SEMMELWEIS EGYETEM

DOKTORI ISKOLA

Ph.D. értekezések

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DOBÓ NOÉMI

Reproduktív medicina

című program

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QUALITY OF LIFE ASSESSMENT AFTER BOWEL RESECTION PERFORMED FOR DEEP INFILTRATING COLORECTAL ENDOMETRIOSIS

PhD thesis

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Budapest

2026

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List of Abbreviations:

ASRM: American Society for Reproductive Medicine
ASA: American Society of Anaesthesiologists
ART: Assisted Reproduction Techniques
BENS: Bowel Endometriosis Symptoms
BMI: Body Mass Index
CLR: Conventional laparoscopic bowel resection
CT: Computer Tomography
DE: Deep endometriosis
DIE: Deep infiltrating endometriosis
DR: Disc resection
EFI: Endometriosis Fertility Index
EHP30: Endometriosis Health Profile 30
ESHRE: European Society of Human Reproduction and Embryology
EQ-5D: European Quality of Life (EuroQOL)
FTDR: Full-thickness disc resection
GI: Gastrointestinal
GIQLI: Gastrointestinal Quality of Life Index
GNRH: Gonadotropin-releasing hormone
HRQoL: Health-related Quality of Life
HJGWH: Center for Endometriosis, Department of Gynecology, Hospital St. John of God and Wilhelminen Hospital
IDEA: International Deep Endometriosis Analysis
KESS: Knowles–Eccersley–Scott-Symptom Questionnaire
LARS: Low Anterior Resection Syndrome
LTADE: Laparoscopic-transanal disk excision
MCS: Mental Component Summary
MRI: Magnetic resonance imaging
NC: Natural orifice specimen extraction colectomy
NOSE: Natural orifice specimen extraction
NSAID: Non-steroidal anti-inflammatory drugs
NVSSR: Nerve and vessel-sparing segmental resection
PCS: Physical Component Summary
QALY: Quality-Adjusted Life Years
QoL: Quality of Life
RCT: Randomized Controlled Trial
RUH: Department of Obstetrics and Gynecology, Rouen University Hospital
RVS: Rectovaginal septum
SF-36: 36-Item Short Form Health Survey
SF-12: 12-Item Short Form Health Survey
SNP: Single Nucleotide Polymorphism
SR: Segmental resection
SU: Department of Obstetrics and Gynecology, Semmelweis University
TVS: Transvaginal sonography

USL: Uterosacral ligament

USP: Urinary Symptom Profile

VAS: Visual analog scale

1. Introduction

1.1 Endometriosis

1.1.1 The definition, prevalence, and epidemiology of endometriosis

Endometriosis is a chronic estrogen-dependent inflammatory disease that impacts 6-10% of women of reproductive age, translating to approximately 190 million women globally (1). It is characterized by the presence of endometrial-like tissue outside the uterus (1, 2). The diagnosed cases of pelvic endometriosis can be classified phenotypically into three subtypes: peritoneal or superficial, which accounts for approximately 80% of cases; ovarian endometriotic cysts (endometriomas); and deep endometriosis (3-5).

Additionally, endometriosis lesions have been identified in extra-pelvic locations, including the abdominal wall, diaphragm, and pleura (known as "thoracic endometriosis"), as well as in the central and peripheral nervous systems (4).

However, the prevalence of endometriosis remains relatively unknown. This condition typically develops during the active reproductive years, as ovarian steroid hormones influence the growth and maintenance of endometriotic implants. As a result, endometriosis is uncommon in pre- or post-menarchal girls and rare in postmenopausal women who are not receiving hormonal replacement therapy(6).

The prevalence of endometriosis shows considerable variability, affecting between 5% and 50% of infertile women, 2% to 11% of asymptomatic women, and 5% to 21% of women hospitalized for pelvic pain (5). Among symptomatic adolescents, it is found in 49% of those experiencing chronic pelvic pain and up to 75% of those whose pain does not respond to medical treatment (5).

Key risk factors for endometriosis include increased menstrual flow, nulliparity, polymenorrhea, hypermenorrhea, and early menarche(6, 7).

1.1.2. Etiology of endometriosis

The causes of this complex and enigmatic disease remain largely unknown, involving a combination of environmental, epidemiological, and genetic factors. Endometriosis has a notable familial component; having a first-degree relative with the condition increases the risk by 7- to 10 times (8). A study of 3096 twins has estimated the heritability of endometriosis, referring to the proportion of disease variance attributable to genetic factors, at approximately 52% (9).

Research focused on the genetic background associated with endometriosis has identified over 40 loci and SNPs that may predispose individuals to developing the disease (10).

These identified genes are involved in various biological processes, including cell proliferation, adhesion, and apoptosis, as well as tumor suppression, detoxification, inflammation, oxidative stress, and autoimmunity. Furthermore, they are crucial in regulating angiogenesis, extracellular matrix remodeling, and hormonal regulation (11, 12). The presence of known mutations and SNPs does not guarantee the development of the disease. Some carriers may never become affected, while individuals diagnosed with the condition may not carry the currently recognized predisposing genetic variations (12). Consequently, the diagnostic value of specific mutations and polymorphisms is limited, and their presence should be interpreted with caution (12).

1.1.3. Pathomechanism of endometriosis

The exact cause of endometriosis remains unclear, and various theories have been suggested. The most widely accepted pathophysiological hypothesis centers on retrograde menstruation, a phenomenon observed in the majority of patients with this condition (13). This process occurs when menstrual tissue containing viable endometrial cells flows backward through the fallopian tubes into the pelvic cavity, where it can implant, grow, and occasionally invade surrounding pelvic tissues (13). Retrograde menstruation is a physiological process that occurs in up to 90% of menstruating women with patent fallopian tubes (14). Normally, the immune system effectively removes the refluxed endometrial tissue from the peritoneal cavity. However, in women with endometriosis, it is hypothesized that these endometrial cells adhere, proliferate, develop a blood supply, and form endometriosis lesions. It is important to note that retrograde menstruation does not fully explain how endometrial tissue grafts onto the peritoneum, suggesting that additional mechanisms play a role in the development of endometriosis (13). Additional factors may include immune system dysfunction, hormones, genetic and epigenetic factors, and environmental elements that facilitate the implantation and growth of endometrial cells (8, 13).

Alternative theories, such as Müllerian metaplasia, have been proposed to provide a better understanding of how endometriosis infiltrates the uterosacral ligaments and the cul-de-sac. The Müllerianosis hypothesis suggests that misplaced endometrial tissue, akin to that found in the cul-de-sac, could develop into endometriosis during fetal organogenesis. Furthermore, the rare presence of endometriosis in atypical locations, such as the brain, liver, or lungs, may be attributed to distant metastasis and the implantation of cells via hematogenous or lymphatic embolization (8).

Furthermore, pre-existing endometrial abnormalities may facilitate the implantation and proliferation of pathological endometrial tissue outside the uterine cavity (15). This process may be driven by factors such as impaired steroid hormone production, including hyperestrogenism, progesterone resistance, or overexpression of aromatase, as well as an enhanced invasive potential of the endometrium associated with neoangiogenesis, endometrial neurogenesis, and an inflammatory profile distinct from that of a disease-free endometrium. However, the precise role of these mechanisms in the development of various endometriosis phenotypes remains incompletely understood(13).

A more recent theory suggests that endometriosis may arise from stem or progenitor cells potentially present during retrograde neonatal uterine bleeding. This hypothesis is supported by the observation that neonatal uterine bleeding occurs in approximately 5% of newborns, the rarity of endometriosis in pre-menarche girls, and the incidence of severe endometriosis in adolescents (16).

The pathogenesis of endometrioma(s) remains a topic of debate. Endometriosis cysts are believed to develop from the surface, originating from superficial ovarian implants of refluxed endometrial tissue located between the pelvic sidewall and the ovary, which is commonly observed during laparoscopy (17). These cysts may be exacerbated by adhesions that connect the ovary to the sidewall, causing active implants of endometrial glands and stroma to invaginate. Over time, menstrual fluid accumulates due to bleeding, leading to the characteristic content found within endometriomas, or the tissue may become trapped within the ovarian cortex, resulting in the progressive formation of cystic lesions. Another hypothesis regarding the formation of endometriomas posits that the peritoneal mesothelium covering the ovary can differentiate into endometrioid epithelium, eventually leading to the development of an invaginating cyst through a process known as metaplasia theory (8, 17). The second theory, proposed by Vercellini, is a variation of the first, as it begins with similar mechanisms- in this case, the implantation of endometrial tissue between the pelvic sidewall and the ovary, resulting in adhesions (18). However, this theory suggests that ovulation is the source of the trapped blood and that, in conjunction with the active implants, a non-resorbed cystic corpus luteum is created, allowing endometriotic cells to invade the newly formed corpus luteum (18). The formation of endometriomas is closely associated with ovulation, as the use of cyclic oral contraceptives has been shown to decrease the risk of endometrioma recurrence by preventing ovulation. It is possible that endometriosis tissue can be seeded

into a hemorrhagic corpus luteum, leading to the progression from a hemorrhagic corpus luteum to an endometrioma (8).

None of these theories is mutually exclusive. Furthermore, all phenotypes of the disease can manifest within the same patient (8).

1.1.4. The symptomatology of endometriosis, its impact on quality of life, and its economic significance

Endometriosis commonly occurs in the pelvis, with the most frequent clinical symptoms including menstrual irregularities, pelvic pain, such as dysmenorrhea and dyspareunia, as well as chronic non-cyclic pelvic pain and infertility (6). It is important to note that there are instances where individuals may remain asymptomatic (13).

These symptoms can be nonspecific and frequently overlap with other clinical conditions, potentially leading to delays in diagnosis and treatment. The symptoms often intensify around the time of menstruation and can vary depending on the affected area. For example, involvement of the urinary tract may cause dysuria and hematuria, while rectosigmoid infiltration can lead to changes in bowel habits, including constipation, diarrhea, dyschezia, tenesmus, and, in rare cases, rectal bleeding (6).

