

Laparoscopic Excision of Endometriosis May Require Unilateral Parametrectomy

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ABSTRACT

Objective: We investigated the effects of laparoscopic excision of endometriosis with unilateral parametrectomy on bladder, rectal, and sexual function as well as patient satisfaction.

Methods: Women who underwent this procedure between February 1, 2006 and November 15, 2007 were enrolled. Patient characteristics, pre- and postoperative findings, and follow-up data were retrospectively collected from a computerized database.

Results: Twelve patients were enrolled in the study. All of the symptoms except dysuria improved after surgery, worsening long after the operation. It seems that all parameters including sexuality, micturition, and defecation are equally important in regards to the final judgement of satisfaction, with a trend towards amelioration long after the operation.

Conclusions: Unilateral parametrectomy may offer successful results in terms of patient satisfaction despite some impairment in bladder, bowel, and sexual function. The risk of permanent functional impairment is high; therefore, surgeons need to maintain the integrity of the contralateral nerve pathway. This is highly important, because pain relief seems to be partially involved in the final judgement of postoperation satisfaction.

Key Words: Complete excision, Endometriosis, Parametrectomy, Nerve-sparing, Voiding disorders.

INTRODUCTION

Endometriosis is the presence of endometrial-like tissue outside the uterus, which induces a chronic, inflammatory reaction. This benign gynecological disorder occurs in from 70% to 80% of women with pelvic pain or infertility¹ and is present in >10% of women within the reproductive age in the United States.² The associated symptoms, such as pelvic pain, dysmenorrhea, deep dyspareunia, dyschezia, dysuria, ovulation pain, and infertility, can severely impact general physical, mental, and social well-being. Medical treatments like oral contraceptives, danazol, and gonadotrophin-releasing hormone agonists are equally effective in the treatment of endometriosis-associated pain, producing temporary relief of symptoms, but none has yet been shown to achieve a long-term cure. Discontinuation of medication usually results in the recurrence of pain within 12 months.^{3,4} The available evidence suggests that the most effective form of treatment is complete laparoscopic excision of endometriosis, which offers good long-term symptomatic relief, especially for those with severe or debilitating symptoms.⁵⁻⁷ Such surgery is neither quick nor simple, with potentially serious complications.⁸⁻¹⁰

Two recent reports recognize the risk of urinary and digestive side effects during complete excision of endometriosis secondary to nerve damage.^{7,11} In a previous article, we confirmed the risk of impairment of urinary, rectal, and sexual function during laparoscopic complete excision of endometriosis.¹² Consequently, we developed a nerve-sparing procedure in patients with deep endometriosis and obliterated cul-de-sac requiring segmental bowel resection.¹² Further experience suggested to us that nerve-sparing surgery is not always feasible on both sides of the pelvis, particularly when endometriosis is deeply embedded in the parametrium. Parametrial involvement has just been mentioned by a few authors,¹³ but none have investigated its treatment. To date, in our experience parametrial involvement with consequent extensive nerve involvement was mainly detected in one side of the pelvis only. These data compare favorably with the well-known asymmetry in distribution of pelvic and abdominal endometriosis. Two authors¹⁴⁻¹⁷ have studied the distribution of deeply infiltrating endometriosis with the aim of attempting to better understand the pathogenesis. These

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studies conclude that uterosacral ligament lesions,¹⁶ intestinal lesions,¹⁴ ureteral lesions,¹⁸ and pelvic deeply infiltrating endometriosis are significantly more often located on the left side.¹⁷ Herein, we first report on 12 patients with parametrial involvement, and we investigate the effect on bladder, rectal, and sexual function as well as patient satisfaction following laparoscopic complete excision of endometriosis with unilateral parametrectomy and inevitable unilateral damage of the hypogastric nerve and the inferior hypogastric plexus due to endometriotic parametrial invasion.

