Management of endometriosis

CNGOF/HAS clinical practice guidelines

Short version

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Abstract

First-line diagnostic investigations for endometriosis are physical examination and pelvic ultrasound. The second-line investigations are: targeted pelvic examination performed by an expert clinician, transvaginal ultrasound performed by an expert physician sonographer (radiologist or gynaecologist), and pelvic MRI. Management of endometriosis is recommended when the disease has a functional impact. Recommended first-line hormonal therapies for the management of endometriosis-related pain are combined hormonal contraceptives (CHCs) or the 52 mg levonorgestrel-releasing intrauterine system (IUS). There is no evidence base on which to recommend systematic preoperative hormonal therapy solely to prevent surgical complications or facilitate surgery. After surgery for endometriosis, a CHC or 52 mg levonorgestrel-releasing IUS is recommended as first-line treatment when pregnancy is not desired. In the event of failure of the initial treatment, recurrence, or multiorgan involvement, a multidisciplinary team meeting is recommended, involving physicians, surgeons and other professionals. A laparoscopic approach is recommended for surgical treatment of endometriosis. HRT can be offered to postmenopausal women who have undergone surgical treatment for endometriosis. Antigonadotrophic hormonal therapy is not recommended for patients with endometriosis and infertility to increase the chances of spontaneous pregnancy, including postoperatively. Fertility preservation options must be discussed with patients undergoing surgery for ovarian endometriomas.

1. Introduction

Clinical practice has changed in the last 10 years, endometriosis receives a great deal more media attention, and patients play a very active role through a host of dedicated patient organizations. It is important to consider these changes and to establish which practices are justified by medical evidence and which are based on fears or beliefs. The aim of the French National Authority for Health (HAS) and the French College of Gynaecologists and Obstetricians (CNGOF) was to update the 2006 CNGOF guideline on the management of endometriosis, to help hospital and community-based healthcare professionals offer patients in France the best possible information and management. This guideline deals with the diagnosis and management of peritoneal, ovarian and deep endometriosis. The management of adenomyosis is not addressed.

The guideline was developed by a working group assembled by the CNGOF and the HAS [1]. Several experts developed an evidence reported by the working group to formulate recommendations, which were circulated to external reviewers in accordance with the methodology developed by the HAS [1].

2. Epidemiology

The prevalence of endometriosis in the general population is difficult to estimate [2]. Studies of its prevalence in women with chronic pelvic pain are heterogeneous, with results ranging from 2% to 74%. The prevalence of endometriosis in women with acute pelvic pain is reported to be over 33%. An annual incidence of about 0.1% has been reported in women aged 15 to 49 years.

3. Natural history of endometriosis

Endometriosis does not necessarily cause pathology and is observed women with no pain or infertility (Level of Evidence (LoE) 4). Progression to painful chronic forms is possible. Endometriosis is a multifactorial disease, resulting from the combined effect of genetic, environmental, and menstruation-related related factors. An association exists between the presence of endometriosis and increased exposure to menstruation (early menarche, heavy menstrual bleeding, short menstrual cycle) (LoE2). The risk of developing endometriosis is five-fold higher for first-degree relatives than in the general population (LoE2). However, there are no data on which to base primary prevention advice [2]. The published data do not suggest that endometriosis progresses over time in terms of the volume or number of lesions (LoE3) [2]. No causal link has been demonstrated between endometriosis and ovarian cancer (LoE2). Endometriosis does not necessarily cause pain symptoms (LoE2). The prevalence of asymptomatic endometriosis in the general population is unknown [2]. There are no data that justify testing or mass screening for endometriosis in the general population. The pain associated with endometriosis can be due to nociception, hyperalgesia, and central sensitization, and these mechanisms may co-exist to varying degrees in a given patient (LoE2).

Management of endometriosis is recommended when it has a functional impact (pain, infertility) or causes organ dysfunction (Expert Consensus). Systematic screening in the absence of symptoms for populations at increased risk, due to genetic factors (a relative with endometriosis) or menstrual risk factors (heavy menstrual bleeding, short menstrual cycle, or early menarche) is not recommended (Grade C). Systematic imaging to monitor patients treated for endometriosis who are asymptomatic is not recommended (Grade C). Screening for ovarian cancer in patients with endometriosis is not recommended (Grade B). Screening for endometriosis in the general population is not recommended (Expert Consensus).

4. Diagnosis and clinical evaluation of endometriosis

4.1. Endometriosis-related pain

The pain symptoms associated with endometriosis vary between patients [3]. The main symptoms suggestive of endometriosis and its location are: severe dysmenorrhoea (a pain intensity score of 8 or more on a 10-point scale, frequently missing school or work, or resistance to step 1 analgesics) (LoE2), deep dyspareunia (LoE2), pain on defecation with menstruation (LoE2), urinary symptoms with menstruation (LoE2), and infertility (LoE2) [3,9]. Note that pain symptoms such as severe dysmenorrhoea and deep dyspareunia are common in the general population (LoE3) and are not necessarily due to endometriosis (LoE3).

When a patient presents with chronic pelvic pain or suspected endometriosis, pain assessment (intensity, impact) and evaluation for symptoms suggestive of endometriosis and its location are recommended (Grade B). The use of a scale to measure pain intensity is recommended when assessing pain or the analgesic efficacy of a treatment (Grade A).

Symptomatic endometriosis impairs patients' quality of life (LoE3). Two quality of life questionnaires are available that are specific for patients with endometriosis and have been validated for use in French-speaking patients (LoE3): Endometriosis Health Profile-30 (EHP-30) and its short version EHP-5. The generic quality of life questionnaire SF-36 has also been validated for use in endometriosis (LoE3). The chronic pain experienced by women with endometriosis can have a major physical, mental and social impact (LoE4). Pain thresholds can be altered in endometriosis, resulting in pain that appears disproportionate to the lesions observed (sensitization) (LoE2) [3].

Quality of life assessment should be included in the management of symptomatic endometriosis (Grade C). Evaluation for symptoms suggestive of sensitization is recommended in patients with endometriosis-related pain (Grade B). If a sensitization syndrome is present, pain evaluation and pain management as described in the 2009 HAS guideline on chronic pain are recommended (Grade C). In patients with isolated dysmenorrhoea, who have no other pain symptoms or immediate desire for pregnancy, evaluation for endometriosis is not recommended if dysmenorrhoea is effectively relieved by hormonal contraception (Expert Consensus).

4.2. Physical examination and signs suggestive of endometriosis

Signs suggestive of endometriosis are: bluish lesions observed during examination with a vaginal speculum, palpable nodules in the uterosacral ligaments or posterior cul-de-sac, uterosacral ligament tenderness, a retroverted uterus, or fixation of the adnexa on bimanual pelvic examination (LoE3) [3].

In the presence of symptoms suggestive of endometriosis, a targeted gynaecological examination is recommended, when possible, including examination of the posterior vaginal fornix (Grade C)

5. Additional investigations (diagnosis and evaluation)

5.1. First-line investigations

Transvaginal ultrasound is an effective technique for confirming or excluding the

diagnosis of endometriomas when lesions are typical (LoE2) [5]. Endometrioma can be diagnosed by physician sonographers who are not experts in endometriosis (LoE2). Care must be taken in postmenopausal women not to mistake a malignant tumour for an endometrioma (LoE2). Pelvic ultrasound and pelvic MRI have similar efficacy for diagnosing typical ovarian endometriosis (LoE2) [4.5.9].