However, these symptoms may also overlap with those of other conditions. An increase in the number of symptoms generally raises the likelihood of a diagnosis of endometriosis. Furthermore, although endometriosis has been diagnosed, the connection between specific pain patterns, such as the frequency and severity of pelvic symptoms, and the phenotype (i.e., the type and location of lesions) remains controversial, as most studies have not established consistent findings (19).

As a result, the condition can significantly affect patients' quality of life, leading to negative effects on their mental health, daily activities, sexual function, and personal relationships. Many patients experience sexual dysfunction due to their symptoms, which imposes a significant psychological burden. Feelings of guilt associated with avoiding sexual activity are common, and many struggle with their sense of femininity(20). Moreover, these factors, coupled with the infertility often linked to the disease, can negatively impact relationships.

The symptoms associated with endometriosis can significantly impact the daily lives of those affected. Many individuals struggle to manage routine activities such as completing work tasks or handling household chores. Additionally, some may experience changes in their appetite and endurance, resulting in decreased participation in social events (21).

Endometriosis is associated with depression, fatigue, decreased stress tolerance, and a decline in sleep quality (22), all of which can diminish work productivity and impose a significant economic burden. Research indicates that these symptoms tend to correlate positively with the patient's age, but there is no evident connection to the stage of endometriosis (23). Considering these effects, endometriosis should be viewed as a public health concern, rather than merely an individual health issue (13).

The Quality-Adjusted Life Years (QALY) method serves as a valuable tool for quantifying changes in quality of life, as it summarizes variations in both lifespan and life quality into a single numerical value (24). A study conducted by ESHRE in 2012 among individuals affected by the condition determined this value to be 0.81 (2), indicating a 19% reduction compared to the best possible health state. A similar result was observed in a study involving Hungarian patients a year later (25).

In addition to the significant physical and emotional challenges posed by the disease, it also imposes a substantial financial burden on those affected.

The economic burden of endometriosis is significant and comparable to other chronic conditions, including diabetes, Crohn's disease, and rheumatoid arthritis. A survey conducted across ten countries revealed that the average annual cost of endometriosis per woman was €9579, encompassing €3113 in healthcare expenses and €6298 in productivity losses (2). Many patients report a reduced quality of life due to pain, the emotional impact of subfertility, frustration over disease recurrence, and uncertainty about the future, particularly about repeated surgeries or long-term medical treatments (2, 26). Moreover, the indirect costs associated with productivity loss are twice as high as the direct healthcare costs related to endometriosis symptoms. This pattern is consistent with other chronic diseases, such as ankylosing spondylitis, where productivity loss accounts for 66% of total expenses, and rheumatoid arthritis, where productivity loss accounts for 57% of total costs (2).

Diagnosing endometriosis remains a significant challenge, often resulting in delays of up to 11 years, which dramatically affects the lives of those impacted by the condition (27). A study conducted by Bokor et al. found that the average time from the onset of the symptoms to the definitive diagnosis was 3.9 years in Hungary (25). Prior to treatment, 89% of patients reported experiencing pain related to endometriosis, while only 28% continued to report pain in the months following treatment ($p = 0.025$). Notably, there was no significant difference in outcomes between patients receiving only surgical

treatment and those undergoing combined surgical and medical therapy ($p = 0.85$). Furthermore, 47% of patients reported a decrease in work productivity, and 40% indicated that their personal relationships were adversely impacted (25).

Research indicates that the cumulative probability of ongoing endometriosis-related pain after surgical treatment can reach as high as 40% to 50% within five years (28). Additionally, surgery for certain subtypes of endometriosis may exacerbate painful symptoms, particularly if repeated following a relapse (4).

1.2 The diagnosis of endometriosis

Endometriosis poses significant diagnostic challenges, as no biomarkers (1) exist to confirm or exclude the condition definitively. Due to its primarily intraabdominal location, and often small size, laparoscopic visualization – preferably accompanied by histologic confirmation - remains the gold standard for diagnosis. Imaging techniques have limited effectiveness in detecting the most common form of the disease, which involves superficial peritoneal lesions. However, endometriomas can be reliably identified using transvaginal ultrasound or magnetic resonance imaging (MRI), boasting over 90% sensitivity and specificity (5). A trained specialist can also detect deep endometriosis and pelvic organ adhesions through transvaginal ultrasound. While MRI demonstrates a sensitivity of 94% for identifying deep endometriosis, its specificity is somewhat lower at 79% (5).

A comprehensive clinical history and gynecological examination may indicate suspicion of endometriosis. Although various symptoms are associated with endometriosis and can aid in the diagnosis of the lesions, it is important to note that endometriosis can coexist with or be misdiagnosed for other conditions, including irritable bowel disease, inflammatory bowel disease, or pelvic inflammatory disease (19).

Clinicians are encouraged to incorporate imaging techniques, such as ultrasound or MRI, into the diagnostic process for endometriosis. However, it is important to recognize that a negative result does not necessarily exclude the presence of endometriosis, especially in cases involving superficial peritoneal disease (1).

A clinical examination, including vaginal examination when appropriate, should be considered to evaluate uterine mobility (1). Neverthless, the sensitivity of physical examination in detecting deep endometriosis of the vaginal wall, uterosacral ligaments, rectovaginal septum, intestine, and endometriomas in patients with suspicion of endometriosis is limited, and its diagnostic accuracy may not be high (1). Furthermore, a

speculum examination can be useful in identifying deep endometriotic lesions affecting the vaginal wall.

Based on these findings, the European Society of Human Reproduction and Embryology (ESHRE) guidelines recommend performing a clinical examination where appropriate. However, it is advisable to consider additional diagnostic steps for patients suspected of having endometriosis, even if the clinical examination yields normal results (1). Furthermore, with advancements in medical technology, there has been a paradigm shift from invasive diagnostic methods to non-invasive imaging techniques.

Recent guidelines advocate using imaging tools such as ultrasound or MRI in the diagnostic process. Among these, transvaginal ultrasound is the preferred first-line technique for identifying deep lesions and endometriomas, notably having a lower environmental impact than MRI or CT scans (1). Furthermore, gynecological ultrasound is widely accessible in daily clinical practice. In 2016, the International Deep Endometriosis Analysis (IDEA) group introduced a consensus opinion on terms, definitions, and measurements necessary for accurately describing the sonographic features of the pelvis in women with suspected endometriosis (29). Accurate mapping of endometriosis is essential for effective diagnosis, surgical planning, and patient counseling. It is crucial to understand that a negative imaging result does not rule out the presence of endometriosis, particularly in cases of superficial peritoneal disease or in extra-pelvic locations. Currently, biological markers obtained from blood, menstrual or uterine fluid, endometrial tissue, urine, or saliva are not recommended for routine clinical practice, as they do not reliably confirm or exclude endometriosis (1). These markers remain the subject of extensive research, and large multicenter studies are required to assess their potential clinical benefit (30). Although some blood biomarkers show promising results during the experimental phase, more external validation and verification are essential.

1.3. The classification of endometriosis: rASRM, ENZIAN, #ENZIAN, EFI

Classifying endometriosis can be challenging due to its various manifestations and symptoms. Numerous efforts have been made to describe and categorize the disease into different stages using various classification systems (31).

Endometriosis is a heterogeneous disease, and most diagnosed cases can be broadly classified into three subtypes within the pelvic cavity: the mildest form, superficial peritoneal endometriosis, which accounts for approximately 80% of cases; ovarian

endometriosis (also referred to as "endometrioma"); and deep endometriosis (3, 5). Additionally, endometriosis lesions have been identified in extra-pelvic regions, including the upper abdominal visceral organs, abdominal wall, diaphragm, pleura (known as "thoracic endometriosis"), as well as in both the central and peripheral nervous systems (4, 32).

The most severe form of endometriosis is deep-infiltrating endometriosis (DIE). This condition is characterized by the invasion of anatomical structures and organs extending more than 5 mm beyond the peritoneum or by lesions that infiltrate the muscularis propria of nearby organs such as the bladder, intestine (with or without obstruction), and ureter. DIE affects an estimated 20-35% of all women with endometriosis (6).

It is essential to recognize that DIE nodules are rarely isolated and generally present in a multifocal distribution. Consequently, DIE is considered an "abdominal-pelvic multifocal disease" rather than being limited to a single organ (13). Moreover, the presence of ovarian endometriomas serves as an indicator of more severe DIE (33, 34). Additionally, adenomyosis—a condition characterized by the infiltration of endometrial-like tissue into the myometrium—is also relevant in this context (13).

The most widely utilized classification system for endometriosis is the revised scoring system of the American Society for Reproductive Medicine (ASRM). This system stages the condition from I to IV, indicating a spectrum from "minimal" to "severe" endometriosis. It assesses the type, location, appearance, and depth of lesion invasion, along with the extent of disease and adhesions (35).

Endometriosis staging is based on a cumulative scoring system, where values are assigned according to the size of endometriotic lesions located in the ovaries, peritoneum, and fallopian tubes and the severity of adhesions at these sites (36).

The rASRM score is primarily utilized in the context of diagnostic laparoscopy. Although this classification system is mainly designed for patients with endometriosis who are pursuing infertility treatment, it falls short in adequately addressing cases of deep endometriosis (DE). Endometriosis can extend beyond the genital tract to involve extragenital structures such as the bowel, bladder, rectovaginal septum (RVS), or ureters (31). It can also result in adenomyosis—features not sufficiently described by the rASRM system (31).

