Prophylactic procedures associated with gynecological surgery for the management of superficial endometriosis and adhesions.
Clinical practice guidelines from the French College of Gynecologists and Obstetricians (CNGOF)

Marion Ouazana MD [1,2]; Yohan Kerbage MD [3,4]; Pauline Chauvet MD [5]; Pierre Collinet MD, PhD [3,4]; Pierre Emmanuel Bouet MD, PhD [6]; Cyril Touboul MD, PhD [7]; Guillaume Legendre MD, PhD [8]; Francois Golfier MD, PhD [9]; Stéphane Ploteau MD, PhD [10]; Pietro Santulli MD, PhD [1,2,11]

The authors should be regarded as joint authors.

Author information:

1 Université de Paris, Faculté de Santé, Faculté de Médecine Paris Centre, Paris, France
2 Service de Gynécologie-Obstétrique II et de Médecine de la Reproduction, AP-HP, Centre Hospitalier Universitaire (CHU) Cochin, 75014, Paris, France
3. CHU Lille, Service de chirurgie gynécologique F-59000 Lille, France
4. Univ. Lille, CHU Lille, F-59000 Lille, France
5 Department of Gynecological Surgery, Clermont-Ferrand University Hospital Estaing, Clermont-Ferrand, France; EnCoV, IP, UMR 6602 CNRS, Université Clermont Auvergne, Clermont-Ferrand, France
6 Department of Reproductive Medicine, Angers University Hospital, Angers 49000, France
7 APHP, GHU East, Tenon Hospital, Department of Obstetrics and Gynaecology, 4 rue de la Chine, F-75020, Paris, France
8 CHU Angers, Department of Obstetrics and Gynaecology, F-49000, Angers, France
9 CHU Lyon, Department of Obstetrics and Gynaecology, F-69000, Lyon, France
10 Department of Gynecology and Obstetrics, Nantes University Hospital, Nantes, France
11 Université de Paris, Department "Infection, Immunity, Inflammation", INSERM U1016, Institut Cochin, Paris, France

Corresponding author:

Prof. Pietro Santulli, MD PhD
Service de Gynécologie-Obstétrique II et Médecine de la Reproduction, CHU Cochin – Bâtiment Port Royal
123 Boulevard de Port-Royal 75679 Paris 14, France
Phone: +33-1-58-41-36-83
Fax: +33-1-58-41-36-72
Email: pietro.santulli@aphp.fr

ABSTRACT

Objective

To provide guidelines from the French College of Obstetricians and Gynecologists (CNGOF), based on the best currently available evidence, for the prophylactic procedures associated with gynecological surgery for benign disease such as superficial endometriosis lesions and adhesions.

Methods

The CNGOF has decided to adopt the AGREE II and GRADE systems for grading scientific evidence. Each recommendation for practice was allocated a grade that reflects the quality of evidence (QE) (clinical practice guidelines).

Results

Endometriosis and pelvic pain

Superficial endometriosis can be entirely asymptomatic. Surgical treatment of asymptomatic superficial peritoneal endometriosis is not recommended in women of childbearing age for the prevention of pelvic pain, especially in case of proximity to noble organs (e.g., the ureters, rectum and sigmoid, and ovaries in nulligravida) as there is no evidence that the disease will progress to become symptomatic (low level of evidence).

In case of accidental discovery of superficial endometriosis in women of childbearing age with pelvic pain, it is recommended that that the lesions are excised, if surgically accessible. Removal of superficial endometriosis lesions in patients with painful symptoms improves quality of life and pain (low level of evidence).

Endometriosis and infertility

It appears that women with isolated superficial endometriosis diagnosed by laparoscopy with histological confirmation have a significantly higher incidence of primary infertility than patients without endometriosis. However, there is no data regarding the impact of treatment of these lesions on the fertility in these women or on the natural course of their disease (low level of evidence).

It is recommended that excision is performed rather than monopolar coagulation of superficial endometriosis lesions in infertile women, as this results in a higher spontaneous pregnancy rate (low level of evidence).

Adhesions and pelvic pain

There is limited data in the literature regarding the benefit of performing systematic adhesiolysis during laparoscopy to prevent pelvic pain when incidental pelvic adhesions are discovered. For patients with pelvic pain, it is probably better not to perform adhesiolysis to prevent pelvic pain, although this can be decided on a case-by-case basis depending on the extent of the adhesions, the topography, and the type of surgery considered (low level of evidence).

For asymptomatic patients, it is recommended not to perform adhesiolysis to prevent pelvic pain due to the lack of clear efficacy both short- or long-term and due to the increased risk of surgical injuries (low level of evidence).

Adhesions and infertility

There is limited data in the literature regarding the potential benefit of performing systematic adhesiolysis when there is an incidental discovery of pelvic adhesions during laparoscopy to prevent infertility.

For infertile women, in the event of fortuitous discovery of adhesions at laparoscopy, it is probably better not to perform complex adhesiolysis. Only adhesiolysis of tubo-ovarian adhesions that are minimal or slight in terms of their extension and/or their nature may be useful to improve the chances of spontaneous pregnancy. However, it remains to be decided on a case-by-case basis depending on other potential causes of infertility (low level of evidence).

For women without known infertility issues, it is probably better not to perform systematic adhesiolysis in order to improve their pregnancy chances, considering the balance between the unknown benefit and the risks of complications inherent to surgery (low level of evidence).

