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Natural History of Very Early Onset Inflammatory Bowel Disease *in North America: A Retrospective Cohort Study*

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Background: The incidence of very early onset inflammatory bowel disease (VEOIBD) is increasing, yet the phenotype and natural history of VEOIBD are not well described.

Methods: We performed a retrospective cohort study of patients diagnosed with VEOIBD (6 years of age and younger) between 2008 and 2013 at 25 North American centers. Eligible patients at each center were randomly selected for chart review. We abstracted data at diagnosis and at 1, 3, and 5 years after diagnosis. We compared the clinical features and outcomes with VEOIBD diagnosed younger than 3 years of age with children diagnosed with VEOIBD at age 3 to 6 years.

Results: The study population included 269 children (105 [39%] Crohn's disease, 106 [39%] ulcerative colitis, and 58 [22%] IBD unclassified). The median age of diagnosis was 4.2 years (interquartile range 2.9–5.2). Most (94%) Crohn's disease patients had inflammatory disease behavior (B1). Isolated colitis (L2) was the most common disease location (70% of children diagnosed younger than 3 years vs 43% of children diagnosed 3 years and older; $P = 0.10$). By the end of follow-up, stricturing/penetrating occurred in 7 (6.6%) children. The risk of any bowel surgery in Crohn's disease was 3% by 1 year, 12% by 3 years, and 15% by 5 years and did not differ by age at diagnosis. Most ulcerative colitis patients had pancolitis (57% of children diagnosed younger than 3 years vs 45% of children diagnosed 3 years and older; $P = 0.18$). The risk of colectomy in ulcerative colitis/IBD unclassified was 0% by 1 year, 3% by 3 years, and 14% by 5 years and did not differ by age of diagnosis.

Conclusions: Very early onset inflammatory bowel disease has a distinct phenotype with predominantly colonic involvement and infrequent stricturing/penetrating disease. The cumulative risk of bowel surgery in children with VEOIBD was approximately 14%–15% by 5 years. These data can be used to provide anticipatory guidance in this emerging patient population.

Key Words: VEOIBD, surgery, epidemiology

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BACKGROUND

Inflammatory bowel disease (IBD) has emerged as a global disease with a rising prevalence in every continent.[1] Many patients are diagnosed early in life; between 5% and 25% of IBD cases develop under the age of 18 years.[2] Pediatric IBD is further classified as early onset IBD (onset under age 10) and very early onset IBD (VEOIBD) defined as onset under 6 years of age.[3, 4] Historically, VEOIBD was thought to comprise approximately 15% of pediatric patients with IBD.[5] However, emerging data suggest that the incidence of VEOIBD is increasing.[6, 7]

Genetic factors are considered to play a more important role in the pathogenesis of VEOIBD and most specifically those patients with disease onset during the first year of life. Several genetic mutations specific to VEOIBD such as IL-10RA, IL10-RB, IL-10, XIAP, ADAM17, EPCAM, FOXP3, LRBA, SKIV2L, TTC37, NCF2/RAC2, and NCF4 have been recently identified.[3, 4, 8, 9] Given the genetic differences in VEOIBD compared with later onset IBD, it is possible that the phenotype, clinical course, and response to treatment may also differ.

With the increasing incidence of VEOIBD, natural history studies of this emerging condition are needed to (1) better understand prognosis, (2) provide anticipatory guidance to patients/families, and (3) risk stratify patients to guide diagnostic and therapeutic decisions (ie, precision medicine). Although many gastroenterologists believe that patients with VEOIBD have a poor prognosis and low response rates to conventional treatment,[10] the natural history of VEOIBD has not been well established.[11] To date, there is a paucity of large cohort studies of representative patient populations, and existing reports have been contradictory. For example, though several studies have suggested that VEOIBD has an aggressive phenotype with poor outcomes and increased frequency of surgery and other complications,[9, 10, 12, 13] more recent studies have shown that risk of surgery in VEOIBD is similar to older onset of pediatric IBD.[13, 14] In fact, a few studies have even suggested the risk of surgery in VEOIBD is less than that of older children,[7, 15] and another study indicated that children with VEOIBD are more likely to have mild disease at diagnosis.[16]

We therefore undertook a large multicenter study across North America to describe the clinical and phenotypic characteristics of VEOIBD at presentation. We also characterized the natural history of VEOIBD including diagnostic reclassification, evolution in disease behavior, and risk of surgery.

