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# Functional Outcomes and Quality of Life After Laparoscopic Nerve-Sparing Radical Treatment of Parametrial Deep Infiltrating Endometriosis

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#### ABSTRACT

**Study objective:** Complete eradication of parametrial nodules of Deep Infiltrating Endometriosis (DIE) is associated with a high risk of iatrogenic nerves damage and pelvic organs dysfunction. The aim of this study is to evaluate the effect of laparoscopic excision of parametrial DIE on quality of life, pain symptoms and post- operative voiding function (bladder and rectal).

Design: Retrospective observational study.

**Setting:** All patients undergoing laparoscopic nerve-sparing excision of parametrial DIE by a single expert surgeon between January 2013 and March 2017 were included in the study.

Patients: Fifty-one patients were included in the final analysis.

**Intervention:** Quality of life (QoL) and Functional outcomes were evaluated using validated questionnaires (EHP-30, NBD score, ICIQ-FLUTS), administered preoperatively and after surgery. Pain scores were collected using Visual Analogue Scale (VAS).

**Measurement and Main Results:** EHP-30 scores had a significant improvement in all the domains analyzed. No differences were found in terms of urinary function. The NBD score showed that intestinal dysfunction was. reported as very minor by 76.4%, minor by 11.8%, moderate by 5.9% and severe by 5.95% of patients. Pain symptoms (VAS score) decreased significantly after surgery except for chronic pelvic pain (p value < .05).

**Conclusion:** Laparoscopic nerve-sparing radical excision of parametrial DIE can favorably impact on patients QoL and reduces pain score and intestinal dysfunction.

Keywords: Deep Endometriosis; Laparoscopy; Nerve-Sparing; Parametrial Endometriosis; QoL

Abbreviations: DIE: Deep Infiltrating Endometriosis; VAS: Visual Analogue Scale; NBD: Neurogenic Bowel Dysfunction; QoL: Quality of Life

# Introduction

Endometriosis is a chronic inflammatory disease, characterized by ectopic proliferation of endometrial glands and stroma [1-3]. The deep infiltrating endometriosis (DIE) is a specific clinical entity characterized by an extension of the disease more than 5 mm under the peritoneal surface, retroperitoneal fibrosis and neural tropism with distortion of the regular pelvic anatomy [4]. DIE affects most frequently uterosacral ligaments (69.2%), rectovaginal septum (14.5%), bowel (9.9%) and bladder (4.2%) [5]. In recent years a growing attention was pointed out on parametrial localization of DIE with studies investigating diagnosis, treatments and clinical outcomes [6-8]. The lateral parametrium contains the nerve branches of autonomic pelvic organs innervation, therefore the complete eradication of the disease is associated with the risk of serious impairment of rectal, bladder and sexual function due to the iatrogenic disruption of inferior hypogastric plexus Radical resection of the posterior parametrium, corresponding to the uterosacral ligament plus rectovaginal ligaments and lateral ligament of the rectum, can also result in injury to the hypogastric nerves, pelvic splanchnic nerves and to the anterior branches of the sacral sympathetic chains. Different authors have described the nerve-sparing approach in case of DIE nodules [9-11]. In 2012, a prospective cohort study compared the laparoscopic nerve-sparing approach to the classical laparoscopic procedure demonstrating the feasibility of radical removal of infiltrating endometriosis tissue from parametrial structures avoiding disruption of autonomic pelvic organs innervation [12].

There has been a growing interest in recent years on analyzing QoL after laparoscopic surgery for endometriosis. However, only a few studies have specifically addressed data on functional outcomes after DIE excision, and, to the best of our knowledge, no one was published investigating patient's QoL with specific validated questionnaires [13,14]. The aim of this study is to use validated questionnaires to evaluate patients' response to laparoscopic nerve- sparing excision of parametrial DIE in terms of self-perceived well-being, pain relief and voiding function.

## **Materials and Methods**

This study was approved by the local Ethics Committee (protocol number 0024582/19), and all patients expressed their informed consent to anonymous data collection. All patients that underwent laparoscopic surgery for endometriosis in the period between January 2013 and March 2017 at Obstetrics and Gynecology Division of the Sassuolo Civil Hospital and at the Endometriosis tertiary level referral center of the University Hospital of Modena were enrolled. All surgeries were performed by the same surgeon with high expertise in laparoscopic treatment of endometriosis (C.A.) Medical records from patients with histologically confirmed laparoscopic resection of posterior and/or lateral parametrium were collected. Exclusion criteria were as follows: age < 18 years, preoperative diagnosis of neurogenic

