Review Article



# Review on endometriosis surgery

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**Background and Objective:** The indication and techniques of endometriosis surgery changed rapidly over the last 40 years since better understanding the disease and an improved diagnosis. This review will therefore include a short discussion of the importance and limits of evidence-based medicine (EBM), the clinical importance and diagnostic value of imaging and the alternative medical treatments.

**Methods:** PubMed was searched for '(endometriosis[Title] AND surgery[Title])' (n=564) and '(endometriosis[Title] AND diagnosis[Title])' (n=634) between January 1th 1985 till November 1th 2021 in English, French, Italian or German language. These articles were used to document endometriosis surgery as experienced by the authors with each an extensive experience of more than 25 years.

**Key Content and Findings:** Surgery is the cornerstone of infiltrating and fibrotic endometriosis and useful for minor endometriosis. We suggest redefining the aim of surgery, as the elimination of all endometrium like cells with genetic or epigenetic (G-E) endometriotic changes. Microscopic endometriosis in the peritoneum, in the bowel wall and in lymph nodes at distance from a deep endometriosis nodule does not need surgery since there is no evidence that it causes pain, infertility or progression into more severe forms of endometriosis. Subtle and typical lesions need excision or destruction since some of them might progress because of G-E changes. Excision of cystic ovarian endometriosis is associated with fewer recurrences, probably since more complete, but with more ovarian damage than superficial destruction of the lining of the cyst. However, since endometriotic infiltration in the cyst wall is less than 2 mm deep, the rest of the capsule being fibrosis, chemical superficial destruction might combine completeness with superficial treatment. For the surgery of deep endometriosis, the authors have reached consensus on many aspects. This comprises the prevention of nerve damage, the complete excision from the vaginal fornix, the complete excision from the bladder preserving the intramural ureter, ureter excision and anastomosis for fibrotic stenosis, short instead of large bowel resections when necessary and the liberal use of sigmoid resections. Other aspects remain debated, such as the excision of fibrotic endometriosis surrounding and extending below the ureter risking to damage the inferior hypogastric plexus, the exact indication of rectum resections versus complete excision with eventual suture of muscularis or mucosa versus limited excision completed by discoid excision with a circular stapler.

**Conclusions:** The concept of completeness of excision of deep endometriosis will be discussed since the outer layers might be metaplastic cells without G-E changes. The treatment of macroscopically fibrotic lesions without endometriotic cells is not clear.

**Keywords:** Endometriosis; surgery; deep endometriosis; cystic ovarian endometriosis; evidence-based medicine (EBM)

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## Introduction

Historically, the development of infertility and endometriosis surgery by laparotomy or laparoscopy and the development of laparoscopic surgery were linked. Laparoscopy was introduced in the early seventies and became widely used for the exploration of pelvic pain and infertility (1-4), and as a result, typical endometriosis was observed to occur in 50% or more in women with infertility or pelvic pain (5). During the same period, microsurgical principles were introduced for open infertility surgery (6,7), emphasising gentle tissue handling and adhesion prevention. Initially, laparoscopic surgery remained limited since performed by 1 surgeon with 1 surgical hand and rudimentary instruments as endocoagulation (8). The introduction of the $CO_2$ laser (9,10) and an operative laparoscope added a second instrument. This permitted treatment of superficial endometriosis, small endometriomas and minimal adhesiolysis (11). Tube video cameras were heavy, with little impact on laparoscopic surgery of endometriosis, which only started when lightweight and light-sensitive CCD video cameras, became available in the second half of the eighties (12,13). The reasonable images permitted surgery with 2 surgeons and 3 hands and thus more complex procedures. Over the following decade, the technique of endoscopic surgery developed rapidly in gynaecology and by the mid-nineties, most gynecologic interventions as hysterectomy, pelvic floor surgery, deep endometriosis and oncologic interventions had been translated into laparoscopic surgery. Simultaneously, abdominal surgeons had embraced laparoscopic surgery, often in cooperation with gynaecologists (14), and many of their interventions were progressively performed by laparoscopy.

This development of endoscopic surgery was facilitated by improved equipment. Milestones were better telescopes, better light sources, video-cameras requiring less light, a high flow insufflator (15), bipolar instruments permitting dissection, improved needle holders and linear and circular staplers. Whereas endoscopic surgery started with infertility surgery and $CO_2$ laser to vaporise superficial endometriosis, the broad field of destructive gynaecological and abdominal surgery brought stronger instruments and stimulated the anatomic dissection of tissues, the development of electrosurgery, and later ultracision and sealing instruments. This innovation which is still ongoing, can be illustrated by suturing and knot tying. Although considered essential skills in surgery, the understanding of knots is an achievement of recent years (16,17).

The development of endoscopic surgery, and more specifically of endometriosis surgery, has been a personal experience for the authors of this manuscript. Many aspects of endometriosis surgery are not yet "evidence-based" with randomised controlled trials. Besides the practical difficulties and the ethical considerations of performing such trials, the development of endometriosis surgery has been so rapid, that most potential trials would have become obsolete before being completed. Moreover, we do believe that the consensus opinion of experts is undervalued in the pyramid of evidence (18). Therefore, this article will be written as an authority based narrative review (19), reflecting the historical experiences and the personal opinions of the authors. Throughout the manuscript, it will be made clear what are consensus opinions of all authors and which topics are still debated in search of a consensus.

## Methods

PubMed was searched for '(endometriosis[Title] AND surgery[Title])' (n=564) and '(endometriosis[Title] AND diagnosis[Title])' (n=634) between January 1th 1985 till November 1th 2021 in English, French, Italian or German language. The articles found were updated with those of a personal endnote database (PK) to document endometriosis surgery as experienced by the authors with each an extensive experience of more than 25 years. The authors have been meeting and discussing endometriosis surgery more than twice yearly for more than 20 years. A draft (PK) reflecting these streamlined opinions was updated with the literature and reviewed and approved by all authors.

## Changing concepts of endometriosis

Endometriosis was described histologically more than 100 years ago and became defined as "endometrium like

