

Review of gynecological endoscopy and endometriosis

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ABSTRACT

In this review we intend to highlight and historically contextualize the value of the Kiel School of Gynecological Endoscopy, focusing on one of our main areas of interest: endometriosis. The identification and treatment of endometriosis is based on guidelines issued by professional societies, both national and international (namely, the German S2k and the ESHRE, ESGE, EGE and WES guidelines for endometriosis). The postulated mechanisms of endometriosis are based on well-known etiological factors. In practice, the recognition and treatment of endometriosis are based on the following parameters: age, description of any pain, knowledge of the patient's medical history and menstrual cycle, gynecological examination of the vagina, cervix and uterus, rectovaginal examination, posterior uterine wall examination, and 2/3D ultrasound with a vaginal and abdominal probe. The treatment of patients with pain differs from that of patients without pain. We also differentiate between patients with endometriomas who desire to become pregnant and those with endometriomas who do not desire pregnancy. Patients with bleeding disorders need special attention and must be investigated by hysteroscopy. A malignancy must always be excluded. The treatment of patients with endometriosis during pregnancy is subject to special criteria. Pregnancies must be monitored, especially with regard to the risk of uterine rupture after previous endometriosis surgery on the uterus, and placenta previa. Therapeutic strategies depend on the endoscopic histological diagnosis and include medications such as Visanne or GnRH agonists, and specific surgical procedures.

KEYWORDS

Gynecological endoscopy, endoscopic surgical diagnosis, gynecological surgery, Kiel School of Gynecological Endoscopy, endometriosis and specific treatment situations.

Introduction and goals of endoscopic surgical diagnosis and therapy

This article is an evaluation of fifty years (Lilo Mettler, 1970–2020) and fifteen years (Ibrahim Alkatout, 2005–2020) of experience in the field of gynecological endoscopy, and it focuses specifically on the application of endoscopic surgery in endometriosis.

The establishment of the Kiel School of Gynecological Endoscopic Surgery was based on a profound understanding of the development of surgery worldwide. The spectrum of techniques used includes robotic-assisted surgery. The goals of

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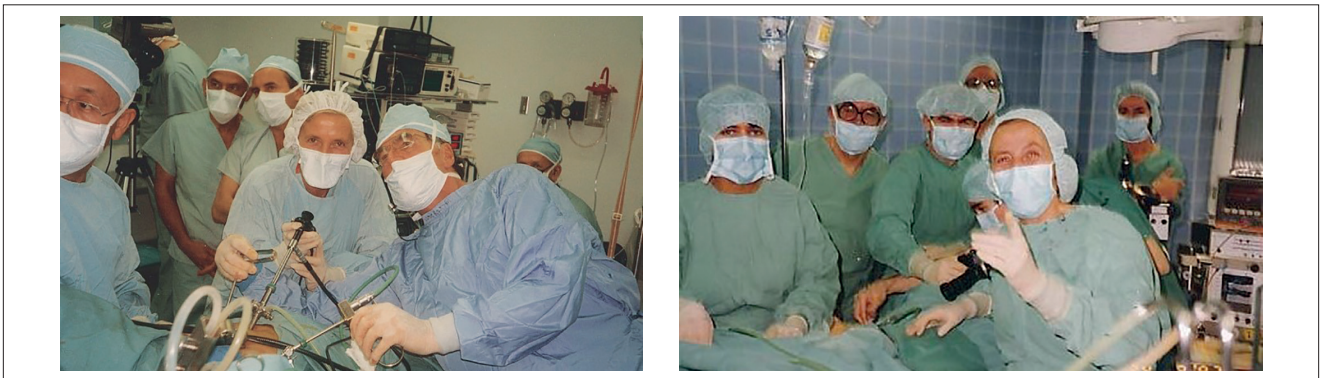
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good surgery are identical whether we are performing laparotomy, laparoscopy or endoscopic procedures, including robotic surgery (regardless of the angle, location or means of access) (Figures 1 and 2).

Figures 1, a and b Professor Kurt Semm (a) and Professor Liselotte Mettler performing laparoscopic surgery by looking directly through the optic device in 1976, prior to the era of video laparoscopy.



Figures 2 Kiel School of Gynecological Endoscopy, Germany, 1970–2020. This picture was taken in 2014.

In short, all types of surgery, including laparotomy, laparoscopy and endoscopic procedures, aim to:

- recognize relevant pathologies;
- allow the possibility of radical treatment in endometriosis and cancer;
- ensure minimal trauma, bleeding and tissue laceration;
- prevent adhesions;
- preserve the genitourinary system in women of reproductive age, provided endometriosis or oncological conditions allow this;
- use the best instruments (with as many degrees of freedom as possible, robotic-assisted systems, etc.).

It remains advisable to adhere to the policy of minimal trauma, maximum vision and good tactile perception, until such time as protons or other “magic bullets” open up new therapeutic pathways. Early identification of disease by means of modern imaging technologies is a significant step forward. Imaging technologies and endoscopy have already merged successfully. Recognition of disease through molecular genetics and human genome sequencing is also expected to improve therapeutic modalities to a notable extent.

