

Laser Surgery for endometriosis

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1 INTRODUCTION

The definitions and our understanding of endometriosis have changed over time. Endometriosis was introduced clinically at the beginning of this century, as ovarian “chocolate cysts”¹ and as adenomyosis externa^{2, 3;4}. It was defined as endometrial glands and stroma outside the uterus, and this morphological definition still is the gold standard. Using this definition, black puckered lesions in the pelvis were soon recognized as endometriosis, making it a frequently diagnosed disease from the seventies onwards, i.e. after the introduction of endoscopy. When, in the 1980’s non-pigmented endometriotic lesions were described⁵⁻⁸, the prevalence of the disease increased from 5% to 20% to over 60% to 80% in women with infertility and/or pelvic pain⁹⁻¹⁸. In parallel with the changing meaning of the word ‘endometriosis’, the increasing awareness and prevalence of endometriosis, our concepts of etiology, pathophysiology, natural history and therapy have evolved.

Endometriosis has been considered for decades as the result of the implantation of retrograde menstruated endometrial cells¹, or as metaplasia^{19;20} induced by this menstrual debris or as lymphatic spread^{21;22}. It has been shown that retrograde menstruation occurs in almost all women^{23;24}, that this fluid contains viable cells²⁵ which can implant on the peritoneum²⁶. The initially nonpigmented or subtle lesions were believed to progress to typical, cystic ovarian endometriosis and/or deep infiltrating endometriosis, and this was assumed to be the natural history of the disease²⁷⁻²⁹. Endometriosis was considered normal endometrial cells at an abnormal location and in an abnormal environment, i.e. the peritoneal fluid.³⁰

In recent years this concept of implantation and progression has been challenged by a new concept which emphasises cellular changes and considers endometriosis as a benign tumour. In this view subtle endometriosis becomes a physiological condition occurring intermittently in all women. Only following cellular changes e.g. a mutation, these lesions evolve into typical, deep or cystic ovarian endometriosis. Therefore subtle endometriosis has been proposed to be called ‘endometriosis’, whereas the benign tumours i.e. typical, cystic and deep, were suggested to be called endometriotic disease³¹.

Treatment of endometriosis consisted of surgical destruction or medical inactivation. Since recurrences were considered to be frequent, surgery was radical. In the last decade, especially since the introduction of endoscopic surgery, concepts as debulking of deep endometriosis and focal therapy of cystic endometriosis have questioned the concept that surgery should be radical, that endometriotic disease is always progressive, and that recurrence rates are high. Hormone replacement therapy given to women with endometriosis has moreover questioned our concepts of medical therapy and peritoneal fluid.³²

In order to evaluate critically surgery for endometriosis we will first discuss the differences in surgical techniques with special emphasis on laser endoscopic excision to evaluate subsequently indications and results of treatment.

2 HISTORY OF SURGICAL TECHNIQUES

To interpret the literature describing the results of surgery for endometriosis, a clear understanding of the evolution and limitations of the various techniques is necessary. Up to the end of the 1970’s, minimal and mild endometriosis was destroyed endoscopically by heat application (endothermia) and by unipolar

or bipolar coagulation. Treatment of more severe endometriotic disease was mostly radical by hysterectomy, often leaving some rectovaginal endometriosis which has not been fully recognised before 1989. In younger women adnexectomies, rarely cystectomies, and anterior resections of the rectum were performed. This period has focused on infertility associated with typical and cystic ovarian endometriosis whereas deep endometriosis – unless very severe, large and painful – was not recognized. We may assume that all publications of this period were “contaminated” by some 5 to 20 percent of undiagnosed and thus untreated deep endometriosis.

In the late seventies and the early eighties microsurgery was introduced, emphasizing gentle tissue handling and careful destruction of superficial endometriosis by bipolar coagulation or resection and removal of cystic ovarian endometriosis followed by reconstruction of the ovary.

From 1986-1987 onwards, the concept of minimal and/or non-pigmented endometriosis was introduced.⁵ This has caused an important shift in the reported incidences of endometriosis, which depend on recognition and awareness. This increasing recognition of endometriosis has resulted in a progressive shift of women, who previously were classified as “normal” to women classified as having minimal endometriosis. To recognise this shift is important for the interpretation of results of surgery, since the group of ‘normal’ women, comprised before 1985 variable numbers of (unrecognized and untreated) women with minimal endometriosis. Simultaneously the severity of the disease in the groups of women with minimal/mild disease progressively decreases, since diluted with women with subtle endometriosis only. The bias of non-recognition of deep endometriotic disease still persists.

After the introduction of endoscopic surgery, several treatments of cystic ovarian endometriosis have been proposed. The removal of the cyst wall by stripping followed by suturing or gluing of the ovary is technically similar to the surgery performed during the microsurgery period. This has been challenged by destruction of the cyst wall, by laser vaporisation, or by bipolar coagulation. This destruction of the cyst wall, however, is poorly defined and ranges from focal treatment of lesions, to superficial destruction of the whole area, to much deeper destruction. These different techniques have been poorly compared and until today differences in opinion persist. It should be realised, however, that differences in technical skills in endoscopic surgery, often are fundamental to these discussions as is suggestion of a combined endoscopic/microsurgical approach.³³

In the nineties, deep endometriosis has been recognized increasingly during laparoscopic surgery^{34,35}, or by clinical examination during menstruation³⁶. “Resection of deep endometriosis” comprises techniques which vary from debulking, to complete discoid excision to resection-reanastomosis of the rectum with large margins mimicking oncologic surgery. These differences are rarely stated clearly in the literature, thus making interpretation difficult. Another important and growing bias is the severity of deep endometriosis reported. In some series deep endometriosis comprises mainly lesions larger than 1 cm² whereas in other reports lesions are limited to somewhat deeper typical lesions in the uterosacral ligaments. It therefore becomes mandatory that all reports on deep endometriosis clearly define volume and depth of the lesions operated upon.

