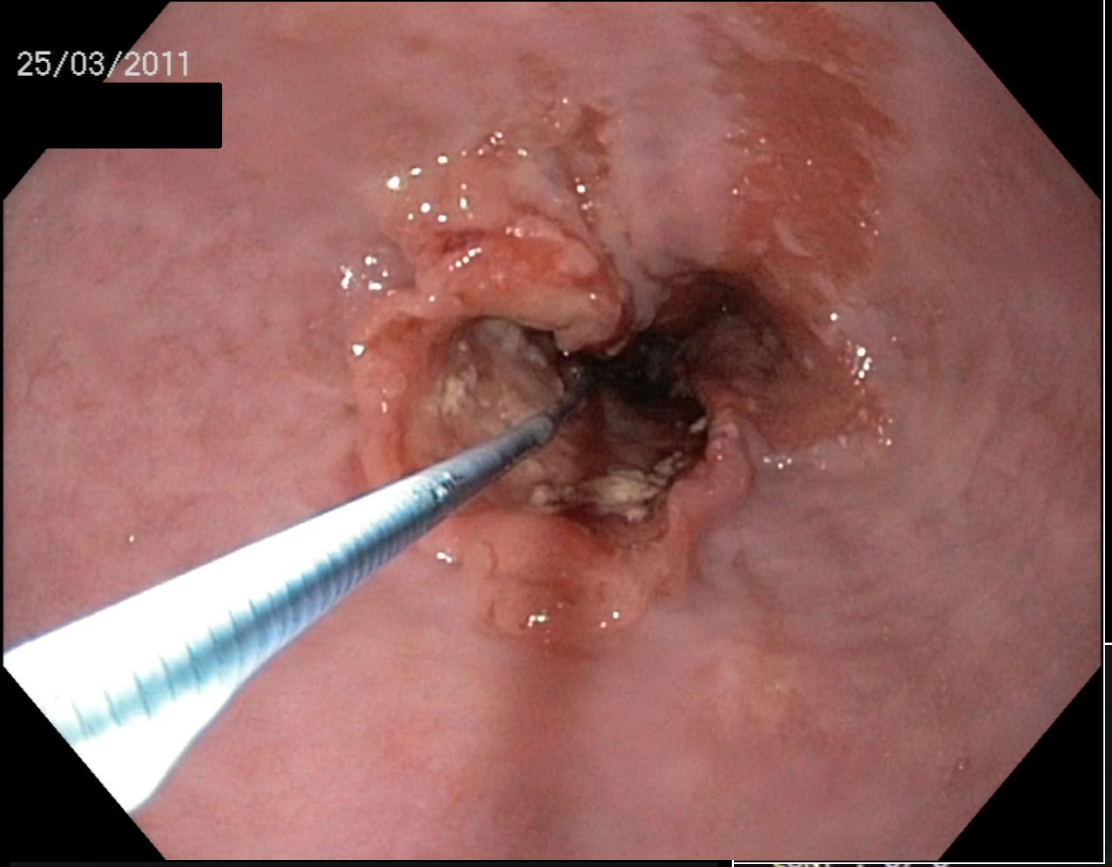
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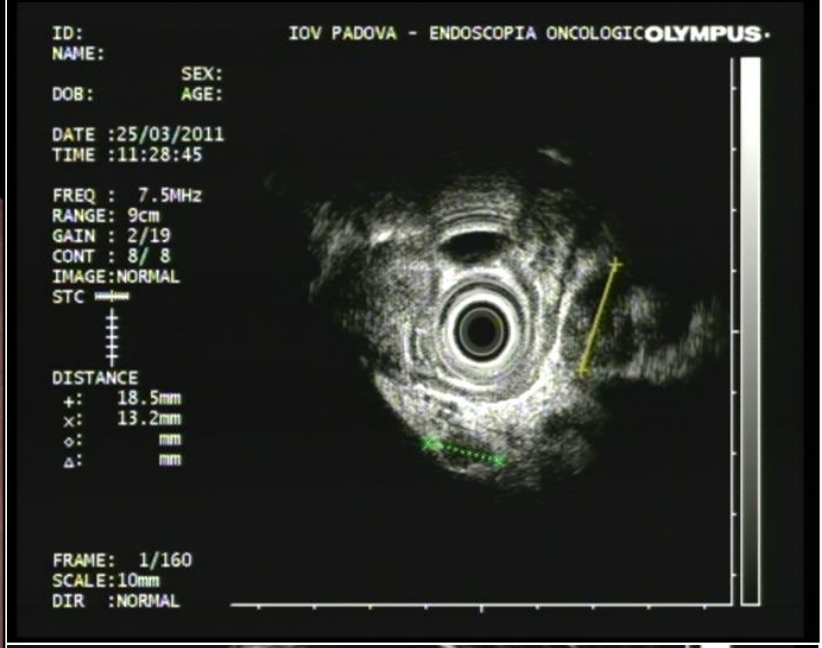
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