Diagnostic Workup of Paediatric Patients With Inflammatory Bowel Disease in Europe: Results of a 5-Year Audit of the EUROKIDS Registry

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ABSTRACT

Objective: In 2005, the Inflammatory Bowel Disease (IBD) Working Group of the European Society for Pediatric Gastroenterology, Hepatology, and Nutrition published consensus guidelines on the diagnostic workup of paediatric IBD, the Porto criteria. According to these guidelines, children suspected of having IBD should undergo an oesophagogastroduodenoscopy (OGD), ileocolonoscopy, and (except in cases of definitive ulcerative colitis) adequate imaging of the small bowel. To audit and evaluate the diagnostic workup of paediatric patients with IBD in Europe, the Working Group created EUROKIDS, a prospective, Web-based registry of newly diagnosed paediatric patients with IBD.

Methods: Patients with IBD (ages 0–18 years) were registered in 44 centres in 18 countries. Data on diagnostic workup were analysed according to the year of diagnosis, type of IBD, and centre size. Diagnostic yield of OGD and ileal intubation were evaluated.

Results: Between 2004 and 2009, 2087 newly diagnosed patients were correctly registered. Both OGD and ileocolonoscopy had been performed in 64% of all of the patients and increased significantly from year 1 (52 %) to 5 (71%, $P < 0.001$). Small-bowel follow-through use decreased during the years (year 1 n = 213, year 5 n = 108; $P < 0.001$), whereas magnetic resonance imaging use increased (year 1 n = 25, year 5 n = 171; $P < 0.001$). Patients diagnosed as having Crohn disease (CD, 59%) and ulcerative colitis (58%) were more likely to have had a complete diagnostic workup than patients diagnosed as having IBD unclassified (45%). In CD, the diagnostic yield of OGD was 7.5% and the yield of ileal intubation was 13%.

Conclusions: The quality of diagnostic workup in paediatric patients with IBD increased steadily between 2004 and 2009. Small-bowel imaging by magnetic resonance imaging superseded the use of small-bowel follow-through. OGD and ileal intubation contributed to a definitive diagnosis of CD.

Key Words: diagnostic workup, diagnostic yield, inflammatory bowel disease, OGD, paediatrics

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Large-scale national epidemiology studies of inflammatory bowel disease (IBD) in children have documented a rising incidence of paediatric IBD (1–5) and have identified that certain features of IBD presenting in childhood are unique to children as compared with adults (6). The IBD Working Group of the European Society for Pediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN) recognised 10 years ago that at the time there were no agreed-upon criteria for diagnosing paediatric IBD. The Working Group agreed that collaboration on a multinational level was needed. To have consistent and reliable data, the essential first step was to ensure an optimal and uniform workup and use of agreed-upon criteria to diagnose IBD. The group then held a number of meetings in Porto, looked at the evidence, and in 2005 published the Porto diagnostic criteria, a consensus guideline for the diagnosis of IBD in children (7). It was agreed that diagnosis of Crohn disease (CD), ulcerative colitis (UC), and IBD-unclassified (IBD-U) should be based on clinical signs and symptoms, endoscopy with histology, and radiology. Every child suspected of IBD should undergo a complete diagnostic program consisting of colonoscopy with ileal intubation, oesophagogastroduodenoscopy (OGD), and in all cases, except in definitive UC, radiological contrast imaging of the small bowel. Additionally, multiple biopsies from all of the segments of the gastrointestinal (GI) tract are needed for a complete histological evaluation. It was also agreed that a diagnosis of IBD-U is acceptable only when the diagnostic program has been fully completed.

To audit the Porto criteria, the group started to prospectively collect anonymous data on new paediatric patients with IBD from May 2004, using an agreed-upon database (EUROKIDS Registry). The primary aim of the present study was to evaluate adherence to the Porto criteria in the first 5 years of the EUROKIDS registry (May 2004–April 2009). The secondary aim was to evaluate the diagnostic yield of OGD and ileal intubation during colonoscopy and the additional value of small-bowel imaging.

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METHODS

EUROKIDS Registry

The EUROKIDS registry is a prospective, Web-based registry of newly diagnosed paediatric patients with IBD in Europe and Israel, established by the IBD Working Group of ESPGHAN. This prospective registry was initiated in May 2004 by 20 paediatric centres in 11 European countries and Israel as a method to audit the diagnostic workup of paediatric patients with IBD in the years following publication of the Porto criteria (7), and to accurately describe disease phenotype in newly diagnosed paediatric patients with IBD. During the first 5 years, the registry has been extended to allow inclusion of patients from 44 centres in 18 countries: Belgium, Croatia, Czech Republic, Denmark, France, Germany, Greece, Hungary, Israel, Italy, Latvia, the Netherlands, Norway, Poland, Portugal, Slovenia, Sweden, and the United Kingdom.

