DISSERTATION

Retrospective dual-center study of the benefit of diagnostic gastroscopy with forward-optic before endoscopy with side-viewing optic

Retrospektive Dual-Center Studie zum Zusatznutzen einer diagnostischen Gastroskopie mit prograder Optik vor der Endoskopie mit Seitenblickoptik

zur Erlangung des akademischen Grades

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List of abbreviations:

ACMI. American Cystoscope Manufacturers Incorporated

AFI. Autofluorescence imaging

ASA. American Society of Anesthesiology

BLI. Blue light imaging

CF. Close focus

DOACs. Direct oral anticoagulation

EGD. Esophagogastroduodenoscopy

EMR. Endoscopic mucosal resection.

ESD. Endoscopic submucosal dissection.

ERCP. Endoscopic retrograde cholangiopancreatography

ESGE. European society of gastrointestinal endoscopy

EUS. Endoscopic ultrasonography

FBS. Frame per second

FNA. Fine needle aspiration

FNB. Fine needle biopsy

GI. Gastrointestinal

GIST. Gastrointestinal stromal tumor

HD^{+}. High definition

LAMS. Lumen apposing metal stent

LCI. linked color imaging

LFT. Liver function test

NBI. Narrow band imaging

PEP. Post ERCP pancreatitis

RDI. Red dichromatic imaging

RFA. Radiofrequency ablation

ROC curve. Receiver operating characteristic curve

SOD. Sphincter of Oddi dysfunction

THI. Tissue harmonic imaging

TXI. Texture and color enhancement imaging

WLE. White light endoscopy

Abstract

Background: Duodenoscopes and echoendoscopes lack flexibility, have narrower field of view, and lack modern optical techniques compared with standard gastroscopes. It is unknown whether gastroscopy should be performed routinely before endoscopy with non-forward optic to avoid missing lesions, create a roadmap and probably reduce the complications associated with endoscopic retrograde cholangiopancreatography / endoscopic ultrasonography (ERCP/EUS). Since no consensus has been reached, the practice is widely variable and depends on the endoscopist's experience and preference.

Aim: This study aimed to determine the proportion of patients with intraluminal relevant lesions when gastroscopy is performed routinely before ERCP or EUS, to determine whether patient's age, hemoglobin level, and intake of anticoagulants are associated with the presence of relevant lesions, and to evaluate the impact of EGD findings on the subsequent ERCP/EUS.

Methods: This is a dual-center retrospective study conducted at the Charité- University Medicine and Vivantes Hospital Spandau, which is an academic center affiliated with Charité, between August 2020 and December 2020. Patients underwent ERCP or EUS for non-luminal diagnosis were included in this study.

Results: A total of 245 patients (145 at Charité- University Medicine and 100 at Vivantes Hospital Spandau) were included in this study. Among them, 95 patients had relevant lesions detected by esophagogastroduodenoscopy (EGD) **(38.78%, 95% confidence interval: 32.89–45.01)**. Patients with relevant lesions were significantly older and had lower hemoglobin levels than those without lesions **(p = 0.029 and < 0.001, respectively)**. No association was observed between the detection of relevant lesions and the intake of anticoagulants **(p = 0.336)**. The EGD findings had a direct impact on the subsequent ERCP/EUS in 17 patients **(6.93%)**. Out of 15 patients with stenosis, dilatation was needed in 6 patients **(2.4%)** to facilitate the passage of duodenoscopes or echoendoscope.

Conclusion: We recommend performing EGD before every non-forward endoscopy to avoid missing relevant lesions, especially in patients aged > 50 years and those with anemia, and probably help to reduce general complications related to ERCP/EUS.

Zusammenfassung:

Hintergrund: Duodenoskope und Echoendoskope sind im Vergleich zu den Standardgastroskopen weniger flexible Instrumente, bei den meistens die modernen optischen Techniken fehlen. Es ist nicht bekannt, ob die Gastroskopie routinemäßig vor der Endoskopie mit Seitenblick-Optik durchgeführt werden sollte, um intraluminale relevante Läsionen zu detektieren, und die mit ERCP/EUS verbundenen Komplikationen zu verringern. Die Praxis ist sehr unterschiedlich und hängt von der Erfahrung und Präferenz des Untersuchers bzw. der endoskopierenden Einrichtung ab.

Ziel der Studie: Bestimmung des Anteils der Patienten mit intraluminalen relevanten Läsionen, wenn die Gastroskopie routinemäßig vor der ERCP oder EUS durchgeführt wird. Außerdem sollte festgestellt werden, ob es einen Zusammenhang zwischen Alter, Hämoglobinspiegel, und Einnahme von Antikoagulantien und dem Vorhandensein relevanter Läsionen gibt.

Methodik: Es handelt sich um eine retrospektive Dual-Center Studie, die an der Universitätsmedizin Charité und Vivantes Klinikum Spandau zwischen August 2020 und Dezember 2020 durchgeführt wurde. Patienten, die eine ERCP oder eine EUS erhalten hatten, wurden eingeschlossen.

Ergebnisse: 245 Patienten wurden berücksichtigt, davon 145 aus der Charité und 100 aus dem Vivantes Klinikum Spandau. Bei 95 Patienten wurden relevante Läsionen mittels Ösophagogastroduodenoskopie festgestellt **(38.78%, 95% Konfidenzinterval: 32.89– 45.01)**. Patienten mit relevanten Läsionen waren signifikant älter und hatten einen niedrigeren Hämoglobinspiegel verglichen mit Patienten ohne Läsionen **(*p* = 0.029 und 0.001, jeweils)**. Es gab keinen statistischen Zusammenhang zwischen der Detektion relevanter Läsionen und der Einnahme von Antikoagulantien **(*p* = 0.336)**. Bei 17 Patienten **(6.93 %)** hatte der ÖGD-Befund eine direkte Auswirkung auf die anschließende ERCP/EUS. Von 15 Patienten mit Stenose war die Dilatation bei 6 Patienten erforderlich **(2.4 %)**, um die Passage des Duodenoskops/ Echoendoskops zu ermöglichen.

Schlussfolgerung: Wir empfehlen die Durchführung einer Gastroskopie vor jeder Seitenblickendoskopie, um relevante Läsionen nicht zu übersehen, insbesondere bei Patienten > 50 Jahre oder mit Anämie. Darüber hinaus können mit hoher Wahrscheinlichkeit die mit ERCP/EUS verbundenen Komplikationen verringert werden.

1. Introduction and a brief history of gastrointestinal endoscopy

The history of gastrointestinal endoscopy is very interesting and impressive. Endoscopes evolved over time from simple rigid and “dangerous” instruments to semisolid and fiberoptic endoscopes in the mid-twentieth century. Modern endoscopes with high optical resolution and the possibility of performing complex interventions are now available.

1.1. Esophagogastroduodenoscopy (EGD)

Rigid endoscopy (1805 –1932)

The first attempts in endoscopy were in the urogenital tract. The main problem with these endoscopes was the lack of flexibility because they were made of metal. Additionally, no suitable source of illumination was found, so the intraluminal vision was significantly impeded [1]. In 1805, Philipp Bozzini developed a “real” endoscope (Figure 1). His endoscope was very simple and made of metal, and for illumination, he used a candle, and the light was then reflected by a mirror [1, 2]. The endoscope was used primarily for the urethra, urinary bladder, and vagina. The clinical usefulness was very limited due to rigidity and restricted visibility [1, 2]. After that, Pierre Salomom Segalas (1826) in France, John Fischer (1827) in Boston, USA, and Desormeaux (1855) in France developed similar endoscopes [1, 2]. The important development in Desormeaux's instrument was using a “lamp fueled with gazogene, which is a mixture of alcohol and turpentine” [1, 2]. Desormeaux was a surgeon at the Necker Hospital in Paris and used his scope to investigate urologic diseases (Figure 2) [1, 2].

Fig. 1 Bozzini's endoscope, 1805. (Source: Achord, J.L. and V.R. Muthusamy, The history of gastrointestinal endoscopy, in Clinical gastrointestinal endoscopy. 2019, Elsevier. p. 2-11. e1, used with friendly permission.)

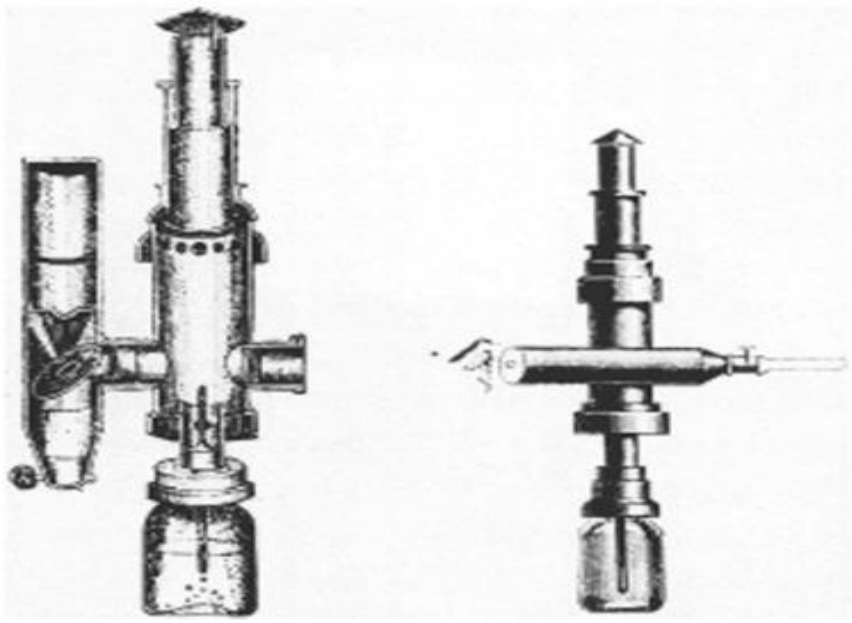


Fig. 2 Desormeaux's endoscope, 1853. (Source: Achord, J.L. and V.R. Muthusamy, The history of gastrointestinal endoscopy, in Clinical gastrointestinal endoscopy. 2019, Elsevier. p. 2-11. e1, used with friendly permission.)

In 1868, Adolf Kussmaul performed the first rigid gastroscopy by “a cooperative sword swallower” [1, 2]. His gastroscope was made of metal, and illumination was provided by a modified Desormeaux's lamp (Figure 3) [1, 2]. This gastroscopy was demonstrated at “the meeting of the medical section of the Society of Naturalists” in Freiburg, Germany [2]. Kussmaul successfully visualized the esophagus and gastric pouch, but with his rigid instrument and the lack of good visibility, he refrained from further attempts [1, 2]. In 1882, an another illumination source was developed by Bruck in Breslau and Milliot in Paris [1, 2]. They used a “platinum wire charged with direct current” [1], but the heat generated from this illumination source was problematic, so a cooling system was necessary [1, 2]. Gustav Trouve, an engineer in Paris, modified the version of Bruck and Milliot by improving the stability and intensity of the light source [2].

Josef Leiter, “an instrument maker in Vienna”, and Johan von Mikulicz, a “surgeon in Vienna”, developed both an esophagoscope and gastroscope [2]. After the invention of the incandescent electric light bulb by Edison in 1879 and the demonstration of this invention at “the International Electrical Exhibition in Vienna” in 1883 [2], Leiter replaced the platinum wire in the esophagoscope with an electric light bulb [2]. Their esophagoscope was usable and practical, but their gastroscope was unsuccessful. Further appreciated efforts in the field of gastroscopy were made by Rosenheim in 1896 in Germany and Jackson in 1900 in the USA [2].

Fig. 3 Kussmaul's gastroscope, 1868. (Source: Achord, J.L. and V.R. Muthusamy, The history of gastrointestinal endoscopy, in Clinical gastrointestinal endoscopy. 2019, Elsevier. p. 2-11. e1, used with friendly permission.)

Hans Elsner and Rudolph Schindler in Germany contributed to the great development of gastroscopy [1]. In 1911, Elsner developed a rigid gastroscope (Figure 4), and in 1922, Schindler modified this gastroscope by adding an "air channel to clear the lens", which was extremely important and helpful [1]. In 1923, Schindler published his "Textbook and Atlas of Gastroscopy" [1].

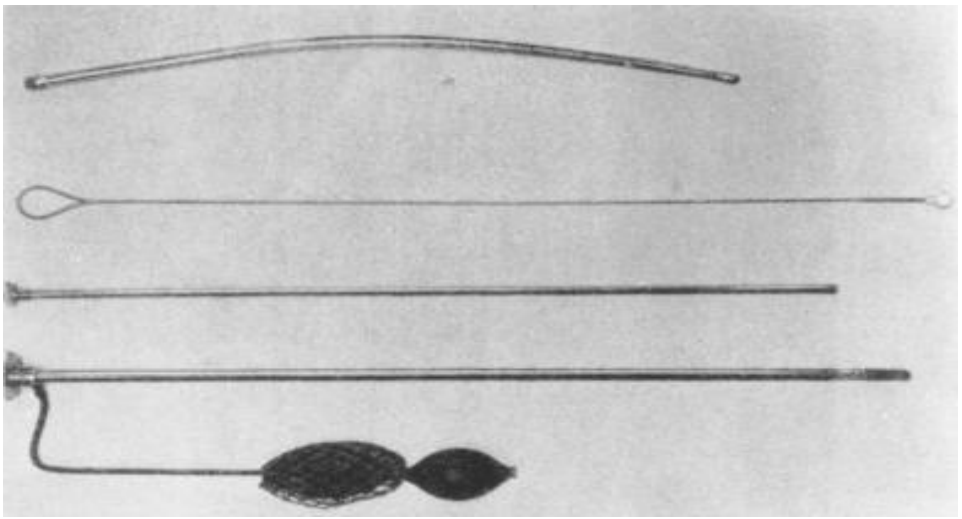


Fig. 4 Elsner's gastroscope, 1911. (Source: Achord, J.L. and V.R. Muthusamy, The history of gastrointestinal endoscopy, in Clinical gastrointestinal endoscopy. 2019, Elsevier. p. 2-11. e1, used with friendly permission.)

Semiflexible endoscopy (1932–1957)

Performing rigid gastroscopy was technically challenging mainly because of the perforation risk. At that time, this was usually a lethal complication. Therefore, the gastroscopy was not widely accepted [1]. In 1932, Schindler, in cooperation with George Wolf, developed an effective semiflexible gastroscope (Wolf-Schindler semiflexible gastroscope, Figure 5) [1]. The distal half of this endoscope consisted of "coiled bronze wire with a protective outer cover of rubber" [1], and the scope could bend up to 34° without distortion of the image [2]. Schindler is considered "the father of gastroscopy" due to his effort and semiflexible gastroscope, and the gastroscopy was turned from a rarely performed dangerous procedure into a relatively safe one in gastroenterology [1]. In 1933, he trained more than 50 doctors from Europe and America to perform gastroscopy [2]. The period of semiflexible endoscopy from 1932 to 1957 is called the "Schindler era" [1].