In conclusion, in order to interpret correctly the data reported in the literature it is important to be aware of the existing biases. (1) The awareness of subtle endometriosis has increased tremendously the apparent prevalence of endometriosis thus decreasing the severity in the group with minimal endometriosis. Simultaneously the normal group of women has changed (2) the awareness and scrutiny of diagnosis of deep endometriosis will determine the incidence of ‘unrecognized’ deep endometriosis in the minimal-mild groups. (3) Reporting depth of penetration and volume of deep disease is necessary to judge whether the series comprise mainly large or mainly small lesions, the smaller ones just fitting the definition of 5mm. (4) The size of cystic ovarian endometriosis, the presence of adhesions, the pathological confirmation of the disease and the technique used, is essential to compare series of cystic ovarian endometriosis.

3 CO₂ LASER SURGERY VERSUS ELECTROSURGERY

CO₂ Laser surgery and electro surgery differ by the energy characteristics and by the mode of application.

The CO₂ laser energy is almost completely absorbed by water. The effect thus is a very superficial heating, and provided sufficient energy, instantaneously heating to temperatures inducing an explosion, i.e. vaporisation of tissue, with little thermal spread, i.e. less than 100µm. In order to be a precise cutting instrument the laser beam has to be focused on a small area. Theoretically spot diameters of less than 0.5 mm can be achieved, but this requires, a perfect lens and working at the exact focal distance. In addition the CO₂ gas in the laser channel of the laparoscope is heated by adsorption of the laser beam and these results in widening of the spot diameter an effect known as blooming. Therefore cooling continuously the CO₂ of the laser channel e.g. with an high flow insufflator³⁷ or using a CO₂ isotope to generate the laser beam are mandatory for a quality cut. Smoke production during vaporisation is so important that continuous evacuation is necessary. The most important difference with electrosurgery is that the energy output is constant of time: therefore the depth of cut is always constant, only depending of the speed of moving the laser beam over the tissue.

Electrosurgery has the advantage of being more versatile, resulting in heating and coagulation below 200V, in sparking with local heating of the air and the adjacent tissue and thus vaporisation above 200V. Higher voltages, will in addition heat the tissue causing coagulation i.e., damage. This was known in the past as blended current in electrosurgical units without voltage stabiliser. The quality of the cut thus is voltage dependent, and at exactly 200 V, i.e. with minimal sparking, the quality of a CO₂ laser and of an electrosurgical cut is comparable with similar limited tissue damage. The most important difference is that the energy output of electrosurgery is not constant since it essentially depends on the impedance of the tissues and on the area of contact between the electrode and the tissue. At higher output settings the intensity of the current will be limited only by the impedance thus being small or higher according to the area of contact, i.e. the depth of cutting. Electrosurgery thus easily cuts to a constant depth notwithstanding an irregular surface. Limiting the energy output, is not realistic, unless with a needle electrode in microsurgery, since any increase in contact area, will result in a drop in voltage and thus will stop cutting and start coagulation.

Another difference between laser and electrosurgery is the angle of access to the tissues: the laser beam used through the laparoscope will have an almost horizontal access to the rectovaginal septum. Energy used though the secondary ports will have a more vertical line of access, and this difference increase when secondary ports are introduced lower in the abdomen.

Finally almost all lasersurgery for endometriosis can be performed with 2 secondary ports only, placed low in the abdomen, i.e. within bikini limits. For electrosurgery, generally 3 secondary ports are necessary, which for ergonomic reasons have to be placed higher in the abdomen.

4 MINIMAL AND MILD ENDOMETRIOSIS

4.1 Methods of destruction

Ideally these endometriosis lesions are vaporized or excised with a high power CO₂ laser. We consider this the method of choice since this treatment rapidly removes all the endometriosis and not more than the endometriosis, leaving a minimal amount of necrotic tissue. The choice between vaporization and excision depends on the size of the endometriotic lesion, larger lesions being excised more rapidly. This method takes full advantage of the characteristics of a CO₂ laser as a bloodless and precise cutting instrument, with little thermal damage to the surrounding tissue.

Alternative methods of destruction are bipolar coagulation, endothermia and, sharp excision. The first method is less adequate than laser vaporization/excision for typical lesions, since depth of infiltration is difficult to assess by inspection and palpation only. Moreover, the amount of necrotic tissue left behind is more important, which could increase the amount of postoperative adhesions. Sharp excision together

with monopolar electrosurgery is theoretically equivalent to CO₂ laser excision. It balances between extensive prophylactic coagulation, which results in more tissue damage, and no prophylactic coagulation which often is associated with capillary bleeding and poor visualization.

4.2 Subtle lesions

If, subtle endometriosis is a natural condition occurring intermittently in all women^{29;38}, it is logic to postulate that treatment is not necessary since it is not a disease, since it will disappear spontaneously and can reappear later at another localization. Anyway subtle endometriosis never has been shown to be a cause of infertility or of pain. From a surgical viewpoint, however, this is an academic discussion, since vaporization of these subtle lesions, is so easily performed without risks, that it might be unwise to leave the possibility that some of these lesions would be or become more invasive or aggressive.