The majority of participating hospitals provide tertiary care, with 6 centres providing both secondary and tertiary care. Several centres from Norway provide secondary care only. Five centres report that they treat only the most severe paediatric IBD cases.

Participating centres prospectively record data on every newly diagnosed child or adolescent (ages 0–18 years) with IBD. The main data are collected at diagnosis and are age at first symptoms and final diagnosis, sex, ethnicity, family history of IBD, type of IBD, presenting symptoms, and height and weight at diagnosis. All of the diagnostic procedures performed at and within 3 months of diagnosis are recorded, as well as disease extent and localisation (endoscopic, histological, and radiological aspect of each segment of the GI tract).

All of the patient data for the present study (inception cohort May 2004–April 2009) were accessed from the online registry on 24 February 2010. Exclusion criteria for the present study were age at diagnosis older than 18 years, type of IBD missing, data recorded retrospectively, IBD diagnosis date after April 2009, or incorrect IBD diagnosis date (ie, diagnosis date >1 month after registration date).

Ethics committee permission was obtained in the United Kingdom, Sweden, and Poland. In the other countries, a Statement of No Objection was released by the local ethics committees because data are anonymously collected.

Definitions

According to the Porto criteria, the workup in patients diagnosed as having CD and IBD-U was considered complete when OGD (with biopsies), colonoscopy with ileal intubation (with biopsies), and adequate imaging of the small bowel were performed (7). A colonoscopy was defined as a procedure reaching proximal to the splenic flexure. Imaging of the small bowel was considered adequate when one of the following modalities was used: conventional radiology (small bowel follow-through [SBFT], enteroclysis), magnetic resonance imaging (MRI, MR-enteroclysis, or MR-enterography), computed tomography (CT) scan, capsule endoscopy, and/or enteroscopy. In patients diagnosed as having UC, a complete workup was defined as performance of OGD and ileocolonoscopy (both with biopsies).

Centre size was determined by the number of newly diagnosed paediatric patients with IBD per year. A ''small centre'' was empirically defined as a hospital recruiting <15 newly diagnosed paediatric patients with IBD per year, a ''medium centre'' as a hospital recruiting 15 to 30 newly diagnosed paediatric patients with IBD per year, and a ''large centre'' as a hospital recruiting >30 newly diagnosed paediatric patients with IBD per year.

We defined the diagnostic yield of OGD and ileal intubation during colonoscopy as the percentage of patients in whom this procedure contributed to a definitive diagnosis of CD. The diagnostic yield of OGD in the evaluation of children suspected of having IBD was determined by the detection of granuloma(s) isolated to the upper GI tract in patients without perianal disease or clear ileocolonoscopic evidence of CD. Perianal disease was defined as the presence of perianal abscess(es) and/or fistula(s), whereas clear ileocolonoscopic evidence of CD consisted of isolated terminal ileitis or ileocaecal disease. Because information on granuloma(s) was not available in the first year of the registry, we determined the diagnostic yield of OGD in patients diagnosed from year 2 onwards, and only in cases that had biopsies from all of the segments of the GI tract. In patients diagnosed as having CD, we used both the isolated detection of granuloma(s) in the upper GI tract and the presence of macroscopic abnormalities in the upper GI tract for determining the diagnostic yield of OGD. Macroscopic abnormalities in the upper GI tract that were considered significant for the diagnosis of CD consisted of ulceration, cobblestoning, or stenosis.

The diagnostic yield of ileal intubation during colonoscopy was evaluated in all of the children registered in years 2 to 5 who had biopsies from the terminal ileum and all of the segments of the colon. The presence of isolated terminal ileitis (without perianal disease or granuloma(s) in the colon) and isolated granuloma(s) in the terminal ileum (without perianal disease or ileocolonoscopic evidence of CD) was used for determining the diagnostic yield. Alternatively, we also determined the disconcordance between the endoscopic and radiological aspect of the terminal ileum in patients who underwent both ileocolonoscopy and adequate imaging of the small bowel.

The additional value of adequate imaging of the small bowel was evaluated using 2 different definitions: abnormal aspect of the terminal ileum on small-bowel imaging in paediatric patients with IBD who had colonoscopy without ileal intubation, and normal aspect of the terminal ileum on endoscopy but an abnormal aspect of jejunum and/or proximal ileum on small bowel imaging in patients who had both ileocolonoscopy and adequate imaging of the small bowel.