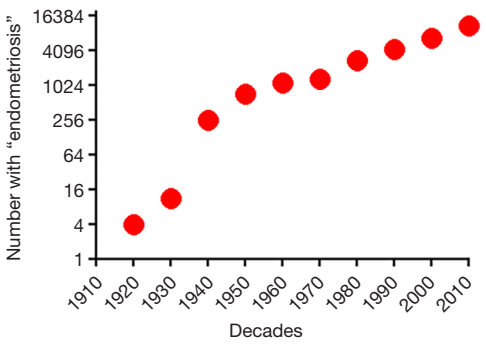


**Figure 1** The number of publications mentioning "endometriosis" increased exponentially since 1940.

glands and stroma outside the uterus". Following initial descriptions of adenomyosis like tissue (20) and severe rectovaginal disease called adeno-myoma (21,22) in the 19th century, the name "endometriosis" was coined by Meighs (23). In the 1920s (24,25) at least 18 articles describe cystic ovarian endometriosis and typical endometriosis or powder-burn black fibrotic lesions but only 4 used "endometriosis" (*Figure 1*). During the following decades, an explosive number of reports described endometriosis lesions found "occasionally" during surgery. By 1960 it was realized that up to 50% of interventions in gynaecology were performed for endometriosis (26,27). However, the true prevalence of endometriosis became apparent only when the frequent use of diagnostic laparoscopy in women with pain and infertility found the presence of typical endometriosis in over 50% of them. Later, when in the mid-eighties non-coloured lesions or subtle endometriosis (28,29) were recognised as endometriosis, the prevalence rose to 70–80% (30). Although severe rectovaginal adeno-myoma's had been described in the late 19th century, the high prevalence of similar, most of them smaller, lesions, was only realized after 1990 (31). As a historical anecdote, when Dan Martin visited Leuven, we went immediately after the excision of a 1 cm × 1 cm × 1 cm nodule to pathology and suggested to have a close look at the specimen. This and the observation that these women suffered from very severe pain, resulted in the first description of "deep endometriosis" (32). Unfortunately, the definition of deep endometriosis as more than 5 mm under the peritoneum, as suggested by the biphasic frequency distribution of depth of lesions (33) was a historical mistake since slightly deeper typical lesions also fitted this definition. Although deep endometriosis lesions were already described in 1989 (34), this overlap with deeper typical lesions still confuses the literature. Typical lesions are often multifocal while large deep endometriosis nodules are mostly unique albeit with cauliflower-like extensions.

The pathophysiology of these endometrium-like cells was explained already in the nineteenth century by metaplasia, a histological concept that indicates the transformation of a differentiated cell into another differentiated cell (24,35,36). The hypothesis of retrograde menstruation and implantation, known as the Sampson theory, was formulated in the nineteen twenties (24,25). This was a logical hypothesis with the then-available data obtained with light microscopy. However, the metaplasia and implantation theories persisted side by side, since the implantation mechanism could not explain all manifestations of endometriosis, e.g., in women without a uterus or endometrium (36). To explain extra-abdominal localisations of endometriosis like tissue the hypothesis of hematogenic or lymphogenic spread was formulated. Later, with the observations that retrograde menstruation was rather the rule than the exception (37), it was unclear why not all women had endometriosis and why the development of clinically more severe lesions occurred in some women only. Important is to realize that the mechanism of metaplasia was neither understood (38) nor explained.

More recently, epigenetics helped to explain how an identical genetic code in all cells of the body can result in histologically very different mature cells, as illustrated by epithelial-mesenchymal plasticity (39,40). However, we are only at the beginning of understanding epigenetic mechanisms, their inheritance, and which changes are reversible or irreversible. It seems likely that histologic metaplastic changes are mediated by epigenetic changes, some of which are reversible while others can become irreversible. Therefore, we will use in the rest of this manuscript instead of histological metaplasia, "reversible metaplasia" or "irreversible metaplasia" to indicate that these cells can or cannot return to normal.

Deep, cystic ovarian and typical endometriosis lesions were shown to be clonal in origin, and several lesions in one woman were found to represent different clones (41,42). All clinical observations on endometriosis as known today can be explained by the genetic epigenetic (G-E) theory (*Figure 2*) (33), which postulates that irreversible G-E changes, either in endometrial cells or in stem cells or even in bone marrow cells, initiate the development of typical, cystic or deep endometriosis lesions. Subtle endometriosis lesions are viewed as implanted normal endometrium or as cells looking like endometrium because of reversible

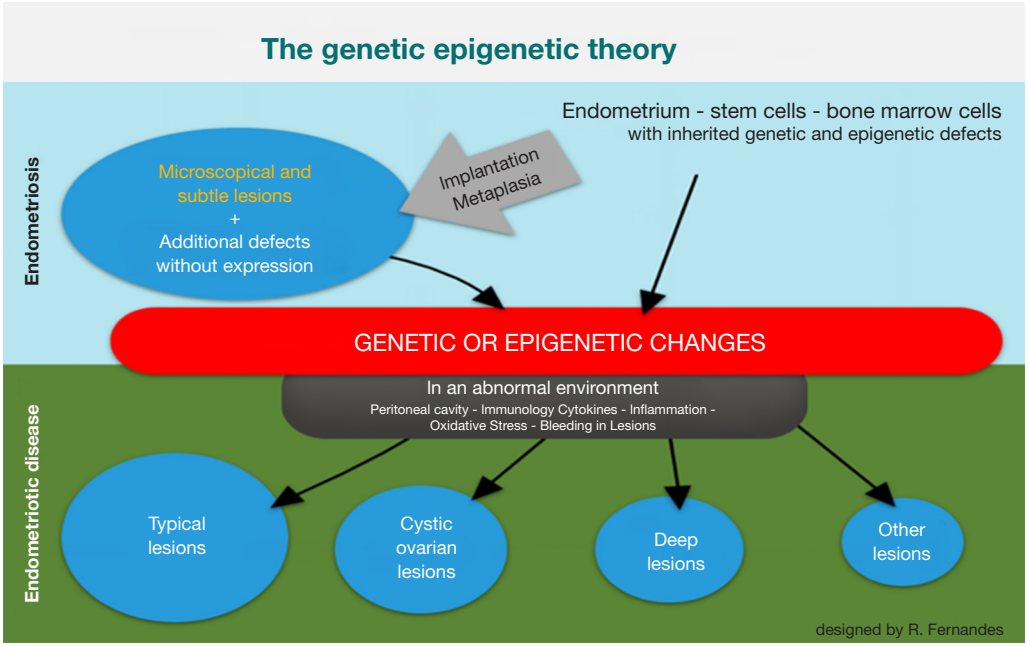


**Figure 2** The genetic epigenetic theory [reprinted with permission (33)]: a set of genetic or epigenetic (G-E) incidents is required to start endometriosis lesions; growth varies with the set of lesions and with the environment (43).

epigenetic changes, i.e., "reversible metaplasia"; however, some lesions that harbour cells with irreversible changes will develop into more severe endometriosis lesions. The growth of these cells with irreversible endometriotic lesions (43) will vary with their G-E incidents, and with the endocrine and immunological environment such as the peritoneal cavity. To understand endometriosis-associated pathology, we need to realize that some of these observations might be a consequence of endometriosis while others such as immunological changes and some changes in the endometrium were inherited as suggested from organoid studies (44). They signal the hereditary predisposition to initiate endometriosis and eventually influence the growth of the lesions (43). The driving motors of developing G-E incidents and thus of the onset of endometriosis lesions, are the inherited predisposition, together with additional incidents caused by irradiation or pollutants, by the oxidative stress of retrograde menstruation or bleeding in lesions and by infection and the microbiome in the pelvis and the upper genital tract (*Figure 3*) (45). Interestingly, the transmural migration of the intestinal microbiome might help to explain the effect of food intake and physical exercise on endometriosis.