4.3 Typical lesions

It is uncertain whether it is useful to treat typical endometriosis to prevent progression. To demonstrate this in randomized controlled trials can be argued to be clinically irrelevant since destruction is so easy. Scientifically it might moreover be practically impossible to achieve. Considering a 60% prevalence of minimal-mild endometriosis with a progression to severe disease in some 10% after 5 years, it would require a randomized trial of hundreds of patients over many years, which is unrealistic.

Typical lesions are associated with pain, and in a series of observational studies and in 2 RCT it has been shown that destruction of typical lesions results in significant better pain relief than in a control group. These studies moreover confirmed the important placebo effect of some 25% lasting for at least 6 months. The activation of spare nociceptors^{39;40} with inflammation and the observation that these lesions are specifically painful when stimulated^{41;42} seem important to understand the pathophysiology.

The usefulness as an infertility treatment remains unclear. During the late seventies an association was shown between endometriosis, luteal phase insufficiency, unexplained infertility and the luteinized unruptured follicle syndrome (LUF)⁴³⁻⁴⁶. To understand why this association has been questioned later, it might be important to realize the shift that had taken place in the groups of women reported by the recognition of subtle nonpigmented lesions⁴⁷⁻⁵⁰. Studies in the baboon confirmed experimentally that endometriosis was associated with the LUF syndrome, that the LUF syndrome was recurrent and that the LUF syndrome diagnosed by inspection of the ovaries, correlated with the absence of ovulation⁵¹. Recently, the Endocan study showed in the human that treatment improved fertility⁵². This study, however, was not blinded, and it can be argued that by telling women that they had endometriosis indeed increased anxiety levels and LUF syndrome and thus decreased fertility rates. The absence of effect observed in the smaller Italian study, and the fact that a 30% cumulative fertility rate in the treated group of the Endocan study was similar to previously reported fertility rates in control groups; support this view.

5 CYSTIC OVARIAN ENDOMETRIOSIS

5.1 Pitfalls of diagnosis

The treatment of cystic ovarian endometriosis remains hampered by misdiagnosing a cystic corpus luteum as a cystic ovarian endometrioma. To the best of our knowledge this problem has not been addressed adequately. Even if only women with pathologically confirmed cystic endometriosis were included, these data do not permit to judge to what extent cystic corpora lutea had been operated upon.

A clinical history of the persistence of a cyst under oral contraceptives or LH-RH agonists is unreliable for diagnosing cystic ovarian endometriosis: over the years we have operated several women with a "chocolate cyst" on ultrasound, persisting for more than 4 months which turned out to be a cystic corpus luteum. We are fully aware that this clinical observation does not allow any conclusion about prevalence. This is consistent with the observation that ovarian cysts can develop during ovarian down regulation⁵³.

Imaging, such as ultrasound and CAT scan has sensitivity of 70% to 80% and a specificity of 90% - 95%^{54-58, 58}. This is a valuable method of diagnosis helping in the clinical management. It will, however, not prevent errors of judgment during surgery. Ovarian flow measurement does not seem to improve substantially⁵⁹, specificity or sensitivity.. CA 125 in chocolate fluid has reported to have a sensitivity and a specificity of nearly 100%^{60;61;61}. Unfortunately until a rapid test becomes available to make the diagnosis during surgery, this remains theoretical.

Our clinical rule of thumb is that, since cystic ovarian endometriosis is so strongly associated with adhesions¹⁸, a “chocolate cyst” without adhesions has a high probability of being a cystic corpus luteum whereas the presence of severe adhesions especially in the fossa ovarica enhances the suspicion of endometriosis. This, together with the inspection of inside of the cyst by ovarioscopy⁶² or by inspection with the laparoscope⁶³, will help to make a correct judgment in the majority of women. Those with a flattened appearance and red or red and brown mottled ridges generally were endometriosis and those with a dark uniform base, an intracavitary clot, or a yellowish rim generally were corpus lutea or albicans

5.2 Physiopathology

The physiopathology of cystic endometriosis is not entirely understood. It is attractive to consider that many cystic ovarian endometriosis originates from invagination of superficial implants⁶⁴. Especially when the ovary becomes adherent to the pelvic wall by endometriotic implants, it seems logic that a “pseudocyst” is formed by the accumulation of old blood and debris, thus stretching the ovarian capsule over this cyst^{65;66;66}. This phenomenon of invagination and stretching of the ovarian capsule can explain that the inside of the cyst wall is not always entirely covered by endometriosis, which is rather localized as focal endometriotic spots. It thus seems logical to postulate that only these endometriotic spots should be destroyed, and that removing the cyst wall is equivalent to removing the ovarian surface. This mechanism of invagination and stretching of the ovarian capsule does not preclude that some cysts have a different origin. A careful histology of the cyst wall moreover reveals that endometriotic glands can be present in the “so called” cyst wall up to a depth of at least 5-6 mm. Whatever the aetiology is, most of the ovarian cysts are clonal in origin, as was repeatedly demonstrated.

5.3 Surgical pragmatism of size

From a surgical point of view, the size of the ovarian cyst is the most important. For smaller cysts (< 5 cm) the cyst wall can generally be stripped easily from the ovary. This process seems to follow a natural plane of cleavage, confirmed indirectly by the fact that it is associated with little bleeding. For cysts larger than 5 cm diameter, the discussion whether the cyst wall should be removed or destroyed, or whether a focal treatment will be sufficient is purely academic. Indeed in these women with a large cyst the remaining ovarian rim will be so thin that resection becomes either technically impossible or practically unrealistic since minimal or no ovarian tissue will be left. Also the extensive vaporization of these very large areas is unrealistic.