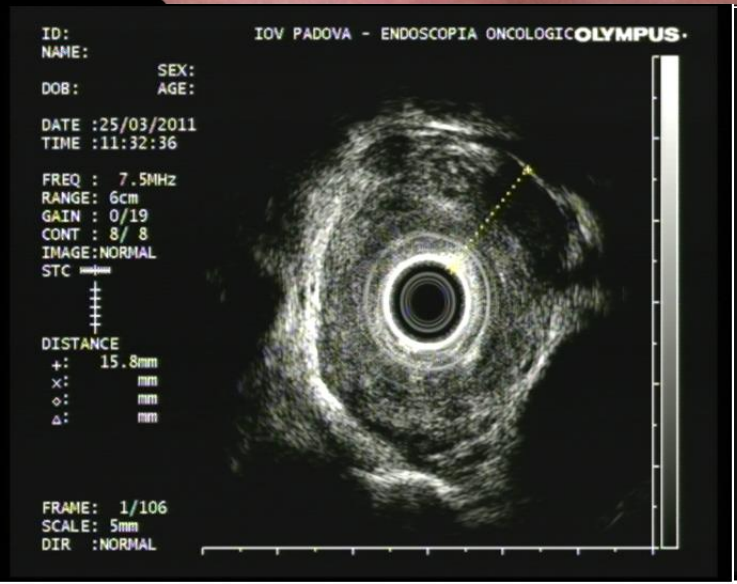
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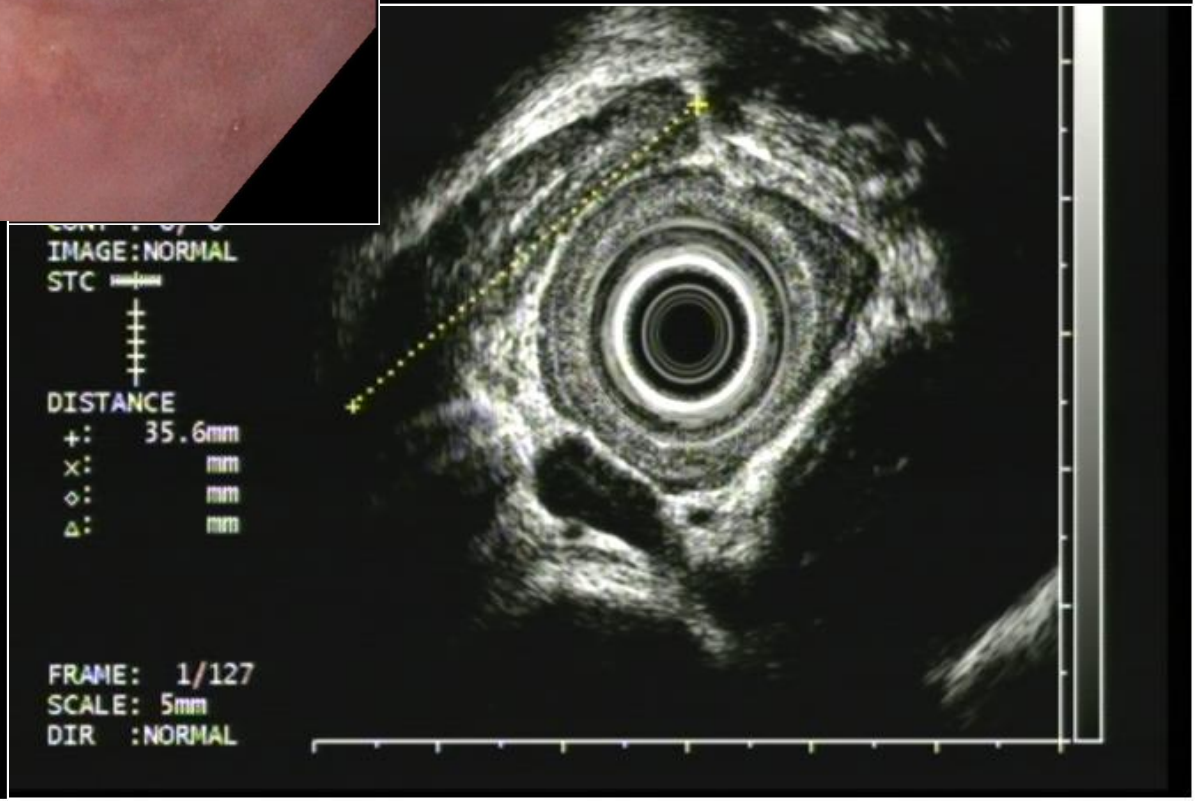
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CME

