Surgery 166 (2019) 670–677

Contents lists available at ScienceDirect

Surgery

journal homepage: www.elsevier.com/locate/surg

Does laparoscopic ileal pouch-anal anastomosis reduce infertility compared with open approach?

Emre Gorgun, MD, FACS, FASCRS[a,*], Turgut Bora Cengiz, MD[b], Erman Aytac, MD, FEBC[a], Alexandra Aiello, MSPH[a], Giovanna da Silva, MD[c], Jeffrey M. Goldberg, MD[d], Stefan D. Holubar, MD, FACS, FASCRS[a], Luca Stocchi, MD, FACS, FASCRS[a], Steven D. Wexner, MD, PhD (Hon), FACS, FRCS, FRCS (Ed), FRCSI (Hon)[c], Scott R. Steele, MD, MBA, FACS, FASCRS[a], Tracy L. Hull, MD, FACS, FASCRS[a]

[a] Department of Colorectal Surgery, Digestive Disease and Surgery Institute, Cleveland Clinic, Cleveland, OH
[b] Department of General Surgery, Digestive Disease and Surgery Institute, Cleveland Clinic, Cleveland, OH
[c] Department of Colorectal Surgery, Cleveland Clinic Florida, Weston, FL
[d] Department of Obstetrics and Gynecology, Cleveland Clinic, Cleveland, OH

ARTICLE INFO

Article history:
Accepted 27 April 2019
Available online 14 August 2019

ABSTRACT

Background: The aim of this study was to assess the association of the mode of surgery on female fertility after restorative proctocolectomy with ileal pouch-anal anastomosis.

Methods: All female patients aged 18 to 44 years who underwent restorative proctocolectomy with ileal pouch-anal anastomosis for ulcerative colitis, familial adenomatous polyposis, or Crohn's disease at the Cleveland Clinic Ohio or the Cleveland Clinic Florida from 1983 to 2012 were sent a standardized fertility questionnaire. Infertility was defined as lack of pregnancy after 1 year of unprotected sexual intercourse. Patients who had attempted to conceive after restorative proctocolectomy with ileal pouch-anal anastomosis were compared based on the surgical approach: laparoscopic ileal pouch-anal anastomosis versus open ileal pouch-anal anastomosis.

Results: A total of 890 female patients were surveyed, of which 519 (58.3%) responded. Of these, 161 (31%) had attempted pregnancy after surgery: 18 (12%) had laparoscopic ileal pouch-anal anastomosis and 143 (88%) had open ileal pouch-anal anastomosis. There were no significant differences regarding demographics between groups. There was no difference in reported infertility rates (61.1% vs 65%, respectively, $P = 0.69$) between the laparoscopic ileal pouch-anal anastomosis and open ileal pouch-anal anastomosis groups. The median time to pregnancy (3.5 months vs 9 months, respectively, log-rank $P = 0.01$) was reduced in patients who underwent laparoscopic ileal pouch-anal anastomosis compared with those who underwent open ileal pouch-anal anastomosis.

Conclusion: Postoperative infertility rates were higher after ileal pouch-anal anastomosis regardless of mode of surgery. However, laparoscopy was associated with a significantly reduced time to conceive compared with the open approach.

Introduction

Restorative proctocolectomy (RP) with ileal pouch-anal anastomosis (IPAA) is the mainstay of the surgical treatment in patients with ulcerative colitis (UC), familial adenomatous polyposis (FAP), and in highly selected patients with Crohn's disease (CD).[1,2] In contrast to proctocolectomy with end ileostomy, RP-IPAA maintains transanal defecation and is associated with improved quality of life in some series.[3,4] Many patients undergoing surgery for UC or FAP are relatively young, and a substantial portion of women who undergo RP-IPAA are at their reproductive age and desirous of children.

It is widely recognized that both the medical and surgical treatments of inflammatory bowel disease are associated with infertility.[5] After RP-IPAA, this problem is likely due to the nature of the extensive dissection leading to intra-abdominal and pelvic

Presented at the 76th Annual Meeting of the Central Surgical Association, Palm Harbor, FL.

* Reprint requests: Emre Gorgun, MD, FACS, FASCRS, Department of Colorectal Surgery, Cleveland Clinic, 9500 Euclid Ave, A-30, Cleveland, OH 44195.
E-mail address: gorgune@ccf.org (E. Gorgun).

https://doi.org/10.1016/j.surg.2019.04.045
0039-6060/

adhesions. The repercussions of these adhesions are especially problematic in female patients when they affect the fallopian tubes and ovaries, potentially hindering reproductive function.[2,6] Female infertility after proctectomy may also be related to transposition of the ovaries; alterations in body image, especially in the presence of an ostomy; and other psychosocial factors. Studies have shown that decreased fertility and fecundity after RP-IPAA are likely due to increased adnexal adhesions, which increased infertility rates in young female patients.[2,7]

The introduction of laparoscopy has decreased abdominopelvic surgical trauma and has been associated with postoperative improvements, including reductions in length of stay, postoperative pain, and overall morbidities.[8,9] Laparoscopic IPAA (L-IPAA) has been shown to be safe and feasible, yet its adoption has been slow owing to technical challenges.[10] Nevertheless, one purported advantage of laparoscopy is decreased intra-abdominal adhesions; hence, one might expect the implementation of laparoscopy in RP-IPAA could decrease surgery-related adhesions and result in increased pregnancy rates compared with the open IPAA (O-IPAA) technique.[11–13]

In this study, we hypothesized that the infertility rate associated with the L-IPAA technique would be lower than that of O-IPAA, and L-IPAA would decrease time to conception compared with O-IPAA in female patients undergoing surgery for UC, FAP, or CD. We aimed to compare the infertility rates after L-IPAA and O-IPAA in patients who attempted to achieve pregnancy after surgery. Our secondary aim was to compare pregnancy outcomes before and after RP-IPAA.