The Enzian classification offers a morphologically descriptive approach to deep endometriosis (DE), focusing on its involvement with the vagina, uterosacral ligaments

(USL), bladder, ureter, bowel, uterus (adenomyosis), and other extragenital locations. This classification assesses the extent of the disease based on size (greater than 5 mm DE), site, and organ involvement. The classification divides the small pelvis into three compartments (axes), each with corresponding anatomical correlates, and grades the disease severity for each compartment (31). Minor peritoneal lesions with an invasion depth of less than 5 mm are excluded. The severity is categorized as follows: grade 1 for invasion less than 1 cm, grade 2 for invasion between 1 and 3 cm, and grade 3 for invasion greater than 3 cm.

In compartment A, DE is evaluated in the rectovaginal septum (RVS), vagina, and the torus of the cervix. The examination of compartment B involves assessing the uterosacral ligaments and parametrial structures in the lateral and dorsolateral directions, with separate categorization for the left and right sides (B left/right). Compartment C concentrates on the bowel segment between the anus and rectosigmoid, using a sagittal section to determine the extent of the disease (31). Particular attention is given to the infiltration of the rectum, specifically the anterior wall, as well as the length of the lesions. Adenomyosis and other extragenital locations (F) are also classified (37).

The EFI system was designed to predict pregnancy rates in patients with surgically confirmed endometriosis who have not attempted conception via in vitro fertilization (IVF) (38). In 2010, Adamson and Pasta introduced the EFI system based on data from 579 infertile patients diagnosed with endometriosis through surgery. Following the development of the scoring system, additional data from 222 patients were collected to correlate actual outcomes (38). The EFI system takes into account historical factors such as age, duration of infertility, and previous pregnancies. For a successful pregnancy, the proper functioning of the fallopian tubes, fimbriae, and ovaries is mandatory.

The least functional score is determined by assessing the function of the ovaries, fallopian tubes, and fimbriae on each side, with the lowest score from both sides combined. Functional scores are assigned by the surgeon and range from 0 to 4 points: 0 indicates absent or nonfunctional, 1 represents severe dysfunction, 2 corresponds to moderate dysfunction, 3 signifies mild dysfunction, and 4 denotes normal function (36). In addition to the least functional score, other surgical factors such as the total rASRM score and the endometriosis lesion score are included. The final EFI score is calculated by summing the historical and surgical scores, ranging from 0 to 10 points, where 10 reflects the best prognosis and 0 indicates the worst prognosis (36).

The use of different classification systems, such as r-ASRM, EFI score, and Enzian, can create overlaps, which can be time-consuming and challenging in routine clinical practice, consequently impacting clinician acceptance (31). Establishing a comprehensive classification system that incorporates ovarian, peritoneal, deep endometriosis, and adhesions is essential. Recently, in 2019 and 2020, the Enzian classification was updated by a panel of experts (#Enzian). This classification system is valuable for both surgical staging and diagnostic evaluation, as deep endometriosis can be accurately diagnosed through transvaginal sonography (TVS) and magnetic resonance imaging (MRI) (31).

1.4. The treatment of endometriosis

When choosing a treatment for endometriosis, it is crucial to consider the patient's predominant symptoms and preferences, the side-effect profile of various treatment options, their age, the extent and location of the disease, prior treatments, and associated costs (5). Managing endometriosis can be particularly complex when it involves the bowel, bladder, ureters, extrapelvic structures, or when pain overlaps with other conditions. Therefore, a multidisciplinary approach is essential. It is worth noting that approximately 50% of women with endometriosis experience recurrent symptoms within five years, regardless of the treatment method employed (5).

1.4.1. Medical treatment

The magnitude of the treatment effect is reported to be consistent across all treatments, yet clinical practice regarding prescribed medications varies significantly. Importantly, none of the hormonal therapies used to manage endometriosis is devoid of side effects. While the contraceptive properties of these drugs can be beneficial for women who do not wish to conceive, they may pose challenges for those facing fertility concerns (4).

The medical treatment of endometriosis primarily focuses on alleviating symptoms and has proven to be an effective therapeutic option for many women (39, 40). Non-steroidal anti-inflammatory drugs (NSAIDs) and other analgesics are commonly used to manage the pain associated with this condition.

Hormonal suppressive therapy is frequently prescribed due to evidence that steroids play a pivotal role in the disease’s pathophysiology. These treatments are often initiated when endometriosis is suspected in young women, even before surgical confirmation of lesions, and are also recommended following surgery if symptoms persist or in cases of recurrent disease (4). The most commonly prescribed medications modify the hormonal environment by either suppressing ovarian function, thereby decreasing the secretion of

endocrine sex steroids, or by acting directly on steroid receptors and enzymes found in the endometrium and lesions. Additionally, these treatments can reduce menstrual bleeding, which may help mitigate retrograde flow and prevent the activation of inflammatory pathways associated with menstrual pain (41).

Examples of treatments include combined oral contraceptives, progestogens (in oral, intramuscular, and intrauterine systems), anti-progestogens, gonadotropin-releasing hormone (GnRH) agonists, GnRH antagonists, and aromatase inhibitors (4). Each of these therapies has demonstrated a significant reduction in pain compared to a placebo, as shown in a multivariate network meta-analysis utilizing visual analog scales for both menstrual and non-menstrual pelvic pain (42, 43). The reported treatment effects appear similar across all therapies, though clinical practice regarding prescription approaches varies considerably. Since these medications target hormone pathways, symptoms typically return upon treatment discontinuation. Additionally, it is crucial to acknowledge that none of these hormonal treatments are free from side effects (4).

1.4.2. Surgical treatment

Surgery may be considered for patients who have not responded to medical treatment, have contraindications or intolerances to hormonal therapies, are attempting to conceive naturally, prefer surgical intervention, or present with specific surgical indications, such as bowel stenosis accompanied by sub-occlusive symptoms or ureteral stenosis (1). The primary objective of surgery is to excise all visible endometriotic lesions and restore the anatomical integrity of the structures. Laparoscopy is now recognized as the standard approach due to its advantages over open surgery (laparotomy), including quicker recovery times and reduced costs (1).

The impact of laparoscopic surgery on pain relief has been thoroughly researched. This type of surgery, which includes the removal of endometriotic lesions, has been shown to significantly reduce pain compared to diagnostic laparoscopy alone (44). While only a limited number of small randomized controlled trials (RCTs) (45, 46) are available, larger observational studies (47-49) also support the finding of pain reduction in patients with endometriosis.

Surgical management of endometriosis is generally well accepted. However, there is ongoing debate regarding the most effective techniques for addressing more advanced cases, particularly deep infiltrating endometriosis (DE) involving the rectum and ovarian endometriomas.

During diagnostic laparoscopy, any visible lesions should be treated within the same surgical session to restore normal anatomy and ensure the complete removal of all endometriotic lesions. Prophylactic use of anti-adhesion agents can be considered during these surgeries (50). Peritoneal endometriosis may be treated through ablation or, in cases requiring histopathological examination or in more advanced disease states, via excision.

Endometriomas are present in 17 to 44% of patients diagnosed with endometriosis and are frequently found alongside deep infiltrating endometriosis (51). When performing surgery for endometriomas, it is crucial to find a balance between minimizing damage to the normal ovarian cortex, which helps to reduce ovarian damage, and ensuring sufficient removal to prevent (early) recurrence. Surgical management of endometriomas can be approached through several techniques: cystectomy, which involves the removal of the cyst wall. This method reduces both the recurrence of endometrioma and endometriosis-associated pain. Ablation, which employs CO2-laser vaporization or plasma energy to destroy the inner surface of the cyst wall; or partial ovarian cystectomy, which combines both excision and ablation techniques.

The surgical management of patients undergoing assisted reproductive therapy necessitates a specialized evaluation. According to ESHRE guidelines, routine surgery prior to ART is not advised for women with rASRM stage I/II endometriosis, as its efficacy in enhancing live birth rates remains unclear. The decision to carry out surgical excision of deep endometriosis lesions prior to ART should primarily be based on the patient's pain symptoms and personal preferences, given the uncertainty regarding its effects on reproductive outcomes due to the lack of randomized studies (1).

Routine surgery for ovarian endometriomas prior to ART is not advised, as current evidence indicates that it does not improve live birth rates and may potentially reduce ovarian reserve. Nevertheless, surgical intervention may be considered to relieve pain associated with endometriosis or to improve follicle accessibility(1).

1.5 Bowel endometriosis

Colorectal endometriosis refers to lesions that infiltrate at least the muscular layer of the bowel wall (52) and is observed in approximately 3-37% of women with a known diagnosis of endometriosis (1, 53). It is most frequently located in the rectum or sigmoid colon (52).

A recent observational study involving 426 patients identified a total of 172 intestinal DIE lesions. Among these cases, the rectum and rectosigmoid junction were affected in

65.7%, followed by the sigmoid colon at 17.4%, the caecum and ileocaecal junction at 4.1%, the appendix at 6.4%, the small bowel at 4.7%, and the omentum at 1.7% (54).

An important consideration when determining the surgical approach for intestinal endometriosis is its multifocal and multicentric nature. The largest lesion is identified as the primary lesion, while all other lesions are classified as satellite lesions (55). Multifocal involvement is defined as the presence of endometriotic lesions within a 2 cm radius of the primary lesion. In contrast, multicentric involvement refers to endometriotic lesions located more than 2 cm away from the primary lesion (55).

Multifocal and multicentric involvement was observed in 62% and 38% of surgical en bloc specimens, respectively (55). This observation may be attributed to the tendency of endometriosis to infiltrate the large bowel wall along the bowel nerves, even at some distance from the visible lesion (56). Furthermore, in nearly 70% of cases, intestinal endometriosis is associated with DIE in other regions, which necessitates specific surgical interventions for the uterosacral ligaments, vagina, bladder, and/or ureter (57).

The depth of infiltration of endometriosis lesions into the bowel wall is a crucial key factor in determining the appropriate surgical approach. It is essential to differentiate between lesions on the bowel serosa and those that penetrate the muscularis.

