Thrombotic and Infectious Risks of Parenteral Nutrition in Hospitalized Pediatric Inflammatory Bowel Disease

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Background: Malnutrition is common in inflammatory bowel disease (IBD), requiring timely and sufficient nutritional supplementation. In patients hospitalized for active disease, symptoms and/or altered intestinal function hinder enteral nutrition feasibility. In this scenario, parenteral nutrition (PN) is used. We aimed (1) to assess the frequency of PN use between 1997 and 2012 among hospitalized pediatric patients with IBD, (2) to determine the risk of in-hospital thrombus and infection associated with PN, and (3) to identify predictors of thrombus and infection in pediatric IBD hospitalizations utilizing PN.

Methods: We performed a cross-sectional analysis of pediatric patients hospitalized between 1997 and 2012. We used the Kids' Inpatient Database (KID) to identify pediatric patients (≤18 years of age) with Crohn's disease (CD) or ulcerative colitis (UC), PN exposure, and primary outcomes including thrombus and infection. We used multivariable regression to identify risk factors for outcomes of interest.

Results: Parenteral nutrition was utilized in 3732 (12%) of 30,914 IBD hospitalizations. Three percent of PN patients experienced a thrombotic complication, and 5.5% experienced an infectious complication. Multivariate analysis showed PN as an independent risk factor for thrombus (odds ratio [OR], 4.3; 95% confidence interval [CI], 3.2–5.6) and infection (OR, 3.8; 95% CI, 3.1–4.6). Surgery was an independent risk factor for thrombus (OR, 2.0; 95% CI, 1.4–2.7) and infection (OR, 2.5; 95% CI, 2.0–3.1) in hospitalizations exposed to PN.

Conclusions: Hospitalized pediatric IBD patients, particularly surgical, receiving PN are at increased risk for thrombosis and infection. Clinicians must balance these risks with the benefits of PN.

Key Words: thrombus, infection, absolute risk, number needed to harm, pediatric, Crohn's disease, ulcerative colitis, parenteral nutrition

INTRODUCTION

Malnutrition is common in inflammatory bowel disease (IBD), requiring timely and sufficient nutritional supplementation. In patients hospitalized for active disease, disease symptoms and/or altered intestinal function may hinder enteral nutrition feasibility. In this scenario, parenteral nutrition (PN) is used.[1] Yet, the benefits of PN must be weighed against the risks, including thrombus formation[2] and systemic infections,[3] associated with using central venous lines (CVLs) for parenteral infusion. Additionally, these risks may be potentiated in patients with IBD due to the hypercoagulable state,[4–6] use of immunosuppressive therapy,[7, 8] and frequent malnutrition.[9]

Although the IBD-specific risks of PN on inpatient thrombus (2%–72%[10–12]) and infection (0.4–13.3/1000 catheter-days[13]) have been established in adult populations, the magnitude of these risks in children with IBD is likely to be quite different given differing age ranges and comorbidity profiles. Therefore, quantifying the absolute risks of PN in the hospitalized pediatric IBD population is needed to inform clinical decision-making. In this study, we leveraged a large national pediatric inpatient database (Kids' Inpatient Database [KID]) to accomplish the following aims: (1) to assess time trends in the frequency of PN use among hospitalized pediatric patients with IBD, (2) to determine the risk of in-hospital thrombus and infection associated with PN use, and (3) to identify factors predictive of these adverse events in pediatric IBD hospitalizations initiating PN.

METHODS

Study Design and Data Source

We performed a cross-sectional analysis using 1997–2012 data from the Kids' Inpatient Database (KID), a nationally representative sample of pediatric hospitalizations from the Healthcare Cost and Utilization Project (HCUP), sponsored by the Agency for Healthcare Research and Quality (AHRQ). KID is the largest publicly available all-payer pediatric

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inpatient database from the United States and includes data from 2–3 million yearly hospitalizations from 1997–2012 HCUP.[14] Utilizing data from up to 44 states depending on the year analyzed, the KID is designed to be nationally representative of pediatric hospital inpatient stays. The database contains more than 75 clinical and nonclinical variables, 25 *International Classification of Diseases, 9th Revision, Clinical Modification* (ICD-9-CM) diagnostic and procedure codes, hospital characteristics, and outcomes.[14]