Conclusion

Further investigations are needed in order to increase the quality of management regarding associated interventions such as the treatment of superficial endometriosis or adhesions performed during a gynecologic surgical procedure and, thereby, bolster these recommendations.

Keywords: superficial endometriosis, adhesions, prophylactic surgery, adhesiolysis, pelvic pain, infertility

INTRODUCTION

Prophylactic management of superficial endometriosis lesions and adhesions is not codified and has not been the subject of a summary work for the drafting of recommendations for clinical practice (RPC). This text is a summary of the RPCs of the working group assembled by the French National College of Gynecologists and Obstetricians (CNGOF) for the management of superficial endometriotic lesions and adhesions discovered unexpectedly in symptomatic or in non-symptomatic patients. The development of these RPCs meets the standards set by the High Authority for Health, with internal and external reviews of the working group. These RPCs are intended to help the practitioners (gynecologist-obstetricians, surgeons) better manage patients with this type of lesion by providing answers to four questions:

- Should superficial endometriosis be treated systematically in case of an unexpected laparoscopic diagnosis in a woman of childbearing age to prevent pelvic pain?
- Should superficial endometriosis be treated systematically in case of an unexpected laparoscopic diagnosis in a woman of childbearing age to prevent infertility?
- Should adhesiolysis be systematically performed in case of an incidental finding of pelvic adhesions during laparoscopy in order to prevent pelvic pain?
- Should adhesiolysis be systematically performed in case of an incidental finding of pelvic adhesions during laparoscopy in order to prevent infertility?

The French College of Gynecologists and Obstetricians (CNGOF) decided to assess good practice guidelines for the management of superficial endometriosis lesions and adhesions in

case of an incidental finding during laparoscopy. Therefore, this study is a literature review to help formulate new guidelines.

METHODS

These guidelines were developed by a committee of experts from the CNGOF (the French College of Gynecologists and Obstetricians).

The committee included specialists in gynecologic surgery with expertise in the management of patients with benign disease, as well as specialists in endometriosis, assisted reproductive technology, and methodologists. Following the formulation of PICO clinical questions (PICO: Patient, Intervention, Comparison, Outcome), the guidelines process continued with a series of teleconference calls and digital media-based discussions between the committee members. Ultimately, a meeting was held to decide on the guideline recommendations. The article research was limited to studies published in English or in French. MeSH terms and non-MeSH terms were used. The keywords used were: “Endometriosis”, “Adhesiolysis”, “Adhesions”, “Laparoscopic adhesiolysis”, “Laparoscopy”, “Diagnostic laparoscopy”, “Minimally invasive surgical procedures”, “Infertility”, “Chronic abdominal pain”, “Pelvic Pain”, “Abdominal pain”, “Chronic Disease”, “Peritoneal”, and “Superficial”.

The guidelines process was conducted independently of any industrial funding.

We used the GRADE® (Grading of Recommendations Assessment, Development, and Evaluation) method to formulate the guidelines, which, after quantitative analysis of the literature, can be used to separately determine the quality of the evidence, i.e., to estimate the confidence one can have in the analysis of the effect of the quantitative intervention and in the level of recommendation. The quality of the evidence was divided into four categories:

● High: future searches will most likely not change the confidence in the estimation of the effect;

● Moderate: future searches will probably change the confidence in the estimation of the effect, and they may modify the estimation of the effect itself;

● Low: future searches will most likely have an impact on the confidence in the estimation of the effect and they will probably modify the estimation of the effect itself;

● Very low: the estimation of the effect is very uncertain.

The quality of the evidence was analyzed for each study, and then an overall level of evidence was defined for a given question and criterion. The final formulation of the guidelines was always binary, i.e., either positive or negative, either strong or weak:

● Strong: Should be undertaken or should not be undertaken (GRADE 1+ or 1-);

● Weak: Should probably be undertaken or should probably not be undertaken (GRADE 2+ or 2-).

The strength of the guideline was determined as a function of key factors validated by the experts after a vote, using the Delphi method and the GRADE grid, according to the various parameters: estimation of the effect; the overall level of evidence (the higher it is, the more likely the guideline will be strong); the balance between wanted and unwanted effects (the more favorable the balance, the more likely the guideline will be strong); the values and the preferences ideally obtained directly from the people involved (patient, doctor, decision-maker).

To formulate a guideline, at least 50% of the participants must have an opinion and less than 20% prefer the opposite proposal. To formulate a strong guideline, at least 70% of the participants must be in agreement.

All of the PICO (**P**atient, **I**ntervention, **C**omparison, **O**utcome) questions and the corresponding recommendations were listed as follows:

"In case of an incidental laparoscopic diagnosis of superficial endometriosis in a woman of childbearing age (P), is the treatment of the lesions (I) more effective than no treatment (C) to prevent pelvic pain (O)?"

"In case of an incidental laparoscopic diagnosis of superficial endometriosis in a woman of childbearing age (P), is the treatment of the lesions (I) more effective than no treatment (C) to prevent infertility (O)?"

"In case of an incidental laparoscopic diagnosis of pelvic adhesions in a woman of childbearing age (P), is adhesiolysis (I) more effective than no adhesiolysis (C) to prevent pelvic pain (O)?"