While bowel endometriosis can often be completely asymptomatic, in many patients, intestinal wall DIE significantly alters the quality of life. This can manifest in various ways, including constipation, diarrhea, hematochezia, intestinal cramping, abdominal bloating, intestinal stenosis or obstruction, and painful defecation (58). Rectal fixation to adjacent structures can result in angulation of the rectum, leading to defecatory pain and constipation. Additionally, fibrosis of nodules can cause rectal constriction and stenosis, while cyclical inflammation of the rectal wall can alter bowel habits, often resulting in diarrhea, with or without rectal bleeding (59).

Symptoms indicative of bowel involvement in endometriosis often overlap with those seen in mild or deep infiltrating endometriosis at non-bowel sites. Cyclic defecation pain or cyclic constipation is reported by the majority of women with rectal endometriosis (ranging from 55% to 65%) but this issue is observed in 25% to 40% of women with minimal endometriosis or deep infiltrating disease at non-bowel areas (8). For patients with rectal disease, many report more frequent and severe symptoms, including bloating, constipation, diarrhea, cramping, and defecation pain. However, these symptoms are not exclusively linked to bowel endometriosis (8).

Colorectal endometriosis can present as large bowel obstruction, making it challenging to differentiate from Crohn's disease or a neoplasm. Similarly, small bowel endometriosis can be difficult to distinguish from Crohn's disease, as both conditions can exhibit similar endoscopic and histologic characteristics (6). Intestinal perforation related to endometriosis can occur in the colon (60) or in the appendix due to transmural endometriosis. A differential diagnosis is essential to differentiate it from other colorectal conditions, including irritable bowel syndrome, diverticular disease, solitary rectal ulcer syndrome, adhesions, and colorectal cancer (6, 61).

1.6 Surgical treatment of bowel endometriosis- discoid resection, segmental bowel resection techniques

Surgical treatment of deep endometriosis (DE) is considered the preferred option for patients who do not respond to medical therapy or assisted reproductive technologies, as well as those experiencing organ dysfunction and/or clinically significant bowel stenosis (62).

While the laparoscopic management of endometriosis is widely accepted, there remains ongoing debate regarding the optimal type of resection. Specifically, the choice between a conservative approach (such as shaving, or disc resection) and a radical technique (wich involves limited resection of the bowel wall while preserving adjacent structures, including the autonomic pelvic plexus and rectal vascular supply- often referred to as "nerve-vessel sparing limited segmental resection"), is still being discussed for the treatment of deep endometriosis infiltrating the rectum.

Effective treatment for colorectal deep infiltrating endometriosis (DIE) depends on factors such as the location and size of the nodule, as well as the depth of invasion, while also considering the woman's quality of life (6).

Optimal treatment strategy for symptomatic deep endometriosis (DE) should aim to enhance quality of life, preserve or improve fertility, maintain gastrointestinal function, and reduce the rates of recurrence and complications. Numerous studies indicate a notable reduction in pain symptoms and improvement in quality of life for women who undergo surgical intervention for colorectal DE (63-66).

When selecting the appropriate surgical approach, it is crucial to consider several factors, including surgical risk, potential complications, functional outcomes, and the likelihood of recurrence. Segmental resection tends to carry a higher risk of complications, such as hemorrhage, anastomotic leakage, rectovaginal fistula formation, and postoperative

voiding dysfunction, compared to techniques like shaving or disc excision, This increased risk may partially stem from the presence of more advanced disease (as denoted by rASRM and #Enzian compartment C) in patients undergoing segmental resection. (67-69).

While rectal shaving is not suitable for all women with colorectal deep infiltrating endometriosis (DIE) due to factors like extensive infiltration and/or multifocal disease, additional factors such as anastomotic height, vaginal involvement, and the surgeon's experience and caseload have also been associated with the occurrence of major complications (62).

However, rectosigmoid resection with a low or ultralow nodule location (8−5 cm and ≤5 cm from the anal verge, respectively) can increase complexity, resulting in a heightened risk of anastomotic leakage, rectovaginal fistula, or postoperative low anterior resection syndrome (70).

Another concern for patients is the potential need for a temporary protective (ileo)stoma to minimize the risk of rectovaginal fistula and associated complications (71).

Typically, the stoma rate is lower when a conservative approach is taken, ranging from 0% to 19.6% in the conservative group (72) compared to 10.3% to 48.2% in those undergoing segmental resection (73, 74). However, in the randomized controlled trial by Roman et al. (75), the stoma rate was 61.7%, with no significant difference observed between the two groups. In terms of functional outcomes, a recent systematic review (76) indicated that patients who underwent conservative surgery experienced fewer instances of constipation and frequent bowel movements than those who had segmental resection. However, when examining the low anterior resection syndrome (LARS) score (77), no clear benefit was found for conservative treatment (76, 78-80). Currently, there is only one randomized controlled trial that has directly compared both techniques within a selected population of patients (specially those with rectal endometriosis up to 15 cm from the anal verge, nodules larger than 20 mm in length, and less than 50% circumference). This study revealed no differences in functional outcomes related to the type of surgery performed (75).

There is a current debate regarding the optimal approach to resecting bowel endometriosis. Limited full-thickness disc excision, whether performed laparoscopically or transanally, entails the selective excision of the bowel endometriosis lesion accompanied by the opening and subsequent closure of the bowel wall (52). In contrast,

full-thickness resection of an entire bowel segment is advised for advanced colorectal DIE, as limited resection techniques may present significant challenges in such cases (72).

A literature review conducted by Meuleman et al. (52) revealed that conservative surgery is associated with fewer postoperative complications, notably reduced rates of pelvic abscess and rectovaginal fistula, in comparison to radical surgery. These findings align somewhat with a case-control study by Fanfani et al. (81), which indicated that segmental resection was linked to a higher incidence of postoperative fever, while discoid resection was more frequently associated with severe rectal bleeding.

Afors et al. (82) noted that the rate of major postoperative complications for discoid resections and for segmental resections was equal (6,6%) in both groups.

In a retrospective study, discoid resection was associated with a shorter operating time and reduced hospital stay, while maintaining a complication rate comparable to that of segmental resection. However, the segmental resection (SR) group did experience a higher rate of voiding dysfunction (83).

Another retrospective study by Roman et al. aimed to evaluate long-term digestive outcomes in 77 women treated with either rectal shaving or colorectal resection for deep endometriosis infiltrating the rectum (84). Patients who underwent rectal shaving demonstrated significantly improved Gastrointestinal Quality of Life Index scores, experienced fewer postoperative constipation symptoms, and exhibited better anal continence. Nonetheless, there were no significant differences in postoperative pelvic pain between the two groups. Rectal recurrence was observed in 8.7% of patients treated conservatively, with 4.3% requiring secondary colorectal resection and an additional 4.3% undergoing rectal shaving. These findings suggest that colorectal resection does not enhance long-term functional outcomes compared to rectal shaving in the management of rectal endometriosis (84).

These results are consistent with the prospective cohort study conducted by Hudelist, which assessed the surgical outcomes of segmental resection and disk resection in relation to fertility, pain symptoms, and quality of life for women suffering from colorectal deep infiltrating endometriosis (72). The study revealed no significant differences between the two surgical techniques in pain alleviation, fertility, or functional outcomes. Long-term follow-up was performed on 112 women (83.6%), with both groups reporting significant improvements in pain symptoms and quality of life scores. Among the 61 infertile women, 42.6% achieved spontaneous pregnancies, while 21.3% conceived via in vitro

fertilization, resulting in an overall pregnancy rate of 63.4%. The overall complication rate (Clavien-Dindo III-IV) was recorded at 5.9%, with no significant difference between the groups. Both conservative disk resection and nerve- and vessel-sparing segmental resection were found to effectively reduce pain symptoms and improve fertility, exhibiting similar morbidity rates (72).

To better understand the long-term therapeutic effects of surgical treatment, the outcomes were re-evaluated, with a median follow-up period of 35.4 months at visit 1 and 86 months at visit 2 (66). This analysis focused on segmental resection (SR) and disc resection (DR), emphasizing pain symptoms, quality of life (QoL), and gastrointestinal symptoms reflected by low anterior resection syndrome (LARS) scores. QoL, assessed on a scale from 0 (worst) to 10 (optimal), and gastrointestinal outcomes measured by lower anterior resection syndrome (LARS), demonstrated significant improvements compared to pre-surgical values in both the SR and DR cohorts. Pain scores for dysmenorrhea (SR $p < 0.001$; DR $p < 0.001$), dyspareunia (SR $p < 0.001$; DR $p = 0.003$), and dyschezia (SR $p < 0.001$; DR $p < 0.001$) showed a significant decrease following the surgery and remained stable throughout the follow-up period. Minor and major LARS was observed in 6.5% and 8.1% of the SR group 13.3% and 6.7% of the DR group at visit 1, and in 3.2% and 3.2% of the SR group and 0% in both categories for the DR group at visit 2, with no significant differences between the two groups (66). The conclusion drawn from this study is that colorectal surgery for deep endometriosis, whether performed by DR or SR, offers long-term, stable pain relief with low rates of permanent gastrointestinal function impairment (66).

Over the past two decades, laparoscopic colorectal surgery has proven to be as effective as open surgery for treating both benign and malignant colorectal conditions. However, it presents notable advantages, including fewer postoperative complications and shorter hospital stays (85).

Laparoscopic surgery is the most widely accepted surgical approach for cases presenting bowel involvement (86-89), although the optimal type of resection remains a subject of ongoing debate (64, 67, 72, 75).

Standard colorectal resection, commonly performed for rectal or sigmoid colon cancer, involves mobilizing the rectosigmoid region as part of total mesorectal excision surgery (72). This procedure necessitates the removal of a significant length of the bowel

surrounding the lesion, along with the adjacent tissue, extending to the plane between the mesorectum and the presacral fascia (72).

