

**Clinical outcome of deep infiltrating colorectal endometriosis surgeries
in the Endometriosis Center of the University of Gießen and Marburg
between 2005-2015**

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1. Introduction

1.1. Definition and pathophysiology of endometriosis

Endometriosis is characterized as endometriotic tissue, glands and stroma, outside the uterine cavity (*Sampson 1921*). Although, endometriosis has been described for a century we still not fully understand the pathophysiology of this benign progressive chronic disease. The mostly accepted theories describe that the implants either originate from uterine endometrium or arise from tissues other than the uterus, such as stem cells, metaplasia of mesothelial cells or induction of embryonic Müllerian rests. Moreover, altered hormonal milieu, environmental factors and genetic components may predispose to the disease (*Burney and Giudice 2012*).

Among the various hypotheses the modified and extended Sampson's theory of retrograde menstruation and implantation of sloughed endometrial tissue is the most popular and has gained widespread acceptance (*Sampson, 1927*). Retrograde menstruation seems to occur in most of the women and endometriosis develops just in some, so many concomitant pathological conditions explain the development of endometriotic lesions. The first crucial step is the survival of the refluxed endometrial cells in the pelvic cavity. This can be explained with a decreased rate of apoptosis (*Jones et al., 1998*) and dysregulated immunological clearance. Ectopic endometriotic cells are resistant to natural killer cell lysis and altered cell-mediated immune response also seems to play an important role of pathophysiology. There are observations about compromised function of NK-cells, macrophages (*Oosterlynck et al., 1991*), neutrophil granulocytes (*Berkes et al., 2014*) and dendritic cells (*Schulke et al., 2009*). The survived endometriotic cells attach on different surfaces of the pelvic cavity, such as the ovaries, tubes, peritoneum, bladder or bowel and invade the affected tissues. Existing damages of the peritoneum may be a predisposing factor of the implantation and determines the site of a lesion development. However, it seems that the menstrual effluent itself can cause damages on the mesothelium as well (*Young et al., 2013*). The implantation of endometriotic cells is followed with invasion of the surrounding tissue caused by a failure to maintain the balance between matrix metalloproteinases and their inhibitors in the extracellular matrix (*Burney and Giudice, 2012*). The further development of endometriotic lesions is supported from a rich vascular supply. Increased amounts of

vascular endothelial growth factor in peritoneal fluid and in ectopic lesions and other angiogenic factors, such as angiogenin, platelet-derived endothelial growth factor and macrophage migration inhibitory factor have been found to contribute to the vasculogenesis of the lesions (*Suzumori et al., 2004; Fujimoto et al., 1999; Yang et al., 2000*).

Endometriosis is believed to be a chronic pelvic inflammatory condition. However, whether the proinflammatory peritoneal and lesional microenvironment is a cause or consequence of the disease remains to be clarified. An increased number of activated macrophages, several cytokins, such as interleukin (IL)-6, macrophage migration inhibitory factor, tumor necrosis factor- α , IL-1 β , IL-8, regulated on activation, normal T cell expressed and secreted (RANTES), and prostaglandins (PG), such as PGF2 α and PGE2 have been observed in the peritoneal fluid of affected women (*Eisermann et al., 1988; Harada et al., 1997; Burney and Giudice, 2012*). Most of these proteins are up-regulated by the transcription factor, nuclear factor kappa B, which is a key protein in the pathophysiology of endometriosis (*Gonzales-Ramos et al., 2012*). The proinflammatory peritoneal and lesional milieu directly activate sensory nerve endings and activate a positive feedback loop, further increasing proinflammatory modulator production and neurogenic inflammation. The enhanced stimulation and activation of peripheral nerve endings in the peritoneal cavity increases the painful stimuli transmitted to the spinal cord, initiating and maintaining chronic pelvic pain (*Maddern et al., 2020*), which is one of the major clinical manifestations of the disease.

Although the extended Sampson's theory is widely accepted it does not explain all clinical aspects of endometriosis. Lately a new holistic genetic/epigenetic theory of pathogenesis has been described. This theory differentiates between physiological and pathological endometriosis lesions. Microscopic and subtle endometriosis is considered to be early intermittently physiological lesions following retrograde menstruation in almost all women and can diminish over the time. Hereditary or acquired genetic incidents are required to develop the endometriotic disease in form of typical-, cystic- and deep endometriotic lesions. The oxidative stress in the uterus during menstruation and in the peritoneal cavity as well as the microbleeding in endometriosis lesions induce genetic and epigenetic changes, resulting subtle and microscopic lesions to progress to more severe ones (*Koninckx et al., 2019*).

Not only the pathophysiology, but also the identification of a non-invasive biomarker of the disease remains elusive. In the last few decades over hundred potential biomarkers

and panels of biomarkers have been tested for endometriosis, but none of them has been proven as a reliable diagnostic tool (*Anastasiu et al. 2020, Berkes et al., 2013*). The gold standard to diagnose endometriosis remains invasive, performing a diagnostic laparoscopy with visual detection and histological confirmation of the lesions.

1.2. Symptoms and clinical manifestations of endometriosis

Endometriosis is the second most common benign gynaecological disease following uterine fibroids and affects around 10-15% of women in the reproductive period. It has been estimated that more than 176 million women worldwide suffer from endometriosis and its associated symptoms (*Adamson et al., 2010*). The real prevalence of the disease is difficult to determine and varies among the subtypes of the disease. Very high incidences of 50-80% have been reported in women with sub- and infertility and even in asymptomatic women in up to 40% subtle endometriosis lesions have been found (*Koninckx et al., 2020*). Endometriosis can cause a huge variety of pain symptoms, such as chronic pelvic pain, dysmenorrhea, dyspareunia, dyschezia and dysuria. The chronic inflammatory peritoneal and lesional milieu and the concomitant severe anatomical distortion of the pelvic cavity, the tubes and ovaries cause sub- and infertility. The symptoms may begin in the early adolescence, but most of the women are affected in the reproductive period. Sometimes the symptoms are still present in women beyond the perimenopause. The symptoms impair the quality of life of affected women and have a negative impact on their family, social and work life. However, endometriosis is a benign condition, increased risk of endometriosis associated ovarian cancer and malignant transformation of deep endometriotic lesions has been also described (*Kvaskoff et al., 2021*).

Depending on the localisation of the ectopic lesions and the depth of infiltration mainly four clinical manifestations of the disease can be distinguished; peritoneal, ovarian, uterine (adenomyosis) and deep endometriosis (DE). Peritoneal endometriosis can be further divided to subtle superficial lesions and to typical infiltrating red, bluish and white lesions. Ovarian endometriosis may affect the ovarian surface or cause cystic lesions in the stroma of one or both ovaries with concomitant adhesions to the surrounding structures, such as tubes, pelvic side wall and bowel, causing large adnexal masses.

DE is defined as endometriotic lesions, infiltrating the surrounding tissue deeper than 5 mm (*Koninckx et al., 2012*). Infiltration the visceral and parietal peritoneum can lead to

involvement of retroperitoneal organs. DE can affect the bowel, bladder, vagina, rectovaginal septum, sacrouterine- and round ligaments, pelvic side walls and the ureters. The deep glandular lesions are often associated with extensive fibrosis leading to distortion of the anatomy, diminishing clear organ boundaries and causing difficulties during surgical treatment (*Keckstein et al., 2020*). The prevalence of DE among endometriosis patients is reported to be 48% (*Cornillie et al., 1990*). The different clinical manifestations and leading symptoms of endometriosis are summarised in **figure 1**.

The therapy of the disease is depending on the pain symptoms, fertility issues, localisation and extension of the disease. The gold standard of the therapy is the surgical removal of endometriotic lesions (*AWMF, Endometriose Leitlinie, 2020*). In case of peritoneal endometriosis, the lesions can be removed with excision or ablation-vaporisation. Cystic ovarian endometriosis can be treated with (i) extirpation of the cyst wall using traction and countertraction, (ii) in selected cases with opening the cyst wall, suction of the chocolate fluid and vaporisation of the cyst wall or (iii) using the combination of both surgical approaches (*Gordts and Campo 2019*). The ovaries should be temporary fixed on the abdominal wall to prevent postoperative adhesions and optimise fertility treatment. Severe adenomyosis of one or both uterine walls can also be treated surgically in selected cases, performing a cytoreductive surgery with excision of the adenomyosis and extensive reconstruction of the uterine wall. In case of DE the surgical treatment is challenging, often involves multivisceral extensive surgery and should be performed in specialised centers with expertise of multidisciplinary teams of gynaecologists, general surgeons and urologists.

The second line of treatment is the pharmacotherapy of endometriosis. Medical therapies are unable to induce complete regression of the lesions and are primary used to decrease pain symptoms, improve quality of life, delay surgical intervention and prevent recurrence of the disease. Endometriotic lesions are oestrogen dependent and most of the medications modulate symptoms by suppressing ovulation or inducing hypoestrogenic state, which results in decidualisation and atrophy of ectopic lesions. Combined oral contraceptives, progestins, gonadotrophin-releasing hormone antagonists and agonists and aromatase-inhibitors are the main pillars of the systematic endocrine therapy (*Schwartz et al., 2020*). Local endocrine treatment can be also applied. The levonorgestrel intrauterine device has been proven to improve endometriosis associated symptoms (*Brown and Farquhar, 2014*) and can be a useful tool for patients suffering from extensive adenomyosis and DE of the rectovaginal septum, vagina and anterior rectal wall.

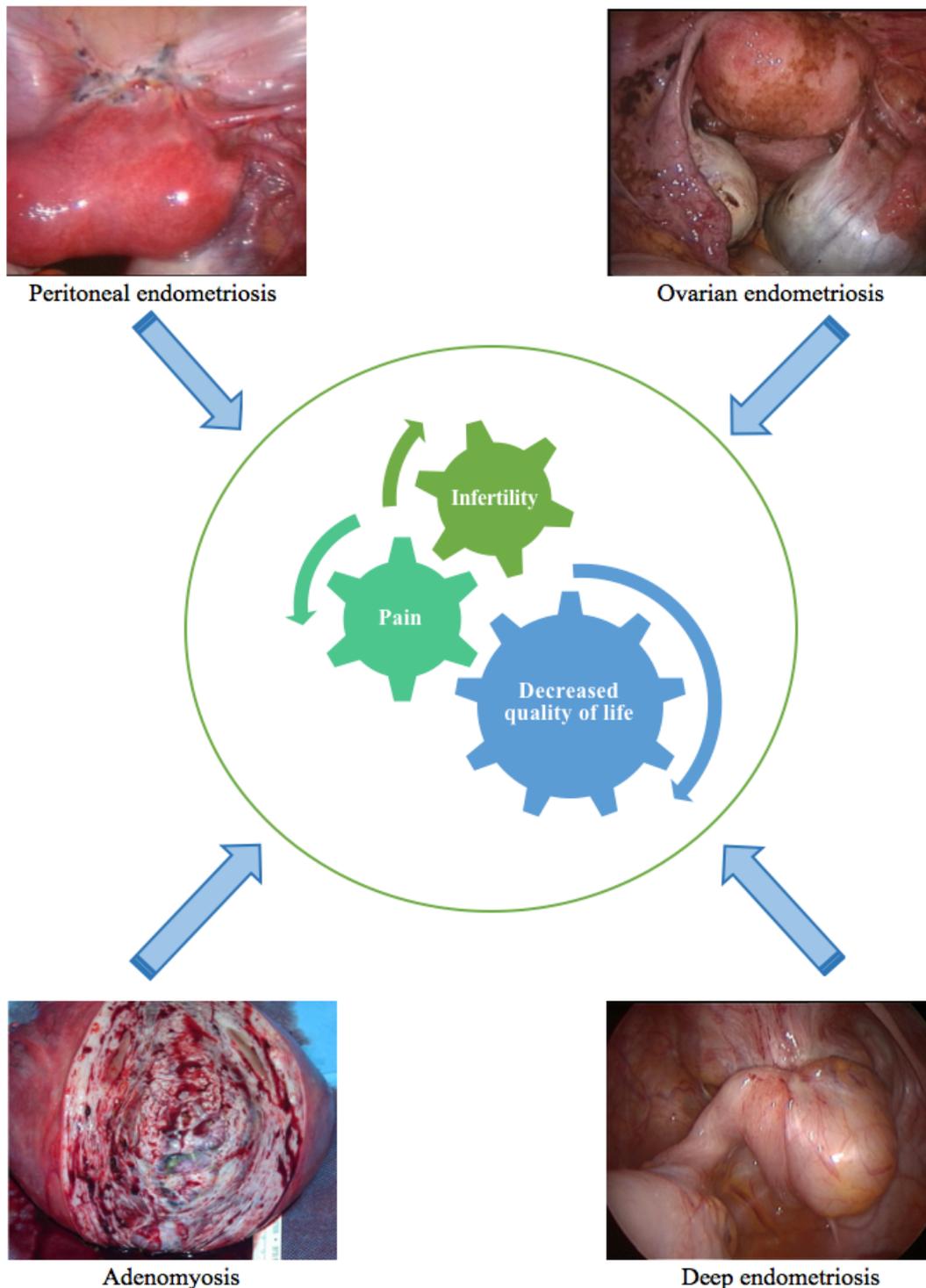


Figure 1. Clinical manifestations and symptoms of endometriosis

Endometriosis has four typical manifestations, which are demonstrated with intraoperative pictures from our centre. Peritoneal endometriosis appears in red, bluish or white lesions. Ovarian endometriosis effects the surface of the ovary or forms a cystic lesion. Adenomyosis infiltrates the uterine muscle and deep endometriosis penetrates retroperitoneal organs, like bowel, bladder, ureters, vagina and rectovaginal space and causes obstruction of the pouch of Douglas. All types of the disease can cause severe pain symptoms, sub- and infertility and burdened quality of life.

1.3. Classification of endometriosis

Several classification systems for the description and staging of endometriosis have been proposed in the last few decades, but none of them describes the disease considering all its aspects. An ideal classification should describe the involved anatomical structures and concomitant adhesions, provide a correlation with clinical symptoms and infertility, predict the surgical difficulty and risks, should be user friendly, validated and give a prognosis about the course of the disease. Currently such classification does not exist, thus the surgical report should include all the widely used systems. The most well-known classification systems are the revised American Society for Reproductive Medicine classification (rASRM), the ENZIAN classification and the endometriosis fertility index (EFI) (Engel *et al.*, 2015). These classifications are based on the extent of endometriosis during the surgery.

The rASRM score describes the size and depth of infiltration of the lesions in the ovaries, peritoneum and the severity of the adhesions in the adnexa and pouch of Douglas. The lesions and adhesions are scored and summed resulting four stages of the disease; minimal-mild, moderate, severe and extensive endometriosis (**figure 2**) (Fertil Steril 1997). The rASRM classification is the most distributed system worldwide and has the advantage of international comparability and description of stages of the disease similar to description of malignant conditions. However, the stages correlate with the extension of the disease, unfortunately it does not correlate with the severity of the symptoms. Patients with minimal stage I endometriosis of the peritoneum might suffer from severe pain, whereas patients with stage IV endometriosis, obliteration of the pouch of Douglas and presence of DE can be completely asymptomatic (Vercellini *et al.*, 2007). The other major disadvantage of the rASRM Classification is the incomplete, almost missing description of DE.

In order to better describe DE, the ENZIAN classification has been introduced in 2002 (Tuttles *et al.*, 2005) and revised in 2011. The ENZIAN classification describes deep infiltrating lesions in three compartments. Compartment A consisting of the rectovaginal septum and vagina, compartment B consisting of the uterosacral ligaments and pelvic walls, including external ureteral endometriosis and compartment C consisting of the rectum. The compartments are further divided according to lesion sizes up to 1 cm, lesions of 1-3cm and lesions larger than 3 cm. DE to other organs in the pelvic cavity and the presence of adenomyosis is expressed as follows: “FA” is defined as adenomyosis, “FB”

as bladder endometriosis, “FU” as intrinsic ureter endometriosis, “FO” as involvement of other locations, and “FI” as involvement of the small intestine (**figure 3**). The system is based on the intraoperative mapping of the disease extension, which is summarised in an acronym. E.g. ENZIAN FA, B2, C3, describes a patient with adenomyosis, DE of the sacrouterine ligament with a lesion size of 1-3cm and involvement of the rectal wall with a lesion larger than 3cm. The ENZIAN classification is a perfect tool to describe DE and it clearly correlates with the extensions of the disease, surgical difficulty and risks. Moreover, it seems to correlate with the presence and severity of different pre-operative symptoms (*Montanari et al., 2019*). Unfortunately, ENZIAN score has gained acceptance mainly in the German speaking countries. The conventional ENZIAN classification has been currently further developed to the #ENZIAN classification to integrate the description of peritoneal endometriosis, ovarian endometriosis as well as tubal distortion to the precise description of DE in the posterior compartment and to consider all endometriosis lesions in the abdominal cavity. The #ENZIAN is applicable for imaging modalities as well, enabling a precise planning for the surgical procedure (*Keckstein et al., 2021*).

The purpose of the development of the EFI score was to describe fertility aspects and predict pregnancy rate after the surgery (*Adamson et al., 2010*). The function of the ovaries, the tubes and the fimbria are evaluated and scored during the surgery. The resulting score is further considered with the rASRM score and historical factors, such as age, duration of infertility and prior pregnancy history. The surgical and historical factors are summed up resulting the EFI score, which describes the probability of being spontaneously pregnant after the surgery in a period of 3 years. The score ranges from 0 to 10 points, with 10 indicating the best prognosis of getting pregnant and 0 the worst (**figure 4**).



AMERICAN SOCIETY FOR REPRODUCTIVE MEDICINE
REVISED CLASSIFICATION OF ENDOMETRIOSIS

Patient's Name _____ Date _____
 Stage I (Minimal) - 1-5
 Stage II (Mild) - 6-15
 Stage III (Moderate) - 16-40
 Stage IV (Severe) - >40
 Total _____

Laparoscopy _____ Laparotomy _____ Photography _____
 Recommended Treatment _____
 Prognosis _____

PERITONEUM	ENDOMETRIOSIS	<1cm	1-3cm	>3cm
	Superficial	1	2	4
Deep	2	4	6	
OVARY	R Superficial	1	2	4
	Deep	4	16	20
	L Superficial	1	2	4
	Deep	4	16	20
POSTERIOR CULDESAC OBLITERATION		Partial	Complete	
		4	40	
OVARY	ADHESIONS	<1/3 Enclosure	1/3-2/3 Enclosure	>2/3 Enclosure
	R Filmy	1	2	4
	Dense	4	8	16
	L Filmy	1	2	4
	Dense	4	8	16
	TUBE	R Filmy	1	2
Dense		4*	8*	16
L Filmy		1	2	4
Dense		4*	8*	16

*If the fimbriated end of the fallopian tube is completely enclosed, change the point assignment to 16.
 Denote appearance of superficial implant types as red [R], red, red-pink, flamelike, vesicular blobs, clear vesicles], white [W], opacifications, peritoneal defects, yellow-brown], or black [B] black, hemosiderin deposits, blue]. Denote percent of total described as R __%, W __% and B __%. Total should equal 100%.

Additional Endometriosis: _____

Associated Pathology: _____

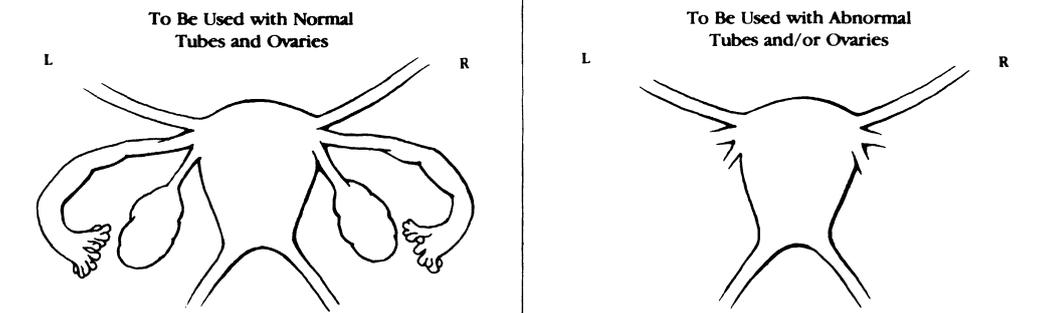


Figure 2. The revised American Society for Reproductive Medicine (rASRM) classification of endometriosis

The lesions of the peritoneum, ovaries and tubes are scored according to size and depth of infiltration, summed up with the score of the adhesions of the adnexa and Pouch of Douglas resulting a four stages system. Stage I with scores up to 5 (minimal-mild), stage 2 with scores 6-15 (moderate), stage III with scores 26-40 (severe) and stage IV with a score beyond 40 (extensive).

ENZIAN 2012

Classification of Deep Infiltrating Endometriosis (according to the Endometriosis Research Foundation, SEF)

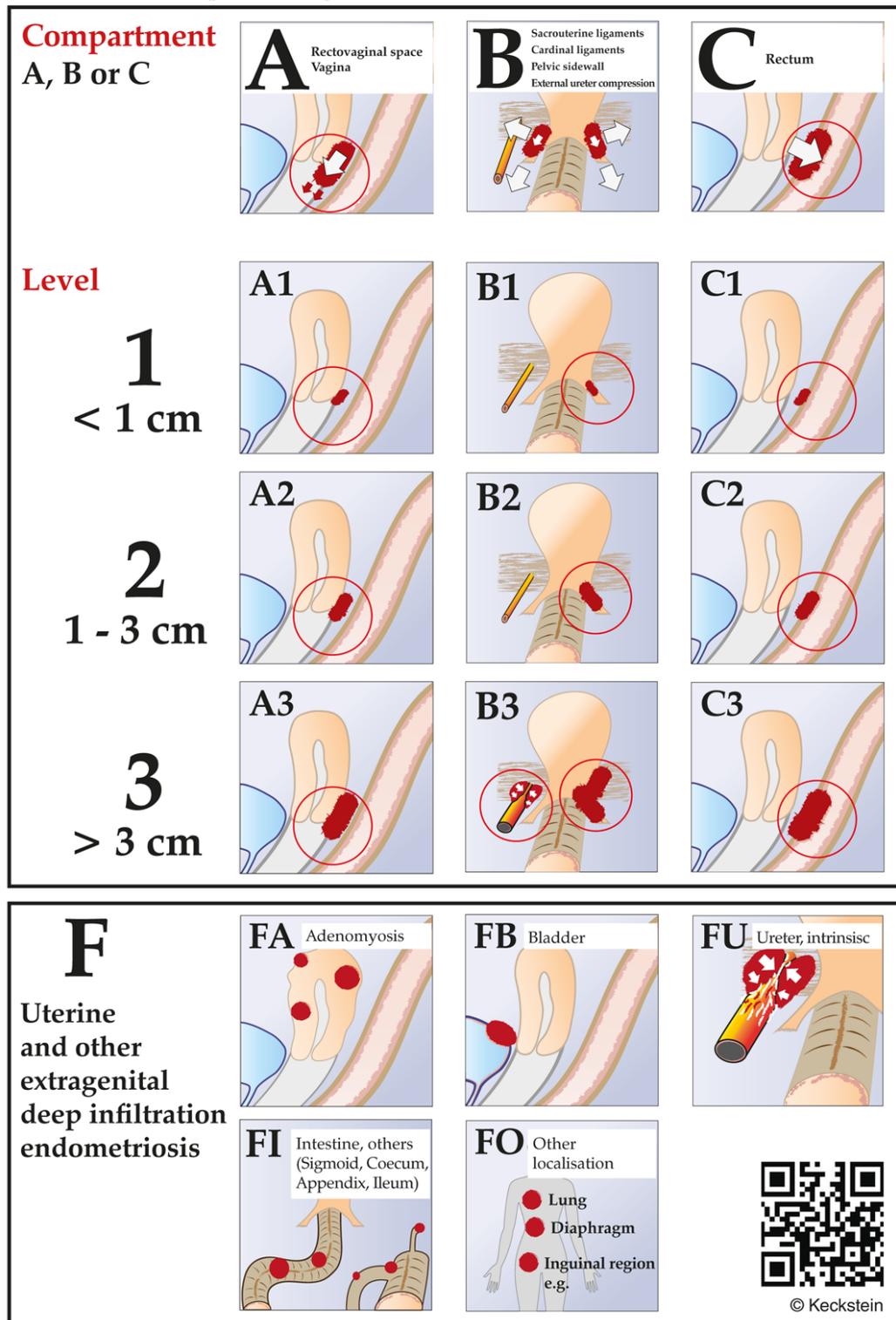


Figure 3. The ENZIAN Classification

The classification describes deep infiltrating endometriosis in compartment A (vagina and rectovaginal space), B (sacrouterine ligaments, cardinal ligaments and pelvic side walls) and C (rectum), the presence of adenomyosis (FA) and further locations, such as bladder (FB), intrinsic ureter (FU) and extrapelvic manifestations (FO).

