Mistakes in the management of gastric polyps and how to avoid them

William Waddingham and David G. Graham

Gastric polyps are usually asymptomatic, with more than 90% found incidentally and a prevalence of up to 6% at upper endoscopy.^{1,2} Fundic gland polyps (FGPs) are the gastric polyps most frequently seen in the Western world, largely due to their long-established association with proton pump inhibitor (PPI) usage.³ In countries where *Helicobacter pylori* infection is prevalent an endoscopist is more likely to encounter hyperplastic polyps and adenomas, which are known to be associated with a higher malignant potential.⁴ Gastric polyps are often regarded as the 'poor relation' to their colonic counterparts and as such clinicians often feel unsure how to identify, assess and appropriately manage these lesions. Endoscopists often lack confidence in the endoscopic characterisation of gastric polyps, feel unsure when to biopsy polyps and, if they are biopsying polyps, how many they should sample, and finally they are not always certain what the longer-term management is. The British Society of Gastroenterology (BSG) guidelines provide a useful flowchart and overview of the management of gastric polyps, and the discussion here is based on those guidelines, guidelines from the European Society of Gastrointestinal Endoscopy (ESGE) and 12 years of clinical experience.^{5,6}



Mistake 1 Inadequate gastric mucosal inspection

Detection of any lesion within the gastrointestinal tract, including gastric polyps, is highly dependent on the quality of mucosal inspection, and to some degree the clinical index of suspicion. Within the stomach, techniques to improve the mucosal view include aspiration of fluid and debris, insufflation to expand the gastric rugae, washing the mucosal surface with water and the use of mucolytics (e.g. simethicone, N-acetylcysteine) or pronase to disperse bubbles and mucus.¹ These interventions should be performed routinely in all cases.

Both the BSG & ESGE guidelines recommend that adequate time is taken for mucosal inspection.^{5,6} Although patients and their tolerance of upper endoscopy vary, a minimum 7-minute examination time is recommended, with data indicating this leads to a threefold increase in the diagnosis of gastric adenomas and cancer.⁷ A high-quality gastroscopy includes assessment of all eight anatomical landmarks (the upper oesophagus, gastro-oesophageal junction [GOJ], fundus in retroflexion, body, incisura in retroflexion, antrum, duodenal bulb, and second part of duodenum) and high-risk stations. For completeness, these landmarks and any lesions detected should be documented photographically.

Mistake 2 Being unaware of the mucosal patterns of gastric polyps

When a lesion is identified it should be documented photographically and its morphology described using the Paris classification (figure 1).^{8,9} For polyps, the description should include their size, location and number (up to 5, greater than 5 thereafter). Optical enhancement (e.g. NBI [Olympus], i-Scan [Pentax], FICE [Fujinon]) with or without magnification improves characterisation of the mucosal surface and pit patterns of polyps. Although not in routine use, an NBI classification system has been proposed to reliably diagnose FGPs and hyperplastic polyps (<1cm) that are known to be low-risk polyps (figure 2).¹⁰ Polyps that are lighter or similar in colour to the background mucosa and with no vessels or isolated vessels have been shown in studies to be low-risk polyps with 94–100% accuracy.¹⁰

In Western populations, up to 77% of gastric polyps will be FGPs (figure 2), and these are typically numerous, small (<1cm) and smooth, hyperaemic and sessile.^{2,11} FGPs occur exclusively in the gastric corpus, and on NBI have a honeycomb appearance with dense



Figure 1 | The Paris classification.

© Waddingham and Graham

William Waddingham and David Graham are based at University College London Hospital and University College London. David Graham is a Consultant Gastroenterologist and Interventional Endoscopist and Clinical Lead at University College London Hospital and an Honorary Senior Lecturerer at University College London. William Waddingham is a Gastroenterology Specialist Registrar and MRC Clinical Research Training Fellow. Images: W. Waddingham and D. Graham Illustration: J R Shadwell Correspondence: david.graham14@nhs.net Conflicts of interest: The authors declare they have no conflicts of interest in relation to this article. Published online: April 20. 2021.

Cite this article as: Waddingham W and Graham DG. Mistakes in the management of gastric polyps and how to avoid them. *UEG Education* 2021; 21: 14–17.