History

A few colleagues who are no longer in our midst served as pioneers of endoscopic surgery in general, and endoscopic gynecology in particular. Others were responsible for the introduction of endoscopy in endometriosis surgery^[1]. They and their main achievements are recalled in the box below:

1. Philipp Bozzini (1773–1809) and the light guide
2. Antonin Jean Desormeaux (1815–1894) and his endoscopes
3. Georg Kelling (1866–1945) and his air insufflation apparatus
4. Max Nitze (1848–1906), an early urological endoscopist who developed cystoscopy
5. Heinrich Kalk (1895–1973) and his insufflation apparatus, which allowed abdominal biopsies of the liver and other organs
6. Raoul Palmer (1904–1985), the European father of endoscopy in the lithotomy position
7. Hans Frangenheim (1920–2001), who built his first abdominal insufflator in 1959
8. Harold Hopkins (1918–1994), who developed the rod lens system of modern endoscopes
9. Karl Storz (1911–1996), who developed the cold light source in 1960
10. Patrick Steptoe, who performed many laparoscopies in Great Britain and developed the human *in vitro* fertilization and embryo transfer technique (IVF–ET) with Robert Edwards
11. Hans-Joachim Lindemann, born in 1920, who performed crucial groundwork for hysteroscopy
12. Kurt Semm (1923–2003), the father of operative gynecological endoscopy and operative endoscopic surgery for all disciplines, who performed the first endoscopic appendectomy as a gynecologist in 1981.
13. Jordan M. Phillips (1923–2008), propagator and “prophet” of gynecological endoscopy throughout the world
14. Gerhard Buess (1943–2012), an enthusiastic promotor of new minimally invasive surgical techniques in operative endoscopy throughout the world.
15. Maurice Antoine Bruhat (1934–2014), driving force of French endoscopy and founder of the Clairmont Ferrand School of Gynecological Endoscopic Surgery
16. Thoralf Schollmeyer (1964–2014), who pursued the teaching of endoscopic surgery in Kiel with great enthusiasm

Benign gynecological surgery

The first endoscopy on a human being was performed in 1901 by von Ott of St. Petersburg, Russia, who examined the abdominal cavity of a pregnant woman through a culdoscopic incision in the posterior vaginal fornix, using a head mirror to reflect the light. In 1901 Dr. Georg Kelling, a professor in Dresden, addressed the German Biological and Medical Society in Hamburg and described the visual examination of the stomach and the esophagus in a human being, and the use of a cystoscope to visualize the viscera of a dog, using air filtered through cotton wool to produce a pneumoperitoneum. Credit for the first true laparoscopy procedure in a human being goes to Hans Christian Jacobaeus in Stockholm, who described his inspection of the peritoneal, thoracic, and pericardial cavities in 1910.

However, the most important advances in gynecological endoscopy have come only over the past fifty years, together with the simultaneous progress of endoscopy in all surgical specialties of medicine. This development has led us up to the present day, culminating in modern robotic-assisted procedures. Current techniques are evaluated in our recent *Practical Manual of Laparoscopic and Hysteroscopic Surgery 2019*^[1].

Gynecological surgery for endometriosis and cancer

With good reason, progress in endometriosis and cancer surgery was slower than the advances made in benign endoscopic surgery. Surgical treatment of deep infiltrating endometriosis (DIE) is more complex than tubal patency testing or ovarian cystectomies. DIE frequently calls for interdisciplinary procedures involving general surgeons and urologists^[2]. However, laparoscopic and hysteroscopic endometriosis surgery were described in detail^[3-8] long before any reports of laparoscopic cancer surgery appeared in the field of gynecology.

Early studies on cervical cancer surgery were published after Dargent's report in 1987^[9]. Endoscopic gynecological surgery developed rapidly and significantly from 1970 to 1990. The simultaneous growth and input of the medical technology industry during this time led, in the late 1980s, to the first reports on subtotal and total laparoscopic hysterectomies and laparoscopic surgery for staging of gynecological cancers. However, studies on endometriosis were published as early as the 1970s^[10]. Early reports on radical hysterectomy by Dargent, Schneider, Nezhat and Querleu were poorly accepted by the gynecological community. Kurt Semm and Hans Frangenheim had to defend their surgeries against the prevailing surgical opinions of the 1970s, and were even asked to prove their mental capacity by undergoing evaluations of their physical and mental health, including electroencephalograms. Laparoscopy gained worldwide acceptance after Nezhat introduced video laparoscopy in 1986^[6]. Advanced instruments and apparatuses made laparoscopy transparent and accessible to the medical community at large^[1].

