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ORIGINAL ARTICLE *Gynaecology*

Conservative surgery versus colorectal resection in deep endometriosis infiltrating the rectum: a randomized trial

Horace Roman[1,2,*], Michael Bubenheim[3], Emmanuel Huet[4], Valérie Bridoux[4], Chrysoula Zacharopoulou[5], Emile Daraï[5,6,7], Pierre Collinet[8], and Jean-Jacques Tuech[4]

[1]Expert Center in the Diagnosis and Multidisciplinary Management of Endometriosis, Rouen University Hospital, 76031 Rouen, France [2]Research Group EA 4308 'Spermatogenesis and Male Gamete Quality', IHU Rouen Normandy, IFRMP23, Reproductive Biology Laboratory, Rouen University Hospital, Rouen, France [3]Department of Biostatistics, Rouen University Hospital, 76031 Rouen, France [4]Department of Surgery, Rouen University Hospital, 76031 Rouen, France [5]Department of Obstetrics and Gynecology, Tenon University Hospital, Assistance Publique Hôpitaux de Paris, Paris, France [6]GRC-6 UPMC, Centre Expert en Endométriose (C3E), Université Pierre et Marie Curie, Paris, France [7]Unité INSERM UMR_S 938, Université Pierre et Marie Curie, 75020 Paris, France [8]Gynaecological Surgery Unit, Jeanne de Flandre Hospital, University Hospital of Lille, Lille, France

*Correspondence address. Clinique Gynécologique et Obstétricale, CHU «Charles Nicolle», 1 rue de Germont, 76031 Rouen, France. Tel: +33-232-888-754; Fax: +33-235-981-149; E-mail: horace.roman@gmail.com

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STUDY QUESTION: Is there a difference in functional outcome between conservative versus radical rectal surgery in patients with large deep endometriosis infiltrating the rectum 2 years postoperatively?

SUMMARY ANSWER: No evidence was found that functional outcomes differed when conservative surgery was compared to radical rectal surgery for deeply invasive endometriosis involving the bowel.

WHAT IS KNOWN ALREADY: Adopting a conservative approach to the surgical management of deep endometriosis infiltrating the rectum, by employing shaving or disc excision, appears to yield improved digestive functional outcomes. However, previous comparative studies were not randomized, introducing a possible bias regarding the presumed superiority of conservative techniques due to the inclusion of patients with more severe deep endometriosis who underwent colorectal resection.

STUDY DESIGN SIZE, DURATION: From March 2011 to August 2013, we performed a 2-arm randomized trial, enroling 60 patients with deep endometriosis infiltrating the rectum up to 15 cm from the anus, measuring more than 20 mm in length, involving at least the muscular layer in depth and up to 50% of rectal circumference. No women were lost to follow-up.

PARTICIPANTS/MATERIALS, SETTING, METHODS: Patients were enroled in three French university hospitals and had either conservative surgery, by shaving or disc excision, or radical rectal surgery, by segmental resection. Randomization was performed preoperatively using sequentially numbered, opaque, sealed envelopes, and patients were informed of the results of randomization. The primary endpoint was the proportion of patients experiencing one of the following symptoms: constipation (1 stool/>5 consecutive days), frequent bowel movements (≥3 stools/day), defecation pain, anal incontinence, dysuria or bladder atony requiring self-catheterization 24 months postoperatively. Secondary endpoints were the values of the Visual Analog Scale (VAS), Knowles–Eccersley–Scott-Symptom Questionnaire (KESS), the Gastrointestinal Quality of Life Index (GIQLI), the Wexner scale, the Urinary Symptom Profile (USP) and the Short Form 36 Health Survey (SF36).

MAIN RESULTS AND THE ROLE OF CHANCE: A total of 60 patients were enroled. Among the 27 patients in the conservative surgery arm, two were converted to segmental resection (7.4%). In each group, 13 presented with at least one functional problem at 24 months after surgery (48.1 versus 39.4%, OR = 0.70, 95% CI 0.22–2.21). The intention-to-treat comparison of the overall scores on KESS, GIQLI,

Wexner, USP and SF36 did not reveal significant differences between the two arms. Segmental resection was associated with a significant risk of bowel stenosis.

LIMITATIONS REASONS FOR CAUTION: The inclusion of only large infiltrations of the rectum does not allow the extrapolation of conclusions to small nodules of <20 mm in length. The presumption of a 40% difference favourable to conservative surgery in terms of post-operative functional outcomes resulted in a lack of power to demonstrate a difference for the primary endpoint.

WIDER IMPLICATIONS OF THE FINDINGS: Conservative surgery is feasible in patients managed for large deep rectal endometriosis. The trial does not show a statistically significant superiority of conservative surgery for mid-term functional digestive and urinary outcomes in this specific population of women with large involvement of the rectum. There is a higher risk of rectal stenosis after segmental resection, requiring additional endoscopic or surgical procedures.

STUDY FUNDING/COMPETING INTEREST(S): This work was supported by a grant from the clinical research programme for hospitals (PHRC) in France. The authors declare no competing interests related to this study.

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TRIAL REGISTRATION DATE: 31 January 2011.

DATE OF FIRST PATIENT'S ENROLMENT: 7 March 2011.