ENDOMETRIOSIS FERTILITY INDEX (EFI) SURGERY FORM

LEAST FUNCTION (LF) SCORE AT CONCLUSION OF SURGERY

Score	Description	Left	Right	
4	= Normal	Fallopian Tube	<input style="width: 40px; height: 20px;" type="text"/>	<input style="width: 40px; height: 20px;" type="text"/>
3	= Mild Dysfunction	Fimbria	<input style="width: 40px; height: 20px;" type="text"/>	<input style="width: 40px; height: 20px;" type="text"/>
2	= Moderate Dysfunction	Ovary	<input style="width: 40px; height: 20px;" type="text"/>	<input style="width: 40px; height: 20px;" type="text"/>
1	= Severe Dysfunction			
0	= Absent or Nonfunctional			

To calculate the LF score, add together the lowest score for the left side and the lowest score for the right side. If an ovary is absent on one side, the LF score is obtained by doubling the lowest score on the side with the ovary.

Lowest Score	<input style="width: 40px; height: 20px;" type="text"/>	+	<input style="width: 40px; height: 20px;" type="text"/>	=	<input style="width: 60px; height: 20px; border: 1px dashed black;" type="text"/>
	Left		Right		LF Score

ENDOMETRIOSIS FERTILITY INDEX (EFI)

Historical Factors			Surgical Factors		
Factor	Description	Points	Factor	Description	Points
Age	If age is ≤ 35 years	2	LF Score	If LF Score = 7 to 8 (high score)	3
	If age is 36 to 39 years	1		If LF Score = 4 to 6 (moderate score)	2
	If age is ≥ 40 years	0		If LF Score = 1 to 3 (low score)	0
Years Infertile	If years infertile is ≤ 3	2	AFS Endometriosis Score	If AFS Endometriosis Lesion Score is < 16	1
	If years infertile is > 3	0		If AFS Endometriosis Lesion Score is ≥ 16	0
Prior Pregnancy	If there is a history of a prior pregnancy	1	AFS Total Score	If AFS total score is < 71	1
	If there is no history of prior pregnancy	0		If AFS total score is ≥ 71	0
Total Historical Factors			Total Surgical Factors		

EFI = TOTAL HISTORICAL FACTORS + TOTAL SURGICAL FACTORS:

<input style="width: 60px; height: 20px;" type="text"/>	+	<input style="width: 60px; height: 20px;" type="text"/>	=	<input style="width: 80px; height: 20px; border: 2px solid black;" type="text"/>
Historical		Surgical		EFI Score

ESTIMATED PERCENT PREGNANT BY EFI SCORE

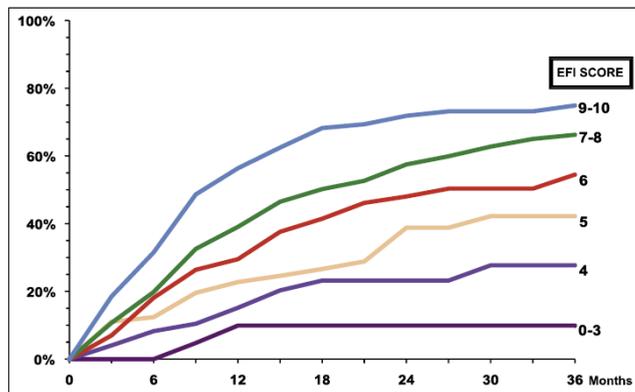


Figure 4. The EFI Score of endometriosis

The EFI score is based on historical and surgical parameters. The historical parameters consider age, duration of infertility and prior pregnancy history. The points are summed up resulting the historical score. The least function score (LF) is calculated by evaluating the function of the ovary, fallopian tube, and fimbria during the surgery. The lowest score on both sides are summed up resulting the LF score. LF is further considered with rASRM lesion and total scores. Finally, The EFI score is calculated by summing the historical and surgical scores. The final result ranges from 0 to 10 points, with 10 points indicating the best, 0 the worst prognosis of getting pregnant within 3 years after the surgery.

1.4. Bowel endometriosis

Bowel endometriosis is one of the most common form of DE with incidence rates of 5-12% of women suffering from endometriosis (*Wills et al., 2008*). The rectosigmoid colon is the most frequently affected segment of the bowel, followed by the appendix and caecum (*De Cicco et al., 2011*). The infiltration of the small intestine is rare. The pathogenesis of bowel endometriosis is similar like on other endometriosis localisations. The retrograde menstruation is followed with implantation of the sloughed endometrial tissue and infiltration of the bowel wall with endometriotic glands and stroma, neoangiogenesis and local inflammation. Furthermore, deep bowel endometriosis is associated with neurogenesis and/or recruitment of local nerve fibres and is capable of invading existing nerves, which in turn may promote fibrosis (*Yong et al., 2020*). The deep infiltration of the bowel wall, the concomitant fibrosis and inflammation cause in most of the cases severe adhesions and distortion of the pelvic cavity, described as frozen pelvis. Some gynaecologists postulate that rectovaginal DE lesions originate from the posterior wall of the cervix and secondarily infiltrate the anterior wall of the rectum. Accordingly, lesions are described such as diabolo-like or hourglass-shaped (*Donnez et al., 2013*). The rectovaginal endometriosis may also extend laterally and involve the pelvic wall, sacrouterine ligaments and ureters. The lesion is located in most of the cases under the peritoneal fold of the pouch of Douglas. However, in many cases the peritoneal fold cannot be clearly detected due to severe adhesions and distortion of the pelvic anatomy.

Bowel endometriosis is a debilitating disease for the patients, causing chronic pelvic pain, dysmenorrhoea, deep dyspareunia, cyclic dyschezia, dysuria, diarrhoea and/or constipation during the period, catamenial rectal bleeding and abdominal cramping. The severe pain symptoms can be explained with a cross organ sensitization of different visceral pelvic organs, as described by Maddern et al. The colon is innervated by spinal afferents traveling via the splanchnic or pelvic nerves and the hypogastric nerve and have cell bodies located within the thoracolumbar and lumbosacral dorsal root ganglia. The central terminals of colon, bladder, uterus and vaginal afferents synapse onto second order dorsal horn neurons in the spinal cord, which ultimately transmit signals to the brain. Accordingly, these different visceral organs share common nerve pathways, allowing the potential for cross-organ sensitization (*Maddern et al., 2020*).

Moreover, DE of the bowel causes sub- and infertility (*Darai et al., 2017*). The severe

symptoms affect dramatically the quality of life causing partnership, social- and working problems.

1.5. Treatment of bowel endometriosis

Bowel endometriosis is a challenging disorder for the gynaecologists and patients should be referred to centre with expertise in diagnosing and treating this severe condition. Depending on clinical aspects, such as patient's age, intensity of symptoms, reproductive desire and anatomical features of bowel affection, such as localisation and extension of the disease conservative or surgical treatment can be applied. The conservative endocrine treatment with application of progestins in a continuous manner improves the symptoms and delay progress, but does not eliminate the disease and is often associated with side effects, such as abnormal uterine bleeding, weight gain, headache and decreased libido (*Vercellini et al., 2016*). Moreover, endocrine therapy causes anovulation and is not appropriate for patients wishing to conceive. The surgical treatment remains the gold standard therapy and should be the first choice for symptomatic patients with a visual analogic scale (VAS) >7 for pain, infertile patients who have previously two or more unsuccessful in vitro fertilization (IVF) cycles, patients not responding to hormonal treatment and patients with signs of bowel obstruction regardless of the intensity of symptoms (*Abrao et al., 2017*). There are mainly three different surgical approaches for the treatment of colorectal endometriosis and all of them can be performed with minimal invasive surgery. Depending on the lesion's characteristics, such as size, depth of infiltration, grade of lumen stenosis and the school of thought "conservative" or "radical" surgical methods can be applied.

The most conservative surgical method to remove bowel endometriosis is the shaving technique. The classical shaving involves the removal of the endometriotic lesion invading the serosa and subserosa (*Abrao et al., 2017*). Some surgeons perform deep shaving of the lesions, which involve the muscularis or even perform "shaving to the mucosa" with consecutive opening of the bowel lumen and suturing the bowel wall (*Donnez and Squifflet 2010*). The moderate conservative surgical modality is the disc excision, which is defined as a full-thickness discoid removal of an endometriotic nodule from the anterior rectal wall. The removal of the affected part of the bowel can be performed transanal with the Rouen technique published by Roman et al. using a transanal

circular stapler device (*Roman et al., 2016*) or transabdominal using either a linear endoscopic stapler device (*Abrao et al. 2017*) or the classical scissor and hand-sewn suture technique.

In contrary to the conservative surgical modalities the radical surgical approach removes a segment of the bowel with the necessity of a termino-terminal e.g. end-to-end or side to end anastomosis using the endoscopic circular stapler device (*Abrao et al., 2017*). There are different ways introducing the anvil of the circular stapler, resulting different anastomosis techniques, such as performing a minilaparotomy, or using a transvaginal or transrectal natural orifice specimen extraction (NOSE) technique (*Bokor et al., 2019*). Depending on the height of the anastomosis from the anal verge, ultra-deep (<6cm), deep (6-10cm) and rectosigmoideal (>10cm) anastomosis can be distinguished (*De Cicco et al., 2011*). The different surgical modalities to treat bowel endometriosis are presented in **figure 5**.

Both conservative surgical techniques enable the removal of smaller bowel lesions with superficial to moderate infiltration of the bowel wall and are associated with lower postoperative complication and morbidity rates. The radical surgical approach of segmental resection shows a high success rate regarding pain symptoms, and improves the quality of life, but carries a high intra- and postoperative complication rate. Whereas earlier the radical segmental bowel resection was the treatment of choice in many centres nowadays there is a trend towards less radical surgical modalities. There are some centres who treat bowel endometriosis in the vast majority of the cases with one surgical modality, e.g. deep shaving (*Donnez O and Donnez J 2020*) or segmental colorectal resection, whereas in other centres all surgical modalities are applied. However, there are many surgical approaches to remove bowel endometriosis with increasing knowledge about indication, complication and outcome it still remains unclear which is the most appropriate technique for the individual to minimise risks of surgery, reduce pain symptoms, restore fertility and prevent recurrence.

In the tertial referral endometriosis centre of the University of Gießen and Marburg we have performed all types of surgical treatment of colorectal endometriosis ranging from the classical shaving and the linear stapler disc excision as conservative surgical approaches to the radical surgical removal of the disease with segmental bowel resection and anastomosis. The decision has been based on the results of preoperative ultrasound and magnetic resonance imaging (MRI), but has been finally made intraoperative depending on the lesions' characteristics. However, we had some criteria, such as size,

location, depth of infiltration, multifocality and multicentricity, the decision varied from surgeon to surgeon. In order to contribute to a better understanding about short- and long-term clinical outcome, risks of surgery and define clear indication for each surgical modality, we analysed the results of our patients operated for colorectal endometriosis over a 10-year period in the tertial endometriosis referral centre of the University of Gießen and Marburg.

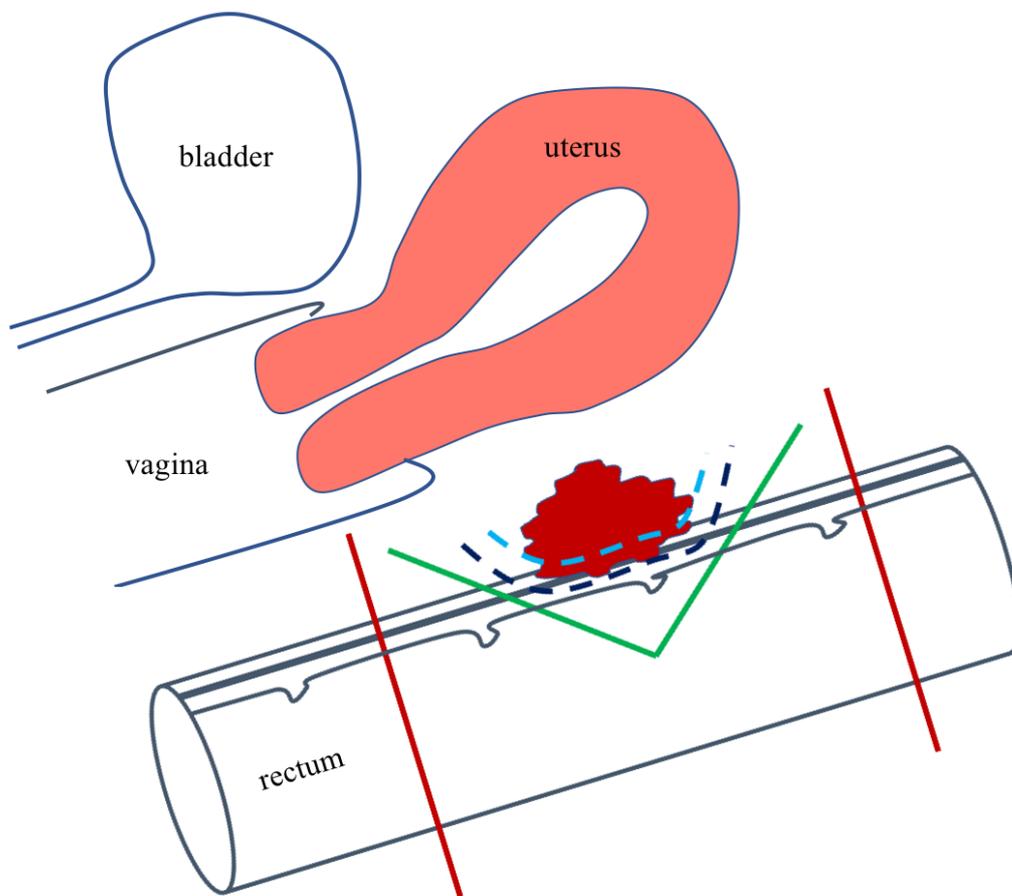


Figure 5. Schematic drawing of conservative and radical surgical treatment modalities of bowel endometriosis

The figure demonstrates the sagittal view of the female pelvis showing the bladder, uterus, vagina and rectum with its layers on the anterior wall (outside line: serosa and subserosa, middle line: muscularis, inner line: submucosa and mucosa). The endometriotic nodule of the anterior rectal wall infiltrates up to the submucosa. The classical shaving (hell blue dashed line) removes the lesion from the serosa and subserosa. The deep shaving (dark blue dashed line) excises the lesion up to the mucosa without opening the bowel lumen. The disc excision (green line) removes a small discoid part of the anterior rectal wall including all its layers and closes the bowel wall with a suture line. The segmental resection (red line) excises a segment of the bowel and restores the bowel integrity with anastomosis.

2. Materials and methods

2.1. Study design and study population

We conducted a retrospective cohort study of patients operated for colorectal endometriosis in the Gynaecological Department of the University of Gießen between 2005 January and 2015 December. We screened the operating theatre plans and collected all patients, who underwent surgery due to intestinal endometriosis. The screening resulted 124 patients with DE of the bowel. We excluded 4 patients with endometriosis of the appendix, coecum and terminal ileum without involvement of the rectosigmoid colon. The final study included 120 patients with DE of the rectosigmoid colon, who were eligible for the retrospective cohort analysis. The patients were treated either because of first diagnosis or recurrence of DE with colorectal involvement.

The study population was further divided according to the type of bowel surgery, to the group of patients with rectal shaving (n 26), disc excision (n 19) and segmental colorectal resection (n 75). We analysed the preoperative medical records, the operating theatre reports, the histology results and the course of hospital stay. In order to assess the short- and long-term clinical outcome of surgery regarding different types of pain symptoms, reproductive results, quality of life aspects and recurrence of the disease we developed a detailed questionnaire, which was sent to the patients in January 2016. The answers were collected until July 2016. The non-responders were interviewed by telephone calls. The ethical committee of the University approved the study (AZ221/13).

The flowchart of the study design is summarised in **figure 6**. The questionnaire is presented in the appendix.

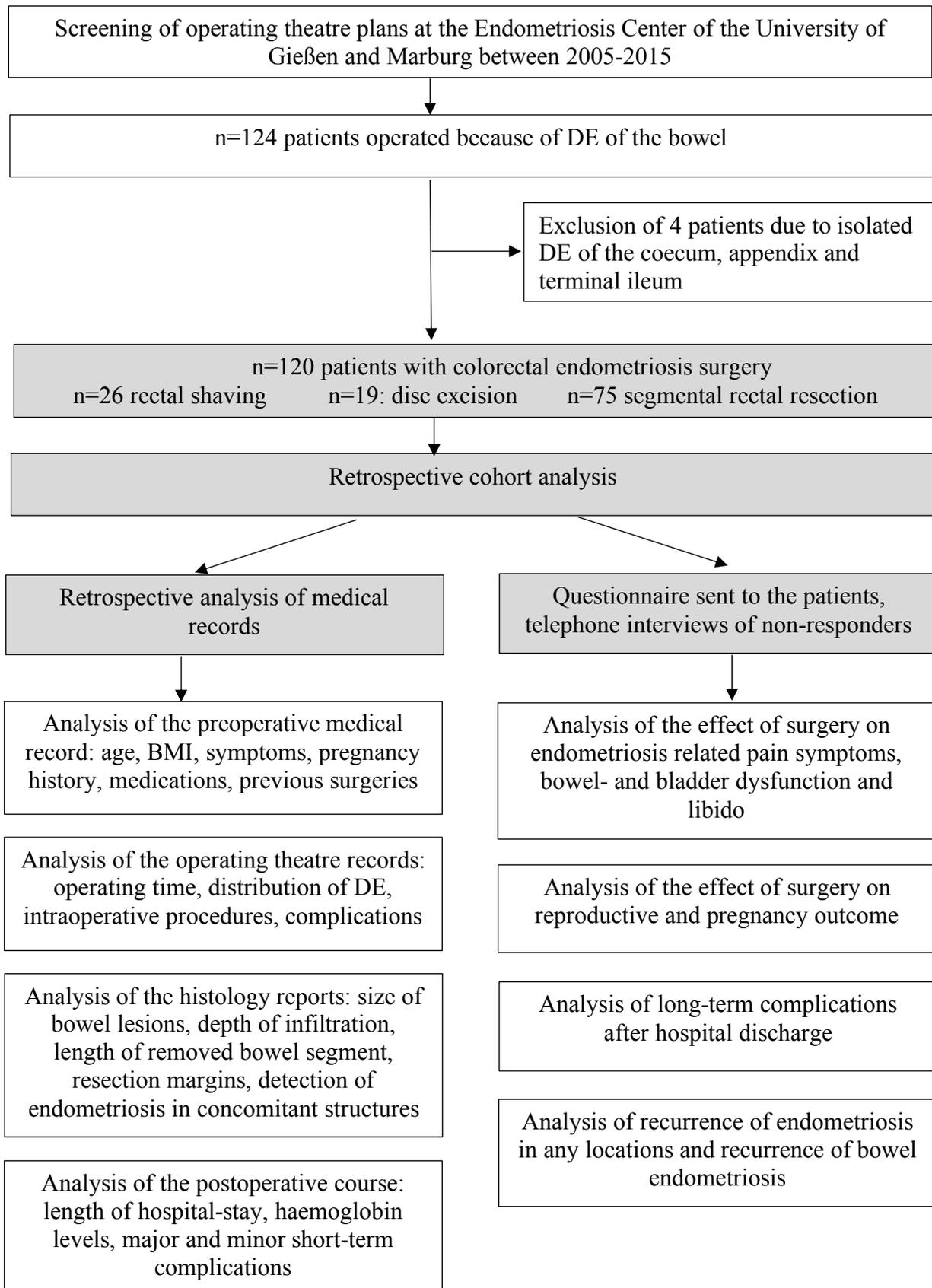


Figure 6. Flowchart of the study design

The flowchart demonstrates the study design and summarises the analysed parameters. (DE: deep endometriosis, BMI: body mass index)

2.2. Preoperative procedures and operative technique

All of the patients were treated in a multidisciplinary setting of gynaecologists, general surgeons, radiologists and if necessary urologists. All patients underwent preoperative a physical examination, including rectovaginal palpation, transvaginal ultrasound and MRI according to a strict protocol, developed in our centre, with application of iv. butylscopolamine (Buscopan®) to reduce bowel motility, rectal and vaginal filling with water and sonography gel, respectively (*Schneider et al., 2016*). One day before the surgery the patients received a mechanical bowel preparation using hydrogenphosphate and dihydrogenphosphate enema. On the day of the surgery a peridural catheter for postoperative pain management as well as a central venous catheter were placed. Regarding the surgical modality, the majority of our patients were treated with segmental bowel resection and end-to-end anastomosis (n 75), whereas a smaller group of them underwent disc excision (n 19) or classical rectal shaving (n 26). The surgical modality was decided based on the results of the transvaginal ultrasound and MRI, but finally depending on intraoperative characteristics of bowel endometriosis, such as lesion`s size, localisation, multicentre or multifocal appearance, depth of infiltration and grade of lumen stenosis. In very extensive endometriosis cases additional surgical procedures were applied. In case of extensive ureterolysis a double J (DJ) catheter was placed. If a vaginal suture was situated directly at the level of bowel anastomosis an omental flap was prepared and inserted between the suture lines to prevent the development of a rectovaginal fistula. In selected cases of ultra-deep rectum resections protective ileostomy was performed. In case of extensive adhesiolysis adhesion barrier was applicated. All patients were intraoperatively scored according to the rASRM and ENZIAN classification.

2.3. Analysis of the descriptive parameter of the study population

The preoperative medical reports were analysed for age, BMI, indication of the operation, symptoms, pregnancy wish and reproductive history, concomitant diseases, medication and previous abdominal surgeries due to endometriosis or other reasons.

2.4. Analysis of the intraoperative data and histology results

The operating theatre reports were analysed for the surgical approach, e.g. open or laparoscopic route, the type of bowel surgery, the distribution of DE and involvement of further anatomical structures of the pelvis and application of additional surgical procedures, such as placement of a DJ-catheter, application of an adhesion barrier and a protective ileostomy. Moreover, we analysed the duration of the surgery as well as minor- and major intraoperative complications. The segmental resection cases were analysed for the height of anastomosis, e.g. ultra deep rectal (< 6cm to the anal verge), deep rectal (6-10cm to the anal verge) and rectosigmoidal (> 10cm to the anal verge) anastomosis depending on the distance of the anastomotic ring from the anal verge as proposed from De Cicco et al (*De Cicco et al., 2011*). The appearance of the bowel lesions was characterised as isolated single lesion (one nodule), multicentric lesions (multiple affection of the bowel wall with two or three nodules with a distance beyond 2cm) and multifocal lesions (multiple affection of the bowel wall with endometriosis lesions within 2cm). The multifocal lesions were described as a long segment affection of the bowel wall.

The histology results were analysed in all removed endometriosis specimens of different anatomical structures of the small pelvis. A lesion was described as histological positive in case of presence of both endometriotic stroma and glands. The solitary appearance of haemosiderin containing macrophages, signs of acute or subacute microscopical bleeding were considered as questionable positive result. In these cases, if a positive immunohistology with CD10 staining was detected, the lesion was considered as positive for endometriosis. The bowel specimens were analysed for length of removed bowel segment, presence of endometriosis in the oral and aboral resection margins, size of the lesions, described with the largest diameter of the nodule as well as depth of bowel wall's infiltration.

2.5. Analysis of the course of hospital stay and postoperative complications

We analysed using the clinical records of the patients the duration of hospital-stay, pre- and postoperative haemoglobin levels, medications and complications. We assessed the postoperative complications as minor and major events according to the Clavien-Dindo

classification of type II (minor) complications, which required a pharmacological therapy or blood transfusion and type III (major) complications, with the necessity of a reoperation, endoscopic or radiological reintervention (*Dindo et al., 2004*). We also analysed the complications after the hospital discharge on a short time (within 6 weeks after the operation) and on a long time (> 6 weeks after the operation) manner, using both the clinical records and the answers of the questionnaire.