Study Sample

We examined discharge data from hospitalizations of patients age 18 years and younger. Hospitalizations with an ICD-9-CM diagnostic code indicating CD (555.xx) or UC (556.xx) at position #1 (primary diagnosis) were eligible for inclusion in this study. In addition, any hospitalization with an ICD-9-CM diagnostic code indicating CD (555.xx) or UC (556.xx) at diagnostic code position #2 or position #3 was included when the primary diagnosis was consistent with an IBD hospitalization. For all hospitalizations where CD or UC was in position #2 or #3, the primary diagnoses that occurred at a frequency of 0.5% or greater were reviewed by 2 pediatric gastroenterologists and classified as "consistent with IBD hospitalization" or "unlikely to be related to an IBD hospitalization." Similar inclusion/exclusion rules have been used in prior HCUP study publications.[15, 16] A final list of codes considered "consistent with an IBD hospitalization" can be found in Supplementary Table 1. Diagnoses with frequencies of less than 0.5% were not reviewed.

Exposure of Interest

The primary exposure was the use of PN during hospitalization, identified by the ICD-9 procedural code 99.15. This code includes PN administration through both central and peripheral catheters.

Outcomes of Interest

We identified outcomes of PN-associated thrombi and infections based on discharge ICD-9-CM codes. We made the a priori decision to evaluate the following thrombotic outcomes: venous or arterial thrombus or embolism of the upper and lower limbs, thrombophlebitis, septic embolism, pulmonary embolism, and embolism or other vascular complications due to transfusion, infusion, or perfusion. No events of septic emboli occurred in the data. We did not evaluate cardiovascular outcomes such myocardial infarction, stroke, or mesenteric ischemia, as these events can be associated with inciting events other than thrombus in children. We made the a priori decision to evaluate the following infections deemed likely to be related to central lines and/or the use of PN: sepsis, bacteremia, septicemia, viremia, systemic inflammatory response syndrome (SIRS), endocarditis, venous catheter infection, cellulitis, and infection/sepsis/septicemia associated with infusion. A final list of included codes for thrombus and infection can be found in Supplementary Tables 2 and 3, respectively. We also analyzed a composite outcome of "any complication," as defined by any of the above thrombus or infection codes. Hospital discharges with both infection and thrombus discharge codes were included only once in the composite outcome.

Covariates

We evaluated patient demographics, including age, sex, race, IBD abdominal hospitalization with abdominal surgery, and primary insurance/payer for the hospitalization. We categorized age as <6 years, 6–12 years, and 13–18 years. We defined race using uniform coding provided by HCUP, where Hispanic patients were uniquely identified without use of a Hispanic modifier code. We combined Asian, Pacific Islander, and Native American ethnicities into a single category based on low individual sample frequencies. We defined payer type as Medicaid, private/HMO, or other. Other combined "no charge," "Medicare," and "self-pay." Hospitalization with abdominal surgery was defined as the presence or absence of ICD-9 procedural coding for small or large bowel procedures. We also analyzed hospital-level characteristics including location and teaching status (rural, urban nonteaching, or urban teaching). A complete list of abdominal surgical procedural codes can be found in Supplementary Table 4.

Statistical Analysis

All analyses were performed using SAS, version 9.4 (SAS Institute, Cary, NC, USA). Descriptive statistics included frequency counts. We used univariate and bivariate analyses to quantify absolute risk, risk difference, and number needed to harm (NNH). We used the chi-square test for bivariate analysis of association between categorical variables. We summarized parametric continuous variables with mean and standard deviation and summarized nonparametric data using median and interquartile range (IQR). We used a Cochran-Armitage test of trend for analysis of triennial prevalence of parenteral nutrition in pediatric IBD hospitalizations.