After that, the German source of gastroscopes disappeared duo to the second world war [1, 2]. Several companies in the USA started producing semiflexible endoscopes. For example, in 1940, Cameron Surgical Specialty Company developed its first gastroscope in cooperation with Schindler in 1940 (Cameron-Schindler flexible gastroscope) [1, 3]. In 1946, Eder-Hufford semiflexible gastroscope was produced [1, 4]. Furthermore, the American Cystoscope Manufacturers Inc. (ACMI) and Eder Company also developed gastroscopes in 1950 and 1953, respectively [1].

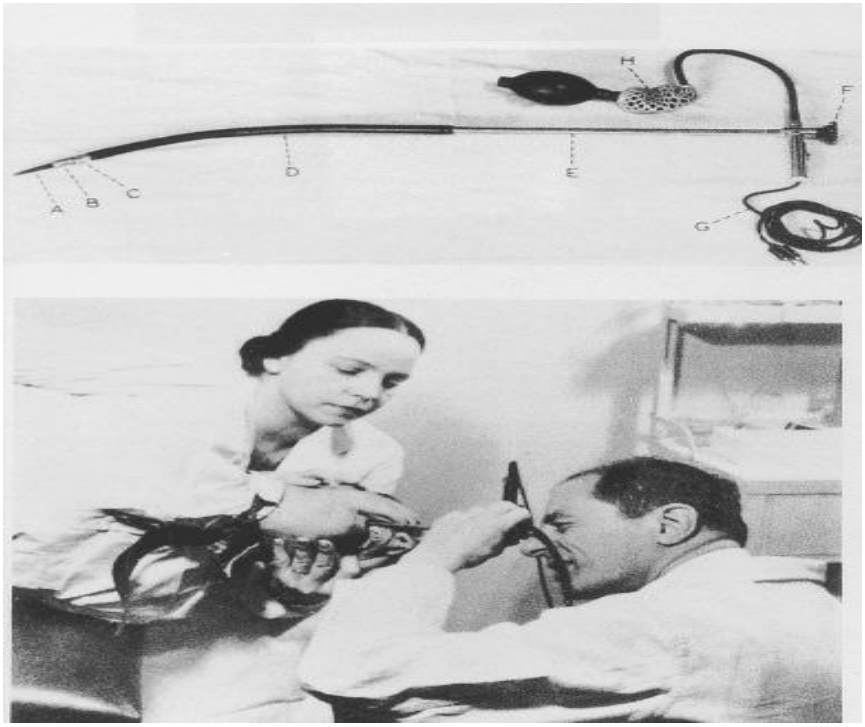


Fig. 5 Wolf-Schindler gastroscope (top). Schindler while performing gastroscopy (bottom). (Source: Achord, J.L. and V.R. Muthusamy, The history of gastrointestinal endoscopy, in Clinical gastrointestinal endoscopy. 2019, Elsevier. p. 2-11. e1, used with friendly permission.)

Furthermore, several instruments were developed to take biopsies from the stomach, for example, Kenamore biopsy forceps in 1940 and Benedict operation gastroscope in 1948 (Figure 6) [1, 2].

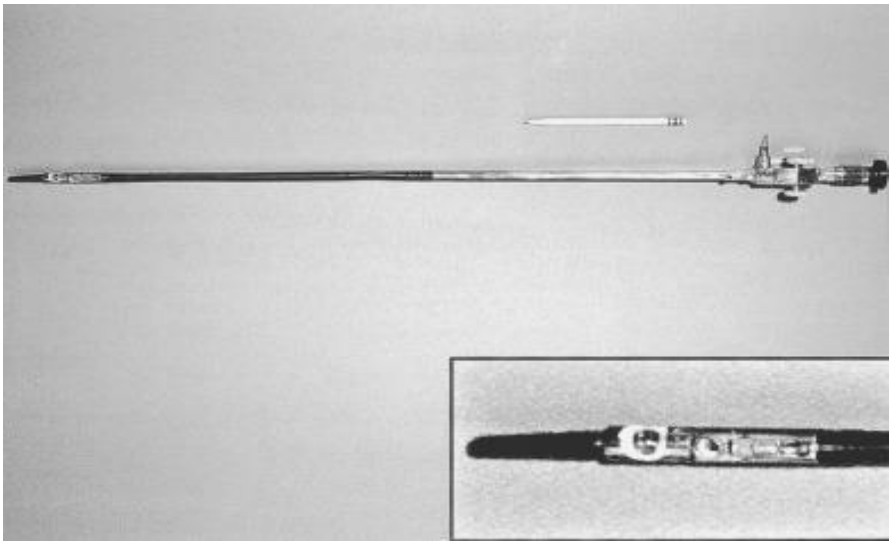


Fig. 6 Benedict operating gastroscope. (Source: Achord, J.L. and V.R. Muthusamy, The history of gastrointestinal endoscopy, in Clinical gastrointestinal endoscopy. 2019, Elsevier. p. 2-11. e1, used with friendly permission.)

Fiberoptics:

Basil Hirschowitz (University of Michigan, Ann Arbor, MI, USA) pioneered the field of flexible gastroscopy and fiberoptics in cooperation with Larry Curtiss and Marvin Pollard [1, 2]. He published his first paper on fiberoptics in 1958 [1, 5]. In October 1960, Hirschowitz in collaboration with ACMI produced “Hirschowitz Gastroduodenal Fiberscope” (Figures 7 and 8) [1, 2].

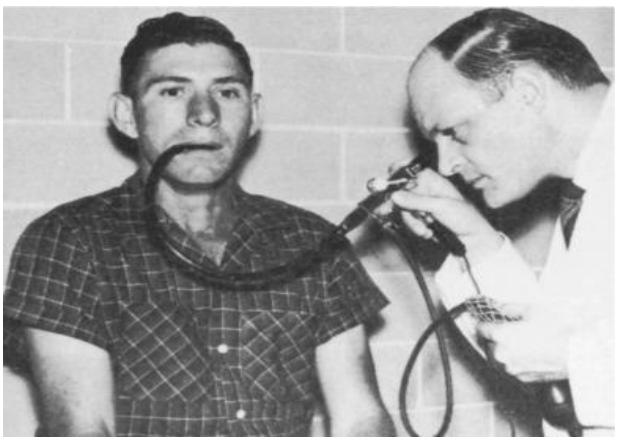


Fig. 7 Hirschowitz examining with his fiberoptic. (Source: Achord, J.L. and V.R. Muthusamy, The history of gastrointestinal endoscopy, in Clinical gastrointestinal endoscopy. 2019, Elsevier. p. 2-11. e1, used with friendly permission.)

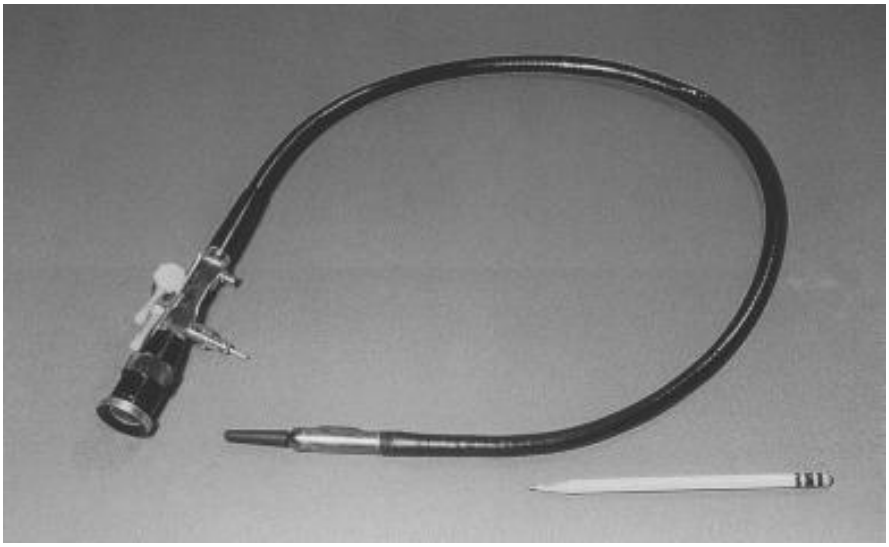


Fig. 8 ACMI fiberscope, 1962. (Source: Achord, J.L. and V.R. Muthusamy, The history of gastrointestinal endoscopy, in Clinical gastrointestinal endoscopy. 2019, Elsevier. p. 2-11. e1, used with friendly permission.)

Several problems with fiberoptics were observed [1], these scopes were too flexible, so intubation of the duodenum was almost always impossible. Furthermore, thermal mucosal injury from the light source at the tip of the endoscope was possible. With side-viewing optic, insertion of the instrument into the pharynx under direct vision and evaluation of the esophagus and some points in the stomach were impossible. Vision restriction also occurred with repeated use of the endoscope because of the defected glass fibers [1]. However, with rapid improvement in production, several modified versions were produced by LoPresti and Olympus and Machida in Japan (Figure 9) [2]. By 1971, the endoscope was lengthened to 105 cm, so the intubation of the duodenum was possible, four- way controlled tip and tip deflection until 180° was introduced [1]. With an integrated so-called “teaching head” the observation of the examination by an additional person was possible. By 1970, the performance of gastroscopy with fiberoptic was standard [1].

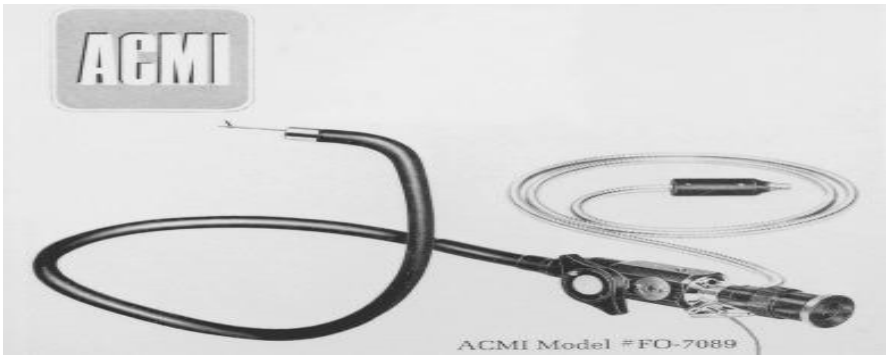


Fig. 9 LoPresti forward-viewing esophagogastroscope, 1970. (Source: Achord, J.L. and V.R. Muthusamy, The history of gastrointestinal endoscopy, in Clinical gastrointestinal endoscopy. 2019, Elsevier. p. 2-11. e1, used with friendly permission.)

1.2. Endoscopic retrograde cholangiopancreatography (ERCP)

With the development of scopes, the direct vision of the ampulla of Vater was possible, as reported by Watson, University of Glasgow, in 1966 [6]. The initial attempts to cannulate the pancreatic duct were made by William McCune and his colleagues at George Washington University in 1968 [7]. Their attempts were partially successful, with a success rate of 25% [1, 7]. In 1970, Machida and Olympus made other attempts to cannulate the ampulla in Japan. They used a side-viewing scope with an elevator to guide the catheter [1]. ERCP with successful bile duct cannulation was further development by Japanese endoscopists in 1970 [8], and Jack Vennes and Stephen Silvis in 1972 in the USA [9]. The first successful endoscopic sphincterotomy and treatment of choledocholithiasis were performed in Japan by Kawai et al. [10] and in Germany by Classen and Demling in 1974 [11]. After that, the procedure developed rapidly. Nowadays ERCP is an established procedure, and it is a part of the training program in the field of gastroenterology.

1.3. Digital endoscopy (video endoscopy)

In 1984, Welch Allen Inc. developed the first video colonoscope, and the first publication was by Sivak and Fleischer [12]. The fiberoptic bundles were replaced with an electronic sensor, which transmits the image to a processor and then to a monitor [1]. Welch Allen Inc. did not produce videoscopes after that, but several companies such as Olympus, Pentax, and Fujifilm began developing videoscopes (Figure 10). Modern video endoscopes with modern techniques are now available in the market, for example, high resolution optic, zoom function, digital chromoendoscopy, and artificial intelligence. The development of video endoscopy was very helpful in the documentation of findings and the teaching process.

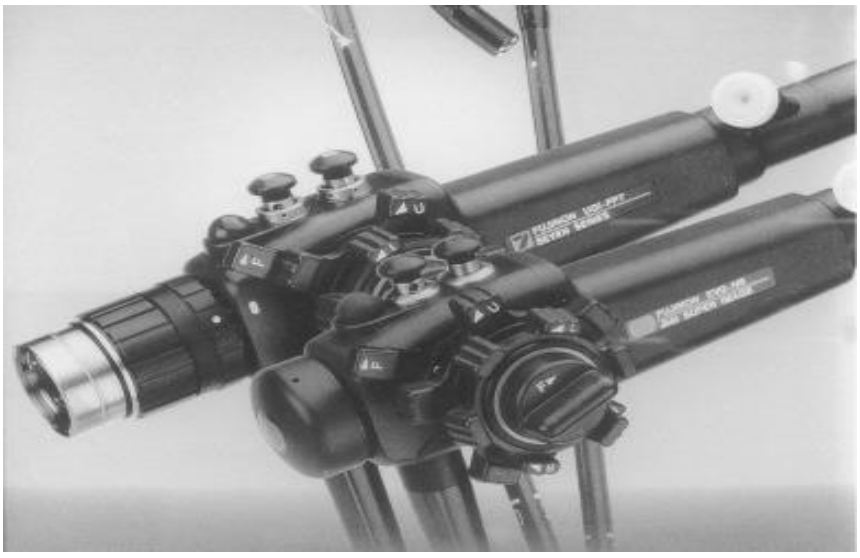


Fig. 10 Fujifilm fiberoptic panendoscope (top) and videopanendoscope (bottom), 1990. (Source: Achord, J.L. and V.R. Muthusamy, The history of gastrointestinal endoscopy, in Clinical gastrointestinal endoscopy. 2019, Elsevier. p. 2-11. e1, used with friendly permission.)

1.4. Endoscopic Ultrasonography (EUS)

The first report on EUS was from Germany. In 1976, Lutz and Rosch reported successful EUS in patients with pancreatic pathology to differentiate between cystic and solid tumors. They used a thin (3-mm diameter) 4 MHz ultrasound probe advanced through the working channel of an Olympus gastroscope [13]. In 1980, EUS devices were developed in Germany as well as Japan and the United States, integrating ultrasound transducers into fiberscopes [14, 15]. Later, ultrasound transducers were integrated into videoscopes (Figure 11).

In 1991, Wiersema et al. reported the first successful experience with EUS fine needle aspiration (FNA) from mediastinal masses and lesions in the upper GI tract and rectum [16, 17]. Modern EUS scopes and processors are now available in the market with several options, such as the Doppler function, tissue harmonic imaging (THI) and elastography. Interventional EUS is now a well-established procedure, for example, celiac plexus block/neurolysis, injection of alcohol or chemotherapeutic agents or radiofrequency ablation (RFA) for tumor lesions, drainage of pancreatic pseudocysts or walled-off necrosis, treatment of gastric varices, biliary drainage and creation of gastrojejunal anastomoses with lumen-apposing metal stents (LAMS), for example, for tumor stenosis [1].