2.6. Analysis of clinical outcome regarding endometriosis related symptoms, reproductive results and pregnancy outcome

We developed and sent a questionnaire to all of the patients who underwent surgery for colorectal endometriosis between 2005-2015. The questionnaire was comprised of 15 sites with two major parts and is presented in the appendix of this work. The non-responders underwent telephone-interviews with the same questions. The first part of the questionnaire involved questions about social anamnesis, such as marital status, job, children, weight and height, postoperative medical therapy, surgical reinterventions due to recurrence of endometriosis or other reasons and reproductive history. The survey about the reproductive history asked about pregnancy wish after the operation, way of conception, outcome of pregnancy, gestational age and way of delivery as well as single or twin pregnancy. The first part of the questionnaire included further questions to evaluate the quality of endometriosis healthcare and time relapse between the first onset of symptoms and diagnosis of endometriosis. Regarding the effect of surgery on endometriosis related symptoms, the patients were asked about presence and intensity of typical pain symptoms, such as dysmenorrhoea, chronic pelvic pain, dysuria, dyschezia, dyspareunia, voiding and digestive dysfunction and libido. The pain symptoms and libido were rated with VAS ranging from 0 to 10, with 0 indicating no symptoms and 10 the highest intensity of symptoms. The patients were asked to complete the questionnaire according to their medical state and symptoms before the surgery, one year after the surgery and at the time of the evaluation (January of 2016). This resulted a follow-up of up to ten years.

The second part of the questionnaire was developed using questions based on the validated Endometriosis-Health-Profile-30 (*Jones et al., 2001*) to evaluate the quality of life aspects, measuring the pain, control and powerlessness, emotional well-being, social

support, self-image, work, intercourse, relationship with children and assessment of treatment quality. The analysis of the quality of life aspects was not addressed in the current study.

2.7. Analysis of the recurrence of endometriosis

The recurrence of the disease was evaluated using the clinical records of the patients as well as the answers of the questionnaire and classified as a conservative recurrence in cases of repeated onset of symptoms or signs of endometriosis with imaging modalities, as surgical recurrence in patients who underwent reoperation with or without histological confirmation of endometriosis and histologically proven recurrence of endometriosis. The histological recurrence was further divided to recurrence of endometriosis in any anatomical location and histological recurrence of bowel endometriosis.

2.8. Statistical analysis

The descriptive statistical parameter, such as patients' age and BMI were compared with Kruskal-Wallis test. The percentages of patients suffering from different types of pelvic pain as well as the VAS Scores before- and one year after the surgery and at the time of the survey were analysed with Wilcoxon test and ANOVA multivariate analysis. P values were two-sided and considered significant if less than 0.05. The cumulative pregnancy and delivery rates were calculated using life table analysis.

3. Results

3.1. Patients' characteristics

Between 2005 and 2015 120 patients were operated with colorectal endometriosis in our centre. All the patients were from Caucasian origin, with a median age of 34 and BMI of 23 kg/m² and were treated either because of first diagnosis of endometriosis or recurrence

of the disease. 78.4% of the patients suffered from different types of pelvic pain, almost every third of the patients had constipation (27%) or diarrhoea (24.3%) and 18.9% of the patients suffered from intestinal cramping, 8.1% from rectal bleeding and 9.9% suffered from other symptoms, such as voiding pain and voiding dysfunction, lower back pain, spotting or bleeding from vaginal cuff and menometrorrhagia. 3.6% of the patients were asymptomatic. More than half of the patients (58.6%) wished to conceive after the surgery. The patients' characteristics are summarised in **table 1**.

Table 1. Patients' characteristics

The table demonstrates age and BMI as median and range (10 and 90 percentile) data as well as symptoms of the patients in the order of their frequency. (BMI: body mass index)

Age	34 (26-43)
BMI	23 (18-33)
Symptoms	
Pain	78.4%
Pregnancy wish	58.6%
Obstipation	27.0%
Diarrhoea	24.3%
Intestinal cramping	18.9%
Rectal bleeding	8.1%
Voiding pain and voiding dysfunction	5.0%
Asymptomatic	3.6%
Menometrorrhagia	2.5%
Bleeding from the vaginal cuff	0.8%

3.2. Diagnosis of endometriosis

The questionnaire and telephone interviews provided information about the time of correct diagnosis of endometriosis after the first onset of symptoms and was available in 66 patients. 25 (37.8%) patients received her diagnosis within 2 years after onset of symptoms. However, 17 (68%) of these patients suffered from recurrent endometriosis, which facilitates the diagnosis. 19 patients (28.8%) had a diagnostic delay longer than 7 years and 16 patients (24.2%) received a correct diagnosis 10 years or even longer after first onset of symptoms. Considering only patients with first diagnosis of endometriosis and excluding those one with recurrence of the disease, the median diagnostic delay was 6 years (**figure 7**).

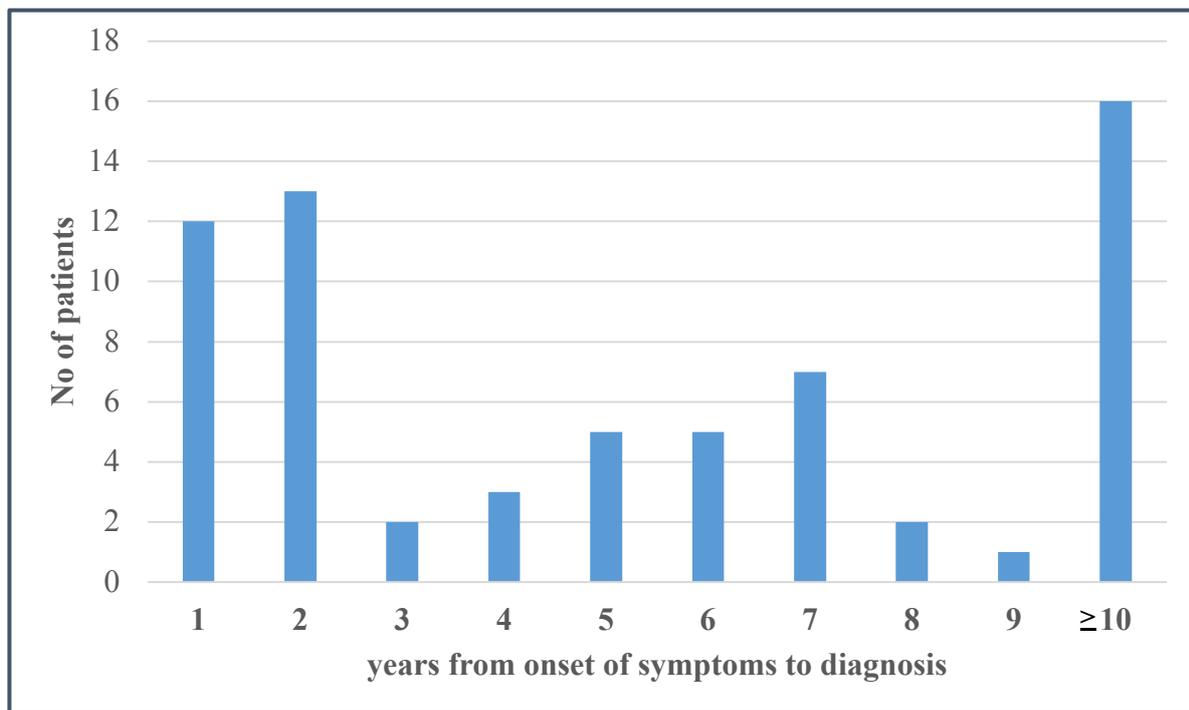


Figure 7. Diagnosis of endometriosis from the first onset of symptoms

The horizontal axis demonstrates the years from first onset of symptoms to correct diagnosis of endometriosis. The vertical axis demonstrates the number of patients. The last column represents patients with a diagnostic delay of ≥ 10 years

3.3. Surgical procedures

Regarding the analysis of the surgical route, e.g. performing the procedure with laparoscopic or open surgery we split the study period for two parts, 2005-2010 and 2010-2015, respectively. During the first observation period 56.2% (n 18) of the patients were operated with laparoscopic surgery, 34.4% (n 11) of them underwent laparotomy and in 9.4% (n 3) of the patients the laparoscopy had to be converted to laparotomy, resulting an overall laparotomy rate of 43.7%. In the second five-year period the rate of laparoscopic procedures increased to 90.9% (n 80), whereas the open approach and the conversion rate decreased to 6.8% (n 6) and 2.3% (n 2) respectively, resulting a decrease of the overall laparotomy rate to 9.1% (n 8) (**figure 8**).

Regarding the type of bowel surgery, the distribution of the different resection modalities did not differ between the first and second observation period. Over the ten years 120 bowel surgeries were performed with 75 (62.5%) segmental resections, 19 (15.8%) disc excisions and 26 (21.7%) shaving procedures, resulting an overall rate of 62.5% and 37.5% for radical and conservative surgical procedures, respectively. Between 2005 and 2010 59.4% (n 19) segmental resections, 15.6% (n 5) disc excisions and 25% (n 8) shavings were performed resulting an overall rate of 59.4% and 40.6% of radical and conservative surgical approaches, respectively. Between 2010 and 2015 the rate of segmental resections, discoid resections and shavings resulted 63.6% (n 56), 15.9% (n 14) and 20.5% (n 18), respectively. The overall rate of radical procedures was 63.6%, whereas 36.4% of patients underwent conservative bowel surgery. The localisation of anastomosis in case of bowel resections showed a similar distribution of rectosigmoid, deep and ultra-deep anterior rectal wall resections over the two observation periods. Ultra-deep rectal resections were performed in 7 (37%) and 15 (27%) patients, deep rectal resections in 5 (26%) and 21 (37%) patients and rectosigmoid in 7 (37%) and 20 (36%) patients, in the first and second observation period, respectively. The distribution of ultradeep, deep and rectosigmoid resections over the ten years resulted 29% (n 22), 39% (n 26) and 35% (n 27), respectively (**figure 9**)

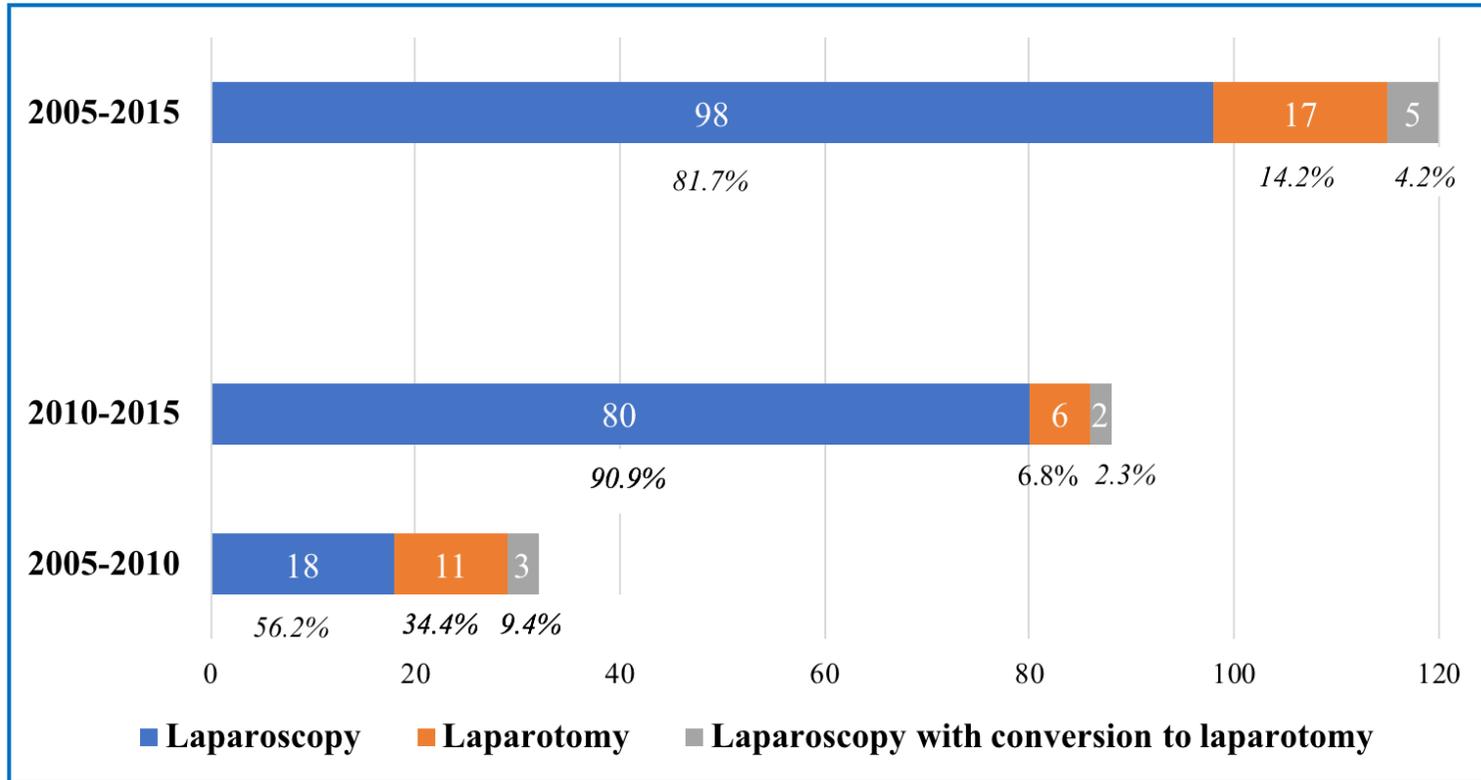


Figure 8. Analysis of the surgical route

Below is presented the analysis of the two observation periods of 2005-2010 and 2010-2015 and above the overall study period. Presented are the absolute and relative number (percentages) of patients, who underwent laparoscopy, laparotomy or conversions of laparoscopy to open surgery. The figure clearly shows how laparoscopy overcome laparotomy as experience increased among gynaecologists and general surgeons.

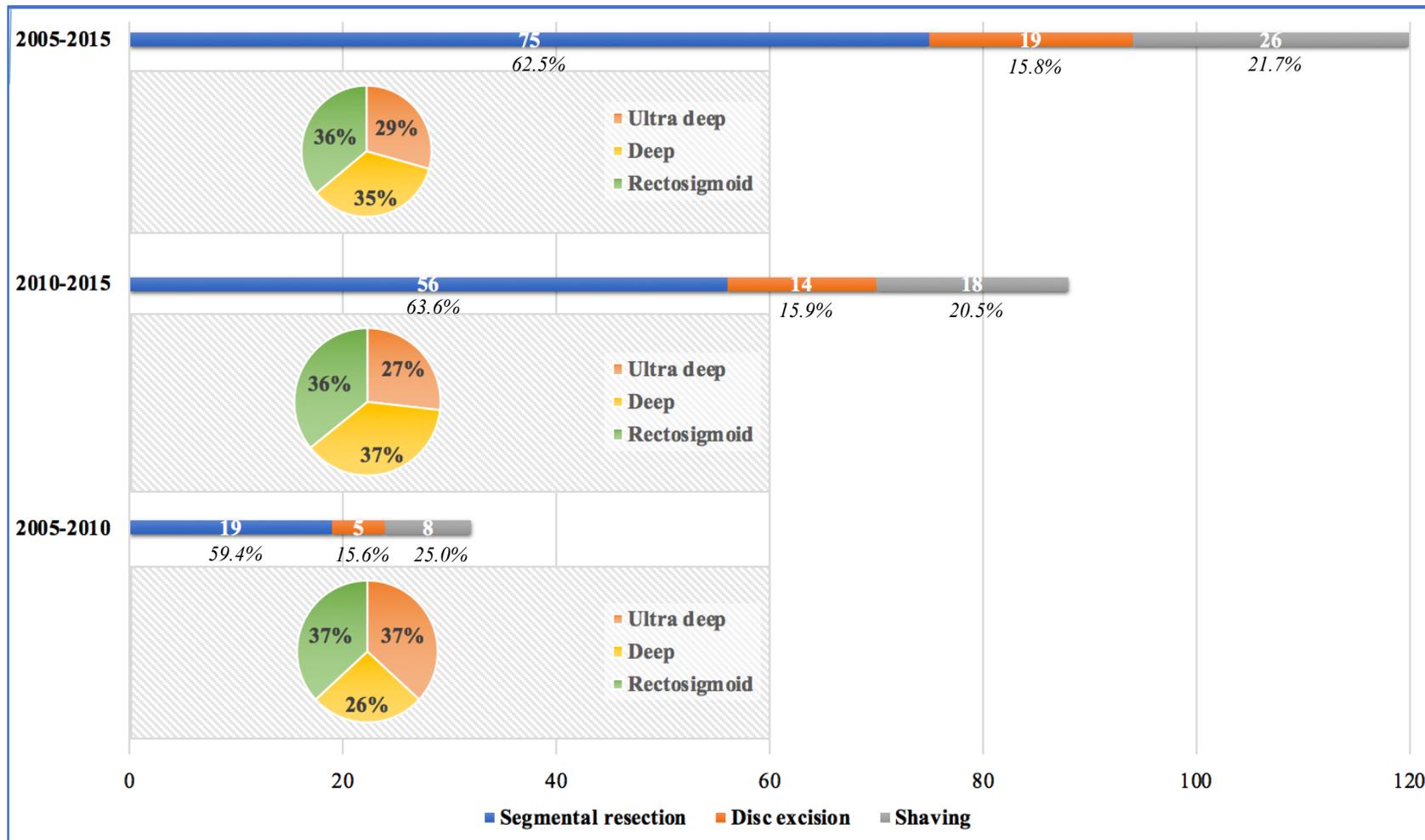


Figure 9. Analysis of conservative and radical surgical approaches for the treatment of bowel endometriosis

Below is presented the analysis of the two observation periods of 2005-2010 and 2010-2015 and above the overall study period with absolute and relative number (percentages) of patients who underwent segmental resection, disc excision or shaving. The distribution of different procedures showed similar results over the two observation periods. The localization of anastomosis, e.g. ultra-deep, deep and rectosigmoid in case of segmental resections is presented in the pie chart as percentages of all segmental resections and shows similar pattern in both observation periods.

The median operating time took 292 minutes (range 162-496 min) over the 10 years. Analysing the data from the first 5 years period, the median operating time took 315 minutes (range 135-518 min) and decreased to median values of 276 minutes (range 161-491 min) in the second 5 years period, resulting a decrease of 39 minutes/procedure (**table 2**).

The patients had a median pre- and postoperative haemoglobin level of 134g/l and 116g/l, respectively.

Almost half of the patients (49.2%) received a double J catheter in order to facilitate the detection of the ureters, but mainly to prevent postoperative complications in cases of radical ureterolysis with compromising the blood supply of the ureter. In 5.1% of the patients the double J catheter was placed before the surgical procedure and in 94.9% during the operation. In 67.8% of the patients the double J catheters was placed on both sides and in 17.9% and 14.3% isolated on the left and right side, respectively.

More than half of the patients (56.7%) received adhesion barrier at the end of the surgery. In most of the cases Hyalobarrier® (hyaluronic acid) was the medium of choice, followed by Adept® solution (4% icodextrine), TachoSil® (human fibrinogen/human thrombin) sponge, CollaGUARD® (type 1 collagen) membrane and Seprafilm ® (sodium-hyaluronate, carboxymethylcellulose). In one case CollaGUARD® and hyalobarrier® were both applicated (**table 2**).

16 (21.5%) patients, who underwent segmental resection received an omental flap to prevent the development of a rectovaginal fistula and 6 (8%) of them a protective double-barrelled ileostomy if ultra-deep rectal resection with high-risk surgical steps was performed. Considering only the ultra-deep rectal resections, the protective ileostomy rate resulted 27.3% (**table 2**).

Table 2. General intraoperative data and additional surgical procedures

The table presents pre- and postoperative haemoglobin levels and operating time with median and range (10-90 percentile) values as well as the percentage of patients with additional surgical procedures, such as placement of DJ- catheter, application of omental flap and double-barrelled protective ileostomy.

Preoperative haemoglobin level	134 g/l (122-145 mg/l)
Postoperative haemoglobin level	116 g/l (92-132 mg/l)
Operating time overall study period 2005-2015	292 min (162-496 min)
Operating time 2010-2015	276 min (161-491min)
Operating time 2005-2010	315 min (135-518 min)
DJ-catheter	49.2% <i>(59/120)</i>
preoperative	5.1% <i>(3/59)</i> 66.7% <i>(2/3)</i> both sides 33.3% <i>(1/3)</i> left side
intraoperative	94.9% <i>(56/59)</i> 67.8% <i>(38/56)</i> both sides 17.9% <i>(10/56)</i> left side 14.3% <i>(8/56)</i> right side
Adhesion barrier	56.7% <i>(68/120)</i>
hyalobarrier	57.4% <i>(39/68)</i>
adept	32.4% <i>(22/68)</i>
tachosyl	4.4% <i>(3/68)</i>
collaguard	2.9% <i>(2/68)</i>
seprafilm	1.5% <i>(1/68)</i>
hyalobarrier and collaguard	1.5% <i>(1/68)</i>
Omental flap	21.5% <i>(16/75)</i>
Protective double-barrelled ileostomy	8% <i>(6/75)</i>

In almost every severe cases of gastrointestinal endometriosis the involvement of the bowel is associated with other localisations of DE as well as adnexal and peritoneal endometriosis causing severe adhesions and frozen pelvis. Thus, we analysed the distribution of DE lesions in the anterior (bladder and round ligaments), midline (uterus, parametria and vagina) and posterior compartments (pelvic side walls, ureters,

rectovaginal septum and sacrouterine ligaments) of the pelvic cavity as well as the affection of the adnexa.

In the anterior compartment 9.2% (n 11) of the patients had bladder endometriosis, necessitating in almost every second case a partial bladder resection. In 4.2% (n 5) and 5% (n 6) of the patients the left and right round ligaments had DE lesions, respectively.

Regarding the midline organs 32.5% (n 39) of the patients showed infiltration of the vaginal wall and 14.2% (n 17) of them the uterus was removed because of severe adenomyosis.

The presence of concomitant endometriotic lesions was the most frequent in the posterior compartment. 36.7% (n 44) of the patients showed DE lesions of the rectovaginal space. The left and right sacrouterine ligaments were affected in 25.8% (n 31) and 30% (n 36) of the patients, respectively. 39.2% (n 47) of the patients presented deep endometriotic lesions on the left and 35.8% (n 43) on the right pelvic wall, with 29.2% (n 35) left and 20% (n 24) right sided affection of the ureter. In case of 2 patients, ureter-neoimplantation was necessary on the left side. Regarding concomitant intestinal endometriosis in 2.5% (n 3) of the cases the coecum was affected and 6.7% (n 8) of the patients underwent appendectomy due to suspicion of endometriosis or involvement of the appendix in massive adhesions.

Regarding endometriosis of the adnexa, the left ovary showed in 50% (n 60), the right ovary in 35.8% (n 43) endometriotic cysts. The ovaries had to be liberated from adhesions in 70% (n 84) on the left side and in 57.5% (n 69) on the right side. In 5.8% (n 7) the left tube and in 2.5% (n 3) the right tube was removed due to hydrosalpinx, and in 30% (n 36) on the left side and 20.8% (n 25) on the right side the tubes had to be liberated from adhesions. The surgical mapping of endometriosis lesions in the pelvic cavity is presented in **table 3**.

In most of the anatomical locations and structures, such as bowel, bladder, sacrouterine ligaments, round ligaments and ureters, the endometriosis was histologically confirmed in the removed lesions with a high detection rate of 83.3-100%. The right pelvic wall showed the least detection rate of 66.7% and the appendix was removed in just 25% of the patients because of endometriosis and in the majority of the patients due to other conditions, such as severe adhesions, elongated appendix and suspicion of chronic appendicitis. Regarding the detection rate of adnexal endometriosis high rates, 92.2% and 82.5% were histological positive for ovarian endometriotic cysts on the left and right side, respectively (**table 3**).

