

Biopsy Sampling in Upper Gastrointestinal Endoscopy: A Survey from 10 Tertiary Referral Centres Across Europe

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Keywords

Gastritis · OLGA · MAPS · Sydney · Biopsy sampling · Gastroscopy · CLO test

Abstract

Background: Guidelines give robust recommendations on which biopsies should be taken when there is endoscopic suggestion of gastric inflammation. Adherence to these guidelines often seems arbitrary. This study aimed to give

an overview on current practice in tertiary referral centres across Europe. **Methods:** Data were collected at 10 tertiary referral centres. Demographic data, the indication for each procedure, endoscopic findings, and the number and sampling site of biopsies were recorded. Findings were compared between centres, and factors influencing the decision to take biopsies were explored. **Results:** Biopsies were

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taken in 56.6% of 9,425 procedures, with significant variation between centres ($p < 0.001$). Gastric biopsies were taken in 43.8% of all procedures. Sampling location varied with the procedure indication ($p < 0.001$) without consistent pattern across the centres. Fewer biopsies were taken in centres which routinely applied the updated Sydney classification for gastritis assessment (46.0%), compared to centres where this was done only upon request (75.3%, $p < 0.001$). This was the same for centres stratifying patients according to the OLGA system (51.8 vs. 73.0%, $p < 0.001$). More biopsies were taken in centres following the MAPS guidelines on stomach surveillance (68.1 vs. 37.1%, $p < 0.001$). Biopsy sampling was more likely in younger patients in 8 centres ($p < 0.05$), but this was not true for the whole cohort ($p = 0.537$). The percentage of procedures with biopsies correlated directly with additional costs charged in case of biopsies ($r = 0.709$, $p = 0.022$). **Conclusion:** Adherence to guideline recommendations for biopsy sampling at gastroscopy was inconsistent across the participating centres. Our data suggest that centre-specific policies are applied instead.

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Introduction

Gastric cancer is a tremendous challenge for health care systems worldwide due to the high mortality associated with this disease. The reason lies in the late stage at diagnosis in most cases, with these patients experiencing no, or rather minor, non-specific symptoms in the initial phase of cancer progression. The identification of *Helicobacter pylori* (*H. pylori*) as the main risk factor and the description of a sequence of inflammation-induced preneoplastic changes of the gastric mucosa has opened the door not only to gastric cancer prevention but also to identification of individuals at increased risk of gastric cancer [1, 2]. The latter group could be offered endoscopic surveillance to enable detection of early stage disease and thereby reduce mortality, as it has been shown for Barrett's and cancer of the oesophagus [3]. While this concept has been implemented in high incidence areas in Asia [4], this approach has not been deemed cost-effective in low-incidence countries in the West [5]. In addition to health-economic concerns, there are also biological and technical issues that render endoscopic surveillance of the stomach more challenging compared to other compartments of the luminal GI tract. Preneoplastic changes in the stomach are more subtle and more dif-

ficult to identify compared to polypoid lesions in the colon. The stomach also comprises a larger surface area compared to a segment of Barrett's metaplasia in the oesophagus.

The updated Sydney protocol remains the gold standard for gastritis assessment asking for only 5 samples from the entire stomach (2 from the antrum, 1 from the incisura angularis, and 2 from the body), in addition to targeted biopsies from any visible abnormalities [6]. The Sydney protocol includes instructions on the histopathological grading of the inflammatory changes. Current national and international guidelines support the application of the Sydney recommendations. Countries without specific national guideline usually adopt the second edition of the European consensus on management of epithelial precancerous conditions and lesions in the stomach (MAPS II) [7–10].

Due to the biology of *H. pylori* gastritis, gastric preneoplastic conditions carry a higher risk of further progression if the gastric body is affected [11], emphasizing further the need for endoscopic surveillance in these patients [12]. Thus, all relevant risk stratification systems require distinct information on the mucosal integrity in both the gastric antrum and the body, and sampling of both areas is required to meet standards for a high quality upper gastrointestinal endoscopy [13]. The need for a complete set of biopsies was demonstrated in a large US study in 2013 analysing over 400,000 sets of biopsies [14]. Separate sampling of both the gastric antrum and the body is furthermore necessary for adequate assessment of pylorip-due *H. pylori* since a shift of the colonisation from the antrum towards the body both occurs in the natural course of the infection and under the influence of medication such as acid blockers [15].

Clinical practice shows that adherence to these recommendations for biopsy sampling is low and depends, among other factors such as local resources, on the expertise as well as personal interests of the investigator [16]. The clinical care setting also plays a role since academic centres are more likely to perform better with regards to guideline adherence [17]. Since academic centres are supposed to set the reference standards, we invited selected tertiary referral centres across Europe with high expertise in diseases of the stomach to collect data on their current practice.

The primary aim of our study was to assess standards of upper gastrointestinal biopsy sampling in patients with endoscopic signs of gastric inflammation in different academic centres across Europe and to analyse factors that might have an influence on the local practice. In addition

to this, the sampling practice was analysed for procedures that were undertaken for different indications, such as anaemia or dysphagia, for comparison.

Materials and Methods

General Study Design

Ten of the 13 centres that were invited to join this survey of local biopsy sampling practice during upper gastrointestinal endoscopy took part in the study, including Rotterdam (The Netherlands), Antwerp (Belgium), Barcelona (Spain), Dublin (Ireland), Kaunas (Lithuania), Magdeburg (Germany), Oxford (United Kingdom), Padua (Italy), Riga (Latvia), and Sofia (Bulgaria). The centres were asked to collect data for all elective oesophagogastroduodenoscopies (OGDs) done during a period of at least 2 consecutive months and submit these in anonymised form to the lead site (Oxford). Only patients 16 years or older were included. Emergency procedures (e.g., bolus obstruction) were not included in the data set.