Key words: colorectal resection / shaving / disc excision / digestive symptoms / bladder dysfunction / deep infiltrating endometriosis / conservative surgery

Introduction

Surgical management of deep infiltrating endometriosis of the rectum has become a topic of increasing interest in gynaecological surgery, leading to much debate. Two surgical approaches are usually employed: a radical approach, mainly based on colorectal segmental resection, and a conservative approach, prioritizing the conservation of the rectum (Roman *et al.*, 2013a). The latter may be performed by shaving and without opening the rectum (Donnez and Squifflet, 2010) or by removing the nodule along with surrounding rectal wall using full thickness or disc excision (Nezhat *et al.*, 1993; Fanfani *et al.*, 2010). Due to the lack of comparative studies (Fanfani *et al.*, 2010; Roman *et al.*, 2010, 2013a), currently available evidence is based on retrospective series reported by surgeons who generally perform only one of these techniques (Darai *et al.*, 2005, 2010; Minelli *et al.*, 2009; Donnez and Squifflet, 2010; Dousset *et al.*, 2010; De Cicco *et al.*, 2011; Abrao *et al.*, 2015; Meuleman *et al.*, 2011).

In our experience, adopting a conservative approach to surgical management of rectal endometriosis appears to yield improved digestive functional outcomes (Roman *et al.*, 2013a, 2016). Despite prospective data recording, our previous studies were not randomized, introducing a possible bias regarding the presumed superiority of conservative techniques due to the inclusion of patients with more severe deep endometriosis who underwent colorectal resection. For this reason, there was no doubt that accurate comparison of conservative and radical approaches should be based on a randomized trial.

The aim of our study was therefore to compare digestive and urinary outcomes in patients managed for deep endometriosis infiltrating the rectum by either conservative rectal surgery, using shaving or disc excision, or by radical colorectal segmental resection.

Materials and Methods

We conducted an unblinded, 1:1 parallel-arms, controlled randomized study to assess the hypothetical superiority of conservative rectal surgery over segmental resection in the management of deep endometriosis infiltrating the rectum (ENDORE, NCT 01291576). Eligible patients were over 18 and under 45 years and managed for deep endometriosis infiltrating the rectum up to 15 cm from the anus, measuring more than 20 mm in length, involving at least the muscular layer in depth and up to 50% of rectal circumference. Between March 2011 and August 2013, patients were enroled in three French referral centres, i.e. Rouen University Hospital, Tenon University Hospital and Lille University Hospital.

All women referred for deep endometriosis had clinical examination by a surgeon experienced in endometriosis, as well as MRI examination. When deep endometriosis was confirmed, endorectal ultrasound was performed to assess whether the rectum was involved and to estimate the depth of rectal wall infiltration. Computed tomography based virtual colonoscopy was often used to measure the length and the height of nodules and to confirm the presence of digestive tract stenosis and associated digestive tract localizations. Complementary examinations, such as cystoscopy and unenhanced helical computed tomography were performed in women with associated involvement of the urinary tract. When deep endometriosis respecting the inclusion criteria was revealed (at least one imaging technique providing rectal infiltration over 20 mm in length), patients were proposed enrolment in the trial and explained the principles and the aim of the study. This study was approved by the local Internal Review Board. Patients underwent randomization before surgery and were duly informed of the results of randomization.

Randomization

Assignment of a patient to conservative surgery or colorectal resection was based on randomization lists drawn up separately for each centre by a statistician with no clinical involvement in the trial (M.B.). The details, like the block size, were not revealed to investigators before the end of the study. Instead, the investigator of each centre received 60 sequentially numbered, opaque, sealed envelopes, which were opened only after the patient had completed all baseline assessments and had given written consent to be enroled in the trial.

To prevent subversion of the allocation sequence, the first two letters of the last name, the first letter of the first name and the date of birth were immediately faxed to the sponsor. Once the fax had been received, the patient could no longer be excluded from the trial.

Patients filled in baseline questionnaires including questions about pelvic complaints related to endometriosis using Visual Analog Scale (VAS), bowel movements and bladder voiding, as well as the Knowles–Eccersley–Scott-Symptom Questionnaire (KESS) (Knowles *et al.*, 2000), the Gastrointestinal Quality of Life Index (GIQLI) (Nieveen van Dijkum *et al.*, 2000), the Wexner scale (Jorge and Wexner, 1993), the Urinary Symptom Profile (USP) (Haab *et al.*, 2008) and the Short Form 36 Health Survey (SF36) (Brazier *et al.*, 1992).

Procedures

Patients enroled in the conservative surgery arm (A) had surgical management of rectal endometriosis by either rectal shaving or disc excision. Rectal shaving was performed using scissors, ultrasound scalpel or plasma energy (Roman, 2013), to a depth allowing complete macroscopic excision of the nodule. The deep subperitoneal space located between the uterosacral ligaments and the rectum was longitudinally opened, in order to avoid injury to hypogastric and splanchnic nerves. Dissection was performed in close contact with the lateral face of the rectum and was directed toward the healthy rectovaginal space located below the endometriosis nodule. Once the lateral faces of the rectum were freed, rectal shaving was performed as deeply as possible into the thickness of the rectal wall, in order to remove abnormal fibrous lesions involving rectal layers, using high magnification endoscopic view. Rectal muscular layer was repaired by resorbable stitches when required. Thus, the nodule was dissected away from the rectal wall, which was then progressively mobilized upward. The deep endometriotic nodule was then treated by resection of the vaginal fornix adjacent to the uterine torus and to the anterior root of the uterosacral ligaments, when infiltrated.

Disc excision was performed using transanal staplers (either semicircular staplers, i.e. the Rouen technique, or end-to-end circular staplers) or directly through the vagina when opened to remove vaginal infiltration (Roman *et al.*, 2017a). The procedure started by achieving rectal shaving, as mentioned above. When the shaved area of the anterior rectal wall was still infiltrated by implants of deep endometriosis, it appeared hollow, rigid and thickened under palpation with a laparoscopic probe. In this context, a more complete treatment was achieved by full thickness disc excision, employing concomitant transanal route. The choice between shaving and disc excision was at the discretion of the surgeon. Hence, the colorectal surgeon used the Contour® Transtar™ stapler when the shaved area was located between 8 and 10 cm above the anus and the EEA circular stapler when it was located in the upper rectum. The thinner and softer the shaved rectal wall, the larger the diameter of the rectal patch that could be removed using the transanal stapler.

