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GASTROINTESTINAL

MRI reveals different Crohn's disease phenotypes in children and adults

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Abstract

Objectives To identify differences between two cohorts of adult and pediatric patients affected by Crohn's disease (CD), with regard to lesion location in the small intestine and colon-rectum, lesion activity, and prevalence of perianal disease (PD), using MRI as the main diagnostic tool.

Methods We retrospectively reviewed 350 consecutive MRI examinations performed between 2013 and 2016 in outpatients or inpatients with histologically proven CD, monitored by the Gastroenterology and Pediatric Units of our Hospital. The magnetic resonance enterography (MRE) protocol for adult and pediatric CD patients routinely includes evaluation of nine different intestinal segments (from jejunum to rectum) and of the anal canal. Intestinal activity was also calculated using a validated score. Perianal disease (PD) was staged. Fisher's exact test was used and the odds ratio (OR) was calculated.

Results Two hundred and nineteen out of 350 MRI studies (118 adults and 101 children) were included. The prevalence of PD was 34.6% in children and 16.1% in adults (OR = 2.8; $p = 0.0017$). Pediatric patients showed more frequent rectal involvement (29.7% vs 13.5%, OR = 2.7; $p = 0.0045$) and higher risk of PD in the presence of rectal disease ($p = 0.043$; OR = 4.5). In pediatric patients with severe colorectal disease, the prevalence of PD was twofold (86.7% vs 40%; $p = 0.072$). Using the clinical Montreal classification for lesion location, no significant differences emerged between the two patient populations.

Conclusions MRI showed a significantly higher prevalence of rectal involvement and perianal disease in the pediatric population. These results may have a relevant clinical impact and deserve further investigation.

Key Points

- *To our knowledge, this is the largest morphological comparative study available in the literature using MRI as the main diagnostic tool to compare adult patients and children with Crohn's disease.*
- *Our study showed significant differences between adults and children: a higher prevalence of rectal and perianal fistulous disease (PD) in pediatric patients and an increased prevalence of PD in the presence of severe colon-rectum involvement.*
- *The association of rectal and perianal disease implies a poorer clinical prognosis and a higher risk of disabling complications in pediatric patients.*

Keywords Magnetic resonance imaging · Crohn disease · Pediatrics · Fistula · Anal canal

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Abbreviations

CD	Crohn's disease
CI	Confidence interval
DWI	Diffusion-weighted imaging
HASTE	Half-Fourier acquisition single shot turbo spin echo
HRMRI	High-resolution magnetic resonance imaging
MEGS	Magnetic resonance enterography global score
MRE	Magnetic resonance enterography
MRI	Magnetic resonance imaging
OR	Odds ratio
PD	Perianal disease
SJH	St. James Hospital
TrueFISP	True fast imaging with steady-state free precession
VIBE	Volumetric interpolated breath-hold examination

Introduction

Crohn's disease (CD) is a chronic inflammatory bowel disease which lasts throughout the patient's life with childhood onset in 10% to 25% of patients [1–4]. Recent epidemiological observations have shown a marked rise in the incidence of pediatric CD during the last two decades [1]. Indeed, recent studies show that location and severity of intestinal lesions may, for unknown reasons, be different in adult and pediatric patients [2, 5–9]. According to the Montreal and Paris Classifications [10, 11], colonic and ileocolonic locations seem to be the prevalent disease locations in children [12, 13].

Recent studies also report an increased incidence of perianal disease (PD) in pediatric patients, up to 50.7%, for still unknown reasons, although the usual incidence reported for both adults and children is nearly 30% [6, 14–17]. Complex perianal fistulas are some of the most disabling CD complications, especially in children and young adults, since these lesions recur in more than 30% of cases despite the most advanced pharmacological and surgical treatments [17–20]. Risk factors for developing perianal fistulas are still unknown, although an association between colorectal disease and anal fistulas has recently been reported [21].

To our knowledge, there are no large-scale comparative studies between adult and pediatric CD patients, particularly regarding the PD prevalence and intestinal disease locations, possibly due to the difficulty in obtaining morphological data on the entire bowel without using invasive procedures. Likewise, correlation between the intestinal disease sites and PD has not been sufficiently investigated yet.

Magnetic resonance enterography (MRE) is currently deemed the least invasive and most accurate diagnostic tool for detecting CD lesions in the small and large bowels, both in adult and pediatric patients, as well as for assessment of lesion activity [22–28]. Likewise, high-resolution magnetic resonance imaging (HRMRI) is considered the most accurate diagnostic imaging method for assessment of PD [25].

The purpose of our study was to investigate the differences between two large cohorts of adult and pediatric patients affected by CD, using magnetic resonance imaging (MRI) as the main diagnostic tool for evaluating lesion location in the small and large bowels, lesion activity, and for the detection and staging of perianal fistulas.

Material and methods

Study population

We retrospectively reviewed 350 consecutive MREs performed between May 2013 and May 2016 on adult and pediatric patients with histologically proven CD, monitored by the adult and pediatric Gastroenterology Units of our University Hospital, both tertiary centers for inflammatory bowel disease. The review included both inpatients and outpatients.