These concepts of the pathophysiology of endometriosis are important for surgical treatment which remains driven by macroscopical and microscopic observations. We need to realise our limited understanding of the relationship between genetic-epigenetic-molecular biological mechanisms and morphological characteristics of endometriosis lesions (*Figure 4*). Unfortunately, today the surgeon cannot distinguish between endometrium like cells with "reversible metaplasia" induced by an external stimulus and cells with irreversible genetic or epigenetic changes. This is important since the former will return to normal after the triggering stimulus is removed, while the latter will remain abnormal. Clinically many subtle lesions, most microscopical endometriosis and endometriosis in lymph node are probably "reversible metaplasia". Subtle lesions can return to normal (46). Endometriosis like cells in lymph nodes were not yet reported to progress into clinical pathology notwithstanding the frequent occurrence in 18% of lymph nodes of women with deep endometriosis of the bowel. Also, the microscopical lesions in the bowel up to 5 cm or more from a deep endometriosis nodule (47,48) do not seem to be pathologic since recurrence rates of deep endometriosis are comparable after conservative nodulectomy, after small bowel resections and large bowel resections. Our interpretation is that the deep endometriosis nodule can induce surrounding cells, even at distance to undergo endometrium like "reversible

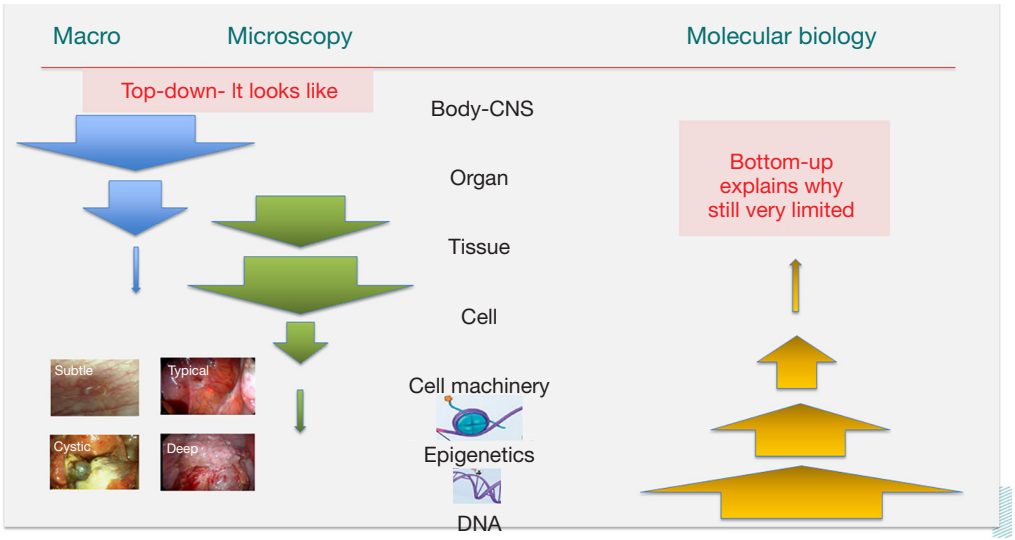


**Figure 3** The relationship of macroscopy and histology with molecular biological, epigenetic or genetic changes is still poorly established. CNS, central nervous system.

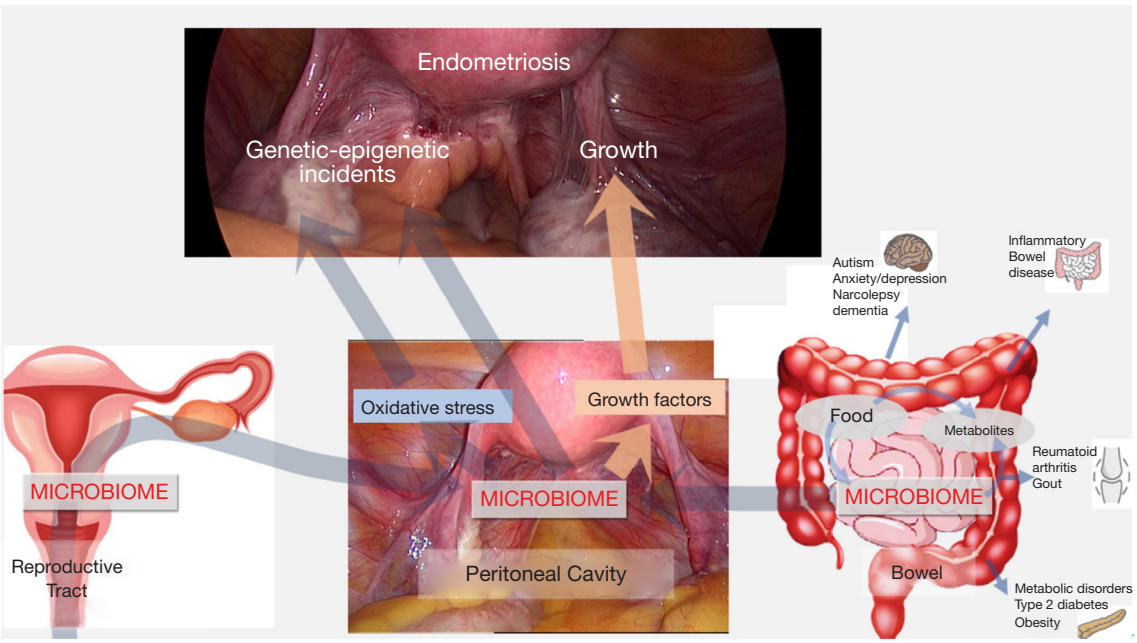


**Figure 4** Infection and the microbiota of the upper genital tract and the peritoneal cavity are cofactors in causing genetic or epigenetic (G-E) lesions leading to endometriosis [reprinted with permission from (45)].

metaplasia". Applied to deep endometriosis nodules, we speculate that the cells surrounding a deep endometriosis nodule are "reversible metaplastic cells", since conservative excision which must be incomplete at the cellular level is not associated with more recurrences. After removal of the nodule, we expect them to disappear or to become inactive (*Figure 5*) (49). Important is that hypotheses about pathophysiology of endometriosis are not used to guide surgery. Surgery remains based on all available evidence. However, theory might help to understand them.

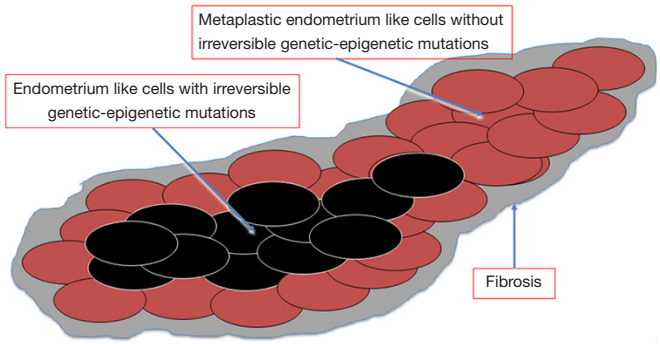


**Figure 5** The outer layer of deep endometriosis might be metaplastic cells without genetic or epigenetic (G-E) changes since recurrence rates are similar after conservative surgery or short or large bowel resections [reprinted with permission (49)].

