Long-term evaluation of quality of life and gastrointestinal well-being after segmental colo-rectal resection for deep infiltrating endometriosis (ENDO-RESECT QoL)

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Abstract

Purposes The primary objective is to assess the long-term quality of life (QoL) and gastrointestinal well-being in patients with endometriosis (DIE) who underwent segmental resection (SR), through specific questionnaires focused on endometriosis and specific gastrointestinal evaluation. The secondary objectives are represented by the evaluation of peri-operative and post-operative outcomes of the procedure.

Methods This observational cohort study ENDO-RESECT (ClinicalTrials.gov ID: NCT03824054) reports all clinical data about women who underwent SR for DIE between October 2005 and November 2017. In the part of the study dedicated to the QoL assessment, the questionnaires adopted were the Endometriosis Health Profile (EHP30), the Psychological General Well-Being Index and the Hospital Anxiety and Depression Scale, the Gastrointestinal Well-being questionnaire and the Bristol Stool chart. Major post-surgical morbidity and obstetric outcomes were also collected.

Results 50 women (18% stage III and 82% stage IV rAFS) were considered for enrollment. EHP-30 interpretation demonstrated a significant improvement in all continuous variables, except for fertility concerns. The overall gastrointestinal QoL and most of the specific symptoms improved after surgery. Frequent bowel movements appeared in the 13% of the series not resulting in an impairment of general and gastrointestinal QoL. Constipation remained unchanged. Patients with depressive mood managed with laparoscopy, benefited the most from SR; moreover, patients with multinodular bowel localizations experienced a greater reduction in abdominal pain. Median FU after SR was 42.5 months (range 12–157 months). Only three (6%) cases of late major grade III complications were documented. The pregnancy rate was 50%.

Conclusions Improvement of general QoL and most of gastrointestinal symptoms was documented after SR.

Keywords Deep infiltrating endometriosis · Intestinal endometriosis · Segmental colo-rectal resection · Quality of life · Gastrointestinal symptoms · Personalized medicine

Introduction

Deep infiltrating endometriosis (DIE) is characterized by the invasion of anatomical structures and organs, which can result in pelvic anatomy distortion [1–4]. DIE predominantly affects women of reproductive age and causes pelvic pain, infertility and gastrointestinal dysfunction [1, 2], which can negatively affect their quality of life (QoL) and psychological well-being [5]. Intestinal-DIE occurs in 3% up to 37% of cases, most commonly affecting the rectum and sigmoid colon [6], and resulting in dyschezia, constipation, rectal bleeding, bloating, flatulence, defecation urgency and/or a sensation of incomplete evacuation [2].

When pharmacotherapy fails or anatomic distortion affects health and causes infertility, surgery is the treatment of choice, which improves QoL and obstetrical outcomes [3, 4]. Laparoscopic treatment is currently the gold standard [7, 8].

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Choosing conservative versus radical surgery should be individually evaluated because the two different approaches have different indications, outcomes, and complications: conservative treatment, such as shaving or full-thickness/discoid resection, is recommended to be applied to selected cases of single and superficial nodules < 3 cm, while radical treatment, such as segmental resection (SR), is recommended in cases of multifocal nodules and in the presence of nodules > 3 cm that deeply infiltrate the colonic wall [9].

While SR certainly improves QoL and reduces pain [10, 11], there are some reports in the literature indicating that conservative treatment produces similar QoL outcomes but lower gastrointestinal symptom incidence [12, 13]. However, general QoL and gastrointestinal well-being after SR were retrospectively evaluated without adopting specific questionnaire for endometriosis and the use of a specific gastrointestinal evaluation. Moreover, the relative small sample sizes and follow-up (FU) duration of these studies would have limited the relevance of the data [12, 14, 15].

The only prospective randomized controlled trial present in the literature failed to demonstrate the superiority of conservative surgery versus SR in terms of gastrointestinal symptoms and voiding disorders; moreover, no specific endometriosis-related Qol questionnaire was adopted [16].

The current literature lacks long-term data about overall quality of life and gastrointestinal well-being evaluation in SR for intestinal-DIE in a large sample of patients.

The primary objective of the present study is to assess the long-term QoL and gastrointestinal well-being in patients who underwent SR for endometriosis; specific questionnaires for DIE-affected patients and for gastrointestinal evaluation were utilized. The secondary objectives are represented by the evaluation of peri-operative and post-operative outcomes.

Patients and methods

This observational cohort study ENDO-RESECT (ClinicalTrials.gov ID: NCT03824054) reports all clinical data about women who underwent surgery for intestinal-DIE between October 2005 and November 2017 in Catholic University Institutions. Local IRB approval was obtained (Institutional Committee [intramural] no. PROT. APROV. IST CICOG-31-10-18\100).

Inclusion criteria were clinically diagnosed intestinal-DIE triaged to SR, and age between 18 and 47 years.

Exclusion criteria were previous or ongoing neoplastic pathology, contraindications to surgery; incomplete surgery, uncontrolled major psychiatric disorders, surgical, spontaneous or pharmacological menopause, intestinal surgery different from SR and colo-rectal anastomosis, and unconfirmed endometriosis at pathology. Ostomy creation and multiple resections were not considered exclusion criteria.