METHODS

Overall Study Design

We conducted a retrospective cohort study of patients diagnosed with VEOIBD (6 years of age and younger) between 2008 and 2013 at 25 North America centers participating in the Crohn's & Colitis Foundation's Pediatric Resource Organization for Kids with Inflammatory Intestinal Digestive Diseases (PRO-KIIDS) network.[17]

Study Population

Inclusion criteria included (1) meeting standardized diagnostic criteria based on endoscopic, histologic, and radiographic evidence of IBD;[18] (2) younger than 6 years of age at the time of diagnosis; and (3) date of diagnosis between 2008 and 2013. Patients with another diagnosis that could account for an IBD-like presentation such as cow's milk protein allergy (CMPA), juvenile polyps, and microscopic colitis were excluded. As per standard of care at the time, patients were not required to undergo genetic testing for mutations associated with VEOIBD.

To minimize the possibility of selection bias, we selected PROKIIDS sites based on their ability to identify and obtain records for all cases of VEOIBD diagnosed at their practices (ie, complete case ascertainment). To avoid referral bias, we included only patients who were diagnosed at participating centers. At each site, all potentially eligible patients were identified. A central biostatistician randomly ordered the list of potentially eligible patients, and sites sequentially reviewed charts to determine final eligibility. Our goal was to review 10 charts at each site. Not all centers identified 10 eligible patients. A few centers elected to review additional participants.

Data Collection

A trained pediatric gastroenterologist with expertise in IBD reviewed medical records and abstracted data related to patient demographics, clinical course, and treatment utilization using a standardized case reporting form. All physicians and study staff received training on standardized data definitions, and any questions or ambiguities identified during chart review were addressed by the study team and disseminated to all centers by the Data Coordinating Center. For each patient, data were abstracted at the after time points when available: diagnosis, 1 year after diagnosis, 3 years after diagnosis, 5 years after diagnosis, and at most recent site visit. All study data were entered electronically using REDCap data capture tools hosted at SickKids Research Institute in Toronto.[19]

Definitions

We defined the date of diagnosis as the date of first endoscopy. We defined initial IBD diagnosis as the original classification of Crohn's disease (CD), ulcerative colitis (UC), or IBD unclassified (IBD-U) at diagnosis (or within the first 3 months). We defined final diagnosis as the most recent classification on final site visit. We described disease extent and behavior using Paris classification.[20]

Statistical Analysis

The final study sample included all patients whose abstracted records included a date of birth and complete disease classification at the time of diagnosis. We used standard descriptive and univariate statistics to characterize our overall

study population and specific subgroups of interest, including reporting of medians (and interquartile range [IQR]) and proportions. The $\times^2$ or Fisher exact tests were used to compare age groups at diagnosis (3 years and older or younger than 3 years of age) on the basis of clinical and phenotypic characteristics, disease location, type, extent, and disease behavior. Kaplan-Meier survival curves were used to compare time to surgical event by age group. *P* values less than 0.05 were considered statistically significant. All analyses were conducted using SAS Version 9.4 (SAS Institute, Cary, NC).

Ethical Considerations

Institutional review board approval was obtained at all participating centers before patient identification and data collection.

RESULTS

The study population included 269 children with VEOIBD across 25 North American centers (see appendix). The median age at diagnosis was 4.2 years (range 0.4–6 y). The characteristics of the study population are displayed in Table 1. A total of 71 (26%) were diagnosed under age 3. The study population was predominantly white (63%), 8% were Jewish, and 7% were Hispanic. Only 5 children (1.7%) had a diagnosed coexisting immunological disorder.

Initial Presentation

Of the 71 patients diagnosed younger than 3 years of age, 26 (37%) had CD, 23 (32%) had UC, and 22 (31%) IBD-U. Of the 198 patients diagnosed between 3 and 6 years of age, 79 (40%) had CD, 83 (42%) had UC, and 36 (18%) had IBD-U (Table 2). In both age groups, the 2 most common symptoms at diagnosis were bloody diarrhea (88%) and abdominal pain (50%). The frequency of these symptoms did not differ between CD, UC, and IBD-U (data not shown). The incidence of any extraintestinal manifestations (EIMs) among Crohn's, UC, and IBD-U was 32%, 8%, and 11%, respectively ($P < 0.0001$). The occurrence of EIMs was similar in both age groups.