Role of Esophageal Stents in Benign and Malignant Diseases

Prateek Sharma, MD[1], Richard Kozarek, MD[2] and the Practice Parameters Committee of the American College of Gastroenterology

These recommendations provide an evidence-based approach to the role of esophageal stents in the management of benign and malignant diseases. These guidelines have been developed under the auspices of the American College of Gastroenterology and its Practice Parameters Committee and approved by the Board of Trustees. The following guidelines are based on a critical review of the available scientific literature on the topic identified in Medline and PubMed (January 1992–December 2008) using search terms that included stents, self-expandable metal stents, self-expandable plastic stents, esophageal cancer, esophageal adenocarcinoma, esophageal squamous cell carcinoma, esophageal stricture, perforations, anastomotic leaks, tracheoesophageal fistula, and achalasia. These guidelines are intended for use by health-care providers and apply to adult, but not pediatric, patients. As with other practice guidelines, these guidelines are not intended to replace clinical judgment but rather to provide general guidelines applicable to the majority of patients. Clinicians need to integrate recommendations with their own clinical judgment, and with individual patient circumstances, values, and preferences. They are intended to be flexible, in contrast to standards of care, which are inflexible policies designed to be followed in every case. Specific recommendations are based on relevant published information. The quality of evidence and strength of recommendations have been assessed using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) system, which is a system that has been adopted by multiple national and international societies. The GRADE system is based on a sequential assessment of quality of evidence, followed by assessment of the balance between benefits vs. downsides (harms, burden, and costs) and subsequent judgment regarding the strength of recommendation.

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INTRODUCTION

This review outlines the role of esophageal stents in benign and malignant disease. The quality of evidence and strength of recommendations have been assessed using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) system (**Tables 1** and **2**) (1–4). Malignant dysphagia is defined as difficulty in swallowing due to cancer resulting from a partially or completely obstructed esophageal lumen (4). Patients frequently do not recognize any symptoms until at least 50% of the luminal diameter is compromised because of the distensible nature of the esophagus, thus explaining the late presentation and poor prognosis associated with esophageal cancers. Esophageal obstruction may be either intrinsic because of esophageal cancer or extrinsic because of compression by lung cancer, lymphadenopathy, etc. The incidence of esophageal cancer continues to increase in the United States and is currently the fastest rising incidence cancer. It is estimated that there were 14,550 new cases of esophageal cancer diagnosed in 2006, with 13,770 cancer-related deaths (5). Unfortunately, the vast majority of cancers are diagnosed at a later stage wherein the cancer has invaded the submucosa and beyond with lymph node involvement or distant metastasis (6). The majority of the cases (>50%) have unresectable disease at the time of diagnosis, either because of distant metastases or unsuitable candidates for surgical resection (7), and the overall 5-year survival rate continues to be dismal (<20%) (8).