Methods

Our study was conducted in Cleveland Clinic Ohio and Cleveland Clinic Florida. All female patients aged 18 to 44 years at the study inception date who had previously undergone RP-IPAA for either UC, FAP, or CD from 1983 to 2012 were identified from a prospectively maintained Institutional Review Board–approved pouch database. After obtaining approval from the Institutional Review Board for further communication with patients, an introductory letter was sent to all patients 2 weeks before the questionnaires. This letter was sent to allow patients to decline participation in this study and to communicate questions to the authors ahead of enrollment. Two weeks after mailing the questionnaires, all patients were contacted by telephone to ensure timely delivery of the questionnaires and to answer questions. Patients who did not return their questionnaires were asked to provide their data by telephone interview or via e-mail. The questionnaire is shown in Appendix 1. Data about pregnancy attempts, time to first pregnancy, details of previous pregnancies, any diagnosis of infertility in patients or in their partners, any infertility therapy used, details of menstrual cycles, delivery methods, and infertility tests (including semen analysis, progesterone level, saline ultrasound, hysterosalpingography [HSG]) performed either before or after surgery were collected.

Patient demographics, including age, body mass index, diagnosis, operative approach, disease duration before surgery, and prior abdominal surgeries before IPAA, as well as perioperative information, including type of pouch, type of operation (total proctocolectomy or completion proctectomy), operative time, intraoperative transfusions, length of stay, and presence of an ileostomy, were retrieved from the database and chart review as needed. Ancillary procedures (adhesiolysis, oophorexy, and anti-adhesive membrane use) were recorded if they were documented in the operative reports.

Patients who attempted to get pregnant after pouch surgery based on the survey response were stratified in to 2 groups, L-IPAA or O-IPAA, based on the operative approach. Patients in whom a laparoscopic operation was converted to open surgery or reoperations necessitating laparotomy were also grouped as O-IPAA.

Patients who did not attempt to get pregnant after surgery and individuals who were diagnosed with male-factor infertility but did not receive any infertility treatment were excluded. Reoperative pouches were also excluded.

Both laparoscopic and open procedures followed the same surgical principles. Laparoscopic surgery was performed in either a laparoscopic or hand-assisted fashion via a Pfannenstiel incision. If a 2-staged procedure was planned, the completion proctectomy and IPAA were done either with a laparoscopic approach or under direct view with pelvic retractors (including hand-assisted laparoscopic surgery), as described in a previous series.[9] All hand-assisted surgeries and surgeries conducted under direct vision were included in the laparoscopic group. We included staged operations along with pouch revisions. Pouch revisions were performed transabdominally for pouch inlet strictures, twisting of the pouch, pouch prolapse, or leaks at the tip of the J-pouch where the previously formed pouch is preserved.

Pregnancy was defined as any pregnancy confirmed by ultrasound imaging including child birth, miscarriage, abortion, extrauterine pregnancy, or ongoing pregnancy. Infertility was defined as failure to achieve any pregnancy despite 1 year of unprotected sexual intercourse. Infertility rates in the groups were calculated as the number of women who failed to become pregnant after a year of unprotected intercourse divided by the number of women who pursued pregnancy. Infertility rate was also assessed after stratifying our cohort into 3 subgroups based on age: 18 to 30, 31 to 35, and 36 to 44 years. The time between commencement of the pregnancy attempt and first pregnancy after surgery was reported as time to conceive. All variables collected through the questionnaire were subjective statements of the participating patients. Postoperative complications were stratified according to the Clavien-Dindo classification.[14] These complications included pouch-related complications (anastomotic leaks, anastomotic strictures, pelvic abscess, pouchitis) as well as infectious (surgical-site infections, urinary tract infections, pneumonia), hematologic (deep venous thrombosis, mesenteric/portal venous thrombosis), and other (ileus, urinary retention) complications.

Categorical variables were reported as frequency (%), and quantitative variables were reported as means ± standard deviations or medians (interquartile ranges). Categorical variables were compared using the Fisher exact test or χ^2 test, whereas quantitative and ordinal variables were compared using the Wilcoxon rank sum test or independent t test between the L-IPAA and O-IPAA groups. The McNemar test or Bowker test of symmetry were used for the dependent variables. Time to conception between the groups was assessed using Kaplan-Meier survival analysis.

Results

Demographics and perioperative outcomes

A total of 890 female patients were surveyed, 519 (58.3%) of whom responded. A total of 161 (30.7%) patients who attempted to become pregnant after IPAA were included in the final analysis. There were 18 (11.1%) patients in the L-IPAA group and 143 (88.9%) patients in the O-IPAA group. Two patients' operations were converted to an open approach and 1 patient in the L-IPAA group necessitated laparotomy on the postoperative day 1 owing to hemorrhage. A summary of baseline characteristics and perioperative data is shown in Table I. The mean years of disease duration (6.9 ± 5.8 vs 5.4 ± 5, respectively), age at the time of diagnosis (19.6 ± 7.9 vs 22.9 ± 7.7 years, respectively), and age at the time of surgery (27.8 ± 5.7 vs 28.2 ± 7 years, respectively) were comparable