Data Collection

Age and sex of the patients were recorded as well as the main indication for each procedure, endoscopic findings, and the number and location of biopsies taken. A set of key indications for referral to OGD were recorded. All indications not listed in online suppl. Table 1 (for all online suppl. material, see www.karger.com/doi/10.1159/000511867) were recorded as “other.” We focused on the primary indication only in those for whom several indications were given. In 7 centres, data were recorded with the help of a one-page questionnaire that was filled out at the end of each procedure. Data were then entered into an Excel database that was submitted to the lead site. Centres using an electronic endoscopy documentation system ($n = 3$) retrieved data in a systematic way at the end of the designated study period.

We also recorded information on the cost for OGDs with and without biopsy for each centre. Centres were further asked to indicate if they followed the MAPS II guidelines on endoscopic surveillance of patients with preneoplastic conditions of the stomach. Histopathology results were not recorded as this was not the focus of the study, but each centre indicated whether histopathology scoring according to the Sydney classification and grading of changes according to the OLGA (Operative Link for Gastritis Assessment) system was done (a) as standard “routine” practice; (b) “upon request” by the endoscopist; or (c) when deemed “feasible” in case of samples with marked preneoplastic changes (or (d) not at all).

Statistical Analysis

Categorical data were compared by χ^2 test. If not otherwise stated, p values refer to the global comparison across all centres. Comparison of numerical data was done by Kruskal-Wallis test and subsequent Mann-Whitney U test as post-test as appropriate. Spearman’s rank correlation test was applied for correlation analyses. Test results were considered as significant for $p < 0.05$. In the case of multiple comparisons, Bonferroni correction was applied resulting in different thresholds. Statistical analysis was performed using IBM SPSS Statistics for Windows, version 25 (IBM Corp., Armonk, NY, USA).

Table 1. General characteristics of each centre and the respective study population

Centre	Centre 1	Centre 2	Centre 3	Centre 4	Centre 5	Centre 6	Centre 7	Centre 8	Centre 9	Centre 10	Total cohort	p value
N procedures	866	885	1,191	408	509	1,879	286	335	194	9,425	na	na
Age median, yrs	59	58	62	62	64	53	58.5	59	60	60	<0.001	<0.001
Age range, yrs	17–93	16–98	16–98	17–90	17–95	17–90	18–89	18–90	17–93	16–98	na	na
Female, %	54	53.1	54	40.5	46.4	69.7	46.9	41.5	44.8	53.8	<0.001	<0.001
Biopsies, %	54.8	84.5	18	66.2	70.9	46.7	65.7	51	67.5	56.6	<0.001	<0.001
Gastric biopsies, %	41.9	76.6	13.0	62.3	57.8	41.0	45.8	47.5	49.5	43.8	<0.001	<0.001
CLO, %	10.2	69.4	9.4	47.1	0.2	44.8	0	1.2	0.5	20.9	<0.001	<0.001
Sydney	1	2	1	1	1	3	3	2	1	–	na	na
OLGA/OLGIM	0	2	0	2	1	3	3	2	0	–	na	na
MAPS	1	1	2	1	1	1	1	2	1	–	na	na
Costs per OGD [€]	241.88	517	27.83	230.56	96	100	115	60	375.45	128.97	189.27	0.437
Additional costs if biopsies taken [€]	61.53	130	3.06	26.76	100	40	34	20	61.48	59.68	0.433	0.433

Statistical tests applied were χ^2 for comparison of categorical variables and Kruskal-Wallis for comparison of age and costs. Statistical significance assumed for $p < 0.05$. Status indicator for application of Sydney gastritis assessment, OLGA/OLGIM risk stratification and MAPS guidelines for surveillance: 0 = not used, 1 = local standard, 2 = upon request, 3 = when feasible (see text for details). CLO, campylobacter-like organism test, also often called RUT (rapid urease test); MAPS, European guidelines on the management of epithelial precancerous conditions and lesions in the stomach [13]; na, not applicable; OGD, oesophagogastroduodenoscopy; OLGA, operative link for gastritis assessment; OLGIM, operative link for gastritis assessment by intestinal metaplasia; SD, standard deviation.

Table 2. Endoscopic findings during OGD per centre

	Centre 1	Centre 2	Centre 3	Centre 4	Centre 5	Centre 6	Centre 7	Centre 8	Centre 9	Centre 10	Total cohort
Duodenitis, %	6.40	15.00	3.40	10.00	4.10	0.50	1.40	19.40	6.60	5.20	6.00
Duodenal ulcer, %	2.10	1.40	5.60	3.40	1.00	2.10	1.00	8.10	1.70	3.10	2.50
Gastritis, %	22.10	36.70	22.90	53.90	39.60	43.50	9.40	52.80	22.00	19.60	30.80
Gastric erosions, %	8.00	1.60	25.00	12.00	9.60	7.50	4.20	11.00	3.80	5.70	8.40
Gastric ulcer, %	4.40	2.40	5.40	4.20	2.40	1.00	2.80	5.40	2.20	4.10	2.80
Gastric cancer, %	0.60	1.40	1.20	2.00	2.00	0.30	1.00	1.80	0.70	0.00	0.90
PHG, %	6.60	2.10	1.50	1.00	4.50	0.10	1.40	6.90	3.60	3.60	2.80
Oesophagitis, %	9.60	21.50	19.60	13.70	10.60	15.30	12.60	35.20	9.50	19.60	14.50
Barrett's oesophagus, %	4.00	5.60	1.00	3.20	7.50	1.10	3.10	1.50	9.30	11.30	5.00
Oesophageal cancer, %	0.50	1.70	1.80	10.00	1.40	0.10	1.00	2.40	1.20	1.00	1.50
Varices, %	9.10	1.50	3.90	1.50	3.50	1.00	3.10	18.50	4.70	6.70	4.20

OGD, oesophagogastroduodenoscopy; PHG, portal-hypertensive gastropathy.

