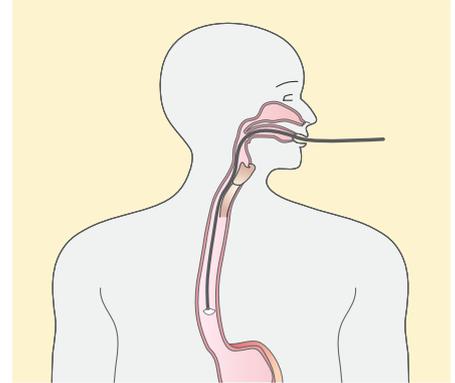


# Mistakes in gastroscopy and how to avoid them

Jochen Weigt and Arne Kandulski

Upper GI-endoscopy is one of gastroenterology's most frequently performed diagnostic and interventional methods. Even though gastroscopy is believed to be a routine investigation – which is the greatest mistake of all – several pitfalls in performance can cause serious problems or misdiagnoses.

Struggles in accurately describing and classifying abnormal findings can occur and concern the correct basic technique of endoscope introduction, and the correct way of investigating the mucosal surface in total, with several available imaging modalities such as virtual chromoendoscopy or magnification. Which classification systems should be used? The decision to perform additional workup needs to be made immediately during the ongoing endoscopy. Is it necessary to take biopsies, or should it even be avoided due to potential interference with a later endoscopic resection? This article answers the questions, highlights the most common mistakes with clinical relevance and expands on how to avoid them.



## Mistake 1 Not taking biopsies

Endoscopy uses numerous classification systems that, with the help of histology, allow for adaptability during the endoscopic procedure. However, histopathology remains the gold standard for diagnosis, risk assessment and determining further clinical management for many diseases. Therefore, current guidelines recommend the obtaining of endoscopic biopsies.<sup>1,2</sup> Mucosal biopsies in malignant disease are essential in providing histopathological proof of diagnosis, proper grading and risk assessment, and molecular targets for personalised oncologic treatments.

Once a certain diagnosis is established, it strongly depends on the clinical situation if further biopsies are necessary, i.e., for clinical follow-up, control of therapeutic response or follow-up of premalignant lesions and conditions. However, as histopathology represents only a small percentage of the mucosal surface, it is essential to describe the detailed distribution pattern of these changes as seen by endoscopy. In a patchy distribution of lesions, performing biopsies from normal mucosa outside the lesions may be helpful. For example, at least six biopsies are recommended for diagnosing eosinophilic oesophagitis and biopsies separately from the gastric antrum and corpus for the proper assessment of *H. pylori*-induced gastritis and Sydney classification; for different localisations and indications, see Table 1.

There is a considerable limitation in the maximum number of biopsies if the endoscopic appearance suggests the possibility of endoscopic resection. Recent ESGE guidelines recommend taking only one to two targeted biopsies of gastric or oesophageal lesions that are potentially suitable for endoscopic resection (Paris classification 0-I, 0-II). This confirms the diagnosis without compromising subsequent endoscopic resection.<sup>1</sup>

In the next paragraph, we provide the recommendations for endoscopic biopsies in different upper GI tract anatomical regions.

## Mistake 2 Not taking the right endoscope

Most endoscopy units are equipped with standard endoscopes with a broad focus range between 2 mm and 100 mm. In most cases, these specifications are good enough to detect and characterize findings in the upper GI tract. However, it is mandatory to take the best endoscope available, which should contain the ability for optical magnification under specific conditions.

Small lesions in the stomach and the oesophagus, especially in the setting of Barrett's metaplasia but also accountable for squamous epithelial changes, demand magnification for correct classification and/or delineation. With various chromoendoscopy techniques combined with magnification, the exact characteristics of the mucosa can be visualized better than without magnification. Signs like light blue crest sign

(LBC) to visually detect intestinal metaplasia in the stomach can be better seen under magnification. Suspicious lesions in the stomach need to be characterized according to magnification classification like the VS classification into definitive benign or suspicious and malignant lesions, which then demand resection or further workup.<sup>5</sup> Most classifications rely on the surface and vascular pattern of the capillary vessels, which can be better seen by magnification—the same accounts for oesophageal changes in squamous epithelial dysplasia or early invasive cancer. The most used classification is the Inoue classification which describes the shape of capillary loops and the presence or absence of background colourization.<sup>6</sup> The use of magnification endoscopy has become widespread as technologies like close focus and stepwise zooming make the endoscopic technique easier and no longer demand distant caps.