Main indications for performing MRE in adult and pediatric outpatients were follow-up examinations during pharmacological therapy, revaluation in non-responding patients, and first diagnostic evaluation at the onset of CD. Main indications in inpatients included disease reactivation and complications.

The routine MRE protocol for adult and pediatric CD patients included assessment of the small and large bowels as well as a preliminary evaluation of the perianal region. Whenever PD was clinically evident and/or suspected and/or detected at MRE, the examination was completed with HRMRI of the pelvis, which was performed within the same session or after a short time interval (1–2 weeks), for a comprehensive fistula staging. According to these criteria, most patients with perianal disease referred by the Adult or Pediatric Gastroenterology Units of our University Hospital undergo HRMRI of the pelvis.

In the present study, all MRI examinations performed on adult (≥ 18 years) and pediatric patients (< 18 years) were retrieved and re-evaluated also considering clinical, endoscopic, and biopsy outcomes. Inclusion criteria were patients with histologically proven CD, complete clinical-endoscopic and follow-up data (over 6 months), and adequate MRI examination of the small and large bowels and perianal region. If a patient had undergone several follow-up examinations within the 3-year period of our study, we evaluated only the examination performed in the most active clinical phase. Details of inclusion and exclusion criteria and clinical data are reported in Table 1 (supplemental materials).

Before the examination, adult patients, parents of pediatric patients, or guardians provided written informed consent. This study was approved by the ethical committee of our Institution.

Clinical evaluation

In both adult and pediatric patients, the initial CD diagnosis was based on ileocolonoscopy (endoscopic assessment of the last 10 cm of the terminal ileum and colon including multiple biopsies), histology, and radiological studies, including ultrasound, CT-enterography, and/or MR enterography, depending on patient age and clinical condition, according to the current clinical guidelines [29].

All patients underwent blood tests, including C-reactive protein, erythrosedimentation rate, white blood count, and orosomucoids. Crohn's Disease Activity clinical score (CDAI in adults, pCDAI in pediatric patients) was calculated in all patients.

All included patients underwent colonoscopy 1–12 weeks from MRE, with the evaluation of lesion location and assessment of the endoscopic activity. In both adult and pediatric patients, CD location was classified in four main categories according to the clinical Montreal classification: L1, ileal; L2, colonic; L3, ileocolonic; and L4, isolated upper gastrointestinal disease.

MRI technique

MRI examinations were performed using a 1.5 Tesla magnet (Magnetom Avanto™, Siemens Healthcare) with a 16-channel phased-array coil. Two different MRI protocols, MRE and HRMRI, were used to evaluate intestinal disease and PD, respectively (Table 2, supplemental material). A biphasic contrast medium (polyethylene glycol-electrolyte solution) was administered orally to all patients, range 300–1000 mL in pediatric patients and up to 1500–2000 mL in adults, depending on the patient's age, weight, and compliance.

The field of view of the MRE included the entire bowel, from the duodenum to the anal canal. The MRE protocol included the following sequences: (a) fast T2-weighted HASTE (half-Fourier acquisition single shot turbo spin echo); (b) fast TrueFISP (true fast imaging with steady-state free Precession); (c) diffusion-weighted imaging (DWI); and (d) T1-weighted fat suppressed VIBE (volumetric interpolated breath-hold examination) after injection of a cyclic gadolinium-chelate contrast agent. The field of view of pelvic HRMRI included the perianal region.

Imaging analysis

A systematic blinded evaluation of the data was carried out by three radiologists: V.B. (< 5 years of experience) retrieved data from the original report; FR.M. (> 20 years of experience in gastrointestinal imaging) reviewed all cases blinded to the previous reports and clinical data; and FA.M. (≥ 5 years of experience) reviewed all cases blinded to the previous reports and clinical data. The three databases were compared by V.B. and synthesized in a single database; in case of discordance, the radiologists revaluated the MRI examinations to reach a final consensus.

Nine different CD locations were considered: the jejunum, proximal-mid ileum, terminal ileum, coecum, ascending colon, transverse colon, descending colon, sigmoid colon, and rectum.

In order to obtain a simplified score, disease activity was assessed in each location using MRI activity features already extensively validated in previous studies, all included in the validated MEGS score (magnetic resonance enterography global score) [30–36]. The following MRI features/parameters were scored from 0 to 3: (a) wall thickness, (b) T2 mural-wall signal, (c) T2 mesenteric edema, (d) post-contrast T1 mural-wall enhancement, (e) length of diseased segments, and (f) active lymph nodes (Table 1). A three-point activity score was obtained at the level of the most inflamed bowel segments, derived from the sum of all parameters: low activity, score 1; moderate activity, score 2; and high activity, score 3 (Table 1).

Patient MRI data were recorded in a secure excel-database: CD location in the nine consecutive segments in the small and large bowels; MRI disease activity at the level of the affected intestinal segments; the presence or absence of PD; and fistula staging according to the Parks [37] and St. James Hospital (SJH) [38] classifications.

Clinical and endoscopic data were reviewed by adult and pediatric gastroenterologists and compared with radiological outcomes. In case of disagreement between clinical and radiological results, a final consensus was reached.