5.4 Methods of treatment

Aspiration and rinsing of cystic ovarian endometriosis has been attempted but the recurrence rate is high⁶⁷⁻⁶⁹. Ultrasound guided aspiration will moreover result the next day in chocolate in the pelvis when we attempted to do so (unpublished data), which might increase adhesion formation⁷⁰ although it was shown that chocolate fluid does not induce adhesions when injected intraperitoneally in mice⁷¹.

For smaller cysts, i.e. less than 5 cm diameter, the method of stripping the cyst from the ovary as initially described by the Clermont Ferrand group is our method of choice^{72;73}. It is rapid, technically easy, and complete treatment also when invading glands would be present. Following adhesiolysis, drainage and rinsing, we incise with the CO2 laser the ovarian capsule around the cyst opening. Once the plane of cleavage is found, the cyst wall is easily stripped from the ovary. The laser is used to assist cleavage in the right plane and prevents the ovarian capsule to be teared in the wrong direction. Closure of the ovary by tissucol or a suture when the remaining ovarian flaps are unequal in size necessary, is suggested

although not proven. . The cyst wall could be vaporized. Some report excellent results⁶⁴. We stopped to use this technique since it was too difficult to judge the correct depth of vaporization. Too superficial destruction resulted in an incomplete treatment and recurrences whereas a too deep destruction often caused bleeding. The cyst wall could be destroyed by unipolar or semi bipolar coagulation. Although attractive, the reported series are too small to compare this technique to vaporization. The third option besides wall excision and wall destruction is focal treatment⁷⁴, but this is generally equivalent to vaporization..

For larger cysts, the pragmatism of size, practically excludes excision and/or vaporization. We favour to keep surgery during the first laparoscopy to a minimum making it a 5 to 10 minute procedure. We make a large window in the cyst wall, followed by rinsing, some focal treatment, no adhesiolysis and postoperatively 3 months of LH-RH agonist treatment is given. If by ultrasound the cyst persists or reforms, this small cyst is treated during a second surgery with excision as If no cyst is found it is unclear whether a second intervention is necessary in the absence of pain or infertility.. This concept has the indirect advantage that the first operation can always be scheduled as a day case, without bowel preparation, whereas the necessity of a bowel preparation for the second intervention will be known in advance. It remains unclear whether it could be preferable during the first surgery to do a full adhesiolysis. It is also unclear whether postoperatively medical therapy is helpful; it is logical since it will prevent a corpus luteum to develop whereas a hypo-estrogenic milieu could reduce adhesion formation. The number of "large" endometriomas is insufficient in most centres to perform randomized trials, whereas the rapid technical evolution of endoscopic surgery has made randomized trials practically impossible until now.

5.5 Results

The results of endoscopic and microsurgical treatment are comparable⁷⁵, ranging between 60 and 80 percent cure of pain, a cumulative pregnancy rate of 60% to 70% after 6 months to 1 year and a recurrence rate between 5% and 20%^{76;77;78;79}. It remains unclear whether preoperative or postoperative medical treatment significantly affects the results⁸⁰.

5.6 Conclusion

Cystic ovarian endometriosis has to be treated, since this condition is associated with pain and infertility and carries the risk of spontaneous rupture. Surgery is the only real treatment, since medical treatment can only inactivate endometriosis without reducing the size of the cyst⁸¹.

Because of technical and practical surgical considerations, we favour excising smaller cysts by stripping, followed by closure of the remaining flaps if necessary. For larger cysts, a minimal first intervention consisting of marsupialisation, rinsing and focal treatment, followed by LHRH agonists for 3 months and a second intervention when a cyst persists is proposed.

6 DEEP ENDOMETRIOSIS

6.1 Diagnosis, types and prevalence

Endometriosis can infiltrate the surrounding tissues resulting in an important sclerotic, and inflammatory reaction which can translate clinically in nodularity, bowel stenosis and ureteral obstruction. The most severe forms such as rectovaginal endometriosis and endometriosis invading the rectum or the sigmoid have been known since the beginning of this century. These conditions, however, are relatively rare with an estimated prevalence of less than 1%. This estimation is derived from the observation in Leuven of some 10% to 20% deep endometriosis in 1988 to 1991¹⁸, a period during which endoscopic surgery was not yet well developed, and in which deep endometriosis was not yet a well known entity. Referrals were thus only those for infertility and pain not for deep endometriosis. Assuming that laparoscopies for infertility are performed in some 10% to 15% of the population and taking into account that Leuven is a tertiary referral centre, the prevalence of deep endometriosis can be estimated to be between 1% (the

prevalence is 10% in younger age group with infertility which can be estimated at 15% of the population, in a tertiary centre the prevalence is probably slightly overestimated) and 3% (prevalence of 20% of the older age group with infertility). Taking into account the observation that by menstrual clinical examination, deep endometriosis is more frequent prevalences between 3% and 10% seem a fair estimate.