The first-line diagnostic investigations for endometriosis are physical examination (a gynaecological examination if possible) and pelvic ultrasound (Expert Consensus). If an indeterminate ovarian mass is seen on ultrasound (not typical of endometrioma), repeat ultrasound by an expert (Grade A) or pelvic MRI (Grade B) are recommended (2013 CNGOF guideline on benign ovarian tumours). Patients with an endometrioma frequently also have deep endometriotic lesions. In this situation, evaluation for deep endometriosis is recommended (Grade C). In patients with chronic pelvic pain, evaluation for deep endometriosis is recommended if they experience pain on defecation during menstruation, cyclic urinary symptoms, or severe deep dyspareunia, or if they are also subfertile (Grade B).

5.2. Second-line investigations and endometriosis work-up

The second-line investigations for suspected endometriosis are a targeted pelvic examination performed by an expert clinician, transvaginal ultrasound performed by an expert physician sonographer and pelvic MRI [3.5.7]. **They are recommended to evaluate the extent of the endometriosis, to plan for specialist management, or when suggestive or localizing symptoms of endometriosis are present, but first-line investigations are negative (Expert Consensus).** The diagnostic efficacy of pelvic ultrasound for deep endometriosis increases with operator

experience (LoE2) [5]. The diagnosis of deep endometriosis can be made when a characteristic deep lesion is identified by ultrasound in a woman with suggestive signs (pain or infertility) (LoE2). The absence of a visible lesion on ultrasound imaging does not rule out deep endometriosis (LoE3). Pelvic MRI is more sensitive and less specific than transvaginal ultrasound for diagnosing involvement of the uterosacral ligaments, vagina, and rectovaginal septum (LoE2) [4]. MRI enables the detection of specific locations such as parametrial disease or extrapelvic bowel locations (LoE3). Transvaginal pelvic ultrasound performed by an operator with expertise in endometriosis is more sensitive than pelvic MRI for diagnosing endometriosis of the rectum and rectosigmoid junction (LoE3). **Both ultrasound imaging and MRI can be used to detect bladder endometriosis, hydroureter, or hydronephrosis (LoE2). Pelvic ultrasound and MRI provide different and complementary information. Whether both investigations should be carried out will require discussion and will depend on the type of endometriosis suspected, the chosen treatment strategy, and the information the patient requires (Expert Consensus).**

In deep pelvic endometriosis, pelvic MRI interpreted by an expert radiologist and/or second-line pelvic ultrasound performed by an expert physician sonographer can be offered in order to confirm the diagnosis (Grade B). If pelvic MRI does not correlate with the clinical or ultrasound findings, a second review of the MRI scan by an expert radiologist can be proposed (Expert Consensus). Pelvic ultrasound performed by an expert or pelvic MRI is recommended before surgical resection of deep pelvic endometriosis, to determine whether any urinary tract or bowel procedures might also be required (Grade C).

Scientific society guidelines concerning the technical requirements for pelvic MRI in the diagnosis pelvic endometriosis are based on multiplanar T2- and T1-

weighted sequences, with and without fat suppression (LoE1); the use of these sequences is therefore recommended for the diagnosis of endometriosis (Grade B). Gadolinium injection is an option with MRI, especially to help visualize a complex adnexal mass (Expert Consensus). Vaginal or rectal opacification is useful in the absence of prior bowel preparation. It is not essential if the patient has already undergone bowel preparation, which is the preferred method (Expert Consensus). An acquisition with the bladder half-full is recommended, so that it does not interfere with interpretation (Expert Consensus). The imaging report (MRI or ultrasound) must describe the size of the lesions as well as the anatomic locations where endometriosis was visualized during the examination (Grade B).

5.3. Third-line diagnostic investigations

These third-line diagnostic investigations are requested by specialists in specific situations.

5.3.1. *Exploration of rectosigmoid endometriosis*

Rectal endoscopic ultrasound (REU) is more effective than pelvic MRI for diagnosing involvement of the rectosigmoid muscularis and evaluating the distance from the anal margin (LoE2) [9]. To diagnose endometrial disease of the rectosigmoid muscularis, the diagnostic performance of transvaginal ultrasound appears at least equivalent to REU. Computed tomography–based virtual colonoscopy is an effective diagnostic technique for rectosigmoid and ileocaecal pelvic endometriosis (LoE3).

Before surgical resection of deep endometriosis with suspected bowel involvement, it is recommended that this involvement be confirmed or excluded

preoperatively so that the patient can make an informed decision and to organize multidisciplinary management if necessary (Expert Consensus). A dedicated investigation is recommended to confirm and characterize bowel involvement (multifocal or unifocal, lesion diameter, infiltration depth, size, circumference, stenosis), which may depend on the available expertise and the lesion locations: transvaginal ultrasound, pelvic MRI, rectal endoscopic ultrasound, or computed tomography–based virtual colonoscopy (Expert Consensus). When first-line imaging studies (transvaginal ultrasound, pelvic MRI) do not confirm endometriotic infiltration of the colon, the recommended second-line investigations are rectal endoscopic ultrasound for rectosigmoid locations, and computed tomography–based virtual colonoscopy for more proximal colonic locations (Grade C). Colonoscopy is not recommended for suspected rectosigmoid endometriosis (Grade C). Colonoscopy can be useful to exclude differential diagnoses (Expert Consensus).

5.3.2. Exploration of urinary tract endometriosis

Hydronephrosis is present in 50-60% of cases of urinary tract endometriosis (LoE3) [18]. It is present in 5% of cases of posterior deep endometriosis and in up to 11% of cases when lesions are >3 cm (LoE3). Hydronephrosis can be reliably identified by renal ultrasound, or MRI with high sections through the renal compartments (LoE1).

Evaluation for hydroureteronephrosis is recommended when deep pelvic endometriosis is discovered (Grade C). When hydroureteronephrosis is present, the opinion of a specialist is recommended to investigate its renal impact (Expert Consensus)

No studies have compared the efficacy of cystoscopy versus imaging in anterior endometriosis [6]. Cystoscopy enables visual diagnosis of endometriotic lesions in half of cases through observation of typical red or bluish nodular lesions (LoE4). **In patients with chronic pelvic pain, lower urinary tract symptoms and suspected endometriosis, MRI or ultrasound imaging performed by an expert physician sonographer are useful to evaluate for bladder or urethral endometriosis (LoE2) and are recommended as first-line investigations (Grade C).**

5.4. Diagnostic laparoscopy and fertiloscopy

When specific, characteristic signs of endometriosis are identified on imaging (cyst and/or deep lesions), laparoscopy solely to confirm the diagnosis is not recommended (Grade B). However, superficial endometriotic lesions cannot be adequately diagnosed by pelvic MRI or ultrasound (LoE2) [4.9]. Diagnostic laparoscopy may be indicated when endometriosis is suspected on the basis of clinical signs but has not been demonstrated in preoperative investigations (Grade C). Such diagnostic laparoscopies are only indicated when warranted by the management strategy for pain or infertility (Grade C). Targeted biopsies (with histological evaluation) are recommended to confirm the diagnosis of endometriosis when typical or atypical lesions are found on diagnostic laparoscopy (Grade B). Biopsy of healthy peritoneum is not recommended (Grade C). When laparoscopy is performed for endometriosis, precise, exhaustive description of the abdominopelvic cavity is recommended, including adhesions and the various types of lesion, describing their macroscopic appearance, size and location, with the aim of correlating the symptoms with the pathology and to guide treatment (Expert Consensus). The use of lesion classification systems is encouraged, to describe the extent of endometriosis and facilitate interprofessional discussions (Expert Consensus). Endometriosis can be ruled out by diagnostic laparoscopy when the abdominopelvic region was adequately explored and no visible macroscopic lesions were visualized (Expert Consensus). Fertiloscopy is not recommended for the purpose of diagnosing endometriosis (Grade C)