Table I
Demographics and perioperative details

Factor	L-IPAA (n = 18)	O-IPAA (n = 143)	*P* value
Age at the time of diagnosis (y)	19.6 ± 7.9	22.9 ± 7.7	.11
Age at the time of surgery (y)	27.8 ± 5.7	28.2 ± 7.0	.82
Interval between surgery and survey (y)	8.4 ± 5.3	13.3 ± 7.1	**.005**
Body mass index	24.0 ± 6.2	23.9 ± 5.5	.94
Prior abdominal surgery	7 (38.9%)	72 (50.3%)	.35
Disease			.43
UC	15 (83.3%)	129 (90.2%)	
FAP	2 (11.1%)	9 (6.3%)	
CD	1 (5.6%)	5 (3.5%)	
Procedure			.10
Total proctocolectomy	11 (61.1%)	58 (40.6%)	
Completion proctectomy	5 (27.8%)	68 (47.6%)	
Revision	1 (5.6%)	15 (10.5%)	
Pouch type			.26
J-pouch	16 (88.9%)	129 (90.2%)	
S-pouch	0	10 (7.0%)	
Operative time (min)	312 ± 95	242 ± 74	**.004**
Estimated blood loss (mL)	200 ± 155	372 ± 231	**.03**
Ileostomy	12 (66.7%)	117 (81.8%)	.12
Adhesiolysis	3 (16.7%)	48 (33.6%)	.14
Oophorexy	2 (11.1%)	33 (23.1%)	.24
Antiadhesives	3 (16.7%)	36 (25.2%)	.42
Intraoperative transfusion	0	14 (9.8%)	.16
Length of stay (days)	5.5 (4–7)	6 (5–9)	.07
Postoperative complication	4 (22.2%)	64 (44.8%)	.08
Clavien-Dindo classification I and II	2	28	.80
Clavien-Dindo classification III and IV	2	36	
Readmission	1 (5.6%)	15 (10.5%)	.50

Data are *n* (%), means ± standard deviation, or median (interquartile range), unless otherwise indicated. Bold *P* values denote statistical significance.

between the L-IPAA and O-IPAA groups. The mean time interval from surgery to survey was 8.4 ± 5.3 years in L-IPAA patients and 13.3 ±7.1 years in O-IPAA patients ($P < .05$). The distribution of the preoperative diagnoses was similar between the groups: 15 (83.3%) versus 129 (90.2%) had UC, 2 (11.1%) versus 9 (6.3%) had FAP, and 1 (5.6%) versus 5 (3.5%) had CD in the L-IPAA and O-IPAA cohorts ($P = .43$), respectively. Both groups had similar mean body mass index ($P = .94$) and rate of previous abdominal surgeries ($P = .35$).

The majority of the patients in the L-IPAA group underwent total proctocolectomy (61.1% vs 40.6%, respectively), whereas completion proctectomy was more common in the O-IPAA group (27.8% vs 47.6%, $P = .10$, respectively). J-pouch was the preferred pouch type in both groups (90% overall, $P = .26$). Diverting ileostomy rates at the time of IPAA were also similar between the L-IPAA and O-IPAA groups (66.7% vs 78.3%, $P = .12$, respectively). Operative time was longer but estimated blood loss was lower in the L-IPAA group. The median length of stay was similar in each group. Adhesiolysis, oophorexy, use of antiadhesive membranes, intraoperative transfusion, postoperative complications, and readmission rates were comparable between the groups.

Before IPAA surgery

No significant differences between the groups were reported by patients in terms of infertility before IPAA construction (details are shown in Table II, all $P > .05$). A total of 7 (38.9%) patients in the L-IPAA group and 69 (48.6%) patients in O-IPAA group had preoperatively attempted to get pregnant. Although 2 (28.6%) vs 18 (26.1%) patients had difficulties getting pregnant, 7 (100%) vs 62 (89.9%) patients were able to conceive in the L-IPAA and O-IPAA groups, respectively. Only 2 (28.6%) patients in the L-IPAA group vs 28 (40.6%) patients in the O-IPAA group failed to conceive despite having at least a year of unprotected sexual intercourse. Eight (5.6%) patients in the O-IPAA group were diagnosed with infertility before RP-IPAA, and all 8 patients received infertility treatment. Ovulation induction was the most common infertility treatment. Five (3.5%) patients in the O-IPAA group had irregular menstrual periods. Four (22.2%) vs 47 (32.9%) patients in the L-IPAA and O-IPAA cohorts, respectively, reported deliveries before surgery, and vaginal delivery was the most common delivery method in the L-IPAA and O-IPAA cohorts.

After IPAA surgery

The details of the pregnancies after RP-IPAA are shown in Table III. Eleven (61.1%) patients in the L-IPAA group and 82 (57.3%) patients in the O-IPAA group reported difficulties getting pregnant ($P = .76$) after surgery. The number of patients who reported a lack of pregnancy despite having 1 year of unprotected sexual intercourse was 11 (61.1%) in the L-IPAA cohort and 93 (65.0%) in the O-IPAA cohort ($P = .74$). There was no difference between the groups when the infertility rates were analyzed in 3 age groups. Eight (44.4%) patients in the L-IPAA group and 77 (53.8%) patients in O-IPAA group who desired to become pregnant were able to conceive after RP-IPAA. There were 46 patients (28.6% overall, 4 in the L-IPAA group and 42 in the O-IPAA group) who were medically diagnosed with infertility after surgery. Among patients diagnosed with infertility, 2 (11.1%) in the L-IPAA group and 16 (11.2%) in the O-IPAA group had abnormal HSG, which was the most common abnormality indicative of infertility post-IPAA. Forty-nine patients received infertility therapy: 4 (22.2%) patients in L-IPAA group and 45 (31.5%) patients in the O-IPAA group. This number included 7 patients who had already been diagnosed with infertility before RP-IPAA. In the L-IPAA and O-IPAA groups, ovulation induction (2 vs 33 patients, respectively), in vitro fertilization (3 vs 17 patients, respectively), artificial insemination (0 vs 16 patients, respectively), and fertility surgery (1 vs 14 patients, respectively) were the infertility therapy methods used. Nine (50%) versus 76 (53.1%) deliveries were reported in the L-IPAA and O-IPAA cohorts, respectively. Cesarean section was more likely to be preferred post-IPAA.

