

## **EFSUMB Gastrointestinal Ultrasound (GIUS) Task Force Group: Celiac sprue and other rare gastrointestinal diseases ultrasound features**

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### **Abstract**

Transabdominal gastrointestinal ultrasound (GIUS) is unique in its capacity to examine the bowel non-invasively and in its physiological condition, including extra-intestinal features such as the splanchnic vessels, mesentery, omentum and lymph nodes- even at the bedside. Despite this, and its extensive documentation for its usefulness, it has only been fully implemented in a few European countries and expert centres. Therefore, the European Federation of Societies for Ultrasound in Medicine and Biology (EFSUMB) established a GIUS Task Force Group in 2014 consisting of international experts from 9 European countries with the objectives to standardize and promote the use of GIUS in a clinical setting. This is achieved by publishing clinical guidelines and recommendations on indications and use of GIUS and so far, 4 guidelines have been published: first on "examination techniques and normal findings", second on "inflammatory bowel disease", third on "acute appendicitis and diverticulitis" and fourth on "transrectal and perineal ultrasound".

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This paper describes the ultrasound features of miscellaneous disorders such as celiac disease, cystic fibrosis, omental infarction, Meckel's diverticle, endometriosis, intestinal neoplasia, mucocele, amyloidosis, GVHD, foreign bodies, vasculitis, and pneumatosis cystoides intestinalis. Bowel ultrasound can be indicated in most of these conditions to investigate intestinal symptoms but in other cases the alterations of the bowel can be also an incidental finding that suggest other examinations which finally help to discover an unknown pathological condition.

**Keywords:** guidelines; sprue; cystic fibrosis; foreign body; vasculitis; tumour; ultrasound; celiac disease; neoplasia; endometriosis

## Introduction

Transabdominal gastrointestinal ultrasound (GIUS) is the imaging method of choice for many indications [1-3], which is represented also in the guidelines [4-9]. The ultrasonographic examination allows a unique combination of focused medical history, clinical examination and imaging to make a diagnosis ("point of care ultrasound") [10-13]. The value of GIUS for diagnosis, differential diagnosis, and follow-up in celiac sprue and other rare and miscellaneous diseases of the gastrointestinal tract is much less known and largely dependent on the individual clinical experience of the examiner. The European Federation of Societies for Ultrasound in Medicine and Biology (EFSUMB) has published general guidelines and recommendations on gastrointestinal ultrasound [14], inflammatory bowel disease (IBD) [15], perianal

applications [16], appendicitis and diverticulitis [17] and other bowel emergencies [11,12,18], as well as functional GIUS [19].

Naturally, as many of these conditions are very rare, there is scarce scientific evidence for some of the diseases included, thus rendering many statements at the level of evidence comparable to expert opinion. Moreover, the chapters are illustrated by many ultrasound images to increase the clinical utility of the paper. The purpose of the paper is mainly focused on the description of rare gastrointestinal diseases. The statements and recommendations may be also helpful in our clinical work to optimize imaging and diagnosis.

The aim of this part of the EFSUMB GIUS guidelines is to describe the sonographic characteristics of and provide statements on celiac sprue and various other rare gastrointestinal diseases of miscellaneous etiologies.

## Objectives

Special knowledge:

- on the value of intestinal ultrasound for the diagnosis, differential diagnosis and follow-up of rare inflammatory and neoplastic diseases, not mentioned in the previous chapters of the EFSUMB GIUS recommendations and WFUMB position papers [11,12,14,15,17,20,21].
- regarding sonographic findings of conditions such as celiac disease, cystic fibrosis (mucoviscidosis), endometriosis, intestinal neoplasia of the small intestine [neuroendocrine neoplasia and gastrointestinal stromal tumours (GIST) and lymphoma of the intestine, amyloidosis, intestinal Graft versus Host Disease (GvHD)].
- of conditions that may result in localized symptoms such as epiploic appendagitis, segmental omental infarction, Meckel's diverticulitis, mucocele of the appendix and foreign bodies.

## Methodological structure and classification of the consensus levels

The work comprises the creation of the Task Force Group (TGF) of GIUS experts, the development of guidelines according to a modified Delphi method and all steps that have led to the statements regarding the definition criteria and landmarks of the US features of rare

intestinal diseases. All statements in this issue include an agreement/disagreement level that has been scored on a five-point Likert scale as follows:

A+: agree; A-: rather agree; I: indecisive; D-: rather disagree; D+: disagree.

## 1. Celiac disease

Celiac disease (celiac sprue) is a chronic autoimmune disease with changes in the intestinal tract, which can be partly visible on GIUS. A key learning point is that the examination must be performed under strict fasting conditions (*nil by mouth* >8 hours) and the motility of the small intestine should be recorded in each of the 4 quadrants for several minutes, with preferably a high-frequency probe. The combination of various nonspecific signs is characteristic for the disease [22-24]: 1) An increase in the distance and a flattening of the Kerckring's folds in the jejunum with a relative increase in the distal ileum; 2) Dilation of the affected small bowel loops >25 mm (first affected jejunal loops and later during the disease also ileum); 3) Kerckring's folds may be only barely visible; 4) Abnormal increase in fluid (only in a fasting state), with active peristalsis, that suddenly causes slow-moving luminal air and chyme to whirl quickly back and forth ("washing machine phenomenon") [22]. HIV enteropathy and autoimmune enteropathy have similar changes [2,3,25] Velvet-like thickening of small intestinal wall [26,27] Lymph nodes with a longitudinal diameter <17 mm [22,24,28-32]. An increase in size and number with significantly reduced irregular echogenicity, cavitation and grouped distribution, should raise the suspect of celiac disease-associated intestinal T-cell lymphoma [33] (fig 1).

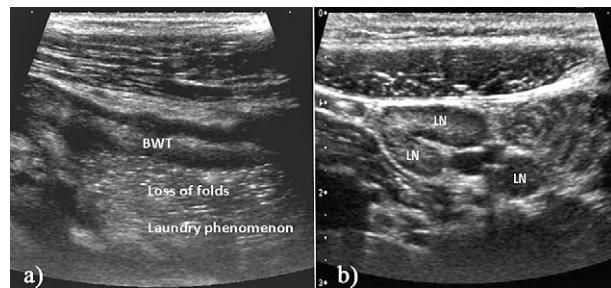
Sonographic accompanying signs of celiac disease are fatty liver, small spleen, enlarged gallbladder, often with sludge, asymptomatic intussusception, dilation of the superior mesenteric artery and reversibly increased (end-diastolic) flow of the superior mesenteric artery [34,35].

