Decrease in primary but not in secondary abdominal surgery for Crohn’s disease: nationwide cohort study, 1990–2014

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Background: Treatment of patients with Crohn’s disease has evolved in recent decades, with increasing use of immunomodulatory medication since 1990 and biologicals since 1998. In parallel, there has been increased use of active disease monitoring. To what extent these changes have influenced the incidence of primary and repeat surgical resection remains debated.

Methods: In this nationwide cohort study, incident patients of all ages with Crohn’s disease, identified in Swedish National Patient Registry between 1990 and 2014, were divided into five calendar periods of diagnosis: 1990–1995 and 1996–2000 with use of inpatient registries, 2001, and 2002–2008 and 2009–2014 with use of inpatient and outpatient registries. The cumulative incidence of first and repeat abdominal surgery (except closure of stomas), by category of surgical procedure, was estimated using the Kaplan–Meier method.

Results: Among 21273 patients with Crohn’s disease, the cumulative incidence of first abdominal surgery within 5 years of Crohn’s disease diagnosis decreased continuously from 54.8 per cent in 1990–1995 to 40.4 per cent in 1996–2000 (P < 0.001), and again from 19.8 per cent in 2002–2008 and 2009–2014 with use of inpatient and outpatient registries. The cumulative incidence of first and repeat abdominal surgery (except closure of stomas), by category of surgical procedure, was estimated using the Kaplan–Meier method.

Conclusion: The 5-year rate of surgical intervention for Crohn’s disease has decreased significantly, but the rate of repeat surgery has remained stable despite the introduction of biological therapy.

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Introduction

Medical therapy, including monoclonal antibodies, constitutes the majority of healthcare costs for patients with Crohn’s disease (CD)1. To what extent the advent of biological therapy has affected the incidence of surgery remains debated, as the favourable efficacy results from clinical trials have not readily translated into real-world effects. A recent observational study2 of all surgery-naïve patients with CD in Stockholm county between 2006 and 2014 reported no difference in bowel resection rates between those maintained on antitumour necrosis factor (TNF) therapy for more than 12 months and those who discontinued treatment earlier.

Population-based studies3–15 of the incidence of abdominal surgery for CD have shown conflicting results, although a decreasing trend was most often reported (Table S1, supporting information). However, the incidence of specific surgical procedures for CD and the risk of repeat surgery remains unknown.
The aim of this study was to use data from a national cohort of patients with CD diagnosed between 1990 and 2014 to provide both the trend and current rate of primary and repeat surgery for CD, as well as to describe rates of surgery based on the type of surgical procedure.

**Methods**

Ethical approval for this study was granted by the Regional Ethics Committee, Karolinska Institutet, Stockholm, Sweden (approval numbers including amendments: 2007/785-31/5; 2015/1030-32).

**Study design and setting**

A population-based nationwide registry was used to create a cohort study of patients with CD who were followed longitudinally. Sweden had a population of 9.7 million inhabitants in December 2014, and has a tax funded healthcare system with universal access. The majority of patients with CD are cared for at hospital-based outpatient facilities or inpatient facilities, and have access to modern pharmaceutical agents.

**Linkage and data sources**

Since 1947, every Swedish resident has been given a unique personal identity number, which is used in all official registries and enables registry linkage. The National Patient Registry (NPR) consists of the inpatient and the outpatient registries. The inpatient registry contains data on all inpatient care since 1964, with full national coverage from 1987, and on hospital-based outpatient surgery since 1997. The non-primary outpatient registry has had full national coverage since 2001.

**Study population**

Patients were included if they had a first-ever diagnosis of CD registered in the NPR between 1 January 1990 and 31 December 2014, as determined by ICD-9 and ICD-10 codes listed in Table S2 (supporting information). To confirm the diagnosis of CD, at least two diagnostic listings with CD as the main or contributory diagnosis in inpatient or outpatient care, or abdominal surgery associated with inflammatory bowel disease (IBD) (Table S3, supporting information) on the same date as the first diagnosis of CD, was required. Patients were excluded if they had a diagnosis of ulcerative colitis or IBD unclassified (IBD-U) before the first diagnosis of CD or underwent intestinal surgery (except appendicectomy) before 1 January 1990.

**Inflammatory bowel disease subtypes during follow-up**

The subtype of IBD (CD, ulcerative colitis or IBD-U) was classified at the end of follow-up according to a previously published algorithm accounting for CD-specific surgery.