Table II
Details of fertility before IPAA surgery

Survey Response	L-IPAA (n = 18)	O-IPAA (n = 143)	*P* value
Attempted to get pregnant	7 (38.9%)	69 (48.6%)	.44
Difficulty getting pregnant before surgery*	2 (28.6%)	18 (26.1%)	.86
Conceived before surgery*	7 (100%)	62 (89.9%)	.90
Preoperative infertility (by definition)*	2 (28.6%)	28 (40.6%)	.69
Number of pregnancies before surgery			.42†
Means ± standard deviation	0.8 ± 1.3	0.9 ± 1.2	
Median (min, max)	0 (0–3)	0 (0–5)	
Diagnosed with infertility before surgery	0	8 (5.6%)	.99
Abnormal laparoscopy	0	2 (1.4%)	
Abnormal HSG	0	0	
Abnormal progesterone level	0	3 (2.1%)	
Abnormal saline ultrasound or hysteroscopy	0	1 (0.7%)	
Unknown	0	2 (1.4%)	
Irregular menstrual periods	0	5 (3.5%)	.99
Received infertility therapy	0	8 (5.6%)	.99
Ovulation induction	0	6 (4.2%)	
Superovulation	0	1 (0.7%)	
In vitro fertilization	0	1 (0.7%)	
Fertility surgery	0	3 (2.1%)	
Who had deliveries	4 (22.2%)	47 (32.9%)	.36
Cesarean section	1 (5.6%)	10 (7.0%)	
Vaginal delivery	3 (16.7%)	35 (24.5%)	
Abortions	0	7 (4.9%)	.99
Miscarriages	3 (16.7%)	17 (11.9%)	.47

Data are *n* (%) or means ± standard deviation, unless otherwise indicated.
* As proportional to the number of patients who had attempted pregnancy.
† Kruskal-Wallis test.

Table III
Details of fertility after IPAA surgery

Survey Response	L-IPAA (n = 18)	O-IPAA (n = 143)	*P* value
Difficulty getting pregnant after surgery	11 (61.1%)	82 (57.3%)	.76
Conceived after surgery	8 (44.4%)	77 (53.8%)	.45
Postoperative infertility (by definition)	11 (61.1%)	93 (65.0%)	.74
Number of pregnancies after surgery			.97*
Means ± standard deviation	1 ± 1.1	1.1 ± 1.1	
Median (min, max)	1 (0–4)	1 (0–5)	
Medically diagnosed with infertility after surgery	4 (22.2%)	42 (29.4%)	.53
Abnormal laparoscopy	1 (5.6%)	7 (4.9%)	
Abnormal HSG	2 (11.1%)	16 (11.2%)	
Abnormal progesterone level	0	6 (4.2%)	
Abnormal saline ultrasound or hysteroscopy	0	8 (5.6%)	
Abnormal semen analysis	0	4 (2.8%)	
Unknown	0	3 (2.1%)	
Irregular menstrual periods	2 (11.1%)	30 (21.0%)	.32
Received infertility therapy	4 (22.2%)	45 (31.5%)	.79
Ovulation induction	2 (11.1%)	33 (23.1%)	
Superovulation	1 (5.6%)	7 (4.9%)	
In vitro fertilization	3 (16.7%)	17 (11.9%)	
Fertility surgery	1 (5.6%)	14 (9.8%)	
Artificial insemination	0	16 (11.2%)	
Who had deliveries	9 (50%)	76 (53.1%)	.80
Cesarean section	8 (44.4%)	67 (46.9%)	
Vaginal delivery	1 (5.6%)	9 (6.3%)	
Abortions	4 (22.2%)	18 (12.6%)	.26
Miscarriages	3 (16.7%)	18 (12.6%)	.62
Tubal pregnancy	0	2 (1.4%)	.99
Time to first pregnancy after surgery (months)			**.01**
Mean	4	16.6	
Median	3.5	9	

Data are *n* (%), means ± standard deviation, or median (interquartile range), unless otherwise indicated. Bold *P* value denotes statistical significance.
* Kruskal-Wallis test.

The patients in the L-IPAA group had significantly lower mean (4 vs 16.6 months, respectively) and median (3.5 vs 9 months, respectively) time intervals to achieve pregnancy compared with the O-IPAA patients (log rank $P = .01$). Kaplan-Meier curve for the time to pregnancy is shown in Figure.