### ► STATEMENT 1

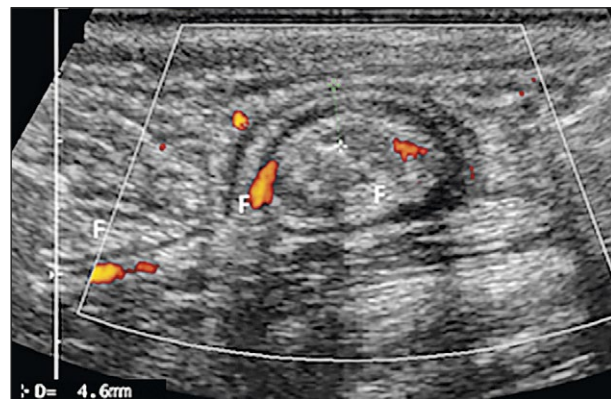
*Although each single sonographic sign of celiac disease is non-specific, their combination is characteristic for the disease. Consensus levels of agreement A+: 16/20; A-: 3/20; D+: 1/20*

## 2. Cystic fibrosis (CF) (mucoviscidosis)

Intestinal complications of CF in children and adults are constipation, dysbiosis, distal intestinal obstruction syndrome (DIOS) [36], intussusception and mucocele of the appendix. There is also an increased risk of gastrointestinal cancer [37] and sometimes stenosing colon fibrosis is described [25,38-44]. There is a thicker echo-rich intestinal wall, in comparison to healthy volunteers. Hy-



**Fig 1.** Celiac sprue. Bowel wall thickening (BWT) of the affected small bowel loops with loss of folds and laundry phenomenon is shown (a). Typically, more than 10 lymph nodes can be seen in the mesentery (b).



**Fig 2.** Cystic fibrosis. The thickened and non-vascular echo rich submucosa of the ileocecal region indicates fibrosis (F).

perchoic accentuation and thickening of the submucosa are the characteristic sonographic features. This thickening of the intestinal wall occurs preferentially in the cecum and is less pronounced in the ascending colon and terminal ileum [2,3] (fig 2).

DIOS is a unique condition in CF characterized by complete or incomplete obstruction of the ileocecal region, with viscous fecal material. It is more frequent in patients with pancreatic insufficiency, previous lung transplantation and a history of meconium ileus [36,45]. It presents with a brief history of abdominal pain and/or distention, a palpable mass in the right lower quadrant and in cases of complete obstruction, vomiting or imaging signs of distended small bowel [45].

Ultrasound may be a useful supplement for diagnosing DIOS [46]. Intussusception is a differential diagnosis for DIOS, easily identified using GIUS [47] as thickened wall bowel with hardened content believed to serve as a lead point. Asymptomatic intussusception is however also quite frequent in CF [42,48]. Appendicitis is less frequent in patients with CF than in the general population [49] and an appendicular diameter >6 mm, is found incidentally in more than half of the CF patients, with

mucooid content (“mucocele of the appendix”) that may be difficult to separate from the mucosa of the appendix without clinical signs of appendicitis [49-51]

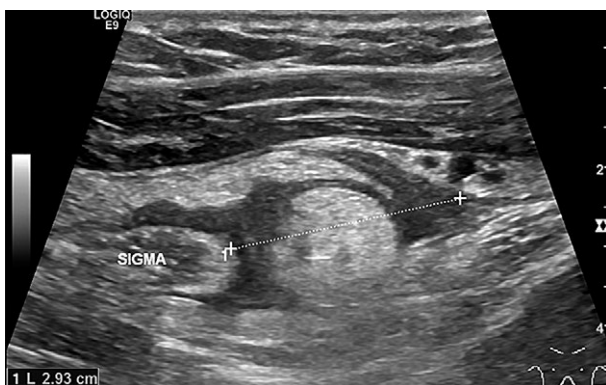
#### ► STATEMENT 2

*Intestinal obstruction syndrome characterized as viscous fecal material in a dilated small bowel, intussusception and mucocele of the appendix are characteristic sonographic features of cystic fibrosis. Consensus levels of agreement A+: 18/20; A-: 1/20; abstention: 1 (no personal experience)*

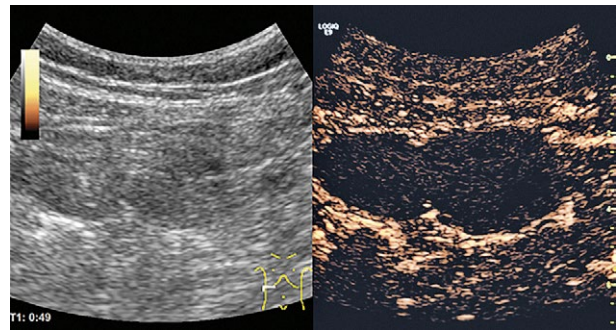
### 3. Epiploic appendagitis

The term “epiploic appendagitis” defines inflammation of the epiploic appendages, small peritoneal pouches containing small vessels and fat, which are more easily seen in the presence of intraperitoneal fluid. Primary and secondary epiploic appendagitis should be differentiated. Primary epiploic appendagitis can result from torsion with ischemia [52,53], or thrombosis in the absence of torsion. Secondary epiploic appendagitis may be adjacent inflammatory processes (diverticulitis, appendicitis, or cholecystitis) [54]. Most patients with primary epiploic appendagitis have non-specific localized acute abdominal pain and confined tenderness related to the colon, mimicking the symptoms of diverticulitis. It is a self-limited disease and under conservative treatment, symptoms in most patients completely resolve within 1-2 weeks.

The characteristic ultrasound finding is a hyperechoic, ovoid, solid, non-compressible mass, with a thin hypoechoic rim at the site of maximum tenderness, located



**Fig 3.** Epiploic appendagitis. Cross-section of the sigmoid colon (SIGMA) with attached hyperechoic fat and a hypoechoic rim (in between markers). This area showed localized tenderness to pressure from the US-probe and was fixed to the abdominal wall during deep respiration.



**Fig 4.** Large fat necrosis of the omentum majus in the right upper abdomen: hyperechoic oval tissue with local pain caudal of the liver. CEUS shows lack of vascularization in the center of the lesion. There is increased peripheral contrast enhancement. The diagnosis was confirmed by laparoscopy.

under the anterior abdominal wall and connected to the adjacent colon [52-54]. This mass can be also completely hypoechoic or contain central hypoechoic areas of hemorrhage and/or can be surrounded by altered, hyperechoic fat, due to inflammatory changes in adjacent tissue [53,55] (fig 3).