6. Informing patients

Information is available from a wide variety of sources, and although this suits some patients with endometriosis, it can also generate anxiety (LoE4) [8]. The information available on the internet varies greatly in quality and is often substandard from a scientific point of view (LoE4). The ability to interact with other women with endometriosis, through patient organizations or health service initiatives, is useful for obtaining additional information and making them feel less alone (LoE3). **The production of printed information is encouraged. It should contain essential information for patients and their partners, be validated by health professionals, and given to patients during the consultation, then explained in terms appropriate to the patient (Expert Consensus). At the time the treatment is chosen, it is recommended that patients be informed about the treatment options, the expected benefits and risks of each treatment and the risk of recurrence, and that the patient's expectations and preferences be taken into account. Before surgery, additional information should be provided about what will happen during the procedure, the aim of surgery, the expected inconveniences and benefits, possible complications, her scars, the postoperative period and convalescence (Grade C). Physicians are invited to fully inform women with endometriosis about fertility (Expert Consensus)**

7. Hormonal therapy for endometriosis-related pain

It is recommended that the choice of treatment be guided by any contraindications, potential adverse effects, existing therapy and the patient's preference (Expert Consensus) [10.13]. Hormonal therapy is not indicated for women with asymptomatic endometriosis unless they request contraception (Grade C).

7.1. Combined hormonal contraceptives

In patients with endometriosis-related pain, a cyclic combined hormonal contraceptive (CHC) alleviates dysmenorrhoea (3- to 9-point decrease in pain intensity on a 10-point scale) (LoE1), dyspareunia, and chronic pelvic pain (LoE3) [13]. The dose of ethinylestradiol (20 versus 35 µg) does not affect the treatment's efficacy against pain (LoE1). The efficacy of vaginally administered CHCs (vaginal ring) has been demonstrated against dysmenorrhoea, non-menstrual pain, and dyspareunia with rectovaginal nodules (LoE3). There is insufficient published data to determine the benefit of continuous over cyclic administration of CHCs in patients with endometriosis-related pain without infertility, who have not undergone surgical treatment and do not have severe dysmenorrhoea [10].

7.2. Progestogens

The 52 mg levonorgestrel-releasing intrauterine system (LNG-IUS), desogestrel contraception, and etonogestrel implant have been shown to have significant efficacy against pain in endometriosis [13]. No recent data have been published about chlormadinone acetate, nomegestrol or medrogestone in this indication. The 52 mg levonorgestrel-releasing intrauterine system reduces pain scores (decrease of about 6 points on a 10-point scale) in endometriosis patients who have not undergone surgical

treatment (LoE2). No data are available on the 13.5 mg LNG-IUS [13]. Desogestrel contraception has been shown to improve patient satisfaction and pain scores (decrease of at least 2 points on a 10-point scale at 6 months) in patients with endometriosis of the rectovaginal septum (LoE3). The etonogestrel implant improves pain control (based on pain scores at 6 and 12 months), and patient satisfaction (LoE3). Depot medroxyprogesterone acetate (DMPA) alleviates pain symptoms in 80–90% of patients (dysmenorrhoea, dyspareunia, and chronic pelvic pain) and the effect persists 6 months after discontinuation (LoE2) [13]. There is no evidence of efficacy for dydrogesterone (LoE3). Dienogest has been well evaluated in endometriosis. In France, it has marketing authorization for use in endometriosis but is not reimbursed by national health insurance schemes. It has been shown to be more effective against pain than placebo (LoE2), and pelvic pain scores are still decreased 12 months after discontinuation (LoE3). There is no difference in efficacy (based on pain and quality of life scores) between dienogest and gonadotrophin-releasing hormone agonists (GnRHas) (LoE1). In the absence of data, the role of chlormadinone acetate, nomegestrol and medrogestone in the treatment of endometriosis in unclear [10].

7.3. Gonadotrophin-releasing hormone agonists (GnRHas)

GnRHas alleviate dysmenorrhoea and pain in patients with endometriosis-related pain, inducing a 3- to 6-point decrease in the global VAS at 10 months (LoE2) [13]. During GnRHa therapy, add-back therapy in the form of concomitant high-dose progestogen and an oestrogen reduces bone mineral density (BMD) loss at 12 months and is superior to a high-dose progestogen alone (LoE2). Add-back therapy including an oestrogen improves quality of life in patients treated with GnRHas (LoE2). No particular add-back therapy can be recommended over the others, due to insufficient scientific data. The use of add-back therapy does not reduce the efficacy of GnRHas in the

management of endometriosis-related pain (LoE1). No studies have evaluated the value of using GnRHa for more than 12 months (the licensed treatment duration) [10].

7.4. Summary of hormonal therapy for endometriosis-related pain

The recommended first-line hormonal therapies for the management of endometriosis-related pain are a CHC or the 52 mg LNG-IUS (Grade B). In light of the risk of thromboembolism, adherence to guidelines on the use of CHCs is recommended (HAS 2013).

The recommended second-line hormonal therapies for the management of endometriosis-related pain are desogestrel low-dose progestogen contraception, an etonogestrel implant, GnRHas with add-back therapy, and dienogest (Grade C).

When a GnRHa is prescribed in endometriosis, concomitant add-back therapy is recommended (Grade B). Add-back therapy must include an oestrogen to prevent bone mineral density loss and to improve patients' quality of life (Grade B). The marketing authorization recommends addition of a progestogen. Add-back therapy can be prescribed before the third month to minimize side effects (Expert Consensus).

8. Hormonal treatments before surgery for endometriosis

Only cyclic CHCs have been evaluated for endometriomas, which reduce the volume of endometriomas by about 50% at 6 months (LoE2) [10.13]. For rectovaginal septum endometriotic disease, cyclic oral CHCs, a CHC vaginal ring, desogestrel contraception, norethisterone acetate, and GnRHas reduce lesion volume by 17–21% at 12 months (LoE3). An increase in volume is observed in 8–16% of patients,

however.

There is no evidence base on which to recommend systematic preoperative hormonal therapy solely to prevent surgical complications, facilitate surgery, or reduce the risk of endometriosis recurrence (Expert Consensus).

9. Hormonal treatments after surgery for endometriosis

When pregnancy is not desired, postoperative hormonal therapy is recommended, to reduce the risk of recurrence of endometriosis-related pain and to improve patients' quality of life (Grade B).

9.1. Combined hormonal contraceptives

Cyclic use of CHCs reduces the risk of recurrence of dysmenorrhoea after surgery by 40–69% (LoE1) [13]. The long-term protective effects do not persist when treatment is discontinued (LoE2). Its effect on non-menstrual pelvic pain and dyspareunia is inconsistent. Continuous use reduces dysmenorrhoea by inducing amenorrhoea but does not appear more effective than intermittent use in the management of non-menstrual pain and dyspareunia (LoE2). CHCs reduce the long-term risk of recurrence of surgically-treated endometriomas while treatment continues (LoE2). Long-term benefit is not observed when the CHC is discontinued after 6 months of treatment (LoE1). The long-term endometrioma recurrence rate is lower when CHCs are taken for a longer period (LoE2). Patient satisfaction rates are similar with continuous versus intermittent CHC use, but continuous therapy is associated with an approximately three-fold risk of discontinuation and more adverse effects (LoE2).