Of the 71 patients diagnosed under 3 years, 8 patients (11%) had a family history of IBD compared with 29 of 198 patients (15%) diagnosed at 3 years and older ($P = 0.55$). We noted consanguinity in <1% of parents of children with VEOIBD.

Over 94% of CD patients in both age groups had inflammatory behavior (B1) at diagnosis (Table 3). The most common disease locations at diagnosis were colonic (L2) and ileocolonic (L3) in both age groups. In children diagnosed under age 3, the proportion with L2 and L3 disease were 70% and 15%, respectively. In children diagnosed between 3 and 6 years of age, the proportion with L2 and L 3 disease were 43% and 29%, respectively. Five subjects (19%) diagnosed under age 3 and 29 subjects (37%) diagnosed over age 3 had upper tract disease; only 2 patients had isolated upper tract disease. Perianal disease was present at diagnosis in 12% of children under age 3 and 20% in children older than 3 years. In total, 62 of 105 children (50%) with CD had granulomas on pathology.

TABLE 1. Demographics of Children with VEOIBD

Demographics of VEOIBD (N = 269)	N (%)
Age at diagnosis	
Median (range)	4.2 (0.4, 6.0)
25th, 75th percentile	(2.9, 5.2)
Age (years)	
0–3	71 (26)
3–6	198 (74)
Sex	
Male	141 (54)
Female	119 (46)
Race	
White	170 (63)
African American	10 (4)
Asian	12 (4)
Amer Indian/Alaska Nat	0 (0)
Other Pacific Islander	0 (0)
Mixed	7 (3)
Unknown	70 (26)
Country of Origin	
USA	41 (15)
Canada	189 (70)
Other	5 (2)
Unknown	34 (13)
Ethnicity	
Jewish	
Yes	21 (8)
No	106 (39)
Mixed	1 (0.4)
Unknown	141 (52)
Hispanic	
Yes	18 (7)
No	142 (53)
Mixed	4 (1)
Unknown	105 (39)
Coexisting immune disorder	
CGD	0 (0)
IL-10/R receptor def	0 (0)
IPEX	0 (0)
NEMO	0 (0)
WAS	0 (0)
X- Agammaglobinemia	1 (0.4)
Other*	4 (1.5)

*The four "others" are Down Syndrome, Epidermolysis Bullosa, NK cell defect and STXBP2 Mutation, and NK cell deficiency.

TABLE 2. Clinical Characteristics of IBD at Diagnosis Based on Age at Diagnosis

	Age at Diagnosis		
Clinical characteristics at diagnosis	0–3 yrs (n = 71) n (%)	3–6 yrs (n = 198) n (%)	*P* value
IBD type			
Crohn's disease	26 (37)	79 (40)	0.08
Ulcerative colitis	23 (32)	83 (42)	
IBD- Unclassified	22 (31)	36 (18)	
GI symptoms			
Diarrhea	65 (88)	171 (88)	1.0
Blood per rectum	66 (93)	165 (84)	0.07
Abdominal pain	30 (48)	132 (70)	0.003
Vomiting	9 (13)	22 (12)	0.68
Decrease appetite	22 (37)	54 (32)	0.53
Weight loss	28(39)	66(33)	
Extraintestinal manifestation			
Erythema Nodosum	0 (0)	3 (2)	0.37
Pyoderma gangrenosum	0 (0)	0 (0)	—
Arthritis	1 (1)	6 (3)	0.68
Arthralgia	2 (3)	15 (8)	0.16
Oral ulcers	2 (3)	6 (3)	1.0
Folliculitis	0 (0)	2 (1)	1.0
Chronic fevers	1 (1)	23 (12)	0.007
Recurrent infections	4 (6)	7 (4)	0.50
Family history of IBD 1st degree	8 (11)	29 (15)	0.55
Surgery <3 months of diagnosis	3 (4)	3 (2)	0.19

In patients with UC, the most common disease location was E3 (extensive hepatic flex) and E4 (pancolitis) in both age groups. Isolated proctitis (E1) was rare (Table 3). Terminal ileal involvement was found in 5% of IBD-U cases diagnosed younger than 3 years of age and in 14% diagnosed between ages 3 and 6.

