In Vitro Fertilization in Women With Inflammatory Bowel Disease Is as Successful as in Women From the General Infertility Population

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BACKGROUND & AIMS: **Inflammatory bowel disease (IBD) affects women of reproductive age, so there are concerns about its effects on fertility. We investigated the success of in vitro fertilization (IVF) in patients with IBD compared with the general (non-IBD) IVF population.**

METHODS: **We conducted a matched retrospective cohort study of female patients with IBD who underwent IVF from 1998 through 2011 at 2 tertiary care centers. Patients were matched 4:1 to those without IBD (controls). The primary outcome was the cumulative rate of live births after up to 6 cycles of IVF. Secondary outcomes included the proportion of patients who became pregnant and the rate of live births for each cycle.**

RESULTS: **Forty-nine patients with Crohn's disease (CD), 71 patients with ulcerative colitis (UC), 1 patient with IBD-unclassified, and 470 controls underwent IVF during the study period. The cumulative rate of live births was 53% for controls, 69% for patients with UC ($P = .08$ compared with controls), and 57% for patients with CD ($P = .87$ compared with controls). The incidence of pregnancy after the first cycle of IVF was similar among controls (40.9%), patients with UC (49.3%; $P = .18$), and patients with CD (42.9%; $P = .79$). Similarly, the incidence of live births after the first cycle of IVF was similar among controls (30.2%), patients with UC (33.8%; $P = .54$), and patients with CD (30.6%; $P = .95$).**

CONCLUSIONS: **Based on a matched cohort study, infertile women with IBD achieve a rate of live births after IVF that is comparable with those of infertile women without IBD.**

Keywords: Reproduction; Ulcerative Colitis; In Vitro Fertilization; Crohn's Disease.

See editorial on page 1647.

Crohn's disease (CD) and ulcerative colitis (UC) are the 2 most common idiopathic inflammatory bowel diseases (IBDs). The median age at onset of these diseases is 35 years, with a quarter of patients developing the disease before age 20.[1] Thus, IBD affects many women of reproductive age and raises concerns regarding the effects of these diseases on fertility. Studies suggest that fertility is unchanged in women with IBD who have received only medical management when compared with the general female population.[2–4] Based on the current literature, patients with UC who require a permanent ileostomy or total proctocolectomy with ileal pouch–anal anastomosis (IPAA) are the only group who have been shown to have

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Abbreviations used in this paper: BMI, body mass index; CD, Crohn's disease; CI, confidence interval; IBD, inflammatory bowel disease; IQR, interquartile range; IPAA, ileal pouch–anal anastomosis; IVF, in vitro fertilization; UC, ulcerative colitis.

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decreased fertility and fecundity, which is thought to be related to tubal adhesions from pelvic surgery.[5–10]

In the general population, up to 15% of women have problems with infertility, leading some to seek assisted reproductive technologies such as in vitro fertilization (IVF).[11] IVF begins with hormonal ovarian hyperstimulation to promote the development of multiple follicles. This may lead to multiple oocytes being retrieved and subsequently fertilized, thereby increasing the probability of a live birth. Ultrasound-guided transvaginal oocyte retrieval is performed after oocyte maturation, and the sperm and ovum subsequently are co-incubated in vitro. Embryos then are cultured and transferred into the uterus.

IVF is not uncommon. In 2010, there were 147,000 IVF treatments performed in the United States.[12] In a previously published study of 6164 patients undergoing IVF, the cumulative live birth rate after 6 cycles was 51% to 72%.[13] Certain factors have been associated with lower IVF success rates, including older maternal age, higher levels of day 3 follicle-stimulating hormone (FSH), fewer oocytes retrieved, fewer embryos transferred, higher body mass index (BMI), and tobacco use.[14–19] Depending on clinical circumstances, certain manipulations such as assisted hatching and intracytoplasmic sperm injection may be used to assist with IVF.

Whether IBD influences IVF success is unknown. In clinical practice, knowledge of these outcomes is relevant in patient–physician conversations regarding treatment decisions for IBD and the impact on future fertility. However, there are only sparse data regarding the use of IVF among women with IBD, primarily in those who have undergone surgery such as an ileostomy, colostomy, or IPAA.[8,20,21] This study compared the live birth rate after IVF in women with and without IBD.