We used multivariable logistic regression to evaluate the association between the primary predictor, PN exposure, and the individual outcomes of thrombus, infection, and composite complication. We controlled for covariates including age, sex, race, disease type, hospitalization with abdominal surgery, year, payer type, and hospital type. Interaction terms for year*PN and for abdominal surgery*PN were included in the model and were not statistically significant. Odds ratios (ORs) and 95% confidence intervals (CIs) are presented. We constructed separate models for CD and UC hospitalizations and a model for overall IBD hospitalizations. All covariates were selected a priori based on clinical relevance and previously published literature.[5, 6, 8, 13, 17]

We developed a second set of models using multivariable logistic regression to evaluate risk factors for outcomes of thrombus, infection, and composite complication in hospitalizations exposed to PN. Covariates included hospitalization with abdominal surgery, year, age, sex, race, payer type, and hospital type. As above, we constructed unique models for CD, UC, and IBD overall.

A 2-tailed *P* value of 0.05 was chosen as the threshold for statistical significance in bivariate analysis and multivariable regression.

Ethical Considerations

Due to the de-identified nature of the data, this study was determined exempt from review by the University of North Carolina Institutional Review Board (IRB).

RESULTS

We identified 30,914 hospitalizations of pediatric patients with IBD in the 1997–2012 KID database. Of these, 19,158 (62%) hospitalizations were for CD, and the remaining were for UC. The median age of the study sample (IQR) was 15 (12–17) years. Approximately half of the IBD patient hospitalizations occurred in females (49%). Just under three-quarters of the IBD hospitalizations were in Caucasians (71%), and the largest contributing payer type was private/HMO insured (71%). Inflammatory bowel disease hospitalizations in this sample occurred most frequently at urban teaching centers (74%).

Use of Parenteral Nutrition

Parenteral nutrition was utilized in 3732 (12%) pediatric IBD hospitalizations (2363 CD and 1369 UC). Table 1 summarizes discharge characteristics for pediatric IBD hospitalizations involving PN and those not involving PN. As shown in Figure 1, the prevalence of PN during hospitalization for pediatric patients with IBD did not differ in the triennial intervals between 1997 and 2012 ($P = 0.78$). Patients hospitalized with CD were no more likely to receive PN than patients

TABLE 1. Clinical and Demographic Characteristics of Pediatric IBD Hospitalizations Using the KID Database from 1997–2012

Characteristics	PN (n = 3732)		No PN (n = 27,182)		Total (n = 30,914)	
	Median	IQR	Median	IQR	Median	IQR
Age, y	15	12–16	15	12–17	15	12–17
	No.	%	No.	%	No.	%
Age categories, y						
<6	208	5.6	1301	4.8	1509	4.9
6–12	891	23.8	6006	22.1	6897	22.3
12–18	2633	70.6	19,875	73.1	22,508	72.8
Female	1796	48.1	13,494	49.6	15,290	49.4
Race						
White	2267	60.7	15,565	57.2	17,832	57.7
Black	406	10.8	2919	10.7	3325	10.7
Hispanic	252	6.7	1992	7.4	2244	7.3
Other	206	5.6	1259	4.7	1465	4.8
Missing	601	16.2	5447	20	6048	19.5
Payer type						
Medicaid	717	19.3	5967	21.9	6684	21.7
Private/HMO	2751	73.7	19,259	70.9	22,010	71.2
Other	257	6.9	1902	7	2159	6.9
Missing	7	0.1	54	0.2	61	0.2
Presence of a surgical procedure	836	16	4396	84	5232	16.9
Hospital type						
Rural	94	2.5	1334	4.9	1428	4.6
Urban/nonteaching	398	10.6	5152	18.9	5550	17.9
Urban/teaching	3086	82.8	19,924	73.4	23,010	74.4
Missing	154	4.1	772	2.8	926	3.1
Disease type						
CD	2363	63.3	16,795	61.7	19,158	61.9
UC	1369	36.7	10,387	38.2	11,756	30.1