Treatments

The various treatments and medications used during the first year after diagnosis are reported in Table 4. Exclusive enteral nutrition (EEN) was used in 10 children (4%). A total of 143 children (55%) had more than 1 course of steroids during the first year of diagnosis, each course lasting 4 to 8 weeks. Additionally, 5-aminosalicylates were used in 191 children (73%), and 112 children (43%) were exposed to immunomodulators (6MP/azathioprine/methotrexate). Four patients were started on tacrolimus and 2 on cyclosporine. A total of 46 (18%) had exposure to biologics during the first year after diagnosis.

Over the course of 5 years of follow-up, cumulative use of immunomodulators and biologics was 60% and 41%, respectively (Table 4). The rate and time to initiation of biologics was not different in patients with CD, UC, or IBD-U or by age at diagnosis (Fig. 1A, B).

Natural History and Outcomes

During follow-up, the diagnosis changed from UC/IBD-U to Crohn's disease in 19 of 164 (11.5%) children. In children younger than 3 years of age, 8 of 45 patients (18%) were reclassified compared with 11 of 119 patients (9%) of the older group (P = 0.17). In children initially diagnosed with CD, 1 child (4%) diagnosed at younger than 3 years of age progressed from B1 to B2/B3 by 5 years. In children diagnosed with CD at 3 to 6 years of age, 4 children (5%) progressed from B1 toB2/B3 behavior.

In CD, the overall risk of bowel-related surgery was 3% by 1 year, 12% by 3 years, and 15% by 5 years. The risk of bowel surgery and time to surgery was not different by age at diagnosis (Fig. 2A). Colectomy risk in UC/IBD-U was 0% by 1 year, 3% by 3 years, and 14% by 5 years, without significant difference by age of diagnosis (Fig. 2B).

DISCUSSION

High quality studies evaluating the clinical characteristics and natural history of VEOIBD in large generalizable samples are lacking. We present findings from a large, multicenter, geographically diverse cohort of VEOIBD patients. Compared with the previously described epidemiological and clinical

TABLE 3. Disease Location and Behavior of IBD Phenotype at Diagnosis

	Age at Diagnosis		
Paris Classification	**0–3 yrs (n = 71) n (%)**	**3–6 yrs (n = 198) n (%)**	***P* value**
CD disease location (Paris) (n = 105)	***(N = 26)***	***(N = 79)***	
L1	0 (0%)	6 (7%)	0.1[a]
L2	18 (70%)	34 (43%)	
L3	4 (15%)	23 (29%)	
Isolated L4	0 (0%)	2 (3%)	
Micro disease only	3 (11%)	10(13%)	
Unknown	1 (4%)	4 (5%)	
L4			
Yes	5 (19%)	29 (37%)	0.14[a]
No	19 (73%)	45 (57%)	
Unknown	2 (8%)	5 (6%)	
CD disease behavior (n = 105)	***(N = 26)***	***(N = 79)***	
B1	25 (96)	74 (94)	0.58[a]
B2 Only	0 (0)	0 (0)	
B3 Only	0 (0)	2 (3)	
Both B2 and B3	0 (0)	0 (0)	
Unknown	1 (4)	3 (4)	
Perianal disease			
Yes	3 (12)	16 (20)	0.39[a]
No	22 (85)	61 (77)	
Unknown	1 (4)	2 (3)	
UC disease location (n = 106)	***(N = 23)***	***(N = 83)***	
E1 (Proctitis)	0 (0%)	3 (4%)	0.18[a]
E2 (Left sided)	2 (9%)	13 (16%)	
E3 (extensive hepatic flex)	1 (4%)	21 (25%)	
E4 (pancolitis)	13 (57%)	37 (45%)	
Not Assessed (complete colonoscopy not performed)	2 (9%)	6 (7%)	
Microscopic disease only	4 (17%)	2 (2%)	
Unknown	1 (4%)	1(1%)	
IBD-U Location (endoscopic) (n = 58)[b]	(N = 22)	(N = 36)	
Proximal Bowel	4 (18)	9 (25)	
Distal Ileum	1 (5)	5 (14)	
Cecum	4 (18)	3 (8)	
Ascending Colon	4 (18)	7 (19)	
Transverse Colon	4 (18)	4 (11)	
Descending Colon	3 (14)	4 (11)	
Recto-Sigmoid	21 (95)	33 (92)	