Statistical methods

To evaluate the difference between the two groups, we used Fisher's exact test. We also calculated the confidence interval (CI) (Wilson method) and the odds ratio (OR). The association between CD location and PD and the association between severity of intestinal CD and PD were calculated with Pearson's chi-square test. Statistical significance was set at $p < 0.05$. Statistical analysis was conducted using STATA v.12 (StataCorp).

Results

Of the 350 studies, 219 were selected according to the described inclusion/exclusion criteria: 118 performed on adults (54%) and 101 on pediatric patients (46%). Most of these patients (80.5% of adults, 70% of pediatric patients) were on long-term pharmacological treatment (biological, anti-inflammatory, immunosuppressant drugs, and/or antibiotics) (Table 1 supplemental material).

A total of 1971 disease locations were evaluated. In case of disagreement between the three radiologists (4.5%), a final

Table 1 MRI activity parameters and scoring system

Parameter	Grade
Wall thickening	Grade 1: 4–5 mm
	Grade 2: 6–8 mm
	Grade 3: >8 mm
Qualitative assessment of signal intensity of wall gadolinium enhancement on T1-weighted fat suppressed images*	Grade 1: low
	Grade 2: moderate
	Grade 3: high
Qualitative assessment of signal intensity of the bowel wall (mural edema) on T2-weighted fat suppressed images **	Grade 1: low
	Grade 2: moderate
	Grade 3: high
Qualitative assessment of signal intensity of perivisceral fat (mesenteric edema) on T2-weighted fat suppressed images**	Grade 1: low
	Grade 2: moderate
	Grade 3: high
Number of active lymph nodes***	Grade 1: 1–2
	Grade 2: 3–4
	Grade 3: > 4
Length of the diseased intestinal segment	Grade 1: 2–10 cm
	Grade 2: 11–25 cm
	Grade 3: > 25 cm

Scoring system: At the level of the most inflamed bowel segments, the 6 parameters were assessed and scored 1–3. A three-point score disease activity score ranging from 1 to 3 was obtained, derived from the sum of all parameters: from 6 to 7 = low activity, score1; from 8 to 13 = moderate activity, score 2; from 14 to 18 = high activity, score 3

*Gadolinium enhancement of the bowel wall was considered: grade 1 if the degree of enhancement at visual inspection was like that of the muscles, grade 2 if similar to the splenic parenchyma, grade 3 if similar to aorta

**Signal intensity of the bowel wall on T2-weighted fat-suppressed images was considered: grade 1 if it was similar to that of the muscles, grade 2 if similar to liver parenchyma, grade 3 if similar ot or higher than that of the spleen or kidneys

***Lymph nodes were considered active if larger than 5 mm and characterized by Gadolinium enhancement and/or a restricted signal in DWI

consensus was reached. In the entire patient population, the primary disease site was the terminal ileum with a prevalence of 82.6%, followed by the coecum (27.4%). In the pediatric population, the primary disease site was the terminal ileum (81.2%), followed by the rectum (29.7%), sigmoid colon (29.7%), coecum (29.7%), and descending colon (22.8%). In the adult population, the terminal ileum was the primary site of disease (83.9%), followed by the coecum (25.4%), sigmoid

Table 2 Prevalence of Crohn's disease lesions at the level of nine different small and large bowel segments

Segment	Total population (N = 219)	Pediatric patients (N = 101)	Adult patients (N = 118)	p value
1. Jejunum	7.3%	8.9% (9/101)	5.9% (7/118)	N.S.
2. Proximal ileum	5.5%	4.9% (5/101)	5.9% (7/118)	N.S.
3. Terminal ileum	82.6%	81.2% (82/101)	83.9% (99/118)	N.S.
4. Coecum	27.4%	29.7% (30/101)	25.4% (30/118)	N.S.
5. Ascending colon	12.3%	11.9% (12/101)	12.7% (15/118)	N.S.
6. Transverse colon	8.7%	7.9% (8/101)	9.3% (11/118)	N.S.
7. Descending colon	19.6%	22.8% (23/101)	16.9% (20/118)	N.S.
8. Sigmoid colon	25.6%	29.7% (30/101)	22% (26/118)	N.S.
9. Rectum	21%	29.7% (30/101)	13.5% (16/118)	0.0045