Table 3. Pelvic distribution of deep endometriosis and histology results of the lesions

The table presents DE lesions in the anterior, midline and posterior compartment of the pelvis and the adnexa as well as the histology results of the removed lesions. Structures, that were frequently infiltrated, defined as $\geq 30\%$ of the patients, are highlighted grey. The percentages of histologically confirmed endometriosis were calculated with exclusion of missing or questionable results. Endometriosis was considered histological positive in case of presence of both endometriotic glands and stroma. #: ovariolysis and ureterolysis because of endometriosis related adhesions and fibrosis

Endometriotic lesions of the pelvis	% of patients (cases/all)	Histologically confirmed endometriosis
DE of the anterior compartment		
○ bladder	9.2% (11/120)	100% (11/11)
○ left round ligament	4.2% (5/120)	100% (5/5)
○ right round ligament	5% (6/120)	83.3% (5/6)
DE of the midline structures		
○ vagina	32.5% (39/120)	96.9% (31/32)
DE of the posterior compartment		
○ rectosigmoid	100% (120/120)	99.2% (119/120)
○ coecum	2.5% (3/120)	100% (3/3)
○ appendix	6.7% (8/120)	25% (2/8)
○ left pelvic wall	39.2% (47/120)	85.7% (36/42)
extrinsic ureter	29.2% (35/120)	86.7% (26/30)
ureterolysis [#]	66.7% (80/120)	
○ right pelvic wall	35.8% (43/120)	66.7% (24/36)
extrinsic ureter	20.0% (24/120)	100% (24/24)
ureterolysis [#]	52.5% (63/120)	
○ rectovaginal space	36.7% (44/120)	100% (42/42)
○ right sacrouterine ligament	30.0% (36/120)	90.6% (29/32)
○ left sacrouterine ligament	25.8% (31/120)	100% (23/23)
Adnexal involvement		
○ left ovary		
cyst	50% (60/120)	92.2% (47/51)
ovariolysis [#]	70% (84/120)	
○ right ovary		
cyst	35.8% (43/120)	82.5% (33/40)
ovariolysis [#]	57.5% (69/120)	
○ left tube		
adhesiolysis [#]	30.0% (36/120)	
hydrosalpinx	5.8% (7/120)	
○ right tube		
adhesiolysis [#]	20.8% (25/120)	
hydrosalpinx	2.5% (3/120)	

3.4. Histology results of bowel specimens

Endometrial stroma and glands were found in all specimens of segmental resections (n 75) and disc excisions (n 19). Regarding shaving procedures (n 26) one patient had histological signs of fibrosis and questionable endometriotic glands, whereas in all other patients (25) the complete histological criteria of endometriosis were fulfilled. This resulted a histological confirmation rate of 99.2% (n 119/120) of bowel endometriosis (**table 3**).

In case of rectal shaving the vast majority of the patients, 88.5% (n 23/26), had a single endometriotic nodule of the bowel wall and a smaller part of patients, 11.5% (n 3/26), had multicentre affection of the bowel with 2 separated nodules with a distance beyond 2cm. This resulted altogether 29 bowel endometriotic nodules, which were removed with shaving procedure. 10.3% (n 3/29) of the nodules infiltrated the serosa, 79.3% (n 23/29) the subserosa and just a few of them, 6.9% (n 2/29) infiltrated the muscularis and 3.4% (n 1/29) the submucosa. These data reflect a rate of 89.7% (n 26/29) of patients with superficial serosal and subserosal infiltration of the bowel wall, eligible for classical shaving procedure. In a smaller amount of the patients, e.g. in 10.3% (n 3/29) of the nodules, a deep shaving was performed due to infiltration of the muscular and submucosal layers. Regarding the size of the removed nodules 75.9% (n 22/29) were smaller than 3cm, 20.7% (n 6/29) were between 3 and 6cm and 1 nodule (3.4%) measured more than 6cm (**table 4**).

Almost all of the patients with disc excision (n 18/19) had a single nodule of the bowel wall, whereas one patient showed a multicentre affection with two separated endometriotic nodules. In case of this patient the lesions were removed with a combination of disc excision and classical shaving. The depth of infiltration was described in 16 nodules and resulted in 6.3% (n 1/16) serosal and in 6.3% (n 1/16) subserosal infiltration. In 75% (n 12/16) of the patients the endometriotic nodule infiltrated the muscular layer and in a remarkable number of patients even deeper layers, in 12.5% (n 2/16) the submucosa and in 6.3% (n 1/16) the mucosa was infiltrated. The resection margin was investigated just in 2 cases resulting a negative histological margin in both. Regarding the size of the removed nodules 35% (n 7/20) were smaller than 3cm, 60% measured between 3 and 6cm and 10% (n 2/20) were bigger than 6cm (**table 5**).

In case of segmental bowel resection 54.7% (n 41/75) of the patients was affected with one single nodule, 9.3% (n 7/75) of the patients with multicenter lesions of two nodules

and 1.3% (n 1/75) with three nodules of the bowel wall. 36% of the patients (n 27/75) showed a multifocal affection of the bowel wall resulting a long segment infiltration. Considering all types of lesions, including the multicenter nodules, altogether 83 bowel lesions were removed. 37.3% (n 31/83) of them were smaller than 3cm, 28.9% (n 24/83) measured between 3 and 6 cm and in 1.2% (n 1/83) the lesion was bigger than 6cm. In 32.5% (n 27/83) the lesions infiltrated the bowel wall on a long segment with several endometriotic thickenings of the bowel wall and small, sometimes microscopic nodules sitting side by side. The length of the removed bowel segment revealed a median of 7 cm (range 4.6-16.3cm), 10.3 cm (range 9.5-10.4cm) and 19.5 cm if one, two or three nodules were present, respectively. In case of multifocal affection with long segment infiltration of the bowel wall the length of the removed bowel-specimen resulted a median of 9cm (range 5.8-19.6cm). Information about the depth of invasion was available in 60 of the 83 lesions. Just a few lesions infiltrated only the serosa (1.7% (n 1/60)) and subserosa (6.7% (n 4/60)). The majority of the lesions involved deeper layers. The muscularis was infiltrated in 60% (n 36/60) of the lesions, the submucosa in 25% (n 15/60) and the mucosa in 6.7% (n 4/60). In 55 and 56 patients the histological report described the oral and aboral resection margins of the removed bowel segment, respectively. Positive oral resection margin was diagnosed just in one patient (1.8%), whereas 10 patients (17.9%) had a positive aboral resection margin. Most of the positive resection margins were associated with a multifocal affection of the bowel wall, having a positive oral and aboral resection margin of 4.8% (n 1/21) and 23.8% (n 5/21) of these cases (**table 6**). From the 11 patients with positive resection margins follow up regarding recurrence of the disease was available in 9 cases. One of them had a recurrence of the pain symptoms, treated conservative and one patient showed a surgical recurrence of endometriosis having two tiny (2mm) peritoneal endometriotic lesions. None of the patients with a positive resection margin showed a recurrence of bowel endometriosis and/or deep infiltrating disease.

Table 4. Histology of shaving procedures

The table presents the histology results of shaving procedures. 88.5% of the patients had 1 removed nodule and 11.5% of them a multicenter affection of the bowel with 2 nodules. Altogether 29 endometriosis nodules were removed with shaving in 26 patients. Presented are the lesions' size and depth of bowel wall infiltration. A summary of all cases is presented in the last row of the table. The most typical features of the lesions are highlighted grey. The majority of the patients had a nodule up to 3cm and infiltration up to the subserosal layer of the bowel wall, indicating that shaving was favourable in case of small lesions with superficial infiltration.

number of bowel lesions	number of patients/total patients	lesion's size	number of cases/total lesions	depth of infiltration	number of cases/total lesions
1	88.5% (23/26)	0-2.9 cm	78.3% (18/23)	serosal	4.3% (1/23)
		3-5.9 cm	21.7% (5/23)	subserosal	91.3% (21/23)
				muscular	--
				submucosal	4.3% (1/23)
				mucosal	--
2	11.5% (3/26)	0-2.9cm	66.7% (4/6)	serosal	33.3% (2/6)
		3-5.9cm	16.7% (1/6)	subserosal	33.3% (2/6)
		≥6cm	16.7% (1/6)	muscular	33.3% (2/6)
				submucosal	--
				mucosal	--
All cases	100% (26/26)	0-2.9cm	75.9% (22/29)	serosal	10.3% (3/29)
		3-5.9cm	20.7% (6/29)	subserosal	79.3% (23/29)
		≥6cm	3.4% (1/29)	muscular	6.9% (2/29)
				submucosal	3.4% (1/29)
				mucosal	--

Table 5. Histology of disc excision procedures

The table presents the histology results of disc excisions. All of the patients had a single nodule out of one patient, who underwent a combination of disc excision and shaving of two isolated bowel nodules. Presented are the lesions' size as well as the depth of bowel wall infiltration. A summary of all cases is presented in the last row of the table. The most typical features of the lesions are highlighted grey. The majority of the cases showed a nodule size of 3-6cm and an infiltration up to the muscular layer (n.e.: not evaluated)

number of bowel lesions	number of patients/total patients	lesion's size	number of cases/total lesions	depth of infiltration	number of cases/total lesions
1	94.8% (18/19)	0-2.9cm	33.3% (6/18)	n.e.	22.2% (4/18)
		3-5.9cm	61.1% (11/18)	serosal	--
		≥6cm	11.1% (2/18)	subserosal	7.1% (1/14)
				muscular	78.6% (11/14)
				submucosal	14.3% (2/14)
				mucosal	7.1% (1/14)
2	5.3% (1/19)	0-2.9cm	50% (1/2)	serosal	50% (1/2)
		3-5.9cm	50% (1/2)	subserosal	--
				muscular	50% (1/2)
				submucosal	--
				mucosal	--
All cases	100% (19/19)	0-2.9cm	35% (7/20)	n.e.	20% (4/20)
		3-5.9cm	60% (12/20)	serosal	6.3% (1/16)
		≥6cm	10% (2/20)	subserosal	6.3% (1/16)
				muscular	75% (12/16)
				submucosal	12.5% (2/16)
				mucosal	6.3% (1/16)

Table 6. Histology of segmental resection procedures

The table presents the histology results of segmental resections. A single nodule of the bowel wall was observed in 41 patients (54.7%). Multicenter affection was detected in 6 patients (8.0%) with 2 nodules and in 1 patient (1.3%) with 3 nodules. Multifocal endometriosis with infiltration of a long segment of the bowel wall was seen in 27 patients (36%). Altogether 83 endometriosis lesions were removed with segmental resection in 75 patients. Presented are the lesions' size, depth of bowel wall infiltration, presence of endometriosis in the oral and aboral resection margins and the length of removed bowel segment with median and range (10 and 90 percentile) data. A summary of all cases is presented in the last row of the table. The most typical features of the bowel lesions are highlighted grey. The majority of the patients had either a nodule up to 6cm or a long-segment multifocal affection of the bowel wall. The infiltration affected mainly the muscular layer and in high number of the patients even the submucosal and mucosal layers. A high percentage of patients (17.9%) had a positive aboral resection margin. (n.e.: not evaluated)

number of lesions	number of patients/total patients	lesion`s size	number of cases/total lesions	depth of infiltration	number of cases/total lesions	oral resection margin	number of patients/total	aboral resection margin	number of patients/total	length of bowel segment (cm)
1	54.7% ^(41/75)	0-2.9cm	53.7% ^(22/41)	n.e.	29.3% ^(12/41)	n.e.	26.8% ^(11/41)	n.e.	24.4% ^(10/41)	7 (4.6-16.3)
		3-5.9cm	46.3% ^(19/41)	serosal	3.4% ^(1/29)	pos.	--	pos.	12.9% ^(4/31)	
				subserosal	6.9% ^(2/29)	neg.	100% ^(30/30)	neg.	87.1% ^(27/31)	
				muscular	58.6% ^(17/29)					
				submucosal	20.6% ^(6/29)					
				mucosal	10.3% ^(3/29)					
2	8% ^(6/75)	0-2.9cm	58.3% ^(7/12)	n.e.	33.3% ^(4/12)	n.e.	50% ^(3/6)	n.e.	50% ^(3/6)	10,3 (9.5-10.4)
		3-5.9cm	33.3% ^(4/12)	serosal	--	pos.	--	pos.	33.3% ^(1/3)	
		≥6cm	8.3% ^(1/12)	subserosal	--	neg.	100% ^(3/3)	neg.	66.7% ^(2/3)	
				muscular	75% ^(6/8)					
				submucosal	25% ^(2/8)					
				mucosal	--					

number of lesions	number of patients/total patients	lesion's size	number of cases/total lesions	depth of infiltration	number of cases/total lesions	oral resection margin	number of patients/total	aboral resection margin	number of patients/total	length of bowel segment (cm)
3	1.3% ^(1/75)	0-2.9cm 3-5.9cm	66.7% ^(2/3) 33.3% ^(1/3)	n.e. serosal subserosal muscular submucosal mucosal	100% ^(3/3) -- -- -- -- --	n.e. pos. neg.	-- -- 100% ^(1/1)	n.e. pos. neg.	-- -- 100% ^(1/1)	19,5
Multifocal	36% ^(27/75)			n.e. serosal subserosal muscular submucosal mucosal	14.8% ^(4/27) -- 8.7% ^(2/23) 56.5% ^(13/23) 30.4% ^(7/23) 4.3% ^(1/23)	n.e. pos. neg.	22.2% ^(6/27) 4.8% ^(1/21) 95.2% ^(20/21)	n.e. pos. neg.	22.2% ^(6/27) 23.8% ^(5/21) 76.2% ^(16/21)	9,5 (5.8-19.6)
All cases	100% ^(75/75)	0-2.9cm 3-5.9cm ≥6cm multifocal	37.3% ^(31/83) 28.9% ^(24/83) 1.2% ^(1/83) 32.5% ^(27/83)	n.e. serosal subserosal muscular submucosal mucosal	27.7% ^(23/83) 1.7% ^(1/60) 6.7% ^(4/60) 60% ^(36/60) 25% ^(15/60) 6.7% ^(4/60)	n.e. pos. neg.	26.7% ^(20/75) 1.8% ^(1/55) 98.2% ^(54/55)	n.e. pos. neg.	25.3% ^(19/75) 17.9% ^(10/56) 82.1% ^(46/56)	9 (5-17.9)

3.5. Intra- and postoperative, short and long-term complications

The median duration of hospital stay was 5 (range 3-11), 6 (range 5-11) and 7 (range 5-15) days in the shaving, disc excision and segmental resection groups, respectively. Two patients in the shaving group, one patient in the disc excision group and 6 patients in the segmental resection group had a long duration of hospital stay owing to major postoperative complications. The data are presented in **figure 10**.

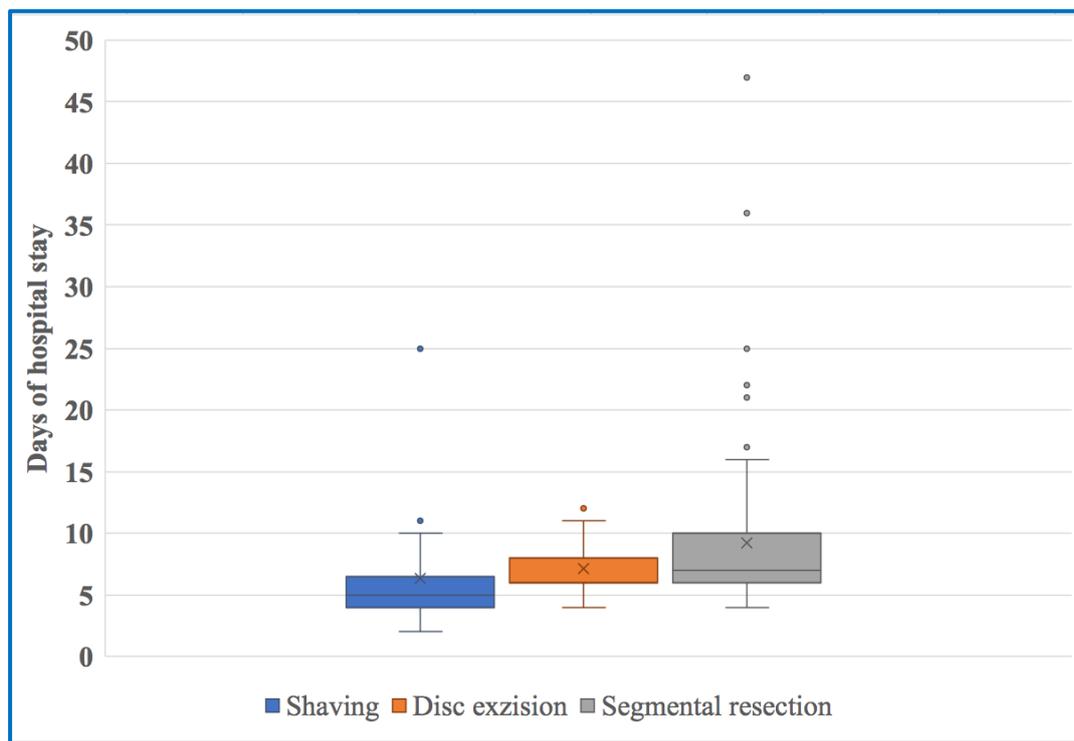


Figure 10. Duration of hospital stay

The plot presents the duration of hospital stay with median (-), mean (x), maximum and minimum values (whiskers) as well as outliers (•). The patients in the shaving, disc excision and segmental resection groups had a median duration of hospital stay of 5, 6 and 7 days, respectively. The outliers represent patients with postoperative complications.

We did not observe intraoperative complications in the shaving procedures. In the disc excision group one patient out of 19 (5.2%) required a blood transfusion. Major intraoperative complication did not occur. The highest intraoperative complication rate of 6.7% (n 5/75) was observed in the segmental resection group. A major intraoperative complication occurred in two patients (2.7%). Both of them suffered an injury of the left ureter with one patient having a preoperative undiagnosed double ureter and injury of the dorsal one. Minor intraoperative complications occurred in three patients (4%). One of

them required a blood transfusion, the other one had an injury of the right epigastric vessel by introducing the 12 mm trocar for introduction of the bowel stapler and in case of the third patient the bowel stapler was defect.

Postoperative complications were defined as events occurring during the hospital stay and classified according to the Clavien-Dindo classification of major and minor complications. The major complications were further divided as bowel-surgery associated and other type of major complications. In the shaving group two patients of the 26 (7.6%) suffered a major and three patients (11.5%) a minor postoperative complication. One patient had a bowel surgery associated major complication with perforation of the rectal wall and concomitant four-quadrant peritonitis resulting a repeated surgery with the necessity of a segmental rectal resection. The other patient showed a hysterectomy associated major complication with hematoma building of the vaginal cuff. She underwent a vaginal revision with opening the vagina, lavage and drainage. The minor postoperative complications involved two patients with bladder infection and one patient with a small hematoma of the abdominal wall, which could be treated conservative. In case of disc excision one patient (5.3%) suffered a major and two patients (10.6%) a minor postoperative complication. None of the patients had a bowel surgery associated complication. The major complication was related to hysterectomy with composition of an abscess of the vaginal cuff treated with a vaginal reoperation with lavage and drainage. Both patients with minor complications required a blood transfusion, moreover one of them developed a small seroma of the abdominal wall and the other one a paradox embolism of the brain associated with temporary neurological deficit.

The segmental resection procedures resulted the most frequent overall postoperative complication rate of 30.7% (23/75) having 8% (6/75) major and 22.7% (11/75) minor complications. In 5.7% (4/75) the major complication was bowel surgery associated. All of the patients developed an anastomotic leakage, which was treated in different ways. Two patients underwent a reoperation with re-anastomosis and application of a protective ileostomy. One of them developed a rectovaginal fistula in the further course, which was closed with over the scope clip (OTSC) rectal endoscopic technique. One patient had a small anastomotic leakage, combined with a rectovaginal fistula and could be treated with OTSC and protective ileostomy. One patient showed a highly complicated postoperative course. The anastomotic leakage was first treated with a relaparoscopy, primary suture of the insufficiency and application of a protective ileostomy. Soon after the revision the patient developed a recurrent small leakage of the bowel wall, which was treated with

endo-vac therapy. This attempt was unsuccessful leading to a four-quadrant peritonitis and concomitant necrosis of the left ureter necessitating a relaparotomy with performing a Hartmann situation and a Psoas-Hitsch plastic. After a year the bowel continuity could be restored with reconstructive bowel surgery.

2.7% (2/75) of the patients showed a major postoperative complication not associated to bowel surgery. One of the patients had a bleeding of the right parametrium, which required a revision with suturing the right uterine vessel. The other patient developed a compartment syndrome of both leg due to the long, uninterrupted Trendelenburg position and undergone repetitive surgeries with fasciotomy of both extremities. The minor postoperative complications (22.7%) involved 6 patients (8%) with neurogenic bladder, urinary retention and/or pyelectasia, 5 patients (6.7%) with temporary positioning injuries, 3 patients (4%) with blood transfusion, 2 patients (2.7%) with bladder infection and 1 patient (1.3%) with a pyelonephritis.

We analysed the short time complications occurring after hospital discharge within 6 weeks to the primary surgery. One patient out of 26 (3.8%) in the shaving group developed a perforation of the sigma at the site of a pseudodiverticulum and required repeated surgery with segmental resection. Short term complication was not observed in the disc excision group, whereas 8% of the segmental resection patients (6/75) suffered a complication. Two patients (2.7%) developed a rectovaginal fistula. One of them could be treated conservative, and the other patient underwent a reoperation with re-anastomosis and application of a protective ileostomy. Two patients (2.7%) developed a pyelectasia, 1 patient (1.3%) had a long-onset neurogenic bladder and 1 (1.3%) patient developed a small subcutaneous serom.

Data of 16, 10 and 52 patients were available for the analysis of long-term complications in the shaving, disc excision and segmental resection groups, respectively. One patient both in the shaving and disc excision group developed a stenosis of the ureter. The patient with shaving could be treated with placement of a DJ ureteric stent, whereas the patient with disc excision underwent a relaparotomy with neo-implantation of the ureter. 7.7% (4/52) of the segmental resection cases showed long-term complications. One patient developed a relative stenosis of the bowel wall treated with endorectal balloon dilatation, 1 patient had 2 small insufficiencies of the rectal wall closed with endo-vac therapy, 1 patient developed a bladder-, retro-rectal- and upper abdominal wall herniation.

The intra- and postoperative as well as the short- and long-term postoperative complications of each surgical modality are summarised in **tables 7, 8 and 9**.

Table 7. Summary of complications of the shaving procedures

Presented are the relative and absolute number of patients with a complication. Intraoperative complications were not observed.

<p>Intraoperative --</p>	<p>major -- minor --</p>		
<p>Postoperative 19.2% (5/26)</p>	<p>major 7.6% (2/26)</p> <p>minor 11.5% (3/26)</p>	<p><u>bowel surgery associated 3.8%</u> (1/26)</p> <p><u>other 3.8%</u> (1/26)</p>	<p>1/26 (3.8%) perforation of the rectum with peritonitis, repeated surgery: laparoscopy with conversion to laparotomy, segment resection of the rectum</p> <p>1/26 (3.8%) hematoma of the vaginal cuff, fever, repeated surgery: vaginal cuff revision, lavage, drainage</p> <p>2/26 (7.7%) bladder infection</p> <p>1/26 (3.8%) small hematoma of the abdominal wall</p>
<p>Short term 3.8% (1/26)</p>			<p>1/26 (3.8%) perforation of the rectosigmoid in a pseudodiverticulum, repeated surgery with sigmaresection</p>
<p>Long term 6.25% (1/16)</p>			<p>1/16 (6.25%) stenosis of the ureter, treated with DJ-catheter</p>

Table 8. Summary of complications of the disc excisions procedures

Presented are the relative and absolute number of patients with a complication. Intraoperative major-, bowel surgery associated postoperative- and short-term complications were not observed.

