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Systematic Evaluation of Diagnostic Delay in Pediatric Inflammatory Bowel Disease

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ABSTRACT

We evaluated the diagnostic delay (time from first symptoms to diagnosis) in 100 pediatric patients with Crohn disease (CD) and 75 patients with ulcerative colitis (UC). Median (interquartile range) diagnostic delay in patients with CD was 4 (2–8) (range 0–82) months compared with 2 (1–7) (range 0–52) months in patients with UC ($P = 0.003$). The time interval from first physician visit to inflammatory bowel disease diagnosis was longer in patients with CD and UC when compared to the time interval from symptom onset to first physician visit (CD: median 3 vs 1 months, $P < 0.001$; UC: median 2 vs 0 months, $P < 0.001$). No specific risk factors were identified for the length of diagnostic delay. Measures should be taken to reduce diagnostic delay.

Key Words: Crohn disease, diagnostic delay, pediatric inflammatory bowel diseases, ulcerative colitis

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What Is Known

- Diagnostic delay in inflammatory bowel disease describes the time from symptom onset until diagnosis.
- Diagnostic delay can be divided into a patient-dependent and a physician-dependent interval.
- Data on length of diagnostic delay and associated risk factors are rare.

What Is New

- Median diagnostic delay in pediatric patients with Crohn disease was 4 months compared to 2 months in patients with ulcerative colitis.
- Physician-related delay was significantly longer than patient-related delay.
- Measures should be undertaken to reduce diagnostic delay.

Diagnosing inflammatory bowel disease (IBD) can be challenging, especially in patients with mild clinical activity and/or an overlap of symptoms with functional diseases. Diagnostic delay can represent an issue in patients with IBD from different countries, considering the literature reporting on patients experiencing symptoms for many years before IBD diagnosis (1–5). Diagnostic delay describes the time interval from first IBD symptom onset until IBD is diagnosed. Diagnostic delay can be separated into a patient's related period (from symptom onset to the first visit of a physician) and a physician-related period (from first physician visit until IBD diagnosis is established). Both patient's related delay and physician's related delay should be evaluated to identify where future improvements might be possible (on patients' or on physicians' side or both). Diagnostic delay may not only decrease quality of life of affected patients but has a major clinical effect as several studies have meanwhile demonstrated that treatment success is increased if therapies are initiated early after disease onset (6,7). In contrast to adult patients there is a paucity of studies having evaluated the length of diagnostic delay and associated risk factors in pediatric patients with IBD (8,9). We aimed to answer the following questions: first, how long is diagnostic delay in pediatric Crohn disease (CD) and ulcerative colitis (UC) patients? Second, which length of diagnostic delay is attributed to patient's delay and which length to physician's delay? And third, what are risk factors for long diagnostic delay in pediatric patients with CD and UC?

METHODS

Data from the nationwide Swiss Inflammatory Bowel Disease cohort study (SIBDCS) were analyzed. The SIBDCS has been

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including pediatric and adult IBD from all over Switzerland starting in 2006. The cohort study is supported by the Swiss National Science Foundation and approved by the local ethical committees (10). Data acquisition focuses on clinical, socioeconomic, and psychosocial data. Written informed consent is mandatory for inclusion into this cohort. Pediatric patients are included from 1 to 17 years of age. Detailed questionnaires focusing on physician-reported outcomes are completed by the IBD physicians, whereas parent-reported outcomes questionnaires are completed by parents together with the affected child. The following analysis evaluates all pediatric patients with CD and UC included into the SIBDCS from October 2006 until July 2013. Patients included in the present study were recruited in the following setting of care: 80% university hospitals and 20% regional hospitals. All pediatric gastroenterologists in Switzerland work in a hospital setting, no one works in a private practice.

The questionnaires recorded 3 distinct time intervals: first, the time interval from first IBD symptoms to first consultation with the physician (the length of this period is mainly dependent on the patient and parents); second, the time interval from physician visit to IBD diagnosis (the length of this period is mainly dependent on the treating physicians); and third, the time from first IBD symptoms to IBD diagnosis (interval 1+2).