Results

General Population Characteristics per Centre

The 10 participating centres recorded their procedures over a period of 2–4 months, covering a total of 29 operational months and 9,425 procedures between January and September 2019. There were significant differences between the centres regarding age and sex of the patient population ($p < 0.001$; Table 1) as well as costs per OGD ($p < 0.001$). There was also a broad variation in the additional fee that was charged if biopsies were taken during the procedure ($p < 0.001$; pathology costs were not included in this consideration).

There was also variation in the indications for each procedure, as far as this was recorded ($p < 0.001$; online suppl. Table 1). About a third of patients were referred for assessment of dyspeptic symptoms. Biopsies were taken in 56.6% of all procedures, but the sampling rate differed between centres, with the highest proportion of patients with biopsies seen in centre 2 (84.5%) and the lowest in centre 3 (18%; Table 1, $p < 0.001$). Biopsies from the stomach were taken in 43.8% of all procedures, again with centre 2 showing the highest sampling rate (76.6%) and centre 3 the lowest (13.0%; Table 1, $p < 0.001$). Similarly, this also accounted for specialised biopsy-based tests such as the rapid urease-based CLO (campylobacter-like organism) test to check for *H. pylori*, which was either used to a negligible degree or in up to 69.4% in centre 2 (Table 1, $p < 0.001$).

Endoscopy Findings

Table 2 shows the occurrence of different endoscopic findings per centre. Since we aimed to assess the rate of bi-

opsy sampling in patients with inflammatory changes of the stomach, patients with signs of “gastritis” and “gastric erosions” were combined in the group “gastric inflammation.” This also included patients with signs of chronic gastritis, such as endoscopic appearance of mucosal atrophy. Endoscopic scoring of atrophy was not done in all centres and was therefore not recorded for this study. Also, patients with “gastric ulcer” were not included in this group because the recommendations for biopsy sampling and endoscopic follow-up differ from non-ulcer patients. Gastric inflammation as defined above was present in 36.0% of the complete cohort with the incidence ranging from 13.6% in centre 7 to 60.5% in centre 4 ($p < 0.001$, Fig. 1a).

When gastric biopsies were taken in patients with endoscopic suggestion of gastric inflammation, these were in 24.1% pairs from antrum and body and in 26.7% sets including a sample from the incisura as required by the updated Sydney classification [6]. In 19.9% of patients with endoscopic gastric inflammation, biopsies from duodenum, antrum, and body were obtained during the procedure. The pattern of biopsies varied considerably between centres (Fig. 1b, $p < 0.001$). In a large proportion of these patients, either no (39.2%) or single-location only biopsies (15.4%) were taken from the stomach.

The proportion of procedures with biopsies taken was significantly higher in patients with gastric inflammation compared to patients without (65.5 vs. 51.9%, $p < 0.001$; Fig. 2a). This was also true for CLO testing (29.5 vs. 16.2%, $p < 0.001$). Most marked in this group of patients was an increase of biopsies taken from the gastric antrum (57.6 vs. 30.5%; $p < 0.001$) and the gastric body (47.1 vs. 23.7%; $p < 0.001$, Fig. 2a).