When multiple nodules were revealed, the rectal nodule was managed using a conservative technique, while associated nodules of the colon, caecum or small bowel were treated separately, by shaving, disc excision or segmental resection (Millochau *et al.*, 2017).

Patients enroled in the radical surgery arm (B) underwent segmental colorectal resection, which could be associated with additional procedures on the left, transverse or right colon, caecum or small bowel, when required. The procedure of laparoscopic colorectal resection was similar

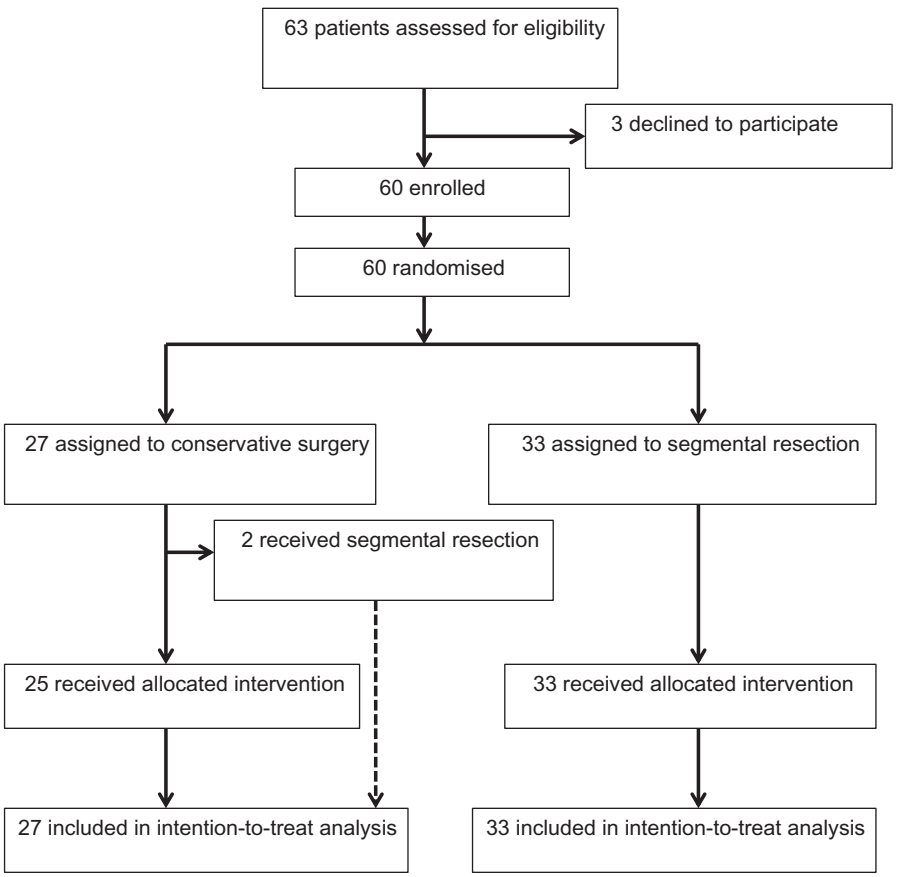

Figure 1 Flow diagram (CONSORT 2010).

to that previously described by other teams (Darai *et al.*, 2005; Dousset *et al.*, 2010; Minelli *et al.*, 2009). Dissection was carried out through the rectovaginal septum and followed the steps described above. Mobilization of the rectum was carried out at least 20 mm below the rectal nodule. Section of the mesorectum and mesocolon was performed in contact with the posterior wall of the rectosigmoid. The stapler was entered into the peritoneal cavity through the inferior right trocar and the rectum was then distally sectioned. A minilaparotomy was carried out in a transverse

Table I Patients' baseline characteristics.

Parameter	Conservative surgery (*n*=27)	Segmental resection (*n*=33)
Age (years)	31 (27–36)	28 (27–36)
Dysmenorrhoea		
VAS of dysmenorrhoea	8 (8–10)	9 (8–10)
Sexual intercourse during past year	24 (88.9%)	31 (93.9%)
Dyspareunia		
VAS of dyspareunia	5 (4–7)	5 (3–7)
Chronic intermenstrual pelvic pain		
VAS of intermenstrual chronic pelvic pain	6 (5–7)	5 (3–8)
Biberoglou & Behrman score	4 (3–5)	5 (4–6)
Digestive symptoms		
≤1 stool/5 days	8 (29.7%)	14 (42.4%)
Defecation pain	21 (77.8%)	24 (72.7%)
≥3 stools/day	11 (40.7%)	12 (36.4%)
Involuntary gas or stool loss	6 (22.2%)	10 (30.3%)
GIQLI score	89 (82–105)	92 (86–104)
KESS score	13 (9–18)	10 (7–19)
Wexner score	0 (0–3)	1 (0–4)
How long were you able to defer defecation?		
<5 min	6 (22.2%)	3 (9.1%)
5–10 min	6 (22.2%)	10 (30.3%)
10–15 min	4 (14.8%)	1 (3%)
>15 min	11 (40.7%)	19 (57.6%)
Urinary symptoms		
USP score	0 (0–3)	0 (0–1)
Catamenial urinary pain or haematuria	8 (29.7%)	7 (21.2%)
Short Form 36 Health Survey score	54 (44–67)	48 (40–61)
Localization of deep nodules of digestive tract		
- Rectal nodules		
1 nodule	26 (96.3%)	32 (97%)
2 nodules	1 (3.7%)	1 (3%)
- Sigmoid colon nodules		
1 nodule	10 (37%)	15 (45.5%)
2 nodules	1 (3.7%)	1 (3%)
3 nodules	1 (3.7%)	0
- Left, transverse, right colon and caecum nodules	2 (7.4%)	2 (6%)
- Small bowel nodules	2 (7.4%)	1 (3%)
Diameter of largest rectal nodule (mm)	30 (26–40)	30 (25–39)
Deepest infiltration of the rectum		
- Muscular layer	17 (63%)	24 (72.7%)
- Submucosa	9 (33.3%)	8 (24.2%)
- Mucosa	1 (3.7%)	1 (3%)
Height of the lowest nodule (mm from anal verge)	80 (60–100)	90 (70–110)