Methods

Study Population

We identified 8684 female patients with IBD who were seen between 1998 and 2011 for possible inclusion in this matched retrospective cohort study from medical records of the gastrointestinal divisions of Beth Israel Deaconess Medical Center (Boston, MA; n = 4028) and Brigham and Women's Hospital (Boston, MA; n = 4656). We also identified all women who underwent their first fresh, nondonor, nongestational carrier IVF cycle at Boston IVF (an affiliate of Beth Israel Deaconess Medical Center; Waltham, MA) and the Brigham and Women's Hospital Center for Infertility and Reproductive Surgery (Boston, MA) during the same time period.

Patients whose diagnosis of IBD occurred before IVF treatment were designated as exposed. The medical records of the remaining women who underwent IVF were electronically searched for references to IBD using the terms "Crohn," "colitis," and "IBD" to exclude patients with IBD who may have been seen at another center. Patients whose records included references to IBD were reviewed individually, and patients with IBD were excluded from the group of unexposed patients. For each exposed woman, 4 unexposed women were matched on the basis of maternal age at the start of the first IVF cycle, the center where the first IVF cycle was performed, parity (nulliparous vs parous), and primary infertility diagnosis (male factor infertility, female factor infertility, or unexplained infertility). Women were followed up until either discontinuation of treatment, completion of 6 IVF cycles, or the delivery of a live infant(s), whichever occurred first. In 4 cases, fewer than 4 unexposed women were available owing to unique patient characteristics (3 women had 1 match, and 1 woman had 2 matches).

The primary outcome was the delivery of 1 or more live infants (cumulative live birth rate) in up to 6 IVF cycles. Any patient who did not deliver at least 1 live infant in a given cycle was eligible to return for care in the subsequent cycle, including patients whose cycle was canceled or those who became pregnant but did not have a live birth. Secondary outcomes included the incidence of pregnancy and live birth for each cycle, number of oocytes retrieved, and number of embryos cryopreserved.

Statistical Analysis

Data are presented as medians with interquartile range (IQR) or a proportion. The cumulative probability of the first live birth, which we refer to as the cumulative live birth rate, was calculated among both exposed and unexposed patients using a competing-risks analysis. The Pepe–Mori test was used to compare the survival curves between exposed and unexposed patients.[22] Although the cumulative live birth rate is a proportion and not a rate, we chose to use this term to mirror what is reported in the literature.[13,23] All analyses were conducted using SAS 9.3 (SAS Institute, Cary, NC) and Stata 12 (StataCorp, College Station, TX). All tests were 2-sided. *P* values less than .05 were considered statistically significant.

Results

We identified 132 patients with IBD who underwent IVF and 470 women without IBD who fulfilled matching criteria. Eleven of the women with IBD were excluded because the diagnosis of IBD could not be confirmed as having preceded the first IVF cycle. Seventy-one patients had UC, and 49 patients had CD; 1 patient had IBD-unclassified. The disease characteristics of the CD and UC patients are described in Tables 1 and 2, respectively.

Patients with CD received a diagnosis at a median of 10.3 years (IQR, 5.6–16.1 y) before initiating IVF. The disease at diagnosis was most often ileocolonic and nonstricturing and nonpenetrating in nature. A total of 53.1% of patients reported a previous surgery for CD. Twenty-three (53.5%) patients with CD were not taking any medications at the time of IVF.

