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Original Article

Surgical management of endometriotic women with pregnancy intention in France: A national snapshot of centers performing a high volume of endometriosis procedures.



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ABSTRACT

Objective: To provide a snapshot of the surgical management of endometriosis in French high-volume activity centers.

Methods: Analysis of prospectively collected data between November 2015 and May 2017 in 21 centers with a high volume of endometriosis surgery in France. Each facility could include up to 40 patients undergoing laparoscopy for endometriosis. Data were collected before and two months after surgery.

Results: 361 patients were enrolled in the study. Twenty-seven patients (7.48%) were lost to follow-up at the month 2 visit. Endometriosis stage was I-II in 33.70% of patients and III-IV in 66.30%. Uterosacral ligament resection was the most frequently performed procedure (50.97%) followed by rectal surgery (31.58%), ovarian procedures for endometrioma, procedures for ureters (21.33%) and the bladder (11.91%). Antiadhesion agents were employed in 215/361 (59.56%) patients. The median length of hospital stay after surgery was 2 (IQR 1 - 4) days. Post-operative complications were recorded in 9.34% of patients. Rectovaginal fistulae occurred in 8 patients (2.41%), pelvic abscess in 4 (1.20%) and bladder atony in 3 (0.90%). 17 patients (5.14%) required a second surgical procedure after a median time of 31 days (IQR 9 - 81). Two months after surgery, 95.09% of patients reported being satisfied or very satisfied with the surgery.

Conclusion: Our study shows that surgical management of endometriosis in centers with a high volume of endometriosis surgery, mainly concerns women presenting with severe disease and deep localizations, with an overall risk of major complications inferior to 10% and a high rate of patient satisfaction.

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Introduction

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Endometriosis is thought to affect around 10% of women of reproductive age [1,2] and is responsible for various disabling symptoms such as dysmenorrhea, dyspareunia, chronic pelvic pain or infertility

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[3,4]. This complex and chronic disease can have a major negative effect on quality of life [5,6]. Despite its prevalence and impact, endometriosis still remains relatively poorly understood by many physicians, and may be associated with prolonged delay in diagnosis and inadequate medical and surgical care [7,8]. As a consequence, complaints from women suffering from endometriosis have been increasingly raised over recent years through the work of associations or personal testimonials [9,10].

In 2016, the DGOS national health care provider (Direction Générale de l'Offre des Soins) and Normandy public health agency (Agence Régionale de la Santé) accredited Rouen University Hospital as an Expert centre in the Diagnosis and Multidisciplinary Management of Endometriosis [11]. Later in 2019, the French government announced the creation of a new action plan to improve the management of endometriosis based on endometriosis networks (filières) [12]. This public health plan focused on three goals: earlier detection of endometriosis, improvement of care pathways and increased public awareness of this chronic disease. Situational analysis is an essential prerequisite to improvement, but data regarding current practices for the management of endometriosis in France are scarce [13]. In 2015, the French coloRectal Infiltrating ENDometriosis Study group (FRIENDS) conducted a national survey of 56 healthcare facilities across France to investigate surgical management of deep infiltrating endometriosis of the rectum and the sigmoid colon [14], thus providing valuable information on national practices and the number of patients requiring surgical management for this specific localization. No such data, however, exists for less severe localizations.

Endometriosis is a polymorphic disease that can affect many different organs, resulting in a broad variety of symptoms [15,16]. This complexity in part accounts for the prevarication and disagreements surrounding its management [17]. Surgical indications are notably a subject of regular debate and remain unclear in many clinical situations [18,19]. In 2016, in response to these challenging issues, Endometriosis Referral centers were created across France, based on the Rouen University Hospital center model [20], with combined advisory, recourse, network coordination, teaching and research roles. To date no study has focused on surgical management performed in centers with a high volume of surgical procedures in endometriosis. This data would be of great value, contributing to a national improvement in the management of endometriosis.

The aim of this study was to provide representative data on surgical management of endometriosis in French centers with a high volume of endometriosis surgery, over a two-year period.

Material and methods

We conducted a secondary analysis on prospectively collected data from the ENDHY cohort (Registration number NCT02612818). This prospective longitudinal multicentric observational study was conducted in centers with a high volume in endometriosis surgery in France between November 2015 and May 2017. The primary endpoint of the study was to assess the relationship between the use of antiadhesion agents during laparoscopy for endometriosis and pregnancy rate 2 years after the procedure. The study was discontinued due to an insufficient number of inclusions at the end of the study period and because of a high rate of loss to follow-up after one year. Original study funding was provided by Nordic Pharma company; however, data analysis and preparation of the present manuscript was carried out by the authors independently of the involvement of the company. This study provides a snapshot of the management of endometriosis in France across various centers with a high volume in endometriosis surgery.

