Characterizing Pediatric Familial Adenomatous Polyposis in Patients Undergoing Colectomy in the United States

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Objective To characterize a multi-institutional cohort of pediatric patients who underwent colectomy for familial adenomatous polyposis (FAP).

Study design In this retrospective cohort study, diagnosis and procedure codes were used to identify patients who underwent colectomy for FAP within the Pediatric Health Information System (PHIS). The inclusion criteria were validated at 3 children's hospitals and applied to PHIS to generate a cohort of patients with FAP between 2 and 21 years who had undergone colectomy between 2009 and 2019. Demographics, clinical and surgical characteristics, and endoscopic procedure trends as identified through PHIS are described. Descriptive and comparative statistics were used to analyze data.

Results Within the PHIS, 428 pediatric patients with FAP who underwent colectomy were identified. Median age at colectomy was 14 years (range 2-21 years); 264 patients (62%) received an ileal pouch anal anastomosis and 13 (3%) underwent ileorectal anastomosis. Specific anastomotic surgical procedure codes were not reported for 151 patients (35%). Endoscopic assessment at the surgical institution occurred in 40% of the cohort before colectomy and in 22% of the cohort following colectomy.

Conclusions In this cohort, colectomy took place at an earlier age than suggested in published guidelines. Ileal pouch anal anastomosis is the predominant procedure for pediatric patients with FAP who underwent colectomy in US pediatric centers. Endoscopic assessment trends before and after surgery suggest that the surgical institution plays a limited role in the care of this population. *(J Pediatr 2022;245:117-22)*.

Familial adenomatous polyposis (FAP) is a well-described inherited adenomatous polyposis syndrome. Affected individuals develop multiple adenomatous colorectal polyps, many of which become apparent during the pediatric and adolescent years; however, great clinical variability is typical.[1-4] Although FAP is rare, occurring in 1 to 3:10 000 births, the clinical implications and associated morbidity are profound.[1] If left untreated, polyps will undergo malignant transformation and progress to colorectal cancer by a mean age of 39 years.[1,2] Following diagnosis, it is recommended that endoscopic surveillance begin during early adolescence or with active symptoms.[1-3]

Although prophylactic colectomy is universally recommended to reduce the risk of colorectal cancer, the optimal timing for colectomy is controversial. Existing recommendations are rooted in consensus expert opinion. Guidelines suggest that most patients with FAP undergo prophylactic colectomy in their late teens to early twenties.[1-3] For patients with FAP undergoing colectomy, there are 2 primary surgical approaches—either colectomy with ileorectal anastomosis (IRA) or proctocolectomy with ileal pouch-anal anastomosis (IPAA). The decision to proceed with one approach over the other is individualized and based on the patient's genotype, colonic and rectal phenotype, as well as the surgeon's experience and discretion.[1-3,5]

There is little known regarding practice trends for pediatric patients with familial adenomatous polyposis undergoing colectomy (pFAP-C) beyond institutional case series. This study seeks to characterize a multi-institutional cohort of patients with pFAP-C and describe colectomy and endoscopic practice trends across the US.

Methods

Developed by the Children's Hospital Association (CHA), the Pediatric Health Information System (PHIS) is a comparative administrative database composed of data from 52 moderate- to large-sized nonprofit tertiary care children's

CHA	Children's Hospital Association
FAP	Familial adenomatous polyposis
IPAA	Ileal pouch anal anastomosis
IRA	Ileorectal anastomosis
pFAP-C	Pediatric patients with familial adenomatous polyposis undergoing colectomy
PHIS	Pediatric Health Information System

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The authors declare no conflicts of interest.