Table 1. Disease Characteristics of Patients With Crohn's Disease

Characteristic	N (%) (N = 49)
Length of diagnosis, median (IQR), *y*	10.3 (5.6–16.1)
Location of disease at diagnosis	
Ileal	9 (18.4)
Colonic	11 (22.5)
Ileocolonic	16 (32.7)
Missing/unknown	13 (26.5)
Disease behavior at diagnosis	
Nonstricturing and nonpenetrating	20 (40.8)
Stricturing	7 (14.3)
Penetrating	7 (14.3)
Missing/unknown	15 (30.6)
Presence of perianal disease	
Yes	9 (18.4)
No	30 (61.2)
Missing/unknown	10 (20.4)
Prior surgical treatment(s)	26 (53.1)[a]
Ileocecal resection	9 (18.4)
Strictureplasty	1 (2.0)
Right hemicolectomy	0 (0.0)
Left hemicolectomy	1 (2.0)
Colectomy and ileoanal pull-through (IPAA)	1 (2.0)
Total proctocolectomy with permanent ileostomy	8 (16.3)
Diverting ostomy	1 (2.0)
Small intestinal resection	11 (22.4)
History of gynecologic surgeries	6 (12.2)
Current medications[b]	
Oral mesalamine	14 (32.6)
Antibiotics	1 (2.3)
Conventional glucocorticoids	2 (4.7)
Nonsystemic glucocorticoids	1 (2.3)
Immunomodulators	2 (4.7)
Biologics	4 (9.3)
Topical/suppository mesalamine	0 (0.0)
Topical/suppository steroid	0 (0.0
Cyclosporine	0 (0.0)
Methotrexate	0 (0.0)
Other	1 (2.3)
No medications	23 (53.5)

[a]Includes patients with multiple surgeries.
[b]Patients may have been on multiple medications; 6 patients were missing information on current medications, therefore the denominator is 43.

Table 2. Disease Characteristics of Patients With Ulcerative Colitis

Characteristic	N (%) (N = 71)
Length of diagnosis, median (IQR), *y*	8.9 (4.6–15.0)
Montreal classification at diagnosis	
E1: ulcerative proctitis	15 (21.1)
E2: left-sided (distal) UC	15 (21.1)
E3: extensive UC (pancolitis)	33 (46.5)
Missing/unknown	8 (11.3)
Surgical treatment(s)	
Colectomy and ileoanal pull-through (IPAA)	22 (31.0)
Total proctocolectomy with permanent ileostomy	3 (4.2)
Current medications[a]	
Oral mesalamine	21 (34.4)
Antibiotics	0 (0.0)
Conventional glucocorticoids	1 (1.6)
Nonsystemic glucocorticoids	0 (0.0)
Immunomodulators	5 (8.3)
Biologics	1 (1.6)
Topical/suppository mesalamine	5 (8.3)
Topical/suppository steroid	5 (8.3)
Cyclosporine	0 (0.0)
Methotrexate	0 (0.0)
Other	0 (0.0)
No medications	34 (56.7)

[a]Patients may have been on multiple medications; 11 patients were missing information on current use of immunomodulators, topical/suppository mesalamine, and topical/suppository steroids, therefore the denominator was 60. Ten patients were missing information on all other current medications, therefore the denominator was 61.

Patients with UC were diagnosed a median of 8.9 years (IQR, 4.6–15.0 y) before initiating IVF. Thirty-three (46.5%) patients had pancolitis. A total of 35.2% of patients underwent a prior total proctocolectomy either with an IPAA or end-ileostomy. Similar to the CD population, many patients with UC (N = 34; 56.7%) were not using medications at the time of IVF.

IBD disease characteristics are stratified further on the basis of prior surgery (Supplementary Table 1). We previously reported that in women with UC who have undergone IPAA, the live birth rate with IVF was comparable with that of women with UC without IPAA and with that of women without IBD.[23] Similarly, in women with CD, the cumulative live birth rate in patients with and without prior surgery was similar ($P = .58$) (Supplementary Figure 1).

Regarding further patient characteristics, patient age, parity, and cycle day 3 follicle-stimulating hormone level did not differ significantly among the non-IBD patients, patients with UC, or patients with CD (all $P > .05$) (Table 3). BMI was lower in the UC group (22.9; IQR, 21.0–25.0) compared with the non-IBD group (24.0; IQR, 21.5–28.0; $P = .05$), but did not differ between patients with CD and patients without IBD. Table 3 presents both primary and secondary infertility diagnoses. An infertility diagnosis of endometriosis was more common in the non-IBD population when compared with both the UC ($P = .04$) and CD ($P = .05$) groups. Tubal factor infertility was more common in the CD population compared with the non-IBD population (24.5% vs 14.0%; $P = .05$). Although this diagnosis also was more common in the UC population, when compared with the non-IBD population, the difference was not statistically significant. Notably, when patients with a primary diagnosis of male factor infertility were excluded, the cumulative live birth rate did not differ among patients with UC ($P = .10$) or CD ($P = .83$) when compared with the non-IBD population.