Initially, all intestinal-DIE cases were diagnosed with pelvic examination and pelvic (trans-vaginal and/or endorectal) ultrasound, while magnetic resonance imaging was used if needed in case of uncertain ultrasound findings [17].

Patients were asked to evaluate pain such as dysmenorrhea, dyspareunia, dysuria, dyschezia and chronic pelvic pain with the visual analogue scale (VAS) [18]. In the part of the study dedicated to QoL, different type of questionnaires were adopted in order to asses general and gastrointestinal well-being.

The Endometriosis Health Profile (EHP30) [19], Psychological General Well-Being Index (PGWBI) [20], Hospital Anxiety and Depression Scale (HADS) [21], gastrointestinal well-being questionnaire (GSRS) [22] and the Bristol Stool chart (BSC) [23] were compiled by the patients who referred their pre-surgical clinical status during the FU period, while the post-surgical status questionnaires were compiled at the moment of the last FU contact. The FU period ended in November 2018.

The EHP30 consists of 30 core questions and 6 modules used to evaluate health profiles of endometriosis patients and has been demonstrated to be more reliable than generic health questionnaires [15, 24, 25]. Module A is related to the effects of endometriosis on the patient's work, module B investigates the patient–child relationship, module C aims to assess the patient's sexual relationships, module D concerns the patient–physician relationship, module E assesses the patient's feelings regarding endometriosis treatment, and module F investigates a patient's feelings concerning fertility [19].

PGWBI is a 22-item questionnaire evaluating self-perceived psychological well-being expressed as a summary score; it has been validated and used in many countries on large, general, and specific, population samples [20].

HADS consists of 14 items divided into two equal subscales for anxiety and depression, in which the patient rates each item on a four-point scale. Higher scores indicate the presence of psychological issues. The cutoff of > 11 implies definite cases, while the cutoff 8–10 indicates probable cases, and the cutoff < 7 defines inconsequential cases [21].

GSRS is a self-reported questionnaire about disease-specific common symptoms of gastrointestinal disorders which has been shown to provide good internal consistency, reliability and responsiveness [22, 26–28]. GSRS contains 15 items, each rated on a seven-point scale ranging from no discomfort (lower scores) to very severe discomfort (higher scores), distributed into five scales exploring, abdominal pain (abdominal pain, hunger pains and nausea), reflux syndrome (heartburn and acid regurgitation), diarrhea syndrome (diarrhea, loose stools, and urgent need for defecation, number of daily defecations ≥ 3), indigestion syndrome (borborygmus, abdominal distension, eructation and increased flatus) and constipation syndrome (constipation, hard stools, and feeling of incomplete evacuation) [22, 26–28].

Though the BSC questionnaire, feces were classified into seven groups [23]; stool form and consistency depend on the time feces spend in the colon, and how they are passed through it, and also on other determinants of its composition including diet, fluids, medications and lifestyle [29]. Patients referring feces type 1 and 2 frequently complain constipation, while referring types 6 and 7 complain diarrhea [23].

The endometriosis-related QoL questionnaires were evaluated by the gynecology team, while gastrointestinal status was evaluated by a gastroenterologist.

The classification of SR in high, low and ultralow resection was performed according to the distance of the rectal margin of transection from the anal verge [29].

Endometriosis was classified utilizing the revised American Fertility Society score (rAFS) [30]. Surgeries were performed by a gynecology team belonging to the same school and well trained in DIE treatment, allowing for standardization and reproducibility of interventions.

During SR, the sigmoid and rectum are mobilized; the rectum is distally transected towards the lesion with a transverse stapler. The proximal bowel is then exteriorized and the affected bowel resected. The circular stapler anvil is secured to the proximal end of the rectum or sigmoid with a purse string suture. The proximal and distal bowel are approximated and anastomosed end-to-end with a trans-anal circular stapler. A temporary loop ileostomy is created in case of ultralow resection or unsuccessful/insecure anastomosis (e.g. leak evidence). Ileostomy reversal is undertaken within 3 months after SR.

The extended Clavien–Dindo classification [31] for postoperative complications was adopted, which characterizes episodes as early (within thirty post-operative days) or late (after thirty post-operative days). *Major complications* were classified as grade III or higher, requiring surgical, endoscopic, or radiological intervention. *Minor complications*, grade I and II, could be resolved with a conservative approach [31]. Only major complications were considered significant for this study.

In cases in which there was no desire for pregnancy, oral contraception (OC) was recommended for 6 months after surgery [32].

Regarding fertility, the pregnancy rate was defined as the number of pregnancies obtained in the population of patients desiring conception. The mode of conception (spontaneous or artificial) was also reported. The live birth rate was defined as the number of deliveries resulting in a live-born neonate [11].

Quantitative variables were reported as median and range and/or as mean ± standard deviation (SD). Qualitative variables were reported as absolute (number), and relative (percentage) frequency. Preoperative and post-operative scores were compared with t test for two dependent means, and alternatively with the Wilcoxon signed-rank test. The Chi-square test was applied for the comparison of group proportions. All tests were two sided. Differences with a $p < 0.05$ were considered statistically significant. All statistical analyses were performed with SPSS version 20.0 (Chicago, IL).

Results

A total of 50 women underwent SR and were enrolled in the study. Histology confirmed intestinal-DIE in all patients enrolled.

