Current role of colonoscopy in infants and young children: a multicenter study

Ryusuke Nambu, Shin-ichiro Hagiwara, Fumihiko Kakuta, Tomoko Hara, Hirotaka Shimizu, Daiki Abukawa, Itaru Iwama, Seiichi Kagimoto and Katsuhiro Arai

Abstract
Background: To evaluate the role of colonoscopy in infants and young children and clarify the distribution of colonoscopy-requiring diseases in this age group.

Methods: Cohorts of colonoscopies performed at three children’s hospitals in Japan between April 2011 and March 2016 including infants and children younger than six years of age were retrospectively reviewed.

Results: In total, 453 colonoscopies were performed in 276 infants and young children. Of these 275 (60.8%) were for diagnostic purposes, 177 (39.2%) were performed as follow-up, and one case was performed for treatment. The median patient age at the time of diagnostic colonoscopy was 2.49 years, and there was a male-to-female ratio of 1.72:1. Abnormal macroscopic and/or histopathological findings were noted in 212 (77.1%) cases. Of these, definite diagnoses were established for the presence of eosinophilic gastrointestinal disorders (EGIDs), inflammatory bowel disease (IBD), and polyp/polyposis in 23, 18.5, and 14% of patients, respectively. Among 51 IBD cases, ulcerative colitis, Crohn’s disease, and IBD-unclassified were identified in 47.1, 33.3, and 7.8%, respectively via endoscopic examination. Of these, 11 (22%) were eventually diagnosed with monogenic diseases via genetic testing. Of those with rectal bleeding, EGIDs, polyps/polyposis, and IBD were found in 27, 19, and 18%, retrospectively. There were significantly more cases of EGIDs and fewer ones of IBD and polyps/polyposis in patients with rectal bleeding younger than two years of age. Furthermore, 68% of all follow-up colonoscopies were performed in children with IBD. There were no serious complications in our study cohort.

Conclusion: We determined the role of colonoscopy in infants and young children. Diseases diagnosed using colonoscopy in this age group included IBD, EGIDs, and polyps/polyposis. The increasing trend of patients with IBD and EGIDs worldwide means that the role of colonoscopy in infants and younger children will be more important in the future.

Keywords: Colonoscopy, Infants and young children, Eosinophilic gastrointestinal disorders, Inflammatory bowel diseases, Monogenic disease

Background
Advances in anesthetic techniques and the evolution in the size and flexibility of endoscopes, have led to an increase in the number of colonoscopies performed in children worldwide, including infants and young children [1]. Although the major role of colonoscopy is the screening and diagnosis of colon cancer in adults [2], there are few children who are diagnosed with colon cancer. Frequently diagnosed diseases during childhood include inflammatory bowel diseases (IBD), polyps/polyposis, and graft versus host disease; however, there have been few reports demonstrating the role of colonoscopy in infants and young children [3, 4].

A large multicenter study conducted in the United States reported that most prevalent indications for pediatric colonoscopy include rectal bleeding (31%), abdominal pain (31%), and diarrhea (24%) [5]. Epidemiological studies have revealed a rise in the incidence of IBD and eosinophilic gastrointestinal disorders (EGIDs) in children including those younger than six years of age.
age. IBD found in this age group may indicate IBD associated with primary immunodeficiency [6–8]. Bequet et al., reported that the most common phenotype found in very early onset IBD was colitis [9], which frequently presents with rectal bleeding.

Over the past decades, the role of colonoscopies in infants and young children has not been well described. The present study aimed to elucidate the role of colonoscopy and the diagnosis requiring for colonoscopy in infants and young children.

Methods
We conducted a retrospective analysis of a cohort of children who underwent colonoscopies at the following three tertiary children’s hospitals in Japan: the National Center for Child Health and Development, Tokyo; Miyagi Children’s Hospital, Miyagi; and Saitama Children’s Medical Center, Saitama. Each institution had at least two pediatric gastroenterologists certified by the Japanese Society for Pediatric Gastroenterology, Hepatology and Nutrition.