Both the IBD and non-IBD patients underwent a median of 2.0 (IQR, 1.0–3.0) cycles; the mean was 2.3 in the IBD group and 2.1 in the non-IBD group. There were no significant differences between the IBD and non-IBD groups with use of intracytoplasmic sperm injection,

Table 3. Participant Characteristics at the First IVF Cycle

Characteristic	Non-IBD (N = 470)	Ulcerative colitis (N = 71)	P[a]	Crohn's disease (N = 49)	P[b]
Age, *y*	35.2 (32.6–39.2)	35.1 (32.6–39.0)	.72	35.4 (32.0–39.1)	.76
Body mass index	24.0 (21.5–28.0)	22.9 (21.0–25.0)	.05	23.0 (21.6–26.0)	.42
Parity			.75		.93
0	333 (70.9)	49 (69.0)		35 (71.4)	
1+	137 (29.2)	22 (31.0)		14 (28.6)	
Cycle day 3 FSH	7.1 (5.7–9.2)	7.0 (6.0–9.1)	.98	7.0 (6.0–9.0)	.84
Infertility diagnosis[c]					
Male factor	119 (25.3)	18 (25.7)	.94	7 (14.3)	.09
Tubal factor	66 (14.0)	16 (22.9)	.06	12 (24.5)	.05
Ovulatory dysfunction	57 (12.1)	8 (11.4)	.87	5 (10.2)	.69
Endometriosis	51 (10.9)	2 (2.9)	.04	1 (2.0)	.05
Diminished ovarian reserve	28 (6.0)	3 (4.3)	.78	3 (6.1)	1.00
Uterine factor	12 (2.6)	2 (2.9)	.70	1 (2.0)	1.00
Unspecified female factor	26 (5.5)	2 (2.8)	.56	2 (4.1)	1.00
Unexplained	131 (27.9)	23 (32.9)	.39	13 (26.5)	.84
Missing	40 (8.5)	4 (5.6)	.41	6 (12.2)	.42

NOTE. Data are presented as medians (IQR) or n (%).
FSH, follicle stimulating hormone.
[a]*P* value compares non-IBD with ulcerative colitis.
[b]*P* value compares non-IBD with Crohn's disease.
[c]Represents both primary and secondary infertility diagnoses.

total dose of gonadotropins, peak estradiol level, oocytes retrieved, embryos cryopreserved, or embryos transferred (all $P > .05$) (Table 4). Fewer patients in the CD group underwent assisted hatching compared with the non-IBD group ($P = .04$). Clinical characteristics of each cycle for the full cohort are included in Supplementary Table 2.

Among women without IBD, 40.9% became pregnant after the first cycle. In the UC and CD groups, 49.3% and 42.9% of women became pregnant, respectively; these proportions did not differ from that of the non-IBD group ($P = .18$ and $P = 0.79$, respectively) (Table 4). After the first IVF cycle, 33.8% of women with UC and 30.6% of women with CD had a live birth, which did not differ from the proportion of women without IBD who had a live birth (30.2%; $P = .54$ and $P = .95$, respectively) (Table 4). Overall cycle outcomes and characteristics for the entire cohort are summarized in Supplementary Table 3.