As reported in Table 1, median age was 38 years (range 24–46); 49 patients (98%) had been already treated surgically for endometriosis in other hospitals. All patients suffered preoperative dysmenorrheal, while dyschezia was reported by 76% of women. Nine patients (18%) were stage III and 41 (82%) stage IV according to the rAFS. Twenty-seven (54%) nulliparous women of child-bearing age were subjected to fertility-sparing surgery.

Table 2 reports the data relative to the clinical status of endometriosis at the time of surgery. Single and multiple colo-rectal nodules were present in 70% and 30% of women, respectively. The median size of bowel nodule was 30 mm

Table 1 Patient characteristics

Variable	N (%)	Median (range)
All cases	50 (100)	–
Age, years	–	38 (46, 24)
Body mass index	–	21 (18, 31)
N of prior surgery for endometriosis		
None	1 (2)	–
1	24 (48)	
> 1	25 (50)	
Preoperative symptoms (VAS)[a]		
Dysmenorrhea	50 (100)	8 (3, 10)
Dyschezia	38 (76)	7 (0, 10)
Dysuria	12 (24)	0 (0, 9)
Dyspareunia	32 (64)	7 (0, 10)
Chronic pelvic pain	29 (58)	5 (0,10)
Stage[b]		
Stage I (minimal)	0	–
Stage II (mild)	0	
Stage III (moderate)	9 (18)	
Stage IV (severe)	41 (82)	
Deliveries		
No	23 (46)	–
Yes	27 (54)	–

[a]Pain is evaluated with the visual analogue scale (VAS) for symptomatic patients

[b]According to rASRM classification

Table 2 Endometriosis clinical status

Endometriosis localization	N (%)	Median (range)
Colo-rectal nodule	50 (100)	–
Single	35 (70)	–
Multiple	15 (30)	–
Dimension (mm)	–	30 (10, 60)
Distance from anal verge (mm)	–	50 (15, 100)
Adenomyosis	22 (44)	–
Endometrioma	33 (66)	
Monolateral	25 (50)	–
Bilateral	8 (16)	
Parametrial nodule	44 (88)	
Monolateral	23 (46)	–
Bilateral	11 (22)	
Periureteral nodule	32 (64)	
Monolateral	18 (36)	–
Bilateral	14 (28)	
Pre-vesical/vesical nodule	16 (32)	–

Table 3 Surgical procedures, intra-operative, post-operative variables and fertility outcomes

Variables	N (%)	Median (range)
Laparoscopy	50 (100)	–
Conversion to laparotomy	8 (16)	–
Bowel resection[a]	50 (100)	–
High	43 (86)	–
Low	6 (12)	–
Ultralow	1 (2)	–
Multiple resection	3 (6)	–
Specimen length (mm)	95 (–)	90 (40, 25)
Association with vagina opening	20 (40)	–
Loop ileostomy creation	13 (26)	–
Parametrectomy	31 (62)	–
Ureterolysis	44 (88)	–
Hysterectomy	8 (16)	–
Estimated blood loss (mL)	–	175 (50, 1000)
Operative time (min)	–	280 (100, 480)
Intra-operative complications	0 (0)	–
Post-operative complications		
Grade[b]	22 (44)	
I	14 (28)	
II	5 (10)	
III	3 (6)	
Ureterovaginal fistula (grade IIIb)	1 (2)	
Anastomotic stenosis (grade IIIc)	2 (4)	
IV	0	
Hospital stay (days)	–	6 (3, 15)
Obstetrics outcome[c]		
Women with desire for pregnancy	16 (32)	–
Pregnancy rate	8 (50)	
Mode of conception		
Natural	3 (19)	
Assisted reproductive technique	5 (62)	
Live birth rate	10 (100)[d]	

[a]Classification of colo-rectal resection

[b]Extended Clavien–Dindo classification of surgical complications

[c]Percentage calculated on the 16 patients with desire for pregnancy

[d]Two twin pregnancies

(range 10–60), and the median anal verge distance was 50 mm (range 15–100).

As shown in Table 3, all surgeries started in laparoscopy, but conversion to laparotomy was necessary in eight (16%) cases due to the need to perform multiple bowel resections in three (6%) cases, and extensive abdominal adhesions. Forty-three (86%) high colo-rectal resections, six (12%) low resections, and one (2%) ultralow resection were performed. Temporary loop ileostomy was performed in 13 (26%) patients: 1 ultralow SR case, 3 multiple SR cases, 8 vagina opening cases due to infiltrating nodules (to avoid the risk of recto-vaginal fistula formation), and 1 post-operative late complication.

Total hysterectomy was performed in eight (16%) women affected by adenomyosis, who no longer intended to conceive.

All patients obtained complete surgical eradication.

No early grade III major complications were registered; conversely three (6%) patients experienced late grade III morbidity (one ureterovaginal fistula, two anastomotic stenosis).

As far as the obstetrics outcome is concerned, of the 27 nulliparous women in child-bearing age, 16 (59%) manifested the desire for pregnancy after surgery; 8 patients (50%) conceived: 3 (19%) spontaneously, 5 (62.5%) with assisted reproductive techniques (ART). The live birth rate was 100%: there were 5 physiological pregnancies, 2 twin pregnancies, and 1 case of severe pre-eclampsia requiring an urgent C-section at 26 weeks of gestational age. Seven other women with a desire for pregnancy failed to conceive (3 of them despite ART). One woman was referred for ART at the time of data collection and four were lost at FU (Table 3).