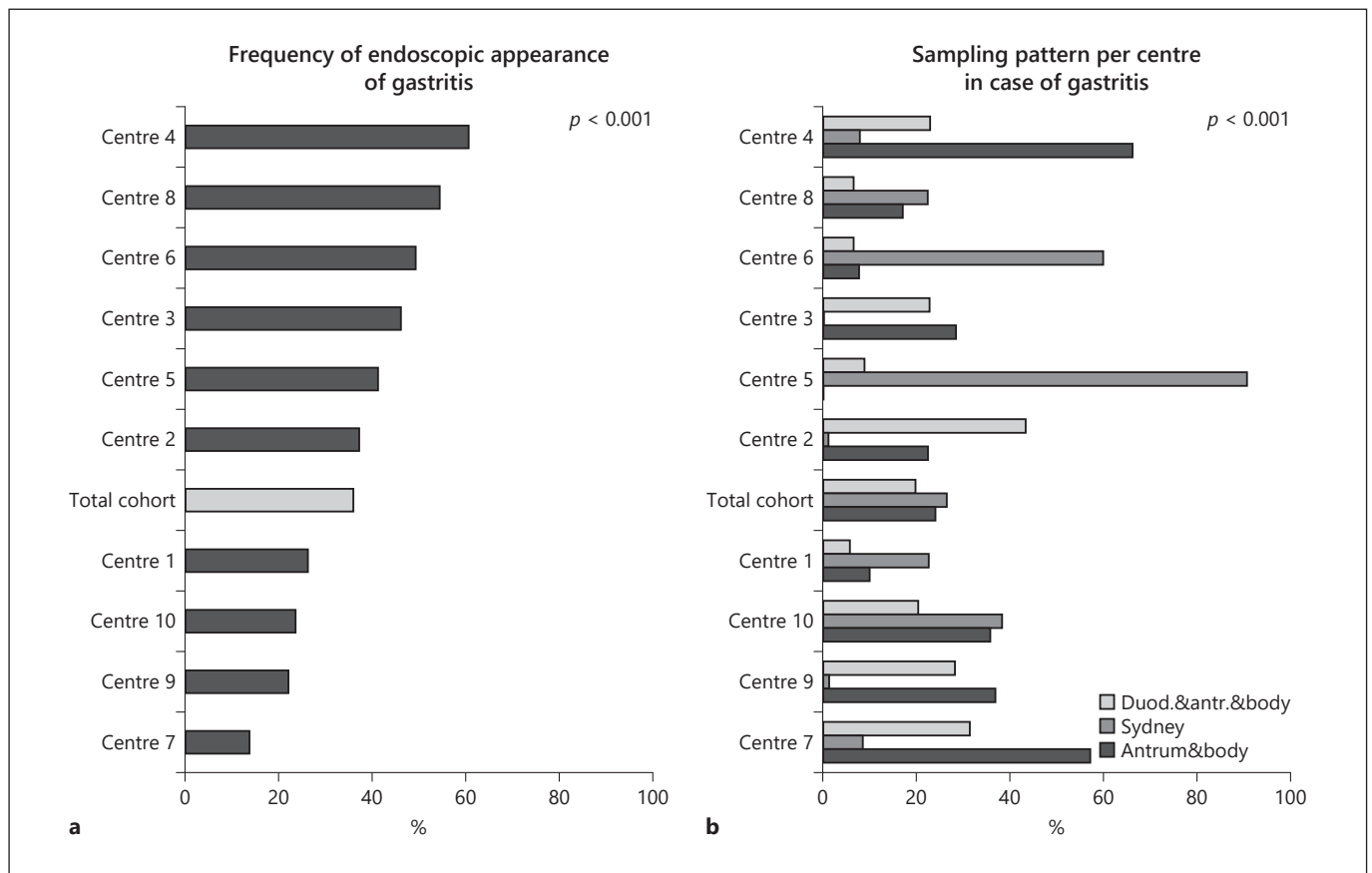


Fig. 1. Frequency of endoscopic signs of gastritis and sampling pattern. **a** Displayed is the prevalence of endoscopic signs of gastritis in the cohort for each centre. This was defined as mucosal irritation, for example, erythema, and presence of erosions, but did not include more advanced changes such as ulcers or tumours. **b** Pro-

portion of sample sets taken per centre in patients with endoscopic signs of gastritis. These were mutually exclusive, but additional samples from the oesophagus might have been taken for each category that were not included in this analysis. Comparisons were done by χ^2 test across all centres as outlined in the methods section.

Influence of Indication on Biopsy Sampling

Dyspepsia was the key indication in 2,623 cases (27.8% of all procedures), gastro-oesophageal reflux in 813 patients (8.6%), dysphagia in 781 procedures (8.3%), and 887 OGDs (9.4%) were done for investigation of anaemia (online suppl. Table 1). The sampling pattern varied significantly with indication across the total cohort ($p < 0.001$; Fig. 2b, c). In the individual assessment, this variation was statistically confirmed in centres 1 ($p = 0.008$) and 10 ($p = 0.001$). Duodenal samples were most frequently added to gastric sample sets for investigation of anaemia (Fig. 2b, c).

For comparison, we analysed the proportion of patients with oesophageal sampling in cases where there was an indication that would prompt biopsies, such as dysphagia (Fig. 3a) or Barrett's oesophagus (Fig. 3b). In

patients investigated for dysphagia, oesophageal biopsies were taken in 44.8% of the procedures. In 13.1% of patients with dysphagia, biopsies from both antrum and body were taken in addition to multi-level oesophageal samples. Of 472 patients with endoscopic Barrett's oesophagus, 150 (31.8%) underwent the OGD for endoscopic surveillance. However, data on this were incomplete (see discussion for further details). Oesophageal biopsies were taken in 71.6% of Barrett's patients compared to 10.5% in patients without this lesion ($p < 0.001$). In 31.4% of the patients with reflux symptoms, also gastric biopsies from multiple locations were taken.

Other Factors Influencing Biopsy Sampling Practice

Across the whole study population, age of subjects had no influence on the decision to take biopsies (57.9 vs. 58.1