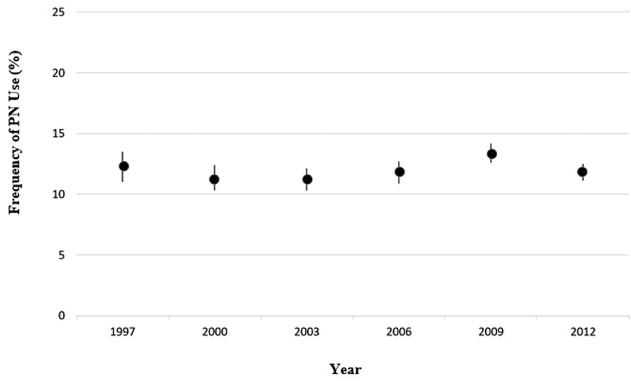

FIGURE 1. Triennial prevalence of PN in pediatric IBD hospitalizations using the 1997–2012 KID database ($P = 0.78$). Point prevalence and 95% CI demonstrate a consistent prevalence from 1997 to 2012.

hospitalized with UC (12.3% vs 11.6%; $P = 0.07$). For CD, UC, and IBD overall, patients hospitalized with abdominal surgical procedures were more likely to receive PN ($P < 0.01$ for all).

Thrombus

Thrombus occurred in 115 pediatric IBD hospitalized patients receiving PN, yielding an absolute risk of 3%. The most common discharge diagnosis codes for thrombi in this population were acute venous embolism of the upper extremity (35%), thrombophlebitis (28%), and pulmonary embolism (22%). In contrast, the absolute risk of thrombus in non-PN-treated patients was 0.6%. This resulted in a risk difference of 2.4% (95% CI, 1.8–3.0) and a corresponding number needed to harm of 42. Table 2 illustrates outcome by disease type.

Adjusted analysis demonstrated an increased risk for thrombus in PN-treated patients as compared with those not receiving PN (CD: OR, 5.8; 95% CI, 3.9–8.5; UC: OR, 3.6; 95% CI, 2.2–4.9; IBD: OR, 4.3; 95% CI, 3.2–5.6) (Table 3A).

Infection

Infection occurred in 207 pediatric IBD hospitalizations receiving PN, resulting in an absolute risk of 5.5%. The most common discharge diagnosis codes for infection in this population were septicemia (35%), cellulitis (26%), and catheter-associated infections (14%). In contrast, the absolute risk of infection associated with hospitalizations not exposed to PN was 1.4%. The risk difference was 4.1% (95% CI, 3.4%–4.9%), with a number needed to harm of 24 hospitalizations.

Adjusted analysis demonstrated an increase in the risk of infection in PN-treated patients, as compared with those not receiving PN (CD: OR, 3.5; 95% CI, 2.8–4.5; UC: OR, 4.4; 95% CI, 3.1–6.1; IBD: OR, 3.8; 95% CI, 3.1–4.6) (Table 3B).

Complication

The absolute risk of either thrombus or infection (composite outcome) was 8% among pediatric IBD hospitalizations receiving PN. The absolute risk of either event in non-PN-treated hospitalizations was 2%, resulting in a risk difference of 6% (95% CI, 5.2%–6.9%) and a number needed to harm of 17 hospitalizations.

Adjusted analysis demonstrated an increase in the risk of complication associated with pediatric IBD hospitalizations receiving PN, as compared with those not receiving PN (CD: OR, 3.9; 95% CI, 3.1–4.8; UC: OR, 3.9; 95% CI, 3.0–5.1; IBD: OR, 3.9; 95% CI, 3.3–4.6) (Table 3C).

Risk Factor for Thrombus and/or Infection in Hospitalizations Associated With PN

Among pediatric hospitalizations for IBD involving PN, we next analyzed the effects of age, gender, race, payer type, hospital type, year, and the presence of abdominal surgery on inpatient events of thrombus or infection. Only hospitalizations with abdominal surgery were a consistent and independent risk factor for these outcomes. A total of 5232 (16%) pediatric IBD hospitalizations involved an abdominal surgical procedure. Of these, 3067 (58.6%) occurred in CD hospitalizations, and the remaining 2165 (41.4%) occurred in UC hospitalizations. After controlling for age, sex, race, payer type, year, and hospital type, hospitalizations with abdominal surgery were associated with an increased risk of thrombus (OR, 1.9; 95% CI, 1.2–3.0),

TABLE 2. Number of Events of Interest and Absolute Risk According to Disease Type and Exposure Status

Outcome	Crohn's Disease						Ulcerative Colitis					
	PN		No PN		Total		PN		No PN		Total	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Thrombus	68	2.8	83	0.5	151	0.8	47	3.4	103	1.0	150	1.2
Infection	133	5.6	253	1.5	386	2.0	74	5.4	131	1.2	205	1.7
Complication	186	7.8	330	0.9	516	2.6	116	8.4	226	2.1	342	2.9
Total sample	2363		16,795		19,158		1369		10,387		11,756	

"Total sample" represents the entire study sample size for disease type and exposure status from the KID Inpatient Database from 1997 to 2012.