The goals of palliative therapy in patients with unresectable cancer are to ameliorate symptoms of dysphagia, treat complications, maintain oral intake, minimize hospital stay, relieve pain, eliminate reflux and regurgitation, prevent aspiration, and ultimately improve their quality of life. Various therapies have been used to palliate dysphagia in patients with esophageal carcinoma, including esophageal stenting, esophageal dilation, radiation therapy, chemotherapy, laser ablation, thermal electrocoagulation, photodynamic therapy, sclerotherapy of the tumor, and nutritional support. Esophageal stents—self-expanding metal stents (SEMSs)—have increasingly been used for palliation of malignant dysphagia and are currently the most common means of palliation. Recently, self-expandable plastic stents (SEPSs) have been used for the management of benign esophageal conditions, such as tracheoesophageal fistulas, benign esophageal strictures, esophageal perforations, and leaks. **Table 3** summarizes various conditions under

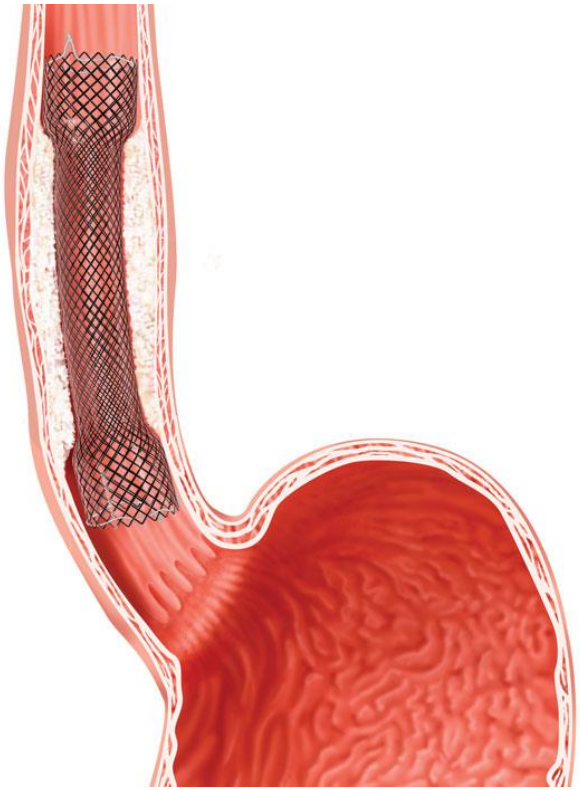

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Table 4b. Selected SEMS currently available in the United States, Europe, or Asia

Stent	Manufacturer	Material	Length (cm)	Diameter shaft/flare (mm)	Covering	Anti-reflux valve	FDA approved
Ultraflex	Boston Scientific	Nitinol	10/12/15	18/23	NC/PC	No	Yes
				23/28			
Wallflex	Boston Scientific	Nitinol	12/12/15	12/28	PC/covered	No	Yes
				23/28			
Esophageal Z	Cook	Stainless steel	8/10/12/14	18/25	PC	Yes (Dua variant)	Yes
Gianturco Z	Cook	Stainless steel	8/10/12/14	18/25	PC	Yes	No
					PC; shaft bars	No	No
Evolution	Cook	Nitinol	8/10/12.5/15	20/25	PC	No	Yes
Alimaxx-E	Alveolus	Nitinol	7/10/12	18/22	Covered	No	Yes
Niti-S	TaeWoong Medical	Nitinol	8/10/12/14	16/20	Covered	No	Yes
				18/23			
				20/25			
FerX-Ella	Ella-CS	Stainless steel	9/10.5/12/13.5/15/16.5/18/ 19.5	20/36	Covered	Yes/no	No
Dostent	MI Tech	Nitinol	6/9/12	18/30	Covered	Yes/no	No
Flamingo Wallstent	Boston Scientific	Stainless steel	12/14	20/30	PC	No	No
Polyflex	Boston Scientific	Polyester	9/12/15	16/20	Covered	No	Yes
				18/23			
				21/28			

FDA, Food and Drug Administration; NC, not covered; PC, partially covered; SEMS, self-expanding metal stent.

Table 1: Indications and contraindications for stent use in esophageal obstruction due to malignancy.