Median follow-up after SR was 42.5 months (range 12–157 months) while the 80% of the series exceeding more than 24 months of FU.

As far as the VAS score is concerned, all patients experienced less pain at the last FU contact; moreover, the 74% of patients resulted pain free, with a mean difference in terms of VAS score ranging from −6.13 for dysmenorrhea to −1.46 for dysuria (Table 4). Regarding QoL, EHP-30 demonstrated a significant improvement in all variables measured, except for concerns about conceiving (Table 5). After surgery, women appeared to be more self-confident,

Table 4 Assessment of pain (VAS score) referred by patients regarding their status before and after surgical treatment

Parameter	Median (range)	Mean (± SD)	Mean diff	p value[a]
Dysmenorrhea PRE	8 (4–10)	7.9 ± 2.1	− 6.13	< 0.00001
Dysmenorrhea POST	0 (0–8)	1.6 ± 2.5		
Dyschezia PRE	7 (0–10)	5.2 ± 3.9	− 2.96	0.000225
Dyschezia POST	0 (0–10)	1.6 ± 3.0		
Dysuria PRE	0 (0–9)	1.8 ± 2.9	− 1.46	0.004728
Dysuria POST	0 (0–5)	0.2 ± 0.9		
Dyspareunia PRE	7 (0–10)	5.5 ± 3.8	− 3.64	< 0.00001
Dyspareunia POST	0 (0–10)	1.7 ± 2.7		
Chronic pelvic pain PRE	5 (0–10)	4.4 ± 3.8	− 3.10	0.000066
Chronic pelvic pain POST	0 (0–8)	1.3 ± 2.4		

[a]Calculated by t test for two dependent means

Table 5 Outcomes in general quality of life evaluated with Endometriosis Health Profile 30 (EHP-30) after surgical eradication of endometriosis and bowel resection compared with referred pre-surgical status

Parameter	Mean (± SD)	Mean diff.	p value[a]
EHP-30 total PRE	53 ± 18.6	− 17.5	< 0.001
EHP-30 total POST	35.5 ± 16.5		
EHP-30 (1) pain PRE	32.8 ± 12.4	− 15.4	< 0.00001
EHP-30 (1) pain POST	17.4 ± 7.8		
EHP-30 (1): control and powerlessness PRE	18.6 ± 8.4	− 6.94	< 0.00001
EHP-30 (1): control and powerlessness POST	11.7 ± 7.2		
EHP-30 (1): feeling of well-being PRE	15.1 ± 7.7	− 3.67	0.000671
EHP-30 (1): feeling of well-being POST	11.4 ± 7.6		
EHP-30 (1): social support PRE	9.5 ± 5.2	− 2.36	0.000205
EHP-30 (1): social support POST	7.2 ± 4.6		
EHP-30 (1): self-image PRE	6.1 ± 3.2	− 1.38	0.004014
EHP-30 (1): self-image POST	4.8 ± 3.1		
EHP-30 (2): work PRE	12.6 ± 6.2	− 5.95	< 0.00001
EHP-30 (2): work POST	6.7 ± 3.8		
EHP-30 (2): looking after children PRE	3.9 ± 2.8	− 1.52	0.006236
EHP-30 (2): looking after children POST	2.4 ± 1.2		
EHP-30 (2): sex PRE	15.3 ± 7.1	− 6.83	< 0.00001
EHP-30 (2): sex POST	8.1 ± 5.6		
EHP-30 (2): feelings about medical professionals PRE	7.3 ± 3.8	− 2.92	< 0.00001
EHP-30 (2): feelings about medical professionals POST	4.6 ± 2.0		
EHP-30 (2): feelings about treatment PRE	6.4 ± 3.7	− 1.21	0.018786
EHP-30 (2): feelings about treatment POST	5.9 ± 3.5		
EHP-30 (2): feelings about conception PRE	10.5 ± 6.2	− 0.29	0.453506
EHP-30 (2): feelings about conception POST	10.6 ± 6.4		

[a]Calculated by t test for two dependent means

and more satisfied at work and with their sexuality. Furthermore, a positive influence on the patient–gynecologist relationship was noted.