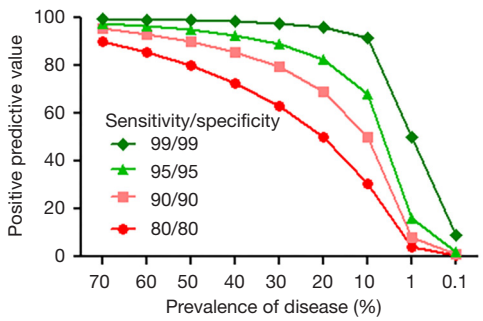


**Figure 6** The positive predictive value of imaging decreases rapidly when the prevalence of the disease is less than 5% [reprinted with permission from (50)].

## Imaging of endometriosis before surgery

The diagnostic accuracy and especially the predictive value of ultrasound and magnetic resonance imaging (MRI) imaging are not clear (50). However, clinical decision making is not based on the accuracy of a test, but on positive and negative predictive values. The clinician needs to know the probability that endometriosis is present or absent. A major problem, well known but poorly recognised, is that predictive values decrease sharply with the prevalence of the disease (*Figure 6*) (50). Therefore, unless accuracy is very high—over 99%—predictive values become unreliable for prevalence below 5%. This should be taken into account for the prevalence of deep endometriosis. Another cause of debate is that imaging generally reports the diagnostic accuracy of symptoms and clinical exam and imaging taken together. Only recently Bayesian analysis was used to investigate the added value of imaging when symptoms and clinical exam are known (51,52). A third problem is that the clinician needs clinical endpoints to be estimated such as the predictive value of a nodule of 1 or 2 cm or the depth of infiltration of the muscularis, etc. This is very different from the accuracy of the diagnosis of all types of deep endometriosis. Superficial endometriosis can't be diagnosed by imaging.

To diagnose cystic ovarian endometriosis, transvaginal ultrasound is the method of choice. However, the diagnostic accuracy to exclude a cystic corpus luteum (53) or ovarian cancer (54) is limited and requires repetitive exams and their prevalence are low. Therefore, the positive and negative predictive values, become unreliable and a cystic corpus luteum needs to be excluded by inspection during surgery. For the same reason surgery for cystic ovarian endometriosis after menopause needs to be done very carefully because of the risk of ovarian cancer.

A full discussion of the value versus the added value of imaging (51,52) in surgery for deep endometriosis is beyond the scope of this manuscript. The added value is controversial for the arguments explained above notwithstanding high sensitivities and accuracies for detecting "deep endometriosis" and bowel invasion. However, imaging is also important for estimating the difficulty and duration of surgery and thus for counselling the patient before surgery. Unfortunately, to the best of our knowledge, the value of imaging to decide before surgery which type of surgery will be needed has only been determined in retrospective descriptive reports (55). The surgeon, therefore, must besides understanding the disease, be able to face different situations and to master the different techniques which may be required.

## Evidence-based medicine (EBM) and Surgery

Diagnosis and therapy should be based on evidence,

obtained without selection bias, patient bias or placebo effect, and observer bias by the believer or surgeon. Therefore, the randomised controlled trial (RCT) became the top of the pyramid of evidence. However, over the last decade, it was realised that the RCT is a slow tool in gathering data and that an RCT is not suited for rare events since a 1% event requires an RCT of 6,000 women to have 30 events in the control group. The RCT is also not suited for multimorbidity or when the variability of disease or treatment is high since strict inclusion and exclusion criteria are needed to avoid prohibitive large numbers to be included and to avoid irrealistic long trials. Also, ethical concerns limit RCTs when the indirect evidence is already reasonably high, as evidenced by the absence of RCTs demonstrating the efficacy of parachutes. EBM thus is a valuable tool with limitations (56-58). Important for the surgeon is to realise that EBM is only the probability that an estimated difference is not caused by chance and that it is an artificial convention that a probability of less than 5% is considered clinically significant. With this definition 5% of significant results might be wrong. Equally important is that "not significant" does not permit the conclusion "not true" since this can be due to many other factors such as a low number of observations. Moreover, the absence of difference does not permit to conclude that there is no difference which requires non-inferiority trials (59) or a different type of statistical analysis needing a much larger sample size.

For these reasons, the RCT is poorly suited to evaluate endometriosis surgery. The disease is variable, ethical concerns and informed consent limit a control group with no treatment or treatment which is considered less good. Therefore, the consensus opinion of expert surgeons (18) is the best alternative to combine multimorbidity and the variability of disease and the many treatment options with a rapidly changing understanding and technology.

Surgery has inherent limitations and biases. Surgical skills and quality of surgery are well known to be variable. However, there is no agreement on which aspects are important and how to evaluate them. For the same reason, video registration (60) as a tool to evaluate the outcome of surgery is not yet accepted.

## Classification of endometriosis

Several classifications of endometriosis have been proposed. Classifications have been a common-sense scoring of the severity of endometriosis and adhesions, but none of them has been validated yet to predict postoperative pain, infertility or recurrence rates (61). The revised American Fertility Society (rAFS) classification (62) is a point scoring system in which adhesions were added to the Acosta classification (63). When analysed, AFS I and II reflect mainly superficial endometriosis with a pelvic area of less or more than 3 $cm^2$ respectively, while AFS III and IV contain cystic ovarian endometriosis. However subtle and deep endometriosis are not reflected in this classification, deep endometriosis being mainly found in AFS II (30). The AFS classification thus, not surprisingly, poorly predicted the outcome of surgery (64). Since localisation and surgical difficulty of deep endometriosis are very variable, the Enzian classification was developed (65,66) describing accurately the localisation and size of deep endometriosis. This scoring correlates as expected, with symptoms and clinical findings (67), with the difficulty and duration of surgery (68) and with postoperative complications (69). This classification was recently updated and expanded with other endometriosis lesions (70). Promising as a preoperative tool is the Enzian scoring by ultrasound (71,72) or MRI (73,74), combining all endometriosis lesions found by ultrasound and MRI with the clinical findings or Enzian score during surgery (*Figure 7*). This might result in improved use of preoperative investigations for the indication and type of surgery.

## Surgery for endometriosis

Surgery for endometriosis has historically been based on the concept of the removal of macroscopically recognised endometriotic tissue.