METHODS

The study was performed in our specialized endometriosis unit of Sacro Cuore General Hospital in Negrar (Verona, Italy). From February 1, 2006 to November 15, 2007, 12 patients were enrolled in the study. They had received a previous diagnosis of endometriosis, and they had stopped medical therapy with progestins, GnRH agonist, or birth control pills for ≥ 3 months before laparoscopic complete excision of all detectable foci of endometriosis and unilateral parametrectomy (ie, cardinal ligament), due to severe endometriosis that involved such parametrial tissue. Parametrial nerve damage during surgery was assessed by laparoscopic surgeons who performed the operation, according to anatomical criteria. Two independent surgeons (RF, RC) confirmed such nerve damage after reviewing the medical record and video of the operation. All surgery was performed due to chief complaints of extremely severe pelvic pain and performed by 4 highly skilled surgeons with general surgical assistance for bowel surgery.

Because deep infiltrating endometriosis involves parametrial tissues, we start with the physiological anatomy of the parametrium to check the integrity of the nerves close to deep infiltrating endometriosis nodules, during and after their surgical removal. The hypogastric nerves run laterally to the uterosacral ligament approximately 5 mm to 20 mm below the course of the pelvic ureter¹⁹ and join at the antero-superior angle of the pelvic plexus and reach the medial part of the cardinal ligament (CL), combining with parasympathetic fibers to form the superior part of the inferior hypogastric plexus.²⁰ The inferior hypogastric plexus is below the medial part of the CL. Medially in the CL 2, separate parts can be distinguished¹: an upper section containing vascular structure (the so-called “pars vasculosa”) and² a lower and medial section (“pars nervosa”) containing the inferior hypogastric plexus. A constant anatomical landmark that we use to represent the

plane dividing the parametrial “pars vasculosa” (ventrally and cranially) from the “pars nervosa” (dorsally and caudally) is the deep uterine vein. It can be considered the most cranial vein directly draining into the inferior hypogastric vein, and normally it originates at the level of the upper third of the vagina.

Differently from the superficial uterine vein, the deep vein is often present and runs across down the ureter in the lateral parametrium crossing the pelvic plexus. The majority of the nerve fibers in the anterior efferent bundle of the pelvic plexus, which provides the autonomous innervation of the bladder (base and neck), pass in the caudal portion of paracervix (deep portion of vesicouterine ligament) for which the deep uterine vein and the parietal pelvic fascia covering the levator ani are the cranial and caudal limits, respectively.¹⁹

Ideally, to perform a nerve-sparing dissection that is carried out more extensively in the cranial part of the CL, the dissection plane should not have exceeded the limit of the shape of the bow of a ship from a lateroventral to mediadorsal position.²¹

The hypogastric nerve and the initial part of the inferior hypogastric plexus are situated in the lateral aspects of the uterosacral ligament (USL). During dissection of the USL and rectal pillar, after incision of the peritoneum of the Douglas pouch, the prerectal space and pararectal spaces are created. Then the medial USL is separated from the lateral nervous fibers.

From then on, the term “parametrectomy” is used to define damage to the inferior hypogastric plexus due to dissection of the CL caudally to the deep uterine vein, damage of the caudal part of the hypogastric nerve and the cranial part of the inferior hypogastric plexus during dissection of the USL, or damage to the fibers of the hypogastric plexus that run to the bladder beside the lateral wall of the vagina at more than 2 cm below the cervix.

The surgical technique used has been described elsewhere.¹² Briefly, video-laparoscopy was initially performed with three 5-mm cannulas inserted under direct vision suprapubically, and in each midquadrant of the abdomen both lateral to inferior epigastric vessels, with a 10-mm laparoscope in the standard umbilical position. Complete excision of pelvic endometriotic lesions was performed using 5-mm bipolar scissors. The laparoscopic procedure usually began with the lysis of adhesions, drainage and stripping of endometriomas, and excision of bladder endometriosis or other pelvic sidewall disease