Data are *n*(%) or median (Q1–Q3). VAS, visual analog scale; GIQLI, gastrointestinal quality of life index; KESS, Knowles–Eccersley–Scott-Symptom; USP, urinary symptom profile.

suprapubic fashion (Pfannenstiel incision). After extraction of the rectal stump, resection of the rectum or the rectosigmoid (depending on the disease extension) was performed. Section of the digestive tract was performed in all cases at an average of 20 mm above and below macroscopic nodule limits. Colorectal anastomosis was performed using end-to-end anastomosis transanal staplers of 28 or 31 mm in diameter.

Multidisciplinary teams included three gynaecologic surgeons (H.R., E.D. and P.C.), who have each performed at least 120 surgeries for colorectal endometriosis, and five general surgeons with at least 5 years of experience in colorectal surgery, who performed all surgical procedures requiring bowel suture. Rectal shaving was performed by the gynaecologic surgeon alone. Independent of allocation, surgeons performed ablation of ovarian endometriomas, ureterolysis, resection of uterosacral ligaments and vagina, bladder or ureter when involved, or hysterectomy in women with severe adenomyosis and no pregnancy intention. Nerve sparing techniques were used to preserve inferior hypogastric plexus, hypogastric nerves and splanchnic nerves at least on one side. Diverting stoma and omentoplasty were used in patients with simultaneous proximal rectal and vaginal sutures. Stomas were closed 3 months after surgery, if rectal barium enema examination ruled out a bowel leakage or a rectovaginal fistula. At least one postoperative visit was planned 6–12 weeks after the procedure to assess immediate postoperative outcomes and to manage postoperative complications. The Clavien–Dindo classification was used to assess postoperative complications (Dindo *et al.*, 2004).

Outcomes

According to the trial's design, patients were followed-up at 6, 12, 18 and 24 month visits after surgery. Digestive and urinary outcomes were assessed using the same questionnaires employed before surgery. Complete data were not recorded in women whose stoma was not yet closed at the time of the visit. The primary endpoint at 24 months post surgery was the proportion of patients experiencing one of the following symptoms: constipation (1 stool/>5 consecutive days), frequent bowel movements (≥3 stools/day), defecation pain, anal incontinence (involuntary loss of gas or stools), dysuria (USP score for dysuria ≥1) or bladder atony requiring bladder voiding by self-catheterization. Secondary endpoints were the values of VAS, KESS, GIQLI, Wexner, USP, SF36 scores.

The randomized parallel arm design was used to compare the two surgical approaches. The study was planned as a randomized clinical trial with a fixed sample size based on the power to find the specified difference. According to our previous observations (Roman *et al.*, 2013a), the percentage of patients presenting with main outcomes was expected to average 10% in arm A versus 50% in arm B. Hence, 60 patients were randomized in order to reach the principal aim with a power of at least 80% and admitting an alpha error of 5% when using Fisher's exact test and accounting for patients who did not receive the allocated treatment. In accordance with the intention-to-treat principle, all randomized patients were included in the analysis.

Statistical analysis

Statistical analyses were carried out using SAS 9.3 software (Cary, NC). The population at the time of randomization, i.e. just before the intervention started, was described using median, first and third quartile (Q1–Q3) if the characteristics had at least ordinal level and were not categorized. In order to compare treatment arms with respect to the presence of functional symptoms at a given time, Fisher's exact test or its generalization by Freeman and Halton was employed for categorical characteristics; otherwise, Wilcoxon's test for independent samples was used. As the analyses regarding the secondary aims were exploratory, each time the *P*-value was <0.05 the corresponding differences were considered to be significant. This study is registered with ClinicalTrials.gov, number NCT 01291576.

The trial was funded by the clinical research programme for hospitals (PHRC) in France and locally registered as 2009/069/HP by the sponsor. The funders had no role in the study design, data collection and analysis, decision to publish or preparation of the article.

Results

A total of 60 patients were enroled in the study: 55 in Rouen, 4 in Paris and 1 in Lille, with 27 patients randomly assigned to arm A (conservative surgery, all in Rouen) and 33 assigned to arm B (segmental resection, 28 in Rouen, 4 in Paris and 1 in Lille). They were recruited from March 2011 to August 2013, and received surgery from March 2011 to October 2013. They attended clinical visits at the time of randomization (baseline) and at 6-month intervals for 2 years, with the last follow-up in October 2015. As no patient was either lost to follow-up or excluded, all 60 patients were analysed for the primary outcome. The flow chart of the trial is presented in Fig. 1.

Table I presents baseline characteristics for each group related to primary and secondary endpoints. Figure 2 presents MRI examination in three patients managed respectively by shaving, the Rouen technique and colorectal resection. Multifocal colorectal endometriosis was recorded in half of patients. The median distance of rectal nodules from the anus corresponded to an infiltration of the mid-rectum.