One gynecologic surgeon from each French center with a high volume in endometriosis surgery (<u>at least 100 procedures per year</u>) was invited to participate in this study.To ensure a balance between centers, each center was able to enroll up to 40 consecutive patients in the study, with a maximum total sample size of 400 patients. Inclusion criteria were women aged 18 to 45, who required surgical management <u>by conventional laparoscopy</u> for any stage of endometriosis and who intended to conceive during the 48 months following the surgery. The use or not of antiadhesion agents, as well as type of antiadhesion agent was dependent on surgeon intraoperative choice and was not required by the study design.

Both surgeons and patients were asked to fill in specific <u>custom-ized</u> questionnaires before and at 2 and 12 months after surgery. Data collected included demographic patient characteristics, intraoperative findings and surgical procedure performed, pain symptoms and satisfaction assessment scores, and fertility outcomes. Pregnancy rate was assessed 24 months after surgery by a phone call to patients not pregnant after 12 months.

The original sample size was calculated to determine the effect of using an anti-adherent agent during laparoscopy for endometriosis on pregnancy rate at 24 months postoperatively. Based on an assumption that use of antiadhesion agents could be followed by a pregnancy rate of 50% vs. 40% in patients without antiadhesion agents, with a bilateral alpha risk of 0.05 and a power of 0.80, 192 patients were required in each group. To anticipate patient loss to follow-up, the sample size was increased to 400, but due to a 30.5% rate of loss to-follow-up at 12 months, the original analysis was abandoned. This study therefore only presents data collected up to 2 months after surgery and aims to provide a snapshot of surgical practices across French centers with a high volume in endometriosis surgery, and their short-term outcomes.

Data are presented as percentages for categorical variables, as means and standard deviations for continuous parametric variables and as medians and interquartile ranges (IQR) for continuous non-parametric variables. These analyses were performed using S.A.S.[®] version 9.3 (SAS Institute, NC, Cary, USA).

Results

Twenty-one surgeons from 21 centers with a high volume in endometriosis surgery participated in the study (**Fig. 1**): 12 were university hospitals, 2 were non-university public hospitals and 7 were private facilities. Each declared routine management of 100 to 300 patients with endometriosis per year (median value 200).

Between November 2015 and May 2017, 377 patients were enrolled in the study of whom 16 patients were later excluded from the analysis, (3 had no endometriosis lesion revealed during surgery, while in 14 patients the use or not of anti-adherent agent was unspecified). Thus, 361 patients were included in the analysis. Twenty-seven patients (7.48%) were lost to follow-up at the month 2 visit, and 110 (30.47%) were absent at the 12-month follow-up visit. Among the 251 remaining patients, 63 (25.10%) got pregnant within 12 months after surgery.

Patient characteristics at baseline are presented in **Table 1**. Mean age was 31.1 ± 5.1 and mean BMI 22.52 ± 4.08 . Most patients were nullipara (68.70%) and more than half had documented infertility (52.11%). The circumstances leading to the presumption of endometriosis were pelvic pain in 68.70% of patients and/or infertility in 32.69%. The diagnosis was preoperatively assessed using pelvic MRI (52.98%) and transvaginal ultrasound (33.63%). Approximately one third of patients had a history of prior surgery, and 21.61% had previously undergone procedures on the digestive tract (appendectomy, bowel resection, etc.). Most frequent baseline complaints were dysmenorrhea (81.72%), dyspareunia (59.83%), chronic pelvic pain (54.57%) and menstrual defecation pain or dyschesia (40.17%). Less than half of the patients were receiving a hormonal treatment before surgery (44.88%).

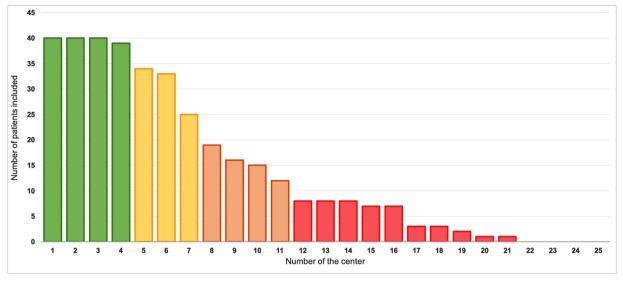


Fig. 1. Distribution of inclusions across the participating centers.

Intraoperative findings and surgical procedures are presented in **Table 2**. Main reasons for surgery were the presence of disabling symptoms (64.82%) and infertility (45.15%). Endometriotic lesions observed during surgery included: endometriomas (45.15%) deep endometriosis of uterosacral ligaments (right in 32.69% and left in 43.21%), rectosigmoid (35.18%), bowel (19.11%), bladder (12.19%), ureter (9.97%), round ligament (1.94%), appendix (1.66%) and diaphragm (1.66%). The r-ASRM classification was assessed and endometriosis stage was minimal (I) or mild (II) in 33.70% of patients, and moderate (III) or severe (IV) in 66.30%. Uterosacral ligament resection was the most frequently performed procedure (50.97%) followed by rectal surgery (31.58%), ovarian endometrioma management, ureter surgery (21.33%) and bladder surgery (11.91%). Rectal shaving (15.24%) was performed more often than colorectal resection and disk excision together (respectively 8.03% and 6.09%).