A total of 1417 colonoscopies were performed in children aged 18 years old or younger between April 2011 and March 2016 at the aforementioned institutions. The following data were collected from the electronic databases of each hospital: age, sex, type of anesthesia, extent of colonoscopy, primary indication, abnormal macroscopic and/or histopathological findings, definite diagnosis, and serious complications. Diagnostic colonoscopy, follow-up colonoscopy, and other reasons for colonoscopy were also distinguished. Patients younger than six years of age were defined as “infants and young children”. Eosinophilic gastrointestinal disorders (EGIDs) were defined as disorders that primarily affect the gastrointestinal tract with eosinophil-rich inflammation in the absence of other known causes for eosinophilia, such as a drug reaction, parasitic infection, and malignancy [10].

Statistical analyses
All data were summarized and present as mean ± standard deviation for continuous variables. We considered values < 0.05 were considered statistically significant. We performed all statistical analyses using EZR, a graphical user interface for R (The R Foundation for Statistical Computing) that is a specifically modified version of R Commander designed to add statistical functions frequently used in biostatistics [11].

Ethics statement
Our study protocol was approved by the human ethics committees of the National Center for Child Health and Development (1460), Miyagi Children’s Hospital (MiyaKoKiriDai327); and Saitama Children’s Medical Center (2016-06-006). Patient information was anonymously handled at each institution, and the opportunity to withdraw from participation was provided to all participants and their guardians by posting flyers around the hospitals.

Results
Of the 1417 colonoscopies performed at the three children’s hospitals, 453 procedures (32.0%) were performed in infants and young children. Of these 453 colonoscopies performed in infants and young children, 275 (60.8%) were performed as “diagnostic procedure” and 177 (39.2%) were “follow-up procedure” (Fig. 1). One colonoscopy was conducted for the decompression of a mechanical ileus secondary to colonic stenosis, which was complicated with necrotizing enterocolitis.

Of the 275 diagnostic colonoscopies, the median age at the time of colonoscopy was 2.49 years (range: 5 days - 5 years 11 months) with a male-to-female ratio of 1.72:1 (Table 1). One hundred twenty-three procedures (44.7%) were performed in children less than two years old. Additionally, 130 (47%), 124 (45%) and 22 (8.0%) procedures were performed with general anesthesia, intravenous sedation, and no sedation, respectively. Nineteen of 22 procedures performed with no sedation were done in infants (<12mo), while the remaining three cases were confined to the sigmoid colon. Ileoscopy was performed in 170 (62%) of the 275 diagnostic colonoscopies. In 111 (85%) cases of the 130 colonoscopies with general anesthesia, terminal ileum were reached. Of note this rate was much higher than that observed in the colonoscopy group with sedation (54/124 procedures. 44%).

Two hundred twelve procedures (77.1%) showed abnormal macroscopic and/or histopathological findings. There were 63 cases of EGIDs (23%), 51 cases of IBD (18.5%), 38 cases of polyps/polyposis (14%), 37 cases of nonspecific colitis (13.5%), 13 cases of hemorrhoid/anal fissure (4.7%), five cases of lymphangiectasis (1.8%), and four with IgA vasculitis (1.5%) (Table 2). These definite diagnoses were made from endoscopic and histological findings coupled with the representative patients’ with clinical courses. Among the 51 patients with IBD, 24(47.1%) were endoscopically diagnosed with ulcerative colitis (UC), 18(33.3%) with Crohn’s disease (CD), one with intestinal Behçet disease, and remaining four were diagnosed as IBD-unclassified (IBD-U), respectively. Eleven (22%) children with IBD were also eventually diagnosed via genetic testing with monogenic diseases, including chronic granulomatous disease (n = 6), familial Mediterranean fever (n = 1), Wiskott-Aldrich syndrome (n = 1), STAT-3 gain of function (n = 1), Hoyeraal Hreidarsson syndrome (n = 1), and activated PI3K-delta syndrome (n = 1). Fifty-three percent of children younger
than two years of age with IBD were later diagnosed with monogenic diseases associated with IBD.

In all diagnostic colonoscopies, rectal bleeding was the most common primary indication (n = 206; 75%) (Table 1). Diagnoses found among the infants and young children showing rectal bleeding included EGIDs (n = 52; 25%), polyps/polyposis (n = 37, 18%), and IBD (n = 36, 17%). We compared the nature of disease distribution in children younger than two years old with that in children with two to five years old. In the former, the most prevalent diagnosis was EGIDs, and the frequency rate of such was higher in comparison with in those aged two-five years old (43% vs. 12%; \( P < 0.001 \)) (Table 3). Conversely, polyps/polyposis and IBD tended to be found more frequently in the older group (polyps/polyposis: 6.8% vs. 26%; \( P < 0.001 \), IBD: 10.8% vs. 23.3%; \( P = 0.06 \)).