**Abdominal surgery**

Information on the date and type of abdominal surgery was extracted from the NPR. Procedures were classified based on anatomical location and expected functional outcome (Tables S3 and S4, and Appendix S1, supporting information): A, resection of small bowel with or without formation of a stoma; B, ileocaecal/ileocolic resection or right-sided hemicolecctiony with or without formation of a stoma; C, segmental resections of colon or rectum with or without formation of a stoma; D, colectomy (with or without concurrent proctectomy) and with or without formation of a stoma (including patients having 3 or more segmental colonic resections); E, proctectomy (with or without concurrent colectomy); or F, other procedures including formation of a stoma and/or strictureplasty as the only procedure. If a patient was coded with procedures from any of the categories A–E and category F (other procedures), the categories A–E had priority, meaning that any other procedures were counted as additional secondary procedures and therefore not recorded.

Procedures for stoma closure and those for adhesive small bowel obstruction were excluded as they were not felt to be related to refractory CD or complications of CD alone.

**Statistical analysis**

Categorical variables are described as number with percentage, and continuous variables as mean(s.d.) or median (i.q.r.). Follow-up time started on the date patients fulfilled inclusion criteria and ended on the date of emigration, death or 31 December 2014, whichever came first. The cumulative incidence of first abdominal surgery overall, as well as for the different surgery types separately (small bowel resection, ileocaecal resection, segmental colorectal resection, colectomy, proctectomy and other procedures) was estimated using the Kaplan–Meier method.

The cumulative incidence of abdominal surgery was compared across different calendar periods (1990–1995, 1996–2000, 2001, 2002–2008 and 2009–2014). The first two intervals included patients identified through the inpatient registry only. The 2001 cohort contained a mixture
unchanged but low risk of repeat surgery for Crohn’s disease

Fig. 1 Study flow chart

First diagnosis of Crohn’s disease between 1990 and 2014
\( n = 33,701 \)

Excluded: < 2 IBD listings and no abdominal surgery on same day \( n = 11,306 \)

Diagnosed twice or had abdominal surgery on same day \( n = 22,395 \)

Excluded \( n = 1,122 \)
Abdominal surgery before diagnosis \( n = 952 \)
Missing birth date/data irregularities \( n = 170 \)

Included \( n = 21,273 \)

IBD, inflammatory bowel disease.

of true incident patients (identified in outpatient or inpatient care) as well as prevalent cases that appeared to be incident as there had been no previous inpatient care. The last two calendar periods contained true incident CD cases identified in outpatient or inpatient care. The differences in cumulative incidence of first operation across calendar periods before and after the start of the outpatient registry were compared using log rank tests.

The cumulative incidence of repeat abdominal surgery (except closure of stomas), overall and according to surgical type, was also compared. For repeat surgery, follow-up started on the day after the patient was released from hospital after the first surgical procedure. In contrast to the analyses of first operation, all patients at risk of repeat surgery had been hospitalized previously, and the cumulative risks could therefore be compared across the entire study interval.

Results

A total of 21,273 incident patients with CD were identified between 1990 and 2014 (Fig. 1 and Table 1). One-third of the patients were diagnosed before 2001. Median follow-up ranged from 20.9 years in the first cohort to 3.0 years in the most recent one encompassing the years 2009–2014.

Table 1 Description of study population by year of first diagnostic listing of Crohn’s disease