Intraoperative 5.2% (1/19)	major -- minor 5.2% (1/19) 1/19 (5.2%) transfusion of 2 units blood
Postoperative 15.8% (3/19)	major 5.3% (1/19) <u>bowel surgery associated</u> -- <u>other 5.3% (1/19)</u> 1/19 (5.3%) abscess of the vaginal cuff, repeated surgery with vaginal cuff revision, lavage, drainage minor 10.5% (2/19) 1/19 (5.2%) transfusion of 2 units blood and seroma of the abdominal wall 1/19 (5.2%) transfusion of 2 units blood and paradox brain embolism
Short term --	
Long term 10% (1/10)	1/10 (10%) stenosis of the ureter, treated with relaparotomy and ureterneimplantation

Table 9. Summary of complications of the segmental resection procedures

Presented are the relative and absolute number of patients with a complication. The highest rate of complications was observed in the segmental resection group. (OTSC: over the scope clip)

<p>Intraoperative 6.7% (5/75)</p>	<p>major 2.7% (2/75) minor 4% (3/75)</p>	<p>2/75 (2.7%) injury of the left ureter 1/75 (1.3%) transfusion of 2 units blood 1/75 (1.3%) injury of the right epigastric vessel 1/75 (1.3%) defect of the bowel stapler</p>
<p>Postoperative 30.7% (23/75)</p>	<p>major 8% (6/75) <u>bowel surgery</u> <u>associated 5.3%</u> (4/75)</p> <p><u>other 2.7%</u> (2/75)</p>	<p>2/75 (2.7%) insufficiency of the anastomosis treated with reanastomosis and protective ileostomy 1/75 (1.3%) insufficiency of the anastomosis and rectovaginal fistula treated with protective ileostomy and endorectal application of OTSC 1/75 (1.3%) insufficiency of the anastomosis, treated with relaparoscopy and primary suture of the insufficiency, application of a protective ileostomy. Recurrence of the insufficiency treated with endo-vac therapy and finally with re-laparotomy, Hartmann procedure, Psoas-Hitsch plastic due to necrosis of the left ureter, after a year reconstructive bowel surgery</p> <p>1/75 (1.3%) bleeding of the right parametrium, reoperation: suture of the uterine vessel 1/75 (1.3%) compartment syndrome of both leg treated with repetitive surgeries</p>

Postoperative	minor 22.7% <i>(17/75)</i>	<p>6/75 <i>(8%)</i> urinary retention and/or pyelectasia</p> <p>5/75 <i>(6.7%)</i> temporary positioning injuries</p> <p>3/75 <i>(4%)</i> blood transfusion</p> <p>2/75 <i>(2.7%)</i> bladder infection</p> <p>1/75 <i>(1.3%)</i> pyelonephritis</p>
Short term	8% <i>(6/75)</i>	<p>2/75 <i>(2.7%)</i> rectovaginal fistula (1 treated conservative, 1 treated with re-laparotomy, reanastomosis and protective ileostomy)</p> <p>2/75 <i>(2.7%)</i> pyelectasia and lower back pain (1 treated conservative, 1 with re-laparoscopy)</p> <p>1/75 <i>(1.3%)</i> long-term onset urinary retention, treated conservative</p> <p>1/75 <i>(1.3%)</i> subcutaneous seroma</p>
Long term	7.7% <i>(4/52)</i>	<p>1/52 <i>(1.9%)</i> relative stenosis of the anastomotic ring treated with endoscopic balloon dilatation</p> <p>1/52 <i>(1.9%)</i> 2 small insufficiencies of the bowel wall treated with endo-vac therapy</p> <p>1/52 <i>(1.9%)</i> bladder and retrorectal rectum herniation treated conservative</p> <p>1/52 <i>(1.9%)</i> herniation of the upper abdominal wall</p>

3.6. Recurrence of the disease

16 (61.5%), 10 (52.6%) and 50 (66.7%) patients had a long-term follow-up and were eligible for the analysis of recurrence rates in the shaving, disc excision and segmental resection groups, respectively. The recurrence rates were analysed as (i) conservative recurrence, defined as recurrence of the symptoms or signs of endometriosis with imaging modalities, eligible for conservative treatment, as (ii) surgical recurrence, defined as necessity of a repeated surgery with or without histological confirmation of endometriosis and as (iii) histologically confirmed recurrence of endometriosis. The histological recurrence was further divided as histologically positive in any locations and histologically positive recurrence of bowel endometriosis. The patients, who underwent disc excision showed neither recurrence of symptoms nor recurrence with ultrasound and/or MRI imaging. The recurrence of symptoms occurred more frequently in the shaving group (18.8%) than in the segmental resection group (16%), however 4% of the segmental resection patients had an asymptomatic recurrence of the disease with ultrasound and/or MRI imaging. None of the observed differences were statistically significant. 12.5% (n 2/16), 20% (n 2/10) and 16% (n 8/50) of the patients underwent a repeated laparoscopy because of persistent or recurrent symptoms in the shaving, disc excision and segmental resection groups, respectively. Histologically proven recurrence of endometriosis occurred in 12.5% (n 2/16), 10% (n 1/10) and 10% (n 5/50) of the shaving, disc excision and segmental resection patients, respectively. None of the patients had a recurrence of bowel endometriosis in the segmental resection group, whereas one patient after shaving and one patient after disc excision developed a histological recurrence of bowel endometriosis. The analysis of recurrence rates including all surgical approaches demonstrates an overall conservative, surgical and histological recurrence of the disease of 17.1%, 15.8% and 9.2%, respectively, having only two patients (2.6%) with histological recurrence of bowel endometriosis. The results are presented in **table 10**.

Table 10. Recurrence rates after bowel endometriosis surgery

The table presents the conservative, surgical and histological recurrence rates after different types of colorectal endometriosis surgery and considering all patients. Presented are the absolute and relative number (percentages) of patients with a recurrence. Patients in the disc excision group did not suffer conservative recurrence. None of the patients in the segmental resection group had a recurrence of bowel endometriosis, whereas each the shaving and disc excision groups had one patient with recurrence of the bowel disease. The overall conservative, surgical and histological recurrence revealed 17.1%, 15.8% and 9.2%, respectively (highlighted grey). Two patients developed a recurrence of bowel endometriosis, both after conservative surgical approach. None of the results showed statistically significant difference comparing the different surgical approaches.

	Shaving	Disc excision	Segmental resection	All cases
Overall conservative recurrence	18.8% (3/16)	--	20% (10/50)	17.1% (13/76)
Recurrence of symptoms	18.8% (3/16)	--	16% (8/50)	14.5% (11/76)
Recurrence with imaging	--	--	4% (2/50)	2.6% (2/76)
Surgical recurrence	12.5% (2/16)	20% (2/10)	16% (8/50)	15.8% (12/76)
Histological recurrence	12.5% (2/16)	10% (1/10)	10% (5/50)	9.2% (7/76)
Histological recurrence of bowel endometriosis	6.3% (1/16)	10% (1/10)	--	2.6% (2/76)

3.7. Symptoms after surgery

The questionnaire and telephone interviews assessed the endometriosis related symptoms before the surgery, one year after the surgery and at the time of the evaluation and provided information in altogether 70 patients (58.3%) of the study population. This resulted a follow up of 18 patients (69.2%) with shaving, 7 patients (36.8%) with disc excision and 45 patients (60%) with segment resection. The median follow-up revealed 40.5 (range 2-88) months. Almost all of the patients suffered from dysmenorrhoea (97%), followed by symptoms of bowel dysfunction (81%), dyspareunia (78%), dyschezia (74%) and chronic pelvic pain (73%) before the operation. A remarkable number of patients suffered from voiding problems (29%) and dysuria (17%). An improvement was observed in all type of bowel surgery regarding the percentages of patients experiencing dysmenorrhoea, chronic pelvic pain, dyschezia and dyspareunia as well as the related

VAS scores one year after the surgery and on a long-time manner compared to the values before the surgery (**figure 11 and 12**). The symptoms did not further improve after a year, as we could not observe a difference between the data observed one year after the surgery and on a long-time manner. The results were statistically significant in all comparisons of the segment resection group and in the majority of the comparisons in the shaving group. The obvious improvement could not reach statistical significance in the disc excision group due to small sample sizes. A significant improvement of libido was observed one year after the surgery and on a long-time manner in the segment resection group, whereas the shaving and disc excision patients did not experience a change of their libido after the surgery. Bowel dysfunction improved significantly in all types of bowel surgery and the improvement remained on a long-time manner. Interestingly, dysuria and voiding problems occurred more frequently one year after the surgery and improved just on a long-time manner, however, none of the results reached statistical significance. However, in the segmental resection group the percentages of patients with dysuria increased after the surgical intervention, the intensity of dysuria measured with VAS values decreased.

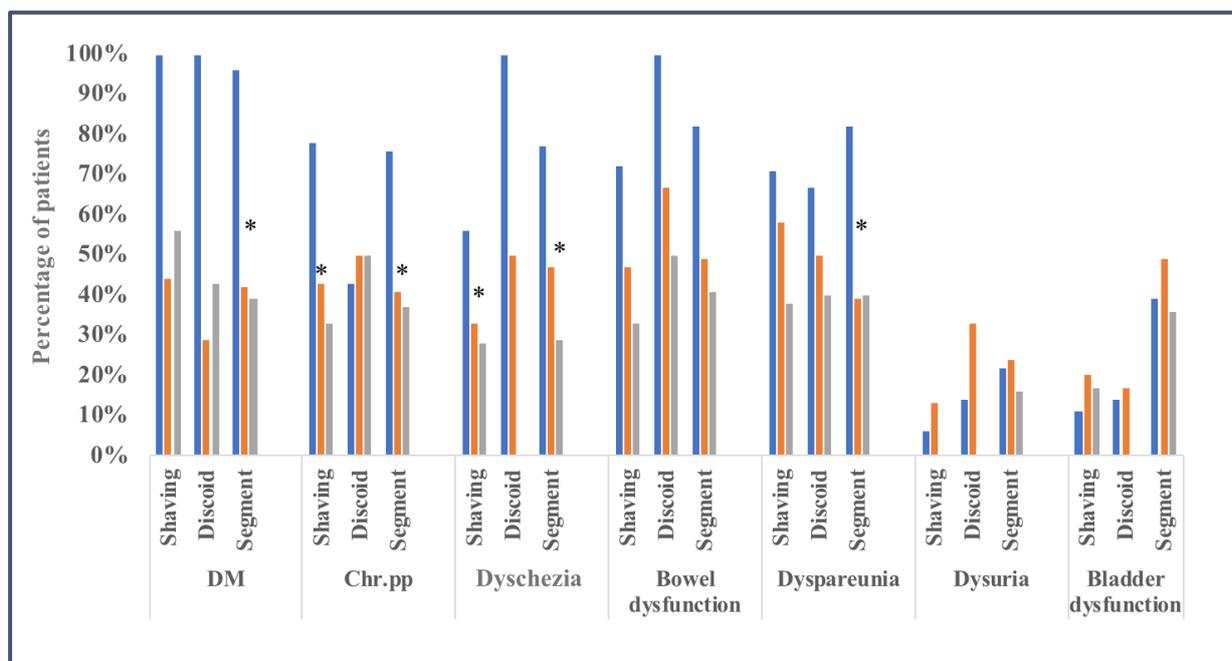


Figure 11. Effect of surgery on endometriosis related symptoms

The figure presents the percentages of patients (vertical axis) with different types of pain symptoms, bowel and bladder dysfunction before the operation (blue), one year after the operation (orange) and at the time of the evaluation (grey). DM: dysmenorrhea, Chr. pp: chronic pelvic pain. * indicates the statistically significant ($p \leq 0,05$) results.

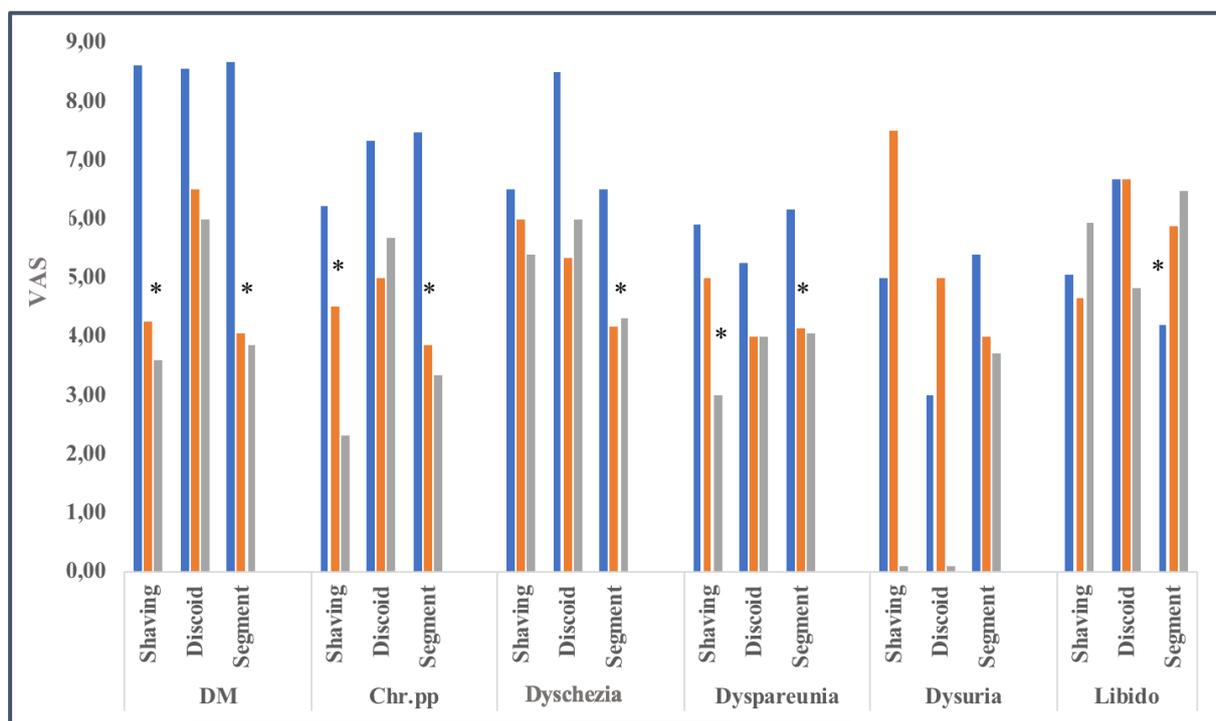


Figure 12. Effect of surgery on pain intensity and libido

The figure presents the median of VAS scores (vertical axis) related to different type of pain symptoms as well as libido before the operation (blue), one year after the operation (orange) and at the time of the evaluation (grey). DM: dysmenorrhea, Chr.pp: chronic pelvic pain. * indicates the statistically significant ($p \leq 0,05$) results.

3.8. Fertility and obstetrical outcome

The fertility outcomes were analysed including all study patients. A subgroup analysis of the different surgical modalities was not possible due to small sample sizes. From the 120 bowel endometriosis patients, 21 (17.5%) underwent a previous or current hysterectomy, 23 (19.2%) did not desire pregnancy, 6 patients were operated in the last 3 months of the study period, thus were not eligible for the obstetrical analysis and in 5 patients the medical record did not report about pregnancy wish. 65 (54.1%) of the 120 patients had a pregnancy wish after the operation and follow up was available for 54 (83.1%) patients. 31 (57.4%) patients became pregnant, defined as clinical pregnancy with positive heart rate and 21 (38.9%) patients had a live delivery. 8 patients were pregnant twice and 4 patients delivered twice resulting a total number of 39 pregnancies and 25 deliveries. 24

of the deliveries were live births and one of them a stillbirth. All of the pregnancies and deliveries occurred within 4 years with 2 years median of being pregnant and 3 years median of having a delivery. The cumulative pregnancy and delivery rate resulted 32%, 50%, 60%, 68% and 8.1%, 32.6%, 42.9%, 49% after 1, 2, 3 and 4 years, respectively (**figure 13**). 1st trimester miscarriage occurred in 6 of the 39 pregnancies (15.4%). None of the patients had a 2nd trimester miscarriage.

Almost equal number of patients conceived naturally (42.1% (n 16/38)) and with IVF (44.7% (n 17/38)). 13.2% (n 5/38) of the patients underwent intracytoplasmic spermium injection (ICSI), resulting a cumulative rate of using assisted reproductive technologies of 57.9% (n 22/38). The majority, 75% (n 18/24) of the patients delivered with caesarean section, 16.7% (n 4/24) had a vaginal delivery and 8.3% (n 2/24) underwent a vaginal operative delivery. 75% (n 18/24) of the deliveries was a single delivery, 20.8 % (n 5/24) a twin delivery and one patient (4.2%) had a triplet delivery. Regarding the age of pregnancy, 61.9% of the patients delivered on term, whereas 38.1% had a premature delivery. The obstetrical outcome is summarised in **table 11**.

Detailed history about the pregnancy and delivery outcomes was available in 15 of the 21 patients (71.4%) and 19 of the 25 pregnancies (76%) leading to delivery. 12 pregnancies (63.2%) showed an uncomplicated pregnancy course, whereas in 7 pregnancies (36.8%) complications occurred. One pregnancy was associated with preeclampsia, two of the pregnancies with HELLP syndrome, two patients suffered from gestational diabetes, one patient developed a cervical insufficiency and one patient underwent a surgery in the first trimester due to simultaneous extrauterine pregnancy. 17 of the 19 deliveries (94.7%) were uncomplicated, whereas 2 patients (10.5%) suffered a severe labour complication. One of them had a rupture of the posterior uterine wall at the 26th gestational week of a twin pregnancy leading to an emergency caesarean section resulting a stillbirth of both twins. The other patient had a rupture of the posterior vaginal vault, which had to be sutured during the secondary caesarean section.

Table 11. Summary of fertility and pregnancy outcome after surgery for deep infiltrating colorectal endometriosis

Presented are the relative (percentages) and absolute number of patients with an obstetrical condition. The pregnancy rate revealed 57.4%. 8 patients were pregnant twice, resulting a total number of 39 pregnancies. 42.1% of the pregnancies conceived naturally and 57,9% with assisted reproductive technologies, IVF or ICSI. The delivery rate revealed 38.9%. 4 patients delivered twice, resulting a total number of 25 deliveries. The majority of the deliveries were caesarean sections (75%). High number of twin pregnancies (25%) and premature deliveries (38.1%) were observed.

Patients	n/total				
previous or current hysterectomy	17.5% ^(21/120)				
no pregnancy desire	19.2% ^(23/120)				
missing data about pregnancy wish	4.2% ^(5/120)				
pregnancy wish	54.1% ^(65/120)				
missing follow up	16.9% ^(11/65)				
followed patients	83.1% ^(54/65)				
Pregnancy rate	57.4% ^(31/54)	Conception	n/total pregnancies		
Total number of pregnancies	39	missing data	2.6% ^(1/39)		
		natural	42.1% ^(16/38)		
		IVF	44.7% ^(17/38)		
		ICSI	13.2% ^(5/38)		
Delivery rate	38.9% ^(21/54)	Way of delivery	n/total deliveries	Multiplicity	n/total
Total number of deliveries	25	missing data	4.0% ^(1/25)	missing data	4.0% ^(1/25)
		vaginal	16.7% ^(4/24)	single delivery	75.0% ^(18/24)
		vaginal operative	8.3% ^(2/24)	twin delivery	20.8% ^(5/24)
		caesarean section	75.0% ^(18/24)	triplet delivery	4.2% ^(1/24)
				missing data	16.0% ^(4/25)
				premature delivery	38.1% ^(8/21)
				mature delivery	61.9% ^(13/21)

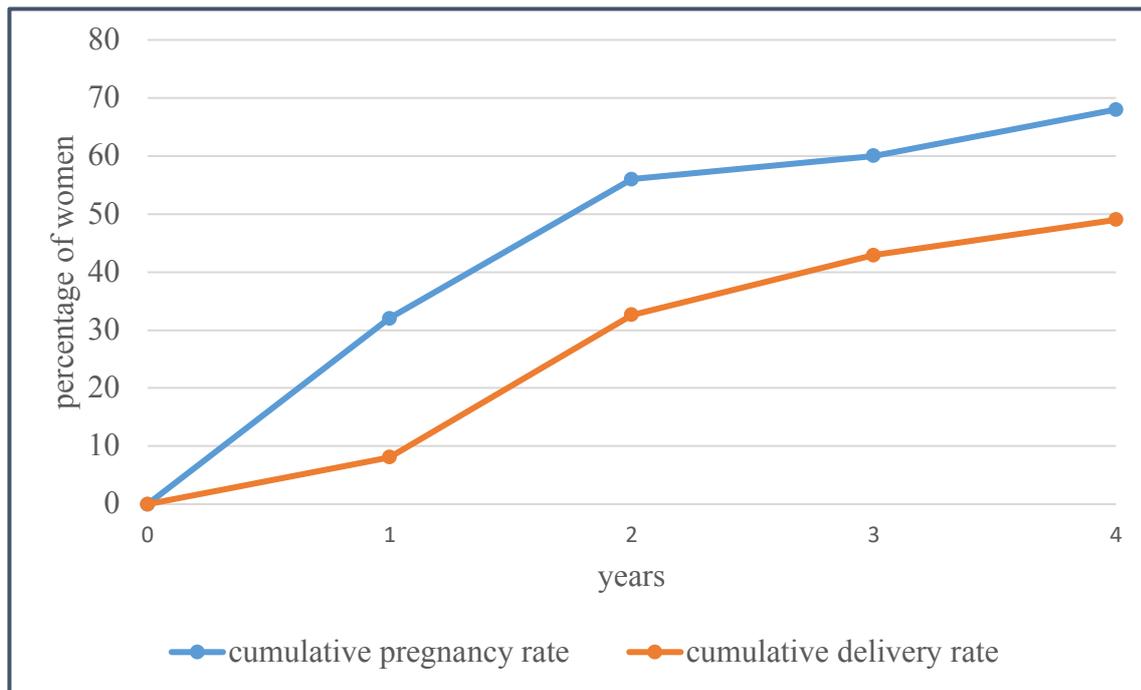


Figure 13. Cumulative pregnancy and delivery rates after surgery for deep infiltrating colorectal endometriosis

Presented are the cumulative pregnancy- and delivery rates over 4 years after surgery. Data were available in 50 patients for the analysis of cumulative pregnancy rates and in 49 patients for analysis of cumulative delivery rates, resulting a cumulative pregnancy and delivery rate of 68% and 49% four years after the surgery, respectively.

4. Discussion

4.1. Types of colorectal endometriosis lesions and their influence on the surgical modality

Bowel endometriosis is one of the most severe forms of DE. It adversely affects the quality of life due to severe pain symptoms, bowel dysfunction, disturbed sexual life, sub-fertility, social- and work life problems. Surgery is the main pillar of treatment strategy and is indicated in all symptomatic patients, in infertility patients after two or more failed IVF cycles and in patients with signs of bowel obstruction regardless of the symptoms (*Abrao et al., 2017*). Although several surgical techniques exist such as segmental resection, disc excision and shaving, there is no consensus which technique is superior to the other regarding clinical outcome. Moreover, there are several described techniques

for disc excision and the definition of the shaving technique varies from centre to centre. The disc excision can be performed (i) using the transrectal circular stapler for nodules up to 2,5cm (*Woods et al., 2003*), (*Landi et al., 2008*), (ii) using the transrectal double circular stapler technique for nodules greater than 2,5cm (*Oliviera et al., 2014*), or (iii) using an intraabdominal linear stapler (*Kamergorodsky et al., 2015*). Similar to the huge variety of disc excision procedures there is no consensus to the definition and technique of the shaving procedure. Generally, it involves removal of a lesion invading no deeper than the subserosal layer. However, there are centres, who perform shaving to the internal muscular layer with consecutive sutures of the rectal wall or even shaving to the mucosa with entering the rectal lumen and double layer suturing (*Abrao et al., 2017*). In case of large nodules the combination of deep shaving with linear stapler or circular rectal stapler disc excision, the “Rouen-technique” have been also described (*Roman et al., 2016*). Due to several applied techniques it is difficult to compare the published results about the clinical outcome of different procedures and define clear indication for each surgical approach.

Whereas earlier the radical segmental resection was favourable to other techniques, nowadays there is a trend towards less radical surgery. In 2011 Meuleman reported in a review of the literature that out of 3894 patients, 71% underwent segmental bowel resection, 10% had full-thickness anterior rectal wall disc excision and 17% were treated with superficial surgery, e.g. with shaving (*Meulemann et al., 2011*). A later work from Roman, which took a snapshot in 2015 about the practising technique in France with enrolment of 56 healthcare facilities and 1135 patients, reflected a tendency towards less radical surgical approaches. Rectal shaving was carried out in 48.1% of the patients, disc excision in 7.3%, whereas colorectal segmental resection was performed in 40.4% of the cases and sigmoid colon segmental resection in 6,4% (*Roman et al., 2017*).