In most cases, the lesion is firmly attached to the anterior abdominal wall, a feature that can easily be visible on sonography during deep patient respiration. The neighboring colon is usually completely normal, although slight thickening of the intestinal wall is visible in about 10% of patients [52,54,55]. There are no color Doppler signals in the hyperechoic mass, but slight to moderate color signals can be seen around the ischemic lesion [54]. With CEUS, masses show a central unenhanced area and broad perilesional enhancement (>1 mm) [56,57].

#### ► STATEMENT 3

*Epiploic appendagitis is characterized by a painful at pressure, non-compressible, typically hyperechoic (sometimes hypoechoic) mass, adjacent to the colon and usually adherent to the parietal peritoneum. Consensus levels of agreement A+: 18/20; I: 1/20; D-: 1/20*

### 4. Segmental omental infarction

Segmental omental infarction has a pathophysiology similar to that of epiploic appendagitis, with the infarcted fatty tissue being part of the omentum. It can occur at any age and may be associated to congenital variations of the omentum or obesity, or more common to trauma, thrombosis, focus of inflammation, previous laparotomy (direct cutting of omental vessels during surgery), or tumor. There is higher frequency of right-sided torsion,

although a few cases of left-sided torsion have been described. Abscess formation has been described, especially in secondary cases to surgery [58]. US show hyperechoic, non-compressible, ovoid or a cake-like mass with central hypoechoic areas [55,59,60] (fig 4).

Sometimes, it is impossible to distinguish epiploic appendagitis from omental infarction on US (or CT) although both are managed conservatively [55]. CEUS shows lack of enhancement in the center of the lesion [2,3]. The key discriminator is to assess the origin of the vasculature to the mass.

#### ► STATEMENT 4

*Segmental omental infarction is characterized by a painful at pressure, typically hyperechoic (sometimes hypoechoic), non-compressible, ovoid or cake-like masses similar to epiploic appendagitis, although the size is larger, and central hypoechoic areas are more common. Consensus levels of agreement A+: 17/20; I: 1/20; D-: 1/20; D+: 1/20*

### 5. Meckel's diverticulum

Meckel's diverticulum (MD) occurs in 2% of the population within 100 cm oral of the ileocecal valve, on the antimesenteric side and is usually up to 6 cm in length [61]. Enterolith formation within MD is rare [62,63]. There are two types of presentation: bleeding in children under the age of 2 years, due to ectopic gastric mucosa [64] and intestinal obstruction and diverticulitis in adults [65,66]. Meckel's diverticulitis can present with the ultrasound appearances of a non-compressible tubular structure, with a blind end and concentric layers. Meckel's diverticulitis can be mistaken for appendicitis, if continuity with the caecum is not investigated [67]. The target sign of MD is typically greater than that found in appen-

dicitis. When obstructing enteroliths are present within the neck of the diverticulum, the ultrasound appearances may be of a rounded hypoechoic mass containing an air-fluid level surrounded by mesenteric inflammation in the periumbilical region similar to CT findings [68-73] (fig 5).

The diverticulum may perforate [74,75]. Enteroliths may spill out the diverticulum and cause small bowel obstruction [76], that also may occur from intussusception due to the inversion of the diverticulum [77]. If a MD is demonstrated, an assessment for an underlying tumor, such as a stromal tumor should be made [78-81]. A differential diagnosis for MD includes duplication cysts, where there will be no communication with the lumen. Peristalsis may be seen in both [82].

#### ► STATEMENT 5

*Meckel's diverticulitis sonographically presents as a non-compressible tubular or round structure, with a blind end and concentric layers. Consensus levels of agreement A+: 18/20; A-: 1/20; D-: 1/20*

### 6. Small bowel diverticula

Acquired jejunoileal diverticula (not Meckel's diverticulum) are less frequent (5%) than colonic or duodenal diverticula. They are usually asymptomatic, but sometimes they may cause symptomatic complications, including diverticulitis, perforation, or hemorrhage. Three-quarter of jejunoileal diverticula are localized in the jejunum [83]. Asymptomatic small bowel diverticula normally cannot be delineated from normal bowel loops by sonography. In cases of acute jejunoileal diverticulitis sonographic criteria are similar to those of acute colonic diverticulitis [17,84]: 1) Short segmental bowel-wall



**Fig 5.** Inflamed Meckel's diverticulum (arrows) with adjacent hyperechoic fatty tissue.



**Fig 6.** Inflamed diverticulum of the jejunum.

thickening (>5 mm); 2) diverticular outpouchings from the affected bowel wall; 3) surrounding hyperechoic tissue changes.

Peridiverticular abscesses may occur. Signs of sealed or free perforation should not be overlooked. Sometimes a large enterolith released from a small bowel diverticulum may cause gastrointestinal obstruction (fig 6).

The symptoms are non-specific and the localization of inflammatory changes of a small bowel diverticulum may be difficult [85]. Nevertheless jejunoileal diverticulitis should be kept in mind as a rare differential diagnosis in patient with acute abdominal pain [86,87].

#### ► STATEMENT 6

*Diverticulitis of acquired jejunoileal diverticula typically show short segmental bowel-wall thickening, diverticular outpouchings, and surrounding hyperechoic tissue changes. Consensus levels of agreement A+: 16/20; A-: 2/20; D+: 2/20*

## 7. Endometriosis

Endometriosis is a common condition, in which functional endometrial tissue is ectopically located outside the uterine cavity, most often involving the ovaries and more dependent portions of the pelvis. The intestinal tract represents the most common site of extragenital endometriosis, observed in 5-27 % of women with endometriosis. The rectum and the rectosigmoid junction, located near the retrocervical area, are the main sites of colorectal involvement (75-93% of cases of bowel endometriosis), followed by the sigmoid colon, terminal ileum, cecum and appendix [88-90]. The implants of endometriosis are typically visualized on US as irregular hypoechoic masses, with obtuse margins, attached to the intestinal wall, causing retraction of the intestinal seg-

ment, showing a characteristic C-shape due to the fibrotic convergence of the serosa [88,91] (fig 7).