A total of 177 colonoscopies were performed as follow-up procedures. Of these, 68% of procedures were performed in patients with IBD (Table 4). In these “follow-up” colonoscopies, six children who were eventually diagnosed with monogenic diseases underwent a total of 29 colonoscopies (4.8 colonoscopies per patient). Similarly, 16 children with UC underwent 52 colonoscopies (3.2 colonoscopies per patient) and 10 children with CD underwent 22 colonoscopies (2.2 colonoscopies per patient). No serious complications such as perforations or severe bleeding occurred.

**Fig. 1** Purpose for colonoscopy in infants and young children in the present study. Colonoscopies were performed in patients aged ≤18 years between April 2011 and March 2016 at three tertiary centers

**Discussion**

As part of the present research, we retrospectively reviewed 453 colonoscopies performed in infants and young children younger than six years of age at three tertiary care children’s hospitals in Japan. To the best of our knowledge, this is the first study to evaluate the role of colonoscopy in infants and young children. The proportion of colonoscopies performed in infants and young children was 32.0% of the 1417 colonoscopies recorded in children aged 18 years old or younger. A cursory review of the literature revealed that this rate was higher than those in other previous studies on the subject of pediatric colonoscopy [12, 13]. We suggest two reasons for this findings; first, our three institutions are the tertiary children’s hospitals having pediatric anesthesia, and second, colonoscopies in children aged 15 to 18 years old in Japan are most often performed by gastroenterologists in adult units. The terminal ileum was reached in 62% of the diagnostic colonoscopies reviewed in this study. Reasons for incomplete colonoscopy include severe colitis with a high risk, cases not indicated for completion by the senior endoscopist, poor bowel preparation, and technical failure. Approximately 75% of the diagnostic colonoscopies revealed abnormal macroscopic and/or histopathological findings. EGIDs and IBD were the most common diagnoses, and rectal bleeding was the most common primary indication for colonoscopy in this population. Approximately 70% of follow-up colonoscopies were performed in IBD patients.
The prevalence of positive macroscopic and/or histopathological findings in diagnostic colonoscopies in our study among infants and young children was compared with the details of other studies on children younger than 16 years or 18 years old. In Asia, the prevalence rates of positive diagnostic findings were 45.8, 50.6, and 70.5% of studies from Korea, Hong Kong and South China, respectively [13–15]. In the United Kingdom, 62% of colonoscopies performed in children younger than 16 years old had abnormal findings [16]. Lissy et al. reported that diagnostic colonoscopy revealed abnormalities in 80% of children referred with rectal bleeding [17]. In practice, negative findings are often as important as positive findings in the management of children with gastrointestinal symptoms. Our study demonstrated that colonoscopies are equally or more important in infants and young children as compared with children of other ages.

The most common diagnoses in children who underwent colonoscopy in this study were, in order, EGIDs and IBD. While a diagnosis for EGIDs requires pathological eosinophil infiltration, macroscopic and microscopic findings are nonspecific [18]. This includes gastrointestinal allergies, such as cow’s milk protein-induced enteropathy, food-protein-induced...

### Table 1 Clinical character and disease distribution of diagnostic colonoscopies

| Characteristic                  | n = 275 |
|--------------------------------|---------|
| Gender, male: female           | 174:101 |
| Age, yr., median ± SD          | 2.49 ± 1.47 |
| age < 2 yr                     | 123 (45%) |
| 2 yr. ≤ age < 6 yr             | 152 (55%) |
| Type of anesthesia             |         |
| General                        | 130 (47%) |
| Intravenous                    | 124 (45%) |
| No sedation                    | 22 (8.0%) |
| Extent of colonoscopy          |         |
| ~ ileum                        | 170 (62%) |
| ~ cecum                        | 8 (2.9%) |
| ~ ascending colon              | 9 (3.3%) |
| ~ transverse colon             | 28 (10.2%) |
| ~ descending colon             | 33 (12%) |
| ~ sigmoid colon                | 27 (9.8%) |
| Abnormal findings              | 212 (77%) |
| Primary indication             |         |
| Rectal bleeding                | 206 (75%) |
| Diarrhea                       | 36 (13%) |
| Abdominal pain                 | 6 (2.2%) |
| Fail to thrive                 | 4 (1.5%) |
| Repetitive intussusception     | 4 (1.5%) |
| Anal fistula                   | 3 (1.1%) |
| Anemia                         | 3 (1.1%) |
| Hypoalbuminemia                | 3 (1.1%) |
| Others*                        | 10 (3.6%) |