We started to use a teaching scope for laparoscopy in 1975, followed by video projection of the procedure on monitors. However, ten years later, it was Camran Nezhat who promoted video laparoscopy globally^[6]. By 1976, all ectopic pregnancies in Kiel were treated via laparoscopy^[10]. As mentioned above, in 1975, Kurt Semm was accused of malpractice due to his use of

laparoscopic surgery. Semm's brain was checked on CT scans and he had to face numerous legal disputes. Here is a short resume of Lilo Mettler's achievements in gynecology:

- Between 1975 and 1976: six months of training in physiology under Robert Edwards at Cambridge, UK. One of the many procedures performed during this time were early egg retrievals together with Patrick Steptoe.
- In 1975, during a training course in Italy, Jordan Phillips realized that operative laparoscopy had a future. He congratulated Kurt Semm and Lilo Mettler for promoting laparoscopy.
- In 1976, Mettler acquired her habilitation degree (academic license to teach at university) in the fields of reproductive medicine, endoscopy and gynecology.
- 1980–1996: 85 trips to the US for endoscopy courses on the East and West Coast and in the Mid-west, organized by Jordan Phillips and AAGL. Mettler wished to acquire sufficient skills to teach laparoscopic and hysteroscopic surgery at the Kiel School.
- 1971: Founding of the AAGL
- 1983: Kurt Semm and Lilo Mettler were threatened with expulsion from the German Society of Obstetrics and Gynecology.
- 1986: Camran Nezhat described video laparoscopy
- 1989: Founding of the International Society for Gynecological Endoscopy (ISGE)
- 1994: Founding of the European Society for Gynecological Endoscopy (ESGE).

Many national gynecological endoscopy societies have been formed in the meantime. The previous German Society of Gynecological Endoscopy was revived in 1984, becoming the AGE (Arbeitsgemeinschaft Gynäkologische Endoskopie e.V.) or Work Group of Gynecological Endoscopy. Other societies that were formed included the French Society of Gynecological Endoscopy, the ESGE, the Australian AGES, as well as Asian-Oceanic, Latin-American, and Canadian societies. These were accompanied by the founding of multidisciplinary societies of endoscopic or minimally invasive surgery/medicine (SLS, SMIT, MITAT).

From 1970 to 1990, we developed gynecological laparoscopic surgery in Kiel under Kurt Semm. We attended numerous national and international endoscopy courses including ones staged in Kiel, Clermont-Ferrand, Brussels, Lyon and Strasburg.

Kurt Semm founded the Kiel School of Gynecological Endoscopy as early as 1970. The school was organized and consolidated by Liselotte Mettler, who served as director from 1980 to 2007. She was succeeded by Thoralf Schollmeyer in 2007, while Ibrahim Alkatout took over as director in 2014. Liselotte Mettler is now an honorary patron. The Kiel School, based on the early work of Kurt Semm, has published ten textbooks over the last fifty years; the most recent one appeared in 2019^[1].

History of endometriosis as a disease

Carl von Rokitansky (1804–1878) published the first histological description of endometriosis in 1860. From a scientific and clinical point of view, endometriosis has already assumed “mythical”

proportions. The disease in its various presentations, including endometriosis, adenomyosis, endosalpingiosis, endosalpingitis nodosa, endocervicosis and müllerianosis, has been and continues to be a challenge for scientists and clinicians.

The pathological anatomy of this chronic occult disease was described as a complex issue in the 19th century. It is hoped that the current elucidation of its immunological and genetic etiology will assist in the development of new treatments in the 21st century.

The most extensive survey of the history of endometriosis was a unique book written by Ronald E. Batt, in which he described the philosophical, poetic, intellectual and pathohistological aspects of the disease^[11]. He attributes the final recognition of endometriosis, by Rokitansky, to the Goethe University-educated Alexander von Humboldt, to Johannes Peter Müller, and to the history of embryology. Rokitansky eventually emerged as the first full-time anatomical pathologist. The Vienna Medical School gave Rokitansky an opportunity to write a manual on pathological anatomy, in which he described the disease which was considered new at the time (1860).

Endometriosis is regarded as a progressive disease, but its recurrence rate after surgical resection is only around 10%. Inactive forms of the disease have been found in addition to active lesions. The actual reasons for the emergence of endometriosis are still not clearly understood.

Sampson's theory of implantation endometriosis^[12] and the coelomic metaplasia theory, which is supported by the metaplastic capacity of the secondary Müllerian system, form the basis of current understanding of endometriosis and have been verified experimentally^[13,14]. Metaplasia was regarded as the source of ovarian endometrioma as well. The spread of endometriosis through the lymphatic and the hematopoietic system is a variation of the implantation theory. The theories are complementary, and differ solely in terms of the inception of endometriosis. However, the theories do not really explain the various clinical manifestations of endometriosis or its development into severe disease, manifested as invasion of the bladder, ureter or bowels.