Postoperative CHC is recommended to prevent the risk of recurrence of surgically-treated endometrioma in patients with no contraindications and when

pregnancy is not desired (Grade B). CHC use is recommended for as long as the treatment is well tolerated and pregnancy is not desired (Grade C). When prescribing postoperative CHC therapy, continuous administration is preferable for women with dysmenorrhoea (Grade B).

9.2. Progestogens and gonadotrophin-releasing hormone agonists (GnRHas)

The 52 mg LNG-IUS lowers the risk of pain recurrence and improves the quality of life of patients after surgery (LoE2), with a similar effect to GnRHas (LoE1). DMPA is superior to cyclic CHCs in the management of dysmenorrhoea after surgery (VAS=0 at 6 months), with no differences in satisfaction rates (>90%), dyspareunia, or chronic pelvic pain (LoE2). Desogestrel contraception reduces pain (3-point decrease on the global VAS 6 months after surgery) but is not superior to CHCs (LoE3). There is no difference in efficacy between dienogest and GnRHas after surgery, based on recurrence of endometriotic lesions on second-look laparoscopy, pain scores, or quality of life scores (LoE2).

A short (3-month) course of GnRHa after surgery does not reduce the long-term (5-year) risk of pain recurrence (LoE2). Several studies comparing GnRHas with other treatments (CHC, LNG-IUS, dienogest) after surgery have demonstrated reduced recurrence and reduced pain after surgery, and improvement in quality of life with GnRHa (LoE2 or LoE3). A 6-month postoperative course of GnRHa does not reduce the risk of recurrence of surgically-treated endometriomas at 18 months in patients with stage 3 or 4 endometriosis (LoE2). Immediate postoperative administration versus administration on day 1 of the following cycle reduces the frequency and duration of bleeding by 15%, with no reduction in the intensity of pelvic pain, dysmenorrhoea or

dyspareunia (LoE2). **GnRHas are not recommended postoperatively for the sole purpose of preventing recurrence of endometrioma (Grade B).**

9.3. Summary of the postoperative hormonal strategy when pregnancy is not desired

After surgery for endometriosis, a CHC or 52 mg levonorgestrel-releasing IUS is recommended as first-line treatment when pregnancy is not desired (Grade B).

10. The role of “novel drugs” for endometriosis

There is insufficient published evidence about the utility in clinical practice of aromatase inhibitors, selective oestrogen receptor modulators, and selective progesterone receptor modulators in the management of endometriosis-related pain [12]. The GnRH antagonist elagolix reduces dysmenorrhoea and non-menstrual pelvic pain at 3 and 6 months but provokes adverse effects such as hot flushes, BMD loss, and headache (LoE2). Preoperative treatment with the anti-TNFα antibody infliximab does not reduce pain symptoms or lesion volume in patients with rectovaginal septum disease (LoE2). In the postoperative setting, goserelin alone for 6 months is associated with a higher 2-year recurrence rate than the combination of goserelin + anastrazole (LoE2). A 6-month course of the selective oestrogen receptor modulator raloxifene after complete surgical excision of endometriosis is associated with more rapid and more frequent recurrence of pain symptoms than with placebo (LoE2).

Selective oestrogen receptor modulators are not recommended after surgery for endometriosis (Grade B). In the absence of data, aromatase inhibitors, selective

oestrogen receptor modulators, selective progesterone receptor modulators, and TNFα inhibitors are not recommended for managing endometriosis-related pain (Grade C). The current data do not yet justify recommending elagolix for the treatment of endometriosis-related pain outside the clinical trial setting (Grade C).

These recommendations could be revised once the results of ongoing clinical trials are available.

11. Hormonal therapy for endometriosis-related pain in adolescents

In light of their efficacy against dysmenorrhoea and endometriosis-related pain in adults, and their tolerability, a CHC or low-dose progestogen contraceptive is recommended as first-line therapy for adolescents with endometriosis-related pain when not contraindicated (Expert Consensus) [14]. If the first-line strategy fails, the opinion of a specialist is recommended in order to determine the best diagnostic and treatment strategy to adopt (Expert Consensus).

Dienogest and GnRHas are effective against endometriosis-related pain in adolescents (LoE2) [14].

Given the risks of bone demineralization, GnRHas are not recommended for adolescent patients (Grade B). GnRHas must not be prescribed before the age of 16 years (18 years of age according to the marketing authorization). The maximum authorized treatment duration is 12 months. GnRHa therapy must be combined with add-back therapy, including at least an oestrogen in order to prevent bone mineral density loss and to improve quality of life (Grade B).

12. Analgesics and non-pharmacological complementary therapies

These therapies apply to all patients with endometriosis-related pain, after comprehensive evaluation of the pain and its impact. When endometriosis-related pain recurs, the pain must be regarded as a chronic pain syndrome with underlying inflammatory and neuropathic mechanisms (LoE1) [11]. No studies have evaluated the efficacy of paracetamol or step 2 and 3 opioids in endometriosis-related pain. Gabapentin and amitriptyline are useful in the treatment of chronic pelvic pain (LoE2/3) but have not been evaluated specifically in endometriosis-related pain. Patients with

chronic pelvic pain commonly use complementary therapies (LoE2). Some therapies have only been evaluated in dysmenorrhoea or chronic pelvic pain. No data are available on the efficacy of the various proposed dietary measures. No studies have assessed the efficacy of herbal remedies or aromatherapy in endometriosis-related pain. Antioxidant and vitamin supplementation has undergone little evaluation. The studies conducted on Chinese herbal remedies appear to show moderate efficacy in certain situations. Caution is required with the forms currently marketed in France or via the internet. It is difficult to conduct blinded studies of physical treatments. It is challenging, if not impossible to devise a credible placebo version. Acupuncture, osteopathy and yoga have been shown to improve the quality of life of patients with endometriosis-related pain (LoE4). Transcutaneous electrical nerve stimulation (TENS) has been shown to be of value in primary dysmenorrhoea (LoE2). It has not been evaluated specifically in endometriosis. An evaluation of Jacobson's progressive relaxation therapy (muscle contraction and relaxation) in Chinese patients with endometriosis found that it reduced anxiety and improved quality of life (LoE3) [11].

Long-term NSAID therapy is not recommended due to its gastric and renal side effects (Grade B). Specific treatment is recommended for pain suspected to be of neuropathic origin (Grade C). No dietary measures or vitamin supplements can be recommended for endometriosis-related pain, due to insufficient evidence (Expert Consensus)

Management of the patient's chronic pain with sustained patient support appears beneficial (LoE4). A holistic, multidisciplinary approach to the care of patients with endometriosis appears useful. Evaluation of the intensity, type, behavioural impact and personal context of the pain ensures a personalized approach to treatment with enhanced efficacy.

Non-pharmacological therapies that have been shown to improve quality of life can be offered alongside the medical management of endometriosis (Expert Consensus). In patients with chronic pain, multidisciplinary evaluation (gynaecologists, pain specialists, sex therapists, psychologists and social workers) is recommended (Expert Consensus).

13. Surgical treatment of endometriosis

The choice between medical and surgical treatment is guided by the woman's expectations of treatment, whether pregnancy is desired, the efficacy and adverse effects of the treatments, the intensity and type of pain, and the severity and location of the endometriosis [23].