PGWBI showed a clear impairment of mental well-being in all women at baseline with significant improvement of all items after surgery (Table 6); even anxious and depressive status and the subjective general state of health resulted significantly improved after surgery (Supplementary tables 1 and 2).
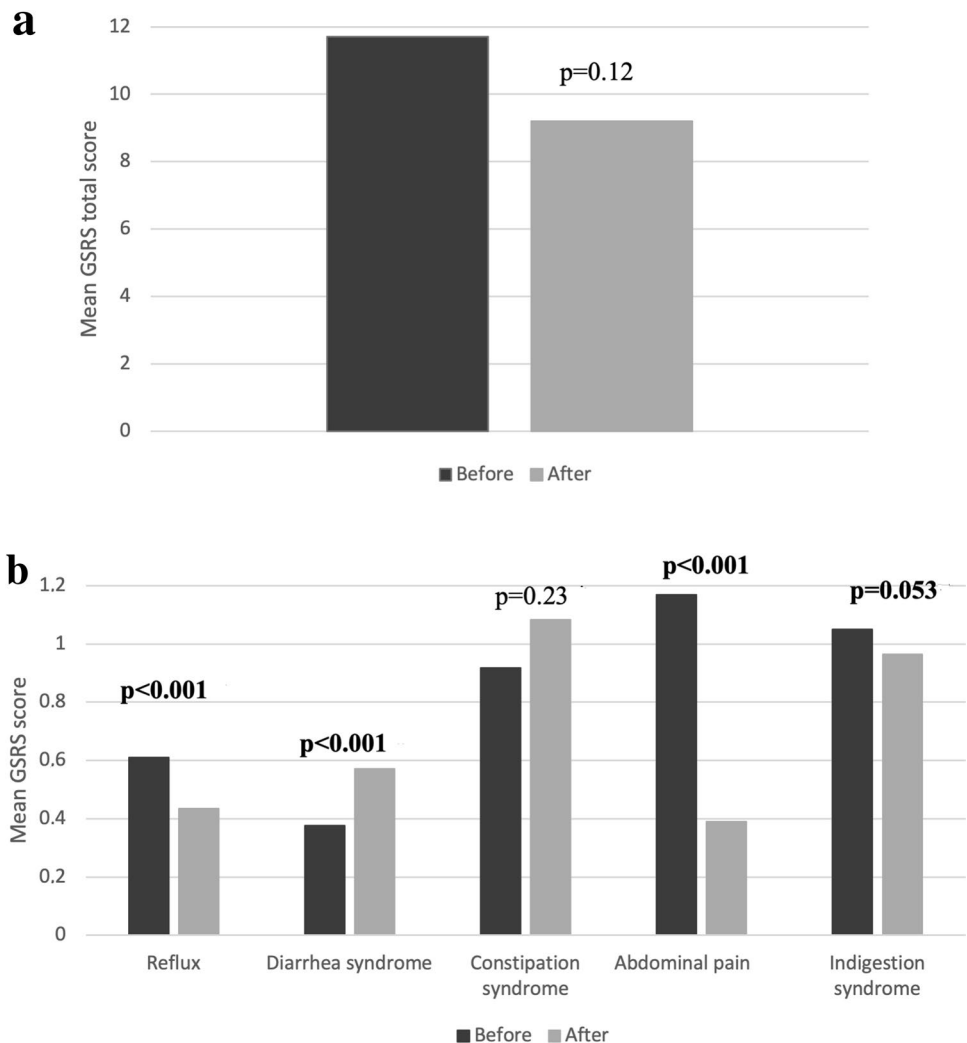
Regarding gastrointestinal outcomes (according to the GSRS), 13 (26%) patients referred overall gastrointestinal impairment for relevant symptoms (score > 17) mostly including abdominal pain followed by indigestion syndrome and constipation at referred pre-surgical status (baseline), while 37 (74%) patients did not report relevant symptoms (score < 17). At last FU period overall gastrointestinal impairment for relevant symptoms was referred by 10 (20%) patients, while 40 (80%) patients did not complain

Table 6 Outcomes in Psychological General Well-Being Index (PGWBI) after surgical eradication of endometriosis and bowel resection compared with referred pre-surgical status

Parameter	Mean ($\pm$ SD)	Mean diff.	p value[a]
PGWBI (anxiety) PRE	62.6 $\pm$ 23.9	22.96	< 0.00001
PGWBI (anxiety) POST	85.5 $\pm$ 22.6		
PGWBI (depression) PRE	76.62 $\pm$ 18.7	10.42	= 0.000015
PGWBI (depression) POST	87.0 $\pm$ 19.4		
PGWBI (general state of health) PRE	47.0 $\pm$ 24.4	35.52	< 0.00001
PGWBI (general state of health) POST	82.5 $\pm$ 19.0		
PGWBI (vitality) PRE	48.4 $\pm$ 30.0	38.9	< 0.00001
PGWBI (vitality) POST	87.3 $\pm$ 18.2		
PGWBI (positivity) PRE	50.3 $\pm$ 22.2	24.6	< 0.00001
PGWBI (positivity) POST	74.9 $\pm$ 21.2		
PGWBI (self-control) PRE	74.9 $\pm$ 20.2	12.52	< 0.00001
PGWBI (self-control) POST	87.5 $\pm$ 18.9		
PGWBI (global index-IGB) PRE	–	2.7	< 0.00001
PGWBI (global index-IGB) POST			

[a]Calculated with Wilcoxon signed-rank test and *t* test for two dependent means

Fig. 1 GSRS scores at referred pre-surgical status and at last FU after surgery. *p* value calculated by *t* test for two means. **a** Mean ($\pm$ SD) general GSRS score and **a** mean ($\pm$ SD) GSRS score for specific symptoms

severe disorders. Figure 1a shows the GSRS score related to the referred pre- and post-surgical evaluation; although an improvement of overall gastrointestinal status was noticed, the difference was not statistically significant ($p = 0.12$). Ten (20%) patients suffered severe abdominal pain at baseline, evaluated with three specific pain questionnaires (Fig. 1b). A statistically significant improvement of symptoms was registered for reflux, abdominal pain and indigestion syndrome. Four (8%) patients referred a new-onset grade 2 diarrhea syndrome after surgery reaching a total symptom incidence of 13%, while grade 3 percentage of patients remained unchanged (2%). The severity (intensity) of diarrhea symptoms did not achieve statistical significance ($p = 0.27$) (Fig. 2).