In other conditions like the inspection of the duodenal papilla, the use of a side viewing endoscope should be preferred. If a side viewing endoscope is unavailable, alternatively, a distal transparent cap can help visualize the papilla when using a straight viewing endoscope.

Two RCTs have been performed and clearly showed the feasibility of inspecting the papillary region with endoscopic caps.<sup>7,8</sup> However, the study by *Shi et al.* failed to prove the non-inferiority of cap-assisted inspection compared to side viewing endoscopes.

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Cite this article as: Weigt J and Kandulski A. Mistakes in gastroscopy and how to avoid them. *UEG Education* 2022; 22: 21–25.

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**Conflicts of interest:** JW receives honorary for lectures and research grant from Fujifilm Europe. AK receives speaker, consultancy and advisory board fees from Roche Pharma AG, Eisai GmbH, Abbvie Deutschland, Janssen-Cilag, Boston Scientific Corp., Micro-Tech Europe, Bayer Vital GmbH, and Bristol Myers Squibb  
Published online: August 25, 2022.

Indication	Site and numbers of biopsies	Comments
<b>Duodenum</b>		
<b>Coeliac Disease (CD)<sup>3,4</sup></b>	Multiple biopsies of duodenum (at least four) should be performed if the diagnosis of CD is considered <sup>6</sup>	Endoscopic features of CD can be patchy and are characterized by mucosal fissuring, nodular mucosa, bulb atrophy with visible submucosal vessels and loss, and reduction or scalloping of Kerckring folds with varying degrees of severity <sup>5</sup>  Endoscopic and histological examination is recommended in refractory patients
<b>Duodenal adenomatosis on the clinical background of familial adenomatous polyposis</b>	Assessment of Spigelman classification to determine the further clinical management <sup>9,10</sup>	Papilla of Vater might be investigated with a side viewing duodenoscope or an attachment cap
<b>Stomach</b>		
<b>Gastritis</b>	Gastric biopsies separately from gastric antrum and corpus should be obtained for the diagnosis and histopathological staging of gastritis according to Sydney classification system. <sup>3</sup> In addition, <i>H. pylori</i> diagnosis by rapid urease test is recommended <sup>11</sup>	Recent guidelines recommend the clinical and endoscopic management of various gastric diseases. The most important development was the definition of <i>H. pylori</i> -induced gastritis as infectious disease <sup>11,12</sup>
<b>Culture and antimicrobial testing of <i>H. pylori</i> after failed eradication therapy</b>		
<b>Gastric ulcer</b>	–	In case of gastric ulcer, documentation of ulcer healing and exclusion of underlying gastric adenocarcinoma is recommended
<b>MALT lymphoma</b>	The initial diagnosis and staging must include multiple biopsies taken from each region of the stomach as well as duodenum and gastroesophageal junction in addition to any site with an abnormal appearance  Following <i>H. pylori</i> eradication, a strict endoscopic follow-up is recommended with multiple biopsies taken two to three months after the eradication followed by a surveillance program every six months within the first two years <sup>14</sup>	Recent clinical and management guidelines recommend gastric biopsies for diagnosis and follow-up of gastric MALT lymphoma
<b>Family history of hereditary diffuse gastric cancer/CDH1 carrier status &gt;70 years old<sup>15</sup></b>	According to the Cambridge protocol, biopsies should be taken from all visible lesions and randomly from pre-pyloric region, antrum, transitional zone, body, fundus, and cardia <sup>17</sup>	Endoscopic surveillance is recommended in CDH1 pathogenic variant carriers if prophylactic gastrectomy is not indicated; in general patients over 70 years and considerable for CDH1 positive variant carriers without gastric cancer or breast cancer in their families. When surveillance endoscopy is offered, high-definition endoscopes with imaging enhancing techniques should be used <sup>15,16</sup>
<b>Chronic gastritis with gastric atrophy and/or intestinal metaplasia<sup>2,18</sup></b>	Biopsies should be taken from at least antrum and corpus labelled in two separate vials.  Additional biopsies should be taken from endoscopic visible lesions  To identify patients with advanced stages of atrophic gastritis and to risk-stratify these patients, histopathological staging system (OLGA and/or OLGIM classification system) can be used. Therefore, additional biopsies from incisura angularis are mandatory <sup>19,21</sup>	Patients with chronic gastritis and gastric atrophy with/without intestinal metaplasia as precancerous lesions are at risk for gastric adenocarcinoma. Therefore, individual surveillance and risk stratification of these patients must be indicated once the diagnosis is set. The updated ESGE MAPS guidelines focus solely on this specific group of patients with clear set management suggestions  High-definition endoscopy with chromoendoscopy or virtual chromoendoscopy is better than high-definition white-light endoscopy alone to guide biopsies
<b>Autoimmune, atrophic gastritis</b>	Biopsies should be taken from gastric antrum and corpus in addition to targeted biopsies from visible lesions	Patients with autoimmune, atrophic gastritis may benefit from endoscopic and bioptic surveillance as well  Both, gastric adenocarcinoma but especially neuroendocrine neoplasm are long-standing complications of chronic autoimmune, atrophic gastritis with pernicious anaemia
<b>Oesophagus</b>		
<b>Oesophageal adenocarcinoma/ adenocarcinoma of the oesophagogastric junction (AOG)</b>	At least six biopsies should be taken from oesophageal ulcer from the base and the edge of the ulcer  In case of suspected advanced oesophageal cancer, at least six biopsies are recommended as well	The appearance of intrapapillary capillary loops (IPCL) and background colorization can predict the depth of invasion in early squamous cell dysplasia and cancer, <sup>24</sup> and may help in decision making right during the investigation
<b>Oesophageal squamous cell cancer (ESSC)</b>	If endoscopic resection is intended, only one biopsy should be obtained in order to prevent scarification from interfering with endoscopic resection techniques	As R0 en bloc resection is important and prognosis of lymphatic invasion is drawn from the resection specimen, one might argue to skip biopsies in resectable lesions and directly perform endoscopic resection without prior biopsy  Endoscopic evaluation and staging of suspected malignant lesions include endoscopic ultrasound and histopathological sampling for grading of the malignant disease <sup>1,25</sup>
<b>Eosinophilic Oesophagitis (EoO)</b>	ESGE recommends two to four biopsies from the distal oesophagus and biopsies from the proximal oesophagus in separate vials  At least six biopsies in total should be taken <sup>1</sup>	This is in concordance with the European evidence-based consensus that recommends six biopsies from different oesophageal locations as well focusing on most visible abnormalities <sup>26</sup>
<b>Barrett's Oesophagus (BO)</b>	Biopsy should be taken from all visible mucosal abnormalities  All endoscopic visible abnormalities should be resected endoscopically  In the absence of visible abnormalities, random four-quadrant biopsies should be collected every 2 cm within the Barrett's segment  Quadrant biopsies should be started from the upper end of the gastric folds collecting biopsies from each site and level in a separate vial	BO is defined by the presence of columnar lined epithelial with a minimum length of 1 cm containing specialized intestinal metaplasia. Surveillance intervals vary for different BO lengths <sup>2,27</sup>  Patients with visible lesions in BO diagnosed with dysplasia or early cancer should be referred to an endoscopic expert centre