working retroperitoneally in the healthy tissue surrounding the disease. Following any ovarian surgery, the ovaries were temporarily suspended by using nonabsorbable suture and then removed on day 2 to day 3 after surgery to improve access to the posterior cul-de-sac and prevent the ovary from becoming adherent to the denuded pelvis postoperatively. Commencing at the pelvic brim, starting on the right hand side, the ureters and main vessels were identified and ureterolysis immediately against the muscular wall of the ureter was performed along its course on the pelvic sidewall until healthy tissue was reached. When endometriosis extended deeply and laterally into the cardinal ligament of one side, the intervention was continued on the opposite side to assess the degree of contralateral involvement. Then, the surgeon decided which side could be sacrificed. On the opposite side, he preceded using the nerve-sparing technique described elsewhere.¹² Unilateral parametrectomy was only done after the surgical team was sure that innervation to the pelvic organs had been spared on the opposite side. In case of bilateral parametrial involvement, the surgeon decided to sacrifice what he judged to be the worst side.

The resection of the parametrial nodule was simply done following the shape of the nodule regardless of the surrounding innervation. When needed, branches of the hypogastric vein, most commonly uterine and vaginal arteries and uterine veins, were sacrificed. Special care was taken to avoid thermal damage to the ureter. When possible, the parametrial endometriosis was resected en bloc with other adjacent endometriotic nodules, namely nodules of the uterosacral ligament, of the rectovaginal septum, of the rectum, and of the vagina.

Prior to the procedure, all patients were counseled regarding the potential risks and benefits of such an intervention and signed a written informed consent. Institutional review board permission was not considered necessary, because treatments and study endpoints were similar to those in our usual clinical practice.

Data about patients was retrospectively collected from our computerized database. The fluctuations in the amount of blood lost during surgery were recorded by measuring aspirated blood volume. The operation time was recorded as well. After the operation, patients' recovery of micturition and passage of stool (through specific queries at 1- and 2-month follow-ups) were recorded. Before surgery, patients were interviewed about dysuria dysmenorrhoea, chronic pelvic pain, dyspareunia, and dyschezia. A subjective scale scoring pain from 0 (absent) to 10 (unbearable) was adopted. Patients were asked to score their pain

in the same way one month after surgery and during the second follow-up visit.

To assess the functionality of bladder, rectum, and vagina, we asked patients whether they were satisfied with their defecation, micturition, and sexuality and asked them to answer "yes" or "no" to our questions at the second follow-up. Additionally, we asked whether the patients were globally satisfied after the operation (in relation to operation recovery, sexual, intestinal, urogenital function, and pain relief).

Statistical Analysis

Continuous variables are described as medians and ranges. Nonparametric Spearman's correlation was searched for between variables, as indicated, and 1-sided Wilcoxon's test for paired data was used to compare median values from pain scales. $P < 0.05$ was considered statistically significant. Traditional conjoint analysis was constructed to assess how much the sexual, urogenital, and intestinal functions matter in patient satisfaction, in relationship to the global judgment of satisfaction, including pain relief.

RESULTS

Patient characteristics are shown in **Table 1**. From the description of the interventions, only one patient underwent "aggressive" surgical excision of endometriosis in our center. All of the others simply underwent ovarian cystectomy and adhesiolysis or diathermocoagulation of endometriosis. One patient had experienced unilateral nephrectomy due to ureteral stenosis by endometriosis. **Table 2** summarizes the surgical laparoscopic procedures for each patient, performed at the time of laparoscopic parametrectomy.

The median operating time was 270 minutes (range, 60 to 480), median blood loss was 350 mL (range, 100 to 800). There are no correlations between blood loss and length of operation ($Rho\ 0.417$, $P=0.167$).

In 3 (25%) patients, the endometriotic implants were so deeply embedded in both parametria that the surgeon decided to remove only one of them, thus leaving some disease in the contralateral one. Eight patients (67%) underwent bowel surgery during the same procedure. The median time needed to resume passage of stool after intervention was 10 days (range, 0 to 60). One patient still has a diverting ileostomy. The median time to resumption of micturition was 7 days (range, 2 to 90). Two patients were still performing self-catheterism at the follow-up time.