Statistical Analysis

Data were analysed in SPSS (version 15.0, SPSS Inc, Chicago, IL). Descriptive statistics were calculated as percentages. For comparisons of proportions, we used the χ^2 test. All reported P values are 2-sided. $P < 0.05$ was considered significant.

RESULTS

As of 24 February 2010, 2606 newly diagnosed paediatric patients with IBD were registered. After excluding 519 patients, a study cohort of 2087 patients remained, of whom 59% were diagnosed as having CD, 9% as having IBD-U, and 32% as having UC (Fig. 1). The mean age at diagnosis was 12.1 years (range 0.6–17.9 years), with 56% being boys. Figure 2 shows the age distribution of the study cohort according to type of IBD.

A total of 424 patients (20%) were reported from small centres (n = 25), 1124 patients (54%) from medium centres (n = 16), and 539 patients (26%) from large centres (n = 3). The distribution of participating centres and patients throughout Europe and Israel is displayed in Table 1.

Endoscopy

OGD was performed in 87% (1811/2087) of all of the paediatric patients with IBD, colonoscopy in 96% (1995/2087), and ileocolonoscopy in 72% (1495/2087). Biopsies were taken in

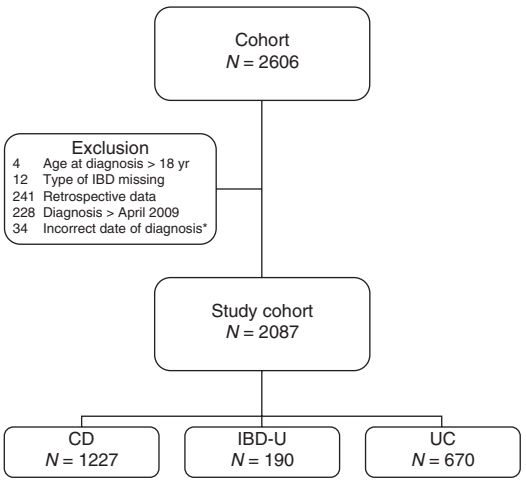

FIGURE 1. Flowchart of the study population in the EUROKIDS registry. ∗ Date of diagnosis >1 month after date of registration. CD = Crohn disease; IBD = inflammatory bowel disease; IBD-U = IBD-unclassified; UC = ulcerative colitis.

95% (1711/1811) of OGD, 98% (1964/1995) of colonoscopies, and 93% (1392/1495) of ileocolonoscopies. Three patients were diagnosed as having CD by surgery. Medical reasons for not inspecting the terminal ileum (ie, risk of perforation, presence of a stenosis, perforation, abnormal caecum with a pseudodiverticulum) were registered in 102 patients (5%). Other reasons were ''technical problem'' (n = 149, 7%), insufficient bowel preparation (n = 50, 2%), lack of time (n = 34, 2%), judged unnecessary by the endoscopist (n = 21, 1%), colonoscopy done elsewhere (n = 9, 0.4%),

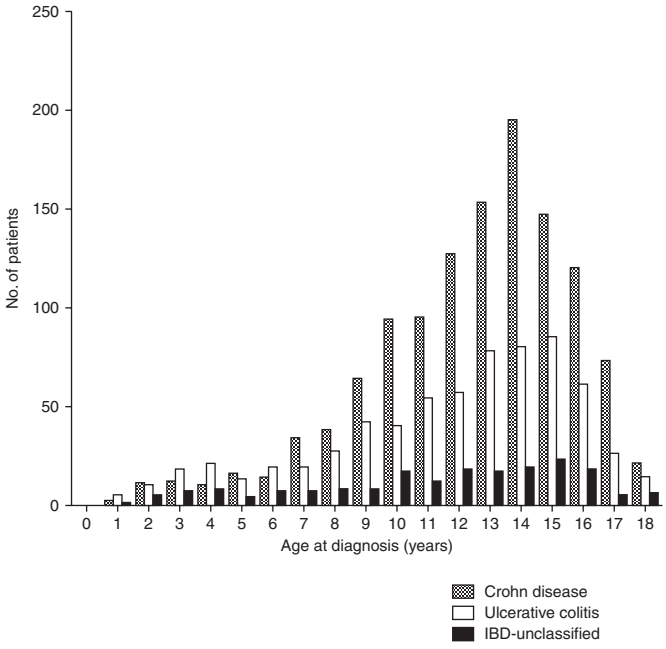

FIGURE 2. Age distribution of newly diagnosed paediatric patients with inflammatory bowel disease in the EUROKIDS registry.