bladder and bowel inflammatory disease, absence of sexual activity and failure to complete the study questionnaires. All patients underwent speculum examination, pelvic bimanual vagino-rectal evaluation and transvaginal ultrasound performed by an expert sonographer expert in endometriosis diagnosis. A transabdominal ultrasound scan of the kidneys was also routinely performed to rule out hydroureteronephrosis. Eventually, they underwent pelvic magnetic resonance with rectal injection of 10-50 ml of sterile gel to confirm dimension and depth of infiltration of the bowel lesions (if any) and to define the parametrial/ureteral involvement. All patients signed a specific informed consent before surgery, specifying all surgical procedures necessary for their complete excision and the potential risks (vascular, neurologic, urologic and intestinal) related to the type of surgery.

All patients were submitted to nerve sparing excision of DIE according to Negrar Method [15]. In case of bowel lesions infiltrating the muscularis interna and causing a stenosis of more than 50% of the lumen in patients symptomatic for bowel dysfunction, a segmental resection with Knight-Griffen technique and end-to-end anastomosis was performed by a general surgeon. A protective ileostomy was routinely done in case of ultra-low rectal segmental resection (resection margin < 5 cm from the dental line). The data on patient age, parity, body mass index, previous abdominopelvic surgery, operating time, amount of blood loss, use of hormonal therapy, length of hospital stay were recorded, while intraoperative, early and late postoperative complications were analyzed according to the Clavien-Dindo classification system [16]. Pain symptoms were investigated using the Visual Analogue Scale (VAS) and the different need of analgesic drugs was evaluated at the preoperative visit and at the follow up evaluation after three months. For the comparative analysis of dysmenorrhea with VAS scale, patients underwent hysterectomy and patients with post-operative continuous hormonal therapy were excluded (22 patients). Quality of life and functional and status outcomes were collected using the Italian validated version of Endometriosis Health Profile-30 (EHP-30) and International Consultation on Incontinence-Female Lower Urinary Tract Symptoms (ICIQ-FLUTS) [17] and the Italian translation of Neurogenic Bowel Dysfunction (NBD) [18], administered one month before surgery and three months after the intervention.

The EHP-30 was used to evaluate the global health profile of the patients [19] and consists of 30 questions about pain, control and powerlessness, emotional well-being, social support and self-image. Currently is the only questionnaire that evaluates QoL specifically in patients with endometriosis. For bowel function the NBD score was used [20]: this questionnaire evaluates intestinal dysfunction and its impact on quality of life in patients with neurological lesions; it is based on 10 items assessing defecation and faecal incontinence with a score ranging from 0 (very low disfunction) to 47 (severe disfunction). The urinary function was evaluated using ICIQ-FLUTS [21,22]. this questionnaire includes 22 items relating to bladder filling, uri-

nation and incontinence; for each question, a score from 0 to 4 is assigned. Higher scores correspond to a higher level of dysfunction. Data were expressed as mean±standard deviation or median (range) for numerical variables and as numbers (percentages) for categorical variables. The Wilcoxon test was used to compare any change in variables before and after the surgical treatment. P value of <0.05 denoted statistical significance. All statistical analyses were performed using SPSS software (version 21, SPSS, Inc., Chicago, IL, USA).

#### Results

During the study period a total of 65 patients underwent nerve-sparing surgery for parametrial deep infiltrating endometriosis. 51 patients met the inclusion criteria and were included for the study analyses. Demographic characteristics of patients are provided in (Table 1). Mean age was  $36.6 \pm 6.2$  years. Eight patients had had previous surgery for endometriosis (15.6%) and 27 were nulliparous (53%). Operative details and procedures are summarized in (Table 2). Dysmenorrhea was the most frequent symptom (84.3%), followed by dyspareunia (74.5%), ovulatory pain (70.6%), dyschezia (51%), chronic pelvic pain (35.3%) and stranguria (27.5%). Laparoscopic approach was used in all cases, no conversion to open surgery occurred. Laparoscopic segmental bowel resection was performed in 15 (%) patients, while discoid resection was performed in only one (%). Three (%) patients needed protective ileostomy for ultra-low rectal anastomosis. The mean operating time was 239 +/-111 minutes. The mean estimated blood loss during surgery was 165 +/- 59.9 mL (range 50-1020 mL). The mean hospital stay was 6 days (range 3-12 days). In 37 patients (62.7%) parametrial endometriosis was unilateral, in 13 patients (22% of cases) both posterior and lateral parametrium were involved and in 9 patients (15.3% of cases) posterior and lateral parametria were involved bilaterally. Right posterior parametrium was involved in 38% of cases (19/50), while the left one was involved in 40% of cases (20/50). Right lateral parametrium was involved by endometriosis in 59.1% of cases (13/22), the left one was involved in 31.8% of cases (7/22), and lateral parametria were involved bilaterally in 9.1% of cases (2/22).