Before versus after surgery

The pooled analysis comparing patients before and after surgery is outlined in Table IV. A total of 76 (47.2%) patients had attempted to get pregnant pre-IPAA. Twenty (26.3%) patients before IPAA and

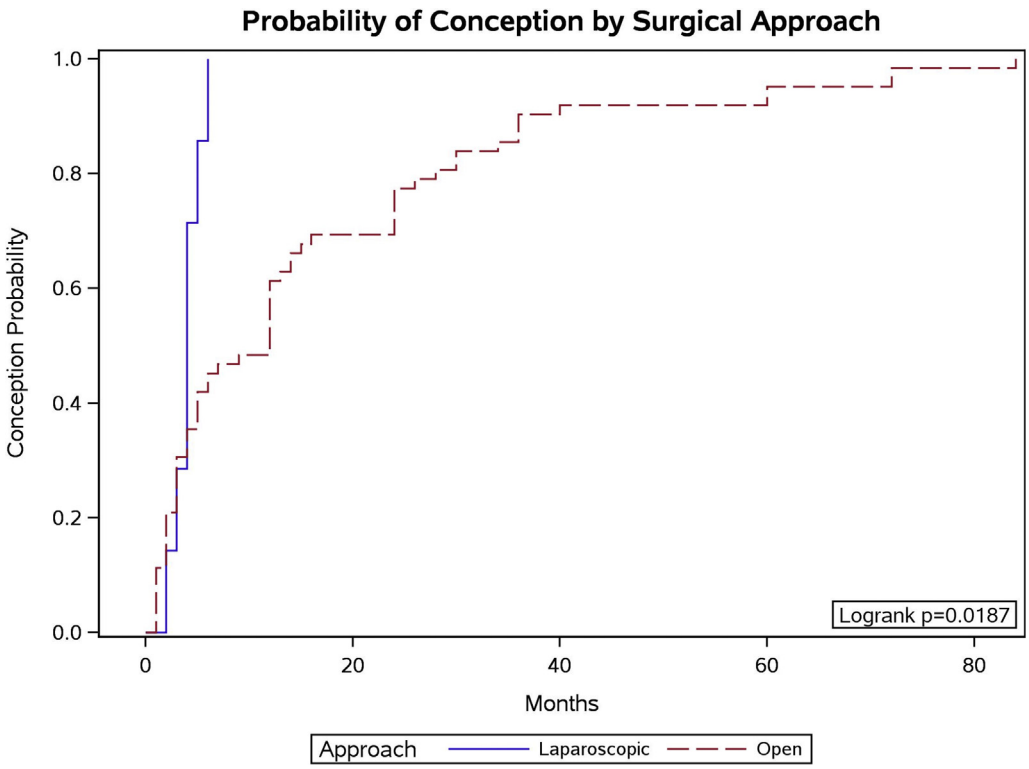

Figure. Kaplan-Meier curve for time to pregnancy for those attempting to conceive after laparoscopic and open IPAA.

93 (57.8%) patients after IPAA had difficulties getting pregnant. Five (3.1%) versus 32 (19.9%) patients experienced irregular menstrual periods pre- and post-IPAA, respectively. The number of patients with a diagnosis of infertility who were receiving infertility treatments was significantly increased after IPAA. Although no patients had abnormal HSG pre-IPAA, 18 (11.1%) patients had abnormal HSG post-IPAA. Among patients who had attempted to get pregnant, 30 (39.4%) patients failed to get pregnant despite 1 year of unprotected sexual intercourse pre-IPAA, but this number surged to 104 (64.5%) patients post-IPAA. Although there was a decrease in the conception rate post-IPAA, it was nonsignificant (69 [90.7%] vs 85 [52.8%] pre- and post-IPAA, respectively).

Discussion

Overall, our major findings were that infertility was common in this patient population both pre- and postoperatively and that mode of surgery did not seem to mitigate the reported increase in postoperative female infertility. A unique and intriguing finding of our study was that the patients in the L-IPAA group were able to conceive a pregnancy dramatically faster than those who had O-IPAA. The implications of this latter finding suggest that laparoscopic pouch construction, vis-a-vis the biologically plausible mechanism of reduced pelvic adhesions, does play a role in maintenance of fertility, and L-IPAA should be strongly considered for young fertile female patients whenever possible.

Many studies reported increased infertility rates post-IPAA. A previous study from our institution showed an 18% increase in infertility (38% pre-IPAA and 56% post-IPAA) after pouch formation.[2] Similarly, the Rajaratnam et al[15] meta-analysis concluded that the risk of infertility is almost 4 times higher (relative risk 3.91 [confidence interval: 2.06, 7.44]) post-IPAA. Herein, we also reported a 25.1% increase in infertility rate post-IPAA. Coherently, the rate of infertility treatment was higher in post-IPAA, which indirectly indicates reduced fertility after RP-IPAA. All of these factors justify the concerns behind reduced fertility and promote further studies.

Pouch surgery has been shown to cause severe abdominal and pelvic adhesions, which is the main suspected reason for impaired fertility in female patients, although postproctectomy tubo-ovarian positional changes likely play a role as well. Oresland et al[16] performed HSG on 21 women who underwent RP-IPAA and found that only 7 patients had entirely normal fallopian tubes, which further supports this theory. To date, several options have been proposed to decrease postoperative adhesions and preserve fertility in female patients undergoing RP-IPAA, including laparoscopic surgery.[17] These include pre- or intraoperative ovarian transposition by fixation to the lower anterior abdominal wall, a practice which has largely been abandoned in IPAA patients, although it is making a resurgence in premenopausal women before they undergo pelvic irradiation.[18,19] Antiadhesion barriers, such as SepraFilm (Genzyme Corporation, Cambridge, MA) and other commercially available products, have been advocated but with limited informative data after colorectal surgery.[20] Thus, the main method of preventing pelvic adhesions is the use of laparoscopic surgery.