Table 1.
Anthropometric and Anamnestic Data of Patients

| | Age | Previous Surgery for Endometriosis (Laparoscopic or Open) | Previous Ovarian Cystectomy | Previous Adhesiolysis | Previous Rectovaginal Septum Surgery | Previous DTC | Previous Ureterolysis | Other Surgery |
|------------|-----|---|-----------------------------|-----------------------|--------------------------------------|--------------|-----------------------|------------------|
| Patient 1 | 28 | 1 | Right | One time | | | | |
| Patient 2 | 36 | 0 | | | | | | |
| Patient 3 | 38 | 2 | | One time | | One time | Left | Left nephrectomy |
| Patient 4 | 32 | 1 | Right | One time | | | | |
| Patient 5 | 35 | 1 | | | | | | |
| Patient 6 | 36 | 4 | | Two times | | | | |
| Patient 7 | 31 | 0 | | | | | | |
| Patient 8 | 29 | 0 | | | | | | |
| Patient 9 | 41 | 1 | Three left cysts | One time | | | | |
| Patient 10 | 33 | 1 | Left & Right | | | | | |
| Patient 11 | 30 | 2 | | | | | | |
| Patient 12 | 35 | 2 | Left & Right | | One time | | | |

Table 2.
Surgical Debulking for Each Patient

| | Parametrectomy | Bowel Surgery | Vaginal Resection | Uterosacral Ligament | Rectovaginal Septum | Ureterolysis | Other Surgery |
|------------|----------------|---------------|-------------------|----------------------|---------------------|--------------|--------------------|
| Patient 1 | Left | Yes | Yes | Left & Right | Yes | Right & Left | |
| Patient 2 | Right | No | No | Left & Right | Yes | Right & Left | |
| Patient 3 | Left | No | Yes | Left | Yes | Right | Total hysterectomy |
| Patient 4 | Left | Yes | Yes | Right | Yes | Right & Left | |
| Patient 5 | Left | No | Yes | No | Yes | Right & Left | |
| Patient 6 | Left | Yes | No | No | No | Left | |
| Patient 7 | Left | Yes | Yes | No | Yes | Right & Left | |
| Patient 8 | Left | Yes | Yes | No | Yes | No | |
| Patient 9 | Right | Yes | Yes | No | Yes | No | |
| Patient 10 | Left | Yes | No | Left & Right | Yes | Left | |
| Patient 11 | Left | No | Yes | No | No | Right & Left | |
| Patient 12 | Left | Yes | Yes | Left | Yes | Right | Stoma |

No unintended injury occurred to bowel or the urinary tract. Re-intervention for hemorrhaging occurred in 2 patients. None of the patients required a blood transfusion. The median time of follow-up was 3.5 months (range, 1 to 13). All of the patients included completed the 1-month visit and postoperative questionnaire.

Pre- and postoperative symptoms are reported in **Table 3**, as collected from the 0 to 10 scoring system questionnaires. All of the symptoms but dysuria improved after surgery. **Table 4** illustrates answers about satisfaction reported by patients on the second follow-up questionnaire. Satisfaction is reported in at least one-half of patients

Table 3.
Pre- and Postsurgical Symptoms at Follow up Visits

| | Pre-intervention† (A) | 1 Month Control Visit† (B) | Follow-up Visit† (C) | A vs B P Value | A vs C P Value |
|---------------|-----------------------|----------------------------|----------------------|-------------------|-------------------|
| Pelvic pain | 7 (0–9) | 1 (0–7) | 1 (0–7) | =0.006 | =0.01 |
| Dysmenorrhea* | 8 (4–10) | 1 (0–4) | 1 (0–8) | =0.003 | =0.004 |
| Dyspareunia | 7 (0–9) | 1 (0–7) | 1 (0–9) | =0.006 | =0.01 |
| Dysuria | 1 (0–3) | 1 (0–1) | 1 (0–4) | =0.05 | =0.076 |
| Dyskezia * | 6,5 (1–8) | 1 (0–4) | 1 (0–8) | =0.024 | =0.012 |

*Results are expressed as median of a scale ranging from 0 to 10.

†11 cases available (had a hysterectomy and 1 had a stoma).