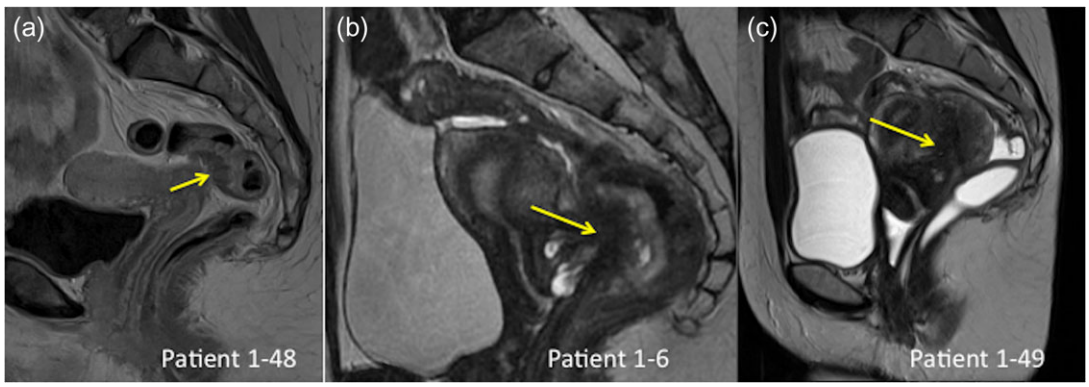

Figure 2 Preoperative MRI assessment in patients managed by shaving (**a**), disc excision (**b**) and segmental resection (**c**).

Table II presents intraoperative findings and additional surgical procedures. In arm A, among the 15 patients managed by disc excision, eight had the Rouen technique, six had disc excision using a transanal end-to-end circular stapler and one had direct transvaginal disc excision. In two women allocated to the conservative surgery arm, the infiltration was too large and too deep to be accurately treated by shaving, and too high to be managed by the Rouen technique (Roman *et al.*, 2017a). Hence, the surgeon decided that colorectal resection was the most appropriate technique. However, and according to the intention-to-treat principle, both these women were analysed in the group of patients managed by conservative surgery.

Table III presents postoperative complications. Symptomatic stenosis of the rectum was significantly more frequent in arm B (five patients had stenosis of colorectal anastomosis; two of them had secondary colorectal resection and three of them had endoscopic dilations under general anaesthesia). Each of the two patients managed by

Table II Intraoperative findings and surgical procedures.

Parameter	Conservative surgery (n = 27)	Segmental resection (n=33)
Operative route		
Laparoscopic	24 (88.9%)	32 (97%)
Laparoscopic converted to open surgery	3 (11.1%)	1 (3%)
Operative time (min)	280 (190–360)	270 (230–300)
Procedure performed on the rectum		
Shaving	10 (37%)	0
Full thickness disc excision	15 (55.6%)	0
Colorectal segmental resection	2 (7.4%)	33 (100%)
Full thickness disc excision	15 (55.6%)	0
Diameter of the specimen (mm)	40 (40–50)	–
Height of rectal suture (mm)	70 (50–90)	–
Colorectal segmental resection	2	33
Length of colorectal specimen (mm)	100 (100–150)	80 (50–150)
Length of rectal segment removed (mm)	60 (60–60)	50 (40–70)
Length of sigmoid colon segment removed (mm)	40 (40–90)	20 (0–60)
Height of colorectal anastomosis (mm)	90 (90–90)	80 (60–100)
Temporary stoma	16 (59.3%)	21 (63.6%)
Ileostoma	0	9 (27.3%)
Colostoma	16 (59.3%)	12 (36.4%)
AFSr score	55 (19–98)	54 (28–91)
Management of ovarian endometrioma	8 (29.6%)	13 (39.4%)
Right ovary	7 (25.9%)	7 (21.2%)
Left ovary	4 (14.8%)	12 (36.4%)
Resection of bladder nodule	3 (11.1%)	1 (3%)
Management of ureteral endometriosis	4 (14.8%)	4 (12.1%)
Advanced ureterolysis	3 (11.1%)	4 (12.1%)
Resection of the ureter and reimplantation into the bladder	1 (3.7%)	0
Segmental resection of sigmoid colon (separated from rectal procedure)	3 (11.1%)	3 (9.1%)
Selective resection of left, transverse, right colon or caecum	3 (11.1%)	2 (6.1%)
Appendectomy	4 (14.8%)	2 (6.1%)
Resection of posterior vagina	24 (88.9%)	20 (60.6%)
Hysterectomy	7 (25.9%)	5 (15.2%)
Adnexectomy	5 (18.5%)	4 (12.1%)
Right	4 (14.8%)	2 (6.1%)
Left	4 (14.8%)	3 (9.1%)
Omentoplasty	18 (66.7%)	25 (75.8%)
Intraoperative blood loss (mL)	200 (200–300)	200 (150–300)
Blood transfusion	0	0

Data are n(%) or median (Q1–Q3). AFSr, American Fertility Society Score.

Table III Postoperative complications.

Complications	Conservative surgery (*n*=27)	Segmental resection (*n*=33)	*P*
Clavien Dindo 1	9 (33%)	7 (21.2%)	0.38
Clavien Dindo 2	12 (44%)	9 (27.3%)	0.19
Bladder atony requiring self-catheterization after Day 7	6[a] (22%)	3 (9.1%)	0.28
Clavien Dindo 3	6[a] (22%)	10 (3.3%)	0.57
Rectovaginal fistula	2[a] (7.4%)	0	0.20
Stenosis of rectal lumen requiring additional procedure	0	5 (15.2%)	0.05
Pelvic abscess	0	1 (3%)	1
Complications related to stoma repair (leakage, abdominal haemorrhage, hernia)	2 (7.4%)	1 (3%)	0.58
Rectorrhage requiring endoscopy in emergency	0	1 (3%)	1

Data are *n*(%) or median (Q1–Q3).
[a]One patient was managed by colorectal resection (conversion).

segmental resection in arm A presented one postoperative complication, respectively rectovaginal fistula and bladder dysfunction requiring long term self-catheterization (postoperative bladder voiding was satisfactory, however, the voiding required systematic contraction of abdomen wall muscles).