The normal appearance of the proper muscle layer of the rectosigmoid colon is replaced with a nodule of abnormal tissue, having their greatest dimension longitudinally along the bowel wall [91]. Endorectal evaluation can detect rectal or rectosigmoid junction implants, that typically have a fusiform shape and can be spiculated at the ends or sides of the thickened area, resembling a comet [92]. In most cases, intestinal lesions are confined to the serosa or the thin hypoechoic proper muscle layer, and are always homogeneous and rarely contain cystic areas [93,94]. The overlying submucosa or mucosa are intact, unlike in primary carcinoma [93]. Internal vascularity on color Doppler can range from scarce to moderate [90,94].

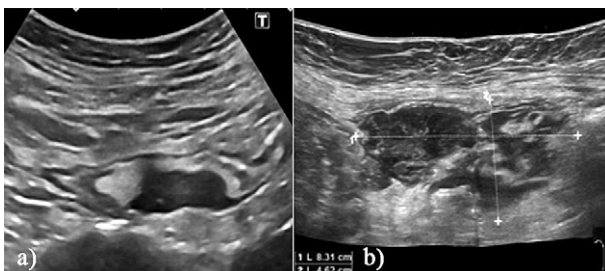
#### ► STATEMENT 7

*Intestinal endometriosis is characterized by asymmetric and irregular hypoechoic masses, attached to the intestinal wall, causing retraction of the intestinal segment, usually sparing the mucosa and submucosa. Consensus levels of agreement A+: 18/20; A-: 2/20*

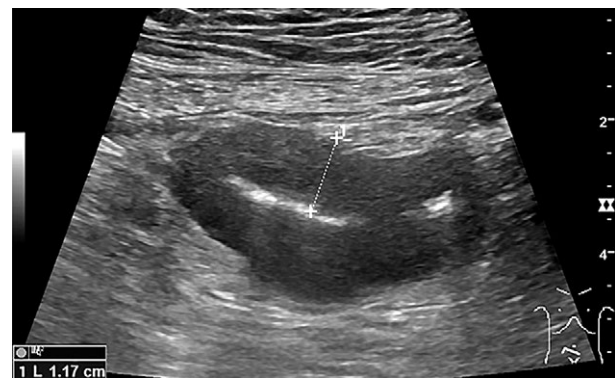
## 8. Intestinal neoplasia of the small intestine

### *Adenocarcinoma of the small intestine*

With approximately 2% of all gastrointestinal malignancies, adenocarcinoma of the small intestine is significantly rarer than colorectal and gastric cancer [33]. Adenocarcinoma is observed most often in the duodenum. GIUS may recognize it as hypoechoic segmental thickening of the bowel wall (pseudokidney sign or target lesion) or as a hypoechoic mass, with an irregular outline, often associated with (sub-) ileus symptoms [2,3] and liver metastases [21,95,96] (fig 8).



**Fig 7.** Endometriosis. The ultrasound image shows a longitudinal orientated sigmoid wall mass with extension to the deep muscle proper layer. Lenticular ends of the sigmoid nodule are noted, described as a comet sign (a). Endometriosis in the left lower abdomen, causing periodic pain (confirmed by laparoscopy) (b).



**Fig 8.** Adenocarcinoma of the small bowel with circular wall thickening and stenosis.

A similar appearance is observed in lymphoma of the small bowel, which are most often located in the ileum [33]. Underlying diseases are indicative for diagnosis [22,25,33]. Intestinal lymphomas (typically T-cell lymphoma) and carcinoma of the small intestine are the most serious complications of long-term adult celiac disease, which has not been treated properly.

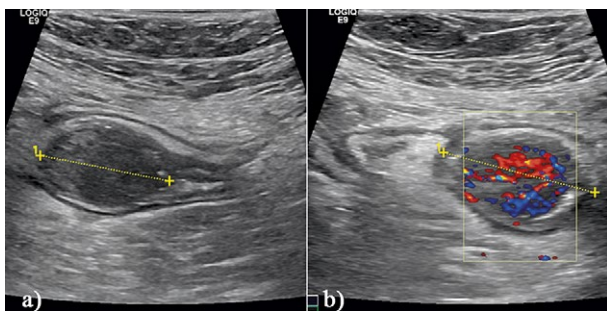
► **STATEMENT 8**

*Adenocarcinomas of the small intestine are characterized by hypoechoic segmental irregular thickening of the bowel wall (pseudokidney sign/target lesion). Consensus levels of agreement A+: 19/20; A-: 1/20*

**Neuroendocrine neoplasia**

Intestinal neuroendocrine tumours (I-NETs) are a heterogeneous group of neoplasms arising from the diffuse neuroendocrine system. Approximately 15–30% of I-NETs are functioning tumours with hormone-related syndromes, and 70–85% of I-NETs are non-functioning, and when small - most likely found incidentally [97]. The most common NET sites are the appendix (50%) and then the small intestine, primarily the ileum [98,99] (fig 9).

EUS provides crucial information on size, depth of invasion and loco-regional metastases of smaller I-NETs. EUS-guided FNA (fine needle aspiration) can also provide a definite diagnosis and useful information (i.e. Ki-67 evaluation) for the correct management of this type of lesion and select candidates for endoscopic resection [100]. At GIUS, I-NETs generally appear as nodular submucosal protuberances, hypoechoic, well-defined, predominantly intraluminal. There is sometimes a hyperechoic rim surrounding the lesions and internal calcifications [101-103]. The lesion can be a lead point for intussusception. Secondary changes in the mesentery, such as metastatic mesenteric adenopathy, intense desmoplastic reaction with rigidity and fixation of the small bowel loops, and kinking of small bowel loops suggest the



**Fig 9.** A NET in the terminal ileum (pT3) (a). Hypervascularisation on color Doppler (b).

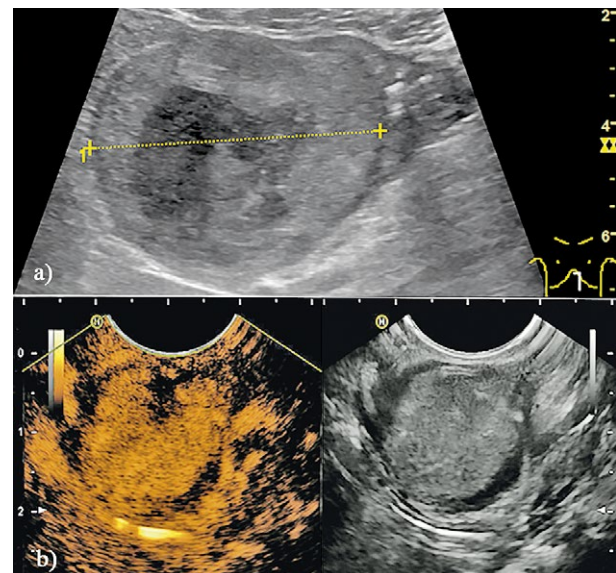
presence of small lesions concealed in the intestinal wall [104,105]. I-NETs and their metastatic lesions are hypervascular and therefore can be demonstrated with CEUS examination. Both primary tumours and metastasis show early and intense arterial enhancement (<20 sec), generally rim-like with well-defined margins, followed by a rapid wash out within 60 sec and a contrast defect in all lesions at the end of the venous and late phase [106,107].