Laparoscopic surgery not only offers superior perioperative outcomes, but it also results in fewer intra-abdominal and pelvic adhesions after IPAA.[8,11,21] Hull et al[11] reported significantly decreased total abdominal adhesion scores (2 vs 8, respectively) in patients who had undergone L-IPAA compared with O-IPAA. Therefore, one might expect to observe lower infertility rates in women who underwent L-IPAA compared with O-IPAA; however, we did not demonstrate this association in our cohort.[13] The L-IPAA group in the present study had a comparable infertility rate to the O-IPAA cohort (61.1% vs 65.0%, respectively), even when stratified by age subgroups. This finding contradicts the literature because L-IPAA is usually associated with reduced infertility rates.[22] Both Bartels et al[23] and Beyer-Berjot et al[24] showed lower infertility rates after L-IPAA compared with their control groups, although the control

Table IV
Comparison of pre- and post-IPAA characteristics

Survey Response	Pre-IPAA	Post-IPAA	*P* value
Attempted pregnancy	76 (47.2%)	161 (100%)	**<.001**
Difficulty getting pregnant*	20 (26.3%)	93 (57.8%)	**<.001**
Infertility (by definition)*	30 (39.4%)	104 (64.5%)	**<.001**
Conception*	69 (90.8%)	85 (52.8%)	.09
Irregular menstrual periods	5 (3.1%)	32 (19.9%)	**<.001**
Diagnosis of infertility	8 (5.0%)	46 (28.6%)	**<.001**
Abnormal laparoscopy	2 (1.2%)	8 (5.0%)	
Abnormal HSG	0	18 (11.1%)	
Abnormal progesterone	3 (1.9%)	6 (3.7%)	.99
Abnormal saline ultrasound/hysteroscopy	1 (0.6%)	8 (5.0%)	.80
Unknown	2 (1.2%)	3 (1.9%)	
Infertility therapy	8 (5.0%)	49 (30.4%)	**<.001**
Ovulation induction	6 (3.7%)	35 (21.7%)	
Superovulation	1 (0.6%)	8 (5.0%)	
In vitro fertilization	1 (0.6%)	20 (12.4%)	
Fertility surgery	3 (1.9%)	15 (9.3%)	
Artificial insemination	0	16 (10.0%)	

Data are *n* (%), unless otherwise indicated. Bold *P* values denote statistical significance.
* Ratios are reported as proportional to the patients who had attempted pregnancy in each group.

group in the latter study was composed of laparoscopic appendectomy patients. This unexpected finding might be due to our study being underpowered by low numbers of patients in the L-IPAA group because our laparoscopic group consisted of only 18 patients while there were 143 patients in the O-IPAA group. Survey response bias likely played a role as well because patients with preserved fertility logically were less likely to be motivated to participate in the study. Nevertheless, our pooled post-IPAA infertility rate was 64.5% (104 of 161 patients), which was in line with a previous meta-analysis in which a 63% weighted average infertility rate post-IPAA (range 44%–82%) was reported.[15] When interpreting this apparently high rate and counseling patients, it is important to focus on the widely accepted definition of infertility after 1 year, and that many options exist for individuals with infertility. Specifically, medically assisted ovulation stimulation, transvaginal egg harvesting, and in vitro fertilization are all potential options for these patients.

Although infertility after pouch surgery has been thoroughly discussed, there seems to be a paucity of studies investigating the time to conception post-IPAA. Beyer-Berjot et al[24] reported a mean time until pregnancy of 11 months in their cohort of 56 patients, of which 15 attempted pregnancy. However, when they compared L-IPAA patients to laparoscopic appendectomy control subjects, they did not observe any difference regarding the time until pregnancy (log-rank $P = .39$).[24] Bartels et al[23] further investigated the time until pregnancy and compared 27 L-IPAA patients with 23 O-IPAA control subjects who had attempted to conceive after surgery. In their cohort, there was a significant difference regarding the time to conceive between the open and laparoscopic groups, including those who underwent in vitro fertilization after RP-IPAA.[23] In the present study, we also observed a similar effect of laparoscopy on time to pregnancy because our L-IPAA group had a shorter mean and median time interval to conceive compared with the O-IPAA group. This particular finding after laparoscopic surgery can be explained by the presumed fewer adhesions, yet time to achieve pregnancy is multifactorial. Nevertheless, we were able to compare the baseline differences before and after surgery (number of pregnancies, details of the menstrual cycles, infertility tests) that could influence conception, which were not comprehensively assessed in the previous reports. Ultimately, the constellation of the advantages of laparoscopy and decreased postoperative adhesions might increase the possibility of achieving an earlier pregnancy after L-IPAA as compared with O-IPAA.[25]

Our study has certain limitations. Apart from the retrospective nature of the study, as stated earlier, we may have been underpowered because there were only 18 patients in the L-IPAA group, and survey response bias may have influenced our outcomes. Second, we included surgeries from 1983 to 2012, during which time the management of UC, FAP, and CD significantly changed. Our first open case was performed in 1983, but our first laparoscopic case was not performed until 1993. Even though all of the surgeries were done by experienced colorectal surgeons, one might expect to see the effects of a learning curve in the laparoscopic group. Also, some patients had surgeries in 1983 and completed the questionnaire in 2014. Therefore, the gap between the dates of surgery to questionnaire completion was up to almost 30 years in some patients, which inevitably leads to recall bias. Because O-IPAA patients were older at the time of survey, we would expect this group to demonstrate the effects of recall bias more commonly than the L-IPAA group. Finally, because tertiary referral centers who see an increased portion of difficult-to-treat cases, referral bias may have influenced our results and limited generalizability. Despite these limitations, our study has several strengths, including the depth and breadth of the cohort, which was selected from the world's largest IPAA registry of more than 5,000 IPAA cases spanning multiple decades with detailed perioperative and longitudinal data, thus representing unique data and insights into this topic, which is very important to young individuals faced with this operation.