Figure 2 | Fundic glandular and hyperplastic polyps. **a** | Fundic glandular polyps seen in the corpus and body. They are either lighter or the same colour as the surrounding mucosa. **b** | On near view, with image enhancement, lacy blood vessels are seen through the translucent surface and the surface shows a pattern of fine grey dots. **c** | Hyperplastic polyps are smooth, red buttered with whitish exudates (fibrin) and are dome shaped. **d** | The surface vascular pattern is more prominent on image enhancement. Reproduced from Banks M, Graham D, Jansen M, et al. *Gut* 2019; 68: 1545–1575.17 © Banks et al. (2019). Re-use permitted under CC BY-NC 4.0 license [http://creativecommons.org/licenses/by-nc/4.0/].

vasculature. In a patient who is taking PPIs and has a normal background stomach, polyps that have these features are almost diagnostic. Any polyps that have a mucosal pattern or morphology not typical of FGPs, or that occur in the context of an abnormal background stomach, warrant consideration of an alternative diagnosis.

Mistake 3 Failing to take appropriate biopsy samples

Gastric polyps detected at endoscopy, including FGPs, should be biopsied at the first endoscopy to confirm the diagnosis and exclude dysplasia.¹ If there are multiple polyps then not all polyps but a representative sample need to be biopsied. Sampling larger polyps >1cm in size with forceps alone may not be representative of the histology of the whole polyp, and as such neoplasia may be missed. A study comparing the histological diagnosis made at polypectomy with biopsy samples for polyps >5mm, found complete concordance for only 55.8% of diagnoses; however, only 2.7% of biopsy samples missed clinically significant diagnoses, such as foci of carcinoma. Although the incidence of clinically significant diagnoses is low this finding should alert the endoscopist that gastric polyps, particularly larger ones, can harbour significant pathology missed at biopsy.¹²

As the majority of gastric polyps found at endoscopy in Western practice will be FGPs occurring on a normal stomach mucosa, routine sampling of the surrounding mucosa is not recommended. However, biopsy samples of the background mucosa should be taken if hyperplastic or adenomatous polyps are found (see Mistake 7 for more detail).

Mistake 4 Thinking that size doesn't matter

Large polyps >1cm in diameter should generally be removed in their entirity to confirm the diagnosis, because malignant potential increases with increasing polyp size. Although FGPs are generally low risk and rarely exceed this size, large FGPs (>1cm) can harbour neoplasia. FGP-associated dysplasia is rare in the case of sporadic FGPs, with >80% occurring in the setting of familial adenomatous polyposis (FAP).¹³ Estimates of the malignant potential of hyperplastic polyps vary significantly from <1–20%. The overall prevalence of carcinoma in hyperplastic polyps is low (up to 1.8%), but this rises with increasing polyp size.¹⁴

In addition to the increased risk of neoplasia, larger polyps can develop surface erosions and blood loss resulting in iron deficiency anaemia. Less commonly, large polyps can become pedunculated and present as gastric outflow obstruction due to their prolapse through the pylorus.¹⁵

The technique for excision of larger polyps will depend on their morphology and size. Generally, endoscopic resection is preferred, with options including endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD). An en-bloc resection with ESD should be considered for larger sessile polyps (>15mm) due to the risk of recurrence.

Mistake 5 Not testing and treating for *H. pylori* infection

Both hyperplastic polyps and adenomatous polyps are associated with H. pylori infection, which should therefore be tested for and eradicated whenever a patient has a positive test result. Diagnosis of H. pylori infection at endoscopy is done by performing a rapid urease test, for example the CLO test (campylobacterlike organism). These are highly reliable diagnostic tests, with studies showing 80-100% sensitivity and 97–99% specificity.7 For best results, two samples—one from the antrum (avoiding areas of ulceration and obvious intestinal metaplasia) and one from normalappearing corpus—are sufficient and provide the highest yield.⁷ The most common reason for false-negative results is recent PPI use, for this reason testing after a 2-week break from PPIs is generally recommended. Histology is another a reliable way of diagnosing *H. pylori* infection, with sensitivity and specificity both as high as 95% and 99%, respectively. This approach is more expensive, and to some degree suffers from interobserver variability, it does, however, provide additional histological information and should be generally be reserved for situations where atrophy, intestinal metaplasia or neoplasia are suspected.