| Age at Crohn’s disease onset (years) | 1990–1995 \( n = 3110 \) | 1996–2000 \( n = 3,184 \) | 2001 \( n = 1,680 \) | 2002–2008 \( n = 7,262 \) | 2009–2014 \( n = 6,037 \) |
|-------------------------------------|-----------------------------|-----------------------------|-----------------------------|-----------------------------|-----------------------------|
| Mean(s.d.)                          | 40.3(19.6)                  | 39.5(19.4)                  | 40.9(18.4)                  | 39.0(20.0)                  | 38.8(20.2)                  |
| Median (i.q.r.)                     | 37(24–54)                   | 36(23–54)                   | 39(26–55)                   | 36(22–55)                   | 34(22–55)                   |
| < 18                                | 333(10–7)                   | 401(12–6)                   | 171(10–2)                   | 1183(16–3)                  | 881(14–6)                   |
| 18–39                               | 1359(43–7)                  | 1358(42–7)                  | 706(42–0)                   | 2909(40–1)                  | 2601(43–1)                  |
| 40–59                               | 816(26–2)                   | 897(28–2)                   | 519(30–9)                   | 1870(25–8)                  | 1360(22–5)                  |
| ≥ 60                                | 602(19–4)                   | 528(16–6)                   | 284(16–9)                   | 1300(17–9)                  | 1195(19–8)                  |
| Sex                                 |                             |                             |                             |                             |                             |
| F                                   | 1640(52–7)                  | 1639(51–5)                  | 865(51–5)                   | 3764(51–8)                  | 2975(49–3)                  |
| M                                   | 1470(47–3)                  | 1545(48–5)                  | 815(48–5)                   | 3498(48–2)                  | 3062(50–7)                  |
| Age at end of follow-up (years)     |                             |                             |                             |                             |                             |
| Mean(s.d.)                          | 59.1(16–7)                  | 54.3(17–7)                  | 53.7(17–6)                  | 48.0(19–5)                  | 41.8(20–2)                  |
| Median (i.q.r.)                     | 57.7(45.5–72.1)             | 51.6(39.7–68.7)             | 52.1(39.6–67.5)             | 45.2(31.5–63.5)             | 36.9(24.6–58.4)             |
| Subtype of inflammatory bowel disease at end of follow-up |                             |                             |                             |                             |                             |
| Crohn’s disease                     | 2909(93.5)                  | 2946(92.8)                  | 1523(90.7)                  | 6653(91.6)                  | 5711(94.6)                  |
| Ulcerative colitis                  | 90(2.9)                     | 100(3.1)                    | 64(3.8)                     | 162(2.2)                    | 5(0.1)                      |
| Unclassified                        | 111(3.6)                    | 138(4.3)                    | 93(5.5)                     | 447(6.2)                    | 321(5.3)                    |
| Duration of follow-up (years)       |                             |                             |                             |                             |                             |
| 0 to <5                             | 229(7.4)                    | 192(6.0)                    | 74(4.4)                     | 414(5.7)                    | 5037(83.4)                  |
| ≥ 5 to <10                          | 181(5.8)                    | 157(4.9)                    | 70(4.2)                     | 4075(56.1)                  | 1000(6.6)                   |
| ≥ 10 to <15                         | 181(5.8)                    | 768(24.1)                   | 1536(91.4)                  | 2773(38.2)                  | 0(0)                        |
| ≥ 15                                | 2519(81.0)                  | 2067(64.9)                  | 0(0)                        | 0(0)                        | 0(0)                        |

Values in parentheses are percentages unless indicated otherwise.
Table 2 Duration of follow-up and surgery events by year of Crohn’s disease onset and type of surgery (first operation only)

| Year of CD onset | Follow-up (years)* | Surgery within 1 year | Surgery within 5 years | Surgery within 10 years | Surgery ever |
|------------------|---------------------|-----------------------|------------------------|-------------------------|-------------|
| 1990–1995        | 20.9 (19.1–22.8)    | 1399 (45.0)           | 1692 (54.4)            | 1855 (59.6)             | 2001 (64.3) |
| 1996–2000        | 15.7 (14.5–17.2)    | 1015 (31.9)           | 275 (40.0)             | 1419 (44.6)             | 1547 (48.6) |
| 2001             | 13.6 (13.2–13.8)    | 202 (12.0)            | 311 (18.5)             | 400 (23.8)              | 436 (26.0)  |
| 2002–2008        | 9.1 (7.2–11.1)      | 956 (13.2)            | 1426 (19.6)            | 1706 (23.5)             | 1753 (24.1) |
| 2009–2014        | 3.0 (1.5–4.4)       | 619 (10.3)            | 842 (13.9)             | 851 (14.1)              | 851 (14.1)  |

Values in parentheses are crude percentages calculated on counts of events without accounting for censoring, unless indicated otherwise; *values are median (i.q.r.). CD, Crohn’s disease. Surgery codes: A, resection of small bowel with or without stoma formation; B, ileocaecal resection/ileocolic resection/right-sided hemicolectomy with or without stoma formation; C, all other segmental resections of colon and rectum with or without stoma formation; D, total colectomy; E, proctectomy; F, other abdominal surgical procedures, including stoma formation as the only procedure.

(Tables 2). A total of 6588 patients (30.9 per cent) underwent a primary abdominal operation and, of these, 1625 (24.7 per cent) had a second abdominal procedure (Table 2 and Fig. 2).