Twenty-two (43%) patients reported pre-surgical constipation with referred feces type 1–2 (Fig. 3). No significant changes concerning constipation were evident at the end of the FU; indeed patients neither reported a significant increase in constipation intensity (Fig. 2c) nor a significant increased presence of hard stool type (53%) (Fig. 3).

Relevant gastrointestinal disorders were globally more prevalent in patients affected by single intestinal nodule compared with multiple intestinal nodule patients with 29% versus 20%, respectively, at baseline; moreover, the prevalence of relevant symptoms decreased at 26% and 7%, respectively, after surgery. Mean GSRS total score did not show statistically significant differences in these

two subsets of patients after surgery. Supplementary figure 1 reports the changes of symptoms between baseline and at the last FU status for single- and multiple-nodule population; patients affected by multiple nodules experienced a greater reduction particularly of abdominal pain ($p < 0.001$), and also reflux ($p = 0.01$) and indigestion syndrome ($p < 0.08$) after surgery while constipation and diarrhea syndrome appeared significantly worsened ($p < 0.001$). For single nodule-affected patients instead, only the reduction of reflux ($p < 0.001$) and abdominal pain ($p = 0.004$) resulted significant, while no statistical worsening of diarrhea and constipation was registered for these patients.

As far as the HADS evaluation is concerned, gastrointestinal symptoms resulted more severe in patients with evident signs of anxiety and/or depressive mood. In particular, relevant gastrointestinal impairment was present in not anxious and anxious patients in the 13% and 50%, respectively, at baseline, and in the 9% and 39%, respectively, at last FU after surgery.

Patients characterized by not depressive and depressive mood, instead, manifested relevant gastrointestinal symptoms in the 13% and 80%, respectively, at baseline, and 20% at last FU after surgery.

Surgery was associated with an overall improvement of gastrointestinal symptoms, particularly in the sub-group of depressive-mood patients ($p = 0.07$).
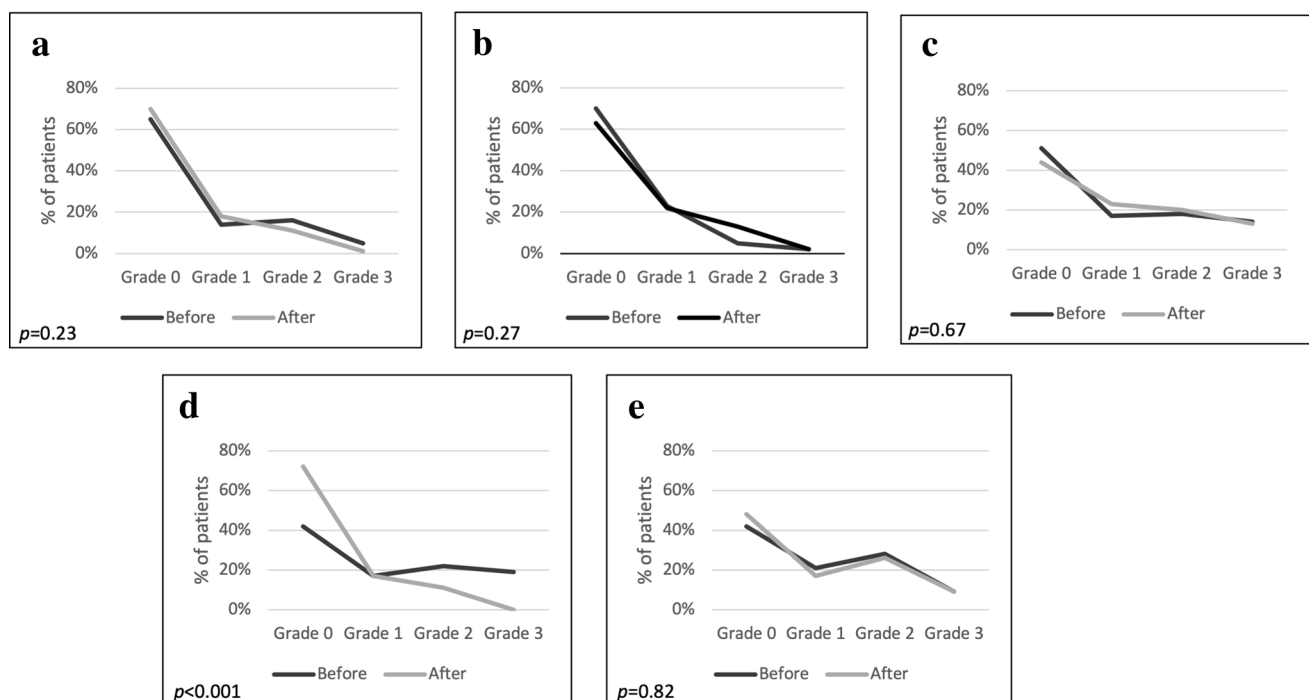