Ovarian endometriomas were managed by complete excision or cystectomy (83/233 (35.62%), laser or plasma ablation (71/233 (30.47%)), bipolar coagulation (59/233 (25.32%)), and partial cystectomy (20/233 (20/233 (8.53%)).

Antiadhesion agents were used in 215 out of 361 (59.56%) cases, more frequently in stages III or IV (153/238, 64.29%) than in stages I or II (62/121, 51.24%) (p = 0.017). These agents were used in 60/114 (52.63%) procedures involving digestive tract surgery, however less frequently when bowel suture was required (disk excision or colorectal resection, 9/51, 17.65%) than in patients managed by shaving (44/ 55, 80.00%) (p < 0.001).

The median length of hospital stay after surgery was 2 (1 - 4) days. Various post-operative complications were recorded at the month 2 follow-up visit in 9.34% of patients. Rectovaginal fistulae occurred in 8 patients (2.41%), pelvic abscess in 4 (1.20%) and bladder atony in 3 (0.90%). Seventeen patients (5.14%) required a second surgical procedure after a median period of 31 days (9 - 81) after the first surgery. Patients received various hormonal treatments after surgery: 35.80% immediately after surgery and 40.55% of patients were receiving continued treatment 2 months after surgery.

The evolution of symptoms two months after surgery is presented in **Table 3**. Two thirds of patients (66.78%) suffering from dysmenorrhea before surgery no longer experienced this pain. Patient rates for relief of chronic pelvic pain and dyspareunia were 70.56% and 73.15% respectively. In most patients (80.60%) the reduction in intensity of symptoms related to a reduction in endometriosis after surgery. Patients were satisfied (37.95%) or very satisfied (57.14%) with the results of the surgery.

Discussion

Our study presents a snapshot of surgical management of patients with endometriosis in 21 centers with a high volume of endometriosis surgery in France. Our data provide information on preoperative assessment, main surgical procedures employed, the use of antiadhesion agents and immediate postoperative outcomes. For these reasons, such data is likely to be useful for public health care policymaking or for raising patient awareness.

The main strength of this study involves the prospective recording of data. Data were collected through standardized questionnaires, ensuring its reliability. Additionally, this study was conducted in facilities which report a high number of patients managed for endometriosis each year. Experienced surgeons were asked to include up to 40 consecutive patients, which allowed to balance inclusions across centers and to prevent the risk of an over-representation of one center with specific practices. Overall, this study provides a reliable, representative sample of patients undergoing surgical management of endometriosis in French centers with a high volume in endometriosis between 2015 and 2017.

Our study also presents several weaknesses. The original ENDHY study aimed to determine the effect of anti-adherent agents on pregnancy rate after surgery. Consequently, the inclusion criteria were not originally shaped to provide a fully representative population, as the study exclusively focused on women with pregnancy intention and presumed probability of natural conception after surgery. Patients who underwent laparotomy or robotically assisted laparoscopy, those benefiting from first line ART and those without pregnancy intention were not included in this study. In addition, despite a significant number of participating facilities (twenty-one), this study was not designed for exhaustivity. The aforementioned FRIENDS study reported a surprisingly high number of facilities performing surgery for rectosigmoid endometriosis (fifty-six) and it is likely that this number would be much higher if less severe forms of endometriosis were taken into consideration. Finally, the low number of inclusions from most of the facilities over two years and the high proportion of lost to follow-up patients in the original study suggest an unequal involvement and motivation of participating centers. These disparities in the number of inclusions across centers could lead to a selection bias and to an over-representation of certain procedures.

Our data are consistent with previous prospective studies on the surgical management of endometriosis, regarding the prevalence of

Table 1.

Patient characteristics at baseline.