"In case of an incidental laparoscopic diagnosis of pelvic adhesions in a woman of childbearing age (P), is adhesiolysis (I) more effective than no adhesiolysis (C) to prevent infertility (O)?"

RESULTS

Endometriosis and prevention of infertility (Table 1)

There is no data in the literature regarding the impact of treatment of superficial endometriosis lesions discovered incidentally in asymptomatic patients.

A follow-up study concluded that there is little risk that an accidentally discovered minimal asymptomatic case of endometriosis will become symptomatic (1). However, this study, conducted in patients who underwent laparoscopy for tubal sterilization, certainly did not study the impact of these lesions in terms of fertility. Moen et al. evaluated the rate of endometriosis diagnosed during these laparoscopies. This was a prospective study in women sterilized between 1986 and 1989. The follow-up was based on a questionnaire provided to the patients in 2001. During this follow-up, 39 patients had at least stage I lesions, while 157 were free of endometriosis. Pelvic pain was more common in the control group than in the women with superficial endometriosis lesions (28% vs. 6%, respectively).

Among the limited indirect data that may point to a benefit of treating these lesions, we selected the work of Reis and Akande (2,3). These authors retrospectively assessed the gynecological

symptoms exhibited by patients with histologically proven superficial endometriosis compared to a control group of asymptomatic patients. This study demonstrated a significant association between superficial endometriosis and primary infertility ([PR] 1.83, 95% CI 1.46–2.24). Therefore, there appears to be a link between superficial endometriosis and primary infertility. This link was also found in the study by Akande et al. The objective of this study was to assess the fertility at 3 years for patients who underwent laparoscopy (without treatment) for unexplained infertility in case of minimal to moderate endometriosis. These patients had a significantly lower probability of pregnancy (36% versus 55%, respectively, $P < 0.05$). However, these results do not provide proof that the treatment of these lesions in asymptomatic patients can provide any benefit in terms of fertility.

It is not possible to make a recommendation regarding the benefit of systematic surgical resection of superficial endometriosis accidentally discovered during laparoscopy in women of childbearing age for the prevention of infertility.

Regarding infertile patients, the literature is more consistent. The meta-analysis by Duffy et al. selected three randomized studies on this topic. The study by Marcoux et al. was the only one to meet sufficient methodological standards. This was a prospective, randomized, controlled study that compared laparoscopy with lesion coagulation versus adhesiolysis with no treatment (diagnostic laparoscopy only) (4). This was a multicenter study involving 25 Canadian centers. Seven hundred and seventeen infertile patients were included, of who 369 were ultimately ineligible mainly due to the lack of histological evidence of endometriosis. The patients, aged 20 to 39, had infertility of at least 12 months, with no other pathology other than stage I or II endometriosis lesions. The pregnancy rate was significantly higher in the surgery group (30.7 vs. 17.7%, respectively) after 36 weeks of postoperative follow-up (OR = 1.95, 95% CI 1.18-3.22). With the inclusion of the trials by Gad and Moini (5,6), thereby involving 528 patients, the authors concluded that the pregnancy rate is higher after laparoscopic treatment with

complete resection of the lesions (OR 1.89, 95% CI 1.25 to 2.86, P = 0.003). Other studies, not included in the meta-analysis, also indicate that operative laparoscopy is associated with a higher pregnancy rate. Finally, several national and international societies have issued recommendations regarding the management of infertile women with endometriosis (ESHRE, ASRM, and RCOG). There is presently a general consensus in favor of laparoscopic destruction of minimal to moderate endometriosis lesions. **Thus, in the event of an accidental discovery of superficial endometriosis during a laparoscopy in an infertile woman of childbearing age, it is recommended that excision of the lesions is performed to prevent infertility (low level of evidence, strong agreement).**

Finally, although the benefit of treating these lesions has not been fully established, the question as to how to treat them also needs to be studied. Again, the literature regarding this subject is somewhat limited (7–9). In case of minimal to moderate endometriosis in an infertile patient, operative laparoscopy with laser vaporization or excision (CO_2) of the lesions has been reported to be associated with a higher cumulative spontaneous pregnancy rate than when monopolar coagulation is used (9). This finding was based on a prospective, randomized study that investigated the effect of four types of treatment on fertility. The 176 infertile patients with minimal to moderate endometriosis included for four years comprised four groups. The first group underwent destruction of the lesions or excision by a CO_2 laser (n = 49). In the second group, the lesions were treated by simple monopolar electrocoagulation (n = 45). The third group only underwent a diagnostic laparoscopy (n = 43). The fourth group received diagnostic laparoscopy followed by treatment with danazol for 3 months (n = 39). The pregnancy rate was significantly higher in the group treated with laser ablation or by excision of the lesions at 1, 2, and 3 years after the surgery. **In conclusion, it is recommended to perform excision rather than monopolar coagulation of superficial endometriosis lesions in infertile women to improve the spontaneous pregnancy rate. (low level of evidence, strong agreement).**

Endometriosis and prevention of pelvic pain (Table 1)