All 60 patients were included in the analysis in the arm assigned by randomization. Analysis of primary outcomes revealed 13 patients in each group presenting one or more functional symptom 24 months after surgery (conservative surgery versus segmental resection: 48.1 versus 39.4%, OR = 0.70, 95% CI 0.22–2.21, $P = 0.70$) (Table IV). Digestive functional symptoms were recorded in arm A and in arm B as follows: constipation in respectively 3 (11.1%) and 3 patients (9.1%), frequent bowel movements in 2 (7.4%) and 7 (21.2%), defecation pain in 5 (18.5%) and 6 (18.2%), and involuntary loss of gas or stools in 3 (11.1%) and 9 (27.3%). As regards secondary outcomes, the values of KESS, GIQLI, Wexner, USP, SF36 and VAS scores were comparable between the two arms (Fig. 3 and Table IV).

During the 24 months of follow-up, 34 patients attempted pregnancy: 13 in arm A (48.1%) and 21 in arm B (63.6%). Among them, 9 (69.2%) and 11 patients (52.4%) respectively conceived during the follow-up ($P = 0.48$). Spontaneous conception was recorded in six (66.7%) and eight patients (72.7%) ($P = 1$) respectively. Using the sum of days at risk of conception (2670 versus 6178 days), namely from the arrest of hormonal treatment to either the first conception (in women who conceived) or the end of follow-up (in women with conception failure), we observed an incidence rate between two consecutive visits (the rate of conception/6 months) of respectively 0.62 and 0.33 (hazard ratio = 0.71, 95% CI 0.40–1.25, $P = 0.23$).

Discussion

In this randomized trial, we compared functional outcomes following conservative colorectal surgery and segmental resection in deep endometriosis responsible for large infiltrations of the rectum. Although previous case-series and comparative observational studies suggested better functional outcomes following conservative surgery, our present trial does not show a statistically significant superiority of conservative surgery for mid-term functional digestive and urinary outcomes in this specific population of women with large involvement of the rectum.

Our study presents some limitations. The presumption of a 40% difference favourable to conservative surgery in terms of postoperative functional outcomes resulted in a lack of power to demonstrate the difference for the primary endpoint. The differences between the frequencies of functional symptoms composing the primary endpoint, as well as the values of GIQLI, KESS and SF36 scores in the two arms suggest that the functional outcomes of the two surgical approaches are close. As regards immediate complications, we found a higher risk of rectal stenosis after segmental resection requiring additional endoscopic or surgical procedures.

The inclusion of only large infiltrations of the rectum does not allow the extrapolation of conclusions to small nodules of <20 mm in length. However, we chose to include only large nodules due to the presumption that many surgeons would consider segmental resection to be an overtreatment in small rectal nodules.

There was an over-representation of patients enroled in the first centre (Rouen) due to the presence of the primary investigator and author of the protocol (H.R.). Despite harmonization meetings and exchanges between investigators, patient enrolment in the two associated centres was still inferior to that of the primary centre. This unbalanced enrolment of patients may raise questions about the external validation of the study. However, the homogeneity of results between the three centres could not be tested, because of the lack of statistical power and allocation of the five patients enroled in Paris and Lille to the same arm. As all surgeons were experienced in the management of rectal endometriosis, it is less likely that unbalanced enrolment of patients significantly impacted the outcomes.

The unblinded design of the trial was specifically required by the ethics committee. No patient had an a priori preference for one or other procedure, thus it was less likely that their answers were impacted by their allocation to either of the two arms. It was unlikely that surgeons influenced patients' answers to the questionnaires or the primary endpoint.

Our trial also has several strengths. The allocation was randomized, which allowed comparison between two arms with similar characteristics, which were managed by only experienced gynaecologic surgeons and general surgeons. The patients were carefully followed-up and

Table IV Clinical assessment 24 months after surgery.

Parameter	Conservative surgery Arm A (*n*=27)	Segmental resection Arm B (*n*=33)	OR	95% CI	*P*
Days of follow-up	729 (726–743)	727 (722–736)	0.58	0.23–1.44	0.25
Assessment of digestive and urinary function					
Patients presenting primary outcome	13 (48%)	13 (39%)	0.70	0.22–2.21	0.60
GIQLI score	111 (97–135)	121 (99–128)	0.80	0.33–1.99	0.64
KESS score	10 (5–15)	9 (5–17)	1.10	0.46–2.67	0.83
Wexner score	0 (0–1)	0 (0–2)	2.10	0.71–6.22	0.23
How long were you able to defer defecation?			0.67	0.26–1.76	0.42
<5 min	5 (19%)	6 (18%)			
5–10 min	4 (15%)	8 (24%)			
10–15 min	3 (11%)	4 (12%)			
>15 min	15 (56%)	15 (45%)			
USP of dysuria	0 (0–1)	0 (0–0)	0.26	0.06–1.14	0.65
Short Form 36 Health Survey score	86 (64–92)	82 (62–87)	0.70	0.28–1.72	0.44
Physical functioning	95 (90–100)	100 (80–100)	0.94	0.37–2.41	0.91
Physical role functioning	100 (50–100)	100 (100–100)	1.56	0.51–4.73	0.44
Bodily pain	84 (62–100)	74 (61–100)	0.56	0.22–1.39	0.21
General health perceptions	72 (50–90)	67 (52–82)	0.84	0.34–2.06	0.71
Vitality	60 (40–75)	55 (40–70)	0.84	0.34–2.06	0.71
Social functioning	100 (75–100)	88 (63–100)	1.28	0.5–3.28	0.37
Emotional role functioning	100 (67–100)	100 (67–100)	2.07	0.7–6.15	0.82
Mental health	76 (52–88)	68 (56–80)	0.62	0.25–1.53	0.31
Assessment of postoperative pelvic pain					
Patients with menstruation during preceding 6 months	9 (33%)	15 (45%)	1.41	0.38–5.22	0.77
Among whom, patients with dysmenorrhoea	4/9 (44%)	8/15 (53%)	1.43	0.2–10.4	1.00
VAS of dysmenorrhoea	3 (2–4)	4 (3–6)	1.24	0.14–11.34	0.86
Months until first recurrence of dysmenorrhoea	12 (5–18)	10 (4–18)	1.00	0.1–10.2	1.00
Patients having sexual intercourse after surgery during preceding 6 months	24 (89%)	32 (97%)	4.00	0.29–216.4	0.32
Among whom, patients with dyspareunia	8/24 (33%)	9/32 (28%)	0.78	0.21–2.9	0.77
VAS of dyspareunia	4 (3–6)	4 (3–7)	1.00	0.19–5.3	1.00
Patients with intermenstrual pelvic pain during preceding 6 months	6 (22%)	10 (3%)	1.50	0.41–6	0.57
VAS of intermenstrual pelvic pain	4 (3–5)	4 (3–6)	1.23	0.21–7.38	0.83