Although we are now aware of the etiology of endometriosis, its various forms such as superficial endometriosis, ovarian cystic endometriosis, and DIE are not fully understood. The peritoneal fluid is a specific microenvironment in patients with endometriosis. The eutopic endometrium in women suffering

from endometriosis is different from that of healthy controls. These cellular differences, together with genetic aspects^[15], help the clinician to recognize and treat endometriosis. According to the endometriosis disease theory, endometriosis is caused by cellular modifications and genetic mutations. It is believed to occur more commonly after irradiation or chemical intoxication, in the presence of poor immune resistance, and other morbidities. However, this is not always the case. Local factors such as peritoneal fluid and cellular modifications are associated with endometriosis in typical locations, including cystic ovaries, superficial peritoneal implants, adenomyosis and deep infiltrating disease^[12,16]

The monthly regeneration of the endometrium after menstrual shedding, and the re-epithelialization of the endometrium after parturition or surgical curettage support the existence of a stem cell pool. Since the basal endometrium is not sloughed along with monthly menstrual bleeding, the stem cells are believed to reside in the basal layer. Clonogenic cells, which are considered to represent the stem cell population in the human endometrium, have recently been identified and implicated in the formation of ectopic endometrial lesions.

Stem cells are undifferentiated cells characterized by the ability to self-renew and differentiate into one or more types of specialized cells. Differentiation is defined as a change in cell phenotype secondary to an alteration in its gene expression, enabling the cell to carry out a specific function. Endometrial self-generation may occur through stem cells in specific niches of the endometrium. Undifferentiated endometrial stem cells may be less responsive to ovarian steroids than their terminally differentiated progeny due to a lack of hormone receptor expression. In addition to resident endometrial stem cells, the incorporation of circulating bone-marrow-derived stem cells may contribute to the cyclic regeneration of the endometrium^[17] (Table 1).

Steps in the diagnosis and treatment of endometriosis

General development of endoscopic endometriosis and the role of surgery

Surgical treatment of endometriosis dates back to the late 18th and early 19th centuries. A variety of surgical modalities evolved during the 20th century, culminating in excessive re-

Table 1 Possible explanations for the etiology of endometriosis.

Theory	Mode of action
Retrograde menstruation	Transport of endometrial cells through the fallopian tubes into the lesser pelvis, allowing the implantation of endometrial lesions
Metaplasia	Transformation of peritoneal tissue/cells into endometrial tissue through hormonal and/or immunological factors
Hormones	Proliferation of endometrial lesions in response to estrogens. Resistance to progesterone-mediated control of endometrial proliferation
Oxidative stress and inflammation	Activation of immune cells and cytokines to promote endometrial growth
Immune dysfunction	Hampers the elimination of menstrual debris and promotes the implantation of endometrial lesions
Genetics	Basis for the increased attachment of endometrial cells and their ability to evade immune clearance
Stem cells	Endometriotic deposits of undifferentiated cells with natural regenerative capacity

section of endometriosis, although with the best of intentions^[2]. Radical surgery was approached with great caution once it became obvious that endometriosis is a lifelong affliction^[18].

Given the absence of evidence-based studies evaluating the medical treatment of endometriosis, Sutton performed a prospective, randomized, controlled double-blind trial of surgery for endometriosis. Until then, no investigation of this nature had ever been attempted. His research team had to resolve the difficult task of recruiting women for the study. Patients who had been referred specifically for laparoscopic laser surgery were asked to participate in a trial in which one arm would undergo diagnostic laparoscopy alone, but with the same incisions as the counter-group. To avoid bias, the details of surgery were sealed and follow-up data were recorded by a research nurse who was unaware of the details of the surgery. Thus, the study was performed in an entirely double-blind manner, comparing treatment and no treatment. In each case, neither the patient nor the nurse involved in her follow up would be aware of the patient's allocation. The results revealed a substantial placebo response in the no-treatment group at three months. However, at six months there was a significant difference between the groups. The patients' visual analog pain scores had improved considerably in the laser treatment group, but returned to preoperative levels in women who only underwent a diagnostic laparoscopy^[19].

Clinical symptoms and pain in specific forms of endometriosis, and their treatment

The manifold disease phenomenon of endometriosis can be tackled effectively through a cooperative effort on the part of gynecologists, endocrinologists, obstetricians, general surgeons, urologists and psychologists, as well as physiotherapists. Complementary approaches such as diet, yoga, sports, swimming, osteopathy and meditation can be helpful.

In the following, we discuss five manifestations of endometriosis, their symptoms and treatment.

Endometriosis and infertility

In cases of infertility (primarily in patients with endometrioma), the woman's wish to conceive is the foremost concern. In the last twenty years, a number of new concepts have been proposed for the treatment of endometriosis in the presence of infertility. An endometrioma need not always be enucleated immediately via laparoscopy.

In the absence of significant pain, clinicians initially focused on the patient's desire of pregnancy. Asymptomatic DIE has, in fact, also been observed during the treatment of infertility. As endometriomas are found in 55% of patients with endometriosis, their location calls for specific attention. When normal ovarian follicles with a maximum size of 4–8 cm were found in addition to endometrioma, the patient could be stimulated with recombinant or urinary extracted gonadotrophins as well as undergo IVF/ICSI treatment, and this approach was given preference. In other words, if the AMH and other ovarian reserve markers permit ovarian hyperstimulation, the endometrioma can be treated later.

Infertility treatment is given priority because the ovarian reserve decreases with advancing age. An endometrioma should not be punctured or aspirated during any assisted reproductive

technology treatment^[2]. If an endometrioma is punctured unintentionally, antibiotic coverage as well as intensive observation during the first week after follicular puncture is advised.