In conclusion, the L-IPAA approach did not confer any advantage over O-IPAA in terms of decreasing the infertility rate after surgery. However, laparoscopy may shorten time to conception, which is a benefit in patients attempting to achieve pregnancy. The increased rate of infertility should be discussed with patients before surgery because our data support the evidence behind a higher incidence of infertility and the subsequent increased rate of infertility treatment following RP-IPAA.

Funding/Support

The authors have no financial ties to disclose.

Conflict of interest/Disclosure

The authors have no conflict of interests to disclose.

Acknowledgments

The authors thank Ali Al Ansari for his help during the manuscript preparation.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at https://doi.org/10.1016/j.surg.2019.04.045.

References

1. Shen B, Remzi FH, Lavery IC, Lashner BA, Fazio VW. A proposed classification of ileal pouch disorders and associated complications after restorative proctocolectomy. *Clin Gastroenterol Hepatol*. 2008;6:145–158; quiz 124.
2. Gorgun E, Remzi FH, Goldberg JM, et al. Fertility is reduced after restorative proctocolectomy with ileal pouch anal anastomosis: A study of 300 patients. *Surgery*. 2004;136:795–803.
3. Fazio VW, O'Riordain MG, Lavery IC, et al. Long-term functional outcome and quality of life after stapled restorative proctocolectomy. *Ann Surg*. 1999;230:575–584; discussion 584–586.
4. McLeod RS, Baxter NN. Quality of life of patients with inflammatory bowel disease after surgery. *World J Surg*. 1998;22:375–381.
5. Ban L, Tata LJ, Humes DJ, Fiaschi L, Card T. Decreased fertility rates in 9639 women diagnosed with inflammatory bowel disease: A United Kingdom population-based cohort study. *Aliment Pharmacol Ther*. 2015;42:855–866.
6. Vender RJ, Spiro HM. Inflammatory bowel disease and pregnancy. *J Clin Gastroenterol*. 1982;4:231–249.
7. Olsen KO, Joelsson M, Laurberg S, Oresland T. Fertility after ileal pouch-anal anastomosis in women with ulcerative colitis. *Br J Surg*. 1999;86:493–495.
8. Braga M, Vignali A, Gianotti L, et al. Laparoscopic versus open colorectal surgery: A randomized trial on short-term outcome. *Ann Surg*. 2002;236:759–766; disscussion 767.
9. Lavryk OA, Stocchi L, Ashburn JH, et al. Case-matched comparison of long-term functional and quality of life outcomes following laparoscopic versus open ileal pouch-anal anastomosis. *World J Surg*. 2018;42:3746–3754.
10. Larson DW, Cima RR, Dozois EJ, et al. Safety, feasibility, and short-term outcomes of laparoscopic ileal-pouch-anal anastomosis. *Ann Surg*. 2006;243(5):667–672.
11. Hull TL, Joyce MR, Geisler DP, Coffey JC. Adhesions after laparoscopic and open ileal pouch-anal anastomosis surgery for ulcerative colitis. *Br J Surg*. 2012;99:270–275.
12. Stommel MWJ, ten Broek RPG, Strik C, et al. Multicenter observational study of adhesion formation after open-and laparoscopic surgery for colorectal cancer. *Ann Surg*. 2018;267:743–748.
13. Indar AA, Efron JE, Young-Fadok TM. Laparoscopic ileal pouch–anal anastomosis reduces abdominal and pelvic adhesions. *Surg Endosc*. 2009;23:174–177.
14. Dindo D, Demartines N, Clavien P-A. Classification of surgical complications: A new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann Surg*. 2004;240:205–213.
15. Rajaratnam SG, Eglinton TW, Hider P, Fearnhead NS. Impact of ileal pouch-anal anastomosis on female fertility: Meta-analysis and systematic review. *Int J Colorectal Dis*. 2011;26:1365–1374.
16. Oresland T, Palmblad S, Ellström M, Berndtsson I, Crona N, Hultén L. Gynaecological and sexual function related to anatomical changes in the female pelvis after restorative proctocolectomy. *Int J Colorectal Dis*. 1994;9:77–81.
17. Fazio VW, Cohen Z, Fleshman JW, et al. Reduction in adhesive small-bowel obstruction by Seprafilm adhesion barrier after intestinal resection. *Dis Colon Rectum*. 2006;49:1–11.
18. Arian SE, Goodman L, Flyckt RL, Falcone T. Ovarian transposition: A surgical option for fertility preservation. *Fertil Steril*. 2017;107:e15.
19. Shandley LM, McKenzie LJ. Recent advances in fertility preservation and counseling for reproductive aged women with colorectal cancer: A systematic review. *Dis Colon Rectum*. 2019;62:762–771.
20. van der Wal JBC, Iordens GIT, Vrijland WW, van Veen RN, Lange J, Jeekel J. Adhesion prevention during laparotomy. *Ann Surg*. 2011;253:1118–1121.
21. Dowson HM, Bong JJ, Lovell DP, Worthington TR, Karanjia ND, Rockall TA. Reduced adhesion formation following laparoscopic versus open colorectal surgery. *Br J Surg*. 2008;95:909–914.
22. Bharadwaj S, Philpott JR, Barber MD, Graff LA, Shen B. Women's health issues after ileal pouch surgery. *Inflamm Bowel Dis*. 2014;20:2470–2482.
23. Bartels SAL, D'Hoore A, Cuesta MA, Bensdorp AJ, Lucas C, Bemelman WA. Significantly increased pregnancy rates after laparoscopic restorative proctocolectomy. *Ann Surg*. 2012;256:1045–1048.
24. Beyer-Berjot L, Maggiori L, Birnbaum D, Lefevre JH, Berdah S, Panis Y. A total laparoscopic approach reduces the infertility rate after ileal pouch-anal anastomosis: A 2-center study. *Ann Surg*. 2013;258:275–282.
25. Whelan RL, Franklin M, Holubar SD, et al. Postoperative cell mediated immune response is better preserved after laparoscopic vs open colorectal resection in humans. *Surg Endosc*. 2003;17:972–978.