	Ν	PatientsN = 361
Age, years, mean \pm SD	361	31.1 ± 5.1
BMI, kg/m2, mean \pm SD	361	22.52 ± 4.08
Obstetrical history		
Nulligesta, n/N (%)	361	240/361 (66.48%
Nullipara, n/N (%)	361	248/361 (68.70%
Cesarean sections, n/N (%)	361	20/361 (5.54%)
Fertility		
Documented primary infertility, n/N (%)	355	137/355 (38.59%
Documented secondary infertility, n/N (%)	355	48/355 (13.52%)
Premature ovarian failure, n/N (%)	185 ^a	34/185 (18.38%)
Tubal infertility, n/N (%)	185	20/185 (10.81%)
Diagnosis		, , ,
Diagnosis circumstances		
Pain symptoms, n/N (%)	361	248/361 (68.70%
Infertility, n/N (%)	361	118/361 (32.69%
Other, n/N (%)	361	13/361 (3.60%)
Means of diagnosis		
MRI, n/N (%)	336	178/336 (52.98%
Ultrasound, n/N (%)	336	113/336 (33.63%
Prior intra-peritoneal surgery		
Laparoscopy, n/N (%)	361	108/361 (29.92%
Laparotomy, n/N (%)	361	26/361 (7.20%)
Visceral surgery, n/N (%)	361	78/361 (21.61%)
Gynecologic surgery, n/N (%)	361	128/361 (35.46%
Symptoms		
Asymptomatic, n/N (%)	361	39/361 (10.80%)
Chronic Pelvic Pain, n/N (%)	361	197/361 (54.57%
VAS chronic pelvic pain, mean \pm SD	311	32.7 (±28.9)
Chronic pelvic pain with posterior irradiation, n/N (%)	361	114/361 (31.58%
Dysmenorrhea, n/N (%)	361	295/361 (81.72%
VAS dysmenorrhea without treatment, mean \pm SD	309	69.0 (±27.0)
VAS dysmenorrhea with treatment, mean \pm SD	299	37.4 (±26.6)
Dyspareunia, n/N (%)	361	216/361 (59.83%
VAS dyspareunia, mean \pm SD		39.3 (±31.1)
Menstrual dysuria, n/N (%)	361	48/361 (13.30%)
Menstrual urinary pain, n/N (%)	361	27/361 (7.48%)
Menstrual defecation pain or difficulty, n/N (%)	361	145/361 (40.17%
Symptom intensity		
Mild, n/N (%)	310	19/310 (6.13%)
Moderate, n/N (%)	310	111/310 (35.81%
Severe, n/N (%)	310	180/310 (58.06%
Pain medication	510	100/310 (30.00%
During menstruation only, n/N (%)	355	110/355 (30.99%
Continuous pain treatment, n/N (%)	355	56/355 (15.77%)
Non-opioids	166 ^b	149/166 (89.76%
Weak opioids	166	20/166 (12.05%)
Strong opioids	166	5/166 (3.01%)
Hormonal Treatment	100	5,100 (3.01%)
No treatment, n/N (%)	361	199/361 (55.12%
Progestins, n/N (%)	361	34/361 (9.41%)
Progestogens, n/N (%)	361	36/361 (9.97%)
Combinations progestogens/estrogens n/N (%)	361	40/361 (11.08%)
GnRH analogues, n/N (%)	361	52/361 (14.40%)
Gintri analogues, n/n (%)	ertile wo	52/501 (14.40%)

^a Most frequent causes of infertility among primary or secondary infertile women (n = 185).

^b Types of pain medication among patients using pain medication continuously or only during menstruation (n = 166).

mensu autom (n = 100).

infertility, painful symptoms, various localizations of the disease and surgical procedures employed to treat them [21–24]. Our study, however, reveals new insights into the specificities of this management in centers with a high volume of endometriosis surgery. Two thirds of the procedures were performed for severe forms of endometriosis. This over-representation of severe disease suggests that centers with a high volume of endometriosis surgery play the role of referral centers, and principally perform surgery in severe cases [11,25]. Management of endometriosis therefore appears to occur naturally in accordance with a center's level of expertise. Mild and moderate endometriosis stages, though probably more numerous in the general population, are performed in centers with a lesser volume of surgery, while severe cases which are rarer, are performed in centers with a high volume of endometriosis surgery. Due to the

associated risks with complex management and potential major impact on patient fertility and quality of life, it appears reasonable that the overall strategy for surgical management of endometriosis should follow that of gynecological cancer care, where the grading of centers depends on the type and number of procedures performed each year. This reasoning is supported by scientific literature which associates quality of surgery to the number of procedures for endometriosis performed and surgeon experience [26,27].

Surprisingly, only half of the patients underwent an MRI examination before surgery. Although the French guidelines state that MRI and ultrasound provide different and complementary information, several authors assert that MRI is mandatory in severe disease to ensure a complete mapping of lesions and a second reading of the examination [13,28].

Table 2.Characteristics of the procedures.