From the above described surgical techniques we performed in our center the segmental resection, the disc excision using the abdominal linear stapler or the classical shaving of the serosal and subserosal layers. The distribution of the procedures showed the segmental resection as the most frequent procedure (62.5%), followed by rectal shaving (21.7%) and disc excision (15.8%) resulting an overall conservative surgical approach rate of 37,5%. The distribution of the different type of surgeries did not change over the 1st and 2nd five years observation period. Regarding the entry to the abdominal cavity in the 2nd half of the study period the laparoscopic route increased from 56.2% to 90.9% of the cases and the conversion rate as well as the laparotomic approach decreased from

9.4% to 2.3% and from 34.4% to 6.8%, respectively. These results are in accordance with the technical development of laparoscopic surgery and increasing expertise of gynaecological and general surgeons. Deep endometriosis surgery is a challenging condition and the success of surgery depends from the surgeon's experience. Patients with severe DE should be referred to expert centres in order to treat with the expertise of a multidisciplinary team of gynaecologists, general surgeons, radiologists and in some cases urologist, like in the tertial referral centre of the University Gießen.

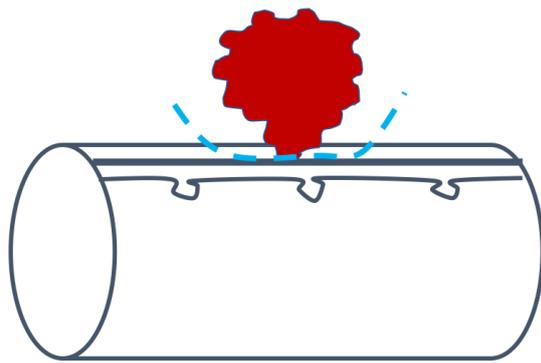
The purpose of our study was to contribute to a better understanding of clinical outcome of bowel endometriosis surgeries and define clear criteria how to choose the most appropriate surgical technique for the different types of lesions. Our data showed that in the majority of the shaving procedures (76%) the nodule measured up to 3 cm. Bigger lesions were observed less often, the lesions revealed between 3-6cm in 20.7% of the patients and in one patient over 6cm. The depth of infiltration showed an involvement of the serosal and subserosal layers in 82.7% of the cases. These results suggest that shaving is appropriate for smaller lesions infiltrating the serosal and subserosal layers. In patients, who underwent disc excision the nodule size showed different distribution. Nodules up to 3cm were observed in 35% of the cases, whereas 60%, the majority of the nodules, measured 3-6 cm and in 10% (2 cases) the nodule was bigger than 6cm. In 75% the muscular layer was infiltrated and in 18.7% even deeper layers, suggesting that disc excision is indicated in case of larger nodules and infiltration of deeper layers of the rectal wall. Regarding patients, who underwent conservative surgical approaches almost all of them had a single nodule and just a few patients two nodules in both the shaving and disc excision groups. This distribution underlies the strategy that conservative surgical approaches are applicable for singular nodular lesions with using the shaving technique for smaller and superficial nodules and disc excision for bigger deeper infiltrating lesions. In case of segmental resection 64% of the patients suffered from nodular lesions with one, two or three isolated nodules. The nodular lesions measured almost in equal parts up to 3cm and beyond 3cm. A large amount, 36% of the patients, had a multifocal affection of the bowel wall, defined as a long segment infiltration.. Our data suggest a clear indication of segmental resection in case of multifocal long segment bowel affection or multicentric involvement. In cases of a single, the muscularis or deeper layers infiltrating nodules, the decision between disc excision and segmental resection relies on the involvement of the bowel lumen circumference. If the nodule compromises more than 1/3 of the bowel circumference segmental resection is preferred. This aspect could not be investigated in

our study, because the histology did not report this parameter, resulting a recommendation relying on our surgical experience.

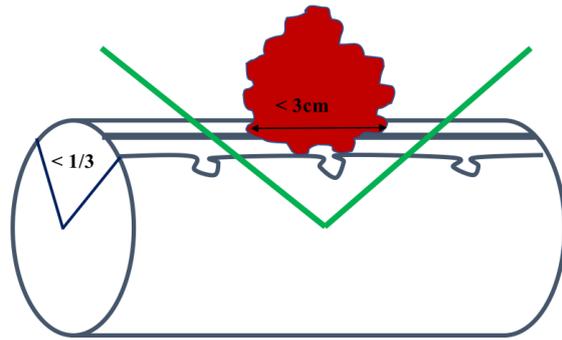
Considering the appropriate surgical technique for bowel endometriosis we have to keep in mind that endometriosis lesions of the bowel differ from those one of bowel cancer. Cancer nodules growth from the mucosal layer, from inside to outside and the major part of the nodule is located inside the bowel wall. In case of endometriosis the nodule invades the bowel from outside to inside, resulting in many cases bulky lesions sitting on the anterior bowel wall with smaller infiltrative portion inside the bowel wall. Thus, it is not the absolute diameter of the endometriotic nodule which is crucial to choose the right way of surgery, but the extension of the nodule sitting in the bowel wall, the involvement of the bowel circumference, the depth of bowel wall infiltration and the multifocal and multicenter character of the lesions. Even large, single bulky nodules, sitting on the anterior rectal wall can be removed with shaving and disc excision and sometimes smaller nodules, which affect a large amount of the bowel circumference or infiltrate the bowel until the submucosa require a segmental resection. In case of long segment multifocal affection of the rectal wall the segmental resection is the only option to remove the disease.

Our results are in accordance with a recent review, which demonstrated a similar distribution of the nodule's size among the different procedures (*Donnez et al., 2017*). A recent work from *Abrao et al*, which analysed the critical factors to consider before surgery, determined the number and size of lesions and bowel circumference involvement as the most relevant parameters in decision making about the surgical technique and defined 3cm as a cut-off for nodule diameter to perform less radical surgery (*Abrao et al., 2015*). In our opinion, this cut-off value should be applied for the infiltrative part of the nodule instead of the complete size of the lesion.

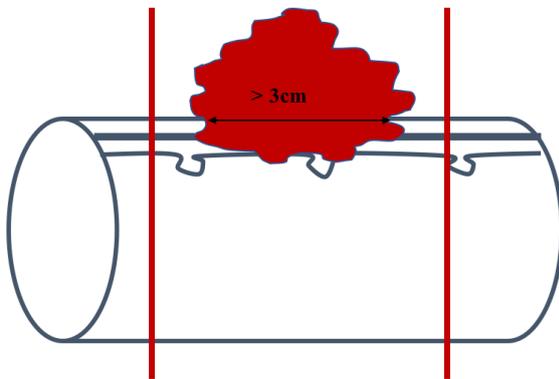
Considering the results of our study and our surgical experience clear criteria can be defined for the decision making during the surgery, which are demonstrated in **figure 14**.



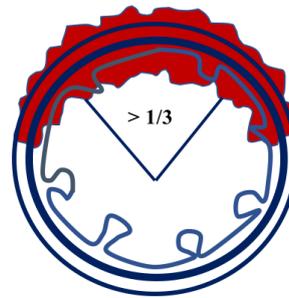
Exophytic lesion with superficial infiltration of the serosa and subserosa
→ Shaving



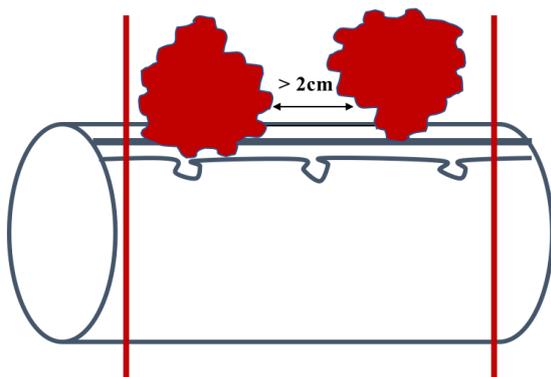
Lesion smaller than 3cm, less than 1/3 bowel circumference involvement, infiltration of the muscularis or deeper
→ Disc excision



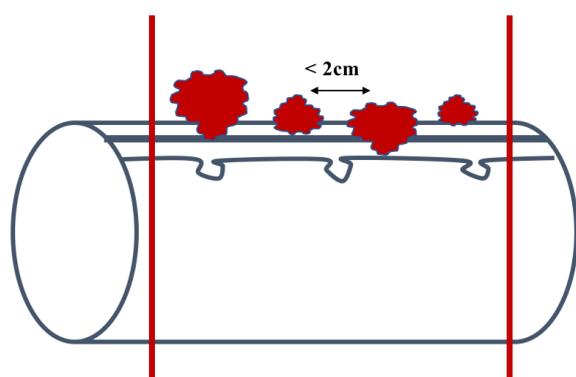
Lesion larger than 3cm, infiltration of the muscularis or deeper
→ Segmental resection



More than 1/3 bowel circumference involvement, infiltration of the muscularis or deeper
→ Segmental resection



Multicenter lesions with nodules of different size and depth of infiltration
→ Segmental resection



Multifocal lesions with long segment affection of the bowel wall
→ Segmental resection

Figure 14. Types of bowel endometriosis lesions

The figure demonstrates bowel lesion types eligible for shaving (dashed blue line), disc excision (green line) and segmental bowel resection (red line). The most important features to consider is the lesion's extension sitting in the bowel wall, depth of infiltration, involvement of bowel circumference as well as multifocal and multicenter character.

4.2. Imaging modalities to evaluate lesion's characteristics and predict the type of surgery

Although transvaginal sonography (TVS), MRI and rectal endosonography (RES) has a high sensitivity of around 90% to detect bowel endometriosis (*Gerges et al., 2020*), the decision making about the type of surgery remains for most of the cases intraoperative. With TVS the height of the lesion and distance to anal verge can be measured appropriate, thus the height of anastomosis and risks of surgery in case of segmental bowel resection can be well estimated. MRI and RES are both capable of detection the muscular layer infiltration. With RES the endometriotic infiltration of the muscular layer can be predicted accurately. The method is less accurate in detecting submucosal and mucosal layer involvement (*Rossi et al., 2014*). MRI is valuable for detecting endometriosis of the rectum and muscular involvement but is even less accurate in detecting submucosal and mucosal involvement than RES (*Kim et al., 2017*). Both MRI and RES are helpful tools to predict the feasibility of rectal shaving, but unable to guide the surgeon about the decision between disc excision and segment resection. The long segment affection of the bowel wall with often superficial but large infiltration areas of the anterior rectal wall is very difficult to predict with imaging modalities. Until now studies of imaging technologies are missing which involve the measurement of important lesion characteristics, such as size, depth of infiltration and involvement of bowel lumen circumference. These characteristics have a great impact on surgical planning, including the selection of intestinal resection type (*Carvalho Moura et al., 2019*).

In our study all patients underwent a preoperative TVS and MRI. We believe, that both imaging modalities should be performed before the surgery in order to predict the involvement of other structures of the pelvis, the extension of the disease, the difficulty of the surgery as well as some useful factors of bowel endometriosis lesions, such as distance to anal verge, infiltration of the muscular layer and multicenter affection. The acquired information about the features of a bowel lesion enable us to create an approximate surgical plan about the type of bowel resection, which is very important for patients' counselling. Unfortunately, we are still not capable to predict precisely the surgical modality and the preoperative surgical plan should be modified in some cases during the surgery.

4.3. Association of bowel endometriosis with other manifestations of deep endometriosis

DE of the bowel occurs seldom isolated and is associated in many cases with an extensive involvement of the posterior compartment and adnexa. In our study we described the distribution of concomitant deep infiltrating lesions and adnexal involvement allowing a precise mapping of DE in the pelvic cavity. Bowel involvement was associated in at least every third women with rectovaginal involvement (36.7%) and vaginal infiltration (32.5%) such as infiltration of the left (39.2%) and right pelvic wall (36.18%) and the sacrouterine ligaments (left 26%, right 30%). Every second women showed an endometrioma of the left ovary (50%) and every third an affection of the right ovary (35.8%). The involvement of the anterior compartment, bladder infiltration and endometriosis of the round ligaments were less frequent. This distribution of DE is in accordance with previous studies and surgical reports (*Chapron et al 2003*). Important to note the association between colorectal and ovarian endometriosis. A recent ultrasound study of 255 women with ovarian endometriosis detected in 44% of the patients DE with 21.5% colorectal involvement during the transvaginal sonography of the pelvis. The authors concluded that ovarian endometriosis should be consider as a marker for posterior compartment deep endometriosis necessitating an accurate ultrasound investigation of the pelvis to determine the extent of the disease and detect severe DE lesions (*Exacoustos et al., 2018*).

4.4. Histology results

There are just few studies in the literature which evaluate the histology findings of bowel lesions and their clinical correlation. A prospective study of Mabrouk et al included 47 patients treated with laparoscopic segmental resection and assessed the relationship between histological findings and clinical characteristics of the disease. They did not observe statistically significant differences in terms of anatomical and pain recurrences, pain symptoms and quality of life improvement among patients with or without positive resection margins and presence of satellite lesions as well as different degrees of vertical infiltration. They reported a mean length of removed bowel segment of 10.3 cm and the mean diameter of the lesion of 2.6cm. They detected multifocal lesions in 64% of the

cases. 19% of the patients had positive resection margins. The muscular layer was infiltrated in 64% of the cases, and deeper layers, such as submucosa or mucosa were involved in 25% and 11% of the cases, respectively (*Mabrouk et al., 2012*). In our study we could observe similar results of the segmental bowel resection group. The length of the removed bowel segment revealed a median of 7cm, 10.3cm and 19.5 cm in case of single nodule, two and three nodules, respectively. 36% of the patients showed a multifocal affection of the rectal wall. In these cases the length of the removed bowel-segment resulted a median of 9cm. The histology results of our study confirm the assumption that the pure size of an endometriosis nodule sitting on the rectal wall cannot directly determine the type of bowel surgery, because even small lesions have been treated with segmental resection and large bulky nodules with disc excision. The most important factor is the extension of the nodule sitting in the bowel wall and the depth of vertical infiltration. We could also observe a high rate of positive aboral resection margins of 17.9%. Most of the cases with positive resection margins were resulted from the multifocal affection of the bowel wall with positive oral and aboral resection margins of 4.8% and 23.8% of the cases, respectively. The presence of a positive resection margin did not correlate with the recurrence of the disease. The depth of infiltration of segmental resection cases revealed a similar distribution like in the study of Mabrouk et al. with infiltration of the muscular, submucosal and musosal layers in 60%, 25% and 6.7% of the nodules, respectively.

4.5. Effect of surgery on clinical symptoms

DE behaves like a chameleon and it can be challenging to diagnose the disease. Many patients are diagnosed too late or first even with a false diagnosis. Hudelist et al conducted a cross-sectional, questionnaire-based multicenter study in tertiary referral centers in Austria and Germany with inclusion of 171 patients with histologically confirmed endometriosis and described a median diagnostic delay of endometriosis from the first onset of symptoms with 10.4 years. 74% of the patients received at least one false diagnosis before detecting the correct diagnosis of endometriosis (*Hudelist et al., 2012*). In our study the median of diagnosing endometriosis from the onset of symptoms was 6 years, every third women had her diagnosis 7 or more years after the first symptoms and a huge number of patients reported even about 10 years diagnostic delay.

Regarding the clinical outcome our data demonstrated that all type of surgery effectively reduces endometriosis related pain symptoms, such as chronic pelvic pain, dysmenorrhoea, dyspareunia and dyschezia as well as bowel dysfunction and increases the libido. The percentage of symptomatic women as well as the intensity of the pain measured by VAS values decreased significantly after all types of surgery. This is in congruence with many other reports about surgical outcome of different colorectal endometriosis procedures. Since the segmental resection was first described by Redwine and Sharpe many reports confirmed the efficacy of the technique regarding clinical symptoms (*Redwine et al., 1991*) (*Sharpe et al., 1992*). Dubernard et al and Bassi et al demonstrated that quality of life was strongly improved after bowel resection and Ruffo et al showed in a large case series of 900 patients a significant improvement of dyspareunia, constipation and pelvic pain (*Dubernard et al., 2006*, *Bassi et al., 2011*, *Ruffo et al., 2010*). Later further studies confirmed, that conservative surgical modalities also effectively improve pain symptoms and can better preserve rectal function. Roman et al and Serrachioli et al showed that shaving technique improved symptoms without negatively altering intestinal function (*Roman et al., 2013*, *Serracchioli et al 2015*, *Roman et al., 2016*). The first report about linear stapler disc excision in a prospective series reported similar clinical results (*Ribeiro et al., 2006*). Fanfani et al reported in a case-control study that disc excision improves endometriosis-related symptoms and could be used as an alternative to the classical segmental resection (*Fanfani et al., 2010*). Roman et al showed in a prospective cohort study that single disc excision is a valid alternative to segmental resection reaching better preservation of rectal function (*Roman et al., 2016*). A recently published randomized trial, which compared the conservative surgical approaches to the radical segmental resection in women with large involvement of the rectum showed a similar postoperative outcome regarding improvement of pain symptoms, but could not confirm the superiority of conservative surgery for mid-term functional digestive and urinary outcomes (*Roman et al., 2017*).

However statistically not significant, but interestingly the dysuria and bladder dysfunction worsened in our study after the surgery and the symptoms decreased just on a long-time manner. These findings may be in accordance with damaging the visceral and splanchnic nerves during the excision of DE lesions from the sacrouterine ligaments, parametria and pelvic side walls causing severe voiding problems after the surgery. With the introduction of nerve sparing operative techniques the incidence of urinary tract dysfunction might decrease in the future (*Dubernard et al., 2008*). However, it is not

always possible to save the nerves during the surgery, because DE not just embrace but infiltrates the nerves making impossible to remove lesions without damaging the nerve fibers. Thus, in case of bilateral severe DE of the sacrouterine ligaments, parametria and pelvic side wall surgeons should make sometimes compromises during the surgery in order to reserve important functions of pelvic organs.

4.6. Effect of surgery on reproductive outcome

DE is associated with disturbed anatomy, severe adhesions, disturbance of the reproductive process including ovulation, fertilization and increased risk of miscarriage (*De Ziegler et al., 2010*). Surgery for DE restores the damaged anatomy and diminish endometriosis associated inflammatory peritoneal and lesional milieu and therefore can effectively increase pregnancy rates. In our study population we observed an overall pregnancy and delivery rate of 57.4% and 38.9%, respectively. We observed an increased miscarriage rate of 18.5% compared to healthy women. Our study confirms similar benefit of surgery like other literature reports. In a review of Darai et al from 2016 the overall pregnancy rate after colorectal surgery was 51.5% compared to a pregnancy rate of 37.9% in patients with surgical removal of DE leaving bowel endometriosis in situ (*Darai et al., 2016*). This work confirmed that bowel endometriosis itself contributes to burdened fertility and surgical removal of the bowel lesion increases pregnancy rate. However, there are increasing reports about the surgical benefit on fertility issues, the effects of bowel surgery itself on spontaneous pregnancy rates and IVF treatment remains controversial and randomised controlled trials are missing. A recent review of Iversen et al from 2017 could not recognise any randomised controlled trial evaluating the effect of bowel endometriosis surgery on fertility outcome. Their analysis included retrospective and prospective observational studies including 905 patients treated with colorectal endometriosis and concluded, that surgery might have a positive effect on fertility outcome. A stronger benefit of bowel surgery on fertility could not be concluded (*Iversen et al., 2017*). Considering the high risks of surgery patients should be informed about the uncertain background of surgical benefits especially in cases, in which infertility is the only clinical manifestation of bowel endometriosis and severe pain symptoms are missing.

We observed a high rate (75%) of caesarean sections, which has been revealed in other

studies as well (*Thomin et al., 2018*). Potential explanation of the high caesarean rates can be an observed increased risk of malpresentations and the high rate of infertility treatment. In our study 42.1% of the patients conceived naturally and 57.9% with assisted reproductive technologies. Information about the indication of caesarean section was not completely available in our study, which limits the interpretation of our results.

There is increasing information that patients with surgically treated DE have a higher risk of pregnancy complications, such as placenta praevia, gestational hypertension, intrauterine growth restriction and preterm birth (*Nirgianakis et al., 2018, Vigano et al., 2015*). Placenta praevia was mostly observed in relation to DE and preterm birth to ovarian endometriosis (*Vigano et al., 2015*). The presence of ovarian endometriosis seems to double the risk of premature delivery compared to community birth records (*Fernando et al., 2009*). Ovarian endometriosis occurs rarely isolated and DE is often associated with ovarian endometriosis as we could also confirm in our study. This might explain the observed increased risk of preterm birth in our study population, however, the small sample size limits the interpretation of the results.

In our study we observed severe labour complications in two patients, having a uterine rupture in one patient and a rupture of the posterior vaginal vault in the other one. An increased risk of labour complications after surgical removal of severe DE, such as a potential life-threatening complication of uterine rupture or rupture of the posterior vaginal vault has been also mentioned in some case reports (*Vystavel et al., 2018*). However, the discussion about the risk of vaginal vault rupture is controversial and there are literature reports, that could not confirm the hypothesis of an increased risk of rupture after extensive surgery (*Allerstorfer et al., 2016*). DE of the bowel often invades the surrounding structures such as the rectovaginal space, sacrouterine ligaments and the posterior wall of the cervix. Because there is no clear cleavage plane during the surgery the extensive excision of the endometriotic nodule may harm the cervix or uterine isthmus causing weakened myometrium possibly predisposing to uterine rupture, as we have seen in our patient at the 27th week of pregnancy resulting in an emergency caesarean section. Although uterine rupture or other endometriosis related acute pregnancy complications, such as intraperitoneal bleeding and ruptured endometrioma (*Vigano et al., 2015*) are very rare caution should be taken in case of severe abdominal pain during the pregnancy or delivery to undertake proper management for achieving the best maternal and neonatal outcome.

4.7. Recurrence of the disease

In our study we observed an overall conservative, surgical and histological recurrence rate of endometriosis of 17.1%, 15.8% and 9.2%, respectively. We could not detect a statistically significant difference between the different surgical approaches. There are similar reports in the literature about recurrence rates of endometriosis after colorectal endometriosis surgery. However, some studies described lower recurrence rates after segmental resection compared to shaving and disc excision (Mangler et al, 2014). We could not observe lower recurrence rates after radical surgery, which might be explained due to the small sample size of the long-term followed patients in our study. Histological recurrence of bowel endometriosis occurred only in one patient in the shaving and one patient in the disc excision groups, whereas patients with segmental resection did not suffer a recurrence of bowel endometriosis, suggesting that the removal of a bowel lesion is more complete if segmental resection is performed. Interestingly, in case of segmental resection we observed relative high rates of histological positive oral and aboral resection margins of 1.8% and 17.9%, respectively, which was not correlated with a higher rate of histological recurrence of the disease. These data confirm the benign clinical behaviour of endometriosis and the importance of macroscopic complete resection, whereas microscopic incomplete resections, e.g. histological positive resection margins do not contribute to disease recurrence in contrary to malignant disorders and does not indicate a repetitive surgery, such it has been described in other papers as well (*Mabrouk et al., 2012, Roman et al., 2016*).

4.8. Complications of bowel endometriosis surgery

The knowledge about the complications of bowel endometriosis surgery and their incidence is essential, since we are dealing with a benign condition in mostly healthy, young women. However, these women suffer from severe pain symptoms, reduced fertility and disturbed quality of life if a severe complication occurs we have to face the problem if the benefits of the surgery worth the risks. Our study provides important information about the procedure related complication rates.