### *Technique of surgery and energy sources*

Endometriosis surgery varies from minor superficial destruction of lesions which can be performed with 1 or 2 secondary ports, to very severe disease requiring dissection and 3 secondary ports. Although a thorough discussion of the different energy sources is beyond the scope of this manuscript, some principles should be clear. An energy source (75) is characterised by its cutting and coagulating properties and by the amount of dead tissue left behind. The $CO_2$ laser is completely absorbed (because of its wavelength) in water or superficial tissue layers. A high-power density thus causes superficial cell heating and vaporisation with minimal tissue damage (less than 100 μ) but also with limited coagulation. Low power densities will heat tissue and necrosis will vary with the duration of contact and heat diffusion. The effect of electrosurgery varies with the

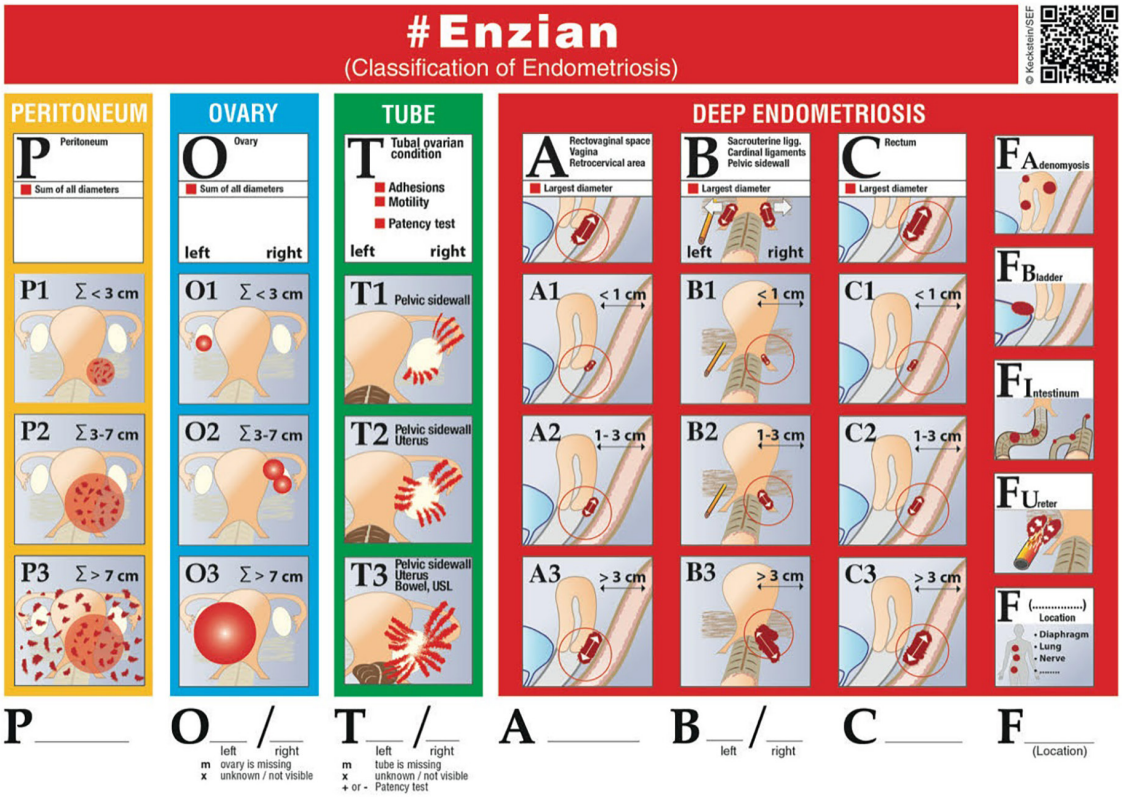


**Figure 7** The new-Enzian classification with all affected organs and compartments. The Enzian classification is based on the known Enzian classification for deep endometriosis using 3 compartments [A: vagina, rectovaginal space (RVS), retro-cervical area; B: sacro-uterine ligaments/cardinal ligament/pelvic sidewall and C: rectum] as well the urinary bladder (FB) the ureters (FU) and other extragenital lesions (FO), it also covers the involvement of the peritoneum (P), ovary (O), other intestinal locations (sigmoid colon, small bowel, etc. FI), as well as adhesions involving the tubo-ovarian unit (T), and optionally, tubal patency.

voltage used. Below 200 V (soft coagulation) the depth of heat generation decreases exponentially with the distance. The vaporising or cutting effect of a spark of 200 V, e.g., with a point electrode, is very similar to a $CO_2$ laser, but higher voltages increase the depth of tissue damage and thus also better coagulation. Electrosurgery is less suited for fat tissue except when used in sealing devices controlling tissue temperature. Electrosurgery is the most versatile source of energy, but needs to be applied correctly in order to avoid complications. The effect of other lasers varies with their wavelength. The argon laser is adsorbed specifically by red colour but is no longer used for endometriosis surgery (76). The wavelength of more recent diode lasers varies. This determines their adsorption and their use with a fibre and their depth of tissue penetration. The plasma jet is used in a similar way as lasers, but the penetration and tissue effect is to the best of our knowledge not clear. Ultrasonic energy has limited lateral spread of heat. Although less suited for point coagulation, is offers excellent cutting and coagulation including fat tissue with minimal tissue damage.

### *Subtle endometriosis*

Many subtle endometriosis lesions may be transient (46), which is logical if considered implanted normal endometrium, or cells with reversible G-E changes. However, it seems wise to destroy them during surgery, since some of them probably will develop into more severe lesions when harbouring 'irreversible endometriotic G-E changes' and since about half of them are painful during conscious pain mapping (77,78). Destruction by coagulation or laser vaporization is moreover fast with minimal surgical risk.

It has not been demonstrated whether the destruction of subtle lesions decreases pain or increases fertility, or

decreases recurrence rates. Considering that many subtle lesions are transient occurring intermittently in most women (79) following retrograde menstruation, it is not surprising that early surgical treatment is associated with high reoperation rates.

### *Typical endometriosis*

Typical endometriosis lesions need excision or vaporisation. Although bloodless $CO_2$ laser vaporisation is faster and more precise than surgical excision (80,81), $CO_2$ laser surgery has become less used over the last decades. First, the optical quality of the (older) operative endoscopes is not as good as the newer generation of straight endoscopes. Since $CO_2$ laser surgery is less suited for the more severe forms of endometriosis requiring dissection, telescopes have to be changed during surgery. Finally, the technique of $CO_2$ laser surgery requires specific expertise and training of the surgeon holding the laser and of the assistant holding 2 instruments including the bipolar for coagulation. As a result, the expertise in $CO_2$ laser surgery is slowly disappearing. This change over time is best illustrated by personal experience (PR Koninckx) using in the nineties always a $CO_2$ laser as a standard set-up, while today we use the $CO_2$ laser only in women with extensive superficial endometriosis. The efficacy of diode lasers used with fibre through a secondary port is not yet clear.

Excision or destruction of typical lesions decreases chronic pelvic pain (82,83). However, it remains unclear whether it affects fertility or recurrence rates (84). The only trial, the endocan trial, demonstrating an increased fertility rate can be challenged since the trial was not blinded. Besides, the fertility rates in the treated group were as expected in women with unexplained infertility whereas fertility in the untreated group was lower than expected. We interpret this trial as suggesting that the fertility in the untreated women decreased after having been told that they still had typical endometriosis, possibly by psychological stress in women with high trait anxiety (85-88) possible secondary to the luteinized follicle syndrome (89-91). Whether surgery of typical endometriosis affects recurrence rates has not been adequately investigated.

### *Cystic ovarian endometriosis*

There are no prospective randomised data comparing superficial destruction of cystic ovarian endometriosis and excision of the cyst wall (92,93). Reported cumulative pregnancy rates (CPR) after surgery are around 60% after 1 year (94). Improvement of pain is assumed to be similar for both techniques. Recurrence rates around 20% after superficial destruction, are believed to be higher compared to the 5% to 7% rate after excision. That excision is more harmful to the ovarian reserve was repetitively reported (95-99) although not confirmed in a recent review (100).