[a]"Unknown" and "Microscopic disease only" are not included in the *P* value computations.
[b]Disease location indicate the region involved but are not mutually exclusive

characteristics of IBD presenting in older children, our findings suggest that VEOIBD is composed of a distinct clinical phenotype but may not necessarily have a more aggressive disease course. Key findings include the following: (1) disease classification at diagnosis is primarily UC or IBD-U, likely due to colitis-predominant disease, (2) diagnostic reclassification to CD is common, (3) internal penetrating/stricturing disease is uncommon, (4) antitumor necrosis factor (anti-TNF) biologics are widely used, including off-label use in patients younger than 6 years of age, and (5) other clinical features and the natural history of VEOIBD seem to be similar to later onset pediatric IBD. Overall, we observed no substantial differences in the

TABLE 4. Exposure to IBD Medications

Cumulative exposure to medications	1st year of diagnosis N (%)	5 th year of diagnosis N (%)
Corticosteroids (>1 course ~4–8 wks)	143 (55)	174 (67)
Oral Enteric (Budesonide)	5 (2)	21 (8)
Oral systemic	132 (51)	166 (64)
IV systemic	23 (9)	53 (20)
Rectal	18 (7)	30 (11)
Biologics	46 (18)	107 (41)
Infliximab/Adalimumab	44 (17)	105 (40)
Other	2 (1)	2 (1)
Immunomodulators	112 (43)	157 (60)
Azathioprine/6-Mercaptopurine	96 (37)	128 (49)
Tacrolimus	4 (2)	5 (2)
Cyclosporine	2 (1)	2 (1)
Methotrexate (IM or oral)	17 (7)	57 (22)
ASA	191 (73)	208 (80)
Sulfasalazine	90 (34)	104 (40)
Mesalamine	111 (43)	137 (52)
Olsalazine	1 (0.4)	1 (0.4)
Exclusive Enteral Nutrition (EEN)	10 (4)	18 (7)

phenotype or natural history of children diagnosed under the age of 3 years compared with children diagnosed between 3 and 6 years of age.

The most common presenting symptoms of VEOIBD observed in our study were chronic diarrhea, bleeding per rectum, and abdominal pain. This was similar to prior published studies.[13, 15, 16] We observed extraintestinal manifestations in 14% of the children diagnosed with VEOIBD at a younger age (younger than 3 y) and in 33% of those diagnosed between 3 and 6 years old, though this difference was not statistically significant. These findings reinforce prior work showing no differences in the prevalence of extraintestinal manifestations in VEOIBD compared with older onset children.[10]

Similar to previously published studies,[5, 12, 13, 15, 21, 22] the most common classification of VEOIBD at diagnosis in our study was UC and IBD-U in more than 60% of patients in both age groups. This is likely a result of the most frequent anatomic location of inflammation being the colon. In children with CD, the most common disease location was colonic (L2), followed by ileocolonic (L3) disease. Isolated ileal disease, more common in adults and older children with CD,[23] was rare in our cohort. We observed no isolated ileal cases in children under age 3 at diagnosis and only 6 (7%) in children 3 to 6 years of age at diagnosis. In children with UC, pancolitis (E4) was the most common disease location in both age groups. Isolated proctitis was rare, which is consistent with other published studies.[13]

Several prior studies have reported that perianal disease is common in VEOIBD, with mutations affecting IL-10 or IL-10 receptor signaling.[24–26] Perianal disease was seen in 34% of VEOIBD from a single-center study.[12] In our study, the presence of perianal disease was less common, seen in only 12% of children diagnosed at younger than 3 years of age and 20% of children between 3 and 6 years of age. Our findings are consistent with those observed in a more recent multicenter study,[13] suggesting probable referral bias in earlier single-center series.