► **STATEMENT 9**

*The ultrasound finding of intestinal NETs is most often a focal and well-defined hypoechoic intraluminal, mural or peri-intestinal round or oval hypervascular lesion, with arterial hyperenhancement on CEUS. Consensus levels of agreement A+: 19/20; A-: 1/20*

**Gastrointestinal stromal tumours (GIST)**

Gastrointestinal stromal tumours (GISTs) are mesenchymal lesions of the GI tract, most commonly found in the stomach. Diagnostic evaluation is based on imaging techniques, such as transabdominal GIUS, CT, MRI, PET, and endoscopic ultrasound. GISTs typically appear as hypoechoic intramural masses originating from the outer hypoechoic layer, with well-delineated margins and normal overlying mucosa [108]. Ultrasound features suggesting high malignant potential are large size and internal heterogeneity [109]. Doppler techniques may help to characterize GISTs versus other submucosal lesions [110]. Vessels observed inside GISTs are correlated with



**Fig 10.** Gastrointestinal stromal tumour (GIST) (a, in between markers). GISTs typically show hyperenhancement in the arterial phase on CEUS and necrotic areas (b).

a higher degree of angiogenesis, with a higher malignant potential [111,112]. Ultrasound guided FNAB has been performed transcutaneously [113], although usually by EUS [114,115]. GISTs are usually harder than other types of mesenchymal tumours. Elastography can be used to assess tumour stiffness to differentiate from other subepithelial lesions such as lipoma [116].

CEUS has been widely applied to characterize GISTs and evaluate response to therapy. Typically, GISTs exhibit an accelerated and uniform uptake in the arterial phase if <20 mm, while venous hypoenhancement is delayed [117] (fig 10).

In GISTs >20 mm typically non-enhancing areas can be identified [112]. CEUS shows hyperenhancement and avascular areas in a high percentage of GISTs, but not in leiomyoma, enabling discrimination between GIST and leiomyoma in most cases [112]. CEUS evaluation can also predict the malignancy risk of GISTs [112,118,119] and monitor the response of liver metastases during imatinib treatment [119-121].

#### ► STATEMENT 10

*Gastrointestinal stromal tumours (GISTs) typically are hypoechoic intramural masses with arterial hyperenhancement and non-enhancing areas. Consensus levels of agreement A+: 18/20; A-: 1/20; D-: 1/20*

#### Lymphoma

Segmental thickening of the intestinal wall, with loss of the intestinal wall layer structure is typically seen in intestinal lymphoma, usually with a close spatial relationship to pathological lymph nodes (enlarged, rounded or oval shaped, clearly hypoechoic) [22,25,33] (fig 11).

Burkitt lymphoma of the intestine may show a similar sonographic image, but the mass lesion is usually larger

[3]. The bowel wall thickening may be circumscribed and mass like or less often diffuse. Mesenterial lymphadenopathy is often found next to neoplastic infiltration (e.g. in intestinal lymphoma and as regional lymph node metastases also in carcinomas).

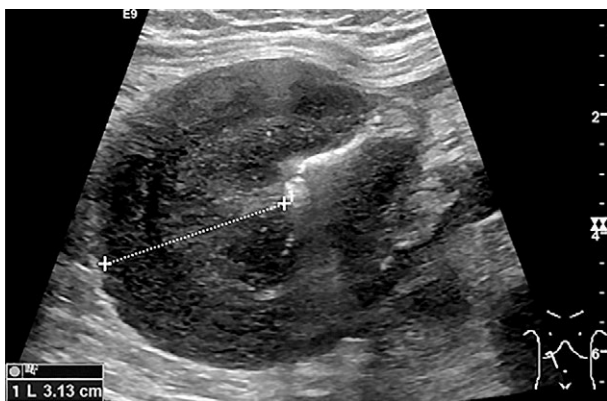
#### ► STATEMENT 11

*Bowel wall thickening in lymphoma is typically transmural, hypoechoic, with loss of wall layers, and with nearby mesenterial lymphadenopathy. Consensus levels of agreement A+: 18/20; A-: 2/20*

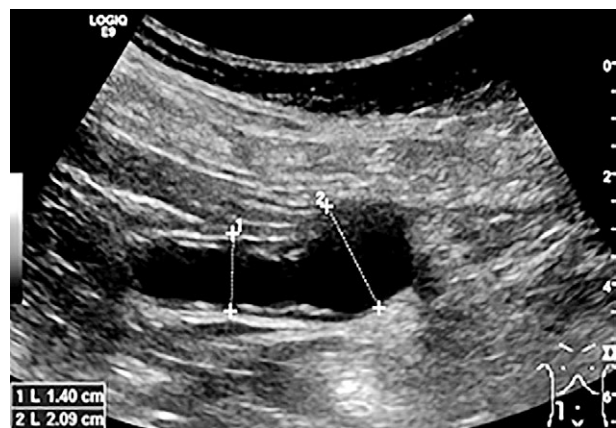
### 9. Mucocele

Appendiceal mucocele (AM) is a descriptive term that refers to a progressive dilatation of the appendix, from the intraluminal accumulation of mucin, secondary to obstruction of the appendiceal lumen. Causal pathologic conditions have been reported including cystic fibrosis, retention cyst, mucosal hyperplasia, cystadenoma, and cystadenocarcinoma. The incidence is 0.2-0.4% of all appendectomy specimens [122,123]. AM is usually an incidental finding, but can present with a variety of non-specific clinical symptoms, including lower right abdominal pain or a palpable abdominal mass. Differentiating between AM and acute appendicitis is crucial as a substantial percentage of AM patients present with symptoms indicative of acute appendicitis.

Typically US shows a distended fluid filled appendix, with variable internal echogenicity depending on the internal content and consistency (aqueous or gelatinous), which may be anechoic, hypoechoic or heterogeneous (onion skin sign) [123-126] (fig 12).