Table 4.
Intervention Satisfaction

| | Sexuality | Micturition | Defecation | Global |
|------------|-----------|-------------|------------|--------|
| Patient 1 | Yes | Yes | Yes | Yes |
| Patient 2 | Yes | Yes | Yes | Yes |
| Patient 3 | Yes | Yes | Yes | Yes |
| Patient 4 | No | Yes | No | No |
| Patient 5 | Yes | No | Yes | Yes |
| Patient 6 | No | No | No | No |
| Patient 7 | Yes | Yes | Yes | Yes |
| Patient 8 | No | No | No | No |
| Patient 9 | Yes | No | No | Yes |
| Patient 10 | Yes | Yes | Yes | Yes |
| Patient 11 | No | No | No | No |
| Patient 12 | Yes | No | No | Yes |
| Importance | 25% | 24.9% | 24.9% | 25% |

regarding sexuality, micturition, defecation, and globally. It seems that all parameters (sexuality, micturition, and defecation) have the same importance for the final judgement of satisfaction, emphasizing that pain relief may be partially involved in satisfaction.

DISCUSSION

Efficient lower urinary tract, rectosigmoid, and sexual functions rely on both autonomic and somatic nerve activity. Injury to the detrusor branches of the pelvic splanchnic nerves can cause detrusor denervation and urinary retention. Given the anatomical distribution of nerve fibers, the dissection of the most lateral part of the cardinal ligament put the inferior hypogastric plexus in

secure jeopardy. Similarly, the dissection of the medial part of the inferior hypogastric plexus may lead to dysfunctional rectal morbidity. Endometriosis has been described in virtually any site of the pelvis, but parametrial involvement has only been mentioned by a few authors.¹³ No report specifically addresses this topic and none have investigated its treatment. Herein, we first report on 12 patients with parametrial involvement in which it was considered technically impossible to completely excise the endometriosis unless parametrectomy and subsequently permanent nerve damage is accepted (Figures 1 and 2).

The reason why we had so many of these “extreme” cases could be that in Italy we are a referral center for this disease, so we usually cope with a select population of patients with the worst cases. It is possible that nerve damage during excision of endometriosis deeply embedded into the parametrium may depend on our limited surgical skill. It can be supposed that in similar circumstances surgeons with greater experience in parametrial resection like oncologic surgeons could try to complete the excision of endometriosis without compromising pelvic innervation. However, all the surgeons were highly trained and have performed more than 200 laparoscopic complete excisions of endometriosis with or without segmental bowel resection. Anaf et al²² demonstrated that deep pelvic endometriotic lesions express the nerve growth factor (NGF) and that the nerves from the inferior hypogastric plexus express Trk-A, the specific receptor for NGF. It has been demonstrated that NGF, a neurotrophin that plays a key role in the occurrence of hyperalgesia, is a positive chemotaxin.^{23,24} Endometriotic lesions were found in close relationship to the nerves of the colon as well and seem to infiltrate the large bowel with predilection around the nerves.²⁵ Such a close anatomical rela-

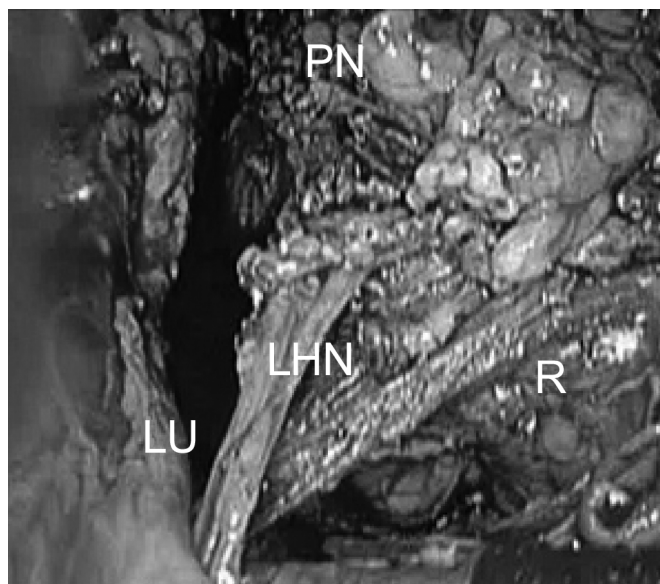


Figure 1. Left Hypogastric Nerve (LHN) that digs into the left parametrium deeply invaded by endometriosis (parametrial nodule = PN). Note how endometriosis strictly adheres to the distal part of the hypogastric nerve so that its transaction was considered necessary to complete the removal of endometriosis (R = rectum; LU = left ureter)