Cumulative live birth rates were similar among women with and without IBD ($P = .13$) (Figure 1). After

Table 4. Characteristics and Outcomes of the IVF First Cycle According to IBD Status

Characteristic	Non-IBD (N = 470)	Ulcerative colitis (N = 71)	P[a]	Crohn's disease (N = 49)	P[b]
Manipulations					
Assisted hatching	81 (17.3)	12 (17.1)	.98	3 (6.1)	.04
Intracytoplasmic sperm injection	132 (36.2)	22 (38.6)	.72	10 (26.3)	.23
Total dose of gonadotropin, *IU*	3000 (1875–4725)	2625 (1735–4050)	.14	2700 (1950–3600)	.57
Peak estradiol level, *pg/mL*	1536 (949–2368)	1807 (1081–2476)	.37	1778 (1210–2293)	.46
Oocytes retrieved	10.5 (7.0–16.0)	11.0 (7.0–18.0)	.15	11.0 (7.0–20.0)	.30
Embryos cryopreserved			.27		.49
0	286 (69.4)	40 (59.7)		31 (68.9)	
1–3	60 (14.6)	12 (17.9)		9 (20.0)	
≥4	66 (16.0)	15 (22.4)		5 (11.1)	
Embryos transferred	2.0 (2.0–3.0)	2.0 (2.0–3.0)	.18	2.0 (2.0–3.0)	.53
Pregnancy	192 (40.9)	35 (49.3)	.18	21 (42.9)	.79
Live birth	142 (30.2)	24 (33.8)	.54	15 (30.6)	.95
Singleton	82 (57.8)	12 (50.0)	.62[c]	9 (60.0)	1.00[c]
Twin	33 (23.2)	8 (33.3)		4 (26.7)	
Triplet	6 (4.2)	0 (0.0)		0 (0.0)	
Unknown	21 (14.8)	4 (16.7)		2 (13.3)	

NOTE. Data are presented as medians (IQR) or n (%).
[a]*P* value compares non-IBD with ulcerative colitis.
[b]*P* value compares non-IBD with Crohn's disease.
[c]*P* value compares the number of live births by IBD status.

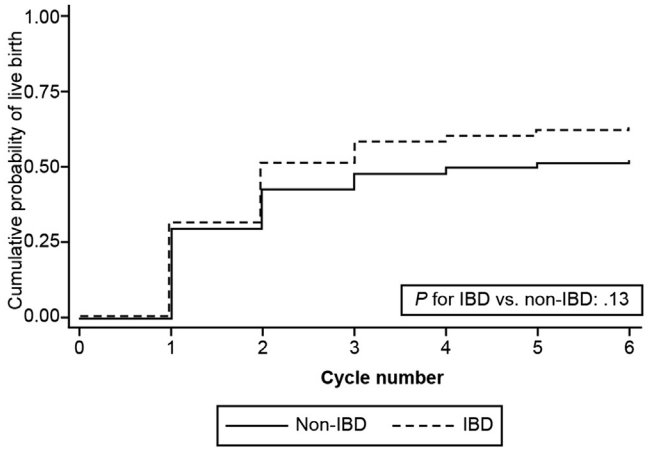

Figure 1. Competing-risks analysis for live births by IBD status. $P = .13$ for IBD vs non-IBD.

up to 6 cycles of IVF, the live birth rate was 69% (95% confidence interval [CI], 58%–79%) in UC patients, 57% (95% CI, 44%–71%) in CD patients, and 53% (95% CI, 48%–57%) in non-IBD patients (Supplementary Table 4 and Figure 2). Compared with non-IBD patients, the cumulative live birth rate did not differ among patients with UC ($P = .08$) or CD ($P = .87$).

Discussion

We evaluated the success of IVF in both medically and surgically treated IBD patients. Our results suggest that women with IBD have similar rates of pregnancy and live births after IVF compared with women without IBD. The cumulative live birth rates were similar to previously reported rates of 51% to 74% after 6 cycles of IVF.[13,24,25] The cumulative live birth rates in the UC cohort were somewhat higher than in the CD and non-IBD populations, although this difference did not reach statistical significance. This potential difference could have been owing to the fact that the UC cohort had a slightly lower BMI than the women in the other groups. As previously