**Fig 11.** High-grade non-Hodgkin lymphoma of the small bowel causing pronounced thickening of the jejunal wall.



**Fig 12.** Mucocele of the appendix, in between markers.



The onion skin sign defined as echogenic layers or a layered appearance of the internal contents of the mass have been described as specific of AM [124]. Appendix diameter 15 mm or more in US examination has been determined as the threshold for AM diagnosis [122]. Smaller diameter may occur in initial stages. The greater the luminal diameter of the appendix the more likely an underlying neoplasm will be present. The wall of the lesion is hazy, slightly different from what one would expect for a cyst wall [123], and a layered structure can be seen. The presence of curvilinear or punctate non-luminal calcification strongly supports a diagnosis of AM. Wall irregularity and nodular contrast-enhancing lesions of the mucocoele may suggest malignancy [125]. The presence of ascites and peritoneal thickening suggests the intraperitoneal spread of neoplastic cells. Intraluminal gas bubbles or an air-fluid level within AM suggests the presence of infection, which needs to be differentiated from an appendicular abscess [127].

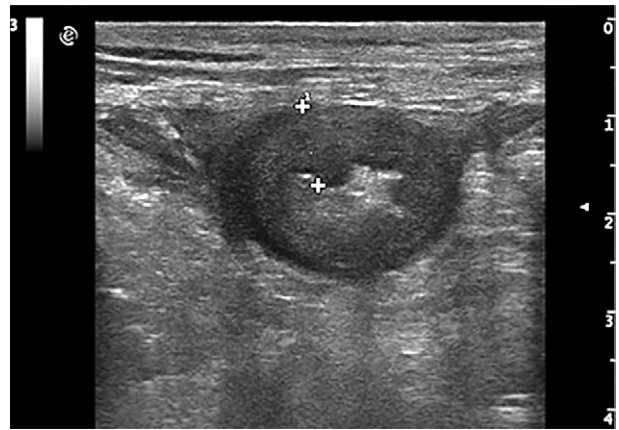
Spontaneous or iatrogenic perforation of the appendix produces *diffuse pseudomyxoma peritonei*, which is characterized by implants of mucinous epithelium on peritoneal surfaces and accumulation of mucus inside the peritoneal cavity [128]. It can present as ascites with multiple internal echoes that do not move, a difference of the ascites with blood, mucus or pus that also has echoes inside but with changes of its appearance with the different movements of the patient or the transducer [127]. Rupture can lead to intraperitoneal spread of neoplastic cells, resulting in mucinous ascites, with adhesions and intestinal obstruction. Ascites due to pseudomyxoma may present multiple septa, as well as scalloping of the hepatic and splenic margins. The diagnosis of appendiceal mucocoele should be considered in appendicitis managed conservatively, where any fluid is seen in the lumen of the appendix on follow up imaging.

#### ► STATEMENT 12

*The diagnosis of appendiceal mucocoele should be considered where there is luminal distension of the appendix, with variable internal echogenicity and a diameter of 15 mm or more. Consensus levels of agreement A+: 19/20; D-: 1/20*

## 10. Amyloidosis

Amyloidosis of the entire gastrointestinal tract usually occurs (80%) in systemic amyloidosis, to which it is in turn rarely associated (3%) [129,130]. The involvement of the small bowel is usually diffuse, throughout the bowel and characterized by infiltration of the entire



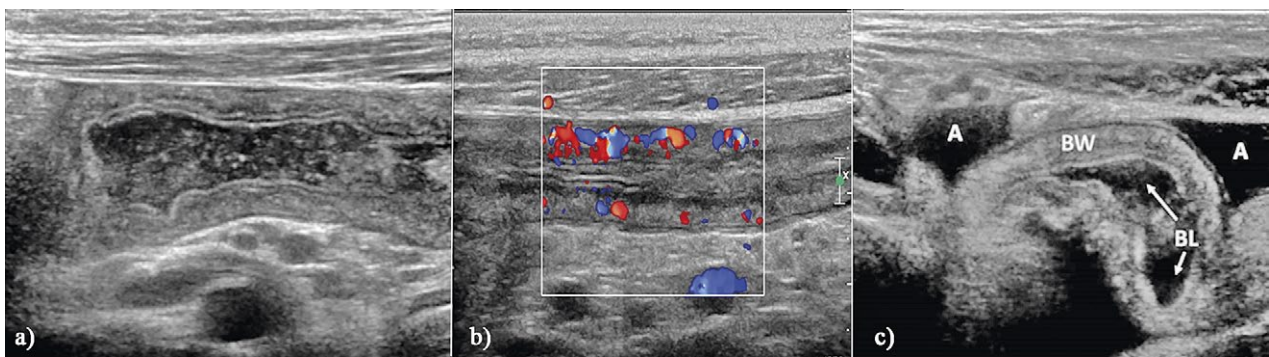
**Fig 13.** Amyloidosis. Ultrasound features of small bowel amyloidosis characterized by wall thickening with disrupted stratification. These findings are associated with decreased vascularity at color Doppler and enlarged mesenteric lymph nodes and mesenteric hypertrophy with dilated vascular structures.

intestinal wall. Clinical symptoms include recurrent pain, weight loss, bleeding, diarrhea as well as intestinal obstruction (ileus), malabsorption and infarction with possible perforation. Generalized edema with symmetrical wall thickening occurs in the end stage due to malabsorption and right heart insufficiency [2,3,25,130]. The sonographic features may be non-specific, and include both hyperechoic and hypoechoic thickening of the bowel wall, mainly of the mucosa with hypoechoic and nodular plicae, reduced peristalsis, bowel dilatation and mesenteric lymph node enlargement [131] (fig 13).

Amyloidosis of the small intestine is typically diffuse and shows slight and largely symmetrical wall thickening on ultrasound [130]. The thickened bowel wall is usually hypovascularized on color Doppler, and associated with dilated vascular structures within the mesentery. There may be focal dilatation of the small bowel alternating with wall thickening [132,133], resembling segmental involvement of Crohn's disease. In addition to the diffuse form, this short segment variant is referred to as "napkin-ring stenosis". There are case reports of focal amyloid deposits in the intestinal wall that appear as subepithelial tumours at colonoscopy and can be delimited endosonographically as submucosal hypoechoic foci.