Segmental resection is considered the most radical approach and is typically recommended for symptomatic patients with deep endometriosis (DE) lesions exceeding 3 cm in diameter or exhibiting multifocal disease (90). The nerve-sparing technique, which aims to prevent potential damage to the inferior hypogastric plexus by carefully dissecting and lateralizing nerve bundles, was first described by Heald et al. (91) in 1982 in a large series study involving colorectal cancer patients (92).

This technique was subsequently adapted for colorectal DE with segmental resection (64, 87). It involves the limited resection of a bowel segment while preserving adjacent structures, particularly the autonomic pelvic nerve plexus and blood vessels. The preservation of these structures is believed to enhance optimal wound healing, resulting in lower rates of severe complications such as anastomotic leakage and fistula formation. Furthermore, some researchers advocate for the preservation of the rectal artery supply by retaining the inferior mesenteric and rectal arteries, suggesting that this approach may benefit the perfusion of the anastomosis (72, 79, 92, 93).

Several lines of evidence indicate that segmental resection (SR) may result in higher complication rates, including anastomotic leakage and fistula formation, when compared to rectal shaving (73, 94). The grade III complications following SR are comparable to those observed with disc resection (DR) (94, 95). Additionally, long-term effects of full-thickness colorectal resection can include low anterior resection syndrome (LARS), which has been observed after both techniques, with no significant benefits associated with either approach (79, 95). Interestingly, SR may also be associated with a greater occurrence of new bowel symptoms, such as constipation (66, 96).

Surgical specimen removal following a segmental bowel resection can be performed either through a mini-laparotomy or by using the natural orifice extraction technique (6, 90, 93, 97).

The conventional method raises concerns regarding the potential disruption of the integrity of the abdominal wall. Furthermore, extraction site laparotomy is associated with higher postoperative pain scores. The occurrence of specific complications, such as incisional hernias and wound infections, is also increased when compared to conventional laparoscopic procedures (93).

To improve outcomes following laparoscopic colorectal surgery, a primary focus has been on minimizing access trauma, leading to the emergence of natural orifice specimen extraction (NOSE) as a promising method (85). Redwine and Sharpe (87) were the first to report a segmental bowel resection for a sigmoid colon endometriosis nodule, which was removed transanally (98).

The NOSE technique involves extracting the specimen through a natural orifice, while the anastomosis is performed intracorporeally. Various methods are available for specimen extraction and creation of bowel anastomosis (93). Currently, specimens can be removed via transcolonically, transrectally, transanally, or transvaginally. Each of these NOSE techniques presents unique challenges in terms of surgical technique and implementation.

Concerns related to the NOSE technique include the risk of bacterial contamination of the peritoneal cavity, an increased postoperative inflammatory response, longer operative times, elevated procedural costs, and a negative impact on postoperative outcomes, including pain, as well as functional and oncological results (85). Intraperitoneal bacterial contamination may occur; however, it does not appear to lead to a higher incidence of infectious morbidity (99).

Conversely, previously published systematic reviews and meta-analyses indicate that the natural orifice specimen extraction (NOSE) procedure is safe, may significantly shorten hospital stays, enhance postoperative recovery, improve cosmetic outcomes, and reduce both postoperative pain and complication rates (85, 100, 101).

A meta-analysis conducted by Liu et al. (102) revealed that NOSE was associated with reduced incidence of surgical site infections and overall perioperative complications; however, it required significantly more operative time compared to conventional laparoscopy. No significant differences were observed between the two groups in terms of anastomotic leakage, blood loss, or intra-abdominal abscess. In contrast, Bokor et al. (93) reported that NOSE was linked to a shorter operative time and hospital stay, with no significant difference in the occurrence of major postoperative complications.

In the retrospective observational study conducted by Grigoriadis et al., a total of 45 NOSE procedures were performed laparoscopically, and five procedures were carried out robotically (98). The specimen extraction occurred vaginally in 29 cases and transanally in 21 cases. In the early postoperative period, 5 patients required reoperation due to complications: 1 case of anastomotic leak, 1 case of postoperative bowel obstruction, 1

case of hemorrhage, and 2 cases of pelvic collection. The overall complication rate was comparable to that of the conventional (minilaparotomy) surgical approach (98).

Several studies have evaluated the oncological and surgical safety of the laparoscopic NOSE technique, confirming that it offers a level of safety comparable to that of conventional laparoscopy for patients with sigmoid and rectal cancer.

A prospective randomized trial involving 276 patients with upper rectal or sigmoid colon cancer revealed that the incidence of postoperative complications was significantly lower in the NOSE group (103). This group also experienced longer operation times, less blood loss, and a lower postoperative visual analog scale score than the non-NOSE group. Additionally, the recovery time for intestinal function (ventilation) and the duration of hospital stay were significantly longer in the non-NOSE group (103). These findings align with the results from Xu's study (101).

Although this technique initially gained limited popularity, there has been a rising interest in it in recent years (98).

1.7. Assessment of quality of life after bowel resection surgeries

Health-related quality of life (HRQoL) is a multidimensional concept encompassing the physical, psychological, and social dimensions associated with a disease or its treatment (104). Nevertheless, only a limited number of studies have specifically focused on HRQoL in patients with endometriosis (2, 105-107). The absence of a consensus on the most effective methods for evaluating quality of life in this context has led to the use of a diverse range of assessment scales. This varied approach presents clinicians with the ongoing challenge of determining the most effective way to assess HRQoL in individuals affected by endometriosis. Conducting routine evaluations of HRQoL in women with endometriosis is essential in clinical practice, offering benefits to both healthcare providers and patients alike.

Endometriosis is a benign chronic condition that primarily affects young women. It is frequently associated with significant pain and has a profound impact on fertility. Furthermore, women experiencing endometriosis often encounter various nonclinical challenges, including depression, feelings of isolation, fatigue, and low energy levels (108). This condition is known to adversely affect physical, mental, and social well-being, as well as overall health-related quality of life (HRQoL) (109). It is noteworthy that a positive correlation exists between the severity of anxiety symptoms and the intensity of

pain (22). Additionally, effective pain management has been associated with a reduction in depression (110-112).

Endometriosis is typically diagnosed 3.9 to 10.4 years after its initial onset (25, 113, 114), and this considerable diagnostic delay negatively impacts health-related quality of life (HRQoL) (115).

Considering the possible complications that may arise during and after surgery, it is essential to assess patients' quality of life both before and after the procedure. While objective measures, such as the length of hospital stays, provide valuable information, there is a growing emphasis on utilizing patient-reported questionnaires to capture their personal experiences and perspectives.

Numerous studies have demonstrated a significant reduction in pain scores and an improvement in sexual functioning among women after the surgical resection of colorectal endometriosis; however, long-term, prospectively collected data on gastrointestinal well-being following segmental bowel resection for deep endometriosis in a large cohort of patients are sparse (72, 78, 79, 116, 117).

1.7.1 Questionnaires

Conducting a comprehensive assessment of postoperative functional status and quality of life is crucial for optimizing surgical techniques. Several validated questionnaires serve as suitable tools for this purpose. However, the interpretability of the results from such studies is often compromised by factors such as overly homogeneous patient populations, small sample sizes, low response rates, and the absence of objective measurement tools.

In this context, I would like to present a selection of questionnaires utilized in the international literature to asses quality of life, particularly concerning endometriosis-related quality of life and gastrointestinal function.

1.7.1.1 The 36-Item Short Form Health Survey (SF-36)

The 36-Item Short Form Health Survey (SF-36) is a widely used instrument for assessing Health-Related Quality of Life (HRQoL). A search on PubMed for the term “SF-36 health survey” yielded 9,722 results. The SF-36 evaluates eight scales: physical functioning (PF), role physical (RP), bodily pain (BP), general health (GH), vitality (VT), social functioning (SF), role emotional (RE), and mental health (MH). Component Analyses have revealed two distinct dimensions: the physical dimension represented by the Physical Component Summary (PCS) and the mental dimension summarized by the

Mental Component Summary (MCS) (118). Each scale contributes to the PCS and MCS scores in varying degrees. Higher scores on the SF-36 indicate improved outcomes (118).

1.7.1.2. The Short Form 12 (SF-12)

The Short Form 12 (SF-12) is a multipurpose and validated generic health status measurement tool, designed as a more concise alternative to the SF-36. It includes 12 items, each derived from one or two questions across eight health scales featured in SF36: physical functioning, role limitations due to physical health, bodily pain, general health, vitality (energy/fatigue), social functioning, role limitations due to emotional problems, and mental health (psychological distress or well-being) (119). Responses are scored and analyzed through a statistical algorithm to generate two summary scores: the Physical Component Summary (PCS) and the Mental Component Summary (MCS). These scores can be compared over time to assess changes in health status (119).

A total of 750 patients were analyzed across 12 studies utilizing the SF-36 along with one study that employed the SF-12. The pooled results demonstrated significant improvements in HRQOL following surgical treatment for bowel endometriosis across all eight domains of the SF-36 and SF-12, as well as in the MCS, PCS, and overall score. The greatest improvement was observed in the Bodily Pain domain (1.39; 95% CI, 0.79−1.98) (63, 75, 120-129). Touboul et al. (127) revisited Daraï et al.'s (121) original cohort with a follow-up period extending beyond four years, reporting sustained improvements, with no significant differences between short- and long-term follow-ups (118).

1.7.1.3. The Visual Analog Scale (VAS)

Self-reported pain is considered the gold standard for pain assessment, requiring the use of scales to enhance accuracy and minimize subjectivity. The Visual Analogue Scale (VAS) is the most commonly employed tool for this purpose. It consists of a 10-cm line with endpoints labeled "no pain" and "worst pain imaginable" (130). Patients indicate their pain level by marking a point on the line, corresponding to a score between 0 and 10 cm based on the distance from the endpoints. Numerous researchers classify endometriosis-related pain as severe when the VAS score is ≥7 cm (130).