We observed relatively high anti-TNF use in our cohort. A total of 122 (42%) children were exposed anti-TNF *by 5 years from diagnosis. Though* infliximab and adalimumab are only FDA approved in patients older than 6 years of age, 46 children in our cohort were younger than 6 years at the time of first exposure to biologics. *We observed no differences in exposure to biologics in those diagnosed younger than 3 years as compared with children diagnosed at 3 to 6 years old.*

We noted a change in diagnosis from UC/IBD-U to Crohn's disease in 19 of 164 (11.5%) of children during follow-up. However, a significant proportion of children with VEOIBD continued to be classified as IBD-U after 5 years of follow-up, suggesting difficulty with making a definitive classification.[7, 13, 16]

Traditionally, VEOIBD has been considered to be a more aggressive phenotype with disease progression.[12] In our cohort, the observed risk of bowel surgery in CD was 3% at 1 year, 12% at 3 years, and 15% at 5 years. Thus, the observed risk of surgery in this VEOIBD cohort is similar to that of children diagnosed with CD at an older age.[14] This finding is consistent with another recent study from Canada showing that the risk of surgery and use of hospital resources were lower in VEOIBD compared with

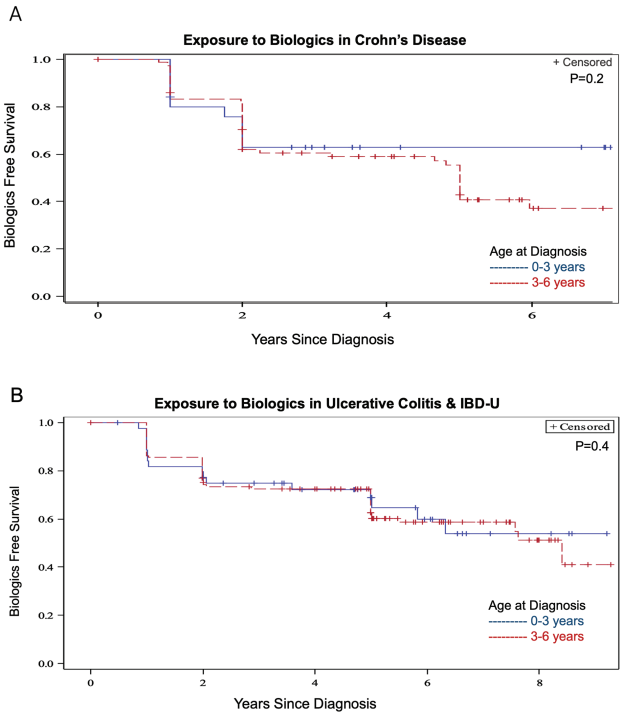

FIGURE 1. A, Biologics free survival in CD. B, Biologics free survival in in UC & IBD-U; *x* axis, years since diagnosis; *y* axis, biologics free survival; blue line, diagnosed younger than 3 years old; red line, diagnosed 3 years and older.