N.S., not significant > 0.05

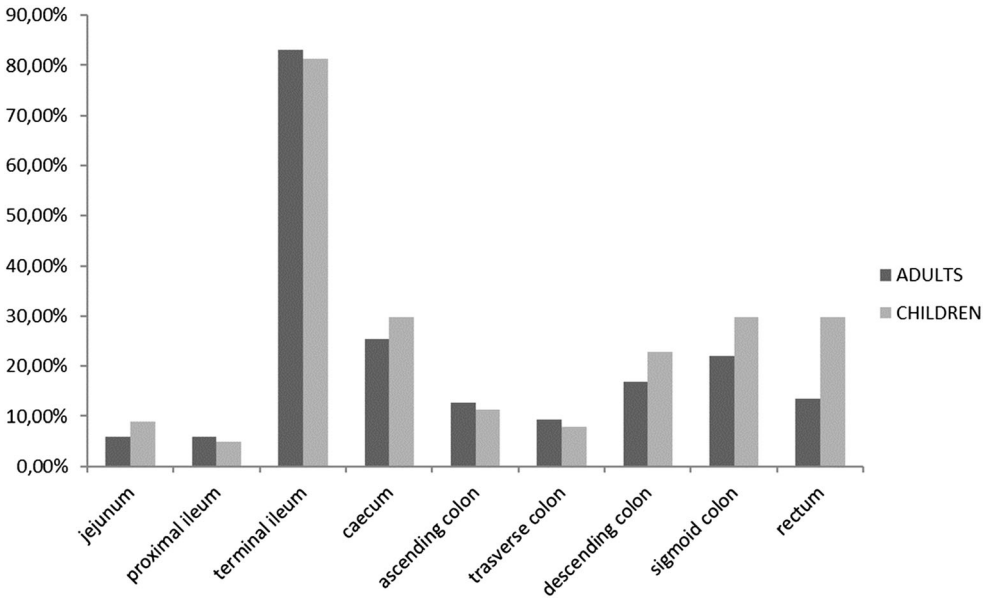

Fig. 1 Prevalence of Crohn's disease lesions at the level of nine different small and large bowel segments

colon (22%), descending colon (16.9%), and rectum (13.5%) (Table 2, Fig. 1).

In pediatric patients, the prevalence of CD in the descending colon, sigmoid colon, and rectum was higher than in adults, but the difference was statistically significant only in the rectum ($p = 0.0045$). Rectal involvement in pediatric patients showed an OR of 2.7 (95% CI, 1.37 to 5.31; $p = 0.0042$).

No significant difference between adults and pediatric patients was found when considering the four locations (L1–L4) included in the Montreal classification (Fig. 2, Table 3).

PD was found in 54/219 examined patients (24.6%); the prevalence of PD in the pediatric and adult population was 34.6% (35/101) and 16.1% (19/118), respectively ($p = 0.0017$) (Fig. 3a, b). The OR of perianal fistulizing disease in pediatric patients was 2.8 (95% CI 1.46 to 5.24; $p = 0.0018$).

No significant differences in fistula staging were observed between the two patient groups, using both the Parks and SJH classifications; complicated fistulas (i.e. inter or transphincteric fistulas complicated by abscesses, or supra-extrasphincteric fistulas, staged as SJH classification grade 2, 4 and 5) were detected in 54.3% of pediatric patients compared to 68.4% of adult patients, with no significant difference (Table 4). The most frequent disease site in both patient groups, the terminal ileum, was associated with PD in 29% of pediatric patients and in 16.2% of adults (Table 5).

Considering patients with PD only, the highest prevalence of anal fistulas was again observed in the presence of disease affecting the terminal ileum, both in adults (84.2%) and in pediatric patients (68.6%). Moreover, in pediatric patients with PD, sigmoid colon disease was present in 56% compared to 23% of adult patients and rectal disease in 60% compared with 25% of adult patients (Table 5). The prevalence of PD in

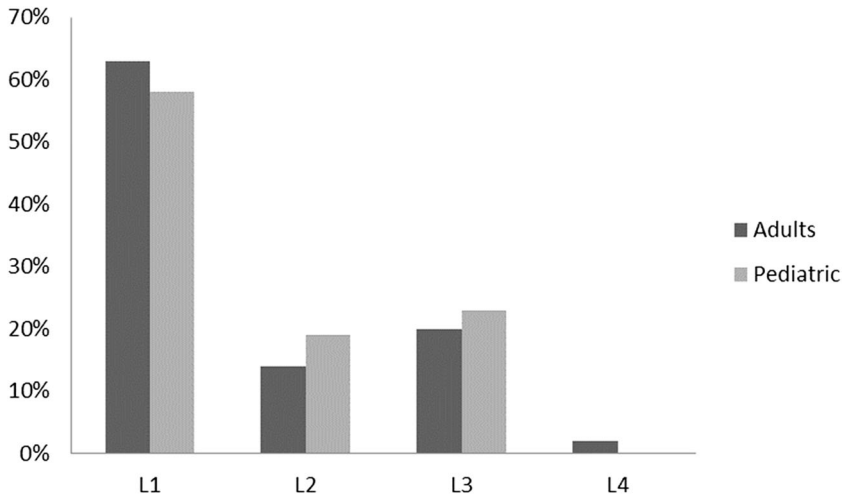

Fig. 2 Prevalence of Crohn's disease lesions according to the Montreal classification

Table 3 Prevalence of Crohn's disease lesions according to the Montreal classification

Montreal classification	Adult patients (118)	Pediatric patients (101)	Total (219)
L1	74 (63%)	59 (58%)	133 61%)
L2	17 (14%)	19 (19%)	36 (16%)
L3	24 (20%)	24 (23%)	47 (22%)
L4	3 (3%)	0	3 (1%)

L1, distal ileal + ileocecal location; *L2*, colonic; *L3*, ileocolonic; *L4*, isolated upper disease

the presence of rectal disease was higher in pediatric patients than in adults, 51.4% versus 21%, the difference being statistically significant ($p = 0.043$) (Table 5), whereas no significant differences were found regarding the remaining intestinal sites. In pediatric patients with PD, a significant OR for rectal involvement was found (OR = 3.9; 95% CI, 1.10 to 14.38; $p = 0.0357$). Furthermore, in pediatric patients, the OR for PD in the presence of rectal involvement was significant (OR = 4.5; 95% CI, 1.17 to 17.30, $p = 0.0286$). Finally, in the entire patient population, the OR of having both rectal CD and PD was 4.0 (95% CI, 2.02 to 8.09; $p = 0.0001$).