Discussion

Dr Timothy Ridolfi (Milwaukee, WI): I'd like to thank the program committee for inviting me to discuss the paper. I'd also like to thank the authors for providing me with their manuscript well in advance. I would like to congratulate the authors as well on an excellent presentation on a pertinent topic.

The authors present fertility outcomes following ileal pouch-anal anastomosis in which patients who attempted to conceive were compared based on surgical approach, mainly laparoscopic IPAA or open. The authors conclude that postoperative infertility rates were higher after IPAA regardless of mode of surgery. However, laparoscopy was associated with a significantly reduced time to conceive compared to open.

The topic is important, as many patients undergoing IPAA are young, within reproductive age, and may desire to have children. A clear understanding of how an approach may influence infertility is important, as it may influence a patient's decision on ileal pouch-anal anastomosis and timing. The authors should be congratulated for receiving an excellent response rate to a very detailed survey. The authors pouch database may be the largest in the world as well.

I do have a few questions for the authors. Why did you choose to only include pouches created before 2012?

Dr Turgut Bora Cengiz: The single best answer would be the study was commenced in 2012, and the data collection took some time, as I stated before. We contacted some patients by phone or e-mails, so the data analysis took some time, but currently we're updating this patient cohort up to 2019, and we'll hope to publish those results soon.

Dr Timothy Ridolfi (Milwaukee, WI): Central to the paper is the idea of splitting these surgeries into an open group and a laparoscopic group. I was wondering if you could provide a little bit more detail on what you considered a laparoscopic surgery and what you considered an open surgery. It's interesting because some of these pouches are done as single-stage and some of them are done as 2-stage procedures or 3-stage procedures.

Sometimes patients have their total abdominal colectomy performed laparoscopically with a hand-assist technique then the proctectomy is performed through the Pfannenstiel incision through the hand-port site. Others have the proctectomy performed through the Pfannenstiel as a second-stage operation and some of them as a hybrid approach. Perhaps you can provide some definition as to who was contained within the laparoscopic group and who was contained within open group.

Dr Turgut Bora Cengiz: Thank you for the great question. We included all hand-assisted laparoscopies under the laparoscopy group, and also we defined direct vision under direct-vision surgery, which was described in one of our papers published in *World*

Journal of Surgery in 2018, defined as an incision <10 cm for completion proctectomy. We also included those patients in the laparoscopy group.

As you stated, right now we are transitioning to a more total laparoscopic approach, and it will be good to see those results, too. But the answer for your question would be hand-assisted and under-direct-vision surgeries were included in the laparoscopy group.

Dr Timothy Ridolfi (Milwaukee, WI): The patients that had the total abdominal colectomy and completion proctectomy performed—I should say total proctocolectomy performed—with direct vision of just removal of the last part of the rectum but coded in the laparoscopic group, but if a Pfannenstiel incision was done for a completion proctectomy for a second-stage operation, those were coded into the open group?

Dr Turgut Bora Cengiz: Correct.

Dr Timothy Ridolfi (Milwaukee, WI): Although there was not a statistical significance between the open and lap group in the patients that were wishing to conceive, the rates were pretty dramatically different. In the laparoscopic group, they were 22%, and in the open group they were 44%. Were there more complications in the open group? Namely leak, as that could increase inflammation and potentially cause there to be a longer length of time for conception.

Dr Turgut Bora Cengiz: Great and interesting question. We actually have the data but we did not assess precisely on the aspect of who got pregnant after surgery. But, as you said, anastomotic leaks, and maybe pelvic abscess, may play a role to time to pregnancy. We'll go back and check that, too, to clear that point.

Dr Timothy Ridolfi (Milwaukee, WI): Did you include redo pouches in the analysis?

Dr Turgut Bora Cengiz: All the redo pouches were excluded.

Dr Timothy Ridolfi (Milwaukee, WI): One of the limitations of the study is there is a temporal difference in your collection period because the first laparoscopic pouch done in 1993 and the first open was in 1983. Have you considered just throwing out all of the open pouches created prior to 1993 so that way there would be no difference in timing of the procedures?

Dr Turgut Bora Cengiz: That's a great point, too, as there is a time-frame difference between those approaches. But as you know, response rate for the questionnaire studies is unpredictable. We just aimed to achieve the highest number of patients possible, and we had the data since 1983–2012 at that time. So, we wanted to have as many patients as we could back at that time. But what you just said could be easily done in the future, and it would be interesting to see the results.

Dr Timothy Ridolfi (Milwaukee, WI): If the findings are the same and you don't lose that many patients, it may reduce one of your limitations of the study. Thank you.

Dr Mary Otterson (Milwaukee, WI): I have a quick comment and maybe a question. The number of laparoscopic ileal pouch-anal anastomoses who are able to become pregnant was 17 women?

Dr Turgut Bora Cengiz: 18.

Dr Mary Otterson (Milwaukee, WI): 18. Do you think that your conclusions might be influenced by your small sample size?

Dr Turgut Bora Cengiz: Yes. However, this would be more pronounced in the infertility rates. Rather than the small sample size, we believe that the time-to-conception analysis was biased due to the variance between fertility and fecundity of our patients. In conclusion, of course, this could be explained by the small sample size, as we tried to emphasize that in the limitations.