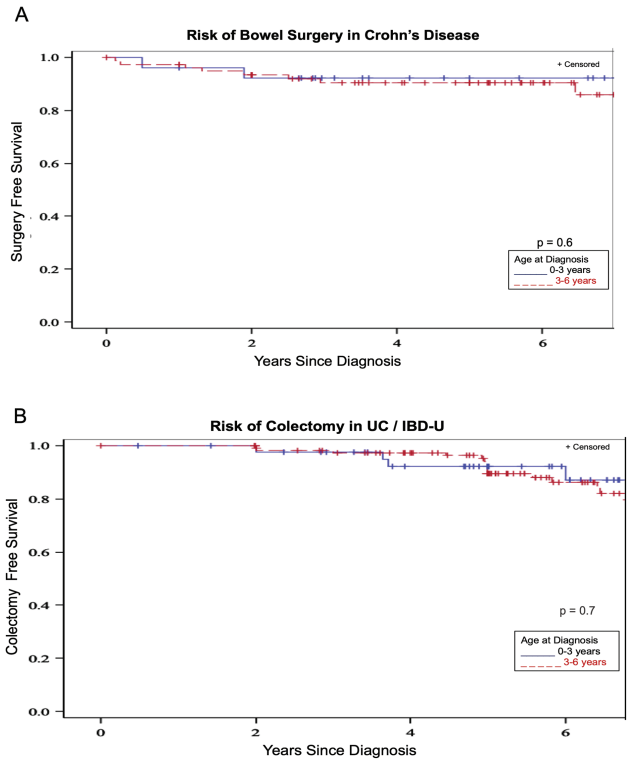

FIGURE 2. A, Surgery free survival (Bowel surgery in Crohn's disease). B, Colectomy free survival (UC & IBD-U); *x* axis, years since diagnosis; *y* axis, risk of bowel surgery; blue line, diagnosed younger than 3 years old; red line, diagnosed 3 years and older.

those with older onset pediatric IBD.[7] We observed the risk of colectomy in UC/IBD-U to be 0% by 1 year, 3% by 3 years, and 14% by 5 years. Prior literature regarding the risk of colectomy in VEOIBD is conflicting. One study demonstrated a higher risk of colectomy in young children[10]; however, a more recent Canadian study showed similar colectomy risk in children diagnosed with VEOIBD vs those with onset later in childhood.[7]

This study is one of the largest cohorts of VEOIBD looking at clinical features in the first 5 years from diagnosis. Other strengths include the large number and geographic diversity of participating centers. We undertook great efforts to minimize recall bias by selecting centers who could identify their complete population of VEOIBD patients and then randomly select participants for chart review. Additionally, we sought to minimize referral bias by excluding patients seen for second opinions after diagnosis. Thus, we believe our sample to approximate a "real world" cohort with robust generalizability.

There were several limitations of the study. As with many retrospective studies, missing data can be an issue. In our study, anthropometric data were not available for 50% of children, and other clinical details and/or dates could not always be ascertained during chart review. Additionally, our sample was predominantly white. Little is known about the distribution of IBD, particularly VEOIBD, among persons of different races and ethnicities. Thus, we cannot evaluate the extent to which our study population is adequately representative of non-European populations. Although we acknowledge that our study centers were largely academic medical centers that potentially could introduce referral bias, we attempted to mitigate this by excluding patients diagnosed at other centers as described previously. Finally, as our cohort had only 9 patients with VEOIBD diagnosed under the age of 1 year old, we could not characterize the clinical course of infantile-onset IBD. Additionally, the majority of patients in this cohort did not undergo genetic testing to describe monogenic disorders in VEOIBD

In summary, our study highlights that VEOIBD patients have a distinct phenotype. In contrast to later onset pediatric IBD, a greater proportion of patients in this VEOIBD cohort were classified as UC/IBD-U, had primarily colonic disease, and infrequently progressed to stricturing/internal penetrating complications. The requirement for surgery seems to be no more aggressive than that of later onset pediatric IBD. The results of this study can be used to counsel families of VEOIBD patients and highlight the need for clinical and comparative effectiveness and safety research in this emerging clinical population. In particular, considering the increasing off-label use of anti-TNF biologics in this patient population, there is a great need for effectiveness and safety research of these medications in VEOIBD.

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Appendix 1. Site List for VEOIBD Study

Study Site	Frequency	Percent
01_Chapel Hill UNC	9	3.85
02_Toronto SickKids	8	3.08
03_Boston	6	3.46
04_Chicago Lurie	10	3.85
05_StLouis CardGlennon	5	1.92
06_Philadelphia CHOP	10	3.85
07_Ottawa CHEO	21	8.08
08_Pittsburgh	10	3.85
09_NewYork Cohen	13	5.00
10_Connecticut	16	6.15
11_Morristown GoryebAHS	10	3.85
12_Providence Hasbro	10	3.85
13_NewYork MtSinai	10	3.85
14_Halifax IWK	10	3.85
15_Baltimore JHMI	11	4.23
16_Rochester Mayo	16	6.15
17_Milwaukee MCW	9	3.46
18_Nashville MonroeCarell	10	3.85
19_Columbus Nationwide	10	3.85
20_Carmel Riley	9	3.46
21_Houston TCH	9	3.46
22_Buffalo	11	4.23
23_SanFrancisco UCSF	10	3.85
24_SaltLakeCity_Utah	8	3.08
25_KansasCity_Mercy	9	3.46
26 Missing	9	