	Ν	PatientsN = 361
Reasons for surgery, n/N (%)		
Failure of the medical treatment	361	41/361 (11.36%)
Disabling symptoms	361	234/361 (64.82%)
Infertility	361	163/361 (45.15%)
Patient's request	361	45/361 (12.47%)
Other	361	34/361 (9.42%)
Endometriotic lesions, n/N (%)	361	
Endometrioma(s)	361	163/361 (45.15%)
Right ovary	361	36/361 (9.97%)
Left ovary	361	66/361 (18.28%)
Both ovaries	361	61/361 (16.90%)
Deep infiltrating lesion(s)	361	243/361 (67.31%)
Right uterosacral ligament, n/N (%)	361	118/361 (32.69%)
Left uterosacral ligament, n/N (%)	361	156/361 (43.21%)
Rectosigmoid, n/N (%)	361	127/361 (35.18%)
Ureter, n/N (%)	361	36/361 (9.97%)
Bladder, n/N (%)	361	44/361 (12.19%)
Bowel, n/N (%)	361	69/361 (19.11%)
Appendix, n/N (%)	361	6/361 (1.66%)
Diaphragm, n/N (%)	361	6/361 (1.66%)
Round Ligament, n/N(%)	361	7/361 (1.94%)
Obliteration of the Douglas Pouch	501	1,001 (110 1.0)
Complete	361	80/361 (22.16%)
Partial	361	78/361 (21.60%)
Size of the largest endometriotic nodule, cm, mean \pm SD	192	2.7 (±1.4)
ASRM revised classification of endometriosis, n/N (%)	102	2 (±111)
I or II (Minimal or Mild)	359	121/359 (33.70%)
III or IV (Moderate or Severe)	359	238/359 (66.30%)
Operative time, minutes, median (min-max)	357	111.6 (±73.8)
Procedures, n/N (%)	557	111.0 (±75.0)
Endometrioma treatment		
Cystectomy, n/N (%)	233	83/233 (35.62%)
Partial cystectomy, n/N (%)	233	20/233 (8.58%)
Bipolar coagulation, n/N (%)	233	59/233 (25.32%)
Laser or Plasma ablation, n/N (%)	233	71/233 (30.47%)
Uterosacral ligament resection	361	184/361 (50.97%)
Ureter surgery	361	77/361 (21.33%)
Bladder surgery	361	43/361 (11.91%)
Rectal surgery	361	114/361 (31.58%)
Shaving	361	55/361 (15.24%)
disk excision	361	22/361 (6.09%)
Rectal resection	361	29/361 (8.03%)
Stoma	361	22/361 (6.09%)
Anti-adherent treatment	361	215/361 (59.56%)
Complication during surgery, n/N (%)	361	4/361 (1.11%)
Length of hospital stay, days, median (IQR)	330	2(1-4)
Post-Operative complications, n/N (%)	332	32/332 (9.34%)
Bladder atony requiring self-catheterization	332	3/332 (0.90%)
Urinary tract infection	332	8/332 (2.41%)
Pelvic abscess	332	4/332 (1.20%)
Rectovaginal Fistulae	332	4/332 (1.20%) 8/332 (2.41%)
Hemoperitoneum	332	2/332 (0.60%)
Surgical reoperation	332 331	2/332 (0.60%) 17/331 (5.14%)
	331 17	
Delay for reoperation, days, median (IQR)		31 (9 - 81)
Hormonal treatment prescribed before discharge	324	116/324 (35.80%)

IQR = Inter-quartile range (25% and 75%).

Similarly to the FRIENDS study, the present study <u>would suggest</u> that rectal shaving is the most frequently performed procedure for rectosigmoid endometriosis [14]. <u>However</u>, given that the displayed objective of the original ENDHY study was to investigate anti-adherent agents which are rarely used in case of digestive tract resection, a selection bias cannot be excluded. Rectal shaving is less standardized than colorectal resection or disk-excision and does not allow to histologically assert complete resection of the rectal nodule. Although it has been suggested that incomplete surgery leads to increased risk of recurrences and impaired post-operative fertility, rectal shaving is also associated with a lower complication rate, offering an explanation for why it is widely performed [21,26,29,30].

Although the most frequent treatment for endometrioma was complete cystectomy, the vaporization of inner cyst wall using plasma or laser were also frequently performed. The place of alternative treatments to cystectomy, considered to be the reference treatment for endometriomas, is difficult to determine from current data in the literature. Two early randomized controlled trials performed more than 16 years ago reported higher pregnancy rates after cystectomy compared with coagulation of the cyst using bipolar current [31,32]. However, coagulation does not mean vaporization, and the diffusion of thermal heat into the ovarian parenchyma is likely to be higher during coagulation, while the destruction of endometrial tissue is less effective. Since 2004, several randomized trials and a comparative study have assessed pregnancy rate after cystectomy vs.

Table 3.

Evolution of symptoms two months after surgery.