* “Others” refers to diseases identified in fewer than two children

### Table 2 Disease distribution of diagnostic colonoscopies

| Disease                         | n = 275 |
|--------------------------------|---------|
| EGIDs                          | 63 (23%) |
| IBD                            | 51 (19%) |
| Normal                         | 41 (15%) |
| Polyps/Polyposis               | 38 (14%) |
| Nonspecific Colitis            | 36 (13%) |
| Hemorrhoid/MPS                 | 13 (4.7%) |
| Lymphangiectasis               | 5 (1.8%) |
| IgA vasculitis                 | 4 (1.5%) |
| Others*                        | 24 (8.7%) |
| Normal                         | 41 (15%) |

EGIDs eosinophil gastrointestinal disorders (including gastrointestinal allergy), IBD inflammatory bowel diseases, MPS mucosal prolapse syndrome
* “Others” refers to diseases identified in fewer than two children

### Table 3 Cause of rectal bleeding required by age group

| Category                        | 0 ≤ yr. < 2 | 2 ≤ yr. < 6 | P-value |
|---------------------------------|-------------|-------------|---------|
| Gender, male: female            | 51:37:00    | 75:43:00    |         |
| Age, yr., median ± SD           | 0.82 ± 0.54 | 3.83 ± 1.09 |         |
| Diagnosis                       |             |             |         |
| EGIDs                           | 38 (43%)    | 14 (12%)    | < 0.001 |
| Polyps/Polyposis                | 6 (6.8%)    | 31 (26%)    | < 0.001 |
| IBD                             | 10 (11%)    | 26 (22%)    | 0.06    |
| Nonspecific Colitis             | 20 (23%)    | 14 (12%)    | 0.05    |
| Hemorrhoid/MPS                  | 1 (1.1%)    | 11 (9.3%)   | 0.01    |
| Others*                         | 6 (6.8%)    | 9 (7.6%)    |         |
| Normal                          | 7 (8.0%)    | 13 (11%)    |         |

* “Others” refers to diseases identified in fewer than two children

### Table 4 Disease distribution in follow up colonoscopies

| Follow-up                      | n = 177 |
|--------------------------------|---------|
| IBD                            | 120 (68%) |
| EGIDs                          | 15 (8.5%) |
| Nonspecific Colitis            | 14 (7.9%) |
| Polyps/Polyposis               | 13 (7.3%) |
| Others*                        | 15 (8.5%) |

EGIDs eosinophil gastrointestinal disorders (including gastrointestinal allergy), IBD inflammatory bowel diseases
* “Others” refers to diseases identified in fewer than two children
enterocolitis, proctocolitis, and allergic eosinophilic gastroenteritis. In Japan, the incidence of EGIDs in neonates and infants has been increasing since the late 1990s [19]. Our three tertiary institutions do not perform colonoscopies in all patients with suspected gastrointestinal allergies. Children with EGIDs do not require colonoscopy for diagnosis because food avoidance and oral food challenges are often sufficient to determine a diagnosis. On the other hand, as EGIDs share common clinical features with IBD, especially in the acute phase, the making of an early diagnosis using colonoscopy is important to ensure the proper management of this vulnerable population [20]. In the present study, the fact that EGIDs and IBD were the most common diagnoses found for children who underwent colonoscopy seems logical. An increase in the number of infants and young children with EGIDs and IBD in Japan would increase the demand for colonoscopies.

As indicated above, IBD was the second leading diagnosis for infants and young children included in this study who underwent colonoscopy. A recent study suggested that the incidence of IBD is increasing in young children aged four years or younger, as well as those aged between five and nine years old [8]. Since infants and young children with IBD frequently have colonic lesions, colonoscopy is important tool when IBD is suspected [9]. The UC-to-CID ratio in this study was 1.3, and this ratio differs from those in Western countries. Griffiths et al. reported that, the occurrence of pediatric UC in Scandinavian countries exceeds that of CD, whereas in both North America and in the United Kingdom, the incidence of pediatric CD was greater than that of UC [21].