TABLE 1. Participants in the EUROKIDS registry

Country	No. participating centres	No. patients
Belgium	2	17
Croatia	1	73
Czech Republic	2	108
Denmark	1	121
France	2	67
Germany	4	195
Greece	1	50
Hungary	1	40
Israel	2	90
Italy	4	181
Latvia	1	4
Netherlands	1	103
Norway	11	41
Poland	3	266
Portugal	1	39
Slovenia	1	33
Sweden	2	155
United Kingdom	4	504

insufficient sedation (n = 4, 0.2%), and biopsies taken in error at the caecum (n = 1, 0.05%). In the remaining patients (n = 219, 11%), it was not clear why the terminal ileum was not visualised by endoscopy.

Figure 3 shows the proportion of newly diagnosed paediatric patients with IBD who underwent OGD, colonoscopy, and ileocolonoscopy during the first 5 years of the registry. Between years 1 and 5, performance of OGDs ($P = 0.003$), colonoscopies ($P = 0.013$), and ileocolonoscopies ($P < 0.001$) increased significantly. A combination of OGD and ileocolonoscopy was performed in 64% of all of the paediatric patients with IBD, and increased significantly by 19% between years 1 and 5 ($P < 0.001$).

OGD was performed significantly more often in patients diagnosed as having CD than in patients diagnosed as having IBD-U and UC (Table 2). Patients diagnosed as having CD also underwent colonoscopy and ileocolonoscopy significantly more often than patients diagnosed as having UC. There were no significant differences in performance of endoscopic procedures between patients diagnosed as having UC and IBD-U.

Cases from large centres were more likely to have had OGD (96%) than those from small centres (85%, $P < 0.001$) or medium centres (83%, $P < 0.001$) but were less likely to have had ileocolonoscopy (58% vs 77% and 76%, both $P < 0.001$).

Imaging of the Small Bowel in Paediatric Patients Newly Diagnosed as Having CD and IBD-U

Information on imaging of the small bowel was available in 99% (1404/1417) of patients diagnosed as having CD and IBD-U. Adequate imaging of the small bowel was performed in 87% (1061/1216) of paediatric patients at or within 3 months of CD diagnosis: SBFT in 58% (n = 707), MRI in 29% (n = 355), CT abdomen in 7% (n = 80), capsule endoscopy in 4% (n = 52), and enteroscopy in 0.4% of patients (n = 5). The small bowel was visualised by >1 imaging technique in 10% (125/1216) of patients diagnosed as

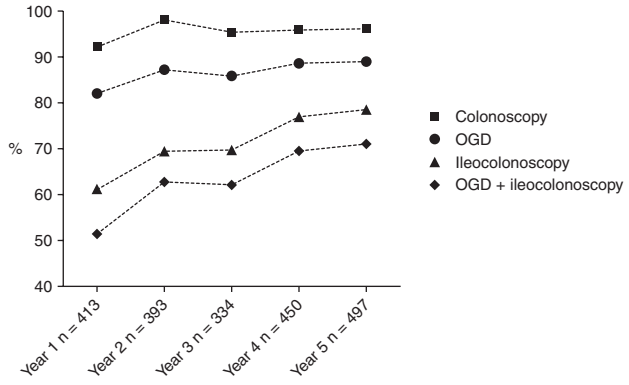

FIGURE 3. Endoscopic procedures in paediatric patients with inflammatory bowel disease during the first 5 years of the EUROKIDS registry. OGD = oesophagogastroduodenoscopy.

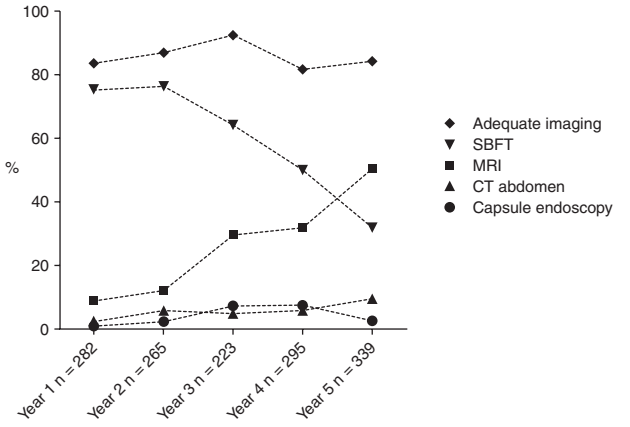

FIGURE 4. Small bowel imaging in paediatric patients diagnosed with Crohn disease and IBD-unclassified during the first 5 years of the EUROKIDS registry. CT = computed tomography; MRI = magnetic resonance imaging; SBFT = small bowel follow-through.