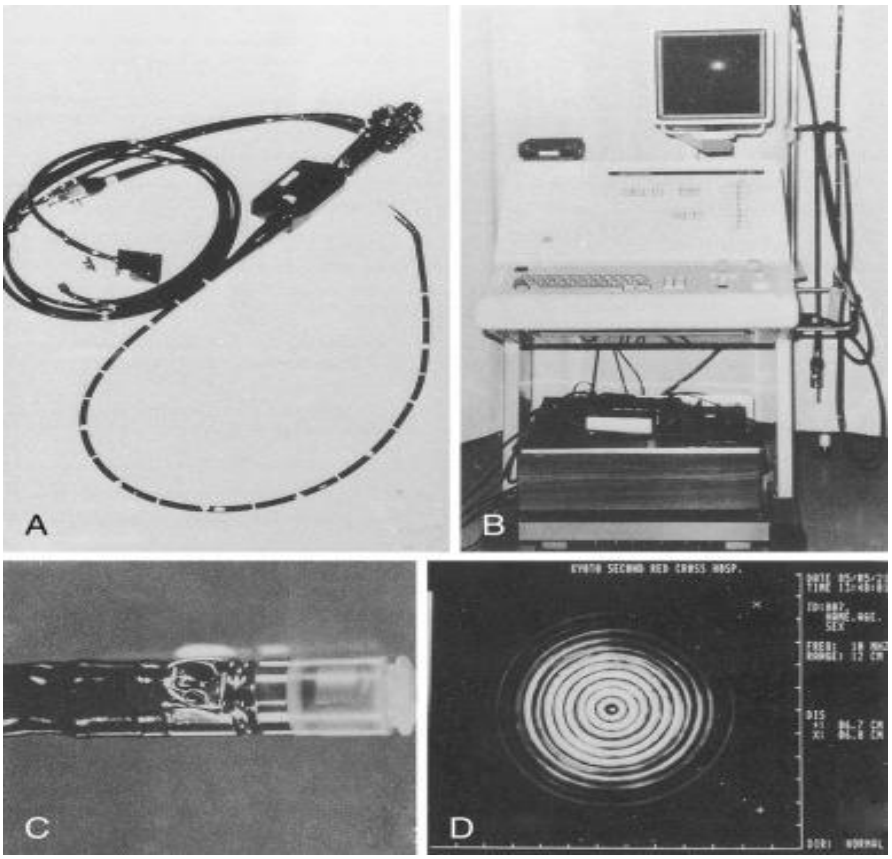


Fig. 11 (A–D) EUS system (scope, monitor, and processor) made by Olympus, 1986. (Source: Achord, J.L. and V.R. Muthusamy, The history of gastrointestinal endoscopy, in Clinical gastrointestinal endoscopy. 2019, Elsevier. p. 2-11. e1, used with friendly permission.)

2. Indications for gastrointestinal endoscopy ** [18]

2.1. Esophagogastroduodenoscopy:

1- Upper abdominal complaints that persist or relapse despite appropriate symptomatic therapy.

2- Upper abdominal complaints when associated with the alarm signs, for example, weight loss or Anorexia, or new-onset symptoms in patients older than 50 years old.

3- Dysphagia or odynophagia.

4- Reflux symptoms, e.g., heat burn or regurgitation, that persist or relapse despite symptomatic therapy.

5- Vomiting of unknown origin.

6- When the presence of upper GI pathology may alter the management. Examples include patients who are scheduled for organ transplantation, patients with planned long-term anticoagulation or nonsteroidal anti-inflammatory drug, and patients with cancer of the head and neck.

7- Familial adenomatous polyposis syndrome (duodenal adenomas possible)

8- For confirmation or exclude of radiologically demonstrated abnormalities in upper GI tract.

9- Gastrointestinal bleeding: acute or chronic. Also, for iron deficiency anemia when the clinical situation suggests an upper GI source of bleeding or when colonoscopy does not provide an explanation or with strong family history of stomach cancer.

10- When sampling of tissue or fluid is indicated.

11- Documented or suspected portal hypertension to screen or treat esophageal/gastric varices.

12- Assess acute injury after caustic ingestion.

13- When clinical situation suggests symptoms of malabsorption, e.g., chronic diarrhea, suspected celiac, or Whipple disease).

14- Removal of foreign bodies.

15- Placement of feeding tubes (e.g., percutaneous endoscopic gastrostomy, percutaneous endoscopic jejunostomy).

16- Intraoperative endoluminal evaluation of anatomic reconstructions (e.g., evaluation of anastomotic leak and patency, fundoplication formation, pouch configuration during bariatric surgery).

Sequential or periodic EGD may be indicated for:

1- Surveillance for malignancy in patients with premalignant conditions (e.g., Barrett's esophagus, polyposis syndromes, gastric adenomas, tylosis, or previous caustic ingestion).

2- Surveillance of healed benign diseases, such as esophagitis and gastric or duodenal ulcer.

EGD is generally *not* indicated for evaluating:

1- Symptoms that are considered functional in origin (there are exceptions in which an endoscopic examination may be done once to rule out organic disease, especially if symptoms are unresponsive to therapy or symptoms recur that are different in nature from the original symptoms).

2- Metastatic adenocarcinoma of an unknown primary site when the results will not alter management.

3- Radiographic findings of: asymptomatic or uncomplicated sliding hiatal hernia, uncomplicated duodenal ulcer that has responded to therapy, deformed duodenal bulb when symptoms are absent or respond adequately to ulcer therapy.

2.2. Indications for endoscopic retrograde cholangiopancreatography ERCP:

1- Jaundiced patient suspected of having biliary obstruction.

2- Patient without jaundice whose clinical and biochemical or imaging data suggest pancreatic duct or biliary tract disease.

3- Evaluation of signs or symptoms suggesting pancreatic malignancy when results of direct imaging (e.g., EUS, US, computed tomography [CT], magnetic resonance imaging [MRI]) are equivocal or normal.

4- Evaluation of pancreatitis of unknown etiology.

5- Preoperative evaluation of patients with chronic pancreatitis and/or pseudocyst.

6- Evaluation of the suspected sphincter of Oddi dysfunction (with manometry).

7- Stent placement across benign or malignant strictures, fistulae, postoperative bile leak, or in high-risk patients with large unremovable common duct stones.

8- Dilation of ductal strictures.

9- Balloon dilation of the papilla.

10- Nasobiliary drain placement.

11- Pancreatic pseudocyst drainage in appropriate cases.

12- Tissue sampling from the pancreatic or bile ducts.

13- Ampullectomy of adenomatous neoplasms of the major papilla.

14- Endoscopic sphincterotomy in indicated in the following situation:

- Choledocholithiasis.
- Papillary stenosis or sphincter of Oddi dysfunction.
- To facilitate placement of biliary stents or dilation of biliary strictures.
- Sump syndrome.
- Choledochocele involving the major papilla.
- Ampullary carcinoma in patients who are not candidates for surgery.
- Facilitate access to the pancreatic duct.

ERCP is generally *not* indicated in:

1- Evaluation of abdominal pain of obscure origin in the absence of objective findings that suggest biliary or pancreatic disease. Magnetic resonance cholangiopancreatography and EUS are safe diagnostic procedures that can obviate the need for ERCP.

2- Evaluation of suspected gallbladder disease without evidence of bile duct disease.

3- Evaluation of proven pancreatic malignancy unless management will be altered.

2.3. Indications for endoscopic ultrasonography EUS:

1- Tumor staging of the GI tract, pancreas, bile ducts, and mediastinum, including lung cancer.

2- Evaluating abnormalities of the GI tract wall or adjacent structures.

3- Tissue sampling of lesions within, or adjacent to, the wall of the GI tract.

4- Evaluation of abnormalities of the pancreas, including masses, pseudocysts, cysts, and acute or chronic pancreatitis.

5- Evaluation of abnormalities of the biliary tree.

6- Placement of fiducials into tumors within or adjacent to the wall of the GI tract.

7- Treatment of symptomatic pseudocysts by creating transgastric or tranduodenal drainage.

8- Celiac plexus neurolysis

9- Providing access into the bile ducts or pancreatic duct, either independently or as an adjunct to ERCP.

10- Evaluation for perianal and perirectal disorders (anal sphincter injuries, fistulae, abscesses).

11- Evaluation of patients at increased risk of pancreatic cancer.

EUS is generally *not* indicated for staging of metastatic tumors when the procedure doesn't alter the management.

3. Contraindications of gastrointestinal endoscopy ** [18]

GI endoscopy is generally contraindicated when:

- The risk of the procedure clearly outweighs the benefit.
- Patient is uncooperative or informed consent cannot be obtained.
- Suspected or documented perforation of a hollow organ.

** from the position statement of the Standards of Practice Committee of the American Society for Gastrointestinal Endoscopy (ASGE), reused with permission.

4. Complications of gastrointestinal endoscopy

According to the ERCP consensus conference, complications are defined as "unplanned events related to the procedure, which require the patient to be admitted to a hospital, stay in the hospital longer than expected, or undergo other unplanned interventions". Other events related to the procedure but not included in this definition are called "incidents" [19, 20].

Complications were classified into three categories according to the length of the hospitalization and outcomes. "Mild: hospitalization of 1–3 days; moderate: hospitalization of 4–9 days; severe: hospitalization of more than 10 days, need for surgery or intensive care, or death attributable to the procedure" [19, 20].

4.1. Adverse events with diagnostic EGD:

The diagnostic EGD is generally a safe, low-risk procedure. The reported mortality in a large study was approximately 1:10,000 [21].

Cardiopulmonary adverse events are often related to sedation. They account for 60% of complications with an incidence between 1:170 and 1:1,000. They include minor events such as transient hypoxia and hypotension or more serious -to- major events such as aspiration, myocardial infarction, cardiac or respiratory arrest, and shock. Risk factors include elderly patients, comorbidity, American Society of Anesthesiologists classification III or IV, prolonged complex procedures, and patients in a prone position [21, 22].

Infectious adverse events are rare with diagnostic EGD and result from the procedure itself or from the equipment. Transient bacteremia after EGD is reported to be as high as 8%, almost without clinical relevance [23]. Current guidelines recommend no antibiotic prophylaxis with EGD [24].

Perforation is very rare with diagnostic EGD, with an incidence of 1: 2,500 to 1: 11,000. Risk factors include Zenker's diverticulum, malignancies, esophageal stenosis, and duodenal diverticula. Early recognition of the perforation is very crucial for management [22, 23].

Bleeding is very rare with diagnostic EGD with an incidence of 0.03%. Mallory-Weiss tears occur in up to 0.1%–0.5% but almost without clinical significance [23, 24].

4.2. Adverse events with ERCP:

Post-ERCP pancreatitis (PEP) is the most common complication of ERCP. The occurrence range is wide and related to the risk profile, from 1.6 % in low-risk patients to 15.7% in high-risk patients, however the overall mortality is low (0.7%) [24-26]. The most used definition of PEP in clinical practice is that proposed by Cotton et al. in 1991 as follows [19]:

- "Mild PEP: clinical pancreatitis (new or worsened abdominal pain) AND amylase at least three times normal at more than 24 hours after the procedure AND requiring admission or prolongation of planned admission to 2–3 days.
- Moderate PEP: pancreatitis (criteria like above) requiring hospitalization of 4–10 days.
- Severe PEP: hospitalization for more than 10 days OR development of hemorrhagic pancreatitis, phlegmon, pseudocyst, infection, OR need for drainage or surgery".

Table 1 shows the risk factors for PEP adopted from the Guidelines of the European Society of Gastrointestinal Endoscopy in 2020 [27].

Table 1. Risk factors for post-ERCP pancreatitis (PEP).

Risk factors for PEP	Odd ratios
Patient-related definite risk factors	
• Suspected sphincter of Oddi dysfunction	2.04 – 4.37
• Female sex	1.40 – 2.23
• Previous pancreatitis	2.00 – 2.90
• Previous PEP	3.23 – 8.7
Procedure-related definite risk factors	
• Difficult cannulation	1.76 – 14.9
• Pancreatic guidewire passages >1	2.1 – 2.77
• Pancreatic injection	1.58 – 2.72
Patient-related likely risk factors	
• Younger age	1.59 – 2.87
• Nondilated extrahepatic bile duct	3.8
• Absence of chronic pancreatitis	1.87
• Normal serum bilirubin	1.89
• End-stage renal disease	1.7
Procedure-related likely risk factors	
• Precut sphincterotomy	2.11 – 3.1
• Pancreatic sphincterotomy	1.23 – 3.07
• Biliary balloon sphincter dilation	4.51
• Failure to clear bile duct stones	4.51
• Intraductal ultrasound	2.41

Bleeding usually occurs after sphincterotomy or precut papillotomy and can be immediate or delayed (up to several weeks after the procedure). It occurs in 0.3% to 2% of cases [24, 26]. Cotton et al. [19] classified bleeding into "mild (hemoglobin drop < 3 g/dl and no need for transfusion), moderate (transfusion of ≤ 4 units and no need for intervention), and severe (transfusion ≥ 5 units or radiologic intervention/surgery needed)". Table 2 shows the risk factors for bleeding adopted from the ESGE Guidelines [27].

Table 2. Risk factors for bleeding by ERCP.

Risk factors for bleeding	Odd ratios
• Anticoagulants	4.39
• Platelets < 50 000/mm^3	35.30
• Cirrhosis	2.05 – 2.85
• End-stage renal disease	1.86 – 13.30
• Intraprocedural bleeding	4.28
• Low-endoscopist experience	1.44
• Unsuccessful cannulation with precut sphincterotomy	3.09

Duodenal perforation occurs in 0.08%–0,6 % of cases [24, 26]. The risk factors for perforation include altered anatomy, sphincterotomy, precut sphincterotomy, dilatation for stricture, papilloplasty, sphincter of Oddi dysfunction, and elderly patients [26, 27]. Stapfer et al. classified the perforation into 4 categories according to the anatomical location and the injury mechanism [28]:

- Type 1: lateral or medial duodenal wall perforation. It usually occurs by a duodenoscope and requires surgery.
- Type 2: periampullary perforation. It is related to sphincterotomy/precut and is the most common form.
- Type 3: distal bile duct injury. It is usually related to instrumentation (e.g., guide wire or basket).
- Type 4: retroperitoneal air on imaging. It is probably related to air insufflation.

Types 2 and 3 could be initially managed conservatively, and surgery is required with signs of peritonitis or persistent leak. Type 4 is usually managed conservatively.