TABLE 3A. Multivariable Analysis, OR and 95% CI of *Thrombus* Among Pediatric IBD Hospitalizations for CD, UC, and Total IBD in the 1997–2012 KID Database

Characteristics	Crohn's Disease		Ulcerative colitis		All IBD	
	OR	95% CI	OR	95% CI	OR	95% CI
Parenteral nutrition	5.7	3.9–8.4	3.2	2.2–4.8	4.3	3.2–5.7
Age category, y						
<6	Ref		Ref		Ref	
6–12	0.4	0.1–1.5	0.7	0.2–1.7	0.6	0.3–1.3
12–18	1.0	0.3–2.8	1.5	0.7–3.4	1.3	0.7–2.5
Female	0.6	0.4–1.0	1.3	0.9–1.9	0.9	0.7–1.2
Race category						
White	Ref		Ref		Ref	
Black	0.8	0.4–1.5	1.3	0.7–2.3	1.0	0.6–1.5
Hispanic	0.9	0.4–2.0	0.2	0.1–0.7	0.5	0.3–0.9
Other	1.2	0.5–2.6	1.6	0.9–2.9	1.4	0.8–2.2
Payer type						
Medicaid	1.4	0.9–2.2	1.2	0.7–1.9	1.3	0.9–1.8
Private/HMO	Ref		Ref		Ref	
Other	1.2	0.6–2.6	0.3	0.1–1.2	0.8	0.4–1.4
Presence of a surgical procedure	1.6	1.0–2.6	2.3	1.5–3.5	2.0	1.5–2.6
Hospital type						
Rural	0.2		0.7		0.5	
Urban/nonteaching	1.3	0.03–1.8	0.7	0.2–2.1	1.0	0.2–1.3
Urban/teaching	Ref	0.8–2.1	Ref	0.4–1.3	Ref	0.7–1.4
Year						
1997	Ref		Ref		Ref	
2000	1.2	0.3–4.3	0.5	0.2–1.6	0.8	0.3–1.8
2003	2.4	0.8–7.3	0.6	0.2–1.7	1.3	0.6–2.6
2006	2.9	1.0–8.7	0.9	0.3–2.1	1.6	0.8–3.1
2009	1.8	0.6–5.5	1.5	0.6–3.2	1.6	0.8–3.1
2012	3.3	1.2–9.5	1.6	0.7–3.4	2.2	1.2–4.1
Disease type						
UC	NA		NA		1.8	1.4–2.3
CD					Ref	

infection (OR, 2.3; 95% CI, 1.6–3.2), and overall complication (OR, 2.1; 95% CI, 1.5–2.7) (Table 4). After stratifying by CD and UC, all associations remained statistically significant, with the exception of thrombus among CD and UC patients, for which we observed a consistent numeric trend (OR, 1.8; 95% CI, 1.0–3.4; and OR, 2.0; 95% CI, 1.0–4.1, respectively). Supplementary Table 5A–C provides the effect estimates for the other covariates.

DISCUSSION

In a nationally representative sample of pediatric hospitalizations, we found that PN was utilized in approximately 12% of IBD hospitalizations. Parenteral nutrition utilization remained stable from 1997 to 2012. Our results confirm that PN is associated with a clinically and statistically increased risk of thrombus, infection, and composite complication in both CD and UC. Lastly, our study demonstrated that the presence of an abdominal surgical procedure during hospitalization is an independent risk factor for these PN-associated adverse events.