Indications
Unresectable malignant esophageal obstruction
Extrinsic esophageal compression by primary or secondary mediastinal tumors
Actual or impending fistula
Malignant gastroesophageal anastomotic leaks
Tumor recurrence after surgery or chemoradiotherapy
Contraindication to chemoradiotherapy
Contraindications
Curable disease by multimodality treatment (relative)
Tumor or stricture within 2 cm of proximal esophageal sphincter
Uncorrectable coagulopathy
Potential for significant airway compression
Recent high-dose chemoradiotherapy (within 3–6 weeks)
Terminal ill patient with limited life expectancy

Table 6. Complications of esophageal self-expandable metal stents

Immediate (at the time of placement)
Aspiration
Airway compromise
Malposition
Delivery system entrapment
Stent dislodgement
Perforation
Early (up to 1 week after stent placement)
Bleeding
Chest pain
Nausea
Late (beyond 1 week of successful stent placement)
Recurrent dysphagia due to reobstruction from tumor or food impaction
Migration
Tracheoesophageal fistula
Bleeding
Gastroesophageal reflux disease/aspiration

Adapted from Baron (65).

Eur J Clin Nutr. 2015 Dec 16. doi: 10.1038/ejcn.2015.206. [Epub ahead of print]

Stents in patients with esophageal cancer before chemoradiotherapy: high risk of complications and no impact on the nutritional status.

Mão-de-Ferro S[1], Serrano M[1], Ferreira S[1], Rosa I[1], Lage P[1], Alexandre DP[2], Freire J[3], Mirones L[4], Casaca R[5], Bettencourt A[5], Pereira AD[1].

Author information

Abstract

Preoperative chemoradiotherapy is the standard of care for locally advanced esophageal cancer, causing persistent deterioration in the nutritional status. We performed a prospective study to evaluate the safety and efficacy of esophageal double-covered self-expandable metal stents in patients with esophageal cancer before chemoradiotherapy. The nutritional status and dysphagia were prospectively recorded. Eleven patients were included: eight were moderate and three were severely malnourished. After stent placement, dysphagia improved in all patients. With regard to complications, one patient developed an esophageal perforation that required urgent esophagectomy. Four patients presented stent migration. Three of these patients required enteral nutrition and none was submitted to surgery because of poor nutritional status. Of the other six patients, only four were operated upon. **Stent placement presented a high complication rate and did not prevent weight loss or malnutrition**. Other alternatives, including naso-gastric tube placement or endoscopic percutaneous gastrostomy or jejunostomy, should be considered.

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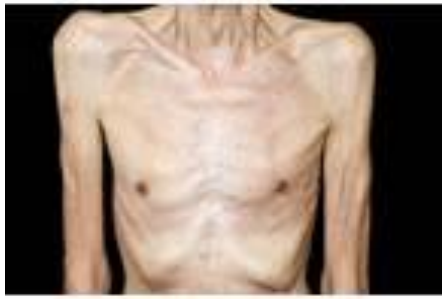
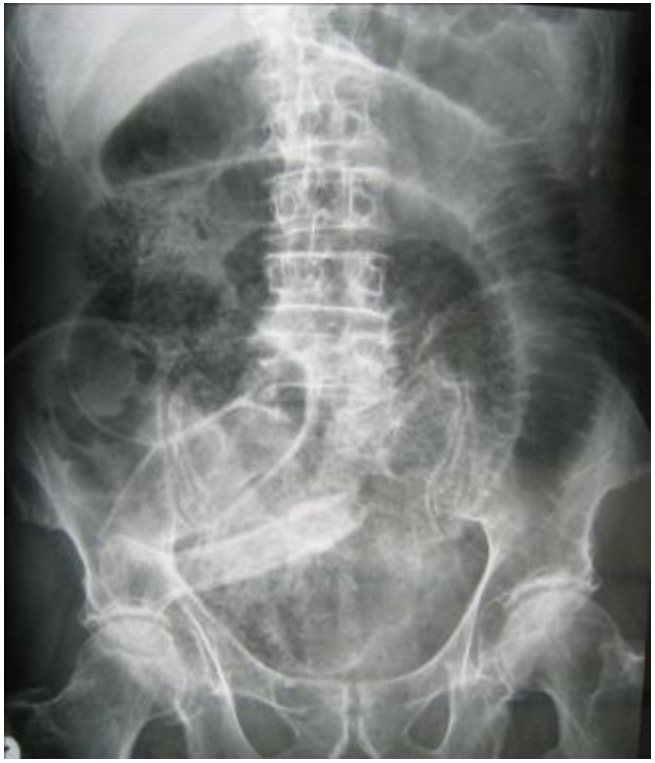


Down-staging of an advanced esophageal carcinoma with chemoradiotherapy leading to stent migration necessitating colectomy.