Data are *n*(%) or median (Q1–Q3).

assessed, allowing for accurate results. Only two conversions were observed in the conservative surgery arm, meaning that 96.7% of patients enroled in the trial received the allocated procedure. Four different conservative procedures were employed to treat patients allocated to the conservative surgery arm, however, we estimated that they would each have a comparable impact on functional outcomes, because all four procedures allowed for systematic preservation of the mesorectum, with only limited variations of the length of rectum and the volume of rectal reservoir. Last but not least, the trial focussed on a question of major interest in the dynamic topic of the management of deep endometriosis.

Exhaustive assessment of digestive function using standardized questionnaires showed that complete removal of large deep endometriosis infiltrating the rectum does not guarantee relief from digestive complaints (Kupelian and Cutner, 2016; Riiskjaer *et al.*, 2016). We had presumed that on average half of all patients managed by segmental resection would report significant abnormal postoperative bowel function, and we were not mistaken. Conversely, our hypothesis that conservative surgery would result in much better functional outcomes was not confirmed. Our presumption was based on a small number of retrospective case-series which reported data on postoperative functional outcomes. However, these retrospective studies may have compared patients with more severe disease managed by colorectal resection and patients with smaller digestive nodules managed by shaving. This unbalanced distribution may have pointed to better postoperative outcomes in patients managed conservatively.

Removal of deep rectal nodules by shaving or disc excision does preserve the mesorectum, rectal vascularization and nerves, as the procedure exclusively concerns the anterior rectal wall and does not modify the overall length of the rectum. However, this did not have a major