having CD. In patients diagnosed as having IBD-U, adequate radiology was performed in 73% (138/188), which was significantly lower than in patients diagnosed as having CD ($P < 0.001$). Fifty-six percent of patients diagnosed as having IBD-U underwent SBFT (n = 106), 18% MRI (n = 33), 2% CT abdomen (n = 3), and 3% capsule endoscopy (n = 5). In 4% (7/188) of patients diagnosed as having IBD-U, >1 imaging technique was used to visualise the small bowel. Radiological examination by abdominal ultrasound alone was performed in 6% of patients diagnosed as having CD (n = 69) and 11% of patients diagnosed as having IBD-U (n = 21, $P = 0.009$).

Variation in small-bowel imaging of patients diagnosed as having CD and IBD-U is displayed in Figure 4. Use of small-bowel imaging increased significantly from 84% in year 1 to 92% in year 3 ($P = 0.004$) but decreased significantly to 81% in year 4 ($P < 0.001$) and returned to 84% again in year 5. Between years 1 and 5, use of SBFT decreased significantly by 44% ($P < 0.001$), whereas use of MRI and CT abdomen increased significantly by 42% and 7% (both $P < 0.001$). Use of capsule endoscopy increased significantly during the first 4 years (year 1: 1%; year 4: 8%; $P < 0.001$), but decreased significantly in the last year (3%; $P = 0.003$).

When examined by centre size, significant variations in use of small bowel imaging were observed. Patients diagnosed as having CD and IBD-U in large centres were more likely to have had SBFT (82%) than those in small centres (43%, $P < 0.001$) or medium centres (51%, $P < 0.001$) but were less likely to have had MRI (10% vs 35% and 34%, $P < 0.001$), CT abdomen (3% vs 10% and 6%, $P < 0.001$), or capsule endoscopy (1% vs 5% and 6%, $P = 0.001$).

Complete Diagnostic Workup According to the Porto Criteria

In total, 57% (1191/2083) of paediatric patients with IBD had a diagnostic workup according to the full Porto criteria. A combination of OGD, ileocolonoscopy, and adequate imaging of the small bowel was performed in 59% (715/1223) of patients diagnosed as having CD and 45% (86/190) of patients diagnosed as having IBD-U ($P = 0.001$). In the patients with a complete diagnostic workup, biopsies from the upper GI tract and from the colon and terminal ileum were taken in 89% (634/715) of patients diagnosed as having CD and 88% (76/86) of patients diagnosed as having IBD-U. If less strict criteria were used (OGD, colonoscopy, and either ileocolonoscopy or adequate imaging of the small bowel), 87% (1061/1223) of patients diagnosed as having CD and 75% (143/190) of patients diagnosed as having IBD-U had this combination of diagnostic procedures. In patients diagnosed as having UC, 58% (390/670) underwent a combination of OGD and ileocolonoscopy. In the patients with a complete workup, biopsies of all of the segments were taken in 87% (338/390).

Adherence to the full Porto criteria increased significantly from 45% in year 1 to 64% in year 5 ($P < 0.001$). When examined by type of IBD, there was a significant time trend in adherence to the full Porto criteria for patients diagnosed as having CD (year 1: 49%; year 5: 64%, $P < 0.001$) and patients diagnosed as having UC (year 1: 41%; year 5: 68%, $P < 0.001$), but not for patients diagnosed as having IBD-U (year 1: 33%; year 5: 44%, $P = 0.35$).

TABLE 2. Endoscopic procedures in paediatric patients with IBD according to type of IBD

	All (n = 2087)	CD (n = 1227)	IBD-U (n = 190)	UC (n = 670)
OGD (%)	1811 (87)	1115 (91)*	161 (85)	535 (80)
Colonoscopy (%)	1995 (96)	1184 (97)**	181 (95)	630 (94)
Ileocolonoscopy (%)	1495 (72)	905 (74)**	129 (68)	461 (69)
OGD + ileocolonoscopy (%)	1333 (64)	831 (68)*	112 (59)	390 (58)

CD = Crohn disease; IBD = inflammatory bowel disease; IBD-U = IBD-unclassified; OGD = oesophagogastroduodenoscopy; UC = ulcerative colitis.
* Significant difference compared with UC ($P < 0.001$) and IBD-U ($P < 0.03$).
** Significant difference compared with UC ($P < 0.03$).