Age, years	36 +/- 6.2	
Weight, kg	62.1 +/- 12.9	
BMI, Kg/m <sup>2</sup>	22.7 +/- 3.9	
Nationality		
·Caucasian	90.1% (46/51)	
·North African	5.9% (3/51)	
· Asian	2% (1/51)	
· Latin American	2% (1/51)	
Marital Status		
·Married	72.5% (37/51)	
·Divorced	· Divorced 11.8% (6/51)	

Table 1: Demographic characteristics of patients.

·Nubile	13.7% (7/51)	
·Widow	2% (1/51)	
Education		
·Secondary school	21.6% (11/51)	
· High school	56.8% (29/51)	
·Degree	21.6% (11/51)	
Occupation		
·Employed	88.2% (45/51)	
·Unemployed	9.8% (5/51)	
·Students	2% (1/51)	
Medical History		
· No prior history	33.3% (17/51)	

Note: Values are given as mean +/- standard deviation or absolute number (percentage).

Table 2: Detail of operative procedures.

OPERATIVE PROCEDURES		
endometrioma enucleation	31/51 (60.8%)	
monolateral adnexectomy	8/51 (15.7%)	
ovarian fossa peritoneum removal	25/51 (49%)	
Total hysterectomy	5/51 (10%)	
Rectosigmoid endometriosis removal	31/51 (60.7%)	
-Shaving	15/51 (29.4%)	
-bowel resection	15/51 (29.4%)	
-discoid resection	1/51 (2%)	
protective ileostomy	3/51 (5.9%)	
Lateral parametrium removal	15/51 (29.4%)	
Unilateral	13/15 (86.6%)	
right	7/15 (46.6%)	
left	6/15 (40%)	
Bilateral	2/15 (13.4%)	
Posterior parametrium removal	44/51 (86.3%)	
Unilateral	36/51 (70.6%)	
right	16/44 (36.4%)	
left	left 20/44 (45.4%)	
Bilateral	8/51 (15.7%)	

Note: Values are given as absolute number (percentage).

The average size of parametrial nodules was 2 +/- 0.5 cm. No case of intrinsic ureteral endometriosis was found. No intraoperative complications occurred. Three postoperative complications were registered: one hemoperitoneum (class IIIb), one rectovaginal fistula (class IIIb) and one case of stenosis of colorectal anastomosis requiring endoscopic balloon dilation (class IIIa). Twenty-seven patients (52.9%) were undertaking hormonal therapy at the 3-month post-operative follow up visit. Pain symptoms severity expressed in VAS score, except CPP, were significantly decreased after the operation (p value < .05) as shown in (Table 3). The EHP-30 score before and after surgery are shown in (Table 4). Surgery improved significantly QoL in many of the domains analyzed such as pain, control and powerlessness, emotional well-being, social support, self-image, satisfaction of treatment, sexual life. It was not possible to evaluate the "infertility" and "relation-ship with children" modules because respectively 21 (41.2%) and 31 (60.8%) patients did not answer the questions. Limited to the small sample analyzed, however, even in these two modules a statistically significant improvement was observed. No significative disfunction were found at post-operative ICIQ-FLUTS questionnaire. Bowel function improved after surgery in patients' subjective perception, although the results are controversial: the NBD score showed that intestinal dysfunction in the whole group was related to constipation, while the surgery was resolutive for diarrhea. Most of the patients

showed mild dysfunction (76.4%), while only three patients had severe dysfunction (5.9%).

Table 3:	VAS score	before	and a	after	surgery*.
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	Median + IQR before	Median + IQR after	p-value
Dysmenorrhea	8 + 5.5	2 + 5.25	0.01
Dyspareunia	6 + 3	4 + 3	0.012
Chronic pelvic pain	0 + 3.5	0 + 0	0.823
Dyschezia	2 + 7.5	0 + 2.5	0.001
Strangury	0 + 4	0 + 0	0.01

Note: VAS score before and after surgery, values are given in median + IQR (interquartile range) \*no continues hormonal therapy l contraceptives.