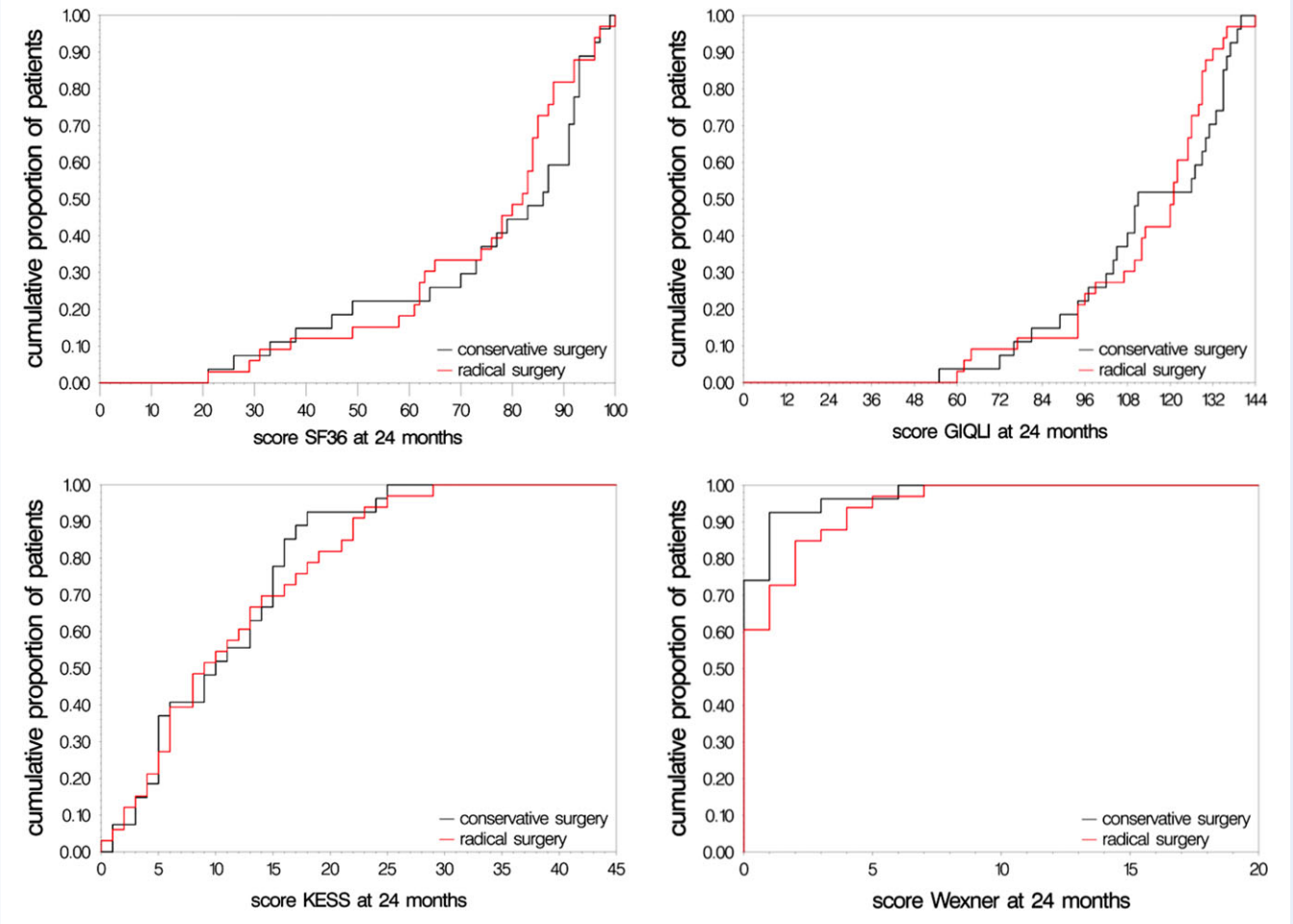

Figure 3 Cumulative distribution functions of different scores: Short Form 36 Health Survey (SF36; Top-left corner), Gastrointestinal Quality of Life Index (GIQLI; Top-right corner), Knowles–Eccersley–Scott-symptom questionnaire (KESS; bottom-left corner) and the Wexner scale (bottom-right corner). Black lines correspond to the conservative surgery group, red lines correspond to the segmental resection group.

positive impact on postoperative rectal function, when compared to colorectal resection. Several explanations might be considered. Deep endometriosis infiltrating the rectum may also involve uterosacral ligaments, vagina, parametrium, inferior hypogastric plexus and splanchnic nerves. Complete resection of large endometriosis lesions may induce postoperative dysfunction of vegetative nerves (Possover, 2011; Bonneau *et al.*, 2013; Roman *et al.*, 2013b; Darwish and Roman, 2017; de Resende *et al.*, 2017). Despite the employment of nerve-sparing techniques (Ceccaroni *et al.*, 2012), it is obvious that inferior hypogastric plexus and splanchnic nerves may be injured by either the disease or the surgeon, resulting in various concerns with bowel and bladder function (Darwish and Roman, 2017). Furthermore, recent studies have shown that patients with colorectal endometriosis may preoperatively present with rectal or bladder dysfunction (Mabrouk *et al.*, 2012), i.e. anal and urethral sphincter hypertonia, and these troubles may be irreversible and not restored by removal of nodules.

The rectum is not the unique localization of deep endometriosis. Hence, the majority of patients had associated vaginal resection, some of them with hysterectomy. Some patients had separate resection of the sigmoid, left or transverse colon, caecum or bladder, along with surgery of the rectum (Table II). Although these additional procedures, sometimes in multiple sites, could have impacted functional outcomes, they could not be cancelled or postponed. However, as the study was randomized no difference was expected between the two arms with respect to the number of sites involved. In addition, the analysis was carried out according to the intention to treat principle, thus multiple procedures were not expected to impact the comparison between the two arms.

Previous studies have revealed a higher risk of rectovaginal fistula and leakage in women managed by colorectal resection when compared to those receiving shaving (Roman *et al.*, 2017b). However, our study was not powered for this relatively rare outcome, which varied from 3 to 12% depending on the characteristics of patients enroled in several series of patients managed for bowel endometriosis. Conversely, bowel stenosis was more frequent in patients enroled in the segmental resection arm, as it is more likely to occur after circular colorectal anastomosis (Maytham *et al.*, 2010) than after semicircular disc excision or shaving.

Although the rate of postoperative complications may appear high, our trial only included women with low colorectal localizations and

frequent association of vaginal infiltrations. Among patients with digestive tract endometriosis, those presenting with infiltration of the rectum are probably exposed to a higher risk of postoperative complications, as well as postoperative digestive and urinary dysfunction. The rate of stenosis of colorectal anastomosis was unexpectedly high; however, this complication may be overlooked in patients in whom postoperative constipation was either not taken into account or explored. Other authors have reported high rates of bowel stenosis after surgery for colorectal endometriosis, which suggests that this complication could be linked to the inflammatory status of the pelvis (Maytham *et al.*, 2010). As regards dysuria, we recorded this symptom both before and after surgery. Although nine patients (15%) required intermittent self-catheterization after surgery, only one of them had to continue over 24 postoperative months, suggesting that immediate postoperative bladder atony may progressively improve (Dousset *et al.*, 2010).

Cumulative pregnancy rates at 24 months post surgery were comparable between the two arms and with data reported in the literature. Furthermore, two-thirds of postoperative conceptions were spontaneous. Consequently, our results suggest that surgery for colorectal endometriosis may be safely offered to young women with severe endometriosis and pregnancy intention.

Our present study did not reveal any endometriosis recurrence during the 24 months following the surgery, however, it was not powered for this outcome, which requires more than 2 years of follow-up. An ancillary study on the recurrence rate of conservative versus radical rectal surgery with postoperative follow-up extended to 10 years is already ongoing. This ancillary study has been approved by the local Internal Review Board.

In conclusion, we were unable to demonstrate that conservative surgery for the management of deep rectal endometriosis improves digestive and urinary functional outcomes, when compared to radical colorectal resection. However, colorectal resection is responsible for a higher rate of bowel stenosis requiring complementary procedures under general anaesthesia. Patients should be informed that there is a risk of abnormal bowel movements in 40% of cases regardless of surgical management. The findings of our trial may be the support for sample size estimations for further randomized trials and may be included in future meta-analyses focusing on functional outcomes after colorectal surgery for endometriosis.

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Authors' roles

H.R. designed the trial, performed the surgery and wrote the first draft of the article. M.B. performed the statistical analysis. E.H., E.D., P.C. and J.-J.T. performed the surgery. C.Z. and V.B. performed the data collection. All the authors contributed to the final article.

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Conflict of interest

The authors declare no competing interests related to this study.

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