Grade 3 disease activity was found in 30.5% of adults and in 35.6% of children (Table 6). Severe (grade 3) terminal ileum disease, found in 29.6% of adults and in 28% of pediatric patients, was associated with PD in 31% and 30%, respectively (Table 7, Fig. 4). Conversely, in both populations, only 18.5% of patients with low-mid-grade terminal ileum disease (grades 1 and 2) had PD. In the entire population, OR for PD in the presence of severe (grade 3) disease of the terminal ileum was 2.0 (95% CI, 0.96 to 4.23; $p = 0.0624$).

In all pediatric patients, OR for PD in the presence of severe colorectal involvement was 9.7 ($p = 0.055$). In pediatric patients with grade 3 left colorectal disease (intended as the disease of at least two left colonic locations, including the transverse colon, descending colon, sigmoid colon, and/or rectum), PD was found in 86.7% of cases, as compared with 40% of adult patients ($p = 0.072$) (Fig. 4).

Discussion

To date, comparative studies between pediatric and adult patients have been scarce and fragmentary in spite of an increasing clinical evidence that pediatric and adult patients may have a different clinical course or "phenotype" [6, 14, 15]. To our knowledge, this is the largest morphological comparative study available in the literature between adult patients and children with Crohn's disease (> 200 patients), where MRI was considered the main diagnostic tool for lesion localization in the small intestine, colon-rectum, and anal region.

In a previous radiological MRI study, we already compared 43 adults and 43 pediatric patients, reporting a higher incidence of lesions in the left colon and rectum in children [39]. Interestingly, several recent clinical studies also found a high prevalence of rectal, colonic, and perianal CD in children [6, 14, 15, 39–41]. Furthermore, a correlation between distal colonic inflammation, perianal disease, and specific molecular pathways has recently been reported [21]. Another study demonstrated the possibility to differentiate two forms of CD, "colon-like" and "ileum-like," based on specific gene expression patterns [42].

The lack of comparative data between adults and pediatric patients has a possible clinical explanation: different specialists manage the two patient groups, i.e., adult and pediatric gastroenterologists.

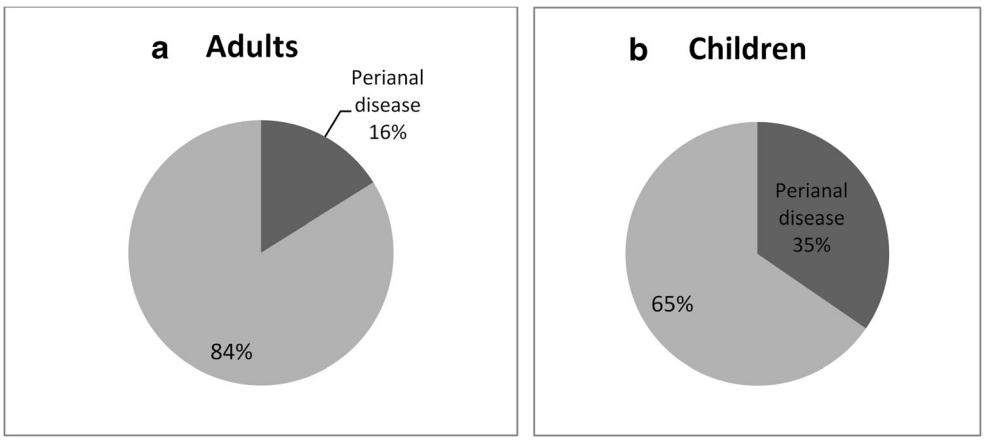

Fig. 3 Prevalence of PD in adults (**a**) and pediatric patients (**b**)

Table 4 Staging of perianal fistulas according to the Parks and St. James Hospital (SJH) classifications in adult and pediatric patients

Parks classification	Total %	Pediatric %	Adults %
Grade 1	57.4	62.8	47.4
Grade 2	31.6	31.4	31.6
Grade 3	5.5	0	15.8
Grade 4	5.5	5.7	5.3
SJH classification			
Grade 1	29.6	34.3	21
Grade 2	31.5	28.6	36.8
Grade 3	11.1	11.4	10.5
Grade 4	20.4	20	21
Grade 5	7.4	5.7	10.5

MRI currently provides unequalled morphological information on CD which cannot be achieved using other diagnostic tools, such as endoscopy or ultrasound. This includes staging of PD and assessment of intestinal disease activity, both in adult and pediatric patients.

In the present study, several differences between the two populations were identified using MRI. The ileal location was, as expected, the primary disease site in both populations. However, in pediatric patients, the second most frequent disease location was the left colon, particularly the rectum (29.7%) and the sigmoid colon (29.7%), whereas in adults, it was the right colon, i.e., the coecum (25%). The higher prevalence of rectal disease in pediatric patients was statistically significant ($p = 0.0045$). Another significant difference was the higher prevalence of PD in the pediatric versus the adult population, 34.6% and 16.1%, respectively ($p = 0.0017$) (Fig. 3a, b). The OR of perianal fistulizing disease in pediatric patients was also significant (2.8, $p = 0.0018$).