Hyperplastic polyps develop in epithelium that is regenerating after a chronic inflammatory stimulus and are seen in the setting of chronic *H. pylori*-related gastritis, pernicious anaemia, and adjacent to ulceration or erosions. For patients who have small hyperplastic polyps (<1cm), *H. pylori* eradication should be considered before undertaking endoscopic resection, with a repeat endoscopy performed 3–6 months later, because in many cases these polyps will regress post eradication.

Gastric adenomas (raised intraepithelial neoplasia) typically occur in the setting of *H. pylori*-related chronic atrophic gastritis (CAG), and should be viewed as a neoplastic precursor to adenocarcinoma. Adenomas should be resected and one must always also test and treat for *H. pylori* as both BSG and ESGE guidelines demonstrate that its eradication is likely to be linked with a decreased risk of progression of CAG.^{5,6}

Mistake 6 Missing synchronous lesions

All gastric polyps, except FGPs and rare inflammatory fibroid polyps, are associated with an increased risk of cancer. There is a strong association between gastric adenomas and synchronous gastric cancer (figure 3), with coexistent cancer being found in up to 30% of patients.¹⁶ A review of the natural history of gastric dysplasia suggests that once high-grade dysplasia has been detected, the risk of progression to cancer or the development of a synchronous malignancy is 60–85% within 4–48 months.¹⁷

Detection of gastric dysplasia and early gastric cancer is especially difficult at endoscopy, with insufflation and careful mucosal washing essential to ensure adequate views. Subtle features include loss of vascular or pit patterns, flattening or abnormal convergence of folds and mucosal depression, as well as ulceration or nodularity.¹⁸ Synchronous dysplasia can be present throughout the stomach; however, there is a slight predominance in the antrum, lesser curve and incisura.

Mistake 7 Not assessing the background stomach

If gastric adenomas or hyperplastic polyps are present, the background mucosa should also be carefully assessed for the presence of precancerous lesions that might predict future cancer risk. This includes CAG and gastric intestinal metaplasia (GIM) (figure 3).

Atrophy is readily identifiable by mucosal pallor, increased visibility of vessels, loss of rugal folds and the presence of an atrophic border. However, a complete assessment should include the use of image enhancement for delineating the presence of GIM, which is often visible as elevated pink patches or plaques—an elongated 'groove type' pit pattern in the body and the light



Figure 4 | Endoscopic appearance of the atrophic border and modified Kimura–Takemoto classification system. a and b | Low power view of atrophic gastritis at white light endoscopy. The abrupt transition at the atrophic border is clearly seen (dotted line) with loss of rugal folds, mucosal pallor and increased visibility of vessels. In this example, the atrophic border is located at the transition between the lesser and greater curve. Using the modified Kimura–Takemoto scoring system, this patient would be staged 'C3, corpus dominant atrophy'. c | Appearance of the atrophic border at enhanced imaging (Olympus, NBI), to the right of the dotted line the normal body pit pattern is lost and the mucosa appears paler (asterisk). d and e | Depicted is the stomach opened up along the greater curvature (d) and in traditional coronal view (e). This schematic representation demonstrates the modified Kimura–Takemoto classification system; antral (C1); antral predominant (C2); corpus predominant (C3) and panatrophy; numbers 1–5 correspond to the location of gastric biopsies, which should be taken according to the updated Sydney system: antrum greater and lesser curve, incisura, corpus greater and lesser curve. **a**-**c** reproduced from Waddingham W, Nieuwenburg SAV, Carlson S, et al. *Frontline Gastroenterol* doi: 10.1136/flgastro-2018-101089. © Waddingham W et al. (2020). **d** and **e** reproduced from Waddingham W, Graham D, Banks M et al. *F1000Research* 2018; 7 (F1000 Faculty Rev): 715. © Waddingham W et al. (2018). Re-use permitted under CC BY-NC 4.0 license [http://creativecommons.org/licenses/by-nc/4.0/].

blue crest seen on NBI are both highly specific signs of GIM.¹⁹

When either CAG or GIM is present the extent should be estimated using the modified Kimura staging system¹⁶ and biopsy samples taken according to the Sydney protocol





(antrum 1 & 2, incisura, lesser curve, greater curve) (figure 4).^{5,6}

Mistake 8 Failing to consider the need for surveillance

After resection of gastric adenomas all patients should undergo a follow-up endoscopy in 6–12 months, followed by yearly endoscopies if appropriate.⁵ The endoscopy interval depends on the highest grade of dysplasia detected and the number and size of polyps resected.