Results of quantitative data are presented either as median plus interquartile ranges (IQR; for non-Gaussian data) or mean ± SD and range (for Gaussian data). The Kruskal-Wallis rank test was used to analyze non-Gaussian quantitative data and to evaluate whether there was a difference in diagnostic delay between the distinct IBD groups (CD, UC). Time delays were then further evaluated by pairwise comparisons using the Wilcoxon rank-sum test with a Bonferroni adjustment. Differences in categorical distribution between groups were evaluated using the Chi square test, or the Fisher exact test in case of small sample size. A $P < 0.05$ was considered statistically significant. A Cox proportional hazards model was calculated to evaluate the length of diagnostic delay with potentially associated factors.

RESULTS

A total of 175 pediatric patients with IBD were recruited, whereof 100 patients (57.1%) had CD, and 75 (42.9%) had UC. Median (IQR) age at enrolment was 14.1 (12.1–15.5) years in patients with CD and 13.6 (11.6–15.3) years in patients with UC. Median age at disease onset was 12 (10–14) years in patients with CD and 11 (7–13) years in patients with UC. Disease location at diagnosis in patients with CD was as follows: ileal, colonic, ileocolonic, upper gastrointestinal tract in 8%, 10%, 47%, and 2% of patients, respectively (the remainder had combinations of these disease locations). Patients with UC presented at diagnosis in 72% with pancolitis, 13.3% with left-sided colitis, and 6.7% with proctitis (8% with unknown disease location).

The analysis of the different time intervals is presented by means of comparative box plots in Figure 1 and by Table 1. Median (IQR) time from first symptoms to IBD diagnosis was 4 (2–8) months in CD compared to 2 (1–7) months in patients with UC. Diagnostic delay in CD was significantly longer than that in UC ($P = 0.003$). Time from first symptoms to physician visit (median, IQR) was 1 month (0–3) in CD compared to 0 months in UC (0–3). No difference between CD and UC was found for the time interval from first symptoms to physician visit ($P = 0.257$). The time interval from first physician visit to IBD diagnosis (median, IQR, range) was 3 months (1–9) for patients with CD and 2 months (1–4) for patients with UC. Again, no difference was found for this time interval between patients with CD and UC (CD vs UC: $P = 0.111$). Furthermore, time from physician visit to IBD diagnosis was longer than the interval from symptom onset to physician visit in patients with CD (median 3 vs 1 months, $P < 0.001$) and patients with UC (median 2 vs 0 months, $P < 0.001$).

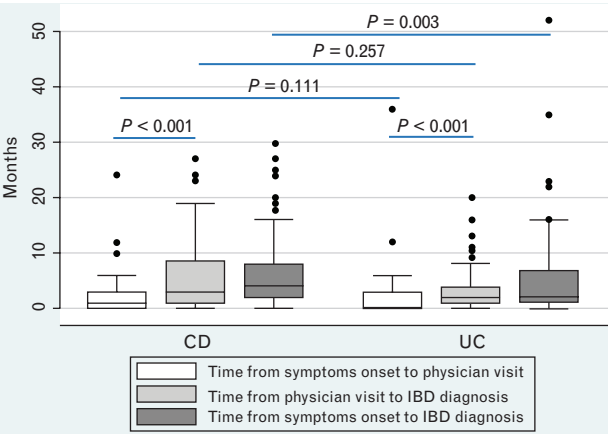

FIGURE 1. Comparative box plots illustrating the different time intervals of diagnostic delay (in months) according to diagnosis. The box contains the 25th to the 75th percentile of the values, the horizontal line in the box corresponds to the median. CD = Crohn disease; IBD = inflammatory bowel disease; UC = ulcerative colitis.

We further evaluated the effect of disease-associated factors on diagnostic delay in children with IBD. In both CD and UC patients the Cox proportional hazards model did not find any significant association between the length of diagnostic delay and the following factors: sex, age at IBD diagnosis, initial disease location, positive family history of IBD (at least 1 first-degree relative with IBD), provenience of parents (urban vs rural), nor education level of the parents.