Cholangitis and Cholecystitis occur in 0,5%–3% and 0.2%–0.5% of patients, respectively [24, 26]. The risk factors include elderly patients > 60, incomplete biliary drainage (for example, hilar cholangiocarcinoma), primary sclerosing cholangitis, prior history of liver transplantation, and cholangioscopy [26, 27].

Other complications related to ERCP include cardiopulmonary events related to sedation, air embolism, pancreatic or bile duct fistula, liver abscess, infective endocarditis, infections transmitted through the duodenoscope, pneumothorax, splenic injury, subcapsular hepatic hematoma, stent migration or dysfunction, impaction of the retrieval basket, and adverse reaction to contrast material [26].

4.3. Adverse events with diagnostic EUS:

Perforation occurs due to the increased stiffness and diameter of echoendoscopes. The perforation rate is slightly higher than that of the conventional EGD. In two retrospective and prospective German studies, perforation (mainly esophageal and duodenal) was reported in 0.03%–0.07% of cases [29, 30]. Gastric and rectal perforations are very rare. Risk factors for perforation include elderly patients, operator inexperience, use of longitudinal echoendoscope, large cervical osteophytes, difficult esophageal intubation, stenosing tumor, dilatation of stenosis before EUS, and duodenal diverticulum [31].

Cardiopulmonary adverse events were reported in 0.41 % of cases in the German registry of the society of ultrasound in medicine [30].

Transient asymptomatic bacteremia was reported in 2% of patients after EUS in a German study [32].

Regarding ***hematogenous tumor cell dissemination*****,** malignant cells were detected in the peripheral blood in up to 24% of patients after rectal EUS by the staging of rectal carcinoma [33]. It is unclear whether this is related to the passage or manipulation with the echoendoscope. Thus, further studies are needed [31].

Patients undergoing EUS fine needle aspiration or biopsy (FNA/FNB) are more likely to have complications and report symptoms after the procedure [29, 30]. A systematic review reported that the complication rate was 0.98%, and the mortality rate was 0.02% [34]. The most common complications were abdominal or thoracic pain after the procedure (34%), acute pancreatitis (34%), fever and infectious complications (16%), bleeding (13%), perforation and bile leak (3%) [34].

Tumor cell seeding is a rare complication with EUS- FNB, and many case reports have reported tumor cell implantation after EUS- FNB [31]. The actual frequency is unknown, but the risk is significantly lower with EUS-FNA than with percutaneous FNB [31, 35].

5. Technical characteristics and differences between gastroscopes, duodenoscopes and echoendoscopes

Table 3 shows the characteristics of gastroscopes, duodenoscopes, and echoendoscopes produced by Pentax Medical.

Product	Insertion tube (mm)	Distal end (mm)	Instrument channel (mm)	Field of view °	Tip deflection up/down °	Tip deflection right/left °	Remarks
Gastroscope							
EG16-K10	5.4	5.2	2	140	210/120	120/120	Transnasal
EG27-i10	9	9.2	2.8	140	210/120	120/120	HD$^+$, CF
EG29-i10	9.8	9.9	3.2	140	210/120	120/120	HD$^+$, CF
EG34-i10	11.6	11	3.8	140	210/120	120/120	HD$^+$, CF
EG-2990i	9.8	10.8	2.8	140	210/120	120/120	HD$^+$
EG-2990Zi	9.8	10.6	2.8	140	210/120	120/120	HD$^+$, MagniView
EG-2490K	8	7.1	2.4	140	210/120	120/120	
EG-2790K	9	9.2	2.8	140	210/120	120/120	
EG-2990K	9.8	10.2	2.8	140	210/120	120/120	
EG-3490K	11.6	11.5	3.8	140	210/120	120/120	
EG-3890TK	12.8	13.2	3.8/2.8	140	180/120	120/120	
Duodenoscope							
ED34-i10T	11.6	13	4.2	100	120/90	105/90	HD$^+$
ED34-i10T2	11.6	13.6	4.2	100	120/90	105/90	HD$^+$
ED-3490TK	11.6	13.2	4.2	100	120/90	105/90	
Echoendoscope							
Linear EG-3270UK	10.8	12	2.8	120	130/130	120/120	
Linear EG-3870UTK	12.8	14.3	3.8	120	130/130	120/120	
Radial EG-3670URK	12.1	10.3	2.4	140	130/60	60/60	Forward optic
Radial EG36-J10UR	12.1	10.4	2.4	140	150/70	70/70	Forward optic
Slim linear EG34-J10U	11.6	12.9	2.8	120	160/130	120/120	
Therapeutic linear EG38-J10UT	12.8	14.3	4	120	160/130	120/120	

HD$^+$: high- definition neu chip. CF: close focus. Source: https://www.pentaxmedical.com/pentax/download/fstore/uploadFiles/Pdfs/Product%20Datasheets/EMEA_BRO_ProductOverview_02.2018.pdf. Last accessed on 08.04.2023, 11:02

Table 4 shows the characteristics of gastroscopes, duodenoscopes, and echoendoscopes produced by Olympus.

Product	Insertion tube (mm)	Distal end (mm)	Instrument channel (mm)	Field of view ◦	Tip deflection up/down ◦	Tip deflection right/left ◦	Remarks
Gastroscope							
GIF-XZ1200	9.9	9.9	2.8	140	210/90	100/100	125x Magnification, NBI, High FPS, TXI, RDI
GIF-H290T	9.9	9.8	3.2	140	210/120	100/100	HD$^+$, NBI
GIF-EZ 1500	9.6	9.9	2.8	140	210/90	100/100	Magnification, NBI, TXI, RDI
GIF -1100	8.9	8.9	2.8	140	210/90	100/100	HD$^+$, NBI, TXI, RDI
GIF-H190N	-	5.4	2.2	140	210/90	100/100	HD$^+$, NBI
GIF-H290EC	9.6	9.7	2.2	140	210/90	100/100	520x Magnification, HD$^+$, NBI
GIF-H290Z	-	9.9	2.8	140	210/90	100/100	Magnification, HD$^+$, NBI
GIF-N180		4.9	2	120	210/120	100/100	Transnasal
GIF-XTQ160		12.9	6	140	200/90	100/100	Therapeutic
GIF -H185		9.2	2.8	140	210/90	100/100	HD$^+$, NBI
GIF-1TH190	10.9	10	3.7	140	210/90	100/100	HD$^+$, NBI
GIF -H190		9.2	2.8	140	210/90	100/100	HD$^+$, NBI
GIF-HQ190		9.9	2.8	140	210/90	100/100	NBI
GIF-FQ260Z		11	2.8	140	210/90	100/100	Magnification, NBI, AFI
GIF-2TH180		12.2	2.8/3.7	140	210/90	100/100	HD$^+$, NBI
Duodenoscope							
TJF-Q190V	11.3	13.5	4.2	100	120/90	110/90	NBI
TJF-Q180V	11.3	13.7	4.2	100	120/90	110/90	NBI
Echoendoscope							
Radial GF-UE190	10.9	13.4	2.2	100	130/90	90/90	
Radial-UE160-AL5	10.9	13.4	2.2	100	130/90	90/90	
Linear GF-UCT180	12.6	14.6	3.7	100	130/90	90/90	NBI
Linear TGF-UC180J	12.6	14.6	3.7	120	180/90	90/90	Forward optic

FBS: frame per second. NBI: narrow band imaging. TXI: texture and color enhancement imaging. RDI: red dichromatic imaging. AFI: autofluorescence imaging. Source: https://www.olympus.de/medical/de/Produkte-und-L%C3%B6sungen/Medizinische-Fachrichtungen/Gastroenterologie/. Last accessed on 08.04.2023, 11:05.

Table 5 shows the characteristics of gastroscopes, duodenoscopes, and echoendoscopes produced by Fujifilm Healthcare.

Product	Insertion tube (mm)	Distal end (mm)	Instrument channel (mm)	Field of view °	Tip deflection up/down °	Tip deflection left/right °	Remarks
Gastroscope							
EG-760R	9.3	9.2	2.8	140	210/90	100/100	LCI, BLI
EG-760Z	9.8	9.9	2.8	140	210/120	100/100	LCI, BLI, Multi Zoom
EG-760CT	10.8	10.5	3.8	140	210/90	100/100	LCI, BLI
EG-740N	5.9	5.8	2.4	140	210/90	100/100	LCI, BLI
EG-720R	9.3	9.2	2.8	140	210/90	100/100	LCI, BLI
EI-740D/S	12.8	12.8	3.7/3.2	140	210/90	100/100	LCI, BLI, dual channel
EG-600WR	9.3	9.2	2.8	140	210/90	100/100	
EG-580NW2	5.9	5.8	2.4	120	210/120	100/100	
EG-530NP	5.1	4.9	2	120	200/90		
Duodenoscope							
ED-580XT	11.3	13.1	4.2	100	120/90	90/110	
Echoendoscope							
Radial EG-580UR	11.5	11.4	2.8	140	190/190	100/100	Forward optic
Linear EG-740UT	12.6	14.5	4	140	150/100	100/100	
Linear EG-580UT	12.4	13.9	3.8	140	150/150	120/120	

LCI: linked color imaging. BLI: blue light imaging. Source: https://www.fujifilm-endoscopy.com/storage/app/media/products/files/3_Guidebook%20Endoscopes.pdf. Last accessed on 08.04.2023, 11:30.

Figures 12–16 show different models of duodenoscopes and echoendoscopes from different companies.

Fig. 12 Echoendoscopes EUS-J10 from Pentax Medical. (left: EG36-J10UR radiales echoendoscope with forward optic, middle: EG38-J10UT linear echoendoscope, right: EG34-J10U linear echoendoscope, both with forward-oblique optic. (Source: https://www.pentaxmedical.com/pentax/en/101/3/Ultrasound-Video-Gastroscope-EUS-J10-line-up. Last accessed on 08.04.2023, 10:58)

Fig. 13 Radial echoendoscope GF-UE160-AL5 with forward-oblique optic from Olympus. (Source: https://www.olympus.de/medical/de/Produkte-und-L%C3%B6sungen/Produkte/Gastroenterology/Ultraschallendoskope.html. Last accessed on 08.04.2023,11:10)

Fig. 14 Linear echoendoscope GF-UCT180 with forward optic from Olympus. (Source: https://www.olympus.de/medical/de/Produkte-und-L%C3%B6sungen/Produkte/Gastroenterology/Ultraschallendoskope.html. Last accessed on 08.04.2023, 11:15)

Fig. 15 Duodenoscope ED-580XT with side-viewing optic from Fujifilm. (Source: https://www.fujifilm-endoscopy.com/products/category/duodenoscopes#down. Last accessed on 08.04.2023, 11:20)

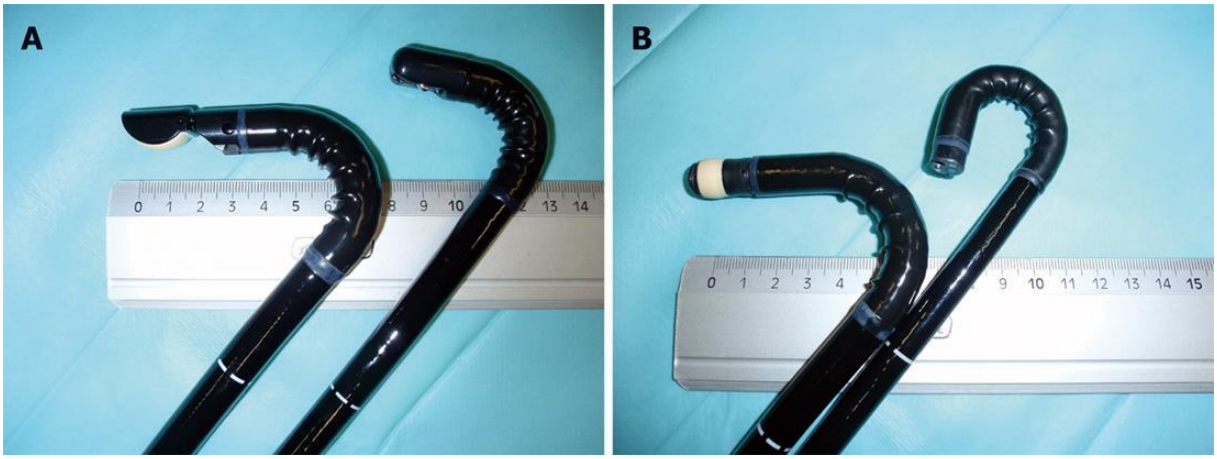


Fig. 16 The differences in terms of flexibility between the echoendoscope, duodenoscope and gastroscope.

A: linear echoendoscope EG-3870 UTK from Pentax (left) with an approximately 50 mm long rigid tip at the distal end and the duodenoscope ED-3490 TK from Pentax (right). B: Radial echoendoscope EG-3670 URK from Pentax (left) with an approximately 50 mm long rigid tip at the distal end and the standard gastroscope EG-2990i from Pentax (right). (Source: Jenssen, C., M.V. Alvarez-Sánchez, B. Napoléon, and S. Faiss, Diagnostic endoscopic ultrasonography: assessment of safety and prevention of complications. World journal of gastroenterology: WJG, 2012. 18(34): p. 4659.)

6. Aim of the Study

ERCP and EUS are frequently performed procedures for various indications in the field of gastroenterology. Because of the anatomical location of the papilla on the medial aspect of the second part of the duodenum, all duodenoscopes have side-viewing optic and elevator to facilitate the manipulation during ERCP. All echoendoscopes have oblique-viewing optic except the radial echoendoscopes from Pentax (EG36-J10UR- EG-3670URK) and Fujifilm (EG-580UR), which have forward-viewing optic. Recently, Olympus has developed a longitudinal echoendoscope (TGF-UC180J) with forward-viewing optic.

Duodenoscopes and echoendoscopes have long rigid tips and limited tip deflection compared with standard gastroscopes. Furthermore, the field of view of duodenoscopes and echoendoscopes is also narrower than that of standard gastroscopes (Tables 3–5). Additionally, many of these scopes are not equipped with advanced options such as HD^{+}, zoom function, narrow band imaging, and other digital chromoendoscopy techniques.

For these reasons, the intraluminal vision with these scopes is limited compared with gastroscopes. Additionally, the ability of targeted biopsies with non-forward optic is limited. It is unknown whether gastroscopy should be performed routinely before endoscopy with side-viewing or oblique-viewing optic to avoid missing lesions [36, 37]. Little data have been reported in the literature, and almost all studies originated from the USA. In up to 30% of patients, relevant lesions were detected using EGD before performing EUS [38, 39]. In one study published in an abstract form, 62% of patients had intraluminal lesions by EGD [40]. EGD findings had a direct impact on the subsequent EUS in up to 12% of patients [38, 40].

Since no consensus has been reached, the practice is highly variable from one center to another. Our practice in the Charité-University Medicine, Campus Benjamin Franklin, and Vivantes Hospital Spandau is that we perform gastroscopy routinely before every ERCP/EUS. This study aimed to retrospectively analyze whether our practice is useful with the goal of standardizing the practice. To the best of knowledge, this is the first study in Germany and Europe to address this issue.