The cancer risk of the background stomach should also be considered—if CAG and or GIM are present they may warrant ongoing surveillance depending on their extent. Patients who have extensive CAG or GIM, meaning it extends into the body of the stomach, should generally be offered ongoing 3-yearly surveillance, while those who have CAG with a history of dysplasia should be offered yearly surveillance.⁵ The surveillance strategies are discussed in the BSG and ESGE guidelines and are based upon the risk of progression of CAG.^{5,6} Estimates of cancer risk for premaligant lesions varies, with studies from low-incidence countries suggesting an annual gastric cancer risk with CAG and/or GIM of 0.1–0.25%,¹⁰ while a recent meta-analysis estimated an annual progression risk of 0.5%.¹¹

Mistake 9 Not considering polyposis syndromes

Management of polyposis syndromes is challenging and recent guidance is available from the ESGE on this topic.²⁰ With regard to gastric polyps, the finding of numerous polyps (i.e. \geq 20) in a patient younger than 40 years of age, should raise the possibility that they have a polyposis syndrome.

FGPs are common in patients who have familial adenomatous polyposis (FAP). In this scenario there are typically multiple FGPs present and they are often seen to 'carpet' the body of the stomach. There is no clear guidance on differentiating sporadic FGPs from FAP-associated FGPs; however, as discussed, the presence of dysplasia should cause suspicion of FAP. When gastric polyps are associated with duodenal adenomas then a familial polyposis syndrome should also be considered and colonoscopy advised if not already undertaken. Importantly, in this scenario the use of a side-viewing scope (duodenoscope) should be considered in order to visualise the Ampulla of Vater due to an association with neoplastic ampullary lesions.

Hamartomatous polyps are rare in the stomach and they include polyps related to Peutz–Jegher's syndrome, Cowden's disease and juvenile polyposis. These rare polyps should all be resected if they are >1cm and patients enrolled into a dedicated surveillance program under the care of a centre that has adequate expertise.¹

Mistake 10 Forgetting about submucosal lesions

Although the vast majority of gastric polyps are epithelial in origin, it should not be forgotten that submucosal lesions occur in the stomach. These lesions are rare and typically found incidentally, they should be considered if the overlying mucosa is normal, and there may be central ulceration (e.g. gastrointestinal stromal tumours [GISTs]). Submucosal lesions tend to be small (<1cm), but as they grow and lead to ulceration of the overlying mucosa they can present with bleeding and pain. A forceps biopsy of these lesions is often unreliable, as the mucosa tends to slide over the submucosal lesion, and the forceps often do not sample the tissue deep enough to make a histological diagnosis. If there is clinical suspicion of a submucosal lesion, the best modality for diagnosis is endoscopic ultrasound (EUS) and fine-needle aspiration (FNA), although other techniques such as submucosal tunnelling and full-thickness resection are options.

Other rarer submucosal lesions include neuroendocrine tumours. These lesions require adequate characterisation of their type and stage, and their management should be undetaken within a neuroendocrine tumour multidisciplinary team.¹ Inflammatory fibroid polyps originate from the submucosa, they represent <0.1% of gastric polyps and are associated with CAG, but they are generally not considered to have neoplastic potential.¹

References

- 1. Goddard AF, Badreldin R, Pritchard DM, et al. The management of gastric polyps. *Gut* 2010; 59: 1270–1276.
- Carmack SW, Genta RM, Schuler CM, et al. The current spectrum of gastric polyps: A 1-year national study of over 120,000 patients. *Am J Gastroenterol* 2009; 104: 1524–1532.
- el-Zimaity HM, Jackson FW and Graham DY. Fundic gland polyps developing during omeprazole therapy. *Am J Gastroenterol* 1997; 92: 1858–1860.
- Morais DJ, Yamanaka A, Zeitune JMR, et al. Gastric polyps: A retrospective analysis of 26,000 digestive endoscopies. Arq Gastroenterol 2007; 44: 14–17.
- Banks M, et al. British Society of Gastroenterology guidelines on the diagnosis and management of patients at risk of gastric adenocarcinoma. *Gut* 2019; 68: 1545–1575.
- Bisschops R, et al. Performance measures for upper gastrointestinal endoscopy: A European Society of Gastrointestinal Endoscopy quality improvement initiative. United Eur Gastroenterol J 2016; 4: 629–656.
- Park JM, et al. Longer observation time increases proportion of neoplasms detected by esophagogastroduodenoscopy. *Gastroenterology* 2017; 153: 460–469.e1.