The surgical interpretation of these observations needs a common-sense evaluation. The superficial destruction of the surface of cystic ovarian endometriosis with $CO_2$ laser, or argon beam coagulator (101) or bipolar coagulation, is difficult to standardise. The depth and completeness of destruction are variable and vary with the expertise and the understanding of the surgeon of completeness of destruction versus ovarian damage. The excision of the wall of the endometrioma can be technically difficult surgery (102) with many associated problems. These are, bleeding needing more coagulation when the plane of cleavage is not correct; bleeding and coagulation of the artery or vein from the hilus with subsequent partial ischemia of the ovary; removal of ovarian tissue because of difficulty or errors in surgical judgment especially when confronted with multiple endometriomas; and finally, excision of large endometriomas leaving a thin rim of a poorly vascularized ovarian capsule. These technical considerations explain that surgery and results vary with the skill and the attitude of the surgeon (103). These aspects become even more important when cysts are large, multiple and when associated with severe adhesions or a frozen pelvis. Advantages and disadvantages of ultrasonic energy in cyst excision is not yet clear.

The capsule of an endometrioma probably is mainly fibrosis (104,105) since the depth of invasion of endometriosis into the cyst wall seems limited to less than 2 mm (106,107). Therefore, chemical destruction, e.g., with alcohol seems a logical approach (108). This technique, however, is poorly standardised and evaluated although preliminary results are encouraging.

The indication for surgery of cystic ovarian endometriosis of less than 3 cm in diameter especially in adolescents and when infertility is the only complaint remains debated. It can be argued that the dilemma is early surgery with the risk of a second intervention for recurrences versus delayed surgery with the growth of the cyst and more ovarian damage and more difficult surgery and more ovarian damage (109). When infertility is the only problem, we know that the results of in vitro fertilisation (IVF) are similar in women without and with a small cystic ovarian endometriosis.

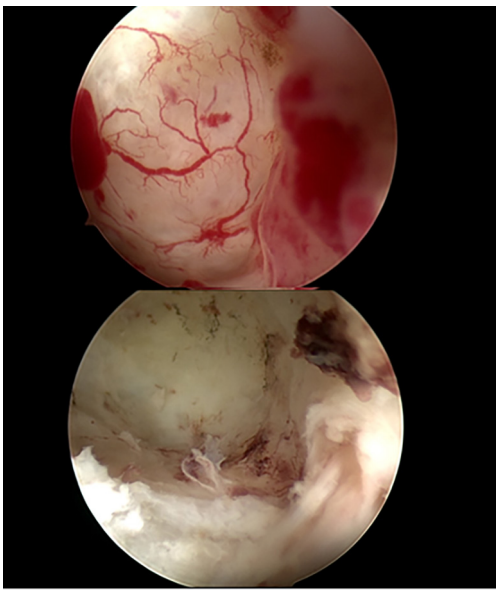

**Figure 8** Transvaginal-hydro-laparoscopy (THL) and inspection of (smaller) cystic ovarian endometriosis followed by underwater bipolar coagulation, without causing postoperative adhesions [courtesy Prof S. Gordts, Belgium and reprinted with permission (49)].

In conclusion, we suggest approaching cystic ovarian endometriosis as follows. Avoid surgery for a cystic corpus luteum by dedicated ultrasonographic exam and inspection during surgery. Unfortunately, this needs clinical judgments since even inspection is wrong in 27% (110). A cystic corpus luteum should be suspected whenever the onset of pain was acute or when confronted with a chocolate cyst without adhesions. In doubt, it is preferable to postpone surgery with ultrasound follow-up. For smaller cysts, especially in young women, the transvaginal-hydro-laparoscopy (THL) with underwater coagulation of small endometrioma's should be considered (111) since the procedure is minimally invasive with minimal or no adhesion formation (*Figure 8*) (92,112). Excision of a cystic ovarian endometrioma of more than 6 cm especially when located centrally in the ovary should be avoided because of the associated risk of ovarian damage. Therefore, a two-step approach is preferable, with drainage and 3 months of gonadotropin-releasing hormone (GnRH) treatment followed by a second intervention with excision if needed. When associated with severe pelvic pain only, the choice between excision and superficial destruction is unclear although we tend to use superficial destruction when cysts are smaller than 2 cm and to excise when between 3 and 6 cm.

### *Deep endometriosis*

Surgery for deep endometriosis can be technically challenging because of distorted anatomy, the involvement of bowels, ureters and bladder. Although the goal of surgery is the excision of the endometriosis lesion, surgery always was a balance between completeness of excision and prevention of complications, as reflected by technical choices. These were initially very different mainly because of local preferences (113), but over the last decades, many aspects of surgery have evolved into a consensus between the authors.

Complete excision of deep endometriosis from the bladder wall, with a muscularis or a full-thickness resection, if necessary, is clear since suturing of the bladder in one or two layers and healing is uneventful. Technically a few rules are considered important. First, when the bladder needs to be opened, enter ventrally to avoid a lesion to the ureter. Second, following a bladder suture, confirm the absence of leakage, and use a bladder catheter which can eliminate blood clots, and leave the catheter for at least 1 week. It is wise to check the healing before removing the catheter. Whereas historically, the nodule was resected first from the uterus, we today prefer to start for larger nodules with a lateral dissection with identification of the ureters. When the trigonum is involved prudence requires two double J stents and it is a surgical choice to balance completeness of excision with postoperative bladder instability.

Excision of deep endometriosis involving the ureter or requiring ureter dissection has become straight-forward. Consensus has been reached that for deep endometriosis it is wise to always identify and/or dissect the ureter respecting the lateral vascularisation to avoid unexpected damage. The systematic use of a double J is not required unless there is stenosis with hydronephrosis. A double J does not protect the ureter, but lesions of the ureter are recognised easier and a ureter resection is facilitated if needed for severe stenosis and hydronephrosis (114-117). The resection and a 4–5 stitch anastomosis of the ureter over a double J (118-120), although technically challenging has become widely adopted since an uneventful procedure (121). The treatment of ureter stenosis, therefore, has evolved towards a more liberal use of resection—anastomosis instead of a difficult and lengthy ureterolysis with the repair of an eventual trauma of a fibrotic ureter. It remains unclear, whether an epiploon flap to accelerate healing and to protect the ureter