The conservative surgical modalities are generally associated with lower complication

rates. A recent review of Donnez O and Roman reported in 1.74% of 4470 shaving procedures an intraoperative perforation of the bowel wall with each case having the bowel sutured without unfavourable postoperative outcome. Postoperative bowel perforation requiring colostomy was reported in 1.7-2.2% of the cases according to smaller studies and 0.13% in the largest series of 3298 cases. Rectovaginal fistulas occurred in 0.24% of the cases in the largest study population and the rate of bladder atony and long-term catheterization revealed 0.19% for a maximum duration of 6 weeks (*Donnez O and Roman, 2017*). Our experience with shaving showed similar excellent results, having just one case with late perforation of the rectosigmoid, making necessary a repeated surgery and performing a segmental resection of the affected bowel segment. We did not experience intraoperative perforation of the rectal wall, although we performed the classical shaving technique up to the subserosal layer in contrary to the deep shaving defined by Donnez involving the muscularis. We did not experience any cases with development of a rectovaginal fistula and cases with urinary retention.

According to the review of Donnez O and Roman the most frequent complication after disc excision procedures was the development of a rectovaginal fistula with incidence rates of 3.6-7.2%. The complication occurred mainly in cases with extensive endometriotic nodules infiltrating not just the bowel wall, but the vagina and in cases with ultradeep located bowel lesions, e.g. less than 6cm to the anal verge (*Donnez O and Roman, 2017*). This high rate was even present if an omentoplasty had been performed. The risk of fistula development was higher than the rate in patients with shaving (1.3%), and comparable to the segmental resection group (3.9%). In our series of disc excision procedures we did not experience any cases with development of a rectovaginal fistula and the overall complication rate was very low anyway. This discrepancy can be described with the different approaches and definitions of the disc excision procedures. It is plausible that e.g. the Rouen technique, which combines the deep shaving with transanal circular stapler disc excision is an extensive and more radical surgical method compared to the linear stapler transabdominal disc excision and is associated with higher amounts of fistula formation.

In our series of disc excisions we did not observe patients with urinary retention. This can be again explained with differences of the operative techniques among different endometriosis centers. Our operative technique enables to save the perirectal splanchnic nerve fibers and preserve bladder and rectal function.

Our study showed that the segmental resection was associated with the highest intra- and

postoperative complication rates. Two cases (2.7%) were associated with a major intraoperative complication both with injury of the left ureter. Major postoperative complications, which indicated a reoperation occurred in 6 cases; 4 of them (5.3%) was bowel surgery associated and in 2 (2.7%) patients a reintervention was indicated due to other reasons, such as bleeding from the right parametrium and compartment syndrome of both leg. Leakage of the operated bowel segment can occur after any of the bowel procedures and appears as a major life-threatening condition. Segmental resection is associated with extensive dissection of the pararectal spaces where important vascular and nerve structures are located which can be harmed compromising the final vascularisation of the bowel wall at the anastomotic line. The damage of the pararectal structures can cause severe morbidity with bowel ischemia, anastomotic leakage and fistulas (*Nezhat et al., 2018*). All of the bowel associated complications in our study showed an insufficiency of the anastomotic ring. Two patients had a severe disruption of the anastomosis and should be treated with a reanastomosis and application of a double barrelled protective ileostoma. Two of the patients showed a tiny insufficiency of the bowel wall which could be treated in one patient with protective ileostomy and endoluminal closure of the bowel wall effectively. In case of the other patient the anastomotic site had been closed with a primary re-suture and performing a protective ileostomy. This management was unsuccessful and the patient developed a recurrence of the insufficiency, which indicated a third revision and necessity of a Hartman procedure. The bowel continuity could be restored just in a year. Our observations are in accordance with the findings of the review of *Donnez O and Roman* from 2017. They reported a leakage rate of 0-4.8% with a mean of 1.72%, in patients with segmental colorectal endometriosis (*Donnez O and Roman 2017*). These data are relying on retrospective analysis and should be carefully interpreted. Unfortunately, there is so far just one randomized controlled trial, which analysed the leakage rate according to the different surgical modalities and showed no differences between the different procedures (*Roman et al., 2018*).

Anastomotic leakage causes severe morbidity, reoperations and up to 15% mortality. Clinical condition of the patients should be optimised to prevent the leakage. These conditions are well known in relation to oncosurgery and should be kept in mind in case of colorectal endometriosis as well. Discontinuation of alcohol intake and smoking, immune-enhanced nutritional supplementation, restrictive application of nonsteroidal anti-inflammatory drugs and avoiding BMI>35 are conditions, which can prevent

anastomotic leakage. Intraoperative factors should be also optimized, such as appropriate fluid administration with avoiding both overload and fluid restriction, avoiding hypotension and anaemia (*Vigueras Smith et al., 2020*). Moreover, the duration of the surgery is positively correlated with major and minor intraoperative complications. Silva-Velazco found an anastomotic leakage increase of 3% every 30 minutes of surgical time (*Silva-Velazco et al., 2016*) with a threshold between 220 and 300 minutes (*Huh et al., 2010*). In our series we observed a median operating time of 292 minutes, with operating time of over 300 minutes in most of the cases, in which anastomotic leakage developed after the procedure. Careful operative steps should be done to prevent or decrease the risk of a leakage; the use of either stapler or handsewns single layer closure anastomosis, intraoperative use of air-leak test, application of protective ileostomy when the nodule is ultradeep located, closure of the vagina before performing bowel resection, use of non-absorbable oral antibiotics one day before surgery and performing tubular resection near the bowel wall and interposition of omental flap on a vascular pedicle in selected cases (*Vigueras Smith et al., 2020*). Our surgeries had been performed following the above principles. We used stapler anastomosis, intraoperative air-leak test and rectoscopy, as well as omentoplasty and protective ileostomy in selected cases. Moreover, we placed great value on gentle tissue handling with avoiding extended coagulation and saving vessel and nerve structures in the pararectal spaces and around the sacrouterine ligaments. Temporary defunctioning stomas may decrease the morbidity and clinical consequences of the leakage in over 65% of low colorectal anastomosis (*Vigueras Smith et al., 2020*). Although ileostomy decrease the morbidity and mortality of anastomotic leakage it does not prevent the development of a leakage itself. In some centers protective ileostomy is recommended in every case of ultradeep rectal anastomosis with highly increased risk for anastomotic leakage, whereas other centers decide individual. In our center we decided upon intraoperative evaluation of risks and performed a protective double-barrelled ileostomy in 8% regarding all cases and in 27.3% regarding ultradeep anastomosis. On the other hand if ileostomy is applied we also have to consider the ileostomy-associated side effects and complications (*Vigueras Smith et al., 2020*), which must be balanced against the risks of anastomotic leakage. Moreover, considering the benign nature of endometriosis and the case, that we are dealing with young healthy patients, the indication for a protective ileostomy must always be determined according to the extent of the disease, risks and patient wish.

Rectovaginal fistula as a long-term complication occurred in 2 cases (2.7%) in our

segmental resection series. This corresponds to literature data, which show an increased risk of fistula formation after segmental resections compared to disc excision and shaving procedures and increases significantly in the presence of concomitant vaginal incision and urinary tract procedures (*Gornes et al., 2020*).

We observed anastomotic stenosis as a long-term complication in 1.9% of the patients with segmental resection. The disc excision and shaving procedures were not associated with rectal stenosis. Our results are favourable compared to the largest reported series of 1643 segmental resections for bowel endometriosis focusing on the analysis of stenotic complications, which described a stenosis rate of 6.3% (*Bertochi et al., 2019*). Stenotic complications after bowel endometriosis surgery may arise more frequently than in patients with other colorectal diseases, suggesting a possible role of the enhanced lesional and peritoneal inflammatory condition related to endometriosis (*Maytham et al., 2010*). Moreover, endometriosis is associated with fibrotic changes in the surrounding tissue. The theory of chronic inflammation and increased fibrotic degeneration is further supported of our observations of having 2 cases with ureteric stenosis as a long-term complication observed in the shaving and disc excision groups.

Voiding dysfunction is a well-known complication of bowel endometriosis surgery. The bladder is innervated by the inferior hypogastric plexus originating from the superior hypogastric plexus (autonomous), the pelvic nerves (parasympathetic) and the hypogastric nerve (sympathetic). Bowel endometriosis can cause urinary dysfunction itself owing to the infiltration of the hypogastric plexus. Moreover, the inferior hypogastric plexus and the hypogastric nerves can be damaged during the dissection of the uterosacral ligaments and pararectal spaces (*Vesale et al., 2020*). Although urinary dysfunction may resolve spontaneously after 1 to 3 weeks, it can also persist for months, years or for a lifetime (*Bonneau et al., 2013*). Unfortunately, conservative therapeutic approaches to restore bladder function are limited. The gold standard remains the intermittent self-catheterisation reducing the quality of life of the patient. Recently neuromodulation techniques have been proposed to overcome the symptoms (*Nyangoh Timoh et al., 2015*). A recently published systematic review and meta-analysis of Vesale et al assessed a total of 5962 patients undergoing surgery for colorectal endometriosis and measured the voiding dysfunction rate and the risk of self-catherisation lasting more than 1 month. They observed an overall rate of voiding dysfunction of 7.6% with a prevalence of 2.4%, 7.5% and 10.1% after rectal shaving, disc excision and segmental colorectal resection, respectively. Self-catheterisation mainly occurred after segmental colorectal

resection (*Vesale et al., 2020*). In our study we observed similar results of voiding dysfunction after surgery. Our shaving and disc excision patients did not develop urinary problems, whereas patients with segmental colorectal resection showed in 9% urinary dysfunction with having one patient treated with a self-catheterisation over a month. Nerve sparing surgery may overcome voiding dysfunctions, as it has been confirmed in a meta-analysis of de Resende et al, who described an odds ratio of 0.19 for the need of self-catheterisation at discharge in the nerve sparing group in relation to the conventional non-nerve sparing surgical technique (*de Resende et al., 2017*).

5. Summary

The gold standard of treatment for colorectal endometriosis is the surgical removal of the lesion with shaving, disc excision or segmental colorectal resection. Which method is the most appropriate is controversial and clear criteria for the choice of surgery are missing. We conducted a retrospective cohort study of 120 patients, who underwent colorectal endometriosis surgery at the Endometriosis Center of the University of Gießen and Marburg between 2005 and 2015 in order to define clear criteria for each surgical modality and assess clinical outcome. We analysed the clinical records of the patients and answers of a self-developed questionnaire as well as telephone interviews.

75 patients underwent segmental colorectal resection, 19 disc excision and 26 shaving. The mean age of the patients was 34 years. 78% of the patients suffered from pain symptoms and 58% had a pregnancy wish. The surgery lasted an average of 292 minutes with a mean hospital stay of 5, 6 and 7 days after shaving, disc excision and segmental resection, respectively. The bowel lesion was associated in every second patient with endometriosis of the ovaries and in every third patient with infiltration of the vagina, rectovaginal space, sacrouterine ligaments and pelvic side walls. The majority of the bowel lesions in the shaving procedures measured up to 3cm and infiltrated the serosa and subserosa. With disc excision mainly lesions between 3-6cm with muscularis layer infiltration were removed. In the segmental resection group every third patient had multifocal, long segment affection of the bowel wall and 10% multicenter lesions with 2-3 nodules. The lesions infiltrated at least the muscularis and in 25% and 7% the submucosa and mucosa, respectively. All procedures improved significantly the pain symptoms, bowel dysfunctions and libido as well as the reproductive results. The pregnancy and delivery rates revealed 57% and 39%, respectively. Two patients underwent a severe labour complication with rupture of the posterior uterine and vaginal vault. We observed a histological recurrence of endometriosis in 9% of the patients, having one patient both in the disc excision and shaving group with recurrence of bowel endometriosis. Recurrence of bowel endometriosis did not occur after segmental resection. The segmental resection was associated with the highest intra- and postoperative complication rates having an injury of the ureter and anastomotic leakage.

We can conclude that none of the procedures are superior to the other one regarding clinical outcome. Small superficial lesions should be removed with shaving. Singular nodules with muscular infiltration are appropriate for disc excision. Lesions with multifocal or multicentre character, or isolated nodules with infiltration up to the mucosa and significant bowel circumference involvement should be treated with segmental colorectal resection

6. List of abbreviations

BMI	body mass index
DE	deep endometriosis
DJ-catheter	double-J catheter
DM	dysmenorrhea
EFI	endometriosis fertility index
ICSI	Intracytoplasmic Sperm Injection
IL	interleukin
IVF	in vitro fertilization
LF	least function score
MRI	magnetic resonance imaging
NOSE	natural orifice specimen extraction
OTSC	over the scope clip
PG	prostaglandin
RANTES	normal T cell expressed and secreted
RES	rectal endosonography
rASRM	revised American Society for Reproductive Medicine
TVS	transvaginal sonography
VAS	visual analogic scale

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10. Appendix

10.1. Questionnaire

Sehr geehrte Teilnehmerin, sehr geehrte Frau,

Sie wurden an der Universitätsfrauenklinik Gießen am aufgrund ihrer Endometriose operativ behandelt.

Im ersten Teil des Fragebogens erhalten Sie Fragen bezüglich einer eventuell erneut erforderlichen Operation nach ihrer operativen Behandlung an der Universitätsfrauenklinik Gießen, nach einer medikamentösen Behandlung, aber auch nach Schwangerschaften und dem Verlauf der Schmerzsymptomatik. Im zweiten Teil des Fragebogens möchten wir Ihre Lebensqualität vor und innerhalb eines Jahres nach der operativen Behandlung an der Universitätsfrauenklinik Gießen, sowie Ihre momentane Lebenssituation erfragen.

Das Ausfüllen des Fragebogens ist freiwillig. Schicken Sie bitte den ausgefüllten Fragebogen, sowie die unterschriebene Aufklärung- und Einwilligung im beigefügten adressierten und frankierten Briefumschlag zurück.

Dr. Eniko Berkes
Oberärztin

Dr. Frank Oehmke
Leitender Oberarzt

Prof. Dr. Dr. h.c. Hans-Rudolf Tinneberg
Direktor der Frauenklinik Gießen

Gießen, den

Bitte Füllen Sie Ihre Personaldaten aus!

Name, Vorname:	Familienstatus: <input type="checkbox"/> ledig <input type="checkbox"/> verheiratet <input type="checkbox"/> geschieden	<input type="checkbox"/> mit Partner lebend <input type="checkbox"/> verwitwet
Geburtsdatum:	Kinder (Anzahl):	
Größe:	Berufstätig: <input type="checkbox"/> ja, Vollzeit <input type="checkbox"/> ja, Teilzeit	<input type="checkbox"/> nein
Gewicht:	Beruf:	

Fragebogen zur tief infiltrierenden Endometriose-Studie Teil I.

Im ersten Teil des Fragebogens erhalten Sie Fragen bezüglich erneuter Operationen, medikamentöser Behandlung und Schwangerschaften nach der operativen Behandlung an der Uniklinik Gießen, sowie über die Schmerz- und andere Symptome vor und nach Ihrer Operation bei uns.

1. Wurden Sie nach der operativen Behandlung an der Uniklinik Gießen in anderen Krankenhäusern/Unikliniken aufgrund der Endometriose oder anderer Krankheiten operiert? Bitte listen Sie diese Operationen auf!

Operation	Operation	Operation
Jahr: Zugang: <input type="checkbox"/> Bauchschnitt (Laparotomie) <input type="checkbox"/> Bauchspiegelung (Laparoskopie) <input type="checkbox"/> Vaginale Operation Grund der Operation: Art der Operation: Krankenhaus/Uniklinik:	Jahr: Zugang: <input type="checkbox"/> Bauchschnitt (Laparotomie) <input type="checkbox"/> Bauchspiegelung (Laparoskopie) <input type="checkbox"/> Vaginale Operation Grund der Operation: Art der Operation: Krankenhaus/Uniklinik:	Jahr: Zugang: <input type="checkbox"/> Bauchschnitt (Laparotomie) <input type="checkbox"/> Bauchspiegelung (Laparoskopie) <input type="checkbox"/> Vaginale Operation Grund der Operation: Art der Operation: Krankenhaus/Uniklinik:

2. Gab es während dieses Krankenhausaufenthaltes Komplikationen, die einen erneuten operativen Eingriff erforderten?

- Ja Nein
- Wenn ja, wurde dieser Eingriff durch eine erneute Bauchspiegelung (Re-Laparoskopie), Ja Nein
 durch einen erneuten Bauchschnitt (Re-Laparotomie) Ja Nein
 oder durch die Kombination einer Bauchspiegelung und Bauchschnitt, durchgeführt? Ja Nein

3. Haben Sie nach der operativen Behandlung an der Uniklinik Gießen eine medikamentöse Therapie erhalten?

- Ja **Wenn ja, welche Therapie und wie lange?** Nein
- Pille von.....bis.....Name:
- Visanne von.....bis.....
- Hormonspirale (Mirena) von.....bis.....
- Hormonspritze von.....bis.....Name:

4. Bestand bei Ihnen vor oder nach der operativen Behandlung an der Uniklinik Gießen Kinderwunsch oder Infertilität (unerfüllter Kinderwunsch)?

- Kinderwunsch: Ja Nein
 Infertilität (unerfüllter Kinderwunsch) Ja Nein

5. Wurde bei Ihnen nach der operativen Behandlung an der Uniklinik Gießen eine künstliche Befruchtung durchgeführt?

- Ja Nein
- Wenn ja, sind Sie schwanger geworden? Ja Nein

6. Wurden Sie nach der operativen Behandlung an der Uniklinik Gießen auf natürlichem Weg schwanger?

- Ja Nein

Im nächsten Abschnitt finden Sie verschiedene Fragen. Bitte beurteilen Sie, ob diese Fragen auf Ihren Zustand vor oder - innerhalb eines Jahres- nach der operativen Behandlung an der Uniklinik Gießen und momentan zutreffen!

1. Haben oder hatten Sie Schmerzen in Zusammenhang mit Ihrer Periode? Trifft dies auf Ihren Zustand vor der operativen Behandlung zu?

Ja Nein

Wenn ja, wann genau? Vor der Periode
 Während der Periode
 Nach der Periode

Wenn ja, wie stark waren die Schmerzen im Durchschnitt auf einer Skala von 1 bis 10?

kein Schmerz stärkster Schmerz
0 1 2 3 4 5 6 7 8 9 10

innerhalb eines Jahres nach der operativen Behandlung zu?

Ja Nein

Wenn ja, wann genau? Vor der Periode
 Während der Periode
 Nach der Periode

Wenn ja, wie stark waren die Schmerzen im Durchschnitt auf einer Skala von 1 bis 10?

kein Schmerz stärkster Schmerz
0 1 2 3 4 5 6 7 8 9 10

zur Zeit zu?

Ja Nein

Wenn ja, wann genau? Vor der Periode
 Während der Periode
 Nach der Periode

Wenn ja, wie stark sind die Schmerzen im Durchschnitt auf einer Skala von 1 bis 10?

kein Schmerz stärkster Schmerz
0 1 2 3 4 5 6 7 8 9 10

2. Haben oder hatten Sie chronische Schmerzen im Unterbauch? Trifft dies auf Ihren Zustand vor der operativen Behandlung zu?

Ja Nein

Wenn ja, wie stark waren die Schmerzen im Durchschnitt auf einer Skala von 1 bis 10?

kein Schmerz stärkster Schmerz
0 1 2 3 4 5 6 7 8 9 10

innerhalb eines Jahres nach der operativen Behandlung zu?

Ja Nein

Wenn ja, wie stark waren die Schmerzen im Durchschnitt auf einer Skala von 1 bis 10?

kein Schmerz stärkster Schmerz
0 1 2 3 4 5 6 7 8 9 10

zur Zeit zu?

Ja Nein

Wenn ja, wie stark sind die Schmerzen im Durchschnitt auf einer Skala von 1 bis 10?

kein Schmerz stärkster Schmerz
0 1 2 3 4 5 6 7 8 9 10

3. Haben oder hatten Sie Schmerzen beim Wasserlassen? Trifft dies auf Ihren Zustand

vor der operativen Behandlung zu?

Ja

Nein

Wenn ja, wie stark waren die Schmerzen im Durchschnitt auf einer Skala von 1 bis 10?

kein Schmerz stärkster Schmerz
0 1 2 3 4 5 6 7 8 9 10

innerhalb eines Jahres nach der operativen Behandlung zu?

Ja

Nein

Wenn ja, wie stark waren die Schmerzen im Durchschnitt auf einer Skala von 1 bis 10?

kein Schmerz stärkster Schmerz
0 1 2 3 4 5 6 7 8 9 10

zur Zeit zu?

Ja

Nein

Wenn ja, wie stark sind die Schmerzen im Durchschnitt auf einer Skala von 1 bis 10?

kein Schmerz stärkster Schmerz
0 1 2 3 4 5 6 7 8 9 10

4. Haben oder hatten Sie Beschwerden der Harnwege außer der Schmerzen beim Wasserlassen? Trifft dies auf Ihren Zustand

vor der operativen Behandlung zu?

Ja

Nein

Wenn ja, was genau?

- Blut im Urin während der Periode
- häufiges Wasserlassen
- erschwertes Wasserlassen
- Selbstkatheterisierung
- Flankenschmerzen
- andere:

innerhalb eines Jahres nach der operativen Behandlung zu?

Ja

Nein

Wenn ja, was genau?

- Blut im Urin während der Periode
- häufiges Wasserlassen
- erschwertes Wasserlassen
- Selbstkatheterisierung
- Flankenschmerzen
- andere:

zur Zeit zu?

Ja

Nein

Wenn ja, was genau?

- Blut im Urin während der Periode
- häufiges Wasserlassen
- erschwertes Wasserlassen
- Selbstkatheterisierung
- Flankenschmerzen
- andere:

5. Haben oder hatten Sie Schmerzen beim Stuhlgang? Trifft dies auf Ihren Zustand

vor der operativen Behandlung zu?

Ja

Nein

Wenn ja, wie stark waren die Schmerzen im Durchschnitt auf einer Skala von 1 bis 10?

kein Schmerz stärkster Schmerz
0 1 2 3 4 5 6 7 8 9 10

innerhalb eines Jahres nach der operativen
Behandlung zu?

Ja

Nein

Wenn ja, wie stark waren die Schmerzen im Durchschnitt
auf einer Skala von 1 bis 10?

kein Schmerz stärkster Schmerz
0 1 2 3 4 5 6 7 8 9 10

zur Zeit zu?

Ja

Nein

Wenn ja, wie stark sind die Schmerzen im Durchschnitt
auf einer Skala von 1 bis 10?

kein Schmerz stärkster Schmerz
0 1 2 3 4 5 6 7 8 9 10

**6. Haben oder hatten Sie Beschwerden des Darmsystems außer der Schmerzen beim Stuhlgang? Trifft dies auf Ihren
Zustand**

vor der operativen Behandlung zu?

Ja

Nein

Wenn ja, was genau?

- Blut auf dem Stuhl während der Periode
- Durchfall während oder um der Periode
- Verstopfung während oder um der Periode
- Durchfall und Verstopfung im Wechsel
während oder um der Periode
- Darmkrämpfe
- andere:

innerhalb eines Jahres nach der operativen
Behandlung zu?

Ja

Nein

Wenn ja, was genau?

- Blut auf dem Stuhl während der Periode
- Durchfall während oder um der Periode
- Verstopfung während oder um der Periode
- Durchfall und Verstopfung im Wechsel
während oder um der Periode
- Darmkrämpfe
- andere:

zur Zeit zu?

Ja

Nein

Wenn ja, was genau?

- Blut auf dem Stuhl während der Periode
- Durchfall während oder um der Periode
- Verstopfung während oder um der Periode
- Durchfall und Verstopfung im Wechsel
während oder um der Periode
- Darmkrämpfe
- andere:

**7. Haben oder hatten Sie Schmerzen beim Geschlechtsverkehr (unter anderem bei tiefer Penetration)? Trifft dies
auf Ihren Zustand**

vor der operativen Behandlung zu?

Ja

Nein

Wenn ja, wie stark waren die Schmerzen im Durchschnitt
auf einer Skala von 1 bis 10?

kein Schmerz stärkster Schmerz
0 1 2 3 4 5 6 7 8 9 10

innerhalb eines Jahres nach der operativen
Behandlung zu?

Ja

Nein

Wenn ja, wie stark waren die Schmerzen im Durchschnitt
auf einer Skala von 1 bis 10?

kein Schmerz stärkster Schmerz
0 1 2 3 4 5 6 7 8 9 10

zur Zeit zu?