7. Patients and Methods

Study design: This was a retrospective dual-center study conducted between August 2020 and December 2020 at the Charité- University Medicine, Campus Benjamin Franklin, Department of Gastroenterology and Hepatology and Vivantes Hospital Spandau (Department of Gastroenterology and Hepatology), which is an academic hospital affiliated with Charité-University Medicine. The study protocol was approved by the Ethics Committee of the Charité-University Medicine (number EA4/222/20).

Inclusion and exclusion criteria: Inclusion criteria included patients who underwent ERCP or EUS for non-luminal diagnosis. Exclusion criteria included patients under the age of 18 years, patients with an indication for EUS for luminal diagnosis, previous surgery in the upper GI tract, signs of GI bleeding, dysphagia, or any significant symptoms in the upper GI tract that made performing EGD independently warranted.

Material and collected data: The patient's files were reviewed, and data were recorded, including age and sex, indication for ERCP/EUS, hemoglobin level at the time of endoscopy, and intake of anticoagulants, including phenprocoumon, direct oral anticoagulants, aspirin, and other platelet aggregation inhibitors. Furthermore, the EGD findings, complications during EGD, and whether any additional procedure after EGD and before ERCP/EUS was needed, such as dilatation, were also recorded. The following scopes were used at the Charité-University Medicine, Campus Benjamin Franklin: gastroscopes GIF-H190, GIF-HQ190, GIF-1TH190 and GIF-XTQ160, duodenoscope TJF-Q190V, radial echoendoscope GF-UE160, and linear echoendoscope GF-UCT180. Procedures at the Vivantes Hospital Spandau were performed using a duodenoscope TJF-Q180V, radial echoendoscope UE160-AL5, linear echoendoscope GIF-UCT180, and gastroscopes GIF-H180, GIF-HQ190, and GIF-ITQ160. All echoendoscopes were with oblique-viewing optic, and all scopes were manufactured by Olympus Germany GmbH.

Primary and secondary endpoints: The primary endpoint was the proportion of patients with relevant lesions detected by EGD. The secondary endpoints were whether the presence of relevant lesions was associated with the patient's age, hemoglobin level, and intake of anticoagulants, and whether EGD findings had a direct impact on the subsequent ERCP/EUS.

Definition of relevant and non-relevant lesions: Any lesion that altered the management of the patient was considered relevant, this is, any lesion that needed new medical, endoscopic, or surgical therapy, when additional imaging/diagnostic workup was needed, when surveillance was needed, or when the lesion had a direct impact on the subsequent ERCP/EUS. The following lesions were considered non-relevant: sliding hernia without esophagitis, cardia insufficiency without esophagitis, Schatzki ring without stenosis, downhill varices, hyperplastic polyps, ectopic gastric mucosa, *H.pylori*-negative gastritis or duodenitis, gastric glandular cysts, ectopic pancreas, and lipoma.

Sample size: The sample size was calculated using Epi lnfo using a large population size of 100,000, an expected prevalence of relevant lesions of 20% (based on previous studies), and

a margin error of 5%. The needed sample size was 245 patients using a 95% confidence interval (95%CI).

Statistical analysis: Statistical analysis was performed using SPSS v28 (IBM Inc., Chicago, IL, USA). Quantitative variables were presented as mean and standard deviation and compared between the two groups using an independent sample *t*-test. Qualitative variables were presented as frequency and percentage (%) and were analyzed using the chi-square test. The receiver operating characteristic (ROC) curve was used to obtain the best cut-off point with the corresponding sensitivity and specificity. A two-tailed *p*-value ≤ 0.05 was considered statistically significant.

8. Results

8.1. Characteristics of the patients: A total of 245 patients (145 (59.18%)) at the Charité-University Medicine, Campus Benjamin Franklin, and 100 (40.82%) at Vivantes Hospital Spandau) were included in this study. Of the 245 patients, 122 (49.8%) were females. The mean age of the patients was 64.83 ± 16.73 years. Regarding the procedure, 43.27% of patients were subjected to ERCP, and the remaining patients were subjected to EUS. Among the patients, 78 (31.84%) were on anticoagulants (Table 6 and Figures 17 and 18).

Table 6. Patients' characteristics.

		N	%
Center	Charité	145	59.18%
	Vivantes	100	40.82%
Sex	Female	122	49.80%
	Male	123	50.20%
Procedure	ERCP	106	43.27%
	EUS	139	56.73%
Anticoagulation	No	159	64.90%
	Yes	78	31.84%
	No data	8	3.27%
Age, years	Mean (SD)	64.83 (16.73)	

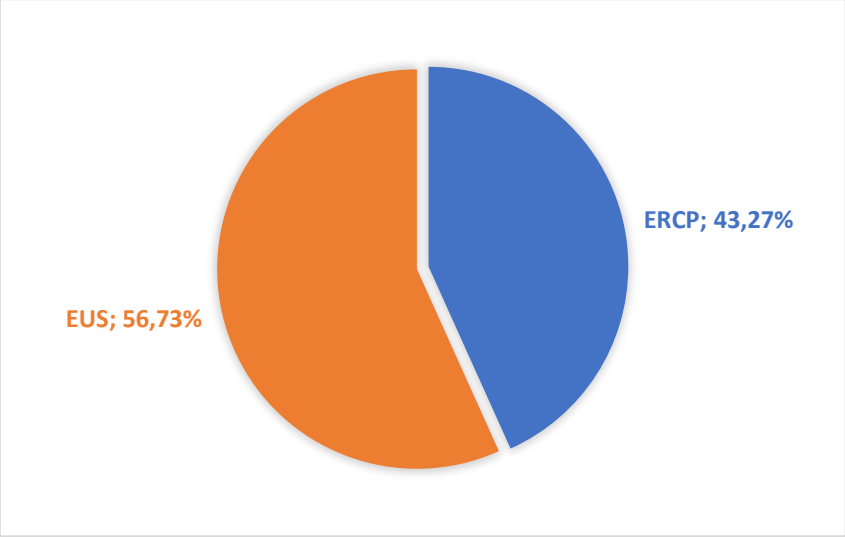


Fig. 17 Procedures performed on the patients.

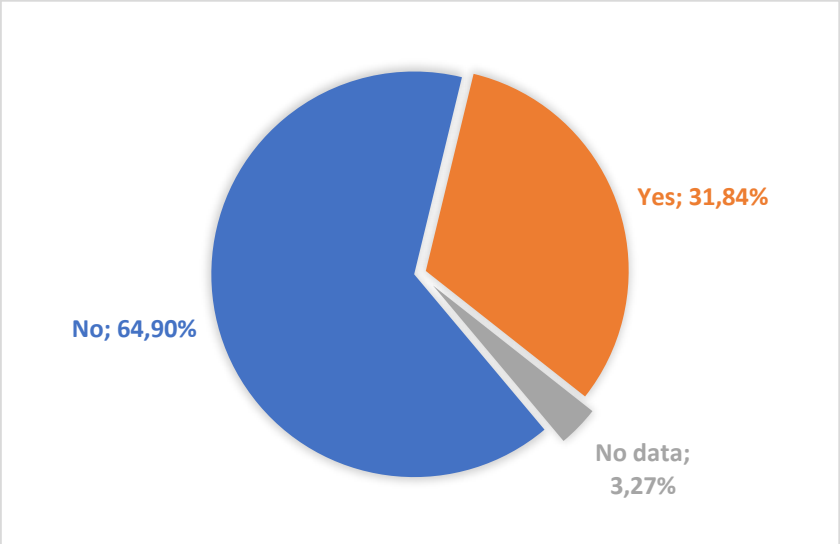


Fig. 18 Intake of anticoagulants of the patients.

8.2. Indications for the endoscopy: Choledocholithiasis was the most common indication for endoscopy in 26.94% of the patients, followed by pancreatic neoplasm in 23.67%, cholestatic liver function test in 20.41%, and pancreatitis in 16.33% (Table 7 and Figure 19).

Table 7. Indications for endoscopy.

	N	%
Choledocholithiasis	66	26.94%
Pancreatic neoplasm	58	23.67%
Cholestatic liver function test	51	20.82%
Acute or chronic pancreatitis	40	16.33%
Cholangiocarcinoma	10	4.08%
Pancreatic pseudocyst	10	4.08%
Mediastinal lymphadenopathy	5	2.04%
Bile leak	5	2.04%

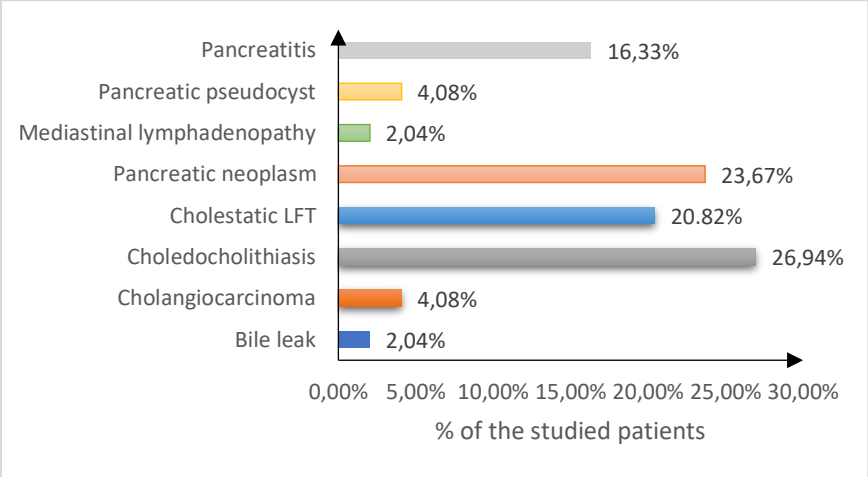


Fig. 19 Indications for endoscopy.

8.3. Relevant and non-relevant Lesions detected by EGD:

A total of 131 relevant lesions were detected: 72 in the esophagus (**54.96%)**, 37 in the stomach (**28.24%)**, and 22 in the duodenum (**16.79%)** (Table 8).

Table 8. Relevant lesions detected during gastroscopy and their sites.

Site	Relevant lesions	N	% of relevant lesions	% of overall lesions	% of overall cases
Esophagus		**72**	**54.96%**	**32.14%**	**29.39%**
	Reflux esophagitis, Los Angeles grade A, B, C, or D	39	29.77%	17.41%	15.92%
	Esophageal varices	12	9.16%	5.36%	4.90%
	Schatzki ring with stenosis	2	1.53%	0.89%	0.82%
	Thrush esophagitis	7	5.34%	3.13%	2.86%
	Barrett's esophagus	6	4.58%	2.68%	2.45%
	Esophageal papilloma	2	1.53%	0.89%	0.82%
	Esophageal stenosis (inflammatory 1; scarred 1)	2	1.53%	0.89%	0.82%
	Eosinophilic esophagitis	1	0.76%	0.45%	0.41%
	Barrett's Adenocarcinoma pT1a m2	1	0.76%	0.45%	0.41%
Stomach		**37**	**28.24%**	**16.52%**	**15.10%**
	Ulcer ventriculi (1 patient with *H.pylori* infection)	13	9.92%	5.80%	5.31%
	Pyloric stenosis (inflammatory 3; scarred 1; and malignant 1)	5	3.82%	2.23%	2.04%
	Gastric fundal varices	3	2.29%	1.34%	1.22%
	Gastrointestinal stromal tumor	1	0.76%	0.45%	0.41%
	Intestinal metaplasia	3	2.29%	1.34%	1.22%
	Portal hypertensive gastropathy	8	6.11%	3.57%	3.27%
	Malignant infiltration in the stomach (from liver metastasis)	1	0.76%	0.45%	0.41%
	Upside-down stomach	2	1.53%	0.89%	0.82%
	Cameron lesion	1	0.76%	0.45%	0.41%
Duodenum		**22**	**16.79%**	**9.82%**	**8.57%**
	Duodenal ulcers (2 patients with *H.pylori* infection)	15	11.45%	6.70%	6.12%
	Stenosis (inflammatory 3; malignant 3)	6	4.58%	2.68%	2.45%
	Adenoma	1	0.76%	0.45%	0.41%
Total		**131**	**100.00%**	**58.48%**	**53.06%**

A total of 93 non-relevant lesions were detected: 46 in the esophagus (**49.46%)**, 41 in the stomach (**44.09%),** and 6 in the duodenum (**6.45%)** (Table 9).

Table 9. Non-relevant lesions detected during gastroscopy and their sites.

Site	Non-relevant lesions	N	% of non-relevant lesions	% of overall lesions	% of overall cases
Esophagus		**46**	**49.46%**	**20.63%**	**18.78%**
	Axial hernia	41	44.09%	18.39%	16.73%
	Schatzki ring without stenosis	1	1.08%	0.45%	0.41%
	Hyperplastic polyp	1	1.08%	0.45%	0.41%
	Ectopic gastric mucosa	2	2.15%	0.90%	0.82%
	Downhill varices	1	1.08%	0.45%	0.41%
Stomach		**41**	**44.09%**	**18.39%**	**16.73%**
	Gastritis	31	33.33%	13.90%	12.65%
	Cardia insufficiency	3	3.23%	1.35%	1.22%
	Gastric glandular cysts	5	5.38%	2.24%	2.04%
	Ectopic pancreas	1	1.08%	0.45%	0.41%
	Lipoma	1	1.08%	0.45%	0.41%
Duodenum		**6**	**6.45%**	**2.68%**	**2.45%**
	Hyperplastic polyp	1	1.08%	0.45%	0.41%
	lipoma	3	3.23%	1.34%	1.22%
	Duodenitis	2	2.15%	0.89%	0.82%
Total		**93**	**100.00%**	**41.52%**	**37.96%**

8.4. Primary Endpoint:

Of the 245 patients, 89 (36.32%) had normal intraluminal findings by EGD, and 156 patients (63.67%) had abnormal intraluminal findings. Among them, 95 (38.78%) were diagnosed with relevant lesions (95%CI: 32.89 –45.01) (Table 10 and Figure 20).

Table 10. The prevalence of relevant lesions detected by diagnostic gastroscopy.

	Cases	Total	%	95% CI	
Relevant lesions	95	245	38.78%	32.89%	45.01%

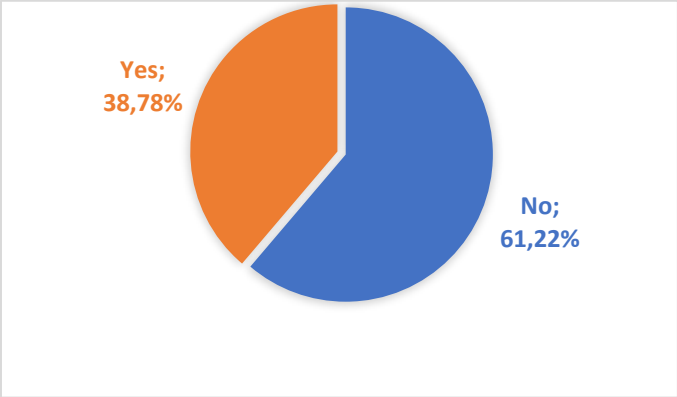


Fig. 20 The prevalence of relevant lesions among the patients.