Fig. 2 Intensity of symptoms for gastrointestinal items at GSRS score at referred pre-surgical status and at last FU after surgery. *p* value calculated with χ^2 test. **a** Reflux, **b** diarrhea syndrome, **c** constipation syndrome, **d** abdominal pain, and **e** indigestion syndrome
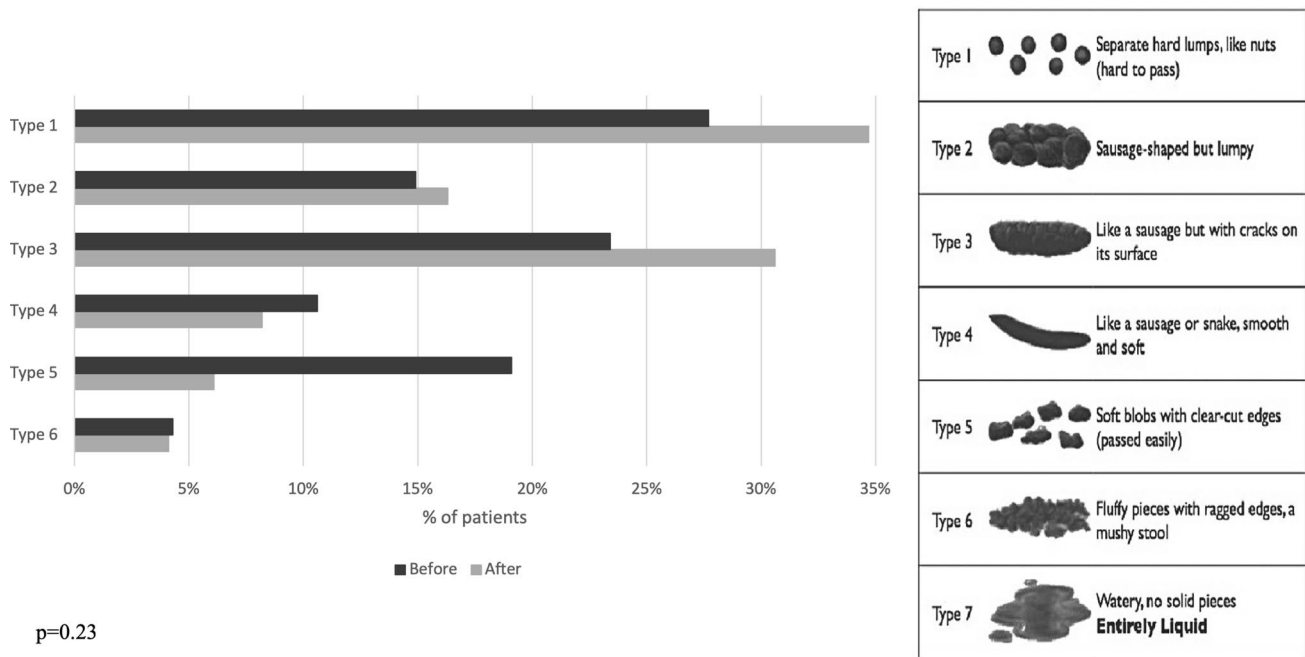
Fig. 3 Bristol Stool Scale distribution at referred pre-surgical status and at last FU after surgery. *p* value calculated with Wilcoxon matched-pair signed-rank test

Supplementary figures 2 and 3 report the changes of symptoms for anxious and depressive-mood population. The symptom abdominal pain resulted improved especially in depressive-mood patients, while diarrhea syndrome appeared worsened in anxious population ($p < 0.001$).

As far as the surgical approach is concerned, the population managed in laparoscopy and laparotomy presented severe gastrointestinal impairment in the 36% and 23%, respectively, at baseline, while in the 9% for laparoscopy and stable in the 23% for laparotomy at last FU after surgery. Laparoscopic approach was associated with a significant overall improvement of gastrointestinal symptoms ($p = 0.02$).

Supplementary figure 4 reports the changes of symptoms regarding surgical approach adopted. Most of the gastrointestinal symptoms resulted improved after laparoscopy (Suppl. figure 4a), while diarrhea, constipation and indigestion syndrome appeared slightly worsened after laparotomy (Suppl. figure 4b).

Discussion

To our knowledge, no prior studies have evaluated concomitantly the specific endometriosis-related QoL (EHP-30) indicators and the gastrointestinal well-being utilizing appropriate questionnaires in such a considerable population sample of patients undergoing SR followed for such a prolonged period [10, 11, 15, 16, 33] (Supplementary table 3).

As far as the primary objective of this study is concerned, our data demonstrate a significant pain and QoL improvement after SR for DIE, which is confirmed by other researchers [10–16, 34, 35]. Moreover, the recent EHP-30 reveals other information available only in a few other studies [13]. In particular, in this cohort, women reported less pain, and an improvement of general well-being and self-awareness. Women sexuality improved with regard to satisfaction, which was previously linked to pain during sexual intercourse [5, 36–38]. QoL improvement had a strong impact on work activities with important economic and social implications. Additionally, social, sexual and work-related satisfaction of women positively influenced the child–mother relationship. An improvement of the gynecologist–patient relationship was also noted, which had a positive impact on the provision of medical care. Statistical significance was not achieved regarding feelings about bearing children. This can be explained by the fact that not all variables of the EHP-30 questionnaire were relevant for all patients. In particular, 23 (46%) women prior to surgery were already mothers, and 7 (14%) of them decided to undergo hysterectomy. The pregnancy rate observed (50%) is in line with the prior literature [11].