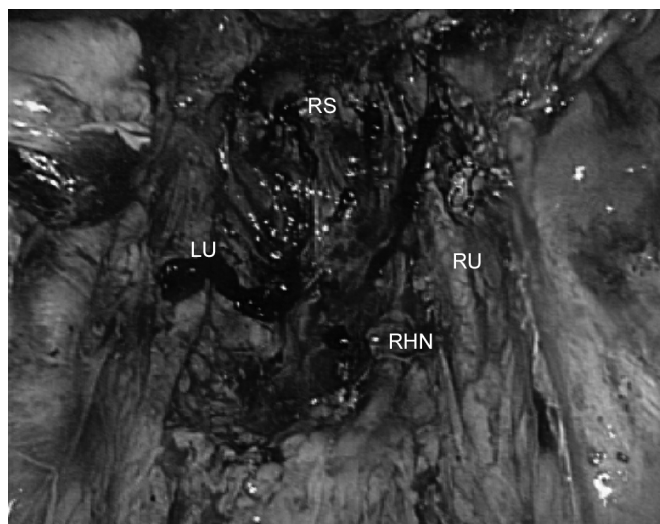


Figure 2. Final result after left parametrectomy and rectosigmoid resection before bowel anastomosis. Note the stump of the left hypogastric nerve (yellow circle). Rectal stump = RS; Right ureter = RU; Right hypogastric nerve = RHN; Left ureter = LU.

tionship among the pelvic plexus and nerves and deep parametrial endometriosis could be the reason, which makes nerve-sparing technically impossible. This study confirms the relief of painful symptoms following aggres-

sive excision for endometriosis except for dysuria. Even if the lower scores for dysuria in the preoperative assessment should underline that bladder endometriosis was not as common and severe as the other localizations, statistical analysis for assessing dysuria relief after surgery has less power than statistical assessment of other pain parameters. Therefore, improvement in dysuria may be possible in the very rare and extreme cases.

In the 3 cases of bilateral parametrial involvement, we decided to resect parametrium on one side, thus only leaving the contralateral side with some endometriosis. However in our experience, detection of nerve structures and vessels is by far more difficult in endometriosis than in cancer, because the closer you are to the endometriotic nodule, the more difficult the dissection becomes. Indeed in some cases, we were not able to identify intraoperatively the deep uterine vein that is an important surgical landmark for nerve-sparing surgery of the parametrium.

The time of the second follow-up was not rigorous. This may have biased the satisfaction judgement in relationship to several checked and unchecked parameters. The main complaint is in regards to urinary symptoms namely the need to use the abdominal torque, intermittent micturition, loss of bladder filling sensation, difficulty in starting micturition, and poor urinary flow. All these symptoms are possibly related to bladder denervation. However, the same importance of sexuality, micturition, and defecation is found from satisfied answers, even if satisfaction seems to be variable. We have not used a scoring system for satisfaction levels, because we judge that it would not be reproducible, as patients are differently involved in judging their dysfunctional symptoms that are related to other functional and nonfunctional parameters (ie, drug therapies, patient backgrounds, previous surgeries, and others). Because use of medicine is more likely after surgery, and patients may bear dysfunctions more positively after intervention, the time of the second follow-up may affect the answers regarding satisfaction. Patients with later follow-ups (more than 6 months) seem to have greater satisfaction with micturition and defecation. Even global judgement of satisfaction and sexuality seem to show a trend toward amelioration. It can be speculated that the reason for higher satisfaction in regards to micturition and defecation in the later follow-up patients may at least partially depend on a resumption of functions that become more evident with the passing of time after surgery. In the animal model, spontaneous sprouting of bladder nerves into the cystoplastic cecal segment has been demonstrated.²⁶ We have no data to support our hypothesis. On the other hand, the global satisfaction judgement in-

volving pain relief should worsen through time, because pain scores worsen long after intervention. Therefore, we could understand that patient satisfaction is strongly linked to functional behavior.

