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Pediatric Gastroenterologists' Approach to Venous Thromboembolism Prophylaxis in Pediatric Inflammatory Bowel Disease

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Abstract

The risk of venous thromboembolism (VTE) is significantly increased in inflammatory bowel disease (IBD) patients. For the adult population, prophylaxis guidelines exist to help guide physicians in their management of high-risk IBD patients. While it is known that children with IBD also experience increased rates of VTE, there is no clear consensus on how best to prevent these unwanted complications. We sought to better understand practicing pediatric gastroenterologists' awareness of this issue and practices surrounding prevention of VTE in their pediatric patients. We found that pediatric gastroenterologists are well aware of the increased risk for VTE in children with IBD, that anticoagulant prophylaxis is infrequently used for pediatric patients, and that the most commonly cited reason for not providing prophylaxis is the lack of available guidelines in the literature.

Inflammatory bowel disease (IBD), comprised of Crohn's Disease (CD) and Ulcerative Colitis (UC), is a condition that causes chronic, relapsing inflammation of the gastrointestinal tract. 20–30% of patients with IBD are diagnosed during childhood, and the

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incidence of IBD in children is increasing.^{1,2} Venous thromboembolism (VTE) is becoming an increasingly recognized complication of IBD that can lead to significant morbidity and mortality.

Studies of adult patients have shown that IBD is an independent risk factor for VTE, with an increased risk of 1.5–3.5 times that of the general population.^{3,4} While pediatric IBD patients are less likely than adults to develop VTE, they too have a significantly increased risk compared to children without IBD.^{5,6} Children with IBD have been reported to develop thromboses in various body regions, including the brain, extremities, liver, and lungs.⁶ Sequelae of VTE can include cognitive dysfunction, post-thrombotic syndrome, and in rare cases, death. In addition to the health burden on the patient, there are increased financial costs associated with VTE causing further strain on the patient and health care system.⁷

Several groups have formally addressed the risk of VTE in adult IBD patients and recommended practices include both mechanical and pharmacological methods.^{8,9} Despite these efforts, many adult gastroenterologists remain unaware of the risk and do not incorporate VTE prophylaxis into their practice.¹⁰ While some pediatric IBD experts have published their recommendations regarding VTE prophylaxis for children with IBD, no formal pediatric guidelines exist.^{7,11} Because of this, we chose to evaluate whether pediatric gastroenterologists are aware of the increased VTE risk among children with IBD, and identify what their practices are regarding prophylaxis.

Methods

This study consisted of a 21-question survey (approved by the Weill Cornell Medicine Institutional Review Board, Supplemental Digital Content 1) that was sent to pediatric gastroenterologists on the NASPGHAN membership list serve. Inclusion criteria required that participants were practicing attending physicians who treated at least 5 IBD patients per year. Survey questions were designed with the help of statisticians with extensive experience in survey-based research, and were pre-tested on members of the division of pediatric gastroenterology at Weill Cornell. Questions were then edited for clarity and content based on pre-test commentary.

REDCap, an electronic data capture tool hosted by the Clinical and Translational Science Center at Weill Cornell, was utilized to collect responses. Survey items included demographic information and questions regarding practice characteristics. Research questions focused on awareness and experience with VTE in IBD patients, practices regarding VTE prophylaxis, and practices regarding thrombophilia evaluation and hematology consultation.

Results

Of the potential 1640 pediatric gastroenterologists surveyed, 162 responded. Nine responses were excluded based on inclusion criteria, leaving 153 surveys eligible for inclusion (a 9.3% response rate.) The majority of respondents reported working at an academic center, as opposed to community hospitals or private practice settings (Supplemental Digital Content 2.) Simple frequencies were used to summarize demographic and practice data. Fisher's

exact test and Chi-square test were used to evaluate relationships between awareness of VTE risk and practice questions, as well as between prophylaxis practice and recent exposure to patients with VTE. All statistical tests were two-sided and $p < 0.05$ was considered statistically significant. Analyses were performed in SAS Version 9.4 (SAS Institute Inc., Cary, N.C.).

When asked how strongly they agreed with the statement “pediatric IBD patients are at increased risk for VTE”, 92% of participants expressed agreement with this statement, with just over 50% strongly agreeing. When respondents were asked about VTE in their IBD patients, approximately 1/3 reported they had not had an IBD patient develop a VTE. When asked about their practices regarding VTE prophylaxis in IBD patients, only 1/3 reported providing VTE prophylaxis to their IBD patients (36% do provide, versus 64% do not provide). Prophylaxis was most commonly provided during an inpatient hospitalization for an IBD flare (Table 1.) Use of mechanical and pharmacological prophylaxis was evenly split among those providing prophylaxis.