First abdominal surgery

The 5- and 10-year cumulative incidence of primary abdominal surgery decreased significantly between 1990–1995 and 1996–2000, with 5-year rates dropping from 54.8 to 40.4 per cent, and 10-year rates from 60.5 to 45.2 per cent ($P < 0.001$) (Fig. 2a). The 5-year cumulative incidence further decreased from 19.8 per cent in 2002–2008 to 17.3 per cent in 2009–2014 ($P < 0.001$). The 10-year cumulative incidence was 25.0 per cent between 2002 and 2008, but remains unknown to date for 2009–2014. Ileocaecal resection was the most common procedure performed, irrespective of time period, accounting for 64.6 per cent of all primary resections (Fig. 2a); 68.8 per cent of these were performed within a year of CD diagnosis (Table 2).

Repeat abdominal surgery

Median follow-up after primary abdominal surgery was 7.3 years. The cumulative incidence of a second abdominal procedure within 5 years of the index operation decreased significantly from 18.9 per cent in 1990–1995 to 16.0 per cent in 1996–2000 ($P = 0.009$) (Fig. 2b). There was no significant decrease across the subsequent calendar periods. The most common repeat surgical procedure was neoleiocolic re-resection (Fig. 3b), which accounted for 28.4 per cent of all repeat resections.

Small bowel resection

The 5-year cumulative incidence of first small bowel resection decreased significantly from 13.6 per cent in 1990–1995 to 8.2 per cent in 1996–2000 ($P < 0.001$). The
Fig. 2 Cumulative incidence of first and second abdominal surgery in relation to year of inflammatory bowel disease onset

(a) First abdominal surgery

(b) Second abdominal surgery

Fig. 3 Cumulative incidence of first ileocaecal resection and first ileocolic re-resection in relation to year of inflammatory bowel disease onset

(a) First ileocaecal resection

(b) First ileocolic re-resection

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cumulative 5-year incidence further decreased from 5.8 per cent in 2002–2008 to 5.0 per cent in 2009–2014 (P=0.020) (Fig. 4a). The cumulative incidence of repeat resection of small bowel within 5 years of first resection ranged from 9.5 to 13.5 per cent, and did not decrease significantly between calendar periods (Fig. 4b).

Ileocaecal or ileocolic resection

The 5-year cumulative incidence of first ileocaecal/ileocolic resection decreased significantly from 36.8 per cent in 1990–1995 to 29.0 per cent in 1996–2000 (P<0.001). There was no significant decrease between 2002–2008 and 2009–2014 (13.3 versus 12.4 per cent; P=0.065) (Fig. 3a). The cumulative incidence of repeat ileocolic resection decreased significantly from 5.5 to 4.4 per cent between 1990–1995 and 1996–2000 within 5 years of diagnosis, and from 13.0 to 8.8 per cent within 10 years (P=0.016) (Fig. 3b). However, no significant decrease was seen thereafter. Median follow-up after a first ileocolic resection was 8.9 years.

Segmental resection of colon or rectum

Patients undergoing segmental resection of the colon or rectum were scarce in all cohorts (Fig. S1, supporting information). The 5-year cumulative incidence of first segmental resection decreased significantly from 7.9 per cent in 1990–1995 to 5.2 per cent in 1996–2000 (P<0.001) (Fig. S1, supporting information). There was no significant decrease between 2002–2008 and 2009–2014 (2.7 versus 2.2 per cent; P=0.246). The cumulative incidence of second segmental resection was low in all cohorts, with no significant decreasing trend. For 2001 and 2002–2008, the incidence within 5 years was 7.6 and 8.3 per cent respectively (P=0.852).

Colectomy

The incidence of colectomy was low and decreased throughout the study interval. The cumulative incidence within 5 years was 1.9 per cent in 2002–2008 and 1.1 per cent in 2009–2014 (P=0.001) (Fig. 5).

Proctectomy

The cumulative incidence of proctectomy was very low in all cohorts, even among those with long-standing disease. The incidence decreased between the two cohorts in the 1990s (3.0 versus 1.9 per cent within 20 years of disease onset; P=0.020). In 2002–2008, with a median follow-up of 9.1 years, the cumulative incidence of proctectomy after 10 years was 0.6 per cent.
Other procedures

The cumulative incidence of other main surgical procedures was low throughout the study, with a rate of 1.7 per cent in the most recent cohort. Strictureplasties were included in this category, but could not be fully ascertained in the registry until 1997.