In the event of failure of the initial treatment, recurrence, or multiorgan involvement, a multidisciplinary team meeting is recommended, involving physicians, surgeons and other professionals (Expert Consensus). A laparoscopic approach is recommended for surgical treatment of endometriosis (Grade B)

13.1. Minimal to mild pelvic endometriosis

Excision and ablation have similar efficacy against pain (LoE2). If minimal to mild pelvic endometriosis (ASRM stages I and II) is discovered in an infertile patient, excision or ablation of the lesions, together with adhesiolysis, increases the spontaneous pregnancy rate (LoE1). The use of adhesion barriers reduces postoperative adhesion scores (LoE2), but the clinical benefit (reduced risk of pain or infertility) has not yet been demonstrated in clinical studies providing high-quality evidence [15].

Surgery for minimal to mild pelvic endometriosis reduces pain in the short and medium term (LoE1). Complete surgical treatment of any pelvic endometriotic lesions discovered during laparoscopy is recommended (Grade B).

13.2. Ovarian endometriomas

Surgery for ovarian endometriomas can reduce ovarian reserve (LoE2) through excision or ablation of the ovarian parenchyma around the cyst, which possibly has negative effects on postoperative fertility (LoE3). This risk is enhanced when endometriomas are large, recurrent or bilateral (LoE3). Evaluation of ovarian reserve may be useful before surgery for endometrioma [16]. When operative treatment is chosen, a laparoscopic approach is associated fewer postoperative complications, less postoperative pain, shorter hospital stays, and lower cost than laparotomy (LoE1).

The recommended technique for the surgical management of endometriomas is laparoscopic intraperitoneal cystectomy (Grade A). In certain situations, cystectomy for endometrioma can lead to partial or total oophorectomy due to intraoperative difficulties. In the absence of cleavage planes, it is best to abandon cystectomy if the patient wishes to preserve the ovary (Expert Consensus).

Isolated ovarian endometrioma is very rare (LoE3). The risk of recurrence is increased after incomplete surgery (LoE3). Evaluation for and treatment of other pelvic locations of endometriosis are recommended when an endometrioma is discovered or during its surgical management (Grade C). Neither expectant management nor ultrasound-guided cyst aspiration is recommended as first-line management for women with pain (Grade C) due to the risk of persistence or rapid recurrence of pain and endometriomas (LoE3). Ethanol sclerotherapy is associated with a lower cyst recurrence rate than aspiration alone (LoE3) and can therefore be offered to patients with recurrent endometriomas (Expert Consensus). Ablation of endometriomas with bipolar coagulation is not recommended (Grade B) due to lower postoperative pregnancy rates and higher rates of recurrence of endometrioma (LoE1).

Laser or plasma energy ablation cannot be recommended over cystectomy due to the lack of high-quality evidence from comparative studies [16].

13.3. Deep endometriosis with infiltration of the bladder

The surgical management of endometriotic lesions of the bladder by partial cystectomy has long-term efficacy against pain symptoms and the risk of recurrence, and has a low rate of severe complications (LoE3). No studies have specifically compared the efficacy of pharmacotherapy versus or in combination with bladder surgery [18].

Surgical treatment of bladder endometriosis by partial cystectomy can be offered to symptomatic patients (Grade C). Resection of an endometriotic nodule of the bladder by the transurethral route alone is not recommended (Grade C), because only the intravesical portion of the lesion is treated, leaving any adjacent infiltration of the myometrium or round ligaments intact, thus increasing the risk of recurrence (LoE3).

The current data from case series on the impact of partial cystectomy on fertility in women treated surgically for bladder endometriosis are inconclusive (LoE4).

13.4. Deep endometriosis affecting the ureters

The surgical management of ureteral endometriosis lesions using conservative (ureterolysis) or radical techniques (ureteral resection with end-to-end anastomosis or ureteral resection and reimplantation into the bladder) is effective for reducing pain symptoms, dilation of the upper urinary tract, and recurrence, with a low rate of severe complications (LoE3). It is not possible, based on the data in the literature, to

recommend specific indications for these three surgical techniques [18].

When radical techniques (anastomosis or reimplantation) are used to treat ureteral endometriosis, management by multidisciplinary surgical team (gynaecological and urological) is recommended (Expert Consensus). Postoperative imaging-based monitoring appears justified, due to the risk of stenosis of the ureteroureteral anastomosis or the reimplantation site, and the risk of minimally symptomatic progressive renal atrophy (Expert Consensus).

13.5. Deep endometriosis with infiltration of the colon and rectum

For patients with colorectal endometriosis, a laparoscopic approach is as effective as laparotomy for relieving pain on defecation and improving postoperative quality of life (LoE2). Compared with laparotomy, laparoscopic surgery reduces opioid analgesic use, blood loss, and serious postoperative complications, and improves postoperative spontaneous pregnancy rates (LoE2). Surgery for colorectal endometriosis reduces the intensity of gynaecological, gastrointestinal, and general symptoms and improves quality of life (LoE2). The relative merits of surgical treatment versus medical hormonal therapy administered before, after or instead of surgical treatment cannot be assessed from the data in the literature [17]. Rectal shaving, anterior discoid resection, and segmental resection are the three techniques used for the surgical excision of colorectal endometriosis (LoE2). In surgical treatment of colorectal endometriosis, a conservative technique (shaving or discoid resection) may reduce the risk of postoperative complications and improve gastrointestinal quality of life scores compared with segmental resection, but the risk of recurrence is probably greater (LoE3). For nodules that infiltrate the rectum over a length of more than 20 mm,

postoperative rectal function is comparable in women who have undergone segmental resection of the rectum or a conservative technique (LoE2). Segmental colorectal resection for endometriosis increases the risk of postoperative symptomatic stenosis requiring further surgical or endoscopic management (LoE2). Discoid or segmental resection for endometriosis of the lower rectum (within 5 cm of the dentate line), especially with concomitant colpectomy, is associated with a greater risk of rectovaginal fistula than with higher locations (LoE4) [17].

Surgery for colorectal endometriosis can be offered to symptomatic patients (Grade C). Surgery for colorectal endometriosis carries a risk of serious postoperative complications (LoE2), of which patients must be informed (Grade B). When endometriosis of the lower rectum is treated surgically, temporary bowel diversion (ileostomy or colostomy) to reduce the complications associated with fistula formation must be discussed and the patient must be informed and receive appropriate preoperative education (Expert Consensus). Due to the absence of studies providing a sufficiently high level of evidence in patients with colorectal endometriosis, it is not possible to make a higher-grade recommendation concerning systematic bowel diversion [20]. Multidisciplinary management is recommended when bowel endometriosis is treated surgically (Expert Consensus).