Thuraisingam AI et al. Gastrointest. Endosc. March 1, 2004. Volume 59, Issue 3; Pages 457-60

Rimozione

ENDOSCOPY

Stent-in-Stent Technique for Removal of Embedded Esophageal Self-Expanding Metal Stents

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OBJECTIVES: **Partially covered self-expanding metal stents (SEMSs) are regularly used for malignant and occasionally for benign esophageal disorders. Safe removal of these stents can be challenging due to embedding of the uncovered stent ends. Our aim is to report the results of removal of embedded, partially covered SEMSs by induction of pressure necrosis using the stent-in-stent technique.**

METHODS: **Consecutive patients referred to three endoscopy units in 2007–2009, treated by the stent-in-stent technique, were reviewed. The partially covered SEMSs were inserted for malignant ($n=3$) or benign ($n=16$) conditions and were left *in situ* for a median of 42 days (14–189). When SEMSs were found to be embedded, a fully covered self-expanding plastic stent (SEPS) or fully covered SEMS was placed inside the partially uncovered SEMS. Subsequent removal of both stents was planned after a period of 10–14 days.**

RESULTS: **In total, 23 stent-in-stent procedures were performed in 19 patients (10 males). Placement of a fully covered stent (SEPS: $n=9$ and SEMS: $n=14$) was technically successful in all patients. In 21 of 23 (91%) procedures, both stents were successfully removed in one procedure after a median of 12 days (5–18). In two patients, a repeat stent-in-stent procedure was needed for persistent embedding of the partially uncovered SEMSs. One (5%) procedure was complicated by severe bleeding, which could be treated endoscopically. In seven (36%) patients, the initial disorder had resolved after stent removal and no further endoscopic interventions were needed. Two (10%) patients were treated with chemoradiation or surgery for esophageal cancer after stent removal. In 10 (53%) patients, a repeat endoscopic intervention was required during follow-up because of progressive dysphagia or a persisting leak or fistula.**

CONCLUSIONS: **The stent-in-stent technique is safe and effective for the removal of partially covered SEMSs that are embedded in the esophageal wall.**

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INTRODUCTION

For the management of malignant dysphagia, self-expanding metal stents (SEMSs) are favored over self-expanding plastic stents (SEPSs). Although equally safe and effective for the relief of dysphagia, SEPSs have been shown to have a higher migration rate (1,2).

For benign esophageal disorders, such as anastomotic leaks, iatrogenic perforations, fistulas, or refractory strictures, no evidence exists on what type of stent is the optimal device of choice. As SEMSs are not Food and Drug Administration (FDA)-approved for these benign disorders, most data are available on the placement of FDA-approved SEPSs for these conditions (3–11).

Despite the lack of FDA approval, SEMSs may be preferable over SEPSs in some benign disorders, especially those not associated with a stricture, such as leaks, perforations, and fistulas. In these disorders, embedding of the uncovered nitinol mesh may serve as an anchor to the esophageal wall, ensuring sufficient sealing (3,12,13).

On the other hand, stent embedding may also be an important limitation of SEMS placement, as this precludes safe stent removal, which is almost always indicated in case of stent placement for benign lesions. The subsequent tissue response, which may enhance the degree of stent embedding, is supposed to be caused

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Argon plasma coagulation: a less-expensive alternative to the "stent-in-stent" technique for removal of embedded partially covered esophageal stents

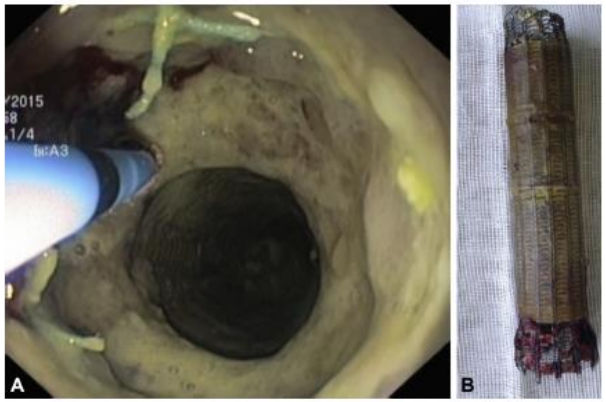

Figure 1. **A**, Argon plasma coagulation of embedded partially covered metal stent. **B**, Partially covered metal stent removed with destroyed ingrown tissue at the edges.