Portions of this study were presented at the Annual Collaborative Group of Americas on Inherited Gastrointestinal Cancer Meeting, November 14-15, 2020 (virtual); and at Digestive Disease Week, May 21-23, 2021 (virtual).

https://doi.org/10.1016/j.jpeds.2021.09.021

hospitals across the US. The PHIS contains demographic information, clinical characteristics, and billing data from inpatient and select outpatient encounters. The CHA and participating hospitals perform data quality and reliability checks before data inclusion. The PHIS has primarily been used in clinical research to better understand variations in practice and outcomes.[6] However, there is potential for analyses and study of rare disease with application of a systematic search strategy following cohort validation using well-defined methodology.[7-10]

Query Development

Query development was accomplished through previously described methods.[10] Patients between 2 and 21 years were included. They were identified within the PHIS through a combination of inclusionary and exclusionary *International Classification of Diseases* diagnostic and procedure codes (*Revisions 9* and *10*). Patients were included if they had an inpatient encounter associated with at least 1 FAP-related diagnosis code in combination with at least 1 colectomy procedure code. Patients were subsequently excluded if the encounter contained specific diagnosis codes indicative of an alternative diagnosis such as inflammatory bowel disease. **Appendix 1** (available at www.jpeds.com) summarizes our search strategy.

Cohort Validation

The query was validated at 3 CHA-affiliated hospitals. Through manual chart review, each hospital generated a list of patients with pFAP-C; 55 were identified among the 3 institutions and served as the "gold standard" patient list. When limiting the query to the 3 validating hospitals, 52 patients were identified within PHIS. Fifty patients were validated as true positives (sensitivity: 90.9%), and there were 2 patients who were false positive, who both underwent colectomy for juvenile polyposis syndrome when manually chart reviewed (positive predictive value: 96.1%). Due to the large number of total admissions reported from each institution to the PHIS, specificity and negative predictive values for the PHIS search were >99%. This study was approved by the institutional review boards of Nationwide Children's Hospital and of the validating hospitals.

Query Application

The validated search strategy was applied to the entire PHIS database between January 1, 2009, and December 31, 2019, to generate a multi-institutional cohort of patients with pFAP-C.

Data Collection

Patient-level variables included sex, race/ethnicity, age at colectomy, and documented comorbidities. Diagnosis codes were reviewed to assess comorbidities, such as desmoid tumor, malignant neoplasm of the colon, stomach and liver, thyroid cancer, and neoplasm of the ampulla of Vater. Surgical outcomes evaluated included in-hospital mortality, length of stay, and need for total parental nutrition. Colectomy procedure codes were used to ascertain the surgical approach. Complications within 365 days of the procedure occurring at the surgical institution were identified using diagnosis codes. Complications included, but were not limited to, anorectal complications (stenosis, bleeding, abscess, fistula), pouch-related complications, adhesive disease or obstruction, abdominal cavity and pelvic infection, stoma complications, and intestinal complications (anastomotic site complication, volvulus, fistula, perforation, malabsorption, and intussusception). Data regarding lower endoscopic procedures pre- and postcolectomy at the surgical institution also were obtained.

Statistical Analyses

Descriptive statistics were generated to describe characteristics of patients undergoing colectomy. Proportions describe categorical data and medians (with first and third quartiles) describe continuous variables. Comparative statistics were generated to evaluate procedure differences by patient age, differences in length of stay by procedure approach, or differences in complications by procedure. χ^2 tests and Wilcoxon Mann–Whitney U tests were employed for these comparisons. Statistical significance was evaluated at an alpha of 0.05, and analyses were conducted in SAS Enterprise Guide, Version 8.1 (SAS Institute).

Results

Patient Characteristics

There were 428 patients with pFAP-C identified within the PHIS across 46 children's hospitals. (**Table I**). Within our cohort, 44% of patients had public insurance, and the

Table I. Patient demographics and surgical characteristics

Demographics and surgical characteristics	N (Median)	Percent (Q1, Q3)
Total	428	100%
Age at colectomy, y	14	(11, 16)
Male	221	52%
Race/ethnicity		
Non-Hispanic White	292	68%
Non-Hispanic Black	38	9%
Hispanic/Latino	69	16%
Asian	6	2%
American Indian	2	1%
Other	21	5%
Comorbid conditions		
Desmoid tumor	21	5%
Malignant neoplasm of colon	2	0.5%
Malignant neoplasm of liver	3	0.7%
Malignant neoplasm of stomach	1	0.2%
Thyroid cancer	2	0.5%
Neoplasm of ampulla of Vater	0	0%
Surgical approach		
Open	115	27%
Laparoscopic	226	53%
Unspecified	87	20%
Surgical procedure		
IPAA	264	62%
IRA	13	3%
Unspecified	151	35%
Length of stay, d	7	(5, 9)

median household income was $40 915. Based on mid-study 2015 US Census Bureau data, 40% of all children in the US had public insurance, and median US household income was $55 775.[11,12]