Table 6 Overall MRI activity scores in adults and children

	Grade 1	Grade 2	Grade 3
Adults	32.2% (38/118)	37.3% (44/118)	30.5% (36/118)
Children	35.6% (36/101)	28.7% (29/101)	35.6% (36/101)

Thus, the most relevant result emerging from our study is that pediatric patients have a higher risk than adults of developing rectal CD as well as a higher prevalence of PD. Furthermore, in the presence of rectal involvement, the OR for PD was significantly higher in children (4.5, $p = 0.0286$). On the basis of these results, we recommend that MRI protocols for CD always include a preliminary assessment of the anal region, particularly in pediatric patients. In general, all patients with rectal or left colon involvement should be considered at high risk of developing perianal fistulas and should therefore undergo clinical and MRI monitoring.

An interesting result emerging from our study is also the apparent inaccuracy of the Montreal clinical classification. Using this classification, no differences emerged between the two patient groups, likely because it does not distinguish between disease locations in the right or left colon-rectum, as it associates all the different colonic locations in a generic colonic (L3) or ileocolonic (L2) disease.

In our opinion, all these results are clinically relevant in the management of pediatric CD patients. Rectal and perianal diseases are well-known negative prognostic factors leading to disabling complications and a higher risk of radical proctectomy [17–20].

Table 5 Counts and percentages of perianal disease (PD) and intestinal disease in the small and large bowels

Location	PD prevalence in all pediatric patients (PD /CD location)	PD prevalence in all adult patients (PD/CD location)	PD prevalence in pediatric patients with PD only (PD/CD location)	PD prevalence in adult patients with PD only (PD/CD location)	*p* value
Jejunum	44.4% (4/9)	14.3% (1/7)	11.4% (4/35)	5.3% (1/19)	NS
Proximal ileum	60% (3/5)	14.3% (1/7)	8.6% (3/35)	5.3% (1/19)	NS
Terminal ileum	29.3% (24/82)	16.2% (16/99)	68.6% (24/35)	84.2% (16/19)	NS
Coecum	43.3% (13/30)	20% (6/30)	37.1% (13/35)	31.6% (6/19)	NS
Ascending colon	41.7% (5/12)	6.7% (1/15)	14.3% (5/35)	5.3% (1/19)	NS
Transverse colon	75% (6/8)	0% (0/11)	17.1% (6/35)	0% (0/19)	NS
Descending colon	52.2% (12/23)	30% (6/20)	34.3% (12/35)	31.6% (6/19)	NS
Sigmoid colon	56.7% (17/30)	23.1% (6/26)	48.6% (17/35)	31.6% (6/19)	NS
Rectum	60% (18/30)	25% (4/16)	51.4% (18/35)	21% (4/19)	0.043

The table shows the absolute and relative prevalence (%) of perianal Crohn's disease (PD) in the presence of intestinal disease at the level of each of the nine considered segments. *NS*, not significant > 0.05

Table 7 Results of MRI activity score in adults and children at the level of each of the nine intestinal locations, in percentages and absolute values

Adult				Children		
Location	Grade 1	Grade 2	Grade 3	Grade 1	Grade 2	Grade 3
Jejunum	42.8% (3/7)	28.6% (2/7)	28.6% (2/7)	66.7% (6/9)	11.1% (1/9)	22.2% (2/9)
Proximal ileum	80% (4/5)	20% (1/5)	0% (0/5)	60% (3/5)	20% (1/5)	20% (1/5)
Terminal ileum	33.7% (33/98)	36.7% (36/98)	29.6% (29/98)	45.1% (37/82)	26.8% (22/82)	28% (23/82)
Coecum	38.7% (12/31)	38.7% (12/31)	22.6% (7/31)	46.7% (14/30)	30% (9/30)	23.3% (7/30)
Ascending colon	33.3% (5/15)	53.3% (8/15)	13.3% (2/15)	33.3% (4/12)	41.7% (5/12)	25% (3/12)
Transverse colon	27.3% (3/11)	54.5% (6/11)	18.2% (2/11)	0% (0/8)	50% (4/8)	50% (4/8)
Descending colon	50% (10/20)	35% (7/20)	15% (3/20)	30.4% (7/23)	30.4% (7/23)	39.1% (9/23)
Sigmoid colon	46.1% (12/26)	38.5% (10/26)	15.4% (4/26)	26.7% (8/30)	36.7% (11/30)	36.7% (11/30)
Rectum	50% (8/16)	31.2% (5/16)	18.7% (3/16)	36.7% (11/30)	36.7% (11/30)	26.7% (8/30)

We also observed an association between severe bowel inflammation and PD, both in adults and pediatric patients suggesting that the severity of intestinal inflammation may be a possible trigger factor for PD (Figs. 5 and 6). Most of the children (86.7%) with severe colorectal disease had PD (Figs. 4 and 5), vs 40% of adults. In both populations, the risk of developing PD was lower in the presence of low-grade colorectal or ileal inflammation.