Fully covered metal stents (FCMSs) are burdened by migration (33% to 89%). Partially covered metal stents (PCMSs), in cases of benign pathologic conditions without any concomitant stenosis, have been used to allow tissue ingrowth at the edges of the stent, thus guaranteeing its adhesion to the lumen. However, this causes difficulties in stent removal. Therefore, deployment of the FCMS for 2 to 7 days has been described to induce necrosis of ingrown tissue, allowing PCMS removal. The so-called "stent-in-stent" technique, although effective, is expensive, requiring the use of a second stent. An esophageal-pleural fistula developed in a 60-year-old woman after she had undergone esophagectomy for cancer. A PCMS was inserted and was left in place for 5 weeks. Removal failed because of ingrown tissue. In the same session, using a standard gastroscope, a 2.3-mm axial probe for argon plasma coagulation (APC) was used to destroy all ingrown tissue at the edges of the PCMS. The settings chosen were: precise coagulation, gas-flow of 1 L/min, 60 W, effect 3. To limit the effect to the superficial layer, thus avoiding trimming of the self-expanding metal stent and esophageal wall injury, APC-induced necrosis of the ingrown tissue allowed easy disentanglement of the stent from the lumen (Fig. 1; Video 1, available online at www.giejournal.org). The fistula healed, and no adverse events related to removal were reported. In conclusion, APC is a safe tool to destroy ingrown tissue and easily remove an entangled PCMS. Moreover, the APC technique is cheap and allows PCMS removal in only 1 step.

This video can be viewed directly from the GIE website or by using the QR code and your mobile device. Download a free QR code scanner by searching "QR Scanner" in your mobile device's app store.

DISCLOSURE

All authors disclosed no financial relationships relevant to this publication.