Comorbidities

Comorbid conditions included desmoid tumor (n = 21, 5%), malignant neoplasm of the colon (n = 2, 0.5%), and malignant neoplasm of liver (n = 3, 1%). Two patients had thyroid cancer (0.5%), and 1 patient had malignant neoplasm of the stomach (0.2%). No patient had an associated diagnosis code to indicate neoplasm of the ampulla of Vater. All comorbid diagnoses were documented at the time of colectomy or within a preceding encounter. Each comorbid diagnosis was associated with a unique patient (Table I).

Colectomy Characteristics

The median age at colectomy was 14 years (range 2-21 years; IQR 11-16 years) (Figure 1). Most patients (n = 226, 53%) underwent colectomy via a laparoscopic approach, whereas 115 patients (27%) underwent colectomy via an open approach (Table I). There were 87 patients (20%) who underwent an undefined colectomy due to nonspecific procedure codes. The median age of patients undergoing colectomy via an open approach was 13 years, whereas the median age of those undergoing colectomy via a laparoscopic approach was 14 years (P = .33). The median length of stay was 7 days (IQR 5-9 days), and there was no significant difference in length of stay among patients undergoing colectomy via an open approach compared with a laparoscopic approach.

Overall, 264 patients (62%) underwent colectomy with IPAA and 13 patients (3%) underwent colectomy with IRA (Table I). Surgical approach could not be determined due to nonspecific procedure codes in 151 patients (35%). The mean age of patients undergoing IPAA was 13 years, whereas the mean age of patients undergoing IRA was 15 years (P = .07).

Surgical Complications and Outcomes

No in-hospital mortality was identified during the colectomy encounter. Sixty-four patients (15%) had documented total parenteral nutrition use during the colectomy encounter.

There were 314 unique surgical complication diagnosis codes documented within a year of colectomy among 169 (39%) patients. Adhesive disease and/or intestinal obstruction occurred in 61 patients (14%) within 1 year of colectomy. Unspecified surgical complications occurred in 56 patients (13%). Stoma-related complications and anorectal complications (abscess, stenosis, fissure, fistula, hemorrhage, prolapse) occurred in 39 patients (9%) and 33 patients (8%), respectively.

Most complications occurred during the colectomy encounter. Of the 314 unique complications, 291 complications (93%) occurred in 168 (39%) patients during the colectomy admission. Four patients (1%) re-presented to the surgical institution with complications within 30 days of discharge. An additional 4 patients (1%) re-presented to the surgical institutions between 30 and 60 days following discharge, and 7 patients (1.6%) re-presented to the surgical institution with colectomy related complications within 1 year of colectomy but beyond 60 days of discharge. Table II details complications and affiliated revisits within 1 year of colectomy.

Hospital Characteristics

During the 11-year study period, 27 hospitals (59% of contributing hospitals) performed, on average, fewer than than 1 FAP-associated colectomies per year, 16 hospitals performed between 1 and 2 FAP-associated colectomies per year, and 3 hospitals performed, on average, more than 2 FAP-associated colectomies per year. There was no difference in