Superficial endometriosis can result in pelvic pain although it can also occur in asymptomatic patients. In a retrospective cohort study, Tissot et al. in 2017 investigated the prevalence of endometriosis in 465 patients who underwent laparoscopic tubal ligation. Fifty-five of these patients exhibited endometriosis lesions (11.8%), 39 of whom had stage I, 7 had stage II, 8 had stage III, and 1 had stage IV. Of note, 39 of the 55 patients were asymptomatic (70.9%). Among 360 asymptomatic patients, the prevalence of endometriosis was 10% (36/360) (10). In addition, the retrospective study by Reis et al. from 2020, which included 203 patients with histologically confirmed superficial endometriosis lesions (patients with ovarian and deep endometriosis were excluded) and 1,292 patients without lesions during laparoscopy, showed that superficial endometriosis lesions were associated with a high risk of primary infertility (adjusted PR 1.83, 95% CI 1.46–2.24), moderate to severe dysmenorrhea (adjusted PR 1.43, 95% CI 1.31–1.52), and moderate to severe dyspareunia (adjusted PR 1.50, 95% CI 1.25–1.75) (2). However, patients with lesions can be asymptomatic, and 19% of them did not have moderate or severe dysmenorrhoea while 53% did not have moderate or severe dyspareunia. A review of the literature does not provide a direct answer to the question "Should superficial endometriosis be treated systematically in the event of an accidental discovery during laparoscopy in women of childbearing age for the prevention of pelvic pain?". There have been no clinical studies to date that evaluated the indication of whether or not to treat superficial endometriosis discovered incidentally.

On the other hand, several studies have evaluated the effectiveness of laparoscopy with destruction or excision of endometriosis lesions in patients experiencing pain. The meta-analysis by Jacobson et al. in 2009 identified five randomized, controlled studies (Abbott 2004; Jarrell 2005; Lalchandani 2003; Sutton 1994; Tutunaru 2006). Two of these were conference reports (Lalchandani 2003; Tutunaru 2006) (7). A total of 246 patients were included in this

meta-analysis. Operative laparoscopy has been compared to diagnostic laparoscopy in terms of the effectiveness in regard to pain. Operative laparoscopy is superior to diagnostic laparoscopy at 3 months (OR 1.36 (0.51-3.64)), 6 months (OR 5.72 (3.09-10.60)), and 12 months (OR 7.72 (2.97-20.06)). These differences are significant. Sutton et al., in a prospective, randomized, double-blind study, compared the efficacy in regard to pain at 6 months of the combination of laser vaporization, adhesiolysis, and sectioning of the uterine vegetative nerves in patients with minimal to moderate endometriosis (stages I, II, and III), thus associating superficial lesions and deep lesions, with an expectant attitude (11). The number of patients was small (74 patients, of who 63 could be followed) and some patients could have deep endometriosis lesions. Nevertheless, they showed the superiority of laparoscopy over the expectation attitude in terms of postoperative pain. The pain improvement rate was 62.5% at 6 months and 56.3% at 1 year in the study group, versus 22.6% at 6 months in the control group ($p < 0.01$). Worsening of the lesions was observed in 29% of the patients in the control group during a second-look laparoscopy performed 6 months later (3 out of 16 patients). The results of the study were, therefore, in favor of surgical treatment with destruction of the endometriosis lesions in painful patients and they suggest the potentially progressive nature of the lesions without treatment. The randomized trial by Abbott et al. involved patients with stage II to IV endometriosis (12). This was a blinded controlled study comparing excision to placebo. The proportion of patients with minimal to moderate peritoneal lesions was, therefore, lower than in the study by Sutton et al. This trial compared the effects at 6 months on pelvic pain and on quality of life of operative laparoscopy with excision of endometriosis lesions versus simple diagnostic laparoscopy. The control group was operated after the assessment at 6 months. Thirty-nine patients were included. A significant improvement in pain at 6 months was observed in 80% (16/20) of the patients in the immediate surgery group versus 32% (6/19) in the simple diagnostic laparoscopy group ($p = 0.002$). A significant improvement in quality of life at 6 months as measured by the

EQ-5D and the SF-12 was also observed. The placebo effect of laparoscopy is, therefore, confirmed at 32%. The results prove the effectiveness of surgery to remove endometriosis lesions in regard to pain symptoms and quality of life. The study by Jarrel et al. was also randomized blind and it included 29 patients, of who only 16 could be followed (13). Excision of lesions (stages I, II, and III) was compared to simple diagnostic laparoscopy. Pain was reduced in both groups at 12 months ($p < 0.05$) but there was no significant difference between the two groups (placebo effect of laparoscopy). Tutunaru et al. included 33 patients operated on for dysmenorrhea. They did not find any difference in the efficacy between the two groups at 6 months. On the other hand, at 12 months, 74% of the patients who underwent operative laparoscopy had improved in terms of pain compared to 22% in the diagnostic laparoscopy group (14).

Can asymptomatic endometriosis progress to painful endometriosis? In one study, Moen et al. evaluated the rate of endometriosis diagnosed during laparoscopies for tubal ligation (and hence a priori asymptomatic) and the development of symptoms such as dysmenorrhea, premenstrual pain, and dyspareunia 12 to 15 years later (1). This was a prospective study involving 196 women sterilized between 1986 and 1989. The follow-up was based on a questionnaire provided to the subjects in 2001. During this follow-up, 39 patients had lesions that were at least stage I, whereas 157 were free of lesions. Surprisingly, pelvic pain was reported more frequently ($p < 0.05$) in the control group than in the group of women with superficial endometriosis lesions (28% vs. 6%, respectively). These results are nevertheless subject to many biases (e.g., the hormonal status at the time of the questionnaire, hysterectomies in the meantime, etc.). **In conclusion, surgical treatment of asymptomatic superficial peritoneal endometriosis is not recommended in women of childbearing age to prevent pelvic pain, especially in the case of proximity to noble organs (e.g., the ureters, rectum and sigmoid, and ovaries in**

nulliparous patients) as there is no evidence that the disease will progress to become symptomatic (low level of evidence, strong agreement).