The endoscopic excision of endometriosis has revealed that endometriosis invading deeper than 5-6 mm is associated with pain and infertility. Three subtypes were described⁸². Type I is characterized by a large pelvic area of typical and sometimes some subtle endometriotic lesions surrounded by white sclerotic tissue. Only during excision does it become obvious that the endometriotic lesion infiltrates deeper than 5 mm. Typically the endometriotic area becomes progressively smaller as it grows deeper, the lesion is thus cone shaped. Type II lesions are characterized by retraction of the bowel. Clinically they are recognized by the obvious bowel retraction around a small typical lesion. In some women, however, no endometriosis can be seen through the laparoscope, and the bowel retraction is the only clinical sign. Diagnosis is generally not too difficult since during laparoscopy the retraction under which an induration is felt, is obvious. In some women however the retraction is hardly seen and the induration can be hardly felt. Only during excision the endometriotic nodule becomes apparent, emphasizing the need for a pre-operative diagnosis and training in recognizing these lesions. Type III lesions are spherical endometriotic nodules in the rectovaginal septum. In their most typical manifestation these lesions are felt as painful nodularities in the recto-vaginal septum. At laparoscopy they generally present as a small typical lesion, and in some women a careful vaginal examination reveals some dark blue cysts (3-4 mm) in the fornix posterior. Type III lesions are the most severe lesions, and they often spread laterally up and around the uterine artery, sometimes causing sclerosis around the ureter. The spread along the uterine artery can be so obvious, that this can be considered as an indirect argument for the hypothesis that deep endometriosis has escaped from the inhibitory influence of peritoneal fluid and is mainly under peripheral circulation control. Whilst being prominent in most women these lesions are very often missed as will be discussed later. Sclerosing endometriosis, invading the sigmoid is similar to the rectal endometriosis, but is situated 10 cm above the rectovaginal septum. This is another form of deep endometriosis, which is fortunately a rare condition and which we could classify as type IV. By pathology, the types II, III and IV are similar and present as adenomyosis externa i.e. glands and stroma in large areas of hyalinous muscular tissue. Since the demonstration of a less deep pouch of Douglas in women with deep endometriosis, it seems logical to postulate that these 3 lesions are pathophysiologically similar, type III being situated in the Douglas on the wall opposing the vaginal wall. Subsequently the Douglas is closed by retraction, giving erroneously the impression that these lesions are situated in the rectovaginal septum, which starts lower. It is logic that these lesions are often vaginally visible since the distance between vaginal wall and peritoneal cavity is hardly 3-4 mm. The type II lesions are situated higher, generally between the back of the uterus and the rectosigmoid, whereas a lesion at the level of the sigmoid generally is not adherent to the surrounding structures, except occasionally to the ureter under the infundibulo pelvic ligament. These concepts seem to constitute another argument to differentiate between slightly larger and deeper typical lesions, the infiltrative type I deep endometriosis, and those with larger nodules, massive retraction and by pathology adenomyosis externa.

Diagnosis of deep endometriosis should be made before surgery. A retrospective analysis showed that by a routine clinical exam only 50% of the larger lesions are diagnosed. A menstrual clinical exam is the most powerful tool actually available to diagnose deep endometriosis type I, II and III. By clinical examination during menstruation³⁵ painful nodularities are found in some 30% of women with pain or infertility. In the absence of cystic ovarian endometriosis these nodularities were in most of the women caused by deep endometriosis. The concentrations of CA 125 are increased in women with deep endometriosis and in women with cystic ovarian endometriosis and were proposed as a screening tool. Although specifically increased during menstruation, the variability does not improve the diagnostic accuracy⁸³. A late follicular sample has a sensitivity of some 70 to 90% of endometriotic disease with a specificity around 95%⁸⁴ Ultrasound and MRI can be used to diagnose deep endometriosis, but their sensitivity is low especially for the smaller lesions. For type IV lesions a contrast enema and/or a

rectoscopy are necessary. Although hard data are not available, we presume that this diagnosis is easily missed, making prevalence higher than actually believed.

In conclusion, the most powerful tool to diagnose deep endometriosis is a menstrual clinical examination whereas a routine clinical exam will reveal mainly the very large lesions. A CA 125 assay is a useful screening aid for deep endometriosis, and it might prove to be useful as screening for type IV lesions which, although severe, are easily missed and cannot be diagnosed by clinical examination. The final diagnosis is the estimation of the depth of infiltration during excisional surgery. The prevalence of the disease increases with age and is estimated at 1% to 10% in the population and at 10% to 30% in women with pain and/or infertility.

6.2 Surgical treatment

Surgery for deep endometriosis is unpredictably difficult with a series of severe complication risks. Therefore a preoperative ultrasound, contrast enema and intravenous pyelography are mandatory, together with a full preoperative bowel preparation. Surgery should be carefully planned. This planning comprises preoperative ureter stenting if gross ureter distortion or hydronephrosis is present together with the eventual collaboration of an urologist to perform ureter re-anastomosis or repair, bladder suturing, ureter re-implantation e.g. in case of an aggressive endometriosis infiltrating deeply the bladder and ureter around the intramural bladder traject of the ureter or to decide about surgery when the trigonum is invaded. Pre-operative planning often requires the collaboration of a colorectal surgeon, since surgery can unpredictably extend from a discoid excision with a muscularis defect, to a resection of the rectum or sigmoid wall necessitating a suture, to a large transmural nodule requiring a resection anastomosis if the defect is too large, or in case of a combined rectal and sigmoid nodule which cannot be sutured a pouch anastomosis requiring mobilisation of the left hemicolon. The exact borders of competence between disciplines are less important. We want to stress however, that the pre-operative planning should be rigorous, that before attempting severe cases it is important to ascertain that the eventual competences which might be required are available, and not accidentally absent. The necessary competences also comprise the anaesthetist, since the ventilation capacity, the obesity and the degree of Trendelenburg can become crucially important to facilitate difficult surgery. The type of lesion, will also determine the position of the secondary trocars which e.g. for a sigmoid lesion have to be placed higher than for a rectum lesion. Finally to grasp and summarise the importance of all this, it should be realised that any surgery should be performed within reasonable time limits, even if unforeseen complications happen such as an instrument break down together with a pouch anastomosis and a ureter re-anastomosis. Prolonging surgery beyond 5-6 hours invariably carries the risk of a severe compartment syndrome of the legs. In conclusion, a careful preoperative planning is mandatory, to predict as precisely as possible what is to be expected, to know which competences should be available, and to judge whether the surgeons competences make it reasonable to expect that the operation time will not have to be extended beyond some 5 hours. Unnecessary to say that assistance and theatre nurses should be trained and experienced. If these conditions are not met, alternative options should be considered such as referral of the patient or a laparotomy. *Primum non nocere* remains the first principle of the surgeon. For this reason any live surgery performed at congresses, should be limited to the expertise of the local situation.