Table 1| Indications for endoscopic biopsies during upper GI endoscopy

### Mistake 3 Not spending enough time investigating the mucosa

In the case of colonoscopy, data clearly show the benefit of a minimum withdrawal time to increase adenoma- and polyp detection.<sup>9,10</sup> Data from EGD demonstrate similar findings. The number of patients identified with premalignant conditions (intestinal metaplasia and atrophy) increases with time spent in the stomach.<sup>11-13</sup> In a study by *Park et al.*, 100,000 endoscopies were retrospectively analysed. Endoscopists with longer investigation times found more preneoplastic and neoplastic lesions.<sup>11</sup>

In this study, the authors chose three minutes as a cut-off value. However, *The et al.*, the cut-off value of gastric mucosal inspection was calculated to be at least seven minutes, to increase the diagnostic yield of preneoplastic lesions.<sup>12</sup> Investigation of Barrett’s mucosa to screen for dysplasia should be performed while spending at least a minute for each centimetre length of Barrett’s mucosa. These time frames are not mandatory but underline the importance of detailed, careful, and sophisticated inspection of the mucosal surface.

### Mistake 4 Not adhering to commonly used classification systems

Endoscopic classification systems are widely available and can help in classifying endoscopic findings. In most cases, the description is the core basis of endoscopic diagnosis through the prediction of histology. First, it is essential to strictly adhere to the classification systems to obtain reliable results. Second, it is helpful to guarantee transferable reports to others.

In other cases, the description of lesions according to distinguished classification systems such as the Paris Classification can predict further diagnostic, therapeutic steps and endoscopic resectability.

The following table shows the most crucial classification systems for upper GI endoscopy.