Ja

Nein

Wenn ja, wie stark sind die Schmerzen im Durchschnitt auf einer Skala von 1 bis 10?

kein Schmerz stärkster Schmerz
0 1 2 3 4 5 6 7 8 9 10

8. Bitte Beurteilen Sie Ihre Libido auf einer Skala von 0-10

vor der operativen Behandlung.

keine Libido

normale Libido
0 1 2 3 4 5 6 7 8 9 10

innerhalb eines Jahres nach der operativen Behandlung.

keine Libido

normale Libido
0 1 2 3 4 5 6 7 8 9 10

zur Zeit.

keine Libido

normale Libido
0 1 2 3 4 5 6 7 8 9 10

Fragebogen zur tief infiltrierenden Endometriose-Studie Teil II.

In diesem Teil möchten wir Ihre Lebensqualität erfragen. Bitte geben Sie bei allen folgenden Aussagen auf einer Skala von 0-10 an, wie stark diese Aussagen für Sie vor der Operation an der Uniklinik Gießen, innerhalb eines Jahres nach der Operation an der Uniklinik Gießen und zur Zeit zutreffen.

Bitte beurteilen Sie folgende Aussagen zu Schmerzarten (Schmerzen während der Regelblutung, chronische Unterbauchschmerzen, Schmerzen beim Geschlechtsverkehr, beim Wasserlassen oder beim Stuhlgang) allgemein. Falls Sie nie unter Schmerzen gelitten haben und auch zur Zeit nicht leiden, fahren Sie bitte mit Frage 12 fort.

1. Ich kann mit den Schmerzen nicht umgehen.

vor der Operation

nicht zutreffend völlig zutreffend
0 1 2 3 4 5 6 7 8 9 10

innerhalb eines Jahres nach der Operation

nicht zutreffend völlig zutreffend
0 1 2 3 4 5 6 7 8 9 10

zur Zeit

nicht zutreffend völlig zutreffend
0 1 2 3 4 5 6 7 8 9 10

2. Ich bin nicht in der Lage wegen der Schmerzen den Haushalt zu erledigen.

vor der Operation

nicht zutreffend völlig zutreffend
0 1 2 3 4 5 6 7 8 9 10

innerhalb eines Jahres nach der Operation

nicht zutreffend völlig zutreffend
0 1 2 3 4 5 6 7 8 9 10

zur Zeit

nicht zutreffend völlig zutreffend
0 1 2 3 4 5 6 7 8 9 10

3. Ich habe beim Stehen Schwierigkeiten wegen der Schmerzen.

vor der Operation

nicht zutreffend völlig zutreffend
0 1 2 3 4 5 6 7 8 9 10

innerhalb eines Jahres nach der Operation

nicht zutreffend völlig zutreffend
0 1 2 3 4 5 6 7 8 9 10

zur Zeit

nicht zutreffend völlig zutreffend
0 1 2 3 4 5 6 7 8 9 10

4. Ich habe beim Sitzen Schwierigkeiten wegen der Schmerzen.

vor der Operation	nicht zutreffend	<input type="checkbox"/>	völlig zutreffend										
		0	1	2	3	4	5	6	7	8	9	10	
innerhalb eines Jahres nach der Operation	nicht zutreffend	<input type="checkbox"/>	völlig zutreffend										
		0	1	2	3	4	5	6	7	8	9	10	
zur Zeit	nicht zutreffend	<input type="checkbox"/>	völlig zutreffend										
		0	1	2	3	4	5	6	7	8	9	10	

5. Ich habe beim Laufen wegen der Schmerzen Schwierigkeiten.

vor der Operation	nicht zutreffend	<input type="checkbox"/>	völlig zutreffend										
		0	1	2	3	4	5	6	7	8	9	10	
innerhalb eines Jahres nach der Operation	nicht zutreffend	<input type="checkbox"/>	völlig zutreffend										
		0	1	2	3	4	5	6	7	8	9	10	
zur Zeit	nicht zutreffend	<input type="checkbox"/>	völlig zutreffend										
		0	1	2	3	4	5	6	7	8	9	10	

6. Ich habe wegen der Schmerzen Schlafprobleme.

vor der Operation	nicht zutreffend	<input type="checkbox"/>	völlig zutreffend										
		0	1	2	3	4	5	6	7	8	9	10	
innerhalb eines Jahres nach der Operation	nicht zutreffend	<input type="checkbox"/>	völlig zutreffend										
		0	1	2	3	4	5	6	7	8	9	10	
zur Zeit	nicht zutreffend	<input type="checkbox"/>	völlig zutreffend										
		0	1	2	3	4	5	6	7	8	9	10	

7. Ich habe wegen der Schmerzen Probleme beim Sport oder anderen Freizeitaktivitäten.

vor der Operation	nicht zutreffend	<input type="checkbox"/>	völlig zutreffend										
		0	1	2	3	4	5	6	7	8	9	10	
innerhalb eines Jahres nach der Operation	nicht zutreffend	<input type="checkbox"/>	völlig zutreffend										
		0	1	2	3	4	5	6	7	8	9	10	
zur Zeit	nicht zutreffend	<input type="checkbox"/>	völlig zutreffend										
		0	1	2	3	4	5	6	7	8	9	10	

8. Ich muss mich wegen der Schmerzen hinlegen oder ins Bett gehen.

vor der Operation	nicht zutreffend	<input type="checkbox"/>	völlig zutreffend										
		0	1	2	3	4	5	6	7	8	9	10	
innerhalb eines Jahres nach der Operation	nicht zutreffend	<input type="checkbox"/>	völlig zutreffend										
		0	1	2	3	4	5	6	7	8	9	10	
zur Zeit	nicht zutreffend	<input type="checkbox"/>	völlig zutreffend										
		0	1	2	3	4	5	6	7	8	9	10	

9. Ich leide unter Appetitlosigkeit oder habe wegen der Schmerzen Schwierigkeiten beim Essen.

vor der Operation	nicht zutreffend	<input type="checkbox"/>	völlig zutreffend										
		0	1	2	3	4	5	6	7	8	9	10	
innerhalb eines Jahres nach der Operation	nicht zutreffend	<input type="checkbox"/>	völlig zutreffend										
		0	1	2	3	4	5	6	7	8	9	10	
zur Zeit	nicht zutreffend	<input type="checkbox"/>	völlig zutreffend										
		0	1	2	3	4	5	6	7	8	9	10	

10. Ich bin nicht in der Lage wegen der Schmerzen an sozialen Aktivitäten teilzunehmen.

vor der Operation	nicht zutreffend	<input type="checkbox"/>	völlig zutreffend										
		0	1	2	3	4	5	6	7	8	9	10	

innerhalb eines Jahres nach der Operation	nicht zutreffend	<input type="checkbox"/>	völlig zutreffend									
		0	1	2	3	4	5	6	7	8	9	10
zur Zeit	nicht zutreffend	<input type="checkbox"/>	völlig zutreffend									
		0	1	2	3	4	5	6	7	8	9	10

11. Ich fühle mich durch die Schmerzen in meinem Alltagsleben eingeschränkt.

vor der Operation	nicht zutreffend	<input type="checkbox"/>	völlig zutreffend									
		0	1	2	3	4	5	6	7	8	9	10
innerhalb eines Jahres nach der Operation	nicht zutreffend	<input type="checkbox"/>	völlig zutreffend									
		0	1	2	3	4	5	6	7	8	9	10
zur Zeit	nicht zutreffend	<input type="checkbox"/>	völlig zutreffend									
		0	1	2	3	4	5	6	7	8	9	10

12. Ich fühle mich im Allgemeinen nicht wohl.

vor der Operation	nicht zutreffend	<input type="checkbox"/>	völlig zutreffend									
		0	1	2	3	4	5	6	7	8	9	10
innerhalb eines Jahres nach der Operation	nicht zutreffend	<input type="checkbox"/>	völlig zutreffend									
		0	1	2	3	4	5	6	7	8	9	10
zur Zeit	nicht zutreffend	<input type="checkbox"/>	völlig zutreffend									
		0	1	2	3	4	5	6	7	8	9	10

13. Ich bin frustriert, weil die Symptome nicht zurückgehen.

vor der Operation	nicht zutreffend	<input type="checkbox"/>	völlig zutreffend									
		0	1	2	3	4	5	6	7	8	9	10
innerhalb eines Jahres nach der Operation	nicht zutreffend	<input type="checkbox"/>	völlig zutreffend									
		0	1	2	3	4	5	6	7	8	9	10
zur Zeit	nicht zutreffend	<input type="checkbox"/>	völlig zutreffend									
		0	1	2	3	4	5	6	7	8	9	10

14. Ich bin frustriert, weil ich die Symptome nicht kontrollieren kann.

vor der Operation	nicht zutreffend	<input type="checkbox"/>	völlig zutreffend									
		0	1	2	3	4	5	6	7	8	9	10
innerhalb eines Jahres nach der Operation	nicht zutreffend	<input type="checkbox"/>	völlig zutreffend									
		0	1	2	3	4	5	6	7	8	9	10
zur Zeit	nicht zutreffend	<input type="checkbox"/>	völlig zutreffend									
		0	1	2	3	4	5	6	7	8	9	10

15. Ich bin nicht in der Lage, die Symptome zu ignorieren.

vor der Operation	nicht zutreffend	<input type="checkbox"/>	völlig zutreffend									
		0	1	2	3	4	5	6	7	8	9	10
innerhalb eines Jahres nach der Operation	nicht zutreffend	<input type="checkbox"/>	völlig zutreffend									
		0	1	2	3	4	5	6	7	8	9	10
zur Zeit	nicht zutreffend	<input type="checkbox"/>	völlig zutreffend									
		0	1	2	3	4	5	6	7	8	9	10

16. Ich habe den Eindruck, dass mein Leben durch die Symptome bestimmt wird.

vor der Operation	nicht zutreffend	<input type="checkbox"/>	völlig zutreffend									
		0	1	2	3	4	5	6	7	8	9	10
innerhalb eines Jahres nach der Operation	nicht zutreffend	<input type="checkbox"/>	völlig zutreffend									
		0	1	2	3	4	5	6	7	8	9	10

23. Ich bin gewalttätig oder aggressiv.

vor der Operation	nicht zutreffend	<input type="checkbox"/>	völlig zutreffend										
		0	1	2	3	4	5	6	7	8	9	10	
innerhalb eines Jahres nach der Operation	nicht zutreffend	<input type="checkbox"/>	völlig zutreffend										
		0	1	2	3	4	5	6	7	8	9	10	
zur Zeit	nicht zutreffend	<input type="checkbox"/>	völlig zutreffend										
		0	1	2	3	4	5	6	7	8	9	10	

24. Ich fühle mich nicht in der Lage, mit anderen über mein Befinden zu sprechen.

vor der Operation	nicht zutreffend	<input type="checkbox"/>	völlig zutreffend										
		0	1	2	3	4	5	6	7	8	9	10	
innerhalb eines Jahres nach der Operation	nicht zutreffend	<input type="checkbox"/>	völlig zutreffend										
		0	1	2	3	4	5	6	7	8	9	10	
zur Zeit	nicht zutreffend	<input type="checkbox"/>	völlig zutreffend										
		0	1	2	3	4	5	6	7	8	9	10	

25. Ich fühle mich einsam.

vor der Operation	nicht zutreffend	<input type="checkbox"/>	völlig zutreffend										
		0	1	2	3	4	5	6	7	8	9	10	
innerhalb eines Jahres nach der Operation	nicht zutreffend	<input type="checkbox"/>	völlig zutreffend										
		0	1	2	3	4	5	6	7	8	9	10	
zur Zeit	nicht zutreffend	<input type="checkbox"/>	völlig zutreffend										
		0	1	2	3	4	5	6	7	8	9	10	

26. Ich fühle mich unverstanden.

vor der Operation	nicht zutreffend	<input type="checkbox"/>	völlig zutreffend										
		0	1	2	3	4	5	6	7	8	9	10	
innerhalb eines Jahres nach der Operation	nicht zutreffend	<input type="checkbox"/>	völlig zutreffend										
		0	1	2	3	4	5	6	7	8	9	10	
zur Zeit	nicht zutreffend	<input type="checkbox"/>	völlig zutreffend										
		0	1	2	3	4	5	6	7	8	9	10	

27. Ich habe den Eindruck, von meiner Umwelt nicht verstanden zu werden.

vor der Operation	nicht zutreffend	<input type="checkbox"/>	völlig zutreffend										
		0	1	2	3	4	5	6	7	8	9	10	
innerhalb eines Jahres nach der Operation	nicht zutreffend	<input type="checkbox"/>	völlig zutreffend										
		0	1	2	3	4	5	6	7	8	9	10	
zur Zeit	nicht zutreffend	<input type="checkbox"/>	völlig zutreffend										
		0	1	2	3	4	5	6	7	8	9	10	

28. Ich bin frustriert, weil ich nicht die Kleider tragen kann, die ich möchte.

vor der Operation	nicht zutreffend	<input type="checkbox"/>	völlig zutreffend										
		0	1	2	3	4	5	6	7	8	9	10	
innerhalb eines Jahres nach der Operation	nicht zutreffend	<input type="checkbox"/>	völlig zutreffend										
		0	1	2	3	4	5	6	7	8	9	10	
zur Zeit	nicht zutreffend	<input type="checkbox"/>	völlig zutreffend										
		0	1	2	3	4	5	6	7	8	9	10	

29. Ich habe den Eindruck, dass die Endometriose Auswirkungen auf mein Aussehen hat.

vor der Operation	nicht zutreffend	<input type="checkbox"/>	völlig zutreffend										
		0	1	2	3	4	5	6	7	8	9	10	
innerhalb eines Jahres nach der Operation	nicht zutreffend	<input type="checkbox"/>	völlig zutreffend										
		0	1	2	3	4	5	6	7	8	9	10	
zur Zeit	nicht zutreffend	<input type="checkbox"/>	völlig zutreffend										
		0	1	2	3	4	5	6	7	8	9	10	

30. Ich leide unter mangelndem Selbstvertrauen.

vor der Operation nicht zutreffend völlig zutreffend
0 1 2 3 4 5 6 7 8 9 10

innerhalb eines Jahres nach der Operation nicht zutreffend völlig zutreffend
0 1 2 3 4 5 6 7 8 9 10

zur Zeit nicht zutreffend völlig zutreffend
0 1 2 3 4 5 6 7 8 9 10

31. Ich spüre Schmerzen während oder nach dem Geschlechtsverkehr.

vor der Operation nicht zutreffend völlig zutreffend
0 1 2 3 4 5 6 7 8 9 10

innerhalb eines Jahres nach der Operation nicht zutreffend völlig zutreffend
0 1 2 3 4 5 6 7 8 9 10

zur Zeit nicht zutreffend völlig zutreffend
0 1 2 3 4 5 6 7 8 9 10

32. Ich habe wegen der Schmerzen Angst, Geschlechtsverkehr zu haben.

vor der Operation nicht zutreffend völlig zutreffend
0 1 2 3 4 5 6 7 8 9 10

innerhalb eines Jahres nach der Operation nicht zutreffend völlig zutreffend
0 1 2 3 4 5 6 7 8 9 10

zur Zeit nicht zutreffend völlig zutreffend
0 1 2 3 4 5 6 7 8 9 10

33. Ich möchte wegen der Schmerzen auf Geschlechtsverkehr verzichten.

vor der Operation nicht zutreffend völlig zutreffend
0 1 2 3 4 5 6 7 8 9 10

innerhalb eines Jahres nach der Operation nicht zutreffend völlig zutreffend
0 1 2 3 4 5 6 7 8 9 10

zur Zeit nicht zutreffend völlig zutreffend
0 1 2 3 4 5 6 7 8 9 10

34. Ich habe Schuldgefühle, weil ich keinen Geschlechtsverkehr haben möchte.

vor der Operation nicht zutreffend völlig zutreffend
0 1 2 3 4 5 6 7 8 9 10

innerhalb eines Jahres nach der Operation nicht zutreffend völlig zutreffend
0 1 2 3 4 5 6 7 8 9 10

zur Zeit nicht zutreffend völlig zutreffend
0 1 2 3 4 5 6 7 8 9 10

35. Ich bin frustriert, weil ich den Geschlechtsverkehr nicht genießen kann.

vor der Operation nicht zutreffend völlig zutreffend
0 1 2 3 4 5 6 7 8 9 10

innerhalb eines Jahres nach der Operation nicht zutreffend völlig zutreffend
0 1 2 3 4 5 6 7 8 9 10

zur Zeit nicht zutreffend völlig zutreffend
0 1 2 3 4 5 6 7 8 9 10

36. Ich muss mich wegen der Schmerzen krank melden.

vor der Operation nicht zutreffend völlig zutreffend
0 1 2 3 4 5 6 7 8 9 10

43. Ich denke, dass Ärzte im Allgemeinen nicht genügend über Endometriose informiert sind.

vor der Operation	nicht zutreffend	<input type="checkbox"/>	völlig zutreffend									
		0	1	2	3	4	5	6	7	8	9	10
innerhalb eines Jahres nach der Operation	nicht zutreffend	<input type="checkbox"/>	völlig zutreffend									
		0	1	2	3	4	5	6	7	8	9	10
zur Zeit	nicht zutreffend	<input type="checkbox"/>	völlig zutreffend									
		0	1	2	3	4	5	6	7	8	9	10

44. Ich habe das Gefühl, dass ich die Zeit der Ärzte unnötig in Anspruch nehme.

vor der Operation	nicht zutreffend	<input type="checkbox"/>	völlig zutreffend									
		0	1	2	3	4	5	6	7	8	9	10
innerhalb eines Jahres nach der Operation	nicht zutreffend	<input type="checkbox"/>	völlig zutreffend									
		0	1	2	3	4	5	6	7	8	9	10
zur Zeit	nicht zutreffend	<input type="checkbox"/>	völlig zutreffend									
		0	1	2	3	4	5	6	7	8	9	10

45. Ich mache mir darüber Sorgen, keine Kinder (mehr) bekommen zu können

vor der Operation	nicht zutreffend	<input type="checkbox"/>	völlig zutreffend									
		0	1	2	3	4	5	6	7	8	9	10
innerhalb eines Jahres nach der Operation	nicht zutreffend	<input type="checkbox"/>	völlig zutreffend									
		0	1	2	3	4	5	6	7	8	9	10
zur Zeit	nicht zutreffend	<input type="checkbox"/>	völlig zutreffend									
		0	1	2	3	4	5	6	7	8	9	10

46. Ich fühle mich minderwertig, wegen der Möglichkeit keine Kinder (mehr) bekommen zu können.

vor der Operation	nicht zutreffend	<input type="checkbox"/>	völlig zutreffend									
		0	1	2	3	4	5	6	7	8	9	10
innerhalb eines Jahres nach der Operation	nicht zutreffend	<input type="checkbox"/>	völlig zutreffend									
		0	1	2	3	4	5	6	7	8	9	10
zur Zeit	nicht zutreffend	<input type="checkbox"/>	völlig zutreffend									
		0	1	2	3	4	5	6	7	8	9	10

47. Ich bin wegen der Möglichkeit, dass ich keine Kinder (mehr) bekommen könnte, depressiv.

vor der Operation	nicht zutreffend	<input type="checkbox"/>	völlig zutreffend									
		0	1	2	3	4	5	6	7	8	9	10
innerhalb eines Jahres nach der Operation	nicht zutreffend	<input type="checkbox"/>	völlig zutreffend									
		0	1	2	3	4	5	6	7	8	9	10
zur Zeit	nicht zutreffend	<input type="checkbox"/>	völlig zutreffend									
		0	1	2	3	4	5	6	7	8	9	10

48. Ich fühle mich durch die Möglichkeit, nicht schwanger zu werden, in meiner Partnerschaft beeinträchtigt.

vor der Operation	nicht zutreffend	<input type="checkbox"/>	völlig zutreffend									
		0	1	2	3	4	5	6	7	8	9	10
innerhalb eines Jahres nach der Operation	nicht zutreffend	<input type="checkbox"/>	völlig zutreffend									
		0	1	2	3	4	5	6	7	8	9	10
zur Zeit	nicht zutreffend	<input type="checkbox"/>	völlig zutreffend									
		0	1	2	3	4	5	6	7	8	9	10

49. Ich habe Schwierigkeiten, mich um meine Kinder zu kümmern.

vor der Operation	nicht zutreffend	<input type="checkbox"/>	völlig zutreffend									
		0	1	2	3	4	5	6	7	8	9	10
innerhalb eines Jahres nach der Operation	nicht zutreffend	<input type="checkbox"/>	völlig zutreffend									
		0	1	2	3	4	5	6	7	8	9	10

zur Zeit nicht zutreffend völlig zutreffend
entfällt, habe noch keine 0 1 2 3 4 5 6 7 8 9 10

50. Ich kann wegen der Endometriose nicht mit meinen Kindern spielen.

vor der Operation nicht zutreffend völlig zutreffend
0 1 2 3 4 5 6 7 8 9 10

innerhalb eines Jahres nach der Operation nicht zutreffend völlig zutreffend
0 1 2 3 4 5 6 7 8 9 10

zur Zeit nicht zutreffend völlig zutreffend
entfällt, habe noch keine 0 1 2 3 4 5 6 7 8 9 10

51. Ich bin wegen fehlender Therapiewirksamkeit frustriert.

vor der Operation nicht zutreffend völlig zutreffend
0 1 2 3 4 5 6 7 8 9 10

innerhalb eines Jahres nach der Operation nicht zutreffend völlig zutreffend
0 1 2 3 4 5 6 7 8 9 10

zur Zeit nicht zutreffend völlig zutreffend
0 1 2 3 4 5 6 7 8 9 10

52. Ich habe Probleme mit den Nebenwirkungen der Therapie umzugehen.

vor der Operation nicht zutreffend völlig zutreffend
0 1 2 3 4 5 6 7 8 9 10

innerhalb eines Jahres nach der Operation nicht zutreffend völlig zutreffend
0 1 2 3 4 5 6 7 8 9 10

zur Zeit nicht zutreffend völlig zutreffend
0 1 2 3 4 5 6 7 8 9 10

53. Ich bin über das Ausmaß der Therapie verärgert.

vor der Operation nicht zutreffend völlig zutreffend
0 1 2 3 4 5 6 7 8 9 10

innerhalb eines Jahres nach der Operation nicht zutreffend völlig zutreffend
0 1 2 3 4 5 6 7 8 9 10

zur Zeit nicht zutreffend völlig zutreffend
0 1 2 3 4 5 6 7 8 9 10

11. Erklärung zur Dissertation

„Hiermit erkläre ich, dass ich die vorliegende Arbeit selbständig und ohne unzulässige Hilfe oder Benutzung anderer als der angegebenen Hilfsmittel angefertigt habe. Alle Textstellen, die wörtlich oder sinngemäß aus veröffentlichten oder nichtveröffentlichten Schriften entnommen sind, und alle Angaben, die auf mündlichen Auskünften beruhen, sind als solche kenntlich gemacht. Bei den von mir durchgeführten und in der Dissertation erwähnten Untersuchungen habe ich die Grundsätze guter wissenschaftlicher Praxis, wie sie in der „Satzung der Justus-Liebig-Universität Gießen zur Sicherung guter wissenschaftlicher Praxis“ niedergelegt sind, eingehalten sowie ethische, datenschutzrechtliche und tierschutzrechtliche Grundsätze befolgt. Ich versichere, dass Dritte von mir weder unmittelbar noch mittelbar geldwerte Leistungen für Arbeiten erhalten haben, die im Zusammenhang mit dem Inhalt der vorgelegten Dissertation stehen, und dass die vorgelegte Arbeit weder im Inland noch im Ausland in gleicher oder ähnlicher Form einer anderen Prüfungsbehörde zum Zweck einer Promotion oder eines anderen Prüfungsverfahrens vorgelegt wurde. Alles aus anderen Quellen und von anderen Personen übernommene Material, das in der Arbeit verwendet wurde oder auf das direkt Bezug genommen wird, wurde als solches kenntlich gemacht. Insbesondere wurden alle Personen genannt, die direkt und indirekt an der Entstehung der vorliegenden Arbeit beteiligt waren. Mit der Überprüfung meiner Arbeit durch eine Plagiatserkennungssoftware bzw. ein internetbasiertes Softwareprogramm erkläre ich mich einverstanden.“

Ort, Datum

Unterschrift

12. Acknowledgement

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