When surgery for deep endometriosis with colorectal involvement is incomplete, and the bowel lesion is left in situ, the rate of postoperative pain recurrence is increased and the postoperative pregnancy rate reduced (LoE3). **When surgical treatment is chosen, it is recommended that resection of the pelvic endometriotic lesions be as complete as possible (Grade C).**

In randomized studies that did not specifically include patients undergoing surgery for colorectal endometriosis, the application of adhesion barriers during abdominopelvic surgery involving bowel anastomosis increased the incidence of serious postoperative complications (LoE1) [17]. **The use of adhesion barriers around the bowel anastomosis at the end of surgery for deep endometriosis is not recommended (Grade C).**

13.6. Value of conservative hysterectomy or hysterectomy with bilateral adnexectomy

When resecting endometriotic lesions, concomitant hysterectomy, with or without bilateral adnexectomy, might reduce the rate of recurrence and repeat surgery compared with resection of endometriotic lesions alone (LoE4) [22]. **When pregnancy is not desired, combined hysterectomy with resection of endometriotic lesions, with or without bilateral adnexectomy, can be offered to reduce the risk of recurrence (Expert Consensus). Given the multiple adverse effects of early menopause on lifespan and quality of life (LoE2), ovarian conservation must be discussed with the patient in the event of hysterectomy for deep endometriosis (Expert Consensus). The use of postmenopausal hormone replacement therapy (HRT) does not appear to worsen the symptoms of endometriosis after bilateral oophorectomy (LoE3). HRT can be offered to postmenopausal women who have undergone surgery for endometriosis (Grade C).**

13.7. Extrapelvic endometriosis: parietal, diaphragmatic, thoracic

Parietal endometriotic lesions usually occur in women with a history of uterine surgery (caesarean section, hysterectomy, myomectomy) or can develop de novo (umbilicus or inguinal canal). The relative merits of surgical treatment versus medical hormonal therapy administered before, after or instead of surgical treatment cannot be assessed from the data in the literature [19]. **A consultation with a gynaecologist is advised when thoracic endometriosis is discovered (Grade C), due to the prevalence of concomitant pelvic involvement (50–80%) (LoE3). Surgical treatment can be offered to symptomatic patients with parietal, thoracic or diaphragmatic endometriosis (Grade C), due to its beneficial effect on pain (LoE3).**

13.8. Endometriosis of nerve roots and the sciatic nerve

Deep endometriosis can compress or infiltrate the sacral roots or the sciatic nerve trunk, leading to cyclic symptoms involving the somatic nervous system (sciatic or pudendal nerve territories) or the autonomic nervous system (bladder, colorectal or vaginal symptoms) (LoE3). Several case series reported by centres of excellence have noted the efficacy of surgery against pain (LoE4) [19]. The relative merits of surgical treatment versus medical hormonal therapy administered before, after or instead of surgical treatment cannot be assessed from the data in the literature.

13.9. Nerve-sparing techniques in surgery for deep endometriosis

In the absence of endometriotic nerve involvement or perineural invasion, techniques to preserve autonomic pelvic nerves improve postoperative urinary function (LoE3) [21]. **Nerve sparing may not be feasible, depending on the distribution and**

stage of endometriosis. During pelvic surgery for endometriosis, preservation of pelvic autonomic nerves is recommended whenever possible (Grade C).

14. Strategies for managing infertility in patients with endometriosis

Endometriosis-related infertility must be managed globally, taking into account any concurrent pain as well as the results of the couple's pre-treatment infertility evaluation (exploration of ovarian reserve, tubal status and the partner's sperm parameters) and the phenotype of the endometriotic lesions [29]. Optimal management is achieved in multidisciplinary teams, including radiologists specialized in female imaging, medical gynaecologists, and gynaecological, urological and gastrointestinal surgeons, practitioners specialized in assisted reproduction, pain practitioners, and psychologists. Antigonadotrophic hormonal therapy does not increase the pregnancy rate in women with endometriosis-related infertility (LoE1) [24].

Antigonadotrophic hormonal therapy is not recommended for patients with endometriosis and infertility to increase the chances of spontaneous pregnancy, including postoperatively (Grade A). The use of postoperative ovarian stimulation, with or without intrauterine insemination, can be considered for non-IVF management when minimal to mild (ASRM stage I or II) endometriosis is proven after laparoscopy (Grade C). After surgery in an infertile patient, the use of the endometriosis fertility index is recommended to guide the strategy for achieving pregnancy (Grade C).

There are insufficient data in the literature to draw conclusions about the role of non-IVF assisted reproduction treatments (ovarian stimulation, with or without intrauterine insemination) in patients with deep pelvic endometriosis or endometrioma [24].

14.1. Principles of IVF to manage infertility in women with endometriosis

In infertile women with endometriosis, neither the presence of endometriosis nor its stage appears to compromise IVF pregnancy and birth rates (LoE3) [25]. The number of oocytes retrieved from women with endometriosis appears reduced, especially with severe endometriosis (LoE3). Studies on ovulation induction for IVF have not shown it to exacerbate the symptoms associated with endometriotic lesions, accelerate progression of endometriosis, or increase the rate of disease recurrence (LoE2). In assisted reproduction, the fertilization method (in vitro versus intracytoplasmic sperm injection (ICSI)) does not affect the cumulative pregnancy rate (LoE3). There is no difference in the pregnancy rates obtained with an agonist protocol and an antagonist protocol in patients with endometriosis undergoing IVF (LoE3). The literature review showed that ovarian suppression with a GnRH agonist (LoE2) or CHC (LoE3) before stimulation for IVF improves the chances of pregnancy.

Endometriosis is not an indication for using ICSI rather than standard IVF in first-line assisted reproduction (Expert Consensus). It is not possible, based on the data in the literature, to recommend choosing an agonist protocol or an antagonist protocol for patients with endometriosis (Grade C). For women with endometriosis undergoing IVF, pre-treatment with a GnRH agonist (Grade B) or CHC (Grade C) is recommended before stimulation.

14.2. *IVF strategy and special cases*

14.2.1. Superficial endometriosis

There is currently no high-level evidence as to whether surgery for superficial peritoneal endometriosis has a positive or negative effect on IVF outcomes (LoE4)

[**Erreur ! Signet non défini.**]. **In women with endometriosis and infertility, surgical treatment of superficial endometriosis solely to increase the chances of pregnancy through IVF is not recommended (Grade C).**

14.2.2. Endometrioma

Endometriomas (size <6 cm) have no impact on embryo quality or final IVF outcomes (pregnancy and birth rates), despite a possible reduction in the number of oocytes retrieved and despite potentially higher gonadotrophin doses (LoE3) [26]. The literature contains no data on endometriomas larger than 6 cm. In women who have previously undergone surgery for endometrioma, IVF outcomes (pregnancy rate and live birth rate) are unchanged (LoE2); however, a slight decrease in ovarian reserve with fewer oocytes retrieved and the use of higher doses of gonadotrophins are observed (LoE2). Many literature reviews show that ovarian cystectomy before IVF does not improve the pregnancy rate (LoE2). The literature does not show improved IVF outcomes for women who underwent ultrasound-guided cyst aspiration before controlled ovarian stimulation (LoE3). **Surgical treatment of endometriomas solely to improve IVF outcomes is not recommended (Grade B). Systematic ultrasound-guided transvaginal aspiration of endometriomas before IVF in order to increase pregnancy rates is not recommended (Grade C). If an endometrioma could interfere with oocyte retrieval, it can be drained by ultrasound-guided transvaginal aspiration, with or without ethanol injection (Grade C).**

14.2.3. Deep endometriosis

Pregnancy rates (spontaneously and after assisted reproduction) achieved after

surgery for deep endometriosis lesions without colorectal involvement range from 40% to 85%. After surgery specifically for colorectal endometriotic lesions, pregnancy rates (achieved spontaneously and after assisted reproduction) range from 47–59%, depending on the study, and are therefore similar to the outcomes obtained in non-colorectal deep endometriosis. The spontaneous pregnancy rates obtained after surgery for colorectal endometriotic lesions range from 27–41%, depending on the study and length of follow-up [27]. The pregnancy rates following IVF in women with in situ deep endometriosis are no different from pregnancy rates achieved through IVF in other indications for assisted reproduction (LoE2). No conclusions can yet be drawn about the value of surgical management for deep lesions before IVF, based on studies comparing the chances of pregnancy after IVF, with or without prior surgery, in patients who did not also have pain symptoms (LoE2). In addition to surgery providing no obvious benefit concerning the chances of pregnancy through assisted reproduction, it must also be borne in mind that it carries a risk of immediate postoperative complications (LoE2) and of reduction of ovarian reserve when surgery is performed on any concomitant endometriomas (LoE3). Few studies have addressed the role of surgery after failure of several IVF trials. Two uncontrolled studies suggest that surgery may improve the IVF pregnancy rate (LoE4).