In the event of accidental discovery of superficial endometriosis in women of childbearing age with pelvic pain, excision of the lesions, if surgically accessible, is recommended, (low level of evidence, strong agreement).

Adhesiolysis and prevention of pelvic pain in symptomatic patients

Few studies to date have investigated the impact of surgical adhesiolysis on preventing pelvic pain in a population of women with chronic pelvic pain.

The current data in the literature are insufficient to establish a link between adhesions and pelvic pain.

Studies evaluating the impact of adhesiolysis have been evaluated in two meta-analyses (15,16). These meta-analyses analyzed and compared the results of laparoscopic adhesiolysis performed for chronic abdominopelvic pain versus diagnostic laparoscopy and therapeutic abstention (15,16).

The meta-analysis by Gerner-Rasmussen et al. included 25 studies, three of which were randomized controlled trials that reported different conclusions. The characteristics of the randomized control trial studies are summarized in Table 2 (17–19).

The study by Swank et al. included 100 randomized patients, of who 52 were in the adhesiolysis group and 48 were in the diagnostic laparoscopy without any intervention group. At one year of follow-up, no benefit was found after adhesiolysis in regard to pain symptoms (evaluated based on pain scores), nor on quality of life evaluated by a MOS SF36 questionnaire, nor on analgesic consumption (18). (Table 1). Seventy-three percent of these patients were followed

for 12 years, and the authors found that the women who had adhesiolysis had a higher pain score compared to those how had diagnostic laparoscopy (8 versus 13, respectively, were pain-free, $p = 0.03$, RR: 1.3)(20).

Nevertheless, the results of this study need to be interpreted with a degree of caution, especially due to potential methodological biases, particularly in regard to the initial hypothesis and the consequent number of subjects that needed to be included. In addition, in case of adhesiolysis, it should be noted that anti-adhesion gel was not used (21).

In the randomized trial by Peters et al., 24 patients who underwent surgical adhesiolysis were compared to 24 patients who did not undergo surgery. It should be noted that in this study, as half of the patients had no history of abdominopelvic surgery, adhesions could be the consequence of an inflammatory mechanism such as endometriosis. Adhesiolysis reduced pain in 46% of the patients, mainly in the subgroup of patients who had surgery for severe adhesions (17) (Table 1).

Finally, the randomized trial by Keltz et al. included a very small number of patients (Table 1). Twenty-five women underwent laparoscopy for chronic pelvic pain, of who 12 were randomized to the adhesiolysis group and 13 to the group without adhesiolysis. Sixty percent of the patients included in the study had endometriosis. Right paracolic adhesions were found in 100% of the patients. The authors were mainly interested in comparison of the effect of right paracolic adhesiolysis versus abstention. They found a significantly greater decrease in chronic pelvic pain in the "right paracolic adhesiolysis" group compared to the control group (reduction in the pain score of -5.2 ± 0.9 versus -1.7 ± 0.9, respectively, $p = 0.0014$) (19). Other therapeutic surgical procedures were performed simultaneously, especially in cases involving endometriosis, and these could help improve the pain, thus making it difficult to interpret these data.

More recently, in the 2017 meta-analysis by van den Beukel et al., out of thirteen studies analyzed, only two controlled and randomized trials could be considered. Both of these studies found that surgical adhesiolysis did not provide any benefit in regard to pelvic pain, pain scores, or quality of life (16). The first trial was the study by Swank et al. described above (18).

The second trial, by Cheong et al., included 50 patients, of who 26 had an adhesiolysis with anti-adhesion gel versus 24 patients who only had a diagnostic laparoscopy. All of the study participants were followed up at 6 months (22) (Table 1).

This study did not find any difference between the two groups in terms of painful symptoms, but it must be interpreted with a degree of caution as it was interrupted at half of the inclusions due to difficulties with including a sufficient number of patients. Moreover, this study involved a heterogeneous population, as there were significantly more patients with severe adhesions in the adhesiolysis group compared to the group without adhesiolysis (the adhesion scores were 15 versus 9, respectively, $p < 0.05$). Other limitations of this study were the small number of patients included and the lack of long-term follow-up (22).

All of these findings must also take into account the risk of adhesions recurrence; the risk of complications due to the surgical procedure, particularly digestive complications; and finally the frequency of negative laparoscopies when the indication for surgery is to diagnose adhesions to explain chronic pelvic pain.

In the literature, the risk of adhesions recurrence after surgery has been reported, and the rate can vary from 55% to 100% (23).

The risk of digestive complications after adhesiolysis appears to be significant. Indeed, the frequency of digestive injuries secondary to adhesiolysis reported in the literature varies from 3% to 24% (23). The risk of ureteral injuries due to adhesiolysis is low and it appears to vary from 0.16% to 0.34% (24,25).

Furthermore, it is interesting to note that an 8% rate of negative laparoscopies was found in the study by Swank et al. (18) and up to 20% in the meta-analysis by van den Beukel (16) when laparoscopy was performed to search for adhesions in chronic pelvic pain.