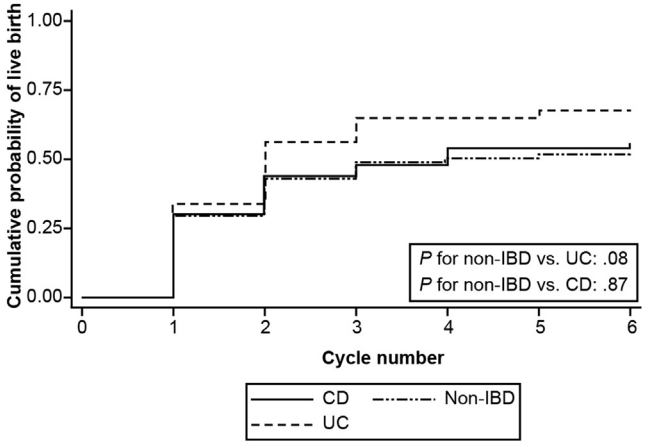

Figure 2. Competing-risks analysis for live births by IBD subgroup. $P = .08$ for non-IBD vs UC; $P = .87$ for non-IBD vs CD.

described, a higher BMI appears to be correlated inversely with the success of IVF.[16,17]

Interestingly, IBD patients had fairly high rates of prior surgeries. This probably is a reflection of the cohort we studied because patients who present with infertility potentially have a higher rate of tubal factor infertility as a result of adhesions from past pelvic surgeries. We did find that tubal factor infertility was more common among patients with IBD compared with those without IBD, particularly in the CD patients. Prior surgery in both our UC and CD cohorts did not influence live birth rates with IVF. The fact that patients with IBD achieved IVF success rates similar to patients without IBD patients is logical because IVF obviates the need for functional fallopian tubes.

This study had numerous strengths including the size of the cohorts. In addition, the matching of our patients with a non-IBD cohort mitigated possible confounding by age, parity, and fertility diagnosis. However, there were several limitations of this multicenter study, including its retrospective nature. Residual confounding by unmeasured variables, such as activity status, could be present. Tobacco use at the time of IVF is known to impact the success of IVF and could not be measured in this study given inconsistent reporting in the charts. Given that patients who undergo IVF are typically a highly motivated group, it seems unlikely that a high proportion of patients were actively smoking at the time of IVF. However, the fact that this variable could not be measured and controlled for was a limitation of our study. In addition, the patients were all from large tertiary care centers, which may somewhat limit the generalizability of the findings. Interestingly, more than half of the IBD patients were not on any medications at the time of IVF. In the UC population, 35.2% of patients had a prior IPAA or total proctocolectomy with ileostomy. Therefore, in this cohort, in which more than half of the patients were on no medications, we would expect that most of these patients were on no medications given the prior IPAA. Although such an explanation is not as straightforward in the CD cohort, we suspect that the high rate of surgery (53.1%) also may account for some patients having been on no medications. Some of these patients would have undergone surgery and not started postoperative therapy. Of those patients who were on medications for CD, a lower number were on immunomodulators or biologic therapy than one might expect. Therefore, it certainly is possible that our CD cohort had fairly mild disease and this should be noted when considering the generalizability of these results.

Overall, our novel data indicate that patients with IBD do not have inferior rates of pregnancy and live births after IVF when compared with the general infertility population. In clinical practice, knowledge of these outcomes is relevant in patient–physician conversations regarding fertility. Future studies should prospectively examine the success of IVF in patients with IBD and

potentially determine which factors uniquely influence the live birth rate in this population.

Supplementary Material

Note: To access the supplementary material accompanying this article, visit the online version of *Clinical Gastroenterology and Hepatology* at www.cghjournal.org, and at http://dx.doi.org/10.1016/j.cgh.2015.03.016.

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Conflicts of interest
These authors disclose the following: Adam Cheifetz has performed consulting and/or research for Janssen, AbbVie, Takeda, and Pfizer; and Alan Penzias has served on the advisory board (with compensation) for OvaScience and Nora Therapeutics, has served as a consultant for ReproSource, Inc, and has served on the speakers bureau for Ferring Pharmaceuticals. The remaining authors disclose no conflicts.