Our study's findings emphasize the need for careful consideration of PN use in pediatric IBD hospitalizations, particularly those hospitalizations involving an abdominal surgical procedure. A prior study of adult IBD revealed a 6.8% absolute risk of thrombus associated with peripherally inserted central catheters (PICCs), frequently present in the setting of PN use. In this study, the authors did not find a statistical difference in the prevalence of thrombus between patients with a CVL exposed to PN vs those with a CVL who were unexposed.[12]

TABLE 3B. Multivariable Analysis, OR and 95% CI of *Infection* Among Pediatric IBD Hospitalizations for CD, UC, and Total IBD in the 1997–2012 KID Database

Characteristics	Crohn's Disease		Ulcerative Colitis		All IBD	
	OR	95% CI	OR	95% CI	OR	95% CI
Parenteral nutrition	3.5	2.8–4.5	4.4	3.1–6.1	3.8	3.1–4.6
Age categories, y						
<6	Ref		Ref		Ref	
6–12	1.0	0.4–2.0	0.6	0.3–1.0	0.7	0.4–1.1
12–18	1.1	0.5–2.2	0.5	0.3–0.9	0.7	0.4–1.1
Female	0.8	0.6–1.0	0.9	0.6–1.2	0.8	0.7–1.0
Race category						
White	Ref		Ref		Ref	
Black	1.5	1.1–2.1	1.3	0.7–2.3	1.5	1.1–1.9
Hispanic	1.1	0.7–1.7	1.6	1.0–2.5	1.3	0.9–1.7
Other	1.2	0.7–2.0	1.4	0.7–2.4	1.3	0.9–1.9
Payer type						
Medicaid	1.2	0.9–1.7	1.4	0.9–2.1	1.3	1.0–1.6
Private/HMO	Ref		Ref		Ref	
Other	1.8	1.2–2.7	1.3	0.7–2.5	1.6	1.2–2.3
Presence of a surgical procedure	2.2	1.7–2.9	3.0	2.1–4.3	2.5	2.0–3.1
Hospital type						
Rural	1.0	0.5–1.8	1.2	0.5–2.8	1.0	0.6–1.7
Urban/nonteaching	0.9	0.7–1.3	0.9	0.6–1.5	0.9	0.7–1.2
Urban/teaching	Ref		Ref		Ref	
Year						
1997	Ref		Ref		Ref	
2000	0.6	0.3–1.1	0.6	0.3–1.4	0.6	0.4–1.0
2003	1.2	0.7–2.0	1.0	0.5–1.9	1.1	0.7–1.6
2006	1.0	0.6–1.7	0.8	0.4–1.6	0.9	0.6–1.4
2009	1.1	0.7–1.8	0.7	0.3–1.3	1.0	0.6–1.4
2012	1.0	0.6–1.6	0.7	0.4–1.4	0.9	0.6–1.3
Disease type						
UC					0.7	0.6–0.9
CD	NA		NA		Ref	

Receipt of PN in this study was determined by the indication reported for placement of the CVL. It therefore may have underestimated the number of PN-exposed patients who initially received the CVL for indications other than PN but who were ultimately exposed. In contrast to these adult data, our data reflect a lower absolute risk (3%) of thrombus in the hospitalized pediatric IBD population studied, likely due to the well-described age-dependent risk of thrombus in the general population[18] and IBD populations.[19]

The adult literature also suggests that PN is associated with an increased risk of infection. Using data from a nationally representative inpatient database, the Nationwide Inpatient Sample, Ananthakrishnan et al. demonstrated a 2-fold risk of infections associated with the use of PN, although this study did not present data on absolute risks.[20]

The pediatric literature regarding the risks associated with PN among IBD patients is more limited. Nylund et al. previously described the increased risk of thrombotic events in hospitalized children with IBD using the KID database.[5] In that study, the authors identified PN as a risk factor for thrombus formation. Our work both confirms and extends these earlier findings. Our results are novel as they highlight the association between PN use and both thrombus and infectious outcomes using absolute risk, risk difference, and NNH associated with PN—the critical inputs of evidence-based medicine and clinical decision-making. Our results reinforce the need to consider age-specific risk and avoid extrapolation of risk estimates taken from adult studies. Our data may be used to inform clinicians and families in decision-making regarding the initiation of PN for inpatient nutrition management in pediatric IBD