Patients with IBD from large centres were less likely to have had a complete diagnostic workup (51%) than patients from small centres (59%, $P = 0.013$) or medium centres (60%, $P = 0.001$).

Diagnostic Yield of OGD, Ileal Intubation, and Additional Value of Small Bowel Imaging

In years 2 to 5 of EUROKIDS, there were 740 paediatric patients with IBD with biopsies from all of the segments of the GI tract. OGD with biopsies led to the isolated detection of granuloma(s) in the upper GI tract (without detection of granuloma[s] in ileocolonic biopsies) in 2.4% (18/740) of paediatric patients with IBD. Five of these patients also had perianal disease or clear ileocolonoscopic evidence of CD (isolated terminal ileitis, ileocaecal disease), which decreased the diagnostic yield slightly to 1.8% (13/740). During colonoscopy, 6 of these 13 patients were also found to have inflammation of the colon, whereas 5 patients had inflammation of both the colon and terminal ileum. The remaining 2 patients had small bowel involvement and upper GI involvement, respectively. In CD, 428 patients had biopsies from all of the segments of the GI tract in years 2 to 5. The frequency of patients diagnosed as having CD whose diagnosis relied on isolated detection of granuloma(s) at OGD was 3.0% (13/428). In addition, there were 19 patients diagnosed as having CD who had ulcerations in the upper GI tract (without perianal disease, ileocolonoscopic evidence of CD, or detection of granuloma[s] in the GI tract). Cobblestoning or stenosis without the other characteristics of CD did not occur. In 10 patients, the type of macroscopic abnormality was missing. When including only the patients with isolated granuloma(s) or ulcerations in the upper GI tract, the total diagnostic yield of OGD was 7.5% (13+19/428).

The diagnostic yield of ileal intubation could be determined in 962 patients with IBD in years 2 to 5 who had biopsies from all of the segments of the colon and the terminal ileum. Fifty-six patients (5.8%) had isolated terminal ileitis without perianal disease or granuloma(s) in the colon. In addition, 19 patients (2.0%) had isolated granuloma(s) in the terminal ileum without the other characteristics of CD (ie, perianal disease or ileocolonoscopic evidence of CD), resulting in a diagnostic yield of 7.8% (75/962). In CD, 559 patients in years 2 to 5 had biopsies from all of the segments of the colon and the terminal ileum. The frequency of patients diagnosed as having CD whose diagnosis relied on ileocolonoscopy (ie, isolated detection of granuloma[s] in the terminal ileum or isolated terminal ileitis) was 13% (75/559). Information on both the endoscopic and radiological aspects of the terminal ileum was available in 875 paediatric patients with IBD. In 152 (17%) patients, the terminal ileum was considered abnormal on endoscopy but normal on adequate small bowel imaging. The opposite combination, a normal endoscopic appearance of the terminal ileum in combination with an abnormal terminal ileum on adequate small bowel imaging, occurred in 58 (7%) patients.

There were 418 paediatric patients with IBD who underwent colonoscopy without ileal intubation but with adequate imaging of the small bowel. The terminal ileum was abnormal in 170 patients (41%) and normal in 194 patients (46%), and data were missing in 54 patients (13%). In 829 paediatric patients with IBD, information was available on the aspect of the terminal ileum by ileocolonoscopy, as well as on the aspect of jejunum and proximal ileum by adequate small bowel imaging. Fifty-one patients (6.2%) had a normal terminal ileum on endoscopy and an abnormal jejunum and/or proximal ileum on small bowel imaging.

DISCUSSION

The Porto criteria recommend a uniform diagnostic workup in children and adolescents suspected of having IBD to reliably classify disease type, extent, and localisation (7). From this workup, disease can be classified according to the Montreal classification (8) or even the more recently published Paris classification (9). In the present study, the IBD Working Group of ESPGHAN has performed an audit to evaluate diagnostic performance in children suspected of having IBD and to analyse the usefulness of a consensus-based guideline during a 5-year period. For this purpose, a Web-based prospective registry, EUROKIDS, was initiated in 2004. Although it is generally known that the incidence of IBD increases with age, the peak incidence occurred at around 14 to 15 years of age in our European cohort. This reflects daily practice, in which adolescents are often diagnosed by ''adult'' gastroenterologists. One of the most interesting results of our study was the clear increase in quality of diagnostic workup during the first 5 years of EUROKIDS.