	Ν	Month 2
VAS dysmenorrhea without treatment, mean \pm SD	187 ^a	29.2 (±28.3)
VAS dysmenorrhea with treatment, mean \pm SD	174 ^a	13.3 (±18.1)
VAS chronic pelvic pain, mean \pm SD	215 ^a	12.0 (±17.7)
VAS dyspareunia, mean \pm SD	198 ^a	11.7 (±17.8)
Patients released from dysmenorrhea, n/N (%)	295 ^b	197/295 (66.78%)
Patients released from chronic pelvic pain, n/N (%)	197 ^b	139/197 (70.56%)
Patients released from dyspareunia, n/N (%)	216 ^b	158/216 (73.15%)
Patients released from menstrual dysuria, n/N (%)	48 ^b	40/48 (83.33%)
Patients released from menstrual urinary pain, n/N (%)	27 ^b	20/27 (74.07%)
Patients released from menstrual defecation pain or difficulty, n/N (%)	145 ^b	110/145 (75.86%)
Evolution of symptom intensity		
Decreased, n/N (%)	307	247/307 (80.60%)
Stable, n/N (%)	307	41/307 (13.3%)
Increased, n/N (%)	307	17/307 (5.5%)
Patient satisfaction		
Very satisfied, n/N (%)	224	128/224 (57.14%)
Satisfied, n/N (%)	224	85/224 (37.95%)
Rather unsatisfied, n/N (%)	224	10/224 (4.46%)
Unsatisfied, n/N (%)	224	1/224 (0.45%)

^a VAS are reported as mean ± standard deviation and are calculated only for patients that presented the corresponding pain at Month 2.

^b Relief from pain are reported as stated by the physicians for patients that presented the corresponding pain at baseline.

vaporization using laser or plasma, none of which revealed better outcomes following cystectomy [33–35].

Anti-adhesion agents were used for more than half of the procedures. This proportion may be an overestimation, as although regular use of anti-adherent agents was not a specified mandatory prerequisite for participation in this study, the approached centers were accustomed to their use. Anti-adhesion agents were more frequently used for moderate to severe endometriosis than for minimal or mild endometriosis. For procedures that involved digestive tract resection (disk excision or colorectal resection), anti-adhesion agents were very rarely used, following evidence that their use in contact with colorectal anastomosis increases risk of leakage and bowel fistula [36,37].

Overall, our study provides evidence that laparoscopic management of endometriosis by experienced surgeons leads to a low rate of severe complications, an improvement in symptoms and a large majority of satisfied patients. This study also gives an unreserved illustration of the difficulties that may be encountered in conducting a multicentric prospective study with limited dedicated human resources and few clinical research technicians dedicated to the study. Although surgeon participation was voluntary, only 3 out of 25 centers achieved inclusion of 40 patients. Over half of the centers included less than 10 patients in the 2-year period and one third of patients were lost to follow-up after one year. These difficulties reflect the absence of dedicated data collection staff. Only one center had a clinical researcher specifically dedicated to endometriosis, in charge of data collection and planning of follow up visit, while surgeons in other centers were required to manage the study in its entirety. Our study protocol was straightforward but additional customized reminders for patients and surgeons are required, both to ensure suitable data collection and to minimize the risk of patients lost to follow up.

Our study presents surgical management of endometriosis in French centers with a high volume of endometriosis surgery and confirms that laparoscopic management of endometriosis is safe and effective in a large majority of patients. It provides an overview of the types of endometriosis managed by experienced surgeons, the techniques used to treat the disease and the use of antiadhesion agents. These results may be of interest to health authorities and contribute to patient preoperative informed choice.

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Declaration of Competing Interest

H.R., C.C. and M.C. are members of the scientific committee of Nordic Pharma (Nordic Group).

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References

- Gordts S, Koninckx P, Brosens I. Pathogenesis of deep endometriosis. Fertility and Sterility 2017;108:872–85 e1. doi: 10.1016/j.fertnstert.2017.08.036.
- [2] Brown J., Farquhar C. Endometriosis: an overview of Cochrane Reviews. Cochrane Database Syst Rev 2014:CD009590. 10.1002/14651858.CD009590.pub2.
- [3] Fauconnier A, Chapron C. Endometriosis and pelvic pain: epidemiological evidence of the relationship and implications. Hum Reprod Update 2005;11:595– 606. doi: 10.1093/humupd/dmi029.
- [4] de Ziegler D, Borghese B, Chapron C. Endometriosis and infertility: pathophysiology and management. Lancet 2010;376:730-8. doi: 10.1016/S0140-6736(10) 60490-4.
- [5] Nnoaham KE, Hummelshoj L, Webster P, d'Hooghe T, Nardone F de C, Nardone C de C, et al. Impact of endometriosis on quality of life and work productivity: a multicenter study across ten countries. Fertil Steril 2011;96:366–73 e8. doi: 10.1016/j.fertnstert.2011.05.090.
- [6] Simoens S, Dunselman G, Dirksen C, Hummelshoj L, Bokor A, Brandes I, et al. The burden of endometriosis: costs and quality of life of women with endometriosis and treated in referral centres. Hum Reprod 2012;27:1292–9. doi: 10.1093/humrep/des073.
- [7] Ballard K, Lowton K, Wright J. What's the delay? A qualitative study of women's experiences of reaching a diagnosis of endometriosis. Fertility and Sterility 2006;86:1296–301. doi: 10.1016/j.fertnstert.2006.04.054.
- [8] Netter A, d'Avout-Fourdinier P, Agostini A, Chanavaz-Lacheray I, Lampika M, Farella M, et al. Progression of deep infiltrating rectosigmoid endometriotic nodules. Hum Reprod 2019;34:2144–52. doi: 10.1093/humrep/dez188.
- [9] Endonymous. Deux ans plus tard : roman graphique autobiographique sur l'endométriose. Endonymous 2020. https://endonymous.fr/ (accessed October 30, 2020).