#### ► STATEMENT 13

*Amyloidosis of the small intestine is typically diffuse and shows sonographically slight and symmetrical bowel wall thickening with reduced peristalsis and hypovascularity. Consensus levels of agreement A+: 17/20; A-: 1/20; abstention: 2 (no personal experience)*



**Fig 14.** Ileal wall thickening (BW) in a 28-year-old patient with IGVD (a), hypervascular (b), associated with fluid-filled bowel lumen (BL) and ascites (A) (c).

### 11. Intestinal graft versus host disease (GVHD)

GVHD is one of the main causes of therapy-related death, after allogeneic haemopoietic stem cell transplantation [134]. GVHD frequently involves both the upper and lower gastrointestinal tract [135-138]. Acute GVHD usually develops 3-5 weeks after transplantation, while chronic GVHD can develop following acute GVHD or it can arise several months after allogeneic stem cell transplantation [139,140]. Gastrointestinal involvement usually presents with high volume secretory diarrhea and abdominal pain, but may also manifest as nausea, vomiting and anorexia. Confirmation of the diagnosis is provided by endoscopic biopsy.

The main GIUS features of acute GVHD is the presence of diffuse or segmental bowel wall thickening mainly resulting from a thickened submucosa and so-called sloughing, i.e. casting off dead tissue (mucosa) [136], associated with dilated fluid-filled bowel loops (fig 14).

These signs in the specific clinical context demonstrated the diagnosis with a 94% sensitivity (95% CI 0.69-0.99), 95% specificity (95% CI 0.73-0.99), and 94.5% accuracy [141]. The ileocecal region is most frequently involved [142]. Color-Doppler evaluation includes the assessment of arterial perfusion of the bowel wall that is increased. A hyperdynamic mesenteric circulation with high peak systolic velocity (PSV) in the superior mesenteric artery (SMA) can be observed. Some patients may show the unique combination of a thickened bowel wall in conjunction with low PSV and high-resistance flow pattern in the SMA, without any diastolic perfusion associated with an ischemic ileocecal bowel wall. These findings seem to be related to a poorer response to therapy and prognosis [136].

CEUS usually shows an enhancement of the bowel wall during the arterial phase, followed by a prolonged venous phase due to the presence of interstitial oedema. In advanced stages, this feature can be lost for increased

fibrosis. This may also be observed in other inflammatory diseases [143]. A more specific CEUS sign reported in acute GVHD is the transmural penetration of microbubbles into the bowel lumen. This could be due to an increased permeability of the damaged gut mucosal barrier, in patients with GVHD [143-145].

#### ► STATEMENT 14

*The main ultrasound features of acute GVHD are the presence of diffuse or segmental bowel wall (submucosal) thickening and so-called “sloughing”, associated with dilated fluid-filled bowel loops. Consensus levels of agreement A+: 18/20; A-: 1/20; abstention: 1 (no personal experience)*

### 12. Foreign bodies

Ultrasound is not routinely performed in the management of ingested foreign bodies with guidelines more concerned about the indications for endoscopy to remove them [13,146]. Emergency endoscopy is indicated for esophageal obstruction, disk batteries or sharp pointed objects. Most foreign bodies pass through the GI tract within a few days [147], but objects longer than 6 cm are unlikely to pass the duodenum. Ultrasound may be more likely used to demonstrate foreign bodies which are not radio-opaque and not seen on other modalities such as CT. The most common of these are fish bones and toothpicks [148] appearing linear and hyperechoic with variable posterior acoustic shadowing. Even with CT scanning, accuracy in the detection of fish bones is dependent on the observer experience [149,150]. Secondary signs, as localized inflammation with thickened segment of the intestine, are often the leading features to detect the localisation of the foreign body [150].

For toothpicks, attenuation can vary with the amount of air and fluid in the wood, with absorption of fluids

increasing after a few days, making it more likely they are seen at CT. Toothpick injuries may mimic other diagnoses such as renal colic and Crohn's disease [151,152], but may also be seen in association with pathology causing strictures such as Crohn's disease itself. Toothpicks should be considered in the over 50's, patients with dentures, alcoholics and in patients with mental health conditions. Mortality is high if not diagnosed. They may erode and perforate any part of the GI tract, appendix and diverticula, into adjacent large blood vessels and major organs including the pleura and pericardium.

After some delay, (migrated) foreign bodies can be found by GIUS as linear structures in abscess formations with hypoechoic or mixed echogenicity.

#### ► STATEMENT 15

*The ultrasound appearance of foreign bodies such as fish bones and toothpicks appear linear and hyperechoic with variable posterior acoustic shadowing. Consensus levels of agreement A+: 18/20; A-: 2/20*

### 13. Other diseases

#### *Vasculitis*

Vasculitis are inflammatory disorders affecting both arteries and veins [153], presenting with systemic symptoms (e.g. fever, skin alterations such as palpable purpura and livedo reticularis, weight loss) and - in some instances - gastrointestinal manifestations. The main vasculitides affecting the gastrointestinal tract are Behcet's disease, Henoch-Schoenlein purpura, Kawasaki disease and polyarteritis nodosa.

These diseases have symptoms such as abdominal pain, diarrhea and/or constipation and blood in the stool



**Fig 15.** Ultrasound features of the bowel wall in Henoch-Schoenlein purpura. Longitudinal views of the bowel in a 10-year old male patient showing a slight thickening of the bowel wall, with a hypoechoic layer, internal to the submucosa (*asterisks*).

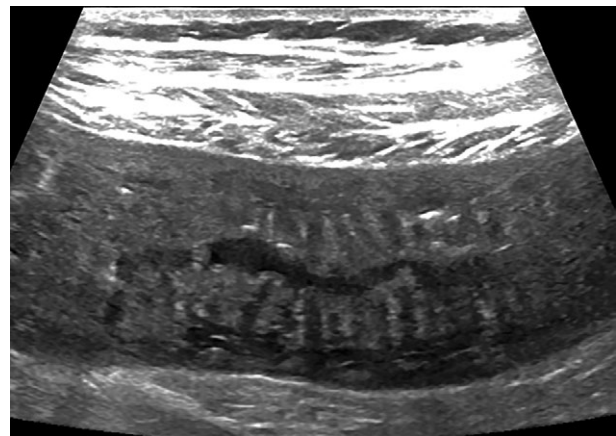
and also common sonographic features, such as bowel wall thickening, wall layers disruption and focal dilatation of the bowel. Specific sonographic features may be observed in some of these diseases. Henoch-Schoenlein purpura, may show as an extra-echoic layer internal to the submucosa as the result of the bleeding within the deep mucosa and submucosa and also may show bowel wall edema due to vasculitis of the supplying vessels [154] (fig 15). Kawasaki disease may be characterized by segmental thickening of the small-bowel wall, with loss or poor differentiation of the wall layers, and segmental intestinal dilatation, usually combined with hydrops of the gallbladder, due to the vasogenic edema [155, 156].