Endometriosis in the presence of bleeding abnormalities

Bleeding abnormalities are warning signs of endometriosis. Patients experience abdominal cramps, pain, dyspareunia, dysmenorrhea, dysuria and dyschezia.

The diagnosis is established by performing 2D or 3D ultrasound examinations, followed by a diagnostic and operative hysteroscopy to obtain material for histological examination. Fluid hysteroscopy helps to identify endometritis, adenomyosis, polyps, myomas, septae, congenital uterine anomalies, cancer, foreign bodies and remnants of placenta. The majority of surgical corrections can be performed during the same procedure.

Endometriosis in the presence of pain

The clinician's approach is based on the principle of neuropelvicology, established by Marc Possover^[20]. Where does the pain come from? Nerves must be involved. The pelvic organs are supplied by nerves of the pelvic organs themselves and those of the lower extremities. The visceral nerves have parasympathetic elements. Somatic pelvic nerves originate from the pudendal plexus, while somatic nerves of the lower extremities originate from the lumbar and sacral plexus. In cases of resection for DIE, care should be taken to preserve the splanchnic and hypogastric nerves. Many surgeons are not even aware of these nerves, and excise them along with the endometriotic lesion, with the result that the patient returns later with a different pattern of pain and functional organ disorders. As early as 2005, Sylvia Mechsner^[21] described nerves associated with endometriosis and concomitant immature vessels. This made it clear that nerves may invade endometriotic lesions. The hypothesis is supported by the fact that all growth factors are found in patients with endometriosis. Even the peritoneal fluid contains substances that support the growth of neural structures. Levels of nerve growth factor (NGF) in peritoneal fluid were significantly higher in patients with endometriosis than in healthy controls. In an *in vitro* growth test for nerve fibers, Mechsner observed new growth of nerve fibers by incubation in the peritoneal fluid of endometriosis patients. This effect could be suppressed by NGF-inhibitors^[22, 23].

Medical treatment consists of analgesics of the NSAID group, such as ibuprofen, paracetamol and naproxen. Hormonal treatments include oral contraceptives, gestagens, and GnRH agonists, aimed at producing hypoestrogenism. Dienogest is given preference at the present time because of its low side-effect profile.

Treatment options still in the experimental stage include letrozole (an aromatase inhibitor), GnRH antagonists, COX-2 inhibitors, selective estrogen receptor modulators, and selective progesterone receptor modulators. Angiogenesis inhibitors and immune modulators are also worthy of mention.

Surgery is based on prior histological diagnosis, and differs according to the location of the disease.

Superficial peritoneal endometriosis with active and inactive lesions:

Complete excision of the lesions without laceration of pel-

vic organs reduces pain and is therefore the primary aim of treatment (Figure 3). However, the superiority of resection over ablation has not been conclusively proven in scientific studies. In a Cochrane analysis, Jacobsen reported similar results for ablation and resection with regard to pain^[24].

Ovarian endometriosis:

Complete endometrioma resection achieved better pain relief for the patient than partial enucleation by the conventional laparoscopic or robotic-assisted approach (Figure 4). With reference to the preceding section on endometriomas in infertile patients, it should be noted that any surgical resection may have a destructive effect on the ovarian cortex. Therefore, the techniques described and defended by Michelle Nissolle, based on the use of minimal coagulation to destroy the endometriosis rather than enucleate the entire cyst, is being given increasing preference even by proponents of aggressive surgery. Healthy ovarian tissue must be preserved for as long as possible.

Deep infiltrating endometriosis:

Of foremost concern in these patients is the identification, correct interpretation, and classification of pain. Damage to organs such as the bladder, ureter or bowel, and hydronephrosis should also be identified. This entity is rated on the Enzian scoring system at every certified endometriosis center in Europe^[25].

Any surgical correction of a frozen pelvis requires thorough knowledge of clinical anatomy and vast surgical experience. The extent of surgery depends on the patient's age and life situation. Preservation of the genital tract is a foremost priority in women of reproductive age. Resection of the uterus, fallopian tubes and ovaries may be considered in postmenopausal women. A variety of laparoscopic techniques are used in bladder, ureter or bowel endometriosis or adenomyosis. Ureteral stents are employed to achieve end-to-end anastomosis after segmental resection. In cases of new implantation of ureters into the bladder, the psoas hitch operation or the Boari-flap technique is performed in cooperation with urologists.

Pain and significantly reduced quality of life call for active

Figure 3 Small red active endometriotic lesions on the roof of the bladder.