8.5. Secondary Endpoint:

The chi-square test showed that the relationship between intake of anticoagulants and the presence of relevant lesions was not significant, as the percentage of relevant lesions among those who used anticoagulants was 42.31%, while the percentage was 35.85% among those not using anticoagulants (p = 0.336). The analysis using an independent sample t-test showed that patients diagnosed with relevant lesions by diagnostic gastroscopy were significantly older with lower hemoglobin levels than those with no lesions **(p = 0.029 and p < 0.001, respectively)** (Table 11 and Figure 21)

Table 11. The association between the presence of relevant lesions and intake of anticoagulants, age, and hemoglobin level.

			Relevant lesion		*p*-value
			No	Yes	
Anticoagulation	No	N (%)	102 (64.15)	57 (35.85%)	0.336
	Yes	N (%)	45 (57.69%)	33 (42.31%)	
Age		Mean (SD)	63.10 (18.29)	67.57 (13.54)	**0.029**
Hemoglobin		Mean (SD)	12.54 (1.72)	11.43 (2.27)	**< 0.001**

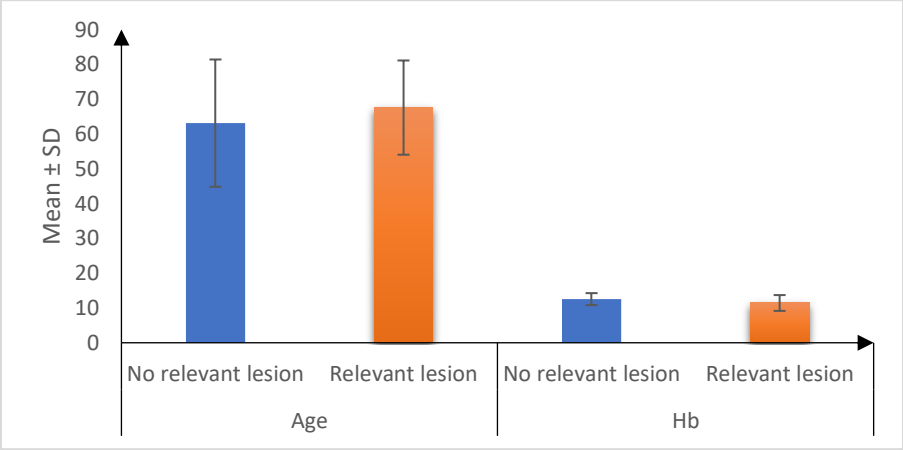


Fig. 21 Association between the presence of relevant lesions and age and hemoglobin (Hb) level.

The ROC curve analysis was performed to obtain the possible cut-off points with the corresponding sensitivity and specificity for age and hemoglobin level to detect relevant lesions. A suggested cut-off point for hemoglobin level was ≤ 13.6, which gives a sensitivity of 80.43% (95% CI: 70.9 –88.0) but low specificity of 27.59% (95% CI: 20.5 –35.6) (Figure 22). A suggested cut-off point for age was >50 years, which gives a sensitivity of 90.53% (95% CI: 82.8 – 95.6), but also a low specificity of 22.67% (95% CI: 16.2 – 30.2) (Figure 23).

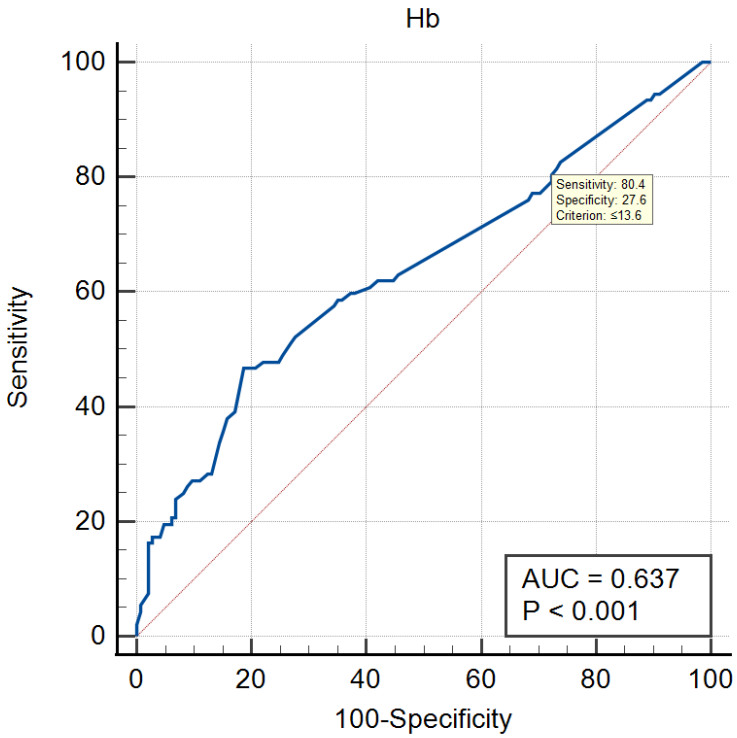


Fig. 22 The receiver operating characteristic (ROC) curve shows the possible cut-off point with the corresponding sensitivity and specificity for hemoglobin level to detect relevant lesions.

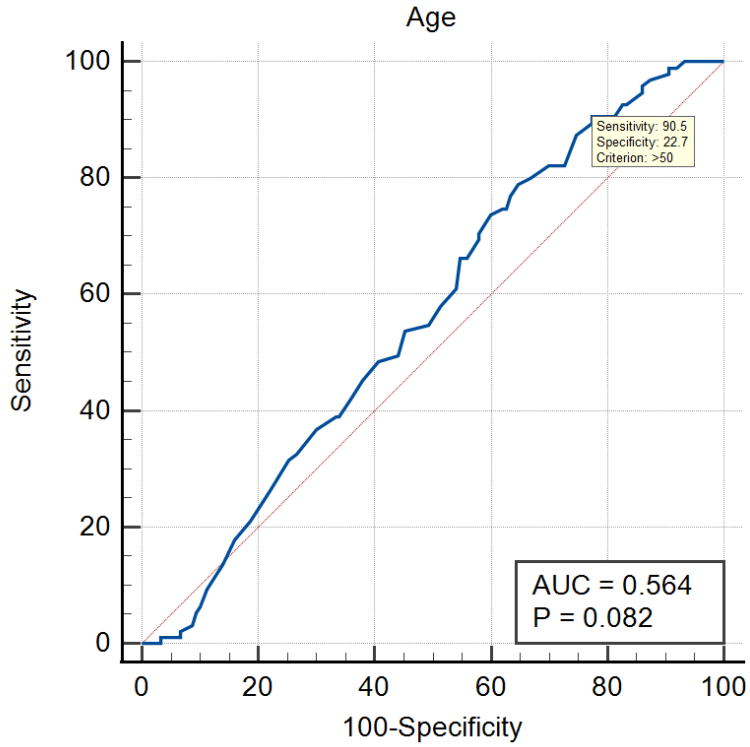


Fig. 23 The receiver operating characteristic (ROC) curve shows the possible cut-off point with the corresponding sensitivity and specificity for age to detect relevant lesions.

Hb possible cut off points	Sensitivity	95% CI for Sensitivity	Specificity	95% CI for Specificity
<6.5	0	0.0 - 3.9	100	97.5 - 100.0
≤6.5	1.09	0.03 - 5.9	100	97.5 - 100.0
≤6.8	2.17	0.3 - 7.6	100	97.5 - 100.0
≤7	4.35	1.2 - 10.8	99.31	96.2 - 100.0
≤7.5	5.43	1.8 - 12.2	99.31	96.2 - 100.0
≤7.8	6.52	2.4 - 13.7	98.62	95.1 - 99.8
≤7.9	7.61	3.1 - 15.1	97.93	94.1 - 99.6
≤8	13.04	6.9 - 21.7	97.93	94.1 - 99.6
≤8.2	16.3	9.4 - 25.5	97.93	94.1 - 99.6
≤8.5	16.3	9.4 - 25.5	97.24	93.1 - 99.2
≤8.6	17.39	10.3 - 26.7	97.24	93.1 - 99.2
≤8.7	17.39	10.3 - 26.7	96.55	92.1 - 98.9
≤8.9	17.39	10.3 - 26.7	95.86	91.2 - 98.5
≤9	19.57	12.0 - 29.1	95.17	90.3 - 98.0
≤9.1	19.57	12.0 - 29.1	94.48	89.4 - 97.6

≤9.2	19.57	12.0 - 29.1	93.79	88.5 - 97.1
≤9.5	20.65	12.9 - 30.4	93.79	88.5 - 97.1
≤9.6	20.65	12.9 - 30.4	93.1	87.7 - 96.6
≤9.7	23.91	15.6 - 33.9	93.1	87.7 - 96.6
≤9.8	25	16.6 - 35.1	91.72	86.0 - 95.7
≤9.9	26.09	17.5 - 36.3	91.03	85.2 - 95.1
≤10	27.17	18.4 - 37.4	90.34	84.3 - 94.6
≤10.1	27.17	18.4 - 37.4	89.66	83.5 - 94.1
≤10.2	27.17	18.4 - 37.4	88.97	82.7 - 93.6
≤10.3	28.26	19.4 - 38.6	87.59	81.1 - 92.5
≤10.4	28.26	19.4 - 38.6	86.9	80.3 - 91.9
≤10.5	33.7	24.2 - 44.3	85.52	78.7 - 90.8
≤10.6	35.87	26.1 - 46.5	84.83	77.9 - 90.2
≤10.7	38.04	28.1 - 48.8	84.14	77.2 - 89.7
≤10.8	39.13	29.1 - 49.9	82.76	75.6 - 88.5
≤11	46.74	36.3 - 57.4	81.38	74.1 - 87.4
≤11.1	46.74	36.3 - 57.4	80	72.6 - 86.2
≤11.2	46.74	36.3 - 57.4	79.31	71.8 - 85.6
≤11.3	47.83	37.3 - 58.5	77.93	70.3 - 84.4
≤11.4	47.83	37.3 - 58.5	77.24	69.5 - 83.8
≤11.5	47.83	37.3 - 58.5	75.17	67.3 - 82.0
≤11.7	48.91	38.3 - 59.6	74.48	66.6 - 81.4
≤11.8	51.09	40.4 - 61.7	73.1	65.1 - 80.1
≤11.9	52.17	41.5 - 62.7	72.41	64.4 - 79.5
≤12	57.61	46.9 - 67.9	65.52	57.2 - 73.2
≤12.1	58.7	47.9 - 68.9	64.83	56.5 - 72.6
≤12.2	58.7	47.9 - 68.9	64.14	55.8 - 71.9
≤12.3	59.78	49.0 - 69.9	62.76	54.3 - 70.6
≤12.4	59.78	49.0 - 69.9	62.07	53.6 - 70.0
≤12.5	60.87	50.1 - 70.9	59.31	50.8 - 67.4
≤12.7	61.96	51.2 - 71.9	57.93	49.5 - 66.1
≤12.8	61.96	51.2 - 71.9	55.17	46.7 - 63.4
≤12.9	63.04	52.3 - 72.9	54.48	46.0 - 62.8
≤13	76.09	66.1 - 84.4	31.72	24.3 - 40.0
≤13.1	77.17	67.2 - 85.3	31.03	23.6 - 39.2
≤13.2	77.17	67.2 - 85.3	30.34	23.0 - 38.5
≤13.4	77.17	67.2 - 85.3	29.66	22.4 - 37.8
≤13.5	79.35	69.6 - 87.1	27.59	20.5 - 35.6
≤13.6	80.43	70.9 - 88.0	27.59	20.5 - 35.6
≤13.7	81.52	72.1 - 88.9	26.9	19.9 - 34.9
≤13.9	82.61	73.3 - 89.7	26.21	19.3 - 34.2
≤14	93.48	86.3 - 97.6	11.03	6.4 - 17.3

≤14.3	93.48	86.3 - 97.6	10.34	5.9 - 16.5
≤14.6	94.57	87.8 - 98.2	9.66	5.4 - 15.7
≤14.9	94.57	87.8 - 98.2	8.97	4.9 - 14.8
≤15	100	96.1 - 100.0	1.38	0.2 - 4.9
≤16	100	96.1 - 100.0	0	0.0 - 2.5
Age possible cut off points	**Sensitivity**	**95% CI**	**Specificity**	**95% CI**
≥18	100	96.2 - 100.0	0	0.0 - 2.4
>18	100	96.2 - 100.0	0.67	0.02 - 3.7
>19	100	96.2 - 100.0	1.33	0.2 - 4.7
>20	100	96.2 - 100.0	2	0.4 - 5.7
>21	100	96.2 - 100.0	2.67	0.7 - 6.7
>25	100	96.2 - 100.0	3.33	1.1 - 7.6
>26	100	96.2 - 100.0	4	1.5 - 8.5
>29	100	96.2 - 100.0	5.33	2.3 - 10.2
>31	100	96.2 - 100.0	6.67	3.2 - 11.9
>32	98.95	94.3 - 100.0	8	4.2 - 13.6
>33	98.95	94.3 - 100.0	8.67	4.7 - 14.4
>34	98.95	94.3 - 100.0	9.33	5.2 - 15.2
>35	97.89	92.6 - 99.7	9.33	5.2 - 15.2
>36	96.84	91.0 - 99.3	12.67	7.8 - 19.1
>37	95.79	89.6 - 98.8	14	8.9 - 20.6
>38	94.74	88.1 - 98.3	14	8.9 - 20.6
>40	93.68	86.8 - 97.6	15.33	10.0 - 22.1
>41	92.63	85.4 - 97.0	16.67	11.1 - 23.6
>42	92.63	85.4 - 97.0	17.33	11.6 - 24.4
>45	91.58	84.1 - 96.3	18	12.2 - 25.1
>46	90.53	82.8 - 95.6	18.67	12.8 - 25.8
>47	90.53	82.8 - 95.6	19.33	13.3 - 26.6
>48	90.53	82.8 - 95.6	20	13.9 - 27.3
>50	90.53	82.8 - 95.6	22.67	16.2 - 30.2
>51	89.47	81.5 - 94.8	22.67	16.2 - 30.2
>52	87.37	79.0 - 93.3	25.33	18.6 - 33.1
>53	82.11	72.9 - 89.2	27.33	20.4 - 35.2
>54	82.11	72.9 - 89.2	30	22.8 - 38.0
>55	80	70.5 - 87.5	33.33	25.9 - 41.5
>56	78.95	69.4 - 86.6	35.33	27.7 - 43.5
>57	76.84	67.1 - 84.9	36.67	29.0 - 44.9
>58	74.74	64.8 - 83.1	37.33	29.6 - 45.6
>59	74.74	64.8 - 83.1	38	30.2 - 46.3
>60	73.68	63.6 - 82.2	40	32.1 - 48.3
>61	70.53	60.3 - 79.4	42	34.0 - 50.3