The surgical excision of deep endometriosis itself relies upon a combination of visual inspection and tactile information. For the treatment of recto vaginal endometriosis up to the recto-sigmoid, we clearly prefer a CO₂ laser (80 Watt, Sharplan) together with a high flow insufflator (Thermoflator, Storz AG)³⁶ mandatory for smoke evacuation and cooling the laser beam.. Guided by visual inspection together with tactile information of the softness of the tissue, the peritoneum is incised below the lesion at the border between the normal soft tissue and the harder endometriosis. Endometriosis moreover glows yellowish under the CO₂ laser beam. *Firstly* the lesion is circumscribed to mark the limits which are useful during later excision. *Secondly* the lateral edges of the nodule are dissected to free the nodule if necessary from the ureter, the uterine artery, and from the spinosacral ligament. This is technically the most difficult part

of the surgery, since very deep and posterior and because of the presence of larger arteries and the nerve. If necessary the lateral borders of the sigmoid have to be dissected and followed with identification of the ureters. *Thirdly* the pararectal spaces are identified. This marks the lateral edges of the nodule, and one identified dissection is bluntly continued downwards. *Finally*, the posterior part of the nodule is dissected from the rectum: We feel it important that during this dissection, the nodule remains attached to the uterus and cervix or vagina thus elevating the nodule whereas the rectum progressively falls down by gravity. This dissection is continued as far as possible, at least until the rectum is completely liberated from the rectovaginal septum. The use of a rectal probe is unclear: it can be useful to identify structures but it is not helpful during dissection. Only after the completion of the dissection of the posterior part up to the vaginal wall, the anterior side of the nodule is dissected from the cervix, and from the vagina. At least in some 20% of women part of the vaginal fornix has to be removed because of endometriotic invasion whereas we estimate that in some 20% of women the rectum has to be opened to permit a complete resection⁸⁵. In the Leuven series it is noteworthy that resection of the rectum has not been necessary in any of these women. Over the years, excision has evolved and become more radical, but simultaneously as a consequence of referral the severity and size of nodules has increased tremendously. This has resulted in a series of resections necessitating the resection of large areas (5*5cm) of rectum wall with subsequent suture. This I consider today the limit of the technique, and although not yet properly reviewed and audited clinical impression of these very large nodules suggest that it maybe is preferable to have a clean excision of the wall than to leave a very thin and devascularised mucosa. This type of surgery obviously implies to be prepared for early and late perforations (estimated at 5 to 10%) with an immediate and early second look laparoscopy permitting to suture these leaks and treat them conservatively without colostomy.

A careful description of the excisional technique is mandatory to understand pros and cons of the reported technique. The advantages of the technique as described is the perfect visualization and the angle of access. Using CO₂ laser excision through the operating laparoscope, excisional surgery is performed with great magnification : excision can be performed with the laparoscope close in since the laparoscope carries the 'knife' ; excision also has to be performed close in since the focal length of the CO₂ laser lens is some 2 cm from the laparoscope. A third advantage is that the direction of access of the rectovaginal septum, and especially the posterior side of the nodule is easier through the laparoscope than through a secondary port. Obviously, this technique requires a high flow insufflator⁸⁵ to maintain a clear picture throughout the excision, and to permit to use the laser continuously, without interruption. Finally this technique takes advantage to the maximum of the haemostatic capacity of the laser.

Three other techniques are used for the resection of deep endometriosis: sharp dissection together with electrosurgery through the laparoscope, sharp dissection together with electrosurgery through the secondary ports and a partial rectum resection followed by reanastomosis usually with a circular stapler. It is obvious that each surgeon performs best using the techniques he is most familiar with, and that few endoscopic surgeons are familiar with all techniques. Most indeed have developed the technique which they started with generally for historical reasons; This however, should not prevent discussion of the relative advantages of the different approaches, as evaluated by expert surgeons performing surgical procedures often arranged on the basis of friendship. Sharp dissection together with electrosurgery through the laparoscope as developed by David Redwine⁸⁶⁻⁸⁹, is technically almost identical to the CO₂ laser excision i.e. permitting a very posterior approach, working close in with great magnification in a bloodless operating field. The disadvantage is that this technique is physically demanding whereas less suited for video-endoscopic surgery thus reducing the possibility of help from an assistant. This technique, however, probably combines the advantage of an improved depth of vision (since not using a video screen) with enhanced tactile information, since also using sharp dissection. Sharp dissection together with electrosurgery through the secondary ports is the most widely used technique^{90-93;93;94;94;95;95;96;97;98-100}, for several reasons. It is derived from the other endoscopic procedures; it does not require a CO₂ laser and possibly even more important a high flow insufflator was not available during its development. Because the angle of access is much sharper, surgeons using this technique generally start dissection at the anterior site of the nodule, thus freeing nodule and rectum from the rectovaginal septum.