### Mistake 5 Not reporting landmarks

In case of significant findings, the investigator should give detailed information about the anatomy. The findings should be recorded in the oesophagus at a distance to the incisors. Important landmarks are the upper oesophageal sphincter, oral tumour/lesion margin and aboral tumour/lesion margin. If tumours cross the oesophagogastric junction (OGJ), the extent into the stomach should be given. In Barrett’s, the most proximal extent of metaplasia should be given, and the beginning of the circular Barrett’s, if present, needs to be given. Both extents are needed for the Prague classification, which additionally utilises the beginning of the rugal folds and the diaphragm pinch. With these landmarks, the exact extent of Barrett and the presence of hiatal hernia is described. These landmarks may have high relevance in the case of risk stratification, especially in surgery. Tumour locations can be given as left-right anterior-posterior. It should be stated whether a tumour is transversal to the scope or not. In the stomach, the locations can be given as anterior/posterior wall, pylorus /antrum/corpus/fundus and cardia, greater and lesser curvature and incisura. In contrast, the corpus may be divided into proximal, distal, and middle parts.

Understanding the difference between the Z-Line and the oesophagogastric junction is essential. The Z-Line is located at the same height as the OGJ only in case of absent Barrett’s metaplasia. OG junction is defined as the beginning of the rugal folds. However, sometimes it is not easy to determine the exact beginning because of air insufflation and distension. We recommend sucking out air and determining the landmarks during the insertion of the endoscope rather than at the end of the examination. In case

of bad visibility, the beginning of the circular veins at the OGJ can be used as an alternative marker.<sup>14</sup> The Z-Line is defined as the junction between the squamous epithelium and the cylindrical epithelium and thus is a paradox to give a height in centimetres for the Z-line in the description of landmarks in Barrett’s metaplasia.

### Mistake 6 Not taking (enough) pictures

Reporting of endoscopic findings should include detailed information about the mucosa and lesions. However, the description in words may never be as good as an image, a short video, or the combination of both. Any finding of the mucosa should therefore be documented as a still image (at least). This guarantees that changes in diagnosis, exact anatomic circumstances and classification can be reviewed, justified, and may be revised. Also, for patient referral, imaging can be crucial since during the clinical course, new aspects may appear that may not be answered with the descriptive report, thus avoiding second endoscopic investigations.

Taking standard endoscopic images can also facilitate the performance of complete investigations. Recent trials using artificial intelligence to investigate the completeness of gastric mucosal inspection have shown that the chances of incomplete inspection are accurate, and that AI can reduce blind spots.<sup>15</sup>

Pictures should show key anatomic landmarks: middle oesophagus, duodenal bulb, body-antrum transition, GOJ junction/Z-line, antrum, incisura, and retroflexion, duodenum d2, pylorus fundus and cardia in retroflexion, greater curvature antegrade.

Whenever additional focal findings are present, the documentation should contain an overview image with visible lesions and borders and, if possible, magnification images with image enhancement like NBI or BLI. Good endoscopic images are taken without coverage of blood or other contents like mucus or food remnants. Images are centered to the lesions and contain only a few light reflections.

### Mistake 7 Pulling out too fast

In clinical reality, many investigators end their examination too early. The scope is often pulled out fast through the tubular oesophagus. This leads to ignoring the mid and proximal parts of this organ. In consequence, specific lesions of the oesophagus are at risk of being overlooked. Especially early squamous cell cancer or dysplasia, heterotopic gastric inlet patches, intramural diverticula or even Zenker’s diverticula are frequently missed.

For heterotopic gastric inlet patches, the prevalence of endoscopic diagnosis varies from 0.1% to 10%. Recent data documents that endoscopic detection strongly depends on the

Disease	Classification System
GORD	Los Angeles classification
Barrett’s Metaplasia	Prague classification
IPCL in early Squamous cell cancer	Inoue classification
Chronic gastritis	Modified Sydney classification
Tumour lesions	Paris classification
Early gastric cancer	VS classification
Peptic ulcer bleeding	Forrest classification
Oesophageal varices	Modified Paquet classification
FAP	Spigelman classification
Oesophago-gastric-junction adenocarcinoma	Siewert classification
Gastric Varices	Sarin classification
Global lesion description	Paris classification

Table 2 | Endoscopic classification systems

awareness of the investigator. At experienced and trained centres, detection rates are significantly high.<sup>16,17</sup>

Similar data is documented for early oesophageal squamous cell cancer in at-risk asymptomatic patients. Abnormal intrapapillary capillary loops (IPCLs) represents a hallmark of areas suspicious of early squamous cell cancer.<sup>6</sup> It appears evident that identifying these lesions is time-consuming and demands magnification endoscopy with image enhancement.