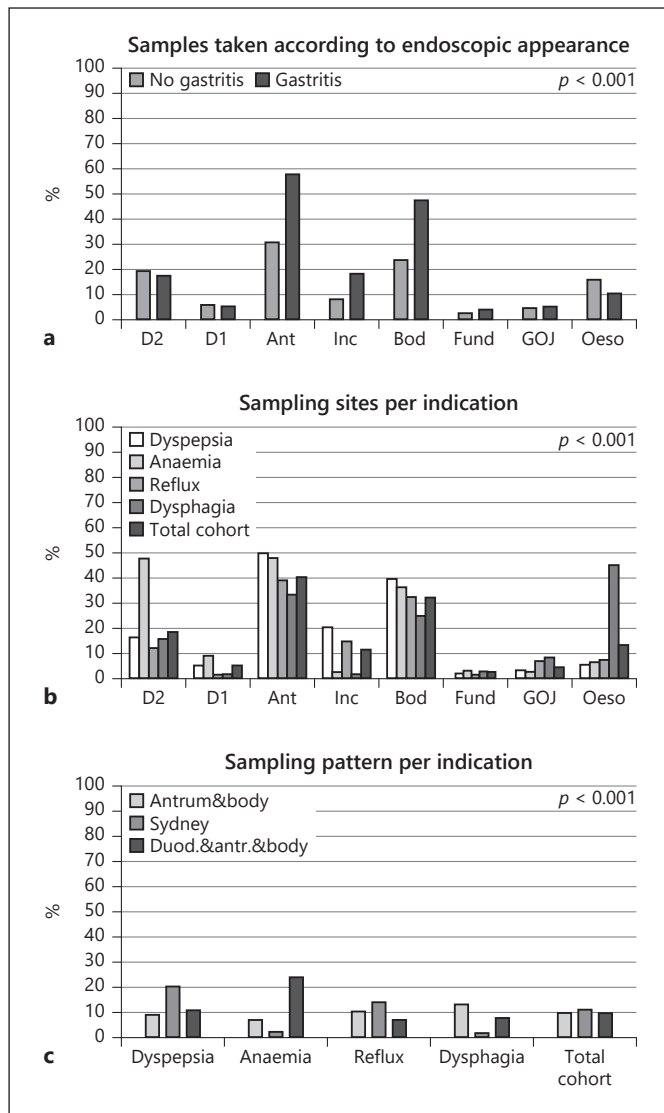


Fig. 2. Sampling pattern variation in procedures undertaken for different indication. **a** Comparison of the rate of samples taken from different locations in patients with and without endoscopic signs of gastritis as defined in the main text. **b** Proportion of biopsies taken from different sampling sites across the whole cohort according to the 4 main procedure indications. **c** Specific sampling patterns according to the 4 main procedure indications. Comparisons were done by χ^2 test across all centres as outlined in the methods section. Ant, gastric antrum; Bod, gastric body; D1, duodenal bulb; D2, second part of the duodenum; Fund, gastric fundus; GOJ, gastro-oesophageal junction; Inc, Incisura; Oeso, oesophagus.

years in patients with and without biopsies, respectively; $p = 0.537$). However, when each centre was assessed individually, biopsied patients were significantly younger in 7 centres and significantly older in 1 compared to patients

without sampling ($p < 0.05$; Fig. 4a). There was an unexpected positive association between costs and the likelihood of biopsies, so that more biopsies were taken in case of higher per procedure costs ($r = 0.709$, $p = 0.022$; Fig. 4b). In line with this, the cost per OGD itself showed a similar trend ($r = 0.600$, $p = 0.067$; data not shown).

The local practice of histopathology assessment and individual risk stratification had an influence on the sampling practice. In centres in which the updated Sydney system was routinely applied for histopathological assessment ($n = 6$), significantly fewer biopsies were taken (46.0%) compared to the 2 centres in which Sydney scoring was done only upon specific request by the endoscopist (75.3%) and the 2 centres in which histopathology grading was undertaken only “when feasible” in patients with marked changes (66.8%; $p < 0.001$; Fig. 5a). This was similar for centres which routinely applied the OLGA stratification when compared to centres where this was done “upon request” or “when feasible” (51.8 vs. 73.0 vs. 65.7%; $p < 0.001$; Fig. 5b). In the 2 centres in which OLGA was routinely established, sampling occurred at the same rate as in the 4 centres which did not apply OLGA at all (51.8 vs. 53.5%; Fig. 5b).

Sampling rates were significantly higher in the 7 centres which subjected their patients to endoscopic surveillance as suggested by the MAPS/MAPS II guidelines when compared to the 3 centres in which this was planned or just recently initiated (68.1 vs. 37.1%; $p < 0.001$; Fig. 5c). In centres already following the MAPS surveillance recommendation more often samples were taken from both antrum and body compared to centres in which this was not yet implemented (34 vs. 21%, $p < 0.001$).

Use of anticoagulants had no significant effect on the decision whether or not to take biopsies. A detailed analysis of the subcohort from Oxford showed that only 53 patients (1.8%) were on anticoagulant treatment which had not been stopped prior to the procedure, including 22 patients on warfarin and 31 patients on a novel oral anticoagulant. Platelet inhibition was given in 38 patients, with 30 patients being on clopidogrel, 12 on aspirin, and 4 on a combination of both. The rate of biopsy sampling was the same across all groups.

Discussion

This study delivers an overview on the current practice of gastric biopsy sampling in 10 European tertiary referral centres with a high degree of expertise in upper gastrointestinal disease. The aim was to assess adherence to na-