>62	69.47	59.2 - 78.5	42	34.0 - 50.3
>63	66.32	55.9 - 75.7	44	35.9 - 52.3
>64	66.32	55.9 - 75.7	45.33	37.2 - 53.7
>65	61.05	50.5 - 70.9	46	37.8 - 54.3
>66	57.89	47.3 - 68.0	48.67	40.4 - 57.0
>67	54.74	44.2 - 65.0	50.67	42.4 - 58.9
>68	53.68	43.2 - 64.0	54.67	46.3 - 62.8
>69	49.47	39.1 - 59.9	56	47.7 - 64.1
>70	48.42	38.0 - 58.9	59.33	51.0 - 67.3
>71	45.26	35.0 - 55.8	62	53.7 - 69.8
>72	42.11	32.0 - 52.7	64	55.8 - 71.7
>73	38.95	29.1 - 49.5	66	57.8 - 73.5
>74	38.95	29.1 - 49.5	66.67	58.5 - 74.1
>75	36.84	27.2 - 47.4	70	62.0 - 77.2
>76	32.63	23.4 - 43.0	73.33	65.5 - 80.2
>77	31.58	22.4 - 41.9	74.67	66.9 - 81.4
>78	26.32	17.8 - 36.4	78	70.5 - 84.3
>79	21.05	13.4 - 30.6	81.33	74.2 - 87.2
>80	17.89	10.8 - 27.1	84	77.1 - 89.5
>81	13.68	7.5 - 22.3	86	79.4 - 91.1
>82	9.47	4.4 - 17.2	88.67	82.5 - 93.3
>83	6.32	2.4 - 13.2	90	84.0 - 94.3
>84	5.26	1.7 - 11.9	90.67	84.8 - 94.8
>85	3.16	0.7 - 9.0	91.33	85.6 - 95.3
>86	2.11	0.3 - 7.4	93.33	88.1 - 96.8
>87	1.05	0.03 - 5.7	93.33	88.1 - 96.8
>88	1.05	0.03 - 5.7	96.67	92.4 - 98.9
>89	0	0.0 - 3.8	96.67	92.4 - 98.9
>91	0	0.0 - 3.8	98	94.3 - 99.6
>93	0	0.0 - 3.8	98.67	95.3 - 99.8
>95	0	0.0 - 3.8	99.33	96.3 - 100.0
>97	0	0.0 - 3.8	100	97.6 - 100.0

8.6. Impact of EGD findings on the subsequent ERCP/EUS:

The EGD findings had a direct impact on the subsequent ERCP/EUS in 17 patients (6.93%). Lesions in these patients included upside-down stomach in 2 patients and stenosis in 15 patients. (esophageal stenosis in 4 patients, gastric stenosis in 5 patients, and duodenal stenosis in 6 patients). Dilatation was required to facilitate the passage of duodenoscope/echoendoscope in 6 patients (2.4%) (Table 12).

Table 12. Number of patients with stenosis and the need for dilatation before ERCP/EUS.

Site of stenosis	dilatation needed	no dilatation	
Esophagus	2	2	
Stomach	2	3	
Duodenum	2	4	
Total	6	9	=15

9. Discussion

Since no consensus has been reached on performing gastroscopy before endoscopy with side-viewing or oblique-viewing optic, the practice is widely variable and depends on the endoscopist's preference. The recommendations in textbooks originate from expert opinions [36, 37]. Some endoscopists prefer to perform EGD routinely before ERCP/EUS to avoid missing lesions and to create a roadmap before any complex procedure with non-forward optic, and this is our routine practice at our institutes. Others believe that this practice is unnecessary and that an adequate intraluminal vision with non-forward optic can be obtained.

Many points support performing EGD before non-forward endoscopy. Duodenoscopes and echoendoscopes lack flexibility (particularly echoendoscopes that comprise a rigid transducer located at the tip of the endoscope) (Figure 16). Therefore, some maneuvers with these endoscopes are difficult or less efficient, for example, retroflexion in the stomach [37]. They have a narrower field of view and are usually not equipped with high-definition optic or digital chromoendoscopy compared with gastroscopes [37]. All these endoscopes have non-forward optic except the radial echoendoscopes from Pentax and Fujifilm and the longitudinal echoendoscope TGF-UC180J from Olympus. The ability for targeted biopsies with these scopes is also limited. Thus, it is logical to assume that relevant intraluminal lesions could be overlooked when EGD is not performed before ERCP/EUS [37]. Another point that supports this practice is that the knowledge of the anatomy of the upper GI tract and the creation of a "roadmap" before ERCP/EUS is informative and might reduce the complications related to these procedures [36, 37]. However, this is not proven in studies [36, 37]. In case of EUS, the detection of lesions in the stomach or esophagus may help exclude pancreatobiliary pathology as a cause of the patient's complaints [37]. Additionally, the endoscopic view of tumors or subepithelial lesions, which is better achieved by EGD, is complementary to the evaluation by EUS [37].

With the increasing role of digital chromoendoscopy and artificial intelligence in gastrointestinal endoscopy, these advanced optical options are available mainly in gastroscopes and are usually absent in duodenoscopes or echoendoscopes. These new techniques enable better visualization and enhancement of the superficial pattern and microvasculature of the lesions. Thus, they are very helpful in detecting early-stage cancer and precancerous lesions in the upper and lower GI tract [41]. These advanced techniques include magnification endoscopy, narrow band imaging, texture and color enhancement imaging, red dichromatic imaging from Olympus, i-Scan from Pentax, blue light imaging, and linked color imaging LCI from Fujifilm (Figures 24 – 26).

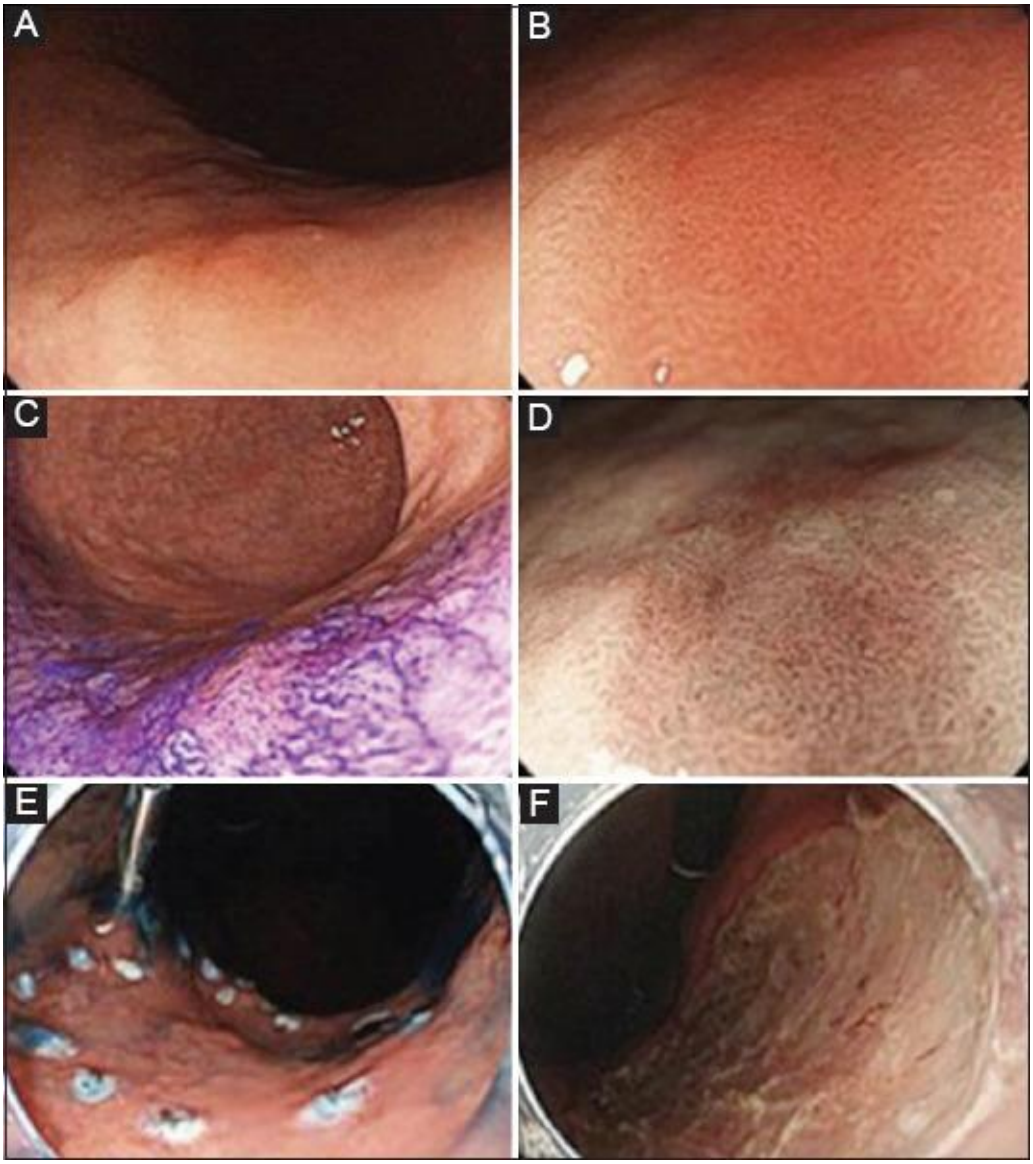
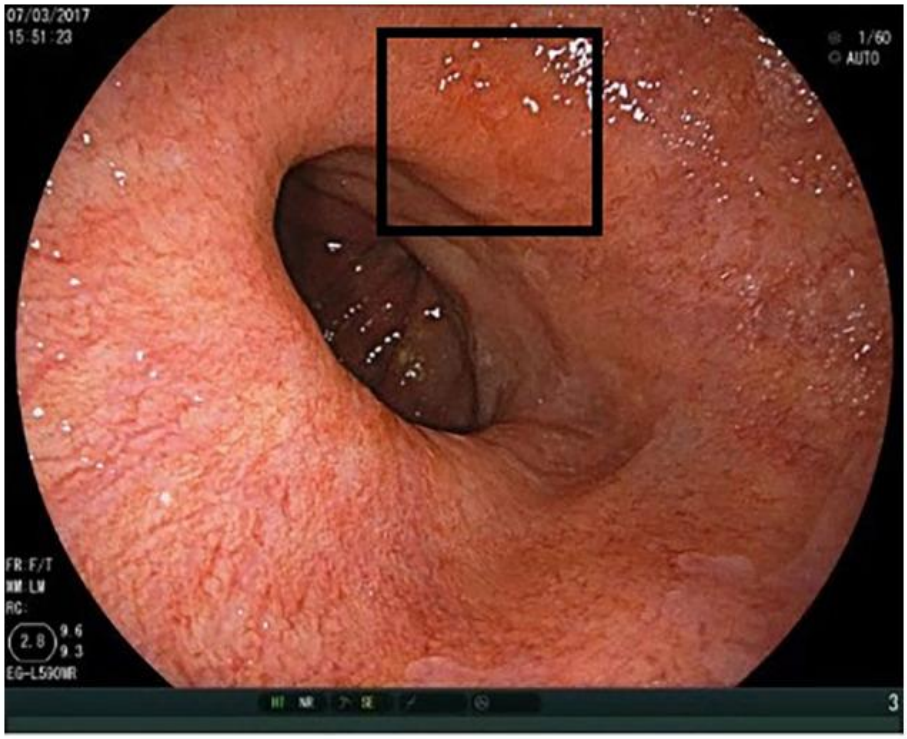


Fig. 24 Gastric cancer in the middle body of the stomach. (A) White light endoscopy WLE showed only a slight redness. (B) High magnification with better visualization of the lesion. (C) Lesion with crystal violent staining. (D) Narrow band imaging NBI high magnification showed demarcation of the brownish lesion with irregular microvasculature. (E and F) Marking and endoscopic submucosal dissection ESD of the lesion. (Source: B. Eleftheriadis, N., Inoue, H., Ikeda, H., Onimaru, M., Yoshida, A., Maselli, R., Santi, G., Hamatani, S., and Kudo, S.E., 2015. Effective optical identification of type “0-IIb” early gastric cancer with narrow band imaging magnification endoscopy, successfully treated by endoscopic submucosal dissection. Annals of Gastroenterology: Quarterly Publication of the Hellenic Society of Gastroenterology, 28(1), p.72.)



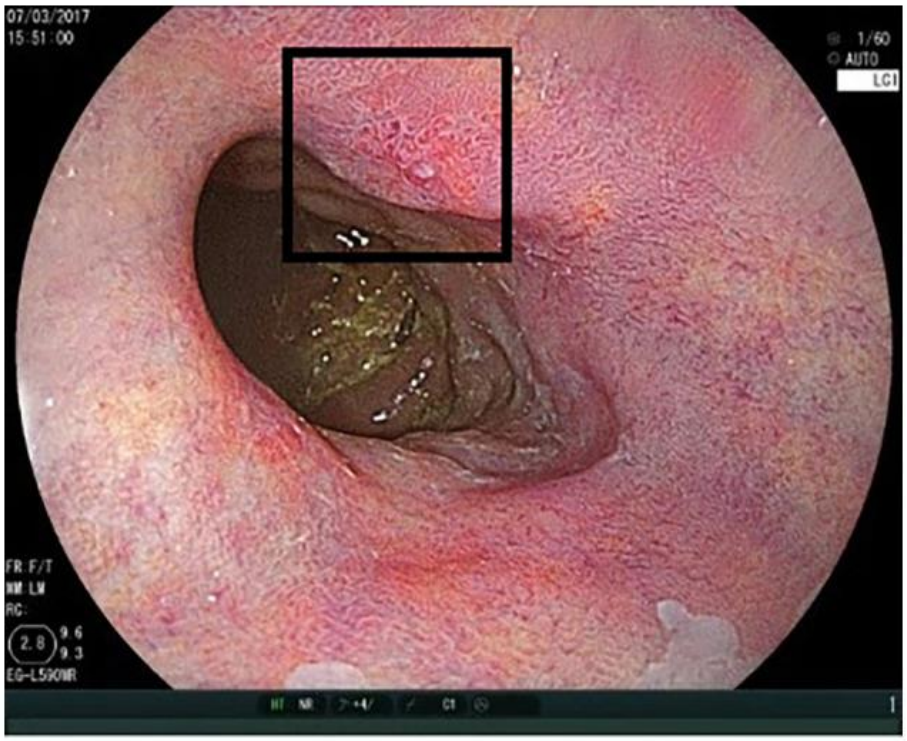


Fig. 25 High-grad gastric intraepithelial neoplasia with white light and linked color imaging. Note the better detection and demarcation of the lesion with linked color imaging. (Source: Lu, J.H., Chen, H.H., Chen, X., Zhang, H., Fan, J. and Zhang, W., 2023. Evaluation of the detection rate of high-grade gastric intraepithelial neoplasia using linked color imaging and white light imaging. Experimental and Therapeutic Medicine, 25(3), pp.1-6.)