IVF can be offered to women with infertility and deep endometriosis to increase pregnancy and birth rates (Grade B). Prior surgical treatment for deep endometriosis solely to improve IVF outcomes is not recommended (Grade C). After one or more unsuccessful IVF cycles in a woman with deep endometriosis, a multidisciplinary team meeting is recommended to discuss surgery for endometriosis (Expert Consensus).

14.2.4. Endometriosis with adenomyosis

Although the diagnosis of adenomyosis remains poorly defined and the groups studied have been heterogeneous, adenomyosis appears to have a negative effect on pregnancy rates in women undergoing IVF [25.27]. The contribution adenomyosis makes to reducing pregnancy rates is difficult to assess in women with concomitant endometriosis. The miscarriage rate appears higher in patients with adenomyosis undergoing IVF (LoE2). The use of an GnRH agonist appears to improve IVF outcomes in women with adenomyosis

14.2.5. Recurrent endometriosis

In women with infertility and recurrent endometriosis, repeat surgery and IVF result in similar pregnancy rates [29]. The management strategy must therefore take account of the symptomatology, the risks of surgery, and any other infertility factors. **For a woman with recurrent endometriosis and infertility, a multidisciplinary team meeting is recommended to discuss appropriate management (Expert Consensus).**

15. The role of fertility preservation in endometriosis.

As no cohort studies specifically addressing fertility preservation in endometriosis have yet been published, it is difficult to make any recommendations. There is evidence that ovarian endometriosis is associated with depletion of the follicle pool (LoE2) and that surgery, especially when bilateral or repeated, can exacerbate the situation (LoE2) [28]. **Fertility preservation options must be discussed with patients undergoing surgery for ovarian endometriomas (Expert Consensus).**

Références

[1]

X. Fritel, P. Collinet, C. Revel-Delhom, M. Canis

RPC endométriose CNGOF-HAS, objectif, méthode, organisation, et limites

[CNGOF-HAS Endometriosis guidelines: Aim, method, organisation and limits]

Gynecol Obstet Fertil Senol (2018), 10.1016/j.gofs.2018.02.018

[2]

B. Borghese, P. Santulli, L. Marcellin, C. Chapron

Définition, description, formes anatomo-cliniques, pathogenèse et histoire naturelle de l'endométriose, RPC endométriose CNGOF-HAS

[Definition, description, clinicopathological features, pathogenesis and natural history of endometriosis: CNGOF-HAS Endometriosis Guidelines].

Gynecol Obstet Fertil Senol (2018), 10.1016/j.gofs.2018.02.017

[3]

C. Huchon, M.D. Aubry, G. Ploteau, A. Fauconnier

Signes spécifiques cliniques évocateurs de l'endométriose (hors adénomyose) et questionnaires de symptômes, de douleur et qualité de vie, RPC endométriose CNGOF-HAS

[Specific clinical signs suggestive of endometriosis (excluding adenomyosis) and questionnaires of symptoms, pain and quality of life: CNGOF-HAS Endometriosis Guidelines].
Gynecol Obstet Fertil Senol (2018), 10.1016/j.gofs.2018.02.022

[4]
I. Thomassin-Naggara, S. Bendifallah, P. Rousset, M. Bazot, M. Ballester, E. Darai
Performances et critères de qualité de l'IRM, du colo-scanner, de l'entéro-IRM/CT pour le diagnostic d'endometriose pelvienne, RPC endométriose CNGOF-HAS
[Diagnostic performance of MR imaging, coloscan and MRI/CT enterography for the diagnosis of pelvic endometriosis: CNGOF-HAS Endometriosis Guidelines].
Gynecol Obstet Fertil Senol (2018), 10.1016/j.gofs.2018.02.023

[5]
C.A. Philip, G. Dubernard
Performances et place de l'échographie dans le diagnostic de l'endométriose, RPC endométriose CNGOF-HAS
[Performances and place of sonography in the diagnostic of endometriosis: CNGOF–HAS Endometriosis Guidelines].
Gynecol Obstet Fertil Senol (2018), 10.1016/j.gofs.2018.02.026

[6]
A. Tardieu, F. Sire, T. Gauthier
Performances des endoscopies diagnostiques (coloscopie, fertiloscopie, hystéroscopie, cœlioscopie), RPC endométriose CNGOF-HAS

[Diagnostic accuracy of endoscopy (laparoscopy, hysteroscopy, fertiloscopy, cystoscopy, colonoscopy); CNGOF-HAS Endometriosis Guidelines].
Gynecol Obstet Fertil Senol (2018), 10.1016/j.gofs.2018.02.024

[7]
N. Bourdel, P. Chauvet, M. Canis
Stratégies diagnostiques dans l'endométriose, RPC endométriose CNGOF-HAS
[Diagnostic strategies for endometriosis: CNGOF-HAS Endometriosis Guidelines].
[Expectations of women with endometriosis: What information to deliver? CNGOF-HAS Endometriosis Guidelines].
Gynecol Obstet Fertil Senol (2018), 10.1016/j.gofs.2018.02.008

[8]
A. Denouël, A. Fauconnier, A. Torre
Attentes des femmes atteintes d'endométriose: quelle information apporter ? RPC endométriose CNGOF-HAS
[Expectations of women with endometriosis: What information to deliver? CNGOF-HAS Endometriosis Guidelines]
Gynecol Obstet Fertil Senol (2018), 10.1016/j.gofs.2018.02.005

[9]
A. Fauconnier, B. Borghese, C. Huchon, et al.
Synthèse épidémiologie diagnostique, RPC endométriose CNGOF-HAS
[Epidemiology and diagnosis strategy: CNGOF–HAS Endometriosis Guidelines].
Gynecol Obstet Fertil Senol (2018), 10.1016/j.gofs.2018.02.012

[10]

S. Geoffron, J. Cohen, M. Sauvan, G. Legendre, J.M. Wattier, E. Daraï, et al.

Traitement médical de l'endométriose : prise en charge de la douleur et de l'évolution des lésions par traitement hormonal, RPC endométriose CNGOF-HAS

[Endometriosis medical treatment: Hormonal treatment for the management of pain and endometriotic lesions recurrence. CNGOF-HAS Endometriosis Guidelines].

Gynecol Obstet Fertil Senol (2018), 10.1016/j.gofs.2018.02.011

[11]

J.M. Wattier

Antalgiques et alternatives thérapeutiques non médicamenteuses pluridisciplinaire, RPC endométriose CNGOF-HAS

[Conventional analgesics and non-pharmacological multidisciplinary therapeutic treatment in endometriosis: CNGOF-HAS Endometriosis Guidelines].

Gynecol Obstet Fertil Senol (2018), 10.1016/j.gofs.2018.02.002

[12]

G. Legendre, L. Delbos, E. Hudon, P.E. Bouet, P. Descamps

Place des nouveaux traitements médicaux dans l'endométriose douloureuse, RPC endométriose CNGOF-HAS

[New medical treatments for painful endometriosis: CNGOF-HAS Endometriosis Guidelines].