Thus, after analyzing the benefit-risk balance (the supposed effect on pain versus the risk of recurrence, digestive injuries, and negative laparoscopy), **it is recommended not to systematically perform adhesiolysis to prevent pelvic pain in symptomatic patients (low level of evidence, strong agreement).**

Adhesiolysis and prevention of pelvic pain in asymptomatic patients

There is no data in the literature regarding asymptomatic patients. Given the risk of potential complications of such a procedure and the lack of data regarding its benefit in a population of asymptomatic patients, **it is recommended not to systematically perform adhesiolysis when pelvic adhesions are discovered in laparoscopic surgery to prevent pelvic pain in these patients (low level of evidence, strong agreement).**

Adhesiolysis and prevention of infertility in infertile women

In case of fortuitous discovery of pelvic adhesions during laparoscopy in infertile women, few studies in the literature have explored what practitioners should do. The frequency of discovery of fortuitous adhesions in patients with unexplained infertility is highly variable, ranging from 8.8% to 40.4% depending on the study (26).

Regarding the impact of adhesiolysis, the main randomized trials were assessed in the meta-analysis by Duffy et al. (27). The results indicate that performing an adhesiolysis had no discernible impact since there was not a significant difference in the clinical pregnancies rates (OR 0.96, 95% CI, 0.44–2.07) or the live births rates (OR 0.67, 95% CI: 0.19–2.32).

The 2010 Collège National des Gynécologues Obstétriciens Français (CNGOF) recommendations had already concluded that a severe adhesiolysis should not be performed in case of infertility, due to the operative risks, the frequency of recurrences, and the minimal benefit of laparoscopic adhesiolysis. Performing an adhesiolysis, on the other hand, can be an option to improve the chances of spontaneous pregnancy in case of minor or mild tubo-ovarian adhesions in terms of their extent and/or their nature (low level of evidence).

This type of adhesiolysis could lead to an increased rate of spontaneous pregnancy without significantly increasing the risk of ectopic pregnancies or the risk of surgical complications. Since these 2010 recommendations were issued, we found another interesting prospective, uncontrolled, study that reported similar results. Bonneau et al. have indeed shown that performing adnexal adhesiolysis during laparoscopy in case of infertility has ample merit as it was associated with a 23.5% probability of spontaneous pregnancy occurring postoperatively (after a 12-month follow-up) (26).

However, these results must take into account the surgical risk associated with performing an adhesiolysis. As already mentioned above, the rate of complications found in the literature is not negligible, especially in terms of the occurrence of digestive injuries (4% in the studies by Swank et al. and van den Bukel et al. (16,18)), and even higher for Herrmann et al. who, through a review of the literature, reported that the rate of digestive injuries varied from 3 to 24% (23), and the risk of adhesions recurrence after performing adhesiolysis ranged from 55% to 100% (23).

Thus, in this context, the benefit/risk balance is not in favor of performing a complex adhesiolysis in infertile women. Only adhesiolysis of minimal or slight tubo-ovarian adhesions in terms of their extension and/or their nature could be of interest to improve the chances of spontaneous pregnancy. However, this remains to be decided on a case-by-

case basis depending on other potential causes of infertility (low level of evidence, strong agreement).

Adhesiolysis and prevention of infertility in patients without known infertility issues

For women without known infertility issues, there is no data in the literature that has explored this issue. For these patients, the risk of operative complications inherent to any surgery and the risk specific to adhesiolysis surgery (mainly the risk of digestive injuries) needs to be taken into account. **Considering the balance between the unknown benefit and the risk of complications related to surgery, we recommend not to perform adhesiolysis to improve the chances of future pregnancy (low level of evidence, strong agreement).**

CONCLUSION AND RECOMMENDATIONS

Systematic surgical treatment of superficial endometriosis accidentally discovered during laparoscopy in women of childbearing age for the prevention of infertility has not been shown to be beneficial.

Performing excision of endometrial superficial lesions is recommended to prevent infertility in the event of accidental discovery.

Excision rather than monopolar coagulation of superficial endometriosis lesions in infertile women is preferable in terms of the effect on the spontaneous pregnancy rate.

Surgical treatment of asymptomatic superficial peritoneal endometriosis is not recommended in women of childbearing age for prevention of pelvic pain, especially in case of close proximity to noble organs (e.g., the ureters, rectum and sigmoid, and ovaries in nulliparous patients).

When pelvic adhesions are discovered in laparoscopic surgery, it is recommended not to systematically perform adhesiolysis in order to prevent pelvic pain.

In infertile women, only adhesiolysis of minimal or slight tubo-ovarian adhesions in terms of their extension and/or their nature should be considered in order to improve the chance of pregnancy, while performing a complex adhesiolysis is not recommended given the high risk of complications.

To strengthen these recommendations, further investigations are needed.