Among those who did not provide prophylaxis, the most common reason cited was the lack of pediatric literature (Table 2.) Concern for risk of bleeding, lack of comfort providing prophylaxis, and patient resistance to anticoagulant medications were also cited by over 10% of respondents. Among those who did not provide prophylaxis, almost all agreed or strongly agreed that children with IBD are at increased risk of VTE. When looking at prophylaxis practices and experience with patients with VTE, there was a statistically significant relationship between providing prophylaxis and exposure to a patient with VTE episodes in the past 24 months (chi-square with one degree of freedom = 4.999, $p=0.025$.) Most respondents reported that their institutions did not have a written protocol for VTE prophylaxis. Of the small number of protocols that did exist, most were based on adult guidelines.

When discussing hematologic evaluations, 18 respondents reported performing a thrombophilia evaluation during assessment of their IBD patients. For those who do perform an evaluation, it was primarily done during first hospitalization or at diagnosis of first VTE. Histories were uniformly obtained and 2/3 reported that they did lab screening. Tests performed included Factor V Leiden, protein C & S levels, and antiphospholipid antibodies.

Discussion

This survey was designed to evaluate pediatric gastroenterologists’ perceptions and practices regarding VTE in pediatric IBD patients. We showed that the vast majority of respondents recognize the increased risk of VTE among children with IBD, and that prophylaxis against VTE is not provided by the majority of participants. The most common reason for this discrepancy was the lack of clear pediatric guidelines. Given the increased incidence of VTE in children with IBD, a prospective, multicenter study assessing the safety and efficacy of anticoagulant VTE prophylaxis seems warranted. Currently, a national quality improvement initiative for children’s hospitals through Solutions for Patient Safety is working to minimize hospital-acquired VTE, and this will likely carry over to children with IBD. There is currently no evidence that a thrombophilia evaluation is warranted in all children with IBD,

and it was interesting that some respondents do screen patients for thrombophilias. Certainly, ensuring that a thorough VTE-relevant personal and family history is obtained in all children with IBD is a reasonable initial screening approach. Collaboration between pediatric gastroenterologists and hematologists would allow for further understanding, more complete clinical assessments, and the opportunity for a more comprehensive and effective prospective, multicenter clinical trial in the future.

Our study had some clear limitations, most noticeably the low response rate. While this limits the generalizability of our findings, we feel that there are still valuable insights that could help inform the development of future clinical trials. Most participants were from academic centers, but because the survey was anonymous, it is not clear how widely distributed those academic centers are, and if many respondents are clustered from larger centers with the same experiences. Some participants did not answer various questions; it is not clear if the questions and/or answers were too vague or if respondents simply chose not to answer them.

Despite its limitations, this study highlights that pediatric gastroenterologists are aware of the increased VTE risk among children with IBD. There is a clear need for a better understanding of the burden of VTE among pediatric IBD patients, as well as the best strategies to utilize to minimize this risk. Our group, utilizing partnership between pediatric hematology and gastroenterology, is working to gain further understanding of this issue. We believe that collaborative research will ultimately allow for the development of pediatric-specific VTE prophylaxis guidelines for children with IBD.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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What is known

- VTE risk is increased in adults and children with IBD
- VTE prophylaxis is recommended in adults with IBD in certain clinical settings

What is new

- Pediatric gastroenterologists are aware of the increased risk of VTE in children with IBD
- VTE prophylaxis is being provided by only about 1/3 of physicians
- The number one reason cited for not providing prophylaxis is lack of published literature, emphasizing the need for collaborative clinical trials and guideline development.

Table 1:

Among those practitioners who do provide prophylaxis, settings when they do provide prophylaxis

Characteristics	Yes	No
Inpatient, not experiencing flare	10 (19.61%)	41 (80.39%)
Inpatient, experiencing flare	52 (96.30%)	2 (3.70%)
Outpatient, not experiencing flare	1 (1.92%)	51 (98.08%)
Outpatient, experiencing flare	5 (9.80%)	46 (90.20%)
Other setting not specified	5 (10.20%)	44 (89.80%)

Table 2:

Among those practitioners who do not provide prophylaxis, reasons why prophylaxis is not provided

Characteristics	Yes	No
Concern for risk of bleeding	38 (48.72%)	40 (51.28%)
Not comfortable prescribing VTE prophylaxis	45 (56.25%)	35 (43.75%)
Lack of pediatric literature	70 (81.40%)	16 (18.60%)
Patient resistance to medication	22 (30.56%)	50 (69.44%)
Other	20 (40.00%)	30 (60.00%)