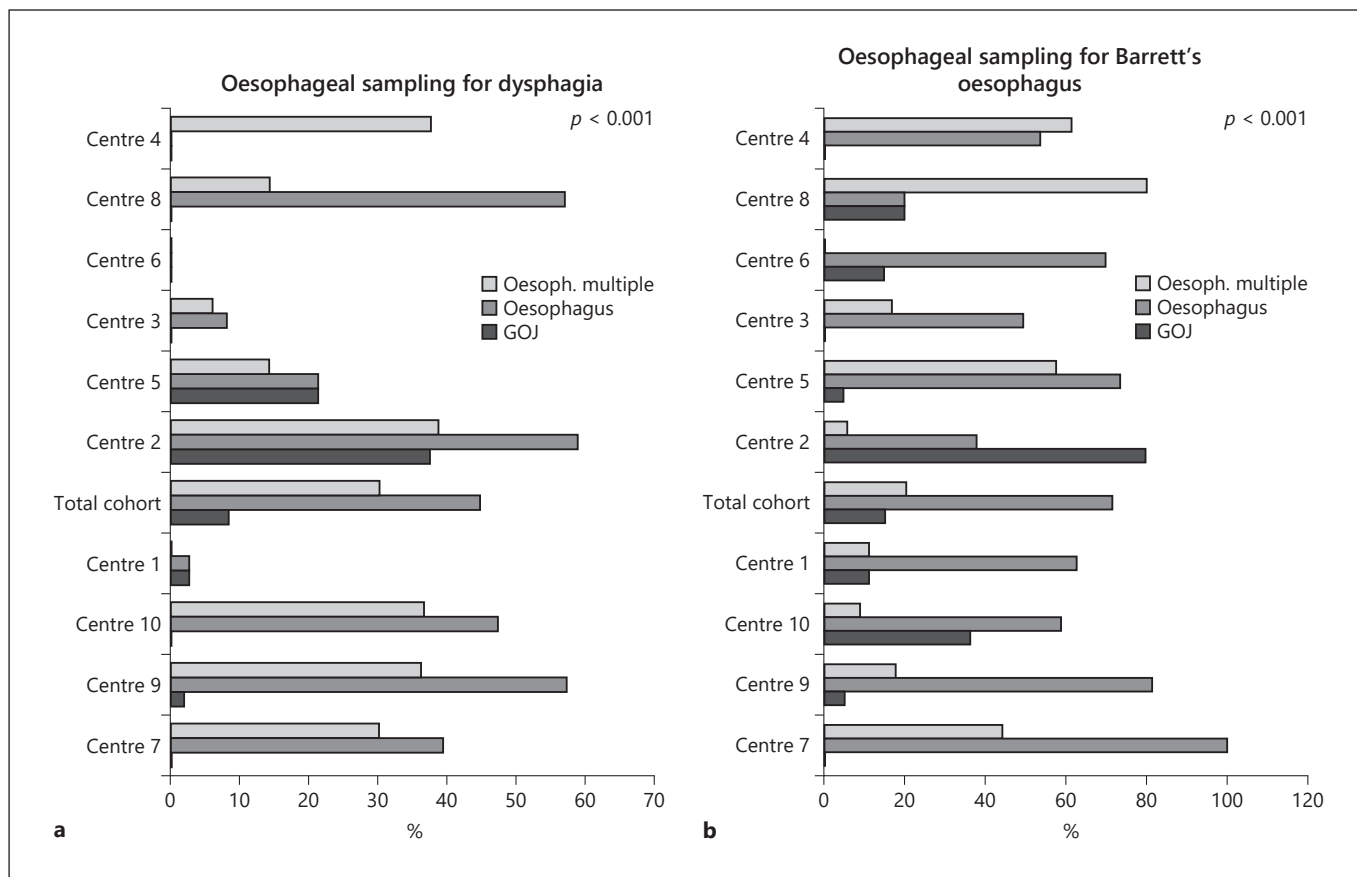


Fig. 3. Sampling of the oesophagus and the GOJ in patients with dysphagia or Barrett's oesophagus. **a** Sampling of GOJ and oesophagus (including multiple level sampling) in patients investigated for dysphagia. **b** Sampling of GOJ and oesophagus (including multiple level sampling) in patients with endoscopic signs of Barrett's

oesophagus. This included both patients under endoscopic surveillance and incidental cases. Comparisons were done by χ^2 test across all centres as outlined in the methods section. GOJ, gastro-oesophageal junction.

tional and international guidance and to emphasize the need for further training and education on this topic.

In our study, gastric biopsies were taken in only 60% of the patients in whom endoscopic signs of gastritis were reported (not including ulcers). Local experience in Oxford demonstrated that the rate of gastric biopsy sampling in these patients increased from 64 to 73% after a local audit undertaken prior to the study period followed by training seminars and instructive posters having been provided in endoscopy rooms. The outcome of a similar approach in Barcelona was more encouraging with a 25% increase in biopsy sampling [16]. However, the effect of training and education on the need for matching biopsies from gastric antrum and body was limited (only 4% increase) in Oxford. Both *H. pylori*-induced inflammation and reactive changes, due to bile reflux, often affect more the distal stomach which makes it likely that samples were

taken from areas with more marked erythema resulting in a higher rate of antrum samples. It is important to emphasize the need for matching body biopsies to enable complete assessment of gastric pathology [12].

The recent update of the European MAPS recommendations [12] and the inclusion of its key recommendations in the National guidelines of Germany [10] and the UK [9] put more weight on the need for an appropriate individual gastric cancer risk assessment, which aligns with recent US guidance [18]. In the current study, significantly more biopsies were taken in centres which already followed the MAPS/MAPS II surveillance recommendations. There is still debate on the most accurate risk stratification system [19]. In 2005, Rugge and Genta [20] proposed the OLGA system for staging of atrophic changes in antrum plus incisura, and body, with large, both retrospective and prospective studies supporting the feasi-

bility and clinical relevance of this staging stratification [21, 22]. Limitations are the interobserver variability of the pathologists scoring the mucosal changes and the need for the endoscopist to take the correct biopsies to avoid underscoring. The suggestions for overcoming the former problem was to replace the assessment of atrophy by IM only (OLGIM) [23], or combine application of OLGA plus OLGIM [24], but this has thus far found only limited acceptance.