1.7.1.4. The European Quality of Life (EQ-5D)

The European Quality of Life (EuroQOL) EQ-5D is a tool designed to evaluate health status across five dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each dimension features three levels of severity: no problem, some

problem, or extreme problem (119). Analyzing survey results from a sample of 3,000 individuals, a numerical health status value can be derived for each patient.

In addition to these dimensions, the EQ-5D includes a visual scale resembling a thermometer. This scale allows respondents to assess their overall health status, scoring 100 for the "best imaginable health" and 0 for the "worst imaginable health." This validated questionnaire effectively captures variations in health status across key population subgroups (119).

The study of Bailly et al. assessed the EQ-5D questionnaire in 41 patients with bowel endometriosis, demonstrating significant improvement in EQ-5D scores following surgery (131).

1.7.1.5. The Bowel Endometriosis Symptoms (BENS)

The Bowel Endometriosis Symptoms BENS score was developed and validated through a cohort of 525 women undergoing medical or surgical treatment for bowel endometriosis at Aarhus and Copenhagen University Hospitals in Denmark (132). This score includes six key factors: pelvic pain, use of analgesics, dyschezia, straining to urinate, fecal urgency, and satisfaction with sexual life. The BENS score ranges from 0 to 28 and is categorized into three levels: 0–8 (no BENS), 9–16 (minor BENS), and 17–28 (major BENS). It represents the first classification system for endometriosis based on the patient-reported symptoms (132).

1.7.1.6. The Low Anterior Resection Syndrome (LARS)

Low Anterior Resection Syndrome (LARS) is a common complication following colorectal surgery. The LARS score is a simple, self-administered questionnaire designed to assess bowel dysfunction after rectal surgery. It includes questions about incontinence, emptying difficulties, urgency, and frequency (133). The calculated score ranges from 0 to 42, with a score of 0-20 representing no LARS, 21-29 representing minor LARS, and 30-42 representing major LARS (77).

Developed by Emmertsen and Laurberg in 2012, the LARS score has been validated in 29 languages. It allows colorectal surgeons worldwide to monitor their patients consistently and report outcomes in a standardized manner. This score has demonstrated particular efficacy in evaluating symptoms originating from a single organ system, specifically the gastrointestinal tract (132).

1.7.1.7. The Endometriosis Health Profile 30 (EHP-30)

The Endometriosis Health Profile 30 consists of five scales: pain, control and powerlessness, emotional well-being, social support, and self-image, totaling 30 items (133). Research has shown that the EHP-30 is more reliable than generic questionnaires. Users can apply six supplementary modules, which can be selected in any combination to evaluate additional areas of health status (104, 134).

The second part of the assessment includes 23 questions related to various aspects of life, such as sexual intercourse, work, relationships with children, perceptions of medical professionals, treatment experiences, and infertility concerns.

1.7.1.8. The Gastrointestinal Quality of Life Index (GIQLI)

The Gastrointestinal Quality of Life Index is a 36-item, patient self-reported instrument specifically designed to assess gastrointestinal-related health quality of life in individuals with gastrointestinal disorders. It encompasses five domains: GI symptoms, emotion, physical function, social function, and medical treatment (133). Subscores range from 0 to 4, resulting in a total score range between 0 and 144, with higher scores indicating better GI health-related quality of life (135, 136).

Four studies (137-140) evaluated HRQOL using the Gastrointestinal Quality of Life Index, all reporting significant improvements in gastrointestinal HRQOL following surgical treatment for bowel endometriosis (118).

1.7.2. Results of quality of life assessments after conventional segmental bowel resection

Numerous studies have demonstrated that conventional segmental bowel resection for bowel endometriosis is an effective therapeutic approach for alleviating symptoms. Results of quality-of-life assessments after the traditional segmental bowel resection surgical method significantly enhance quality of life (63, 105, 126, 129, 141). However, assessing outcomes remains challenging due to the limited availability of large-scale prospective studies ($n > 150$) in the literature (63, 126, 141). Nevertheless, all completed studies have reported positive outcomes.

In a systematic review conducted by de Cicco, 34 studies were analyzed, which included a total of 1,889 cases of segmental bowel resection for deep endometriosis. Although pain relief was not assessed prospectively, the postoperative outcomes indicated that between 71.4% and 93.6% of women were pain-free at one year of follow-up. The recurrence of symptoms over a follow-up period of 2 to 5 years varied from 4% to 54%, likely due to

inconsistencies in how recurrence was defined (64). The rate of pain recurrence requiring additional surgical intervention ranged from 0% to 34%, while confirmed recurrence of bowel endometriosis was reported in 0% to 25% of cases (64).

It is essential to emphasize that bowel resection can alleviate dysmenorrhoea, non-cyclic pain, and various gastrointestinal symptoms.

The previously indicated results align with the findings of the study conducted by Darai et al. Notably, all gynecologic symptoms showed significant improvement following laparoscopic segmental colorectal surgery, including dysmenorrhea ($P < .0001$), nonmenstrual pelvic pain ($P = .001$), and dyspareunia ($P = .0001$) (89). Furthermore, the severity of pain experienced during defecation significantly decreased postoperatively ($P < .0005$). Interestingly, although there was a reduction in pain intensity during bowel movements, the change was not statistically significant, likely due to the occurrence of new-onset constipation and diarrhea. While asthenia showed a tendency to improve, lower back pain remained unchanged (89).

The results from Bassi indicated that laparoscopic segmental resection of the rectosigmoid effectively achieves its primary goal of treating endometriosis with bowel involvement (126). This procedure significantly enhances patients' quality of life, as evidenced by a notable improvement ($p < .001$) in all pain-related symptoms. Additionally, there was a significant increase ($p < .001$) in scores across all SF-36 domains, reflecting improved overall physical and mental health components (126).

In the study conducted by Seracchioli, noncyclic pelvic pain scores demonstrated significant reductions at both 6 and 12 months ($P < 0.05$). However, a high recurrence rate was observed, as 4 out of 12 women reported improvements. Symptoms such as constipation, diarrhea, and rectal bleeding showed consistent improvement in all affected women during the follow-up period. After three years, dysmenorrhea either resolved or improved in 18 of the 21 women, while three remained unchanged. Dyspareunia was either resolved or improved in 14 out of 18 women, with four reporting no change. Pain during defecation remained unchanged in two women, and one woman continued to experience lower back pain (53).

In Bertocchi’s study, EQ-5D-5L scores revealed a significant decline at the time of discharge, followed by an improvement at 4 to 6 weeks post-surgery when compared to preoperative levels. The initial decrease in quality of life (QoL) immediately after surgery may be linked to the multidisciplinary nature of the procedure, as many patients were

discharged with either an urinary catheter or a protective ileostomy. By the 4 to 6 weeks post-surgery (T2), the questionnaire indicated a significant improvement in QoL both to the discharge (T1) and preoperative (T0) scores (142). In the short term, the surgery appeared to be an effective treatment for endometriosis, particularly among women who had not responded to prior medical therapies or those facing infertility (142).

To better understand the impact of laparoscopic segmental bowel resection on quality of life and gastrointestinal function, it is essential to evaluate both mid- and long-term outcomes in treating severely symptomatic women with deep infiltrating intestinal endometriosis. This evaluation should utilize health-related QOL questionnaires as well as endometriosis-specific assessments. Research confirms that notable improvements in quality of life can be observed even several years following the surgical intervention.

In Dubernard's study, the median follow-up period was 22.5 months, ranging from 2 to 55 months. The results indicated significant improvements in several symptoms, including dysmenorrhea ($P < 0.0001$), dyspareunia ($P < 0.0001$), bowel movement pain or cramping ($P < 0.0001$), pain during defecation ($P < 0.0001$), diarrhea ($P < 0.016$), lower back pain ($P < 0.0001$), and asthenia ($P < 0.0002$) (129). However, no improvement was noted in tenesmus, rectorrhagia, or constipation. Additionally, all components of the SF-36 Health Status as well as overall quality of life scores demonstrated significant improvement following colorectal resection for endometriosis (129).

A prospective observational cohort study was conducted to evaluate changes in quality of life (QOL) using the SF-36 questionnaire over a one-year follow-up in patients undergoing laparoscopic colorectal resection to treat deep endometriosis. The most significant median increases were observed in the physical functioning, role physical, social functioning, and role emotional domains throughout the study period (125). In contrast, the pain, general health, vitality, and mental health domains exhibited moderate improvements, although they did not increase as substantially as the previous group. Overall, all SF-36 domains demonstrated significant improvements ($p < 0.05$), with physical health-related QOL domains exhibiting more significant enhancement compared to mental health domains (125).

The study conducted by Touboul aimed to evaluate the long-term outcomes regarding symptoms, quality of life (QOL) using the SF-36 questionnaires, as in the previous study, as well as fertility, in women who underwent either laparoscopically assisted or open surgery for colorectal resection due to endometriosis (127). The findings revealed that

improvements in both symptoms and QOL were sustained for over four years, with no significant differences observed between the two surgical techniques (127).

Meuleman's study evaluated 56 patients who underwent multidisciplinary surgery, focusing on their quality of life and symptoms both before and after the procedure. The patients completed the Oxford Endometriosis Quality of Life questionnaire, a sexual activity questionnaire, and visual analog scales (VAS) to assess dysmenorrhea, chronic pelvic pain, and deep dyspareunia. The median follow-up period after multidisciplinary CO_2 laser surgery was 29 months with a range of 6 to 76 months. Postoperative VAS scores for chronic pelvic pain, dysmenorrhea, and deep dyspareunia were significantly lower than preoperative scores ($P < 0.001$) (105). Notably, 93% of patients experienced improvement in chronic pelvic pain, 100% in dysmenorrhea, and 90% in deep dyspareunia. Additionally, 86% (49 out of 57) of patients reported complete satisfaction with the surgical outcome.