Subsequently the rectum is dissected from the nodule which has become freely mobile. Most of these procedures aim at debulking the endometriosis, rather than performing a complete resection. The word 'debulking' is chosen when the surgeon prefers not opening the rectum, even if the resection is less complete. It is difficult to estimate whether this 'debulking' attitude is a consequence of the technique used, or a consequence of the philosophy often dictated by local and medico-legal considerations. My (PK) experience was that resection of endometriosis using this technique is much more difficult than using the CO₂ laser approach, and that the best method to avoid bowel lesions was by avoiding traction and using gravity only. These same considerations could explain why some authors -probably in order to perform a complete resection and to avoid recurrences, perform a partial resection and anastomosis in women with larger nodules. At this moment it is not known whether those performing a complete resection, are overtreating their patients or whether those aiming at debulking the lesion, are undertreating the endometriosis.

A few years ago I wrote that Type IV endometriosis requires a resection and subsequent reanastomosis. Since then I started to do conservative excisional surgery in these women. This is feasible, but results almost invariably in large wall defects. As discussed for the rectal lesions, these lesions will be reviewed carefully, before it will be claimed that this is the treatment of choice. Considering, however, the duration of surgery in some and some complications in others, I am reluctant to propose this as mainstream surgery today. Taking into account only the repair sutures, easily comprising some 25-30 stitches, in a difficult angle it must be obvious that this will not be mainstream surgery to-morrow.

6.3 Complications, treatment and prevention ¹⁰¹

When part of the rectum wall has to be removed, or when the rectum is accidentally opened, the pelvis is rinsed with a 1% hibitane solution and the wall is sutured endoscopically with 2 layers of 3x0 Vicryl (Ethicon, USA). A defect in the posterior vaginal fornix is sutured either vaginally or endoscopically. Care is taken to suture these defects water-tight. I prefer to suture these defects laparoscopically, for reasons of sterility: during laparoscopic suturing a continuous flow of CO₂ from the abdominal cavity to the vagina prevents contamination.

Surgical excision of deep endometriosis is thus difficult surgery since it often necessitates dissection far laterally around the ureter and uterine artery. Also the excision from the bowel wall is difficult, since in 10 % of women part of the bowel wall will have to be resected. In 20 % of women, especially those with rectovaginal endometriosis i.e. type III lesions, excision has to be performed up to and including the posterior vaginal fornix. It is important that neither resection of part of the bowel wall nor resection of the vaginal fornix should be considered as complications of surgery, since the postoperative follow up has been uneventful in a series of over 300 women.

Complications of surgery during the initial series (n=225) have been the transection of the uterine artery in 2 women necessitating clipping, a ureter lesion in 1 woman and a late bowel perforation in 6 women. A ureter lesion is a serious complication, and therefore we advocate a preoperative intravenous pyelogram, a careful dissection of the ureter from its landmarks at the pelvic brim and a liberal preventive stenting if necessary. This is judged even more important, since it became evident that a ureter which is only half cut, can rather easily be sutured endoscopically over a double J¹⁰². A late bowel perforation is an even more serious complication which has occurred in 6 women : 2 women with a type II lesion (1989 and 1991) and 1 woman with a type III lesion (1992) were readmitted after a week with progressively increasing symptoms of peritonitis; 1 woman (1992) with a type I lesion and a history of pouch anastomosis for colitis ulcerosa, was observed for 1 week with atypical symptoms which later proved to be a rectum perforation; 2 women (1994) with a type II lesion had acute pelvic pain, 12 hours following surgery and 2 days following surgery respectively. Although symptoms of peritonitis were minimal, an immediate laparoscopy revealed a bowel perforation in both.

It is important to realize that bowel perforations can occur during the early postoperative days thus necessitating a low fiber diet and eventually hospitalization. A perforation generally occurs during straining, with acute pelvic pain as the only symptom. Disturbingly this pain disappears over the

subsequent hours with slight peritoneal irritation as the only symptom. A liberal use of early second look laparoscopies is advocated in these women before symptoms of peritonitis develop. In some 10 women we indeed recently demonstrated that even a bowel perforation can safely be sutured endoscopically thus avoiding a colostomy.

Prevention of a late perforation is even more important. Since January 1996, liberal prophylactic suturing of the rectum was introduced, whenever a suspicion of lesion to the muscularis existed. Since then this complication had virtually disappeared. Over the last years after resection of larger portions of the bowel wall, thus replacing resection –anastomosis this complication has reappeared. It is too early to have a final judgment.

6.4 Medical treatment

Medical therapy before surgery has been discussed for many years and surgeons have claimed that deep lesions were less vascularised following medical therapy. Recently it was demonstrated that a pretreatment for 3 months with an LH-RH agonist could shrink the volume of deep lesions^{103;104}. Indeed, in this series decapeptyl (3.75 mg/month) has been given specifically to women with the most severe disease, especially deep lesions. Analysis of data showed that women pretreated with this LH-RH agonist had a higher rAFS score at surgery than those without treatment confirming the selection bias. Similarly pretreated women had more and larger cystic ovarian endometriosis also pointing to the selection bias. As expected, women with pretreatment had a smaller pelvic area of endometriosis. Pretreated women had, however, a smaller volume of deep endometriosis notwithstanding the fact that because of the selection bias, they almost certainly had a much higher volume before treatment. For this reason we advocate pretreating women with severe deep endometriosis medically for 3 months with a GnRH agonist. We have the impression that Danazol might be equally effective but our series was too small to prove this statistically. Other medical therapies have not been used frequently enough to be evaluated.