Table 1 CHARACTERISTICS OF THE RANDOMIZED THE STUDIES REGARDING SUPERFICIAL ENDOMETRIOSIS TREATMENT

Author (Year)	Study design Population	Patients	Outcomes	Results (95% CI)	IR	Decrease				Increase			QP
						B	P	C	A	E	DE	CF	
Duffy, 2014	Metanalysis of randomized control trials	246 Diagnostic laparoscopy vs. ablation or excision of superficial endometriosis	Pain at 3 months Pain at 6 months Pain at 12 months	OR 1.36 (0.51-3.64) OR 5.72 (3.09-10.60) OR 7.72 (2.97-20.06)	+4	-1	-1						2
		382 Diagnostic laparoscopy vs. ablation or excision of superficial endometriosis	Pregnancy rate	OR 1.94 (1.20-3.16)	+4	-1	-1						2

IR: Initial rate
B: Bias
P: Precision
C: Inconsistency
A: Applicability
E: Effect
ED: Dose-effect
CF: Confusion factors
QP: Quality of proof

TABLE 2: CHARACTERISTICS OF THE RANDOMIZED CONTROL TRIAL STUDIES REGARDING ADHESIOLYSIS

Study	Patients and intervention	Location of pain/Adhesions	Diagnosis	Follow-up	Outcomes	Results
Peters et al. (1992)	48 women N=24 Midline laparotomy and surgical adhesiolysis N=24 No adhesiolysis	Stage II-IV pelvic adhesions		9-12 months	-Improvement of pain: McGill Pain score. -Subjective pain assessment. -Impact on daily activities.	Less pelvic pain after adhesiolysis in the subgroup of women with severe, vascularized, and dense adhesions involving the bowel (stage IV)
Swank et al. (2003)	109 patients (general surgery) 87% female Pain history was not reported N=52 Laparoscopic adhesiolysis with ultrasound dissection without anti-adhesion barrier N= 48 No adhesiolysis	Not reported	History taking, physical examination, and imaging on indication, diagnostic laparoscopy	12 months	-Improvement of pain -Pain scores -QOL * (MOS-SF36*) -Complication Negative laparoscopies	No improvement at 12 months for: -Pain scores -QOL* (MOS-SF36) -Use of analgesics
Keltz et al. (2006)	25 patients with chronic pelvic pain N=12 Laparoscopic adhesiolysis of right paracolic adhesions In addition to lysing: electrosurgical coagulation Other procedures were performed (lysis of adnexal adhesions, resection, or ablation of endometriosis) N=13: No adhesiolysis	At laparoscopy, 60% had endometriosis, 32.0% had evidence of prior pelvic infection, 48.0% had pelvic adhesions. Right-sided paracolic adhesions were found in 100% of subjects.	Detailed history Pain mapping (verbal pain scale: 0 to 10) Utilized at 9 locations on the anterior abdominal wall	4 to 8 weeks postoperatively	-Pain mapping and a verbal pain scale (0-10)	Significant reduction of right and left lower quadrant pain (P<0.001) following the operative laparoscopy. Right paracolic adhesiolysis had significantly greater right pelvic pain reduction than the other (P=0.014).
Cheong et al. (2014)	50 women N=26 Laparoscopic adhesiolysis with anti-adhesion barrier icodextrin 4% solution N= 24 diagnostic laparoscopy 40% had previous surgery to treat pelvic pain	Pelvic	History taking Physical examination Diagnostic laparoscopy	6 months	-Improvement of pain Pain scores VAS* -QOL* measures (SF-12 EHP-30) -Complications Negative laparoscopies	This study stopped before recruitment reached a sufficient sample size for statistical power. In the selected population: adhesiolysis in those who had adhesions may be of benefit in terms of improvement of pain and quality of life.

*QOL Quality of life; Visual analog scale scores (VAS); MOS SF-36 (medical outcomes study with a 36-item short-form health survey

Acknowledgments: The authors wish to thank the French College of Gynecologists and Obstetricians **(**CNGOF) for their funding of the linguistic correction.

REFERENCES

1. Moen MH, Stokstad T. A long-term follow-up study of women with asymptomatic endometriosis diagnosed incidentally at sterilization. Fertil Steril. Oct 2002;78(4):773-6.

2. Reis FM, Santulli P, Marcellin L, Borghese B, Lafay-Pillet M-C, Chapron C. Superficial Peritoneal Endometriosis: Clinical Characteristics of 203 Confirmed Cases and 1292 Endometriosis-Free Controls. Reprod Sci. Jan 2020;27(1):309-15.

3. Akande VA. Differences in time to natural conception between women with unexplained infertility and infertile women with minor endometriosis. Hum Reprod. 1 Jan 2004;19(1):96-103.

4. Marcoux S, Maheux R, Bérubé S. Laparoscopic Surgery in Infertile Women with Minimal or Mild Endometriosis. N Engl J Med. 24 Jul 1997;337(4):217-22.

5. Gad M, Badroui M. Evidence-based therapy for infertility associated with early stage endometriosis. International Journal of Gynaecology and Obstetrics 2012;S531-S867:S548.

6. Moini A, Bahar L, Ashrafinia M, Eslami B, Hosseini R, Ashrafinia N. Fertility outcome after operative laparoscopy versus no treatment in infertile women with minimal or mild endometriosis. International Journal of Fertility and Sterility 2012;5(4):235-40.

7. Jacobson TZ, Duffy JM, Barlow DH, Farquhar C, Koninckx PR, Olive D. Laparoscopic surgery for subfertility associated with endometriosis. In: The Cochrane Collaboration, éditeur. Cochrane Database of Systematic Reviews [Internet]. Chichester, UK: John Wiley & Sons, Ltd; 2010 [cited 28 Sept 2020]. p. CD001398.pub2. Available at: http://doi.wiley.com/10.1002/14651858.CD001398.pub2

8. Nowroozi K, Chase JS, Check JH, Wu CH. The importance of laparoscopic coagulation of mild endometriosis in infertile women. Int J Fertil. Dec 1987;32(6):442-4.