Gynecol Obstet Fertil Senol (2018), 10.1016/j.gofs.2018.02.009

[13]

M. Sauvan, N. Chabbert-Buffet, S. Geoffron, G. Legendre, J.M. Wattier, H. Fernandez, et al.

Traitement medical de l'endométriose douloureuse chez l'adolescente, RPC endométriose CNGOF-HAS

[Management of painful endometriosis in adolescents: CNGOF-HAS Endometriosis Guidelines].

Gynecol Obstet Fertil Senol (2018), 10.1016/j.gofs.2018.02.029

[14]

M. Sauvan, N. Chabbert-Buffet, S. Geoffron, G. Legendre, J.M. Wattier, M. Canis, et al.

Traitement médical de l'endométriose douloureuse sans infertilité, RPC endométriose CNGOF-HAS

[Medical treatment for the management of painful endometriosis without infertility: CNGOF-HAS Endometriosis Guidelines].

Gynecol Obstet Fertil Senol (2018), 10.1016/j.gofs.2018.02.028

[15]

S. Ploteau, B. Merlot, H. Roman, M. Canis, P. Collinet, X. Fritel

Endométriose minime à légère : résultats du traitement chirurgical sur la douleur et l'infertilité et modalités techniques. Quelles stratégies thérapeutiques ? RPC endométriose CNGOF-HAS

[Minimal and mild endometriosis: Impact of the laparoscopic surgery on pelvic pain and fertility. CNGOF-HAS Endometriosis Guidelines].

Gynecol Obstet Fertil Senol (2018), 10.1016/j.gofs.2018.02.004

[16]

C. Rubod, E. Jean dit Gautier, C. Yazbek

Traitement chirurgical des endométriomes. Modalités et résultats en termes de douleur, fertilité et récidive des techniques chirurgicales et de ses alternatives. RPC endométriose CNGOF-HAS

[Surgical management of endometrioma: Different alternatives in term of pain, fertility and recurrence. CNGOF-HAS Endometriosis Guidelines].

Gynecol Obstet Fertil Senol (2018), 10.1016/j.gofs.2018.02.013

[17]

M. Ballester, H. Roman

Prise en charge chirurgicale de l'endométriose profonde avec atteinte digestive. RPC endométriose CNGOF-HAS

[Surgical management of deep endometriosis with colorectal involvement: CNGOF-HAS Endometriosis Guidelines].

Gynecol Obstet Fertil Senol (2018), 10.1016/j.gofs.2018.02.003

[18]

P.A. Bolze, P. Paparel, F. Golfier

Localisations urinaires de l'endometriose. Resultats et modalites techniques de la prise en charge chirurgicale. RPC endométriose CNGOF-HAS

[Urinary tract involvement by endometriosis. Techniques and outcomes of surgical management: CNGOF-HAS Endometriosis Guidelines].

Gynecol Obstet Fertil Senol (2018), 10.1016/j.gofs.2018.02.016

[19]

B. Merlot, S. Ploteau, A. Abergel, C. Rubob, C. Hocke, M. Canis, et al.

Endométriose extra-génitale : atteinte pariétales, thoraciques, diaphragmatiques et nerveuses. RPC endométriose CNGOF-HAS

[Extragenital endometriosis: Parietal, thoracic, diaphragmatic and nervous lesions. CNGOF-HAS Endometriosis Guidelines].

Gynecol Obstet Fertil Senol (2018), 10.1016/j.gofs.2018.02.001

[20]

J. Loriau, E. Petit, A. Mephon, B. Anglieviel, E. Sauvanet

Moyen de prévention des complications anastomotiques digestives dans la chirurgie de l'endométriose profonde. RPC endométriose CNGOF-HAS

[Evidence-based ways of colorectal anastomotic complications prevention in the setting of digestive deep endometriosis resection: CNGOF-HAS Endometriosis Guidelines].

Gynecol Obstet Fertil Senol (2018), 10.1016/j.gofs.2018.02.007

[21]

B. Rabischong

RPC endométriose CNGOF-HAS

[Nerve sparing techniques in deep endometriosis surgery to prevent urinary or digestive functional disorders: Techniques and results: CNGOF-HAS Endometriosis Guidelines].

Gynecol Obstet Fertil (2018), 10.1016/j.gofs.2018.02.031

[22]

J. Niro, P. Panel

Intérêt de l'hystérectomie avec ou sans annexectomie bilaterale dans le traitement chirurgical de l'endometriose, RPC endométriose CNGOF-HAS

[Interest of hysterectomy with or without bilateral oophorectomy in the surgical treatment of endometriosis: CNGOF-HAS Endometriosis Guidelines].

Gynecol Obstet Fertil Senol (2018), 10.1016/j.gofs.2018.02.019

[23]

H. Roman, M. Ballester, J. Loriau, M. Canis, P.A. Bolze, J. Niro, et al.

Synthèse des stratégies et prise en charge chirurgicale de l'endométriose, RPC endométriose CNGOF-HAS

[Strategies and surgical management of endometriosis: CNGOF-HAS Endometriosis Guidelines]. Gynecol Obstet Fertil Senol (2018), 10.1016/j.gofs.2018.02.020

[24]

J. Boujenah, P. Santulli, E. Mathieu-d'Argent, et al.

Prise en charge de l'infertilité en première intention hors FIV : performances du traitement médical ? Performances de la stimulation ovarienne ? Performances des inséminations ? RPC endométriose CNGOF-HAS

[First line management without IVF of infertility related to endometriosis: Result of medical therapy? Results of ovarian superovulation? Results of intrauterine insemination? CNGOF-HAS Endometriosis Guidelines].

Gynecol Obstet Fertil Senol (2018), 10.1016/j.gofs.2018.02.021

[25]

C. Chauffour, J.L. Pouly, A.S. Gremeau

Prise en charge en FIV en cas d'endométriose, RPC endométriose CNGOF-HAS

[Management by assisted reproductive technology in women with endometriosis: CNGOF-HAS Endometriosis Guidelines].

Gynecol Obstet Fertil Senol (2018), 10.1016/j.gofs.2018.02.015

[26]

C. Chauffour, J.L Pouly, A.S. Gremeau

Endométriome et prise en charge en FIV, RPC Endométriose CNGOF-HAS

[Endometrioma and management by assisted reproductive technology: CNGOF-HAS Endometriosis Guidelines].

Gynecol Obstet Fertil Senol (2018), 10.1016/j.gofs.2018.02.014

[27]

E. Mathieu-d'Argent, J. Cohen, C. Chauffour, J.L. Pouly, J. Boujenah, C. Poncelet, et al.

Endométriose profonde et infertilité. RPC endométriose CNGOF-HAS

[Deeply infiltrating endometriosis and infertility: CNGOF-HAS Endometriosis Guidelines].

Gynecol Obstet Fertil Senol (2018), 10.1016/j.gofs.2018.02.006

[28]

C. Decanter, E. Mathieu-d'Argent, J. Boujenah, C. Poncelet, C. Chauffour, P. Collinet, et al.
Endométriose et préservation de la fertilité, RPC endométriose CNGOF-HAS [Endometriosis and fertility preservation: CNGOF-HAS Endometriosis Guidelines].
Gynecol Obstet Fertil Senol (2018), 10.1016/j.gofs.2018.02.010

[29]
P. Santulli, P. Collinet, X. Fritel, et al.
Stratégies de prise en charge de l'infertilité en Assistance Médicale à la Procréation dans un contexte d'endométriose, RPC endométriose CNGOF-HAS
[Management of assisted reproductive technology (ART) in case of endometriosis related infertility: CNGOF-HAS Endometriosis Guidelines].
Gynecol Obstet Fertil Senol (2018), 10.1016/j.gofs.2018.02.025