Significant enhancements were observed in general health ($P < 0.0001$), physical health ($P < 0.001$), and mental health, including emotional well-being ($P < 0.0001$), sense of control ($P < 0.0001$), social support needs ($P = 0.008$), and self-image ($P = 0.0007$) (105). Furthermore, anxiety-related fear and depression associated with infertility concerns decreased significantly following the surgery ($P = 0.0008$). Moreover, sexual function significantly improved, with increased pleasure ($P < 0.0001$), reduced discomfort ($P < 0.0001$), and a higher frequency of sexual intercourse ($P = 0.0003$). (105).

In Turco's study, the interpretation of EHP-30 showed significant improvement in all continuous variables, except fertility concerns. Overall gastrointestinal quality of life (QoL) and most specific symptoms improved following surgery. Frequent bowel movements were observed in 13% of cases but did not negatively impact general or gastrointestinal QoL (143). Meanwhile, constipation remained unchanged. Patients experiencing depressive moods who underwent laparoscopy derived the most significant benefit from segmental resection (SR), whereas those with multinodular bowel involvement experienced a more substantial reduction in abdominal pain (143).

Kössi et al. conducted the first study to employ the 15D questionnaire in evaluating the impact of surgical treatment for bowel endometriosis on various quality of life aspects (58). One year after surgery, patients received a mailed questionnaire that evaluated endometriosis-related symptoms, quality of life, and sexual function, using both the 15D Questionnaire and the McCoy Female Sexuality Questionnaire.

Health-related quality of life scores showed significant improvements in several domains, including usual activities ($P = 0.04$), discomfort and symptoms ($P < 0.001$), distress ($P < 0.001$), vitality ($P < 0.001$), and sexual activity ($P < 0.001$) when compared to baseline values. Additionally, the overall 15D score demonstrated a significant increase, rising from 0.85 to 0.91 ($P < 0.001$) (58).

Riiskjaer's study evaluated urinary, sexual, and bowel function before and after laparoscopic bowel resection for rectosigmoid endometriosis (78). The findings indicated a significant and clinically relevant improvement in urinary and sexual function one year post-surgery. Furthermore, a notable increase in defecation frequency was observed postoperatively, likely attributed to reduced reservoir capacity. However, the mean overall LARS (Low Anterior Resection Syndrome) score remained unchanged one year following surgery. A majority of patients experienced either minor or major LARS both before and after the procedure. At the one-year follow-up, 26.5% of patients reported no LARS symptoms, 27.4% had minor LARS, and 46.2% experienced major LARS. These results closely resemble those seen in rectal cancer patients who underwent low anterior resection, where the respective rates were 29.0%, 25.1%, and 45.9%. Interestingly, the presence of a nodule in the lower rectum or the implementation of a defunctioning stoma did not increase the risk of worsened bowel function (78). Considering the significant prevalence of bowel function impairment persisting one year after surgery, where 73.5% of patients continued to experience minor or major LARS, it is evident that impaired bowel function alone should not be the sole indication for recommending bowel surgery (78).

Hudelist et al. conducted a study to examine changes in gastrointestinal (GI) function before and after surgery, comparing a modified nerve and vessel-sparing segmental resection (NVSSR) with full-thickness disc resection (FTDR) (80). In addition, the researchers prospectively assessed health profiles, pain symptoms, fertility outcomes, and major postsurgical complications.

The primary outcome focused on changes in GI function, measured by the prevalence of low anterior resection syndrome (LARS) and the GI function-related quality of life (GIQLI) score. Secondary outcomes included changes in pain levels—measured using the visual analog scale (VAS) for dysmenorrhea, dyspareunia, dyschezia, and dysuria—as well as Endometriosis Health Profile-30 (EHP-30) scores, postsurgical complication rates (classified by Clavien–Dindo), and fertility outcomes which encompassed

pregnancy rate, time to conception, miscarriage rate, preterm and term delivery rates, and ongoing pregnancy rates (80).

The study demonstrated that both NVSSR and FTDR techniques for treating colorectal deep endometriosis (DE) resulted in a notable impairment of GI function. This improvement was reflected in a postoperative decrease in LARS-like symptoms, low rates of new-onset LARS, and enhanced GIQLI scores. Both techniques significantly alleviated pain, improved quality of life, and were associated with low incidences of severe complications. Furthermore, total preoperative EHP-30 scores showed a significant decrease following surgery, with notable improvements in subscale ratings related to pain, control, and powerlessness, emotional well-being, social support, self-image, and sexual life (80).

The objective of Roman's randomized study was to compare digestive and urinary outcomes in patients with deep endometriosis infiltrating the rectum, treated either through conservative rectal surgery (using techniques such as shaving or disc excision) or with radical colorectal segmental resection (75). The primary endpoint was the proportion of patients experiencing one or more of the following symptoms 24 months postoperatively: constipation (defined as having fewer than one stool every 5 consecutive days), frequent bowel movements (3 or more stools per day), defecation pain, anal incontinence, dysuria, or bladder atony requiring self-catheterization. Secondary endpoints included scores from the Visual Analog Scale (VAS), Knowles–Eccersley–Scott-Symptom Questionnaire (KESS), Gastrointestinal Quality of Life Index (GIQLI), Wexner scale, Urinary Symptom Profile (USP), and Short Form 36 Health Survey (SF36).

The results of this trial did not show a statistically significant advantage of conservative surgery over radical resection regarding mid-term functional digestive and urinary outcomes in women with extensive rectal involvement (75).

An annual evaluation of gastrointestinal function and quality of life, using standardized scoring systems, was conducted in Roman’s study to compare excision and radical rectal (colorectal resection) surgery. The findings highlighted a rapid and significant improvement in GIQLI and SF-36 scores for both groups, as well as an improvement in the KESS score for the conservative surgery group (95). These improvements were observed one year post-surgery and remained stable over five year period. No statistically significant differences were observed between the two groups regarding GIQLI and SF-

36 scores at the five-year follow-up, nor in the overall trends of improvement within each group. Based on these results, both conservative and radical rectal surgery are recommended as effective and long-lasting treatment options for patients suffering from pain and digestive issues due to deep infiltrating endometriosis of the rectum (95).

Bokor's retrospective international multicenter cohort study aimed to compare two surgical techniques—laparoscopic-transanal disk excision (LTADE) and nerve and vessel-sparing segmental resection (NVSSR)—for full-thickness excision of rectal deep endometriosis (DE) with an anastomotic height of ≤7 cm from the anal verge. The study focused on the incidence of LARS, postoperative outcomes, and fertility results. The incidence of LARS did not show a significant difference between the LTADE (31.7%) and NVSSR (37.9%) groups (P = .4) (79).

The findings from Darici's study confirm that colorectal surgery for deep endometriosis (DE), whether performed through segmental resection (SR) or disc resection (DR), results in significant and lasting pain relief, along with improved QoL for at least two years postoperatively, with stable benefits for up to seven years (66).

Quality of life (QoL) scores demonstrated a significant increase, while symptom scores for dysmenorrhea, dyspareunia, and dyschezia significantly decreased after surgery during the initial follow-up visit and remained stable throughout the follow-up period during the second visit for both the segmental resection (SR) and disc resection (DR) groups (66).

Notably, dysuria decreased at the first postsurgical visit in the SR group, but increased by the second visit, while in the DR group, there was no significant reduction at either follow-up point. Furthermore, no significant differences were observed in LARS scores between the two groups over the follow-up period ($p = 0.45$ and $p = 0.79$, respectively).

Additionally, the long-term prevalence of digestive complaints, as measured by LARS scores, remained low, with minor and major LARS rates reported at 8.1% and 3.2% in the SR group and 6.7% and 0% in the DR group, respectively (66).

Among patients eligible for long-term follow-up, 80% of those in the DR group and 96% in the SR group stated that they would choose to undergo the surgery again despite its consequences (66).

1.7.3. Quality of life assessment following Natural Orifice Specimen Extraction (NOSE) colectomy

Traditional large tissue resections often necessitate extended skin incisions to facilitate effective specimen removal. In contrast, NOSE employs the use of natural body orifices, such as the anus, for tissue extraction. This approach offers several advantages, including faster recovery times and a decreased risk of postoperative hernias. Although there are concerns related to contamination risks and anastomosis integrity during bowel surgery, emerging research supports NOSE as a viable alternative to conventional mini-laparotomy (144). While this technique represents a significant advancement, it also introduces new challenges, such as apprehensions about fistula formation and infection, particularly among general surgeons (85, 144).

The systematic review and meta-analysis conducted by Kar et al. encompassed six studies with a total of 372 patients. It examined the efficiency, safety, and technical challenges associated with NOSE compared to mini-laparotomy for bowel resection due to endometriosis. The findings suggest that NOSE may represent a valuable alternative, offering the benefit of a shorter hospital stay without significantly increasing intraoperative blood loss or prolonging operative time.

The duration of surgery showed no significant difference between NOSE and mini-laparotomy, which is consistent with recent studies indicating comparable times across NOSE and traditional approaches. This reflects a broader trend toward minimally invasive techniques that maintain surgical efficiency(144).

However, it is worth noting that only a limited number of multidisciplinary centers currently utilize this approach for the surgical treatment of bowel endometriosis.

2. Objectives

2.1. Primary objectives

The primary objective of our single-center, randomized, open-label, two-arm, parallel-group controlled trial was to report the short- and medium-term outcomes of bowel function reflected by the Low Anterior Resection Syndrome score after NOSE versus conventional nerve- and vessel sparing-colectomy for colorectal endometriosis (77).

Our second study compared two surgical approaches: laparoscopic-transanal disc excision and nerve- and vessel-sparing segmental resection (LTADE, NVSSR) for the full-thickness excision of rectal DE. The analysis considered cases with an anastomotic height of ≤7 cm from the anal verge regarding the incidence of LARS, postoperative outcomes, and fertility results (79).