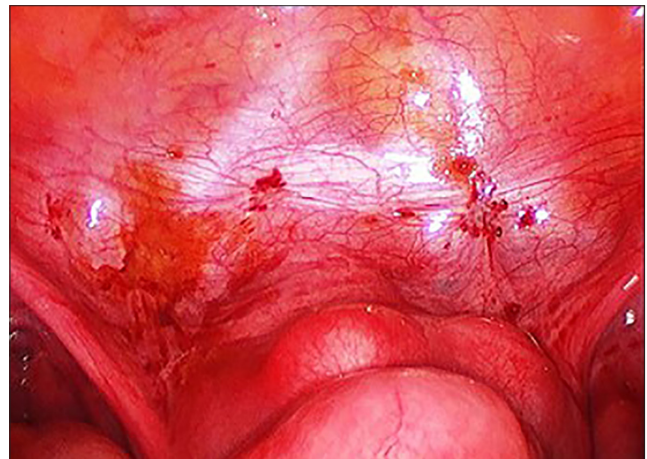
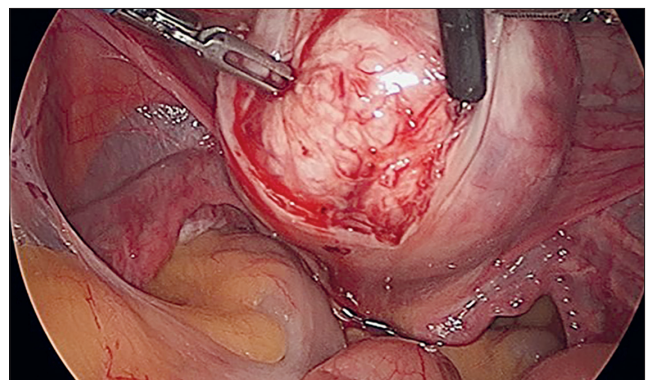


Figure 4 Laparoscopic resection of a 5 cm endometriotic cyst.



surgical intervention in patients with bowel endometriosis. Depending on the infiltration depth of endometriosis as demonstrated on preoperative rectal ultrasound or MRI, the surgeon and patient decide to perform one of the following three procedures: 1) Superficial shaving of the rectal wall, 2) partial bowel resection, or 3) segmental bowel resection^[26-28]. The surgical procedure is planned in close cooperation with general surgeons (Figure 5.1, 5.2 and 5.3).

Figure 5.1 A) Laparoscopic segmental resection of a recto-sigmoid endometriotic lesion located 7 cm above the anus using the DaVinci robotic technique. **B)** Schematic illustration of laparoscopic recto-sigmoid resection

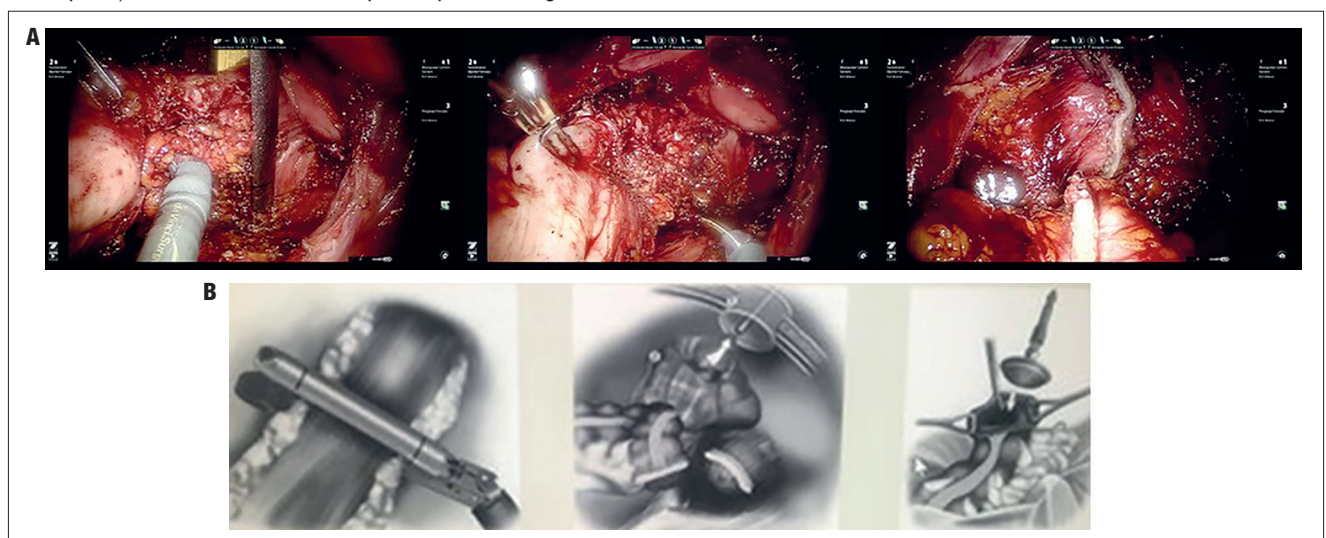


Figure 5.2 **A)** Extracorporeal images showing the introduction of the upper connecting part of the circular stapler into the healthy sigmoid loop that is at that moment out-side the body. It is then reinserted into the abdomen. Later transrectally the lower connecting part of the circular stapler is inserted and the anastomosis performed with the circular stapler under laparoscopic vision (see Fig. 5.3). **B)** Resected recto-sigmoid tumor, 10 cm in size.