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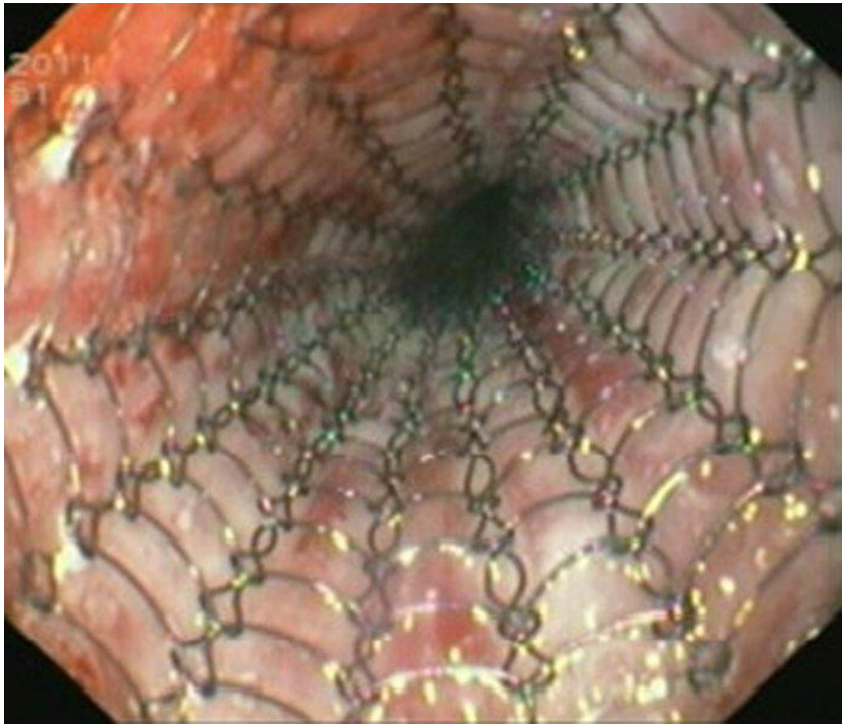
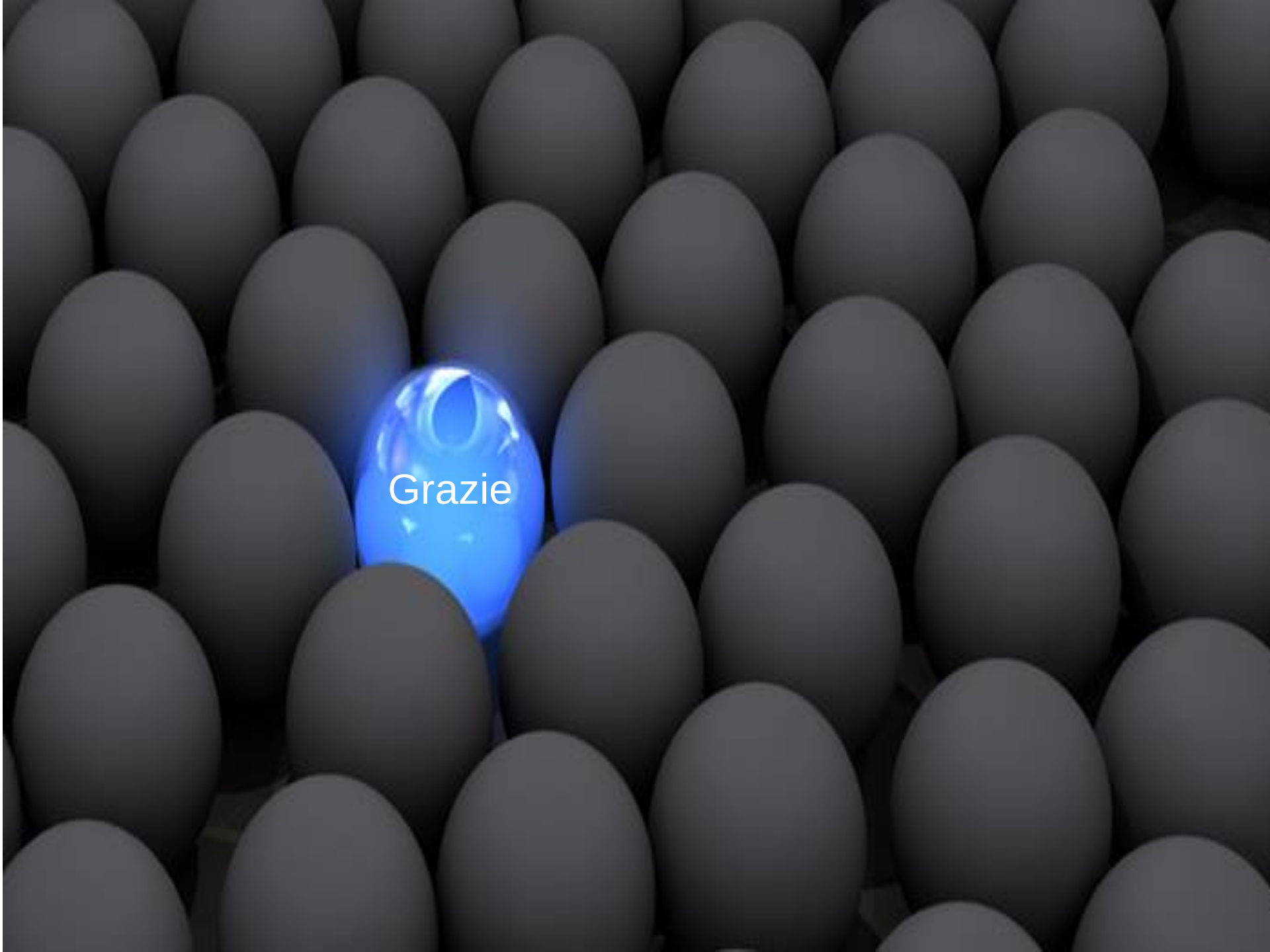
Il loro posizionamento dovrebbe essere deciso dal **Team Multidisciplinare** del centro di riferimento

- Possono creare disturbi alle metodiche radiologiche in fase di stadiazione e ristadiazione
- Ostacolare l'intervento chirurgico
- Peggiorare il quadro clinico (fistola, compressione etc)

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