In our population, a significant increase of up to 26% of patients with overall gastrointestinal-related complaints, and up to at least 50% of patients presented symptoms similar to "irritable bowel syndrome" with severe to moderate abdominal pain, constipation more than diarrhea and indigestion syndrome at baseline [39, 40].

The overall GSCG core improved after surgery, particularly with regard to reflux and abdominal pain and indigestion syndrome.

This study confirms that SR produces an evident clinical benefit in terms of general and specific gastrointestinal QoL for the selected population [13, 15–17]. Furthermore, none of the patients experienced a relapse, nor required re-operation for endometriosis and benefits obtained resulted long-lasting and constant over time. These results are supported by the long follow-up period achieved. Patients with an increased likelihood of post-surgical improvement were those with depressive mood who underwent laparoscopic surgery; moreover, women with multinodular disease experienced a greater reduction in abdominal pain.

However, some post-surgical gastrointestinal *sequelae* were noted, but these did not appear to affect the QoL of patients.

Constipation appeared to be slightly worsened after surgery without reaching statistical significance. This worsening could be explainable by the evidence that patients with preoperative constipation are less likely to achieve normal bowel movements after surgery [41]. Women affected by multinodular bowel localizations, moreover, experienced more post-operative constipation.

A significant increase of "diarrhea syndrome" was also noted after surgery. Since a post-operative incidence of liquid/diarrheal-type stools (types 5–6–7) was not reported with the BSC and the most recorded feces types were the normal types 2–3, the increase in diarrhea syndrome should be considered as a mere rise in numbers of daily-formed feces defecations (frequent bowel movements) (FBM) as also suggested by the recent literature [16].

No relationship between the onset of FBM and multiple resections, the length of specimen removed, and the level of SR was observed.

Interestingly, women with FBM were those suffering from anxiety and multinodular bowel localizations than depressive mood and single nodule.

Since overall QoL did not result affected, considering these results, an adequate counseling is necessary for patients undergoing SR with regard to the FBM onset, even in the long term, especially when anxiety and multinodular disease are present. It is reasonable to assume that the presence of anxious mood in patients undergoing SR may be a factor that worsens surgical outcomes since anxiety is generally strongly associated with fecal urgency and diarrhea syndrome already in normal conditions [40, 42–44].

While patients affected by multinodular disease benefited more than single-nodule population regarding abdominal pain reduction, at the same time one part of them experienced a constipation worsening and another part FBM after surgery. This study failed to identify the reasons for these divergent results although the possible determining factors have been statistically evaluated.

Further studies are needed to confirm the contribution of patient physical and mental characteristics reported above, in addition to surgical factors, that determine negative gastrointestinal outcomes following surgery, to tailor surgical treatment [41].

As far as the secondary objectives are concerned, the incidence of major intra- and post-operative complications was comparable with the previous literature [13, 45, 46], but doubled compared to the recent prospective trial on bowel surgery for endometriosis (6% vs 3.3%) [16]. Anastomotic stenosis rate registered in this cohort, however, was lower (4% vs 15%) than the recent literature incidence [16].

Moreover, the onset of major post-operative complications had no impact on the improvement of patients' QoL, as already shown in other literature [33].

The percentage of laparotomy conversions observed in this study (16%) is consistent with data reported in the literature in which the conversion rate was up to 20% [13]. This result can be explained by the fact that 3 (6%) women underwent multiple resections and part of patients who underwent previous surgeries (98%) in other hospitals presented with extensive abdominal adhesions. Laparotomy did not negatively influence post-operative general QoL [30], but gastrointestinal post-operative well-being of women who underwent laparoscopy clearly improved, possibly because of less adhesion formation [47].

The strengths of this study are the large population sample subjected to the same type of surgery by the same team of gynecologists, the long FU period, the adoption of the EHP-30, specific for QoL assessment in DIE patient, and the assessment of gastrointestinal well-being with ad hoc questionnaires evaluated by a dedicated gastroenterologist.

The weakness of this study is the retrospective data collection of preoperative patient clinical status. However, the retrospective nature of the preoperative data collection does not affect the quality of the results collected at the last visit of FU concerning the long-term assessment of quality of life related to endometriosis and gastrointestinal well-being after SR, primary endpoint of this study.

A relative weakness could be represented by the loss of information about the period preceding the last follow-up contact; the aim of this study, however, was to investigate the *definitive* status of patients. In the first post-operative months, in fact, patients often presented with diverse and more intense gastrointestinal symptoms, such as tenesmus, diarrhea, and abdominal discomfort or constipation in connection with surgery [34] which progressively improved after 12 months following resection [14, 48, 49]. The collection of data following this transition period allows for the exclusion of possible bias in definitive QoL assessment.

Finally, an adequate follow-up period allowed, first, to observe the real incidence of anastomotic stenosis [16, 50].

The present study has the advantage of informing clinicians with the FU reached, about the long-term outcomes of SR that resulted acceptable in terms of general and gastrointestinal QoL [12, 14, 15, 34].

Physicians should consider the optimal surgical approach (radical or conservative) on a case by case basis, being cognizant of the pros and cons of each type of surgery, to recommend the best tailored treatment for patients [9–16, 34, 35].

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee (No. PROT. APROV. IST CICOG-31-10-18\100) and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This article does not contain any studies with animals performed by any of the authors.

Informed consent Informed consent was obtained from all individual participants included in the study.

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