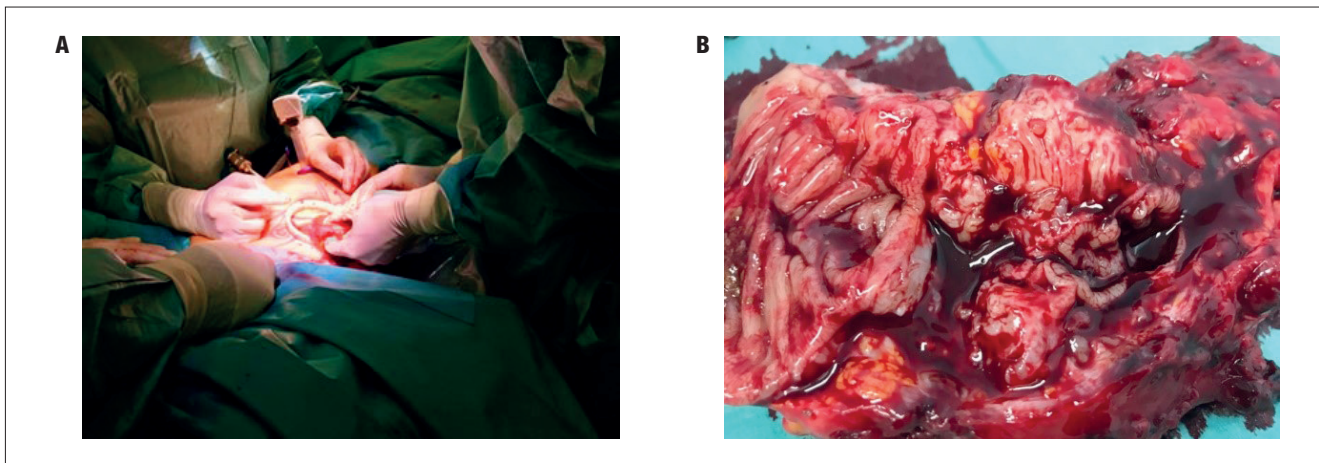
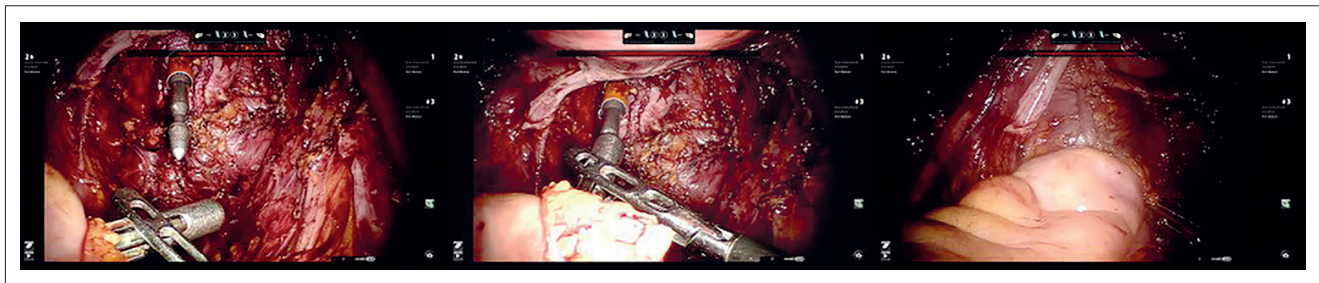


Figure 5.3 After repositioning of the healthy sigmoid into the abdomen, end-to-end anastomosis of the rectum and the sigmoid colon performed with the circular stapler.



Endometriosis in pregnancy

Endometriosis has been associated with a risk of abortion and ectopic pregnancy in the first trimester. Potential preterm deliveries and complications have been observed in the third trimester. Pregnant women with endometriosis do not always experience an improvement of their disease. Inflammation and alterations within the uterine cavity may jeopardize implantation and intrauterine development of the fetus. Moreover, endometriosis is an independent risk factor for placenta previa.

Spontaneous bowel perforations, rupture of endometriotic cysts, uterine ruptures, and intraabdominal bleeding of decidualized endometriotic lesions occur more frequently in patients with endometriosis than in other patients. Any woman who becomes pregnant after complex endometriosis surgery must be monitored and observed carefully^[29].

Post-operative bowel complications during pregnancy after IVF stimulation may occur in patients with DIE, in particular. As a reason for these findings, Antonio Setubal suggests that the endocrine environment of pregnancy does not always prevent progression of the disease. Therefore, the aforementioned spontaneous bowel perforations should not be forgotten^[30].

How is endometriosis differentiated from malignancies?

Endometriosis, and particularly endometriomas, are established risk factors for ovarian cancer. The risk of developing an epithelial or clear cell or endometrioid ovarian carcinoma is definitely higher in patients with endometriosis than in the general population^[18]. Common predisposing factors are early

menarche, short menstrual intervals, and nulliparity.