From the little data available, with 2 patients dissatisfied with the procedure out of 3 with bilateral parametrial involvement, it is impossible to draw any conclusion about whether it is worth leaving endometriosis in one parametrium. However, these preliminary data are encouraging.

Our study remarkably reports for the first time a series of 12 patients with parametrial invasion by endometriosis. From our data, unilateral parametrectomy with inevitable unilateral damage of the hypogastric nerve and the inferior hypogastric plexus during laparoscopic complete excision of endometriosis seems to be feasible and may offer good results in terms of patient satisfaction despite some impairment in bladder, bowel, and sexual function. It has been reported in experimental animals that normal urinary function could be maintained when at least one side of the sympathetic nerves has been preserved.²⁷ In addition, normal urinary function has been maintained in humans by applying autonomic nerve preservation to the noninvaded side in patients with stage IIb cervical cancer, who have parametrial invasion only in one side.²⁸

However, the risks of permanent functional impairment are very high, and surgeons have to be absolutely sure about the integrity of the contralateral nerve pathway. To undervalue the damage of the contralateral nerve pathway may lead to disastrous consequences for a patient's quality of life. If intraoperative judgement of nerve sparing is very difficult and subject to misunderstanding due to interobserver variability, in our experience it is virtually impossible to assess the extent of nerve damage of a previous surgery. For this reason, we think that this procedure should only be considered for patients at the first intervention. Larger series with longer follow-ups are needed to confirm our results.

CONCLUSION

From our experience in some cases, nerve-sparing complete excision of endometriosis may be technically impossible, and in these patients unilateral parametrectomy may be considered. Our experience suggests that patients' subjective satisfaction increases with the passing of time and that more than 6 months are needed to assess the results of surgery. However, considering the high risks of this kind of surgery, currently we suggest considering unilat-

eral parametrectomy only during the first surgery, in extremely select patients who are "desperate" with a very poor quality of life and with pain refractory to medical therapy, after a detailed informed consent.

References:

1. Koninckx PR, Meuleman C, Demeyere S, Lesaffre E, Cornillie FJ. Suggestive evidence that pelvic endometriosis is a progressive disease, whereas deeply infiltrating endometriosis is associated with pelvic pain. *Fertil Steril.* 1991;55:759–765.
2. Goldman MB, Cramer DW. The epidemiology of endometriosis. *Prog Clin Biol Res.* 1990;323:15–31.
3. Waller KG, Shaw RW. Gonadotropin-releasing hormone analogues for the treatment of endometriosis: long-term follow-up. *Fertil Steril.* 1993;59:511–515.
4. Miller JD, Shaw RW, Casper RF, et al. Historical prospective cohort study of the recurrence of pain after discontinuation of treatment with danazol or a gonadotropin-releasing hormone agonist. *Fertil Steril.* 1998;70:293–296.
5. Redwine DB, Wright JT. Laparoscopic treatment of complete obliteration of the cul-de-sac associated with endometriosis. Long-term follow-up of en-bloc resection. *Fertil Steril.* 2001;76:358–365.
6. Garry R. The effectiveness of laparoscopic excision of endometriosis. *Curr Opin Obstet Gynecol.* 2004;16:299–303.
7. Darai E, Thomassin I, Barranger E, et al. Feasibility and clinical outcome of laparoscopic colorectal resection for endometriosis. *Am J Obstet Gynecol.* 2005;192:394–400.
8. Nezhat C, Nezhat C, Nezhat F, Ocampo J, Nutis M, Dávalos et al. Outcome after rectum or sigmoid resection: A review for gynecologists. *J Minim Invasive Gynecol.* 14:529–530, 2007; author reply 530.
9. Mereu L, Ruffo G, Landi S, et al. Laparoscopic treatment of deep endometriosis with segmental colorectal resection: short-term morbidity. *J Minim Invasive Gynecol.* 2007;14:463–469.
10. Remorgida V, Ferrero S, Fulcheri E, Ragni N, Martin DC. Bowel endometriosis: presentation, diagnosis, and treatment. *Obstet Gynecol Surv.* 2007;62:461–470.
11. Thomassin I, Bazot M, Detchev R, et al. Symptoms before and after surgical removal of colorectal endometriosis that are assessed by magnetic resonance imaging and rectal endoscopic sonography. *Am J Obstet Gynecol.* 2004;190:1264–1271.
12. Landi S, Ceccaroni M, Perutelli A, et al. Laparoscopic nerve-sparing complete excision of deep endometriosis: is it feasible? *Hum Reprod.* 2006;21:774–781.
13. Donnez J, Pirard C, Smets M, et al. Surgical management of endometriosis. *Best Pract Res Clin Obstet Gynaecol.* 2004;18:329–348.