2.2. Secondary outcomes

Our secondary outcomes of the randomized study assessed Visual Analog Scale scores, Gastrointestinal Quality of Life Index (135, 136), Endometriosis Health Profile 30 (104, 134), rate of complications, length of hospital stay, and recovery after NOSE versus conventional nerve- and vessel sparing–colectomy for colorectal endometriosis.

3. Methods

3.1. Data collection

This prospective randomized study was designed in accordance with the Declaration of Helsinki and approved by the Institutional Ethical and Review Board of the University for the protection of human subjects (no.:58723-4/2016/EKU) on December 8, 2016 (133).

In our retrospective, international, multicenter cohort analysis, data were retrospectively collected from a prospectively maintained electronic database used across all three participating centers. Patient baseline characteristics, intraoperative findings, surgical procedures, and follow-up information were systematically recorded in the North-West Inter Regional Female Cohort for Patients with Endometriosis (CIRENDO, 17 January 2019) database (NCT02294825) at RUH. For SU, data were retrieved from the NOSERES database (NCT04109378), while HSGWH used the TIE database. All databases and the study received approval from the local institutional ethics and review boards at RUH and SU to ensure the protection of human subjects (nos 58723-4/2016/EKU [8 December 2016]; HSJGWH No: WSP-1-GYN; Barmherzige Brüder Ethikkommission [5 September 2017]) (79).

3.1.1. Patients participating in the study

We conducted a single-center, randomized, open-label, two-arm, parallel-group controlled trial to assess functional outcomes and endometriosis-related pain changes in women undergoing NOSE colectomy (NC) or conventional laparoscopic resection (CLR) for the management of colorectal deep endometriosis (DE) between September 30, 2019, and December 31, 2020, at University Hospital. The secondary outcomes included complication rates and fertility outcomes. The mean follow-up time was 14±2.6 months (133).

Our second study was conducted as a retrospective, international, multicenter cohort analysis, involving all premenopausal women with deep endometriosis (DE) affecting the lower rectum all of whom were scheduled for surgical treatment. The study encompassed three tertiary referral centers: the Department of Obstetrics and Gynecology at Rouen University Hospital in Rouen, France (RUH); the Department of Obstetrics and Gynecology at Semmelweis University in Budapest, Hungary (SU); and the Center for Endometriosis, Department of Gynecology, at St. John of God Hospital and Wilhelminen

Hospital in Vienna, Austria (HJGWH). The study period extended from October 2009 to December 2018 (79).

3.1.1.1. Inclusion criteria

Inclusion criteria of our randomized trial were being clinically diagnosed (by at least one imaging technique or via a previous surgery) as having intestinal deep infiltrating endometriosis up to 15 cm from the anus, involving at least the muscular layer in depth, and at least 50% of the recto-sigmoidal circumference in case of patients complaining of pain and/or infertility, and age18 to 45 years(133).

The inclusion criteria for our second study were defined as follows: women aged 18 to 45 years (inclusive) presenting with endometriosis-related pain and/or infertility, with a confirmed diagnosis of deep endometriosis (DE) that infiltrates at least the muscular layer of the lower rectum, located within 7 cm of the anal verge. Eligible patients were those managed surgically by either LTADE or NVSSR (79).

3.1.1.2. Exclusion criteria

Ongoing pregnancy and suspected malignancy were excluded. Written informed consent was obtained from all patients before randomization (133).

Patients with a history of previous colorectal surgery or chronic inflammatory diseases of the gastrointestinal tract were excluded from the retrospective, international, multicenter cohort analysis, along with those who suffered from chronic defecation dysfunction due to other factors, such as birth trauma (79).

3.1.2. Preoperative assessment

The process started with an initial consultation, where the patient's file was completed in detail. All selected women underwent clinical examination by a gynecologist experienced in colorectal surgery for endometriosis, as well as a transvaginal ultrasound examination. Transvaginal sonography was performed to assess whether the rectum was involved and estimate the depth of rectal wall infiltration according to the IDEA protocol (29). In case of parametrial involvement, a pelvic MRI was also performed. If surgery was deemed necessary, the patient was scheduled for elective hospitalization, which is the standard of care (133). For patients who were eligible for the study, participation in the study was offered at this stage. If the patient agreed, they completed the informed consent form and study-related questionnaires. All the surgeries were performed by the same surgical team (133).

3.1.3. Postoperative assessment

Postoperative follow-up care was provided at several stages: Four weeks postoperatively, the surgeons conducted a postoperative check-up, and the patient completed study-related questionnaires, sent via email. A clinical examination was also performed at this time. Six months after surgery, the patient had another postoperative check-up with one of the members of the surgical team. By this time, the patient was asked to complete the study-related questionnaires sent via email. During this visit, a clinical examination, an assessment of pain and childbearing desires, and a gynecological ultrasound were performed. Twelve months postoperatively, the patient returned for a one-year follow-up visit. Study-related questionnaires were completed via email, and the surgeon performed a clinical examination. This visit included an anamnesis concerning pain and any wishes related to childbearing, as well as both a gynecological and an abdominal ultrasound.

3.1.4. Recruitment and consent

Women diagnosed with deep endometriosis that infiltrates at least the muscularis layer of the rectum and who are planned for surgical laparoscopic treatment were eligible for the study. Eligible participants were invited to join the study. Eligible women could enter the study only after providing written informed consent.

This written informed consent was obtained from capable, eligible women after they were thoroughly informed about the study. Each patient received a patient information letter along with an informed consent form, both approved by the Ethics Committee. During the informed consent process, all participants were encouraged to ask questions.

The right of participants to decline participation without providing reasons were respected under all circumstances. Furthermore, participants retained the legal right to withdraw from the study at any time point, even after randomization and treatment without giving reasons and without compromising their further treatment options.

3.2. Theory, calculation

3.2.1. Questionnaires

In our prospective randomized trial patients were asked to complete baseline questionnaires including questions about pelvic organ function, pelvic pain, and quality of life-related to endometriosis using the Visual Analog Scale (dysmenorrhea, dyspareunia, dyschezia, dysuria, and chronic pelvic pain), Endometriosis Health Profile 30 (pain, control and powerlessness, emotional well-being, social support, self-image, sexuality) (104, 134), the Gastrointestinal Quality of Life Index (GIQLI) (135, 136), and

the Low Anterior Resection Syndrome (LARS) (77) score to assess bowel function preoperatively (T0), and at 30 days (T1), six months (T2), and one year (T3) post-operatively (133).

In our retrospective, international, multicenter cohort analysis, patients were asked to present for a postoperative check-up 4 weeks and 6 months after surgery. The postoperative evaluation of digestive function was assessed using the validated LARS at least 12 months after surgery (79).

3.2.2. Infertility assessment

The Endometriosis Fertility Index (38) was calculated for each procedure, and the clinical pregnancy rates were calculated during the first postoperative year (133).

3.2.3. Randomisation

Assigning patients to NOSE or conventional colorectal resection was based on a randomization list using a simple randomization method. To determine the allocation sequence, computer-based coin flipping (www.random.org) was carried out by a staff member with no clinical involvement in the study. Randomization started after the patient had completed all baseline assessments and provided written consent to be enrolled in the trial. Patients were analyzed within the group to which they were allocated, irrespective of whether they had experienced the intended intervention (intention-to-treat analysis). Blinding in our study was not feasible (133).

3.2.4. Statistical analysis

The study data were evaluated using descriptive statistical methods such as average, median, range, frequency, and distribution. Variables were tested for normality using the Kolmogorov-Smirnov-Lilliefors and the Shapiro-Wilk tests; skewness and kurtosis were also examined. Groups of values without a normal distribution were compared using the Mann-Whitney U test, Kruskal-Wallis test, Fisher's exact test, or Wilcoxon signed-rank test. Where the distribution allowed, an independent samples t-test was used for continuous variables. The evolution of quality of life and digestive symptoms was tested based on the records at 12 months.

All tests were two-sided, and $P<.05$ was accepted as a significant difference. Statistical analyses were performed using IBM SPSS version 17 (IBM Corp., Armonk, NY, USA) (133).

3.2.5. Sample size calculations

Based on the results of our previously published (79) multicenter, retrospective study on the data of 205 patients with low rectal endometriosis undergoing laparoscopic surgery, we ascertained that in our center, the mean LARS scores were 29±12 in the CLR group and 21±9 in the NC group at one year postoperatively. In our present study, the randomized case selection enabled us to build a cohort where at least 80% statistical power was set as the target. LARS is the key characteristic/measure of a technique's outcome, supporting the power calculation performed (https://clincalc.com/Stats/SampleSize.aspx) using our previous data. To detect low anterior resection syndrome using the LARS score as a continuous variable by assessing two independent study groups with a mean of 29±12 for the CLR group and 21±9 for the NC group, a sample size of 70 patients was required with 80% power at 0.05 alpha. Based on our previous experience, we predicted a drop-out/loss to follow-up rate of 22%; therefore, our final sample size was 91 patients (133).

3.3. Surgical procedures

The primary objective of surgery was to achieve a visibly complete elimination of all endometriotic lesions, regardless of the technique used. The team included two gynecological surgeons with extensive experience in endometriosis surgery. Nerve- and vessel-sparing techniques were used to preserve the inferior hypogastric plexus, hypogastric nerves, and splanchnic nerves on at least one side (Figure 1.) (133).

Figure 1. Steps of laparoscopic conventional vs. NOSE colectomy (133)

All patients were placed in the modified dorsal lithotomy position. Pneumoperitoneum was induced by inserting a Veress needle (Karl Storz, Tuttlingen, Germany) into the

umbilicus. A 4-port approach was used. Subsequently, the patient was placed in the steep