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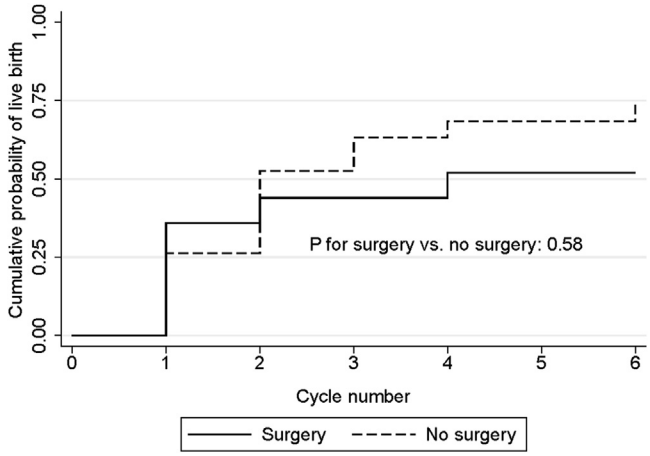

Supplementary Figure 1. Competing-risks analysis for live birth among patients with Crohn's disease by surgery status. $P = .58$ for surgery vs no surgery.

Supplementary Table 1. Characteristics of Patients by Disease and Surgery Status

Characteristic	Ulcerative colitis		Crohn's disease	
	IPAA (N = 22)	No IPAA (N = 49)	Surgery (N = 26)	No surgery (N = 23)
Had surgery	22 (100.0)	3 (6.1)	26 (100.0)	0 (0.0)
On current medication[a]	1 (5.3)	27 (64.3)	12 (48.0)	8 (44.4)
Length of diagnosis, median (IQR), *y*	11.9 (8.5–16.2)	7.2 (4.4–11.3)	13.2 (5.1–21.9)	8.3 (5.6–11.1)
Location at diagnosis				
Ileal	–	–	6 (23.1)	3 (13.0)
Colonic	–	–	5 (19.2)	6 (26.1)
Ileocolonic	–	–	11 (42.3)	5 (21.7)
Missing/unknown	–	–	4 (15.4)	9 (39.1)
Behavior at diagnosis				
Nonstricturing and nonpenetrating	–	–	8 (30.8)	12 (52.2)
Stricturing	–	–	4 (15.4)	3 (13.0)
Penetrating	–	–	7 (26.9)	0 (0.0)
Missing/unknown	–	–	7 (26.9)	8 (34.8)
Presence of perianal disease				
Yes	–	–	8 (30.8)	1 (4.4)
No	–	–	15 (57.7)	15 (65.2)
Missing/unknown	–	–	3 (11.5)	7 (30.4)
Montreal classification at diagnosis				
E1: ulcerative proctitis	0 (0.0)	15 (30.6)	–	–
E2: left-sided (distal) UC	2 (9.1)	13 (26.5)	–	–
E3: Extensive UC (pancolitis)	16 (72.7)	17 (34.7)	–	–
Missing/unknown	4 (18.2)	4 (8.2)	–	–

[a]Some patients were missing information on current medications, and the number missing and the resulting denominators are as follows: UC with IPAA group (3 missing; denominator, 19); UC and no IPAA group (7 missing; denominator, 42); CD and surgery group (1 missing; denominator, 25); and CD and no surgery group (5 missing; denominator, 18).