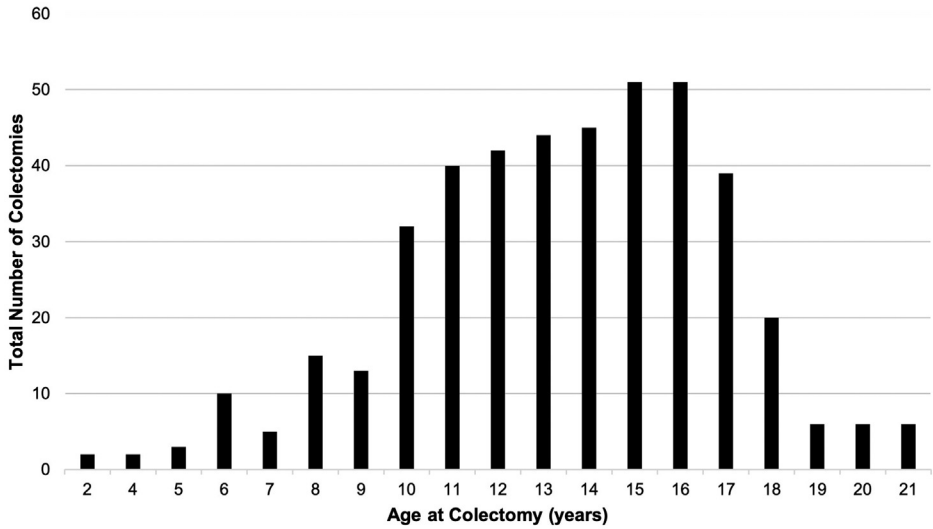

Figure 1. Distribution of age at colectomy.

Table II. Complications and revisits to surgical institution within 1 year of colectomy in our cohort of 428 patients with FAP who underwent colectomy*

Complications	N	Percentage
Patients with complications	169	39%
Adhesive disease/obstruction	61	14%
Stoma complications	36	8%
Anorectal complications (stenosis, bleeding, abscess, fistula)	33	8%
Nonspecific surgical complication	56	13%
Pouch-related complication	15	3%
Abdominal and/or pelvic cavity infection	15	3%
Infectious complication	12	3%
Intestinal complication		
Anastomotic complication	18	4%
Volvulus	3	1%
Fistula	7	2%
Perforation	7	2%
Malabsorption	13	3%
Intussusception	1	0.2%
Other	2	0.5%
Postprocedure bleeding complications	10	2%
Incision/abdominal wall complication	9	2%
Other	16	4%

*Refer to **Appendix 2** (available at www.jpeds.com) for details regarding timing of complications in relation to discharge.

the age at time of colectomy between the lowest- and highest-volume hospitals. The average annual FAP-associated colectomy case volume decreased by 48% during the 11-year study period.

Endoscopic Procedure Trends

Precolectomy. Ninety-one patients (21%) had 1 lower endoscopic evaluation at the surgical institution before colectomy. Sixty-two patients (14%) had 2-3 colonoscopies before colectomy, 13 patients (3%) had 4-5 colonoscopies, and 5 patients (1%) had 6 or more colonoscopies before colectomy; 257 patients (60%) did not have documented lower endoscopic procedures associated with the surgical institution (**Figure 2**). Of the 171 patients with documented precolectomy colonoscopy, 167 (97.7%) had a documented biopsy, polypectomy, or other excision of tissue in their final preoperative colonoscopy as identified by procedural codes; 54% (n = 91) of these encounters were biopsies performed at a median of 5.6 months preoperatively; 21% (n = 35) were polypectomies performed at a median of 5.1 months preoperatively; and 24% (n = 40) of patients had a biopsy and polypectomy performed at a median of 4.9 months preoperatively. One patient had an unspecified excision of tissue at 4.2 months preoperatively. Ten of the 171 patients (2%) with documented precolectomy colonoscopy had the procedure within 30 days preceding the colectomy encounter. Overall, the median time separating last endoscopic evaluation and colectomy encounter was 5 months (IQR 2.5-10.8 months). The median duration of time over which there were documented colonoscopies at the surgical institution was 14.1 months (IQR 4.2-39.4 months).

Postcolectomy. Sixty-five patients (15%) had 1 lower endoscopic evaluation at the surgical institution postcolectomy, 20 (5%) had 2-3 lower endoscopies, and 10 patients (2%) had 3 or more lower endoscopies following colectomy. The majority of patients (333 patients, 78%) did not have postcolectomy lower endoscopic procedures at the surgical institution (**Figure 2**). The median amount of time between colectomy and first lower endoscopic procedure was 11.2 months (IQR 3.3-24.3 months).