The acceptance in Europe of performing an OGD during the first diagnostic workup of a paediatric patient with IBD was high, starting with 82% in year 1 and reaching almost 90% in year 5. In UC and IBD-U, the number of OGDs was significantly lower than in CD but still between 80% and 90%. The routine use of OGD at diagnosis is not recommended in all of the guidelines on paediatric IBD. According to the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition, OGD with biopsies should be ''considered'' in children suspected of having IBD, but more research on the diagnostic value of OGD is mandatory (10). In our study, we evaluated the diagnostic yield of OGD, based on both endoscopic and histological criteria, while also taking into account the endoscopic and histological findings from ileocolonoscopy. Mild, nonspecific mucosal changes (eg, erythema, erosions, aphtae) in the upper GI tract are common in both CD and UC.

Because ulcerations, cobblestoning, and stenosis are rarely seen in UC (9), we used only these specific abnormalities for determining the diagnostic yield of OGD. This yield was 7.5%, indicating that OGD contributed to a diagnosis of CD in 1 of 13 paediatric patients diagnosed as having CD. Previous studies on the diagnostic role of OGD have focused primarily on the isolated detection of granulomas in the upper GI tract. The results of these studies were summarised in 2009: the frequency of paediatric patients diagnosed as having CD whose diagnosis relied on isolated detection of granulomas at OGD seemed to range between 2% and 21% (11). This large range of granuloma detection may vary with number and site of biopsies, as well as the quality of histological workup in the pathology laboratory. We have no data concerning the number of biopsies taken in our patients, other than the guideline advice to take 2 or more biopsies from each segment. Using another definition for diagnostic yield of OGD, Lemberg et al (12) reported that endoscopic and histological assessment of the upper GI tract established a diagnosis of CD in 13 of 38 patients (34%) with otherwise nonspecific pancolitis. Taken together, all of these results indicate that OGD contributed to a diagnosis of CD in a substantial number of patients, justifying its use in the initial assessment of children suspected of having IBD. Besides the diagnostic implications of OGD, knowledge about involvement of the oesophagus, stomach, and duodenum may have therapeutic consequences. For example, it has been shown that in paediatric patients with oesophageal CD, disease course has a high probability for early need of azathioprine (13).

In addition to the increasing numbers of OGDs, the success rate of ileal intubation increased steadily from 61% in year 1 to 79% in year 5. This significant increase may be the result of the process of continued registration within the EUROKIDS study group. An even more dramatic improvement in success rate of ileal intubation was reported in a study from 2002. Batres et al (14) analysed paediatric colonoscopies from 1994 through 2000 and found an increase in ileal intubation from 22% between 1994 and

1996 to 66% in 2000. Possible explanations for this improvement were the technical developments of endoscopes, video images, and screens in the 1990s, as well as growing experience and skills of paediatric endoscopists.

The terminal ileum was not visualised by endoscopy in 28% of the patients with IBD. Medical reasons (eg, risk of perforation, presence of a stenosis) were responsible for examinations terminated outside the terminal ileum in at least 5% of all of the procedures. The adult IBD literature has reported ileal intubation rates of 95% of all colonoscopies (15), which also emphasises that in approximately 95% of all patients, the terminal ileum should be possible to reach. Technical problems should be overcome by teaching and training, whereas lack of time, insufficient colon preparation, and insufficient sedation can be avoided by optimising protocols for bowel preparation and the timing of procedures.

Ileal intubation with ileal biopsies has been shown to increase the diagnostic yield of CD in adult patients presenting with symptoms of IBD (16). In our dataset, the diagnostic yield of ileal intubation in patients diagnosed as having CD was 13%. Ileal intubation can also contribute to a diagnosis of CD in patients with nonspecific pancolitis who have distinct macroscopic lesions in the terminal ileum, such as cobblestoning and linear ulcerations. This information was not registered in our database. The role of ileal intubation was also highlighted by de Matos et al (17), who found isolated granulomas in the terminal ileum in 26 of 112 (23%) untreated paediatric patients diagnosed as having CD.

A combination of OGD and ileocolonoscopy was performed in 64% of all patients with IBD and in even fewer patients diagnosed as having IBD-U (59%). This low performance rate is primarily caused by lack of ileal intubation (in 28% of patients). Eighty-four percent of all paediatric patients with IBD underwent both OGD and colonoscopy, thus reflecting a high grade of endoscopic examination of the upper and lower GI tract. Differences in numbers of OGDs and ileocolonoscopies between patients diagnosed as having CD and UC are probably inherent to the differences in disease distribution. Although not in accordance with guidelines, paediatric endoscopists may decide to refrain from ileoscopy and OGD to save time when the macroscopic aspect of the colon is typical for UC. Small and medium centres perform fewer OGDs but have a higher success rate of ileal intubation than large centres. The reasons for these differences are not clear, but the results could have been biased because there were only 3 large centres in 2 countries (UK and Poland). Other reasons may be differences in technical experience, limited time for the diagnostic program, and different in-house strategies, although these not in accordance with guidelines and not based on any evidence.