Discussion

During the past decade, several population-based studies have assessed temporal trends in CD surgery, but results have been conflicting (Table S1, supporting information)\(^{21,22}\). A meta-analysis\(^{22}\) of population-based studies of patients diagnosed with CD between 1955 and 2011 reported decreasing rates of surgery, with a 24 per cent probability of surgery within 5 years of diagnosis after 2000. In another meta-analysis\(^{23}\) of population-based studies the risk of a second abdominal procedure within 10 years was 33.2% in studies conducted after 1980. In the present nationwide longitudinal cohort study of more than 21 000 patients with CD, the 5-year cumulative incidence of primary intestinal resection decreased by two-thirds over the study interval. In contrast to the continuously decreasing incidence of primary intestinal resection, the cumulative incidence of repeat abdominal surgery within 5 years of primary surgery remained constant after an initial decrease during the 1990s.

Consistent with another population-based study\(^{11}\), ileo-caecal resection remained the most common procedure during the whole study period. This is likely because CD most commonly affects the terminal ileum, creating the most bowel wall damage in that location, in combination with the narrower lumen of the small bowel being more prone to obstructive symptoms than the colon. Interestingly, colectomies and small bowel resections were the only categories of abdominal surgery with a continual decrease in incidence over the study. This is somewhat surprising given the recent increase in the incidence of colonic CD\(^{24}\), which is now similar to that of ileal disease\(^{24,25}\).

Studies from Denmark\(^{12,13}\), Manitoba\(^{8}\), UK primary care\(^{14}\) and the Netherlands\(^{15}\) have all reported decreasing rates of intestinal resection for CD over time. The Dutch group even noted decreasing surgical rates for all anatomical locations and repeat resections during the entire period. Of note, the incidence of surgery was, however, based on an estimated, rather than known prevalence of CD in the Netherlands\(^{15}\). Other studies have reported conflicting data. A French study\(^{26}\) of 2573 patients during the years 1978–2002 and an analysis\(^{11}\) of 310 patients from Olmsted County in the USA during 1970–2004 did not find a decrease in the incidence of abdominal surgery. Reports from administrative databases in Ireland between 2000 and 2010\(^{27}\), and the USA between 1988 and 2011\(^{28}\), similarly did not document a decrease in the rates of surgery.

IBD, inflammatory bowel disease. \(P = 0.002\) (1990–1995 versus 1996–2000), \(P = 0.001\) (2002–2008 versus 2009–2014) (log rank test).
decreased rates in the present Swedish cohort study may be related to the fact that more than half of the included patients with CD were diagnosed after the introduction of TNF inhibitors, in the era of early immunomodulator use, more conservative management of patients, including the introduction of endoscopic balloon dilatation for anastomotic stricture, improved diagnostics and surveillance, reduced tobacco use, improved active disease monitoring, and increased use of postoperative medical prophylaxis during the study interval.

The use of a nationwide population-based design allows stratification by calendar period and type of surgical procedure for data analysis. In a recent validation of this study design, 93 per cent of patients with at least two recorded diagnoses of IBD in the NPR had a correct diagnosis according to the Copenhagen criteria. The surgical procedure codes have also recently been validated with a positive predictive value of 99 per cent and sensitivity of 94 per cent. Limitations of the analysis are the short follow-up in the most recent cohort, lack of fully comparable data on incidence before and after start of the outpatient register, and lack of complete information on tobacco and medication use.

Updated surgical risk estimates, relevant to current treatment paradigms, are essential for both patients and doctors when making therapeutic decisions. Patients can be educated regarding the decreased rates of bowel resection, even in those with colonic and rectal disease, a phenotype that has become more common in recent years. In fact, the present results have shown that the risk of proctectomy is very low, even in patients with long-standing disease. However, to what extent this trend will continue with the introduction of new medical therapies, in contrast with data from the LIRIC trial that support early surgery, remains an unanswered question.

In a Swedish population-based database, the cumulative incidence of a first abdominal surgical procedure after a diagnosis of CD has decreased by two-thirds over the past 25 years, whereas the incidence of repeat abdominal surgery has not decreased since the introduction of biological therapies.

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**Supporting information**

Additional supporting information can be found online in the Supporting Information section at the end of the article.