#### ► STATEMENT 16

*The main ultrasound features of vasculitis are segmental bowel wall thickening with prominent hypoechoic folds. Consensus levels of agreement A+: 16/20; A-: 3/20; D-: 1/20*

#### *Angioedema*

Abdominal angioedema can occur in patients with hereditary angioedema, an autosomal dominant deficiency of C1-esterase inhibitor, and recently more frequently as a complication of angiotensin-converting enzyme inhibitors therapy and other infrequent causes. This condition presents with acute abdominal pain mimicking a surgical emergency. Ultrasound features of this condition, in particular when GIUS is used as a bed-side point-of-care ultrasound, include segmental bowel wall thickening, with prominent hypoechoic folds, intestinal swelling - on the initial day of the episode of abdominal pain - and ascites (fig 16).



**Fig 16.** The main ultrasound feature of angioedema is segmental bowel wall thickening with prominent hypoechoic folds.

Edema regresses rapidly, whereas free peritoneal fluid may persist for at least 3 days. It is therefore important to perform the intestinal ultrasound in the acute phase, to demonstrate the intestinal edema, and to repeat GIUS examination to show its regression after symptomatic relief [157-160]. Various other acute diseases may present with a similar sonographic appearance and must be differentiated [19].

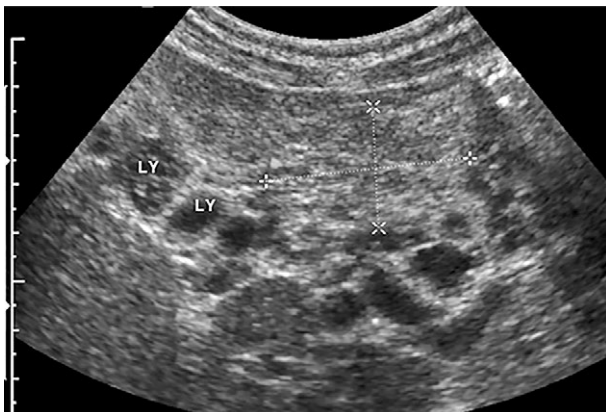
#### ► STATEMENT 17

*The main ultrasound feature of angioedema is segmental bowel wall thickening with prominent hypoechoic folds. Consensus levels of agreement A+: 19/20; D-: 1/20*

#### *Intestinal lymphangiectasia*

Intestinal lymphangiectasia can be classified as congenital or acquired forms. The resulting protein loss in patients can lead to a serious disease. Patients with the congenital form usually become symptomatic in childhood. Peripheral edema, intermittent abdominal pain, and signs of malabsorption with dominant steatorrhea occur. The dilated lymph vessels are primarily located in the small intestine including duodenum; a segmental location is possible (fig 17).

Sonographic features of intestinal lymphangiectasia can be a diffuse and regular thickening of bowel wall, dilated and fluid-filled bowel loops with well-defined or hypertrophic folds and maintained, although reduced, peristaltic activity. The mesentery may be hypertrophic or edematous with dilated lymphatic vessels. Enlarged lymph nodes are absent while thickening of the wall of the colon, gallbladder and urinary bladder may be present [161], together with ascites and pleural effusions.



**Fig 17.** Sonographic features of histologically proven duodenal lymphangiectasia are edematous folds and sometimes dilated lymphatic vessels (LY). The pancreatic head is shown in between markers.

#### ► STATEMENT 18

*Sonographic features of lymphangiectasia are edematous folds and sometimes dilated lymphatic vessels. Consensus levels of agreement A+: 15/20; A-: 4/20; abstention: 1 (no personal experience)*

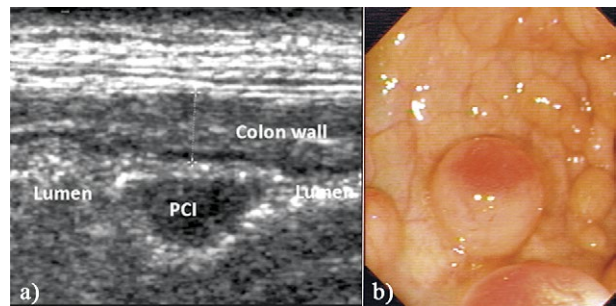
#### *Pneumatosis coli*

Pneumatosis coli (pneumatosis cystoides intestinalis) is a rare condition that may be associated with a variety of diseases [162]. The presenting clinical picture may be very heterogeneous. The majority of cases of pneumatosis coli are associated with a preexisting condition such as necrotizing enterocolitis in childhood, leukemia, lymphoma, chronic granulomatous disease, collagen vascular disease, congenital immunodeficiency states, bowel ischemia/inflammation/obstruction, pneumo-mediastinum, and hepatic, renal, and bone marrow transplants [163]. Pneumatosis coli is characterized by visible cysts particularly in the submucosa (fig 18).

The diagnosis of pneumatosis coli may be underestimated despite the fact that ultrasound is frequently required for the initial evaluation of patients with acute abdominal symptoms. The cystic cavities are filled with mucus and gas. Due to the often difficult differentiation between intraluminal and intramural gas and the susceptibility of ultrasound to artifacts, this clinical picture can only rarely be primarily detected on ultrasound [3,23]. The gas tends to diffuse into the portal vein, the peritoneal cavity or the systemic veins, rarely into the retroperitoneal space.

#### ► STATEMENT 19

*Pneumatosis coli intestinalis is characterized by visible mucinous and/or air cysts in the bowel wall. Consensus levels of agreement A+: 17/20; A-: 2/20; D+: 1/20*



**Fig 18.** Pneumatosis intestinalis coli (PIC, pneumatosis coli) is characterized by visible mucinous and/or air cysts (a). The cystic cavities in this case were filled with mucus. The endoscopic view before removal is also shown (b). The colon wall and lumen are also indicated.

In **conclusion**, GIUS is often the first and decisive imaging method in patients with clinical challenging diseases. Besides acute conditions, it is one of the most relevant and widely used imaging techniques for the follow-up of bowel diseases.

**Conflict of interest:** none with relevance to this paper.

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