In our study, a complete set of biopsies, as recommended by the Sydney system (including a sample from the incisura), was only taken in one out of 6 patients with endoscopic suggestion of gastric inflammation. This result is furthermore skewed by 1 centre where Sydney samples were taken in 84% of these patients, including a sample from the incisura which was reported to increase the yield for detecting preneoplastic conditions by 13% [25]. It is likely that economic factors, including time constraints during the procedures and additional costs for further biopsies, limit the willingness to obtain this additional sample with the opinions of pathologists and endoscopists slightly differing on this issue. It was a surprise that the ratio of procedures with biopsies was lower in centres in which Sydney scoring and OLGA stratification were routinely applied when compared to those in which this was not routine practice. Once again, costs might play a role here since the workload for pathologists increases substantially when these grading systems are routinely

applied. It is possible that endoscopists at the respective centres take this in consideration and sample only in the case of more marked changes. Since we did not grade the endoscopic appearance of the mucosal changes, we could not fully address these issues in our study. It is of note, that despite the inclusion of centres with great expertise in gastric pathology, national and local standards varied between centres and in most departments taking part in this study endoscopic scoring of atrophic changes was not part of the clinical routine. Therefore, we did not include this factor in the lists of data to record (similarly with intestinal metaplasia) since we wanted to capture the current routine at each centre rather than creating a study setting. Future studies should include this factor, in particular, since a recent study from Porto ignited again the discussion about the actual need for gastric biopsies when appropriate endoscopic scoring of the mucosal changes is performed [26].

We did not include the histopathology costs for additional biopsies since the variables that would need to be taken into consideration (e.g., additional staining methods, routine OLGA staging, etc.) were too diverse to allow a comparison between centres in this small study.

Our study has further limitations: we did not include data on PPI intake. Samples for diagnostic assessment of *H. pylori* infection are usually not taken in patients on PPI. Furthermore, since the focus of this study was inflammatory changes of the stomach, some standard indi-

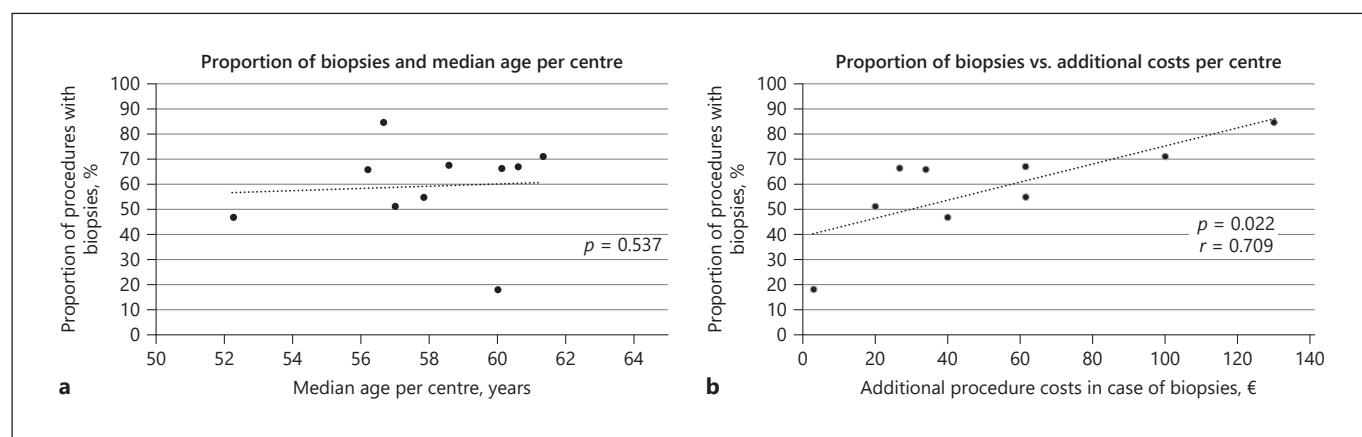


Fig. 4. Association of biopsy sampling with influencing factors. **a** Proportion of procedures with biopsies taken in relation to the patients' age in years as displayed on the *x* axis. No statistically significant association was found. **b** Relative proportion of procedures with biopsies taken per centre in relation to additional costs for biopsy sampling in € as displayed on the *x* axis. This did not include costs for pathology, but the fixed rate added to regular fees

in case any biopsies were taken. Interestingly, biopsies were taken significantly more often in centres where these extra costs were higher. There was a significant association with $r = 0.709$, $p = 0.022$. Spearman's rank correlation test was applied for statistical analysis. MAPS, European guidelines on the management of epithelial precancerous conditions and lesions in the stomach; OLGA, Operative Link for Gastritis Assessment.

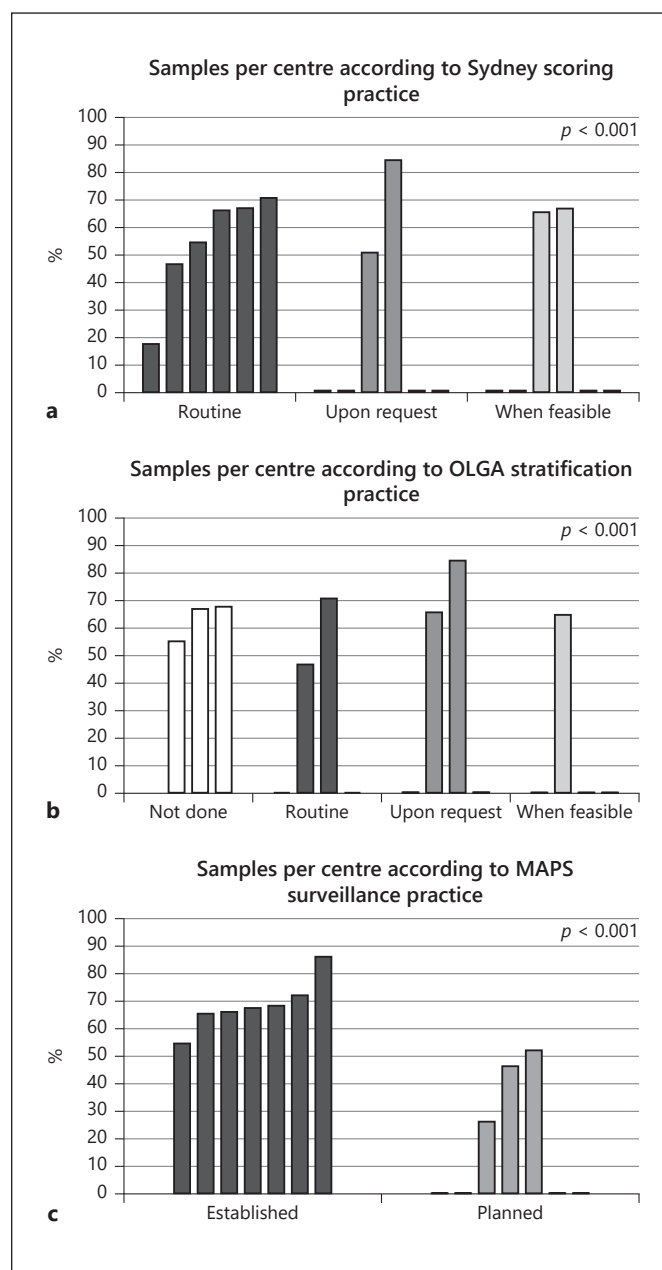
cations (e.g., coeliac screening) were not included and noted under “other.” When several indications were listed, we tried to stratify according to the lead indication (e.g., “dysphagia” had priority over “reflux”) which might have introduced some bias. We did not systematically exclude repeat procedures (i.e., possible inclusion of patients in whom biopsies have been taken already at a previous OGD). In Oxford, the rate of repeat procedures was about 6% and did not influence the statistical outcome of the final results.

