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Factors influencing disease recurrence after ileocolic resection in adult and pediatric onset Crohn's disease

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Abstract

BACKGROUND: Factors influencing recurrence of ileocecal Crohn's disease (CD) after surgical resection may differ between adolescents and adults.

METHODS: CD patients who underwent ileocecectomy were retrospectively divided into pediatric onset (age at diagnosis $\leq$ 16 years, n = 34) and adult onset (>16, n = 108) patients to evaluate differences in risks of endoscopic and clinical recurrence.

RESULTS: In 142 patients, rates of any recurrence, endoscopic recurrence, and clinical recurrence at 5 years were 78%, 88%, and 65%, respectively. Risks of recurrence were similar between groups. Younger patients were more likely to be on immunologics preoperatively and more likely to be started on immunoprophylaxis postoperatively. Immediate postoperative prophylaxis was predictive of delayed clinical recurrence only in the older group.

CONCLUSIONS: Despite increased preoperative and postoperative immunoprophylaxis in younger patients, recurrence rates of CD after ileocecectomy do not differ between these groups. Immediate postoperative prophylaxis was predictive of delayed clinical recurrence only in patients with adult onset CD.

Crohn's disease (CD) is a chronic inflammatory gastrointestinal disorder with an unpredictable clinical course and a high rate of recurrence. Despite increased use of immunomodulators and biologic therapy, surgical resection is still required in approximately 70% to 80% of patients with CD, and up to 70% of patients will require a second operation.[1,2] Subclinical endoscopic recurrence precedes the development of symptoms. One year after surgical resection, more than 70% of patients have evidence of anastomotic endoscopic recurrence.[3,4] Thirty percent of patients progress to symptomatic recurrence at 3 years, and 60% have endoscopic recurrence by 5 years.[2,3] The pathophysiology of recurrence is poorly understood, and importantly,

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there is little consensus on the best algorithm to prevent recurrence. While several small randomized clinical trials have identified potential treatment options, details of patient selection and timing of prophylaxis remain elusive.[5]

Several factors have been evaluated as potential risk factors for postoperative recurrence. Smoking, prior resection, genetic markers, perforating disease type, ileocolonic location, and short disease duration before first surgery may increase risk of postoperative recurrence.[1,6,7] Some studies indicate that a younger age of disease onset is associated with an increased incidence of surgical recurrence.[8–10] Additional studies demonstrate a more aggressive phenotype of CD in young patients.[11,12] Studies evaluating differences in risk factors associated with postsurgical recurrence in pediatric compared with adult onset CD are sparse.[13,14]

In this study, we review the records of patients with pediatric onset CD (age at diagnosis $\leq$ 16 years) compared with older patients with CD (age at diagnosis $>$ 16 years) who underwent ileocecal resection. The purpose of this study was to investigate whether predictors of postoperative disease recurrence in patients undergoing ileocecectomy for CD differ with age. We hypothesized that there are distinct differences between early-onset and adult-onset CD and that different risk factors are associated with recurrence.

Methods

Study population

After obtaining institutional review board approval, patients who underwent ileocecectomy or right hemicolectomy for CD between January 2004 and October 2013 at Case Western University Hospitals Case Medical Center and Rainbow Babies and Children's Hospital in Cleveland, Ohio, were identified from a prospectively maintained database of colon and rectal surgery patients and from the hospital medical records department. A retrospective chart review was performed on all patients. Patients were excluded if pathology report was negative for CD. Patients with concomitant procedures (such as additional bowel resection, stricturoplasty, treatment of perianal disease) were included provided that the main focus of the surgery was active terminal ileum or ileocecal CD. Our retrospective chart review included surgical and gastroenterology office notes, surgical and endoscopic operative reports, hospital admission and discharge notes, pathology reports, and radiology studies.

Patients were divided into 2 groups based on age at diagnosis of CD: pediatric onset group (age at diagnosis $\leq$ 16 years) and adult onset group ($>$16 years). This division was based on prior studies that have shown distinct physiologic characteristics between pediatric and adult onset CD[11,15,16] and use the age of 16 as a cutoff to differentiate early and adult onset inflammatory bowel disease.[17,18] Demographics, operative and perioperative data, short- and long-term outcomes were recorded. Patients who underwent surgery on admission or during an index admission were considered "emergent" or "urgent" surgery, respectively. Study data were collected and managed using REDCap electronic data capture tools hosted at University Hospital Case Medical Center.[19]

Study outcomes

The primary outcome of interest was time to any recurrence of CD at the neoterminal ileum, which was defined as endoscopic, clinical, or surgical recurrence. The secondary endpoints were endoscopic, clinical, and surgical recurrence at the neoterminal ileum. Endoscopic recurrence was demonstrated by Rutgeerts score of i2 or greater on postoperative colonoscopy.[3] Patients requiring initiation or augmentation of medical therapy, hospitalization, or other interventions to control symptoms of CD were categorized as having a clinical recurrence at the earliest date of interventions. Patients who required reoperation at the neoterminal ileum were considered to have a surgical recurrence. Time to recurrence was measured from the date of surgery to the earliest date of recurrence, whether clinical, endoscopic, or surgical.

Statistical analysis

Statistical analysis was performed using SPSS version 21.0 (SPSS, Inc, Chicago, IL). Descriptive statistics were used to generate frequencies and percentages for categorical variables and mean with standard deviations for continuous variables. Categorical variables were compared using the chi-square test and continuous variables were compared using independent-sample *t* test. To evaluate factors associated with recurrence, we developed a Cox proportional hazards model of both endoscopic and clinical recurrence and performed univariate and multivariate analyses separately for younger and older adults. Crude and adjusted hazards ratios (HRs) with 95% confidence interval and *P* values are reported. All variables with a *P* value of less than .150 on univariate analysis were included in the multivariate model. Patients who were lost to follow-up were censored at the time of last follow-up. Time to recurrence between the 2 groups was compared using the Kaplan–Meier method and the log-rank test. A *P* value of less than or equal to .05 was considered statistically significant throughout the analysis.

Results

One hundred and sixty-three patients underwent ileocecectomy or right hemicolectomy for CD between June 2004 and October 2013. Three patients were excluded because of cecal cancer, 4 were excluded because the pathology report was not consistent with CD, 6 were excluded because the date of diagnosis could not be obtained, and 8 were