Recent advances in diagnostic tools, particularly in the field of genetics, have placed a spotlight on the existence of primary immunodeficiency associated gastrointestinal disorders such as monogenic diseases among IBD patients, especially in those diagnosed with IBD before the age of six years. Atypical endoscopic and histological findings of IBD in this age group always challenge pediatric gastroenterologists, and some studies have classified this particular group of IBD cases as displaying UC-like or CD-like disease. Patients with monogenic diseases may suffer from serious infections due to the use of immunosuppressive drugs to treat IBD. On the other hand, hematopoietic stem cell transplantation may cure some of the known monogenic diseases such as interleukin 10 abnormalities, X-linked lymphoproliferative disorder type 2, or chronic granulomatous disease. It is becoming increasingly critical to suspect the monogenic IBD when making the diagnosis of IBD in infants and young children. In the present study, 22% of patients diagnosed by the age of six years and 53% diagnosed by
Conclusions
In the present study, we elucidated the role of colonoscopy in infants and young children. The most common diseases found by colonoscopy in this age group were EGIDs, IBD, and polyps/polyposis. The increasing trend of patients presenting with IBD and EGIDs worldwide means that the role of colonoscopy in infants and younger children will be more important in the future.

Abbreviations
CD: Crohn’s disease; EGIDs: Eosinophilic gastrointestinal disorders (including gastrointestinal allergy); IBD: Inflammatory bowel diseases; MPS: Mucosal prolapse syndrome; UC: Ulcerative colitis

Acknowledgments
This work was supported in part by a Grant-in-Aid for the National Center for Child Health and Development from the Ministry of Health, Labour and Welfare, Japan (27-12 to KA). The authors also would like to thank Enago (https://www.enago.jp/) for the English language review.

Authors’ contributions
All authors assisted with manuscript preparation and revisions. RN and KA conceptualized and designed the study, collected data, carried out the initial analyses, drafted the initial manuscript, and reviewed and revised the manuscript. SH and FK collected data, carried out the initial analyses, and reviewed and revised the manuscript. TH, DA, and II collected data and reviewed and revised the manuscript. HS and SK reviewed the manuscript. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

Funding
This work was supported in part by a Grant-in-Aid for the National Center for Child Health and Development from the Ministry of Health, Labour and Welfare, Japan (27–12 to KA). This funding body played roles in the collection data and in writing the manuscript.

Availability of data and materials
The datasets generated and analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate
Our study protocol was approved by the Human Ethics Committees of the institutions. Determining these complications would have enabled us to enhance the usage profile for colonoscopy in infants and young children. Further follow-up including additional immunological or genetic testing may reveal more monogenic or other Mendelian forms of IBD.