EHP-30 questionnaire	<b>BEFORE SURGERY</b>	AFTER SURGERY	P-value
Pain	47.2 (+/- 25.3)	10.1 (+/-14.8)	< .001
Control and powerlessness	56.3 (+/-25.7)	13.2 (+/-15.6)	< .001
Emotion	53.4 (+/-24)	23.3 (+/- 20.7)	< .001
Social support	38.8 (+/-26.5)	22.2 (+/-21.5)	< .001
Self-image	30.7 (+/-23.9)	19.7 (+/- 22.5)	< .001
work module	38.8 (+/- 28.3)	9.3 (+/-16.7)	< .001
relationship with children	20 (+/-26.1)	6 (+/-12.9)	0.002
sexual intercourse	49.2 (+/- 27.8)	20.6 (+/-22.6)	< .001
medical profession	21 (+/-26.7)	3.9 (+/- 8.7)	< .001
treatment module	38.3 (+/- 29.1)	15.5 (+/- 21.9)	< .001
infertility module	48.8 (+/- 27.8)	30.2 (+/- 30.0)	.007

 Table 4: EHP-30 scores before and after surgery.

Note: Values are given as mean +/- standard deviation or absolute number (percentage), if not otherwise expressed.

#### Discussion

The parametrium has been described as the supporting system of the uterus that anchors the organ to the lateral pelvic wall and has both supply-drainage and fascial functions. More often DIE lesions are at the level of the posterior and lateral part of the parametrium associated to retrocervical, bowel and ureteral nodules [23]. This pattern of lesions distribution can be associated with ureteral and bowel function impairment and often with chronic pelvic pain symptoms expressed as dyspareunia and dyschezia [8,24]. Due to these symptoms, endometriosis may have a profound impact on quality of life and mental health of the patients affected. In 2004 (Abbot, et al. [25]) demonstrated that surgical excision of endometriosis determines a symptomatic improvement. significantly more than placebo. According to this evidence, surgical eradication of DIE represents the treatment of choice in symptomatic patients unresponsive to medical treatment. The preservation of the pelvic autonomic system may be challenging in case of large nodules and surgical treatment of deep infiltrating endometriosis needs adequate surgical skills and expertise to minimize the risk of surgical complication; in fact only a few series, with limited sample size, have demonstrated the feasibility of nerve-sparing surgery in case of parametrial DIE [26-28] To the best of our knowledge this study is the first to analyze the impact of laparoscopic nerve-sparing surgery for parametrial deep infiltrating endometriosis on quality of life using EHP-30 questionnaire. We observed that this type of surgery improved quality of life of patients and reduced all the painful symptoms, except for chronic pelvic pain.

This evidence suggests that a "symptom guided approach" and a radical surgery are associated with better postoperative outcomes. The main post-operative improvement in term of quality of life relates to domains affecting social and relationship life. This represents an important goal considering that the average age of the patients enrolled is 36 years, with a percentage of working and married women being respectively 88.2% and 72.5%, and that 47% of them are engaged in the management of children. Furthermore, the eventuality of surgical complications associated with this technique was low. Patients reported a subjective improvement in bowel function at NBD

questionnaire, excepted for constipation. This evidence is in accordance with a retrospective study by (Abo, et al. [29]) on 371 women undergoing surgery for colorectal endometriosis. The results of the ICIQ-FLUTS questionnaire on urinary function showed that incontinence was more frequent in patients undergoing posterior parametrial resection than those undergoing lateral or resection of both parametria. However, a conclusion can't be achieved because of size discrepancy between the three groups (36/51 patients underwent resection of the posterior parametrium, 7/51 of the lateral parametrium and 8/51 of both parametria). The main bias of our study is related to the lack of pre-operative data on urinary function. Many authors have studied the incidence of urinary symptoms in patients with endometriosis (Fauconnier, et al. [24]).

Related specific symptoms to anatomical locations of DIE but did not evaluate the correlation between urinary symptoms and posterior DIE; (Darai, et al. [30]) reported a high incidence of urinary symptoms in patients with deep infiltrating endometriosis, but without being able to correlate the presence of symptoms with well-defined anatomical lesions. Among the possible limitations of this study, we mention the small sample size, the lack of a comparison arm of patients not receiving nerve-sparing approach and the short follow up [31,32]. On the other hand, our study provides the first analysis of the impact of nerve-sparing surgery on quality of life, using validated questionnaires and it gives good and promising results for the systematic use of this type of approach.

## Conclusion

In conclusion, the use of nerve sparing technique by expert surgeons warrants good results in term of improvement of QoL and pain control and provides good functional outcomes. The development of surgical skills based on anatomical knowledge can lead to a more extensive use of the nerve-sparing technique with a persistent improvement in the quality of life of the patients with parametrial localization of DIE.

## **Conflict of Interest**

Authors have no conflict of interest and economic interest to declare. The authors declare no conflict of interest. This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors. The data that support the finding of this study are available from the corresponding authors upon reasonable request.

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