Unfortunately, we did not collect complete data on the proportion of patients undergoing the procedure for endoscopic surveillance. This included not only the indications relevant for biopsy sampling such as surveillance of atrophic gastritis and Barrett’s oesophagus but also patients with portal hypertension and oesophageal varices. Although some centres provided some information on this issue, data are far from complete, as indicated by the fact that only 32% of the patients with Barrett’s oesophagus were marked as “surveillance” as well as only 54 patients, that is, 0.6% of the whole cohort with gastric atrophy under surveillance. However, we believe that the influence on the main analysis of this study is minor due to these rather small numbers (compared to the 3,393 patients with endoscopic signs of gastritis).

Although oesophageal pathology was not the focus of the study, we find it encouraging that oesophageal samples were taken in 45% of patients with dysphagia compared to 14% in the total cohort, and in 72% of patients with Barrett’s oesophagus compared to 11% without. Duodenal biopsies were taken in 49% of patients investigated

for anaemia compared to 17% in the total cohort. The data do not reflect the national practice for each country. It is of note that only in Germany and in the UK, evidence-based guidelines on gastritis assessment have been published [9, 10] and that other countries rely on international consensus recommendations [8, 12]. An additional bias may be introduced by the healthcare infrastructure within each respective national health care system. Some countries, such as Latvia or the UK offer open access endoscopy (by direct primary care referral without specialist gastroenterology review prior to the proce-

Fig. 5. Association of biopsy sampling with local clinical practice. **a** Relative proportion of procedures with biopsies taken according to local histopathology practice. Displayed are the ratios for centres which routinely score inflammatory changes routinely according to the updated Sydney protocol, those which score upon request by the endoscopist and those which score when feasible, that is, when marked changes are present. **b** Relative proportion of procedures with biopsies taken according to local histopathology practice. Displayed are the ratios for centres which routinely stratify patients according to the OLGA system, those which stratify upon request by the endoscopist, and those which give a staging when feasible, that is, when marked changes are present. Four centres do not apply OLGA at all. **c** Relative proportion of procedures with biopsies taken according to local clinical practice. Displayed are the values for centres in which surveillance regimens according to MAPS/MAPS II are fully established and for those who have planned to implement these. Comparison was done by χ^2 test as outlined in the methods section. MAPS, European guidelines on the management of epithelial precancerous conditions and lesions in the stomach; OLGA, Operative Link for Gastritis Assessment.



ture). This often results in referral of younger, more “healthy” patients often leading to stricter criteria as to when to take biopsies (e.g., only in patients above a certain age).

In conclusion, adherence to guideline recommendations for biopsy sampling during OGD seems to be poor even in academic centres across Europe. It has to be noted that only academic centres with high expertise in gastric pathology have been included in this study and that the data presented here cannot be directly extrapolated to conditions in community hospitals and specialist practices. A unified approach for a broader Europe-wide roll-out of quality control of gastritis assessment would help to address some of the limitations of the current study and to understand the factors influencing current practice. An automated online tool facilitating a uniform database for collection of quality indicators would be ideal but setting this up is hampered by different healthcare systems and a broad variation in endoscopy documentation systems. Until this is feasible, teaching and dedicated training, which were demonstrated to be effective [16], must be supported to raise further awareness of the need for accurate assessment of inflammatory and preneoplastic changes of the stomach.

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Statement of Ethics

The study was locally registered as audit ID:5398 at Oxford University Hospitals, NHS Foundation Trust. Local ethics approval was sought and confirmed at each participating centre as appropriate.

Conflict of Interest Statement

S.A., F.B., E.L.B.L., J.B., H.C., Z.D., M.F., G.F.E., G.L.H., J.K., A.L., M.L., I.L., T.M., L.M., R.N., S.A.V.N., A.O’C., S.R., H.D.S., A.S., M.C.W.S., I.T., T.T.N., T.U., and J.W. have no conflict of interest with regard to the data presented here.

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Author Contributions

J.B. designed the study and prepared the main draft of this manuscript. All authors contributed to the data collection and analysis. All authors contributed to editing and revision of this manuscript, including approval of the submitted version.

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