- Participants in the Paris Workshop. The Paris endoscopic classification of superficial neoplastic lesions: esophagus, stomach, and colon: November 30 to December 1, 2002. Gastrointest Endosc 2003; 58 (6 Suppl): S3–S43.
- Endoscopic Classification Review Group. Update on the Paris classification of superficial neoplastic lesions in the digestive tract. *Endoscopy* 2005; 37: 570–578.
- Colling C, Asztalos I, Buchner AM, et al. Mo2037 Narrow-band imaging classification system for gastric polyps may reduce the need for biopsies. *Gastrointest Endosc* 2017; 85: AB531.
- Shaib YH, Rugge M, Graham DY, et al. Management of gastric polyps: An endoscopy-based approach. *Clin Gastroenterol Hepatol* 2013; 11: 1374–1384.
- 12. Muehldorfer SM, Stolte M, Martus P, et al. Diagnostic accuracy of forceps biopsy versus polypectomy for gastric polyps: A prospective multicentre study. *Gut* 2002; 50: 465–470.
- Lloyd IE, et al. A clinicopathologic evaluation of incidental fundic gland polyps with dysplasia: implications for clinical management. Am J Gastroenterol 2017; 112: 1094–1102.
- Zea-Iriarte WL, et al. Carcinoma in gastric hyperplastic polyps. A phenotypic study. *Dig Dis Sci* 1996; 41; 377–386.
- Parikh M, Kelley B, Rendon G, et al. Intermittent gastric outlet obstruction caused by a prolapsing antral gastric polyp. *World J Gastrointest Oncol* 2010; 2: 242.
- Rugge M, et al. Gastric epithelial dysplasia in the natural history of gastric cancer: A multicenter prospective follow-up study. *Gastroenterol Off J Am Gastroenterol Assoc* 1994; 107: 1288–1296.
- Sung, JK. Diagnosis and management of gastric dysplasia. *Korean J Intern Med* 2016; 31: 201–209.
- Wang L, Huang W, Du J, et al. Diagnostic yield of the light blue crest sign in gastric intestinal metaplasia: A meta-analysis. *PLoS One* 2014; 9: e92874.
- Kono S, et al. Can endoscopic atrophy predict histological atrophy? Historical study in United Kingdom and Japan. *World J Gastroenterol* 2015; 21: 13113–13123.
- Van Leerdam ME, et al. Endoscopic management of polyposis syndromes: European Society of Gastrointestinal Endoscopy (ESGE) Guideline. Endoscopy 2019; 51: 877–895.

Your gastric polyps briefing

Online courses

- Gastric polyps [https://ueg.eu/p/109].
- Hereditary gastrointestinal polyposis syndromes [https://ueg.eu/p/108].

UEG Week

- "Gastric polyps and polyposis: Help!" session at UEG Week 2019 [https://ueg.eu/library/session/ gastric-polyps-and-polyposis-help/156/2200].
- "Clinical presentation and endoscopic assessment of gastric lesions" session at UEG Week 2019 [https://ueg.eu/library/session/ gastric-polyps-and-submucosal-lesions/156/2123]
- "Endoscopy meets pathology: Polyps and polyposis syndromes in the upper GI tract" at UEG Week 2016 [https://ueg.eu/library/session/

endoscopy-meets-pathology-polyps-and-polyposissyndromes-in-the-upper-gi-tract/144/1606].

 "Gastric polyps: Diagnostic and therapeutic approach" session at UEG Week 2016 [https://ueg.eu/library/session/ gastric-polyps-diagnostic-and-therapeuticapproach/144/1567].

Standards and Guidelines

- Banks M, et al. British Society of Gastroenterology guidelines on the diagnosis and management of patients at risk of gastric adenocarcinoma. *Gut* 2019; 68: 1545–1575.
- Van Leerdam ME, et al. Endoscopic management of polyposis syndromes: European Society of Gastrointestinal Endoscopy (ESGE) Guideline. *Endoscopy* 2019; 51: 877–895.