9. Chang FH, Chou HH, Soong YK, Chang MY, Lee CL, Lai YM. Efficacy of isotopic 13CO2 laser laparoscopic evaporation in the treatment of infertile patients with minimal and mild endometriosis: a life table cumulative pregnancy rates study. J Am Assoc Gynecol Laparosc. Feb 1997;4(2):219-23.

10. Tissot M, Lecointre L, Faller E, Afors K, Akladios C, Audebert A. Clinical presentation of endometriosis identified at interval laparoscopic tubal sterilization: Prospective series of 465 cases. J Gynecol Obstet Hum Reprod. Oct 2017;46(8):647-50.

11. Sutton CJG, Ewen SP, Whitelaw N, Haines P. Prospective, randomized, double-blind, controlled trial of laser laparoscopy in the treatment of pelvic pain associated with minimal, mild, and moderate endometriosis**Supported by Birthright Research Grant (Ref:S3/90), Royal College of Obstetricians and Gynaecologists, London and Laserscope, Cwmbran, United Kingdom. Fertil Steril. Oct 1994;62(4):696-700.

12. Abbott J, Hawe J, Hunter D, Holmes M, Finn P, Garry R. Laparoscopic excision of endometriosis: A randomized, placebo-controlled trial. Fertil Steril. Oct 2004;82(4):878-84.

13. Jarrell J, Mohindra R, Ross S, Taenzer P, Brant R. Laparoscopy and Reported Pain among Patients with Endometriosis. J Obstet Gynaecol Can. May 2005;27(5):477-85.

14. Tutunaru D, Vladareanu R, Dumitrascu M, Alexandru B. Placebo effect of diagnostic laparoscopy alone in mild endometriosis. Gynaecology and Obstetrics. 2006;2:144.

15. Gerner-Rasmussen J, Burcharth J, Gögenur I. The efficacy of adhesiolysis on chronic abdominal pain: a systematic review. Langenbecks Arch Surg. Jul 2015;400(5):567-76.

16. van den Beukel BA, de Ree R, van Leuven S, Bakkum EA, Strik C, van Goor H, et al. Surgical treatment of adhesion-related chronic abdominal and pelvic pain after gynaecological and general surgery: a systematic review and meta-analysis. Hum Reprod Update. 01 2017;23(3):276-88.

17. Peters AA, Trimbos-Kemper GC, Admiraal C, Trimbos JB, Hermans J. A randomized clinical trial on the benefit of adhesiolysis in patients with intraperitoneal adhesions and chronic pelvic pain. Br J Obstet Gynaecol. Jan 1992;99(1):59-62.

18. Swank DJ, Swank-Bordewijk SCG, Hop WCJ, van Erp WFM, Janssen IMC, Bonjer HJ, et al. Laparoscopic adhesiolysis in patients with chronic abdominal pain: a blinded randomised controlled multi-centre trial. Lancet Lond Engl. 12 Apr 2003;361(9365):1247-51.

19. Keltz MD, Gera PS, Olive DL. Prospective randomized trial of right-sided paracolic adhesiolysis for chronic pelvic pain. JSLS. Dec 2006;10(4):443-6.

20. Twelve-year outcomes of laparoscopic adhesiolysis in patients with chronic abdominal pain: A randomized clinical trial - PubMed [Internet]. [cited 14 Jul 2020]. Available at: https://pubmed.ncbi.nlm.nih.gov/27866713/

21. Roman H, Hulsey TF, Marpeau L, Hulsey TC. Why laparoscopic adhesiolysis should not be the victim of a single randomized clinical trial. Am J Obstet Gynecol. Feb 2009;200(2):136.e1-4.

22. Cheong YC, Reading I, Bailey S, Sadek K, Ledger W, Li TC. Should women with chronic pelvic pain have adhesiolysis? BMC Womens Health. 4 Mar 2014;14(1):36.

23. Herrmann A, De Wilde RL. Adhesions are the major cause of complications in operative gynecology. Best Pract Res Clin Obstet Gynaecol. Aug 2016;35:71-83.

24. Outcome of laparoscopic repair of ureteral injury: follow-up of twelve cases - PubMed [Internet]. [cited 25 Sept 2020]. Available at: https://pubmed.ncbi.nlm.nih.gov/22100442/

25. Ureteral injuries during classic intrafascial supracervical hysterectomy: an 11-year experience in 1163 patients - PubMed [Internet]. [cited 25 Sept 2020]. Available at:

https://pubmed.ncbi.nlm.nih.gov/18539094/

26. Bonneau C, Chanelles O, Sifer C, Poncelet C. Use of laparoscopy in unexplained infertility. Eur J Obstet Gynecol Reprod Biol. Jul 2012;

27. Duffy JMN, Johnson N, Ahmad G, Watson A. Postoperative procedures for improving fertility following pelvic reproductive surgery. Cochrane Gynaecol Fertil Group Ed Cochrane Database Syst Rev Internet [Internet]. 15 Jul 2009; Available at: http://doi.wiley.com/10.1002/14651858.CD001897.pub2