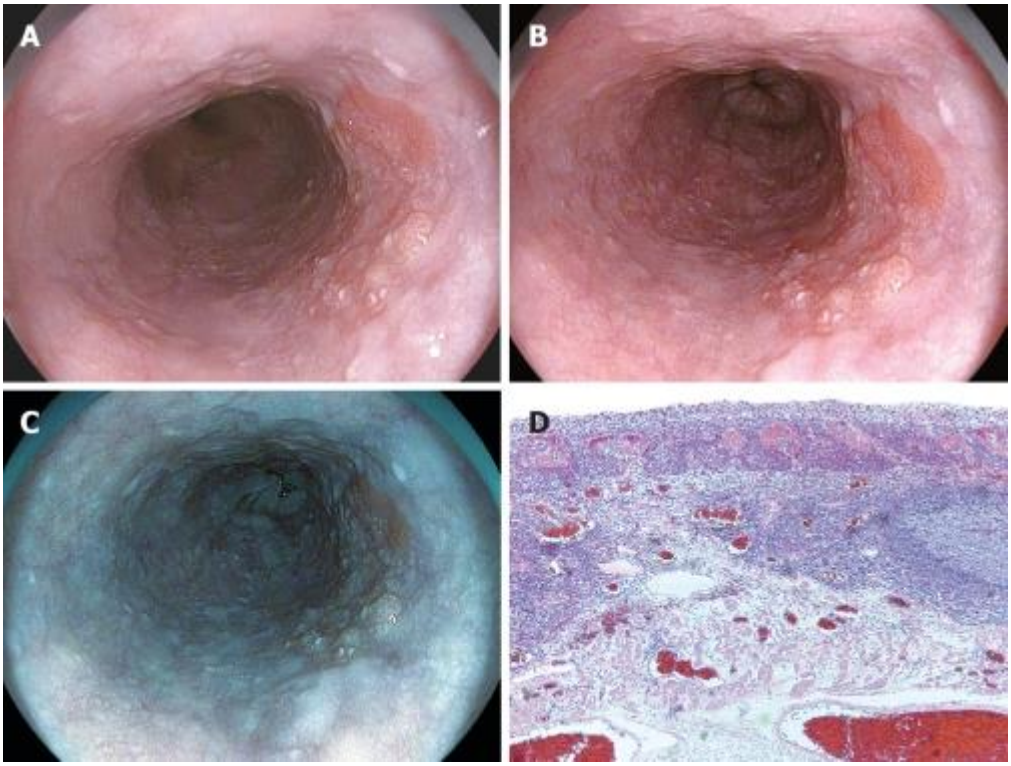


Fig. 26 A case of early esophageal cancer in the middle esophagus. (A) White light endoscopy WLE showed a slightly elevated reddish lesion. (B and C) i-Scan Imaging enabled better visualization and demarcation of the lesion. (D) Histologic confirmation of carcinoma in situ. (Source: Kodashima, S. and Fujishiro, M., 2010. Novel image-enhanced endoscopy with i-scan technology. World journal of gastroenterology*:* WJG, 16(9), p.1043.)

However, a few points are against performing EGD before ERCP/EUS. For example, this practice exposes patients to prolonged sedation and increases procedure costs [36, 37]. Some endoscopists believe that the intraluminal orientation with non-forward optic is adequate. Thus, they perform EGD only in patients with symptoms such as dysphagia, patients with known or suspected stenosis and diverticula, or patients with altered anatomy in the upper GI tract [36, 37].

This study showed that 38.78 % of patients had relevant lesions by EGD when performed before ERCP/EUS. This result is consistent with other studies in the literature. In two prospective studies, the proportion of patients with relevant lesions was 22% and 29%, respectively [38, 39]. In one retrospective study, this rate was as high as 62% [40].

In this study, lesions such as reflux esophagitis, thrush esophagitis, eosinophilic esophagitis, ulcer ventriculi, Cameron lesion, and duodenal ulcers altered the medical management of the patients. Patients with histologically confirmed Barrett's esophagus without dysplasia

and those with intestinal metaplasia in the stomach were scheduled for endoscopic surveillance. Among the patients, one was diagnosed with focal Barrett's adenocarcinoma, which was treated with endoscopic mucosal resection and subsequent radiofrequency ablation for the remaining Barrett's mucosa. One patient was diagnosed with a small gastrointestinal stromal tumor <2cm in the stomach and was scheduled for endoscopic surveillance. Patients diagnosed with esophageal/gastric varices or portal hypertensive gastropathy without known liver cirrhosis underwent a diagnostic workup. Depending on the size of the varices and risk profile, some patients had endoscopic therapy and others were scheduled for endoscopic surveillance. Endoscopic removal of the lesions was performed in two patients with esophageal papilloma, which can rarely develop into a malignancy.

In this study, 15 patients were diagnosed with stenosis (4 with esophageal stenosis, 5 with gastric stenosis, and 6 with duodenal stenosis) and 2 patients were diagnosed with an upside-down stomach. In these 17 patients (6,9 %), the EGD findings had a direct impact on the subsequent ERCP/EUS because, without awareness of these lesions, the advance of the duodenoscope/echoendoscopes would be harmful due to the risk of perforation. Dilatation was needed in 6 cases representing 2,4 % of the patients. These results are consistent with two studies, which showed that the EGD findings had a direct impact on the subsequent EUS in 9.8 % and 12% of the patients [38, 40]. In this study, we have not diagnosed patients with esophageal/duodenal diverticula, which would also be relevant for the subsequent ERCP/EUS due to an increased risk of perforation. We have diagnosed 16 patients (6.5 % of cases) with a large axial hernia > 3cm. By some endoscopists, this finding would also be relevant for the advancement with a non-forward endoscope. However, we did not include these patients in the final analysis.

Many of these lesions detected by gastroscopy would also be detectable by non-forward optic. In the Literature, few studies have compared forward optic with non-forward optic. Thomas et al. conducted a retrospective study on 168 patients and showed that, in 18% of cases, relevant lesions were detected by EGD but missed in EUS or ERCP [42]. In a prospective study conducted on 200 patients, the EUS had a sensitivity of 80% compared with EGD to detect intraluminal lesions. However, in this study, many duodenal and esophageal lesions were overlooked with EUS [43]. Kim et al. showed in a prospective study on 175 patients that the detection rate of lesions by EGD and linear EUS was comparable, but the intraluminal vision in the proximal and middle esophagus with a standard gastroscope was better than that with echoendoscope [39]. In this study, EUS was performed only by experienced endoscopists. Therefore, this result cannot be generalized to other endoscopists with fewer skills in manipulating with non-forward scopes. In a prospective study conducted on 386 patients, the detection rate of lesions by gastroscope and side-viewing duodenoscope was comparable, but the vision in the esophagus and antrum was better with the gastroscope [44]. In two other studies, the intraluminal evaluation by gastroscopy and EUS was comparable, but in one of these studies, a forward

optic echoendoscope from Pentax was used [45, 46]. In summary, we believe that the intraluminal evaluation with side-viewing or oblique-viewing endoscope is, in general, inadequate, and once a lesion during non-forward endoscopy is detected (in case of EGD not performed before), a switch to standard gastroscopy should be strongly considered for better evaluation, avoiding missing other lesions, and, if necessary, taking targeted biopsies.

The novelty of this study is that, it showed an association between age and hemoglobin level and the detection of relevant lesions by EGD. Patients with relevant lesions were significantly older and had lower hemoglobin levels (***p* = 0.029 and < 0.001**, respectively). According to the ROC curve analysis, a cut-off point of 50 years for age and 13.5 g/dl for hemoglobin level had a sensitivity of 90% and 80%, respectively, for detecting the relevant lesions, but the specificity was low. No association was observed between the detection of relevant lesions and the intake of anticoagulants (***p* = 0.336**).

This study has some limitations. First, it is a retrospective study and lacks a control group. Second, performing EGD before every ERCP/EUS may lead to increased time of procedure and cause sedation-related complications. However, this seems not to be clinically relevant. In one prospective study, the average duration of EGD before EUS was 5 min. [38]. In this study, we recorded zero complications during EGD. Other studies showed that EGD before EUS was also a safe procedure [38, 47]. Third, the costs for diagnostic EGD including other materials, such as biopsy forceps, and endoscope reprocessing are high, but these costs could be justified by the detection of relevant lesions, which would be a burden on the healthcare system when they are detected later. Further studies are needed to clarify the cost-effectiveness. Fourth, we do not know if our practice can reduce the complications related to ERCP/EUS. Thus, large cohort prospective studies are needed to clarify this issue.

In **conclusion**, we recommend performing EGD before ERCP/EUS to avoid missing relevant lesions, especially in patients older than 50 years and in those with anemia. EGD probably helps to reduce the complications related to ERCP/EUS. Further prospective studies are needed to support our retrospective observations.

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Declaration (Eidesstattliche Versicherung)

Ich, Adnan Alkurdi, versichere an Eides statt durch meine eigenhändige Unterschrift, dass ich die vorgelegte Dissertation mit dem Thema: "Retrospective dual-center study of the benefit of diagnostic gastroscopy with forward-optic before endoscopy with side-viewing

optic. Retrospektive Dual-Center Studie zum Zusatznutzen einer diagnostischen Gastroskopie mit prograder Optik vor der Endoskopie mit Seitenblickoptik" selbstständig und ohne nicht offengelegte Hilfe Dritter verfasst und keine anderen als die angegebenen Quellen und Hilfsmittel genutzt habe.

Alle Stellen, die wörtlich oder dem Sinne nach auf Publikationen oder Vorträgen anderer Autoren/innen beruhen, sind als solche in korrekter Zitierung kenntlich gemacht. Die Abschnitte zu Methodik (insbesondere praktische Arbeiten, Laborbestimmungen, statistische Aufarbeitung) und Resultaten (insbesondere Abbildungen, Graphiken und Tabellen) werden von mir verantwortet.

Ich versichere ferner, dass ich die in Zusammenarbeit mit anderen Personen generierten Daten, Datenauswertungen und Schlussfolgerungen korrekt gekennzeichnet und meinen eigenen Beitrag sowie die Beiträge anderer Personen korrekt kenntlich gemacht habe (siehe Anteilserklärung). Texte oder Textteile, die gemeinsam mit anderen erstellt oder verwendet wurden, habe ich korrekt kenntlich gemacht.

Meine Anteile an etwaigen Publikationen zu dieser Dissertation entsprechen denen, die in der untenstehenden gemeinsamen Erklärung mit dem/der Erstbetreuer/in, angegeben sind. Für sämtliche im Rahmen der Dissertation entstandenen Publikationen wurden die Richtlinien des ICMJE (International Committee of Medical Journal Editors; www.icmje.og) zur Autorenschaft eingehalten. Ich erkläre ferner, dass ich mich zur Einhaltung der Satzung der Charité – Universitätsmedizin Berlin zur Sicherung Guter Wissenschaftlicher Praxis verpflichte.

Weiterhin versichere ich, dass ich diese Dissertation weder in gleicher noch in ähnlicher Form bereits an einer anderen Fakultät eingereicht habe.

Die Bedeutung dieser eidesstattlichen Versicherung und die strafrechtlichen Folgen einer unwahren eidesstattlichen Versicherung (§§156, 161 des Strafgesetzbuches) sind mir bekannt und bewusst."

Curriculum vitae (Lebenslauf)

Mein Lebenslauf wird aus datenschutzrechtlichen Gründen in der elektronischen Version meiner Arbeit nicht veröffentlicht.

List of publications

Alkurdi, A., Rubin, D., Seelhoff, A. and Herbst, H., 2021. Brown Bowel Syndrome: An Exceedingly Rare Condition with Longstanding Malabsorption and an Unusual Cause of Colon Pseudo-Obstruction. Case Reports in Gastroenterology, 15, pp.960-965.

Alkurdi, A., Buchkremer, J., Branchi, F., Treese, C., Daum, S., Schumann, M., Siegmund, B. and Bojarski, C., 2023. Benefits of diagnostic gastroscopy before endoscopy with side-viewing optic: A retrospective dual-center study. Zeitschrift für Gastroenterologie, 61(08), pp.e376-e377.

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Certificate of the accredited statistician

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Bescheinigung

Hiermit bescheinige ich, dass Herr Adnan Alkurdi innerhalb der Service Unit Biometrie des Instituts für Biometrie und klinische Epidemiologie (iBikE) bei mir eine statistische Beratung zu seinem Promotionsvorhaben „**Retrospektive Dual-Center Studie zum Zusatznutzen einer diagnostischen Gastroskopie mit prograder Optik vor der Endoskopie mit Seitenblickoptik** " wahrgenommen hat. Folgende Beratungstermine wurden wahrgenommen:

- Termin 1: 03.02.2021
- Termin 2: 02.03.2021
- Termin 3: 05.07.2022
- Termin 4: 29.08.2022

Folgende wesentliche Ratschläge hinsichtlich einer sinnvollen Auswertung und Interpretation der Daten wurden während der Beratung erteilt:

- Empfehlung der Nutzung des Statistik-Programms „IBM SPSS Statistics" zwecks statistischer Auswertung der erhobenen Daten
    - Weiterhin Instruktion über die adäquate Eingabe der Werte
- Instruktion über die adäquate Deskription der kategorialen und metrischen Variablen
- Empfehlung zur korrekten Anwendung geeigneter statistischer Test in Abhängigkeit von den Fragestellungen: unabhängiger t-test und Chi-Quadrat-Test.
- Empfehlung zur Verwendung von ROC-Analysen zur Bestimmung optimaler Cut-offs
- Hinweis auf die evtl. angebrachte Verwendung multipler Regressionsmodelle zur Adjustierung bzgl. potenzieller Confounder
- Hinweise zur Interpretation der Ergebnisse

- Hinweis auf Erwähnung, dass es sich um eine retrospektive Studie mit explorativem Charakter handle und daher keine Adjustierung bzgl. multiplen Testens (z.B. Bonferroni-Korrektur) vorgenommen werden müsse
- Hinweis auf Erwähnung im Diskussions-Abschnitt der Monographie, dass die in dieser explorativen Arbeit gefundenen Resultate durch weitere unabhängige Studien bestätigt werden müssen

Diese Bescheinigung garantiert nicht die richtige Umsetzung der in der Beratung gemachten Vorschläge, die korrekte Durchführung der empfohlenen statistischen Verfahren und die richtige Darstellung und Interpretation der Ergebnisse. Die Verantwortung hierfür obliegt allein dem Promovierenden. Das Institut für Biometrie und klinische Epidemiologie übernimmt hierfür keine Haftung.

Datum: 01.02.2023 Name des Beraters/ der Beraterin:

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