In our study, no significant difference was found between pediatric and adult patients as regards PD staging, using both Park's and SJH classifications. Complicated fistulas were more frequently found in the adult population, likely due to the longer existence of PD.

The main limitations of our study include its retrospective and single-center nature.

With regard to the single-center nature of the study, both adults and pediatric patients were referred to our Department from large Gastroenterology IBD Units; thus, if selection bias is present, it should affect both patient populations to the same extent. However, our study does not intend to be an epidemiological but a strictly radiological study, comparing two patient populations sufficiently large to provide adequate data for a statistical analysis. Nevertheless, the prevalence of rectal and perianal disease found in our study is in agreement with epidemiological and clinical data recently reported in pediatric patients [5–9]. Patients < 8 years were not included due to low compliance; similarly, children and adults with extensive intestinal resections were excluded in order to correctly assess intestinal lesion distribution; overall, they represented < 5% of the entire patient population.

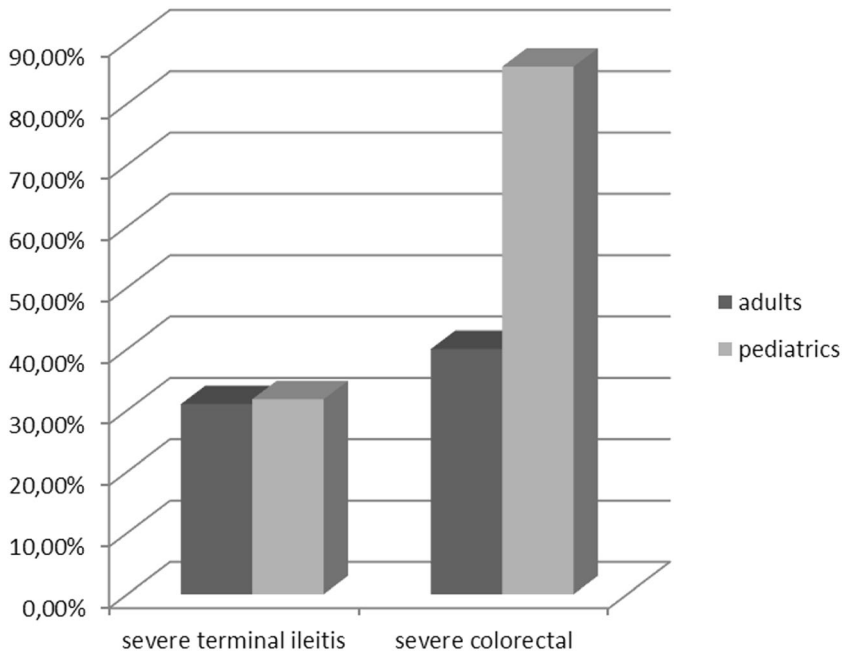

Fig. 4 Prevalence of PD in the presence of severe disease activity

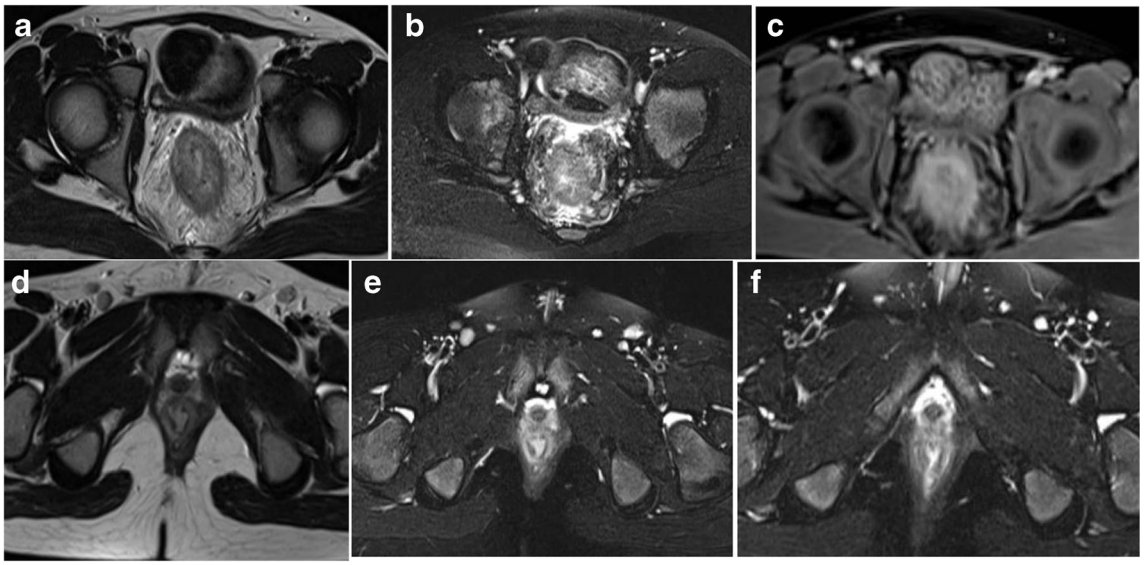

Fig. 5 Eleven-year-old boy, with CD of the sigmoid colon and rectum. **a**, **b** High-resolution TSE T2-weighted fat suppressed and plain axial image showing severe circumferential rectal wall thickening (up to 15 mm) and severe mural and mesorectal fat edema. **c** Marked gadolinium wall enhancement is observed, with irregular outer borders. Multiple mesorectal and inguinal inflammatory lymph nodes were also present (**d**, **e**). These findings are suggestive of severe colorectal Crohn's disease, MRI activity score 3. **d** T2-weighted high-resolution TSE axial image, obtained at the level of the anal canal, shows a subtle posterior intersphincteric fistula. **e**, **f** The T2-weighted fat-suppressed axial images highlight the hyperintense intersphincteric linear course of the fistulous tract, with the internal opening at six-o-clock (Parks' type 1)