Radiological examination of the small bowel by SBFT, as proposed in the Porto criteria, was highest in the first 2 years of EUROKIDS, when 76% of patients diagnosed as having CD and IBD-U underwent SBFT. As stated in the Porto criteria, SBFT with barium contrast provides information on the extent and possible complications of small bowel involvement in CD, including stenosis, stricture, or internal fistulas (7). In the years following, the use of SBFT decreased significantly and was replaced by the use of MRI. This technique has no radiation exposure, whereas SBFT is responsible for 16% to 36% of all radiation exposure in children with IBD, as was demonstrated in recent studies (18,19). In addition, adult and paediatric data have shown that MRI was even more sensitive than fluoroscopy in detecting ileitis and inflammatory changes in the bowel wall (20–23). In a recent ESPGHAN-endorsed European Crohn's and Colitis Organisation guideline on paediatric CD, MRI is recommended as a primary investigation tool for small-bowel imaging in children with IBD (24), but local expertise should also be taken into account when choosing a small bowel imaging technique. For instance, evaluation of MRIs requires experienced radiologists because interpretation and scoring of MRI findings can sometimes be difficult (23).

Use of CT also increased significantly through the years, with 9% of patients diagnosed as having CD and IBD-U undergoing a CT in year 5. CT has been shown to be superior to SBFT in both sensitivity and specificity (25). Although comparative data on MRI and CT are limited, evidence from small adult studies suggests that both imaging techniques show similar accuracy in detecting active inflammation in the small intestine of patients with CD (25,26). Despite its obvious advantages, CT also causes significant radiation exposure (25%–43% of all radiation exposure in paediatric IBD) (18,19).

A diagnosis of IBD-U is usually reserved for patients with IBD who have features that make the clinician uncertain as to whether the diagnosis is CD or UC. According to the Porto criteria, a diagnosis of IBD-U is only acceptable when a complete diagnostic workup has been performed. In our study cohort, 9% of paediatric patients with IBD were diagnosed as having IBD-U, which is similar to the prevalence reported in other large paediatric IBD cohort studies (6,27); however, that patients were labelled as IBD-U may have been the result of an incomplete diagnostic workup (in 55%). It may be that this diagnosis could be changed to CD or UC after a full workup had been performed. Establishing a definitive diagnosis of CD or UC is essential, especially in the context of choosing therapeutic options and discussing long-term prognosis with a patient.

Previous studies on adherence to adult gastroenterological guidelines (eg, evaluation and management of osteoporosis in patients with IBD, surveillance colonoscopy in UC, colon polyp surveillance) have demonstrated that adherence is frequently suboptimal amongst clinicians (28–31). This was also shown in our study, with overall adherence rates to the full Porto criteria varying between 45% and 59%, depending on the type of IBD. There was a positive and significant time trend, showing the positive effect of the guideline audit on clinical practice. The even higher rate of 87% of patients diagnosed as having CD and 75% of patients diagnosed as having IBD-U, who underwent at least OGD and colonoscopy plus either ileal intubation or small bowel imaging, documents the high level of acceptance of the criteria and suggests that other factors play a role in implementation. For example, centre size had an influence on performance rates, indicating that the results mirror daily practice in diagnosing IBD more than keeping to a study protocol with additional checks and routines.

In summary, this first analysis of the EUROKIDS registry shows that the performance of OGD and ileocolonoscopy has been constantly rising since the publication of the Porto criteria. Taking serial biopsies for histology is an accepted standard. Small bowel imaging by MRI has increased over the years and has superseded the use of SBFT. In some cases, CT and capsule endoscopy contribute to the diagnosis. The diagnostic workup can be further improved by increasing the success rate of ileal intubation in all patients with IBD and by stimulating the use of small bowel imaging, especially in patients diagnosed as having IBD-U. The diagnostic yield of OGD (7.5%) and ileocolonoscopy (13%), combined with the additional value of small bowel imaging, emphasises the importance of a full diagnostic workup in children and adolescents with a suspicion of having IBD. In the near future, data from this 5-year EUROKIDS cohort will provide accurate and reliable information on the unique phenotype of paediatric-onset IBD.

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APPENDIX

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