In an evaluation of 550 patients who had undergone surgery for endometrioma from 1995 to 2004, we observed two ovarian cancers in five years post-surgery. The overall risk of ovarian cancer in patients with endometriosis is 1.3–13.2%^[31-34]. The genetic pattern of the endometrium, endometriotic tissue and ovarian cancer revealed a variety of up-regulating and down-regulating genes^[15]. Moreover, oxidative stress, local inflammatory processes, and hyperestrogenism play an important role in the genesis of ovarian cancer. Increased levels of proinflammatory cytokines such as IL-1, IL-6, IL-8, and TNF α may cause a ten-fold increase in COX2 promoter activity in the ectopic endometrium compared to the eutopic endometrium. This may be interpreted as a sign of neoplastic transformation.

In cultivated endometriosis, endometrium and ovarian cancer tissue samples, we tried to identify specific gene patterns that might indicate the progression of endometriosis into ovarian cancer. However, we were unable to generate repetitive genetic patterns for the early differentiation of ovarian cancer from endometriosis. Although Fuminori Taniguchi⁽³⁵⁾ described fibroblast growth factors (FGFR2) that were overexpressed in endometriosis, we may safely conclude that research on the progression of endometriosis into ovarian cancer is not complete yet.

Lifelong gynecological surveillance is warranted in patients with ovarian malignancies who have undergone endometrioma surgery. Early recognition of any transformation into ovarian cancer is a prime concern. Obviously, atypical patho-

logical lesions must be followed up in patients who have undergone any type of infertility treatment. Total excision is one of the main approaches in this setting. If surgical clarification is not possible despite pain and the presence of atypical lesions on ultrasound or MRI, the patient must be cautioned about the high risk of ovarian cancer.

Discussion and future perspectives in gynecological endoscopy for the five types of endometriosis

Modern gynecological surgery is only 150–200 years old. Access routes include the vaginal pathway, the transabdominal route, gastrointestinal or transvesical entry into the abdomen, and image-guided entry. Hysteroscopy offers the advantage of granting direct entry into the uterine cavity using continuous flow technology. Laparoscopy involves direct entry, under CO₂ expansion of the abdominal cavity, by the conventional or robotic approach.

Surgery is used for the diagnosis and treatment of benign and malignant endometriosis. Samples of the endometrium and of ovarian cancer tissue cannot be distinguished easily. Knowledge of clinical anatomy constitutes the basis of any surgical procedure. Endoscopic and image-guided surgery are well-established procedures for benign and malignant conditions. Hysteroscopy and laparoscopy are both of great value in the diagnosis and treatment of endometriosis.

It took about fifty years for endoscopic surgery to be integrated into the medical curriculum at almost every surgical unit and institution around the world. Kurt Semm's wish came true. Endoscopy has become a ubiquitous procedure. Despite certain shortcomings of the technique, our vision of teaching this type of surgery in conjunction with imaging technologies will pave the way for further benefits in the future.

With good reason, each surgical specialty is handled separately. In fact, super-specialization has allowed surgeons to focus on expertise in specific fields. However, healthy cooperation and exchange of ideas between general surgeons, urologists, gynecologists, neurologists and orthopedic surgeons will continue in the interests of mutual benefit.

Neuropelvelogy, a new discipline founded by Marc Possover, highlights important areas of interaction^[20], especially in the field of endometriosis.

In 2016 we founded the Kurt Semm Center for Endoscopic Conventional and Robotic Surgery in Kiel, Germany, as an interdisciplinary center for urologists, general surgeons, gynecologists and other specialists. We intend to continue our work while adhering strictly to the guidelines established by professional societies in our country and throughout the world. In the interest of patients and doctors, we focus on clinical research and the acquisition of new data. Although a number of skilled and astute individuals do not accord surgery the status of a science, surgery nevertheless remains the most effective tool for the diagnosis and treatment of endometriosis, and deserves to be validated as such.

Targeted efforts to transform a dream into reality have resulted in fruitful cooperation between gynecologists, especially gynecological endoscopic surgeons, general surgeons, endocrinologists, geneticists, and basic researchers, as well as internists, neurologists, psychologists, physiotherapists and specialists of complementary medicine.

Summary

The identification and treatment of endometriosis is based on guidelines issued by professional societies, both in our country and internationally (namely the German S2k and the ESHRE, ESGE, EGE and WES guidelines for endometriosis)^[36-38].

The postulated mechanisms of endometriosis are based on well-known etiological factors. In practice, the recognition and treatment of endometriosis are based on the following parameters: age, description of any pain, knowledge of the patient's medical history and menstrual cycle, gynecological examination of the vagina, cervix and uterus, rectovaginal examination, posterior uterine wall examination, and 2/3D ultrasound with a vaginal and abdominal probe^[39-41].

The treatment of patients with pain differs from that of patients without pain. We also differentiate between patients with endometriomas who desire to become pregnant and those with endometriomas who do not desire pregnancy. Patients with bleeding disorders need special attention and must be investigated by hysteroscopy. A malignancy must always be excluded. The treatment of patients with endometriosis during pregnancy is subject to special criteria. Pregnancies must be monitored especially with regard to the risk of uterine rupture after previous endometriosis surgery on the uterus, and placenta previa.

Therapeutic strategies follow the endoscopic histological diagnosis and include medications such as Visanne or GnRH agonists, and specific surgical procedures.

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