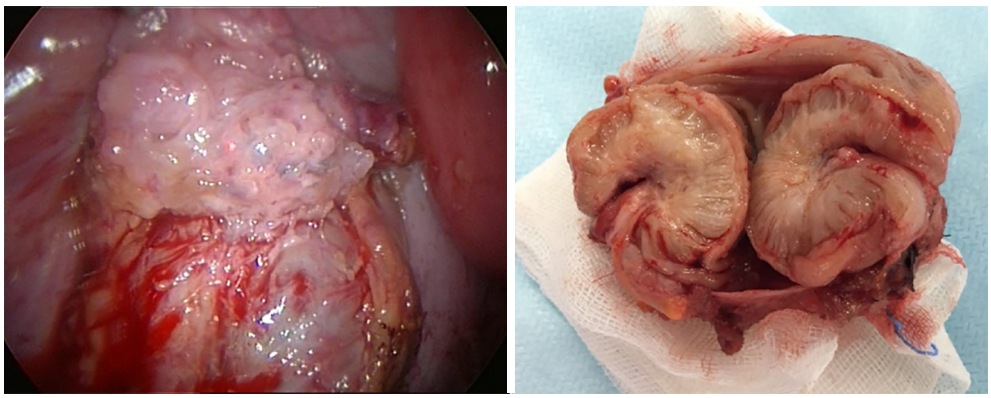

**Figure 9** Images of conservative excision of an endometriosis nodule from the bowel up to the mucosa (left) leaving a large muscularis defect to be sutured and of a short bowel resection (right) [reprinted with permission (49)].

is helpful. When a larger segment of the ureter needs to be resected with traction on the anastomosis, and when the resection is close to the bladder wall, reimplantation with a psoas hitch should be considered.

The conservative excision of an endometriosis nodule from the sigmoid is feasible for nodules up to 2 cm. However, this is complication prone and technically difficult surgery. Most sigmoid nodules require a transmural discoid resection which is difficult to suture, because of the mobility of the sigmoid and because of its location cranial from the secondary trocars. The sigmoid also is often difficult to reach with a circular stapler. Since the complication and leakage rate of sigmoid resections is very low a liberal use of short sigmoid resections has reached consensus [for review (49)].

Consensus has not yet been reached for the low rectovaginal nodules, which can be excised conservatively or treated with bowel resection and anastomosis. The main argument in favour of a conservative excision of low rectum and high rectovaginal nodules is that it can be done with a similar postoperative complication rate and a similar recurrence rate than following a resection anastomosis (49). This avoids the higher leakage rates and the nerve damage with bowel and bladder instability and sexual disturbances after low rectum and ultra-low rectum resections (122). Resection anastomosis, on the other hand, has the advantage of being better standardised and faster surgery. It also is the favoured technique of bowel surgeons. The choice of technique therefore mainly depends on the size of the nodule.

Besides these arguments, the debate is also caused by the background and the expertise of the surgeons. Traditional bowel surgery starts with the mobilisation of the rectum and thus with dissection between the nodule and the uterus/vagina. However, this results in a mobile rectum and makes the resection of the nodule more difficult. Those who started with infertility surgery and thus with a $CO_2$ laser left the nodule attached to the uterus/vagina to pull the nodule upwards and started dissection between the nodule and the rectum. Only after the rectum has been freed from the endometriosis, the nodule is dissected from the posterior wall of the uterus or vagina. This approach can result in a large muscularis defect when the nodule is bulging into the rectum (*Figure 9*) necessitating large single or double-layer sutures, a procedure which most gynaecologists and bowel surgeons are not used to do. Over the last decades, both approaches have evolved in the same direction. Following a conservative debulking of the nodule from the rectum, the remaining endometriosis is removed with a circular stapler (123). This approach has the advantage that bowel openings are avoided, and that difficult and lengthy suturing is replaced with a circular stapler. Another important recent innovation is the short bowel resection (*Figure 9*) limiting the resection to that part of the bowel containing the nodule. The required dissection and the reduction of the reservoir function of the rectum are less. Preliminary results suggest that healing is fast and that recurrence rates are not increased (personal communication A Wattiez). A short resection thus favourably replaces the larger bowel resection based on vascularisation. It is too early to discuss the advantages and disadvantages of a short bowel resection versus a more conservative approach. It is also difficult to compare the results of suturing with the outcome of a wedge resection with a circular stapler since the quality of suturing is

surgeon dependent. Emerging elements are the use of indocyanine green to check vascularisation of the rectum and thus the safety of sutures and anastomoses (124-127).

## Prevention of postoperative adhesion formation

Prevention of postoperative adhesions is important for all abdominal and endometriosis surgery because of the associated infertility, the chronic pain and the occasional bowel occlusions. The suggestions formulated by microsurgery, have been investigated and confirmed recently (128).

Before surgery, it is important to treat eventual vaginal infections since they are associated with a less favourable peritoneal cavity microbiome. It is unclear whether preoperative anti-oxidants are useful. Surgery should be performed with gentle tissue handling, as fast as possible, with a minimal insufflation pressure and with the addition of some 10% of $N_2O$ to the $CO_2$ pneumoperitoneum. Blood and fibrin deposits should be avoided while saline as a rinsing liquid should be replaced with Ringers lactate. The pneumoperitoneum should be kept between 25 and 31 °C without desiccation. Dexamethasone at the end of surgery is probably beneficial. With the combined use of gentle tissue handling, 10% of $N_2O$, low insufflation pressure, lower temperature, adequate rinsing liquid, coined peritoneal conditioning, and a barrier at the end of surgery adhesion free surgery has become feasible (129,130).

## Prevention of complications

The main complications of typical endometriosis and cystic ovarian endometriosis surgery are postoperative adhesions and the decrease in ovarian reserve. The former can be decreased by adequate surgery and peritoneal cavity conditioning (129,130). The cause of the eventual decreased ovarian reserve following ovarian endometriosis surgery is the cumulative effect of a decreased ovarian reserve caused by the endometrioma, and the damage during surgery. It has been suggested that careful surgery by a skilled surgeon is associated with minimal damage to the ovarian reserve (102,131).

Deep endometriosis surgery is complication prone surgery involving the bladder, the ureter and the bowel. The first aspect of prevention consists of a checklist at the end of surgery (132) to judge eventual risks. This checklist will result in the decision to use a drain, a double J, postoperative antibiotics, etc. The second and most important prevention of serious postoperative complications is an early diagnosis by checking the patient twice daily, by daily C-reactive protein (CRP) (personal communication PR Koninckx) measurements and by the liberal use of a second look laparoscopy. The patient should always improve and CRPs should decrease from day 3 onwards, otherwise, something is wrong. An early repeat laparoscopy will be beneficial in case of bleeding, infection or ureter or bladder leak. It is mandatory for bowel perforation, most of them occurring after surgery (133) since this pathology can be treated conservatively with suturing of the bowel lesion and lavage if diagnosed within 24 hours.

## The alternative therapy of endometriosis: medical and IVF

A full discussion of the pro and cons of medical therapy (134) is beyond the scope of this manuscript. Progestins and the absence of estrogens reduce or prevent the proliferation of the endometrium. Sampsons implantation theory suggested that this was also true for endometriosis. However, endometriosis lesions are clonal and thus individually variable and heterogeneous. Some of them are resistant to progesterone while some have an increased aromatase activity (135). Some lesions with strong progesterone resistance therefore will escape the effect of progesterone while others can grow when treated with estroprogestins (136). Some lesions can grow when plasma estrogen concentrations are low as demonstrated by growing deep endometriosis lesions after menopause and in the absence of estrogen treatment (137). Solid data concerning clinical prevalence are not yet available.