References
1. Croffle JM. Advances and new technologies in adult endoscopy: can they be adapted to pediatrics? Curr Gastroenterol Rep. 2007;9:208–13.
2. Levin B, Lieberman DA, McFarland B, Andrews KS, Brooks D, Bond J, et al. American Cancer Society colorectal Cancer advisory group; US multi-society task force; American College of Radiology Colon Cancer Committee. Screening and surveillance for the early detection of colorectal cancer and adenomatous polyps, 2008: a joint guideline from the American Cancer Society, the US multi-society task force on colorectal Cancer, and the American college of radiology. Gastroenterology. 2008;134:1570–95.
3. Kawada PS, O’Loughlin EV, Stormon MO, Dutt S, Lee CH, Gaskin KJ. Are we overdoing pediatric lower gastrointestinal endoscopy? J Pediatr Gastroenterol Nutr. 2017;64(6):898–902.
4. Eltisur Y, Teitelbaum JE, Rewalt M, Nowicki M. Clinical and endoscopic data in juvenile polyposis syndrome in preadolescent children: a multicenter experience from the United States. J Clin Gastroenterol. 2009;43:734–6.
5. Gilger MA, Gold BD. Pediatric endoscopy: new information from the PEDS-COR project. Curr Gastroenterol Rep. 2005;7:234–9.
6. Uhlig HH, Schwed T, Koltezk S, Shah N, Kammermeier J, Elkadi A, et al. The diagnostic approach to monogenic very early onset inflammatory bowel disease. Gastroenterology. 2014;147:990–1007.
7. Kelsen JR, Baldassano RN. The role of monogenic disease in children with very early onset inflammatory bowel disease. Curr Opin Pediatr. 2017;29:566–71.
8. Benchimol EI, Mack DR, Nguyen GC, Snapper SB, Uijtdehaage A, Lozada LM, et al. Incidence, outcomes, and health services burden of very early onset inflammatory bowel disease. Gastroenterology. 2014;147:803–13.
9. Bequet E, Sarter H, Fumery M, Vasere F, Armengol-Delpeyr E, Picarete B, et al. Incidence and phenotype at diagnosis of very early-onset compared with later-onset Paediatric inflammatory bowel disease: a population-based study [1988–2011]. J Crohns Colitis. 2017;11:519–26.
10. Rothenberg ME. Eosinophilic gastrointestinal disorders (EGID). J Allergy Clin Immunol. 2004;113:11–28.
11. Kanda Y. Investigation of the freely available easy-to-use software EZR for medical statistics. Bone Marrow Transplant. 2013;48:452–8.
12. Yoshikawa S, Takedatsu H, Funakaga S, Kuwaki K, Yamasaki H, Yamauchi R, et al. Study to determine guidelines for pediatric colonoscopy. World J Gastroenterol. 2017;23:5773–9.
13. Lee YW, Chung WC, Sung HJ, Kang VG, Hong SL, Cho KW, et al. Current status and clinical impact of pediatric endoscopy in Korea. Korean J Gastroenterol. 2014;64:333–9.
14. Tam YH, Lee KH, Chan KW, Shioe JD, Cheung ST, Mou JW. Colonoscopy in Hong Kong Chinese children. World J Gastroenterol. 2010;16:1119–22.
15. Lei P, Gu F, Hong L, Shioe JD, Cheung ST, Mou JW. Pediatric colonoscopy in South China: a 12-year experience in a tertiary center. PLoS One. 2014;9:e95933.
16. Stringer MD, Pinfield A, Revell L, McClean P, Puntis JW. A prospective audit of paediatric colonoscopy under general anaesthesia. Acta Paediatr. 1999;88:199–202.
17. de Radder L, van Lingen AV, Tamini H, Jenning MA. Rectal bleeding in children: endoscopic evaluation revisited. Eur J Gastroenterol Hepatol. 2007;19:317–20.
18. Kolezko S, Niggemann B, Arias A, Dias JA, Heuschkel R, Husby S, et al. Diagnostic approach and management of cow’s-milk protein allergy in infants and children: ESPGHAN Gi committee practical guidelines. J Pediatr Gastroenterol Nutr. 2012;55:221–9.
19. Nomura I, Monta H, Ohya Y, Saito H, Matsumoto K. Non-IgE-mediated gastrointestinal food allergies: distinct differences in clinical phenotype between Western countries and Japan. Curr Allergy Asthma Rep. 2012;12:297–303.
20. Ishige T, Yagi H, Tatsuki M, Hatori R, Nishida Y, Takizawa T, et al. Endoscopic findings in the acute phase of food protein-induced enterocolitis syndromes. Pediatr Allergy Immunol. 2015;26:90–1.

Received: 16 January 2019 Accepted: 30 July 2019
Published online: 20 August 2019
21. Griffiths AM. Specificities of inflammatory bowel disease in childhood. Best Pract Res Clin Gastroenterol. 2004;18:509–23.
22. Suzuki T, Sasahara Y, Kikuchi A, Kakuta H, Kashiwabara T, Ishige T, et al. Targeted sequencing and immunological analysis reveal the involvement of primary immunodeficiency genes in pediatric IBD: a Japanese multicenter study. J Clin Immunol. 2017;37:67–79.
23. Kammermeier J, Dziubak R, Pescarin M, Drury S, Godwin H, Reeve K, et al. Phenotypic and genotypic characterisation of inflammatory bowel disease presenting before the age of 2 years. J Crohns Colitis. 2017;11:60–9.
24. Levine A, Griffiths A, Markowitz J, Wilson DC, Turner D, Russell RK, Fell J, Ruemmele FM, Walters T, Sherlock M, Dubinsky M, Hyams JS. Phenotypic modification of the Montreal classification for inflammatory bowel disease: the Paris classification. Inflamm Bowel Dis. 2011;17:1314–21.
25. Gupta SK, Fitzgerald JF, Croffie JM, Chong SK, Pfefferkorn MC, et al. Experience with juvenile polyps in north American children: the need for pancolonoscopy. Am J Gastroenterol. 2001;96:1695–7.

Publisher’s Note
Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.