TABLE 1. Time delays (mo) in children with Crohn disease (n = 100) and ulcerative colitis (n = 75), stratified according to overall diagnostic delay and time from first symptoms to physician visit and from physician visit to establishment of inflammatory bowel disease diagnosis

Time intervals, mo	Time from first symptoms to IBD diagnosis		Time from first symptoms to physician visit		Time from physician visit to IBD diagnosis	
Disease percentile, %	CD	UC	CD	UC	CD	UC
1	0	0	0	0	0	0
5	1	0	0	0	0	0
10	1	1	0	0	0	0
25	2	1	0	0	1	1
50	4	2	1	0	3	2
75	8	7	3	3	9	4
90	19	12	6	6	19	10
95	24	22	11	12	27	15
99	82	52	24	36	82	20
Range	0–82	0–52	0–24	0–36	0–82	0–20

The listing of percentiles allows the readout of the percentage of patients diagnosed at specific time intervals.

CD = Crohn disease; IBD = inflammatory bowel disease; UC = ulcerative colitis.

DISCUSSION

Our study is the first one to systematically assess distinct time intervals of diagnostic delay in pediatric patients with IBD and has several clinically important messages. First, diagnostic delay is longer in children with CD compared to children with UC. Second, parents seem to address children quickly for workup of IBD-related complaints, whereas the period from first physician visit to establishment of the IBD diagnosis may require some time. And third, no specific risk factors could be identified for the length of diagnostic delay in children with CD or UC.

In children with CD the median diagnostic delay from first symptom onset to diagnosis was 4 months, which is significantly longer than that in patients with UC (2 months). Our data are in accordance with 3 studies that systematically evaluated the diagnostic delay in pediatric patients with IBD. Sawczenko and Sandhu (9) evaluated diagnostic delay among 739 newly diagnosed pediatric patients with IBD in Great Britain and Ireland. They found a median diagnostic delay of 5 months. Diagnostic delay was comparable when comparing CD patients with persons experiencing UC (median 0.5 vs 0.4 years). Similar to our data, they found that one-fifth of the IBD population presented with a delay of more than 1 year. Delays were most common in patients with CD and in younger children. Of note, only 1 quarter of patients with CD presented with the classical symptoms of diarrhea, weight loss, and abdominal pain (9). Our Swiss data are in line with findings from Heikenen and coworkers (8) who found an average diagnostic delay of 7.1 months in patients with CD and 6.7 months in patients with UC. Length of diagnostic delay in patients with CD depended on disease location (10.5 months for small intestinal CD; 7.5 months for ileocolonic CD; and 6.4 months for colonic CD). They found that children experiencing growth failure presented with the longest diagnostic delay. In contrast to the findings described by Sawczenko, most patients with IBD presented with abdominal pain, diarrhea, hematochezia, and weight loss. Timmer and coworkers (11) evaluated the length of diagnostic delay in a German group of 2436 pediatric patients with IBD. They documented a median diagnostic delay of 4 (IQR 2–8) months. Patients with CD experiencing ileal location were found to be associated with delayed diagnosis. In line with data from Heikenen, the authors found that growth failure was observed more frequently in patients with delayed diagnosis. In contrast, the chances for early diagnosis increased with increasing age (11).

How can we reduce the diagnostic delay in pediatric patients with IBD? Our data reveal that pediatric patients with IBD are referred relatively quickly to the physician. There may, however, be a problem with a delay on physician's side. We think that the use of fecal biomarkers such as fecal calprotectin or lactoferrin has the potential to reduce diagnostic delay in pediatric patients with IBD (12,13). The high sensitivity of fecal calprotectin in detecting bowel inflammation can help in the decision which patients are in need for rapid endoscopic workup (12,13). The question may arise if it is at all clinically relevant to keep the diagnostic delay as short as possible. Increasing evidence indicates that this should indeed be a primary goal given the increased therapy success in early disease (14–16).

In summary, we demonstrate in a large nationwide Swiss cohort that the diagnostic delay in patients with CD is significantly longer than that in patients with UC. Increased awareness among members of general public and health practitioners is mandatory to decrease the diagnostic delay in pediatric patients with IBD.

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