- [10] Endofrance : Association Française de lutte contre l'Endométriose. Association EndoFrance n.d. https://www.endofrance.org/ (accessed October 30, 2020).
- [11] Roman H, Chanavaz-Lacheray I. l'équipe Rouendométriose. [The Rouen Expert center in the diagnosis and multidisciplinary management of endometriosis: A French pilot experiment]. Gynecol Obstet Fertil Senol 2018;46:563–9. doi: 10.1016/j.gofs.2018.06.006.
- [12] Ministère des Solidarités et de la Santé. Agnès Buzyn, ministre des Solidarités et de la Santé, annonce un plan d'action pour renforcer la prise en charge de l'endométriose. Ministère des solidarités et de la santé 2019. https://solidarites-sante.gouv. fr/actualites/presse/communiques-de-presse/article/agnes-buzyn-ministre-dessolidarites-et-de-la-sante-annonce-un-plan-d-action (accessed October 29, 2020).
- [13] Collinet P, Fritel X, Revel-Delhom C, Ballester M, Bolze PA, Borghese B, et al. Management of endometriosis: CNGOF/HAS clinical practice guidelines - Short version. J Gynecol Obstet Hum Reprod 2018;47:265–74. doi: 10.1016/j. jogoh.2018.06.003.
- [14] Roman H. FRIENDS group (French coloRectal Infiltrating ENDometriosis Study group). A national snapshot of the surgical management of deep infiltrating endometriosis of the rectum and colon in France in 2015: A multicenter series of 1135 cases. J Gynecol Obstet Hum Reprod 2017;46:159–65. doi: 10.1016/j. jogoh.2016.09.004.
- [15] Zondervan KT, Becker CM, Missmer SA. Endometriosis. N Engl J Med 2020; 382:1244–56. doi: 10.1056/NEJMra1810764.
- [16] Montanari E, Dauser B, Keckstein J, Kirchner E, Nemeth Z, Hudelist G. Association between disease extent and pain symptoms in patients with deep infiltrating endometriosis. Reprod Biomed Online 2019;39:845–51. doi: 10.1016/j. rbmo.2019.06.006.
- [17] Nezhat C, Vang N, Tanaka PP, Nezhat C. Optimal Management of Endometriosis and Pain. Obstet Gynecol 2019;134:834–9. doi: 10.1097/ AOG.000000000003461.
- [18] Kho RM, Andres MP, Borrelli GM, Neto JS, Zanluchi A, Abrão MS. Surgical treatment of different types of endometriosis: Comparison of major society guidelines and preferred clinical algorithms. Best Pract Res Clin Obstet Gynaecol 2018;51:102–10. doi: 10.1016/j.bpobgyn.2018.01.020.
- [19] Leonardi M, Gibbons T, Armour M, Wang R, Glanville E, Hodgson R, et al. When to Do Surgery and When Not to Do Surgery for Endometriosis: A Systematic Review and Meta-analysis. J Minim Invasive Gynecol 2020;27:390–407 e3. doi: 10.1016/ j.jmig.2019.10.014.
- [20] Golfier F, Chanavaz-Lacheray I, Descamps P, Agostini A, Poilblanc M, Rousset P, et al. The definition of Endometriosis Expert Centres. J Gynecol Obstet Hum Reprod 2018;47:179–81. doi: 10.1016/j.jogoh.2018.02.003.
- [21] Abo C, Moatassim S, Marty N, Saint Ghislain M, Huet E, Bridoux V, et al. Postoperative complications after bowel endometriosis surgery by shaving, disc excision, or segmental resection: a three-arm comparative analysis of 364 consecutive cases. Fertil Steril 2018;109:172–8 e1. doi: 10.1016/j.fertnstert.2017.10.001.
- [22] Roman H, Chanavaz-Lacheray I, Ballester M, Bendifallah S, Touleimat S, Tuech J-J, et al. High postoperative fertility rate following surgical management of colorectal endometriosis. Hum Reprod 2018;33:1669–76. doi: 10.1093/humrep/ dey146.
- [23] Roman H, Tuech J-J, Huet E, Bridoux V, Khalil H, Hennetier C, et al. Excision versus colorectal resection in deep endometriosis infiltrating the rectum: 5-year followup of patients enrolled in a randomized controlled trial. Hum Reprod 2019;34:2362–71. doi: 10.1093/humrep/dez217.