14. Vercellini P, Frontino G, Pietropaolo G, et al. Deep endometriosis: definition, pathogenesis, and clinical management. *J Am Assoc Gynecol Laparosc.* 2004;11:153–161.
15. Vercellini P, Fedele L, Aimi G, et al. Reproductive performance, pain recurrence and disease relapse after conservative surgical treatment for endometriosis: the predictive value of the current classification system. *Hum Reprod.* 2006;21:2679–2685.
16. Chapron C, Dubuisson JB. Management of deep endometriosis. *Ann N Y Acad Sci.* 2001;943:276–280.
17. Chapron C, Chopin N, Borghese B, et al. Deeply infiltrating endometriosis: pathogenetic implications of the anatomical distribution. *Hum Reprod.* 2006;21:1839–1845.
18. Vercellini P, Pisacreta A, Pesole A, Vicentini S, Stellato G, Crosignani PG. Is ureteral endometriosis an asymmetric disease? *BJOG.* 2000;107:559–561.
19. Ercoli A, Delmas V, Gadonneix P, et al. Classical and nerve-sparing radical hysterectomy: an evaluation of the risk of injury to the autonomous pelvic nerves. *Surg Radiol Anat.* 2003;25:200–206.
20. Raspagliesi F, Ditto A, Kusamura S, et al. Nerve-sparing radical hysterectomy: a pilot study. *Tumori.* 2003;89:497–501.
21. Trimbos JB, Maas CP, Deruiter MC, et al. A nerve-sparing radical hysterectomy: guidelines and feasibility in Western patients. *Int J Gynecol Cancer.* 2001;11:180–186.
22. Anaf V, Simon P, El Nakadi I, et al. Hyperalgesia, nerve infiltration and nerve growth factor expression in deep adenomyotic nodules, peritoneal and ovarian endometriosis. *Hum Reprod.* 2002;17:1895–1900.
23. Gundersen RW, Barrett JN. Characterization of the turning response of dorsal root neurites toward nerve growth factor. *J Cell Bio.* 1980;87:546–554.
24. Yamamoto M, Kondo H, Iseki S. Nerve growth factor receptor (NGFR)-like immunoreactivity in the perineurial cell in normal and sectioned peripheral nerves of rats. *Anat Rec.* 1992;233:301–308.
25. Anaf V, El Nakadi I, Simon P, et al. Preferential infiltration of large bowel endometriosis along the nerves of the colon. *Hum Reprod.* 2004;19:996–1002.
26. Frederiksen H, Davidsson T, Månsson W, et al. Sprouting of bladder nerves into cystoplastic cecal segment in the rat. *Urol Res.* 1999;27:476–482.
27. Liang JT, Chien CT, Chang KJ, et al. Neurophysiological basis of sympathetic nerve-preserving surgery for lower rectal cancer—a canine model. *Hepatogastroenterology.* 1998;45:2206–2214.
28. Sakuragi N, Todo Y, Kudo M, et al. A systematic nerve-sparing radical hysterectomy technique in invasive cervical cancer for preserving postsurgical bladder function. *Int J Gynecol Cancer.* 2005;15:389–397.