Supplementary Table 2. Clinical Characteristics According to IVF Cycle

Characteristic	Cycle 1	Cycle 2	Cycle 3	Cycle 4	Cycle 5	Cycle 6
Overall cohort, n/total n (%)[a]	591/591 (100.0)	331/427 (77.5)	177/245 (72.2)	87/145 (60.0)	46/74 (62.2)	21/37 (56.8)
Type of cycle, n (%)						
Fresh	591 (100.0)	270 (81.6)	152 (85.9)	72 (82.8)	40 (87.0)	19 (90.5)
Thaw	0 (0.0)	61 (18.4)	25 (14.1)	15 (17.2)	6 (13.0)	2 (9.5)
Manipulations, n (%)[b]						
Assisted hatching	96 (16.3)	78 (29.0)	60 (39.5)	32 (44.4)	23 (57.5)	12 (63.2)
Intracytoplasmic sperm injection	164 (35.7)	90 (44.6)	50 (43.9)	20 (38.5)	15 (46.9)	8 (50.0)
Total dose of gonadotropin, *IU*[b]	2850 (1875–4500)	3600 (2325–6000)	4050 (2475–5700)	5400 (2925–6600)	4350 (2100–6600)	5100 (3300–6600)
Peak estradiol level, *pg/mL*[b]	1646 (968–2370)	1367 (886–2150)	1292 (884–1959)	1308 (714–2135)	1157 (719–1970)	1289 (1208–2616)
Oocytes retrieved[b]	11.0 (7.0–16.0)	9.0 (6.0–14.0)	10.0 (6.0–14.0)	10.0 (5.0–16.0)	10.0 (6.0–14.0)	11.0 (5.0–16.0)
Embryos cryopreserved[b]						
0	357 (68.0)	177 (76.3)	107 (82.3)	53 (88.3)	28 (75.7)	16 (94.1)
1–3	81 (15.4)	32 (13.8)	14 (10.8)	4 (6.7)	6 (16.2)	0 (0.0)
≥4	87 (16.6)	23 (9.9)	9 (6.9)	3 (5.0)	3 (8.1)	1 (5.9)
Embryos transferred[b]	2.0 (2.0–3.0)	2.0 (2.0–3.0)	3.0 (2.0–3.0)	3.0 (2.0–3.0)	2.0 (2.0–4.0)	3.0 (2.0–5.0)

NOTE. Data are presented as medians and IQR except where noted.
[a]The denominator is the number of women eligible to return for that IVF cycle (calculated as the number of women in the previous cycle minus the number of women with a pregnancy resulting in a live birth).
[b]These data were calculated only for fresh transfer cycles.

Supplementary Table 3. Cycle Outcomes

Cycle	Cohort, n	Patients who did not return for treatment[a]	Pregnancies[b]	Live births[b]	Deliveries[c]			
					Singleton	Twin	Triplet	Unknown
1	591	Not applicable	248 (42.0)	181 (30.6)	103 (56.9)	45 (24.9)	6 (3.3)	27 (14.9)
2	331	96/427 (22.5)	131 (39.6)	86 (26.0)	54 (62.8)	19 (22.1)	1 (1.2)	12 (14.0)
3	177	68/245 (27.8)	59 (33.3)	32 (18.1)	21 (65.6)	8 (25.0)	0 (0.0)	3 (9.4)
4	87	58/145 (40.0)	26 (29.9)	13 (14.9)	7 (53.9)	4 (30.8)	0 (0.0)	2 (15.4)
5	46	28/74 (37.8)	17 (37.0)	9 (19.6)	5 (55.6)	4 (44.4)	0 (0.0)	0 (0.0)
6	21	16/37 (43.2)	9 (42.9)	5 (23.8)	4 (80.0)	1 (20.0)	0 (0.0)	0 (0.0)

NOTE. The n/total n (%) are shown.
NA, not applicable.
[a]The denominator is the number of women eligible to return for that IVF cycle (calculated as the number of women in the previous cycle minus the number of women with a pregnancy resulting in a life birth).
[b]The denominator is the number of women in the cycle cohort.
[c]The denominator is the number of live births in the cycle.

Supplementary Table 4. Cumulative Live Birth Rate and 95% Confidence Intervals for All Women and by IBD Status

Cycle	All women (N = 591)[a]	Non-IBD (N = 470)	Ulcerative colitis (N = 71)	Crohn's disease (N = 49)
1	0.31 (0.27–0.35)	0.30 (0.26–0.35)	0.34 (0.24–0.46)	0.31 (0.20–0.46)
2	0.45 (0.41–0.49)	0.43 (0.39–0.48)	0.56 (0.45–0.68)	0.45 (0.32–0.60)
3	0.51 (0.47–0.55)	0.49 (0.44–0.53)	0.65 (0.54–0.76)	0.49 (0.36–0.64)
4	0.53 (0.49–0.57)	0.50 (0.46–0.55)	0.65 (0.54–0.76)	0.55 (0.42–0.69)
5	0.54 (0.50–0.58)	0.52 (0.47–0.57)	0.68 (0.57–0.78)	0.55 (0.42–0.69)
6	0.55 (0.51–0.59)	0.53 (0.48–0.57)	0.69 (0.58–0.79)	0.57 (0.44–0.71)

[a]One woman had IBD-unspecified.