Medical treatment following excision of deep endometriosis has not been evaluated properly. If excision has been performed completely, medical treatment is probably not necessary. Medical therapy, however, should be considered instead of repeat or more radical surgery for recurring symptoms or failures of excision.

Medical treatment alone has not been addressed specifically in any study because of a lack of a clearcut diagnosis of deep endometriosis without excision. Medical treatment either by danazol, GnRH agonists, or gestrinone^{87;105;106;106;107} does not cure endometriosis. They inactivate the endometriotic lesions which reappear rapidly after treatment has been stopped¹⁰⁸. None of these therapies have an important beneficial effect on subsequent fertility¹⁰⁹. They all improve pelvic pain and the effect persists often for many months after therapy has been stopped¹¹⁰. Since deep endometriosis is strongly associated with pelvic pain, and since cystic ovarian endometriosis does not respond well to medical therapy, it is suggested that the observations and conclusions concerning severe pelvic pain, are probably related to deep endometriosis.

6.5 Results

Nehzat⁹⁷ reported 25 pregnancies in 67 women following excision of deep endometriosis. We (PK) evaluated cumulative pregnancy rates (CPR) in a consecutive series of 900 women with primary or secondary infertility without severe tubal damage and with a severe subfertile husband. Cumulative pregnancy rates were slightly lower in advanced stages of endometriosis according to the revised AFS classification being 62 % and 44 % in classes I and IV respectively. When, however, the duration of infertility was taken into account, - which was the strongest predictor of subsequent conception - the differences in CPR between classes I to IV disappeared. Suggesting that the differences found between mild and severe endometriosis were mainly a consequence of differences in duration of infertility and possibly in age of the women.

The only single group with a significantly higher CPR following surgery were women with deep endometriosis. By Cox multivariate regression analysis the following model was established: pregnancy was predicted most strongly by a shorter duration of infertility and by the surgical treatment of cystic ovarian endometriosis and/or of deep endometriosis. From these results it can be concluded that aggressive and complete excision of deep endometriosis can be advocated, with subsequent spontaneous pregnancy rates up to 60 % within 1 year. These results can be considered excellent taken into account the severity of disease and the large denuded area in the pelvis following excision of deep endometriosis. It remains unclear whether those women who did not conceive after 1 year, should be oriented towards in vitro fertilization or to a second look laparoscopy. Medical treatment alone, as can be derived from indirect evidence is probably not the treatment of choice for deep endometriosis and infertility. As has been pointed out, medical pretreatment seems to be useful to facilitate surgery as has been suggested for cystic ovarian endometriosis. Both surgical and medical treatment was reported to be highly successful in treating pelvic pain. Candiani⁹⁶ reported absence of dyspareunia and dysmenorrhea in 6 and 4 women out of 10 after 40 months. Nezhat⁹⁷ reported moderate to complete pain relief in 162 women out of 175 but in some 2 or more interventions had been necessary. Preliminary analysis of our results in 250 women in whom deep endometriosis has been excised with a CO₂-laser showed a cure rate of pelvic pain in 70 % with a recurrence rate of less than 5 % with a follow up period up to 5 years. These data should be interpreted carefully, since the completeness of excision has steadily increased. The results of recent years, strongly suggest an almost complete cure rate without recurrences; this however could be an overoptimistic clinical impression which will have to be proven by careful analysis of the data. In addition medical treatment of pelvic pain is highly efficient, and the effect of treatment often persists after treatment has been stopped¹¹¹.

7 DISCUSSION AND CONCLUSIONS

We advocate a first line approach to the diagnosis and treatment of endometriosis, which relies on a menstrual clinical examination, an ultrasound scan and eventually an assay of CA125. Following these exams, 4 groups of women can be considered. When the clinical examination during menstruation does not reveal any nodularities, no ovarian cysts are found at ultrasound scan and the CA125 concentration is normal, women with infertility and/or pain are scheduled for a day case diagnostic laparoscopy. If an endometrioma is found, larger than 5 cm in diameter, these women are also scheduled as a day case for an initial procedure during which the cyst is opened, rinsed and focally treated. Postoperatively these women are treated for 3 months with a GnRH analog, and eventually scheduled for a second intervention. If a small endometrioma is found on scan, these women are also scheduled for day case. They are advised that the probability that a bowel preparation would be necessary cannot be excluded, but that the probability is probably less than 5%. If a deep endometriotic nodule is found, the necessity of a preoperative medical treatment and of a preoperative contrast enema and intravenous pyelography should be considered. These women always receive a bowel preparation and are admitted in the hospital for at least 48 hours.

This approach has the advantage that the preoperative clinical exam together with the ultrasound scan are used to decide whether the patient will be admitted to the hospital or treated in the one day clinic, and whether a bowel preparation will be given. From our experience over the last years, the accuracy of this procedure is close to 100% since unexpected deep endometriosis and unnecessary bowel treatments have virtually disappeared from the department.

Surgery remains the cornerstone of the treatment of endometriosis. Medical treatment seems to be indicated, besides pre- and postoperatively as discussed, for women with recurrent pelvic endometriosis and pain, or when adequate surgery is not available or too dangerous.

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