- [24] Lier MCI, Vlek SL, Ankersmit M, van de Ven PM, Dekker JJML, Bleeker MCG, et al. Comparison of enhanced laparoscopic imaging techniques in endometriosis surgery: a diagnostic accuracy study. Surg Endosc 2020;34:96–104. doi: 10.1007/ s00464-019-06736-8.
- [25] Roman H, Chanavaz-Lacheray I, Forestier D, Magne E, Celhay O, Pasticier G, et al. [Early postoperative complications in a multidisciplinary surgical center exclusively dedicated to endometriosis: A 491-patients series]. Gynecol Obstet Fertil Senol 2020;48:484–90. doi: 10.1016/j.gofs.2020.03.009.
- [26] Carmona F, Martínez-Zamora A, González X, Ginés A, Buñesch L, Balasch J. Does the learning curve of conservative laparoscopic surgery in women with rectovaginal endometriosis impair the recurrence rate? Fertil Steril 2009;92:868–75. doi: 10.1016/j.fertnstert.2008.07.1738.
- [27] Guo S-W. Recurrence of endometriosis and its control. Hum Reprod Update 2009;15:441–61. doi: 10.1093/humupd/dmp007.
- [28] isenblat V, Bossuyt PMM, Farquhar C, Johnson N, Hull ML. Imaging modalities for the non-invasive diagnosis of endometriosis. Cochrane Database Syst Rev 2016;2: CD009591. doi: 10.1002/14651858.CD009591.pub2.
- [29] Stepniewska A, Pomini P, Bruni F, Mereu L, Ruffo G, Ceccaroni M, et al. Laparoscopic treatment of bowel endometriosis in infertile women. Hum Reprod 2009;24:1619–25. doi: 10.1093/humrep/dep083.
- [30] Roman H, Moatassim-Drissa S, Marty N, Milles M, Vallée A, Desnyder E, et al. Rectal shaving for deep endometriosis infiltrating the rectum: a 5-year continuous retrospective series. Fertil Steril 2016;106:1438–45 e2. doi: 10.1016/j.fertnstert.2016.07.1097.
- [31] Alborzi S, Momtahan M, Parsanezhad ME, Dehbashi S, Zolghadri J, Alborzi S. A prospective, randomized study comparing laparoscopic ovarian cystectomy versus fenestration and coagulation in patients with endometriomas. Fertil Steril 2004;82:1633–7. doi: 10.1016/j.fertnstert.2004.04.067.
- [32] Beretta P, Franchi M, Ghezzi F, Busacca M, Zupi E, Bolis P. Randomized clinical trial of two laparoscopic treatments of endometriomas: cystectomy versus drainage and coagulation. Fertil Steril 1998;70:1176–80.
- [33] Mircea O, Puscasiu L, Resch B, Lucas J, Collinet P, von Theobald P, et al. Fertility Outcomes After Ablation Using Plasma Energy Versus Cystectomy in Infertile Women With Ovarian Endometrioma: A Multicentric Comparative Study. J Minim Invasive Gynecol 2016;23:1138–45. doi: 10.1016/j.jmig.2016.08.818.
- [34] Carmona F, Martínez-Zamora MA, Rabanal A, Martínez-Román S, Balasch J. Ovarian cystectomy versus laser vaporization in the treatment of ovarian endometriomas: a randomized clinical trial with a five-year follow-up. Fertil Steril 2011;96:251-4. doi: 10.1016/j.fertnstert.2011.04.068.
- [35] Candiani M, Ottolina J, Posadzka E, Ferrari S, Castellano LM, Tandoi I, et al. Assessment of ovarian reserve after cystectomy versus "one-step" laser vaporization in the treatment of ovarian endometrioma: a small randomized clinical trial. Hum Reprod 2018;33:2205–11. doi: 10.1093/humrep/dey305.
- [36] Beck DE, Cohen Z, Fleshman JW, Kaufman HS, van Goor H, Wolff BG, et al. A prospective, randomized, multicenter, controlled study of the safety of Seprafilm adhesion barrier in abdominopelvic surgery of the intestine. Dis Colon Rectum 2003;46:1310–9. doi: 10.1007/s10350-004-6739-2.
- [37] Berdah SV, Mariette C, Denet C, Panis Y, Laurent C, Cotte E, et al. A multicentre, randomised, controlled trial to assess the safety, ease of use, and reliability of hyaluronic acid/carboxymethylcellulose powder adhesion barrier versus no barrier in colorectal laparoscopic surgery. Trials 2014;15:413. doi: 10.1186/1745-6215-15-413.