TABLE 3C. Multivariable Analysis, OR and 95% CI of *Complication* Among Pediatric IBD Hospitalizations for CD, UC, and Total IBD in the 1997–2012 KID Database

Characteristics	Crohn's Disease		Ulcerative colitis		All IBD	
	OR	95% CI	OR	95% CI	OR	95% CI
Parental nutrition	3.9	3.1–4.8	3.9	3.0–5.1	3.9	3.3–4.6
Age category, y						
<6	Ref		Ref		Ref	
6–12	0.8	0.4–1.5	0.6	0.4–1.1	0.7	0.4–1.0
12–18	1.0	0.5–1.8	0.8	0.5–1.3	0.9	0.6–1.3
Female	0.8	0.6–1.0	1.0	0.8–1.3	0.9	0.7–1.0
Race category						
White	Ref		Ref		Ref	
Black	1.4	1.0–1.8	1.3	0.9–2.0	1.3	1.1–1.7
Hispanic	1.0	0.7–1.5	0.9	0.6–1.4	1.0	0.7–1.3
Other	1.2	0.8–1.9	1.5	1.0–2.3	1.3	1.0–1.8
Payer type						
Medicaid	1.3	1.0–1.6	1.3	1.0–1.8	1.3	1.1–1.6
Private/HMO	Ref		Ref		Ref	
Other	1.6	1.1–2.2	0.9	0.5–1.6	1.3	1.0–1.7
Presence of a surgical procedure	2.0	1.6–2.5	2.7	2.1–3.5	2.3	1.9–2.7
Hospital type						
Rural	0.8	0.4–1.5	1.0	0.5–2.0	0.9	0.6–1.4
Urban/nonteaching	1.0	0.8–1.4	0.9	0.6–1.3	1.0	0.8–1.2
Urban/teaching	Ref		Ref		Ref	
Year						
1997	Ref		Ref		Ref	
2000	0.6	0.4–1.1	0.6	0.3–1.2	0.6	0.4–1.0
2003	1.3	0.8–2.1	0.9	0.5–1.6	1.1	0.8–1.6
2006	1.2	0.7–1.9	0.8	0.5–1.5	1.0	0.7–1.4
2009	1.2	0.8–1.9	1.0	0.6–1.6	1.1	0.8–1.5
2012	1.3	0.8–1.9	1.0	0.6–1.7	1.1	0.8–1.6
Disease type						
UC					1.0	0.9–1.2
CD	NA		NA		Ref	

hospitalizations. Our results are also strengthened by our use of a nationally representative data set for pediatric hospitalizations, thereby providing more generalizable conclusions than previously published single-center studies.[17, 21]

An additional novel aspect of our study is the use of a composite outcome of either thrombus or infection associated with PN use. We believe this composite outcome serves as a clinically useful outcome to aid in clinical decision-making. Indeed, an 8% absolute risk of PN related complications is high, resulting in a corresponding NNH of 17; however, prior studies have not evaluated the absolute risk of a composite outcome, making it difficult to compare our findings with previous results.

We also identified that, among IBD hospitalizations initiating PN, the presence of an abdominal surgical procedure conferred a 2–3-fold risk of developing thrombus, infection, or the composite event. Though not robustly researched in pediatric IBD, adult IBD studies have demonstrated an increased risk of both thrombus[22] and infection[20] in post–abdominal surgery adult IBD patients exposed to PN. Our results were statistically significant for all comparisons, with the exception of thrombus formation in the CD- and UC-stratified hospitalizations receiving PN. In both subgroups, we noted a numeric trend demonstrating elevated risk of adverse outcomes associated with surgical procedures. Though not statistically significant, each disease type demonstrated a 95% CI for hospitalization associated with the surgical procedure and adverse outcomes in those exposed to PN with lower bounds at 1.0. Despite this lower bound, adverse outcomes of thrombosis and infection in surgical hospitalizations remain a clinically significant problem.