With these considerations, medical treatment before surgery is not recommended. There is no proven benefit while small lesions might be missed (138). It is unclear whether medical treatment can jeopardise complete excision of extensions of deep endometriosis nodules. Medical treatment for many years without a diagnosis, especially in those with incomplete pain relief, should be avoided since many women risk to be treated for endometriosis without having endometriosis, while some lesions can continue to grow during medical treatment. The latter is suggested by the repetitive observations by the authors (PR Koninckx, A Ussia, J Keckstein, L Adamyan, M Malzoni, A Wattiez) of severe deep endometriosis nodules in women who had been taking medical therapy for more than 10 years. That adequate ultrasonographic follow-up can prevent this is likely but not yet demonstrated. Also, the promotion

of medical treatment as prevention of surgery (139) is inappropriate as most reports review selectively the risks of endometriosis surgery (140). They fail to balance the benefits and risks of surgery and fail to address the potential harm done by postponing surgery, ignore the eventual growth of lesions and more difficult surgery later.

An inconvenient truth is that traditional statistical analyses are not suited to analyse heterogeneity. Homogeneity of a population is a fundamental and necessary assumption for statistics. This consideration cast doubt on all published data of medical therapy including RCTs since the traditional statistical analyses can hide subgroups of women in whom medical therapy might be damaging (136).

Many reports describing the results of IVF treatment in women with endometriosis should be considered critically. The pregnancy rates of IVF treatment in women with cystic ovarian endometriosis is similar with or without prior surgical treatment. This observation does not exclude that IVF may be harmful in these women and that the ultimate CPR will be lower. The procedure of oocyte pick-up may induce pelvic adhesions, a risk that is possibly enhanced by the increased pelvic inflammation in endometriosis. Massive pelvic adhesions indeed are a repetitive observation during surgery following several IVF attempts (PR Koninckx, A Ussia, J Keckstein, L Adamyan, M Malzoni, A Wattiez unpublished data). Severe complications of deep endometriosis nodules during pregnancy are well known (141) and probably underreported in the literature. Because of pregnancy complications and adhesion formation, it seems unwise to proceed with IVF in women with untreated deep endometriosis nodules and possibly also those with cystic ovarian endometriosis. Counselling and involving the patient cannot solve the absence of solid data and conclusions. Unfortunately, the complementary values of surgery and IVF (142) have not been investigated adequately.

## Discussion

Endometriosis surgery has been reviewed repetitively (143,144). Endometriosis surgery requires a balanced consideration of the diagnosis of endometriosis, the indication of surgery, the quality surgery and the postoperative care, taking into account alternative treatments. Unfortunately, a comprehensive discussion including all aspects is rarely available, since literature reports are mostly specific and selective. Also, reports are written by specialists in their field, which often lack a clear understanding of the other aspects. Every specialist is moreover often emotionally biased since as humans we tend not to cut the branch of a tree on which we are sitting. We are fully aware of this risk since this review is written exclusively by endometriosis surgeons.

The pitfalls of surgery for endometriosis begin with the diagnosis. Endometriosis is a probability, based on the age and background of the woman and her symptoms, the clinical exam and imaging. Unfortunately, the diagnosis of endometriosis remains a probability which often needs a diagnostic laparoscopy to confirm or exclude the diagnosis. The question of when to do surgery for endometriosis, therefore, should be separated into two sequential questions. The first question is whether a diagnostic laparoscopy is indicated to confirm the diagnosis since at least subtle and typical endometriosis require a laparoscopy for diagnosis. The second question is what should be done when during laparoscopy endometriosis is found, and for this aspect preoperative imaging can help helpful. Women with a clear diagnosis because of a big palpable and painful nodule or cystic ovarian endometriosis need surgery. In all other women, it remains an art, based on clinical experience to judge symptoms, severity and localisation of pain, duration of infertility, clinical exam and imaging and to translate them into a decision to perform a laparoscopy and to anticipate surgery. A frequent misunderstanding in the literature is that the value of imaging and other additional exams is rarely judged separately as the added value to make the indication for laparoscopy or as a guide to anticipate surgery. Clinically important is the added value of these exams when symptoms and clinical exams are known already. This, however, requires Bayesian analysis which only recently started to be performed for endometriosis. It should be understood that imaging cannot add to a diagnosis which was already made, e.g., in women with a vaginally visible deep endometriosis nodule. The value of imaging in preparing for surgery and counselling is poorly investigated and beyond this discussion. When during a diagnostic laparoscopy the diagnosis of endometriosis is confirmed, whether to proceed with surgery or to schedule surgery during another intervention becomes a surgical judgement. This requires balancing the circumstances, the skills of the surgeon and the anticipated difficulty of surgery, which unfortunately can become apparent only during the intervention. It seems likely that preoperative imaging might help in this.

Quality of surgery has many variables and is difficult

to judge. Although opinions may vary, surgeons overall recognise the quality of surgery. It is easier to recognise good surgery than to describe the rules and elements, similar to "it is easier to recognise a miracle than to do a miracle".

Adequate surgery and postoperative care require an experienced team. Although this seems obvious, the importance of the team and their experience are uncommonly discussed and are not transparent in the literature of surgery.

It is unclear whether asymptomatic endometriosis does require therapy. In the absence of symptoms, superficial endometriosis will remain undiagnosed but might progress. Unfortunately, the value of imaging in monitoring progression is speculative today. Similarly, the risk of progression with ovarian damage of small cystic ovarian endometriosis is unclear, especially in puberty. Asymptomatic deep endometriosis nodules do not need treatment, although it might be unwise to proceed to IVF without surgery with the risk of pregnancy complications. Medical therapy does not cure endometriosis although it can be effective in reducing pain. The indications of medical therapy are not yet clear and anyway beyond the scope of this review. In the absence of data, it is unclear whether surgery should be postponed when medical therapy is effective in abolishing pain. It remains unclear whether monitoring the development and progression of the disease by ultrasound is clinically useful (145).

In conclusion, the diagnosis of superficial endometriosis needs a laparoscopy. The diagnosis of severe endometriosis can often be made clinically or by imaging as discussed. Severe endometriosis with severe pain needs surgery in the absence of contraindications. During surgery, all endometriosis lesions should be removed. We do not have data to balance the risks of surgery and the risks during pregnancy or the risk of progression in asymptomatic deep endometriosis. If during the laparoscopic inspection the surgeon estimates not to have the appropriated skills matching the expected difficulty of surgery it is preferable not to proceed and to refer the patient. If the patient refuses surgery medical therapy can be discussed, knowing that medical therapy will not cure the disease and will not prevent progression in all women. However, medical therapy for many years is not indicated in the absence of a diagnosis, and is rarely indicated when surgery was incomplete because of the estimated difficulty. Therefore, medical therapy is mainly indicated after a diagnostic laparoscopy with surgery. The aim of medical therapy after surgery is not the treatment of pain if excision has been complete. We postulate, however, that medical therapy, might have an important role in preventing recurrences by reducing retrograde menstruation and oxidative stress and by preventing ascending infection.

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