Finally, adults and pediatric patients enrolled in this study were heterogeneous with regard to treatment regimes since patients before, during, and after treatment were included. CD is a chronic disease treated with different drugs over long periods of time; therefore, untreated ("naïve") patients are usually very few compared to patients undergoing treatment. Disease activity, however, may be high in naïve patients as well as in non-responding patients during treatment and in case of relapse after treatment. This heterogeneity, therefore, should not affect our results regarding the correlation between PD and activity.

In conclusion, using MRI as a main investigation tool in two large cohorts of CD patients, we observed an association

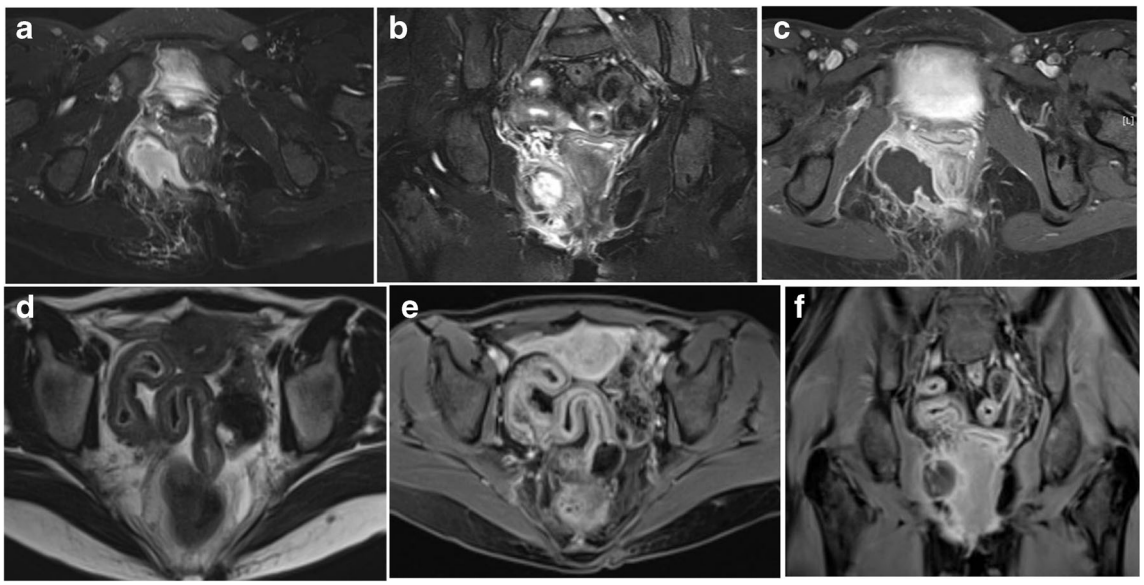

Fig. 6 Thirty-five-year-old female, with a severe relapse of CD of the mid-distal ileum and severe perianal disease. **a**, **b** High-resolution TSE T2-weighted fat-suppressed coronal and axial images showing a large abscess in the right ischio-anal sub-levator ani space, originating from a horse shoe fistula. **c** T1-weighted post-contrast image showing marked peripheral gadolinium enhancement of the large abscess and adjacent fat tissue. The perianal disease was staged Parks type 2, S. James Hospital 4. **d** Axial T2-weighted image showing multiple severely inflamed ileal loops, characterized by marked wall thickening. **e** Post-contrast axial T1-weighted image showing marked and severe gadolinium enhancement of the ileal loops. MRI activity was classified scored 3. **f** Post-contrast coronal T1-weighted image showing marked and severe gadolinium enhancement of the ileal loops, associated with severe perianal disease

between rectal disease and perianal fistulas, and between the activity of intestinal disease and prevalence of perianal disease, both in adults and pediatric patients. We also found a significant difference between the two patient groups, i.e., a higher prevalence of rectal involvement, a higher risk of PD, and more severe colorectal disease in children compared with adults. If confirmed by further studies, these results may have a significant clinical impact.

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Compliance with ethical standards

Guarantor The scientific guarantor of this publication is Francesca Maccioni.

Conflict of interest The authors of this manuscript declare no relationships with any companies, whose products or services may be related to the subject matter of the article.

Statistics and biometry One of the authors has significant statistical expertise.

Informed consent Written informed consent was obtained from all subjects (patients) in this study.

Ethical approval Institutional Review Board approval was obtained.

Methodology
- retrospective
- observational
- performed at one institution

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