Discussion

In this large multi-institutional cohort of patients with pFAP-C in the US, the median age at colectomy was 14 years and the majority of patients received an IPAA. Because of the large volume of patients captured from 46 geographically diverse children's hospitals, this cohort represents a broad reflection of practice trends among children's hospitals across the US.

Guidelines recommend prophylactic colectomy in late teens to early twenties; however, they acknowledge clinical and personal circumstances impact colectomy timing. Available data from adult institutions and polyposis centers suggest that most patients undergo colectomy at an age consistent with guideline recommendations.[13-15] Our data demonstrate a median age of 14 years at time of colectomy, which is similar to previously reported pediatric data but younger than suggested in published guidelines or reported from major polyposis centers.[16-18] It is unknown whether our cohort represents a unique subset of patients with pFAP-C more likely to undergo early colectomy. Munck et al found that one-half of the children identified in their multi-institutional cohort with a "hot spot" mutation at codon 1309 underwent colectomy before age 11, suggesting that patients with a severe genotype may be more likely to undergo early colectomy.[18]

Genotype and phenotype data are unknown in our cohort. However, 97.7% of patients undergoing colonoscopy at the surgical institution had colonic tissue obtained via biopsy or polypectomy before their colectomy, suggesting histologic findings may have contributed to the decision to proceed with colectomy. Improved understanding for colectomy indication among our cohort would provide insight into whether this cohort represents a unique FAP population possibly benefiting from early colectomy or reflects practice trends and care variation among US children's hospitals. Prospective multi-institutional data collection efforts are necessary to fully understand and answer these questions.

Understanding colectomy practices in pediatric patients with pFAP-C is relevant to potential future chemoprevention trials that seek to offer a safe and effective way to defer surgery. The relatively young age at colectomy observed in our cohort could influence the design of future pediatric FAP chemoprevention trials seeking to maximize drug effect and recruitment. Currently, there are no agents approved for this use in the US, and it remains an active area of investigation.[1,19]

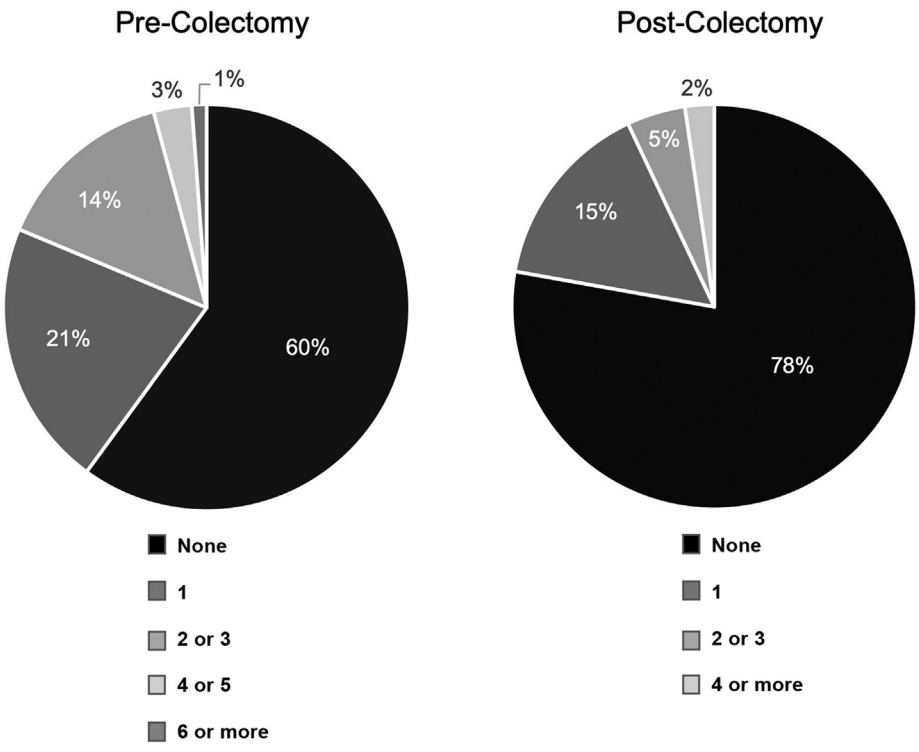

Figure 2. Lower endoscopic procedures per patient at surgical institution.