TABLE 4. Adjusted or and 95% CI for Adverse Outcomes Comparing Surgical Pediatric IBD Hospitalizations Receiving Parenteral Nutrition With Nonsurgical Pediatric IBD Hospitalizations Receiving Parenteral Nutrition in the 1997–2012 KID Database

Outcome	Crohn's Disease		Ulcerative Colitis		All IBD	
	OR	95% CI	OR	95% CI	OR	95% CI
Thrombus	1.8	1.0–3.4	2.0	1.0–4.1	1.9	1.2–3.0
Infection	1.8	1.1–2.8	3.6	2.1–6.3	2.3	1.6–3.2
Complication	1.7	1.2–2.5	2.7	1.7–4.2	2.1	1.5–2.7

Also stratified by disease type. Analysis adjusted for age, sex, race, payer type, year, and hospital type.

Furthermore, hospitalizations associated with an abdominal surgical procedure likely involve sicker patients who may require longer exposure to PN, thus raising the absolute risk for adverse outcomes. As a result, development of thrombus or infection in these post–abdominal surgery IBD hospitalizations exposed to PN is a reasonable finding.

Our study has multiple strengths, including the use of a nationally representative sample of pediatric IBD hospitalizations to evaluate risks of PN use. The HCUP KID database provides a large sample size, facilitating a broad evaluation of the risks of PN use in pediatric IBD hospitalizations. Additionally, this regionally diverse and nationally representative database provided 15 years of data for analysis, allowing for trends in the prevalence of PN use to be reported on.

We acknowledge several limitations in our study. As with most epidemiologic studies that utilize administrative data, misclassification of patient condition, exposures, or outcomes identified by diagnosis or procedure codes is always possible. Despite this limitation, the KID database has been widely used in studies of pediatric IBD.[5, 23–26] Additionally, the use of the specific ICD-9 procedure code to identify PN exposure in the KID database and the adult Nationwide Inpatient Sample (NIS) is also well accepted in the medical literature.[5, 27] Another limitation to our study was the inability to measure and control for disease severity, prior PN use, and prior hospitalizations. Although we considered adjusting for additional clinical factors such as malnutrition and hypercoagulability, we decided against this given that the diagnosis codes were recorded in less than 1% of the entire sample, raising questions about validity. Thus, there is the potential for unmeasured confounding by indication, as sicker patients may be more likely to be started on PN and more susceptible to thrombi and infection. Furthermore, our study did not distinguish between the use of peripheral PN and central PN. Hence, differentiation between the risk of peripheral PN and central PN is beyond the scope of this manuscript, though prior studies have observed the risk of infections with peripheral PN to be quite small (0.1–0.5 per 1000 catheter-days).[28] Additionally, the KID database does not contain data regarding medication dispensing. Hence, we could not account for the use of thrombus prophylaxis in our analyses. Lastly, we acknowledge a number of limitations related to the cross-sectional structure of the KID database. First, the KID is structured at the level of the individual discharge rather than the individual patient. Thus, we could not differentiate between admissions for unique patients vs patients admitted multiple times. This may have slightly overestimated the risk of PN on thrombosis and infection. We also could not differentiate between patients whose PN started before vs during their hospitalization. Similarly, we could not assess the temporal relationship between the use of PN and the occurrence of thrombus and infection, though we speculate that thrombus and infection likely occurred after rather than before PN initiation in most instances.

In summary, we used a nationally representative sample of pediatric IBD hospitalizations to demonstrate that PN use in hospitalized patients is associated with an increase in absolute risk for thrombus, infection, and composite complication. In pediatric IBD hospitalizations involving PN, the presence of an abdominal surgical procedure is independently associated with an increase in the risk for adverse outcomes as well. Moving forward, these data can be used to inform risk–benefit trade-offs in the nutritional management of hospitalized pediatric IBD patients and can contribute to the development of clinical practice guidelines for the inpatient nutritional management of this patient population, with the ultimate goal of delivering safer, more effective care through risk awareness and management. At a minimum, these data emphasize the need for judicious use of intravenous nutrition, particularly in abdominal surgical patients.

SUPPLEMENTARY DATA

Supplementary data are available at *Inflammatory Bowel Diseases* online.

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