### Mistake 8 Underestimating the training in magnification and Image Enhanced Endoscopy (IEE)

As mentioned for different indications, high-definition endoscopy, including magnification endoscopy, image enhanced endoscopy (IEE) or chromoendoscopy improve the quality of endoscopy when detecting and characterising suspicious lesions. Therefore, specific training is mandatory. After introducing narrow-band imaging (NBI) in 2005, based on optical filters and a selection of wavelengths corresponding to the peak light absorption of haemoglobin, a second-generation of equipment-based IEE technology has been launched by different endoscopic companies over the last few years. This second-generation IEE includes NBI developments, i-Scan Optical Enhancement and Blue Laser / Light Imaging (BLI), as well as Linked Color Imaging (LCI), to mention the most important ones.<sup>18</sup>

Whilst the first-generation of IEE did not significantly improve adenoma detection rates in colorectal cancer screening compared with white light endoscopy,<sup>19</sup> the new generation of IEE has shown much better performance detecting superficial neoplastic lesions. LCI has been demonstrated to have higher adenoma detection rates in randomized trials.<sup>20</sup>

For the detection of preneoplastic lesions in the stomach, there is significant evidence for the advantage of conventional dye-based chromoendoscopy with high accuracy.<sup>21</sup> Similar results were obtained for first-generation NBI, mainly with magnification. The accuracy of the intestinal metaplasia diagnosis was 84 % and 95 % for dysplasia. However, it must be emphasized that these results were generated in expert centres and strongly depend on training.<sup>22-24</sup>

The second-generation IEE has been shown to further increase gastric intestinal metaplasia detection rates with high accuracy and a proposed endoscopic scoring system.<sup>25,26</sup> LCI has been emphasized to significantly increase detection rates of intestinal metaplasia in the stomach.<sup>26,27</sup>

As for the stomach, detection of mucosal lesions in Barrett's oesophagus and further characterization have been greatly improved by

the technical developments of IEE. For BLI imaging, the BLINC classification system has been proposed as an endoscopic classification system with high sensitivity and a promising training tool.<sup>28</sup>

In addition, using next-generation IEE with BLI and LCI improved the visualization of BO even by non-experienced endoscopists.<sup>29</sup>

### Mistake 9 Taking biopsy from or even resecting benign lesions

In general, the investigation during EGD should adhere to the following pattern that presumes the aforementioned skills in classifying mucosal lesions.

Start with the mucosal inspection, in case of detection, followed by optical diagnosis, followed by the decision to biopsy, to resect or to report. Optical diagnosis of benign fundic gland polyps is almost 100% reliable without biopsy and never demands endoscopic resections. The only exception is gastric adenocarcinomas of the fundic-gland mucosa lineage, which are rare entities.<sup>30</sup> It seems more important to notice fundic gland polyps as an associated lesion to genetic carcinoma syndromes such as FAP<sup>31</sup>, and to screen the colon of patients discovered with numerous fundic gland polyps for adenoma and cancer.

The misinterpretation of remnant normal gastric mucosa in patch atrophy as a polypoid lesion should be considered. Atrophy can be irregularly distributed in the stomach leading to pseudopolypoid lesions of remnant gastric non-atrophic mucosa besides severe atrophy. In cases where most of the mucosa is atrophic, these islands of the non-atrophic gastric mucosa may be misinterpreted as polypoid lesions. A simple examination of the pit pattern can help in identifying the foveolar openings and, in many cases, even a regular superficial capillary network.

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## Your gastroscopy briefing

### UEG Week

- 'Upper GI endoscopy in hereditary syndromes' session at UEG Week Virtual 2021 [<https://ueg.eu/library/upper-gi-endoscopy-in-hereditary-syndromes/247922>]
- 'A deep-learning based system reduces the miss rate of gastric neoplasms in upper endoscopy: a tandem clinical trial' session at UEG Week Virtual 2021 [<https://ueg.eu/library/a-deep-learning-based-system-reduces-the-miss-rate-of-gastric-neoplasms-in-upper-endoscopy-a-tandem-clinical-trial/248422>]
- 'Dyspepsia: To scope or not to scope?' session at UEG Week Virtual 2021 [<https://ueg.eu/library/dyspepsia-to-scope-or-not-to-scope/247921>]
- 'Training in endoscopy' session at UEG Week Virtual 2021 [<https://ueg.eu/library/training-in-endoscopy/248167>]

### Standards and Guidelines

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