Data regarding colectomy approach are limited by nonspecific coding and should be interpreted cautiously. The majority of patients underwent an IPAA. This may suggest that these children had a more aggressive phenotype with significant rectal involvement necessitating IPAA rather than IRA. Although not statistically significant, the average age of patients undergoing IPAA was 2 years younger than patients undergoing IRA, 13 and 15 years, respectively (P = .07), again suggesting younger patients undergoing colectomy may present with more severe rectal polyposis. We are unable to make meaningful conclusions regarding surgical complications, as data are limited by available diagnosis codes, nonspecific procedure codes, and captured encounters exclusive to the surgical institution; thus, reported complication data are likely underestimates and cannot be reliably compared between procedure approaches.

We analyzed frequency of lower endoscopic procedures pre- and postcolectomy at the surgical institution to better understand endoscopic surveillance trends; however, because procedure indication was not identifiable and data collection was limited to the surgical institution, we could not draw concrete conclusions regarding surveillance trends. Most patients (60%) had no documented colonoscopy at the surgical institution before their colectomy. The majority of patients with documented colonoscopies underwent 3 or fewer before colectomy. In the context of our cohort, 3 or fewer colonoscopies align with current surveillance guidelines, which recommend initial endoscopic evaluation between 12 and 14 years.[1] However, this cohort could represent a unique subset of patients with pFAP-C with severe disease, potentially prompting surveillance at an earlier age. Thus, this cohort may undergo greater numbers of surveillance colonoscopies than otherwise expected per guideline recommendations. Following colectomy, only 22% of patients had a documented lower endoscopic procedure at the surgical institution. This may be due to an alternative site of care, lack of postcolectomy surveillance, and/or the procedure occurred within an encounter type not submitted to the PHIS. Given these trends, we speculate that the pediatric surgical institution may be a discrete participant in the care of pediatric patients with pFAP-C, leaving to question whether these patients have a consistent medical home before and after surgical care. Gaining a better understanding of pediatric FAP postsurgical endoscopic surveillance practices will be important to the establishment of long-term patient expectations that are critical for this population, who require lifelong cancer surveillance and who would benefit from the care provided at adult FAP centers of excellence.

Cancer diagnoses were rare in our cohort. Notably, 1 patient was identified as having had a malignant neoplasm of the stomach before colectomy. Unfortunately, patient level and histologic details regarding this individual are unknown, as this significant observation warrants documentation in the medical literature.

Our cohort of patients with pFAP-C had a lower median household income than that of the general US population, suggesting possible socioeconomic differences. We

hypothesize that this population's suspected lower socioeconomic status adversely impacts access to care and argues in favor of strong multidisciplinary teams through routine social work involvement and relationships with adult polyposis centers to provide transitional care.

Our study has several limitations. Genotype, phenotype, and endoscopic findings, both gross and microscopic, are not data elements captured within the PHIS. Understanding these details would provide important context and possibly insight into our observed practice trends. In addition, nonspecific *International Classification of Diseases* coding limited our ability to make conclusions regarding colectomy practices and related complications. Further, care occurring at non-PHIS institutions was not captured; thus, data related to endoscopic procedures, comorbidities, and surgical complications are likely underestimates. Future studies, using similar methodology, could sample this error through manual chart review during cohort validation.

Although this cohort represents a subset, our data suggest that pediatric patients with pFAP-C, cared for at a children's hospital, who undergo colectomy, do so at earlier ages than suggested in adult literature. Future collaborative multi-institutional prospective studies are needed to better characterize the variations in pediatric FAP colectomy practices observed in our study. ■

Submitted for publication Jun 22, 2021; last revision received Aug 16, 2021; accepted Sep 15, 2021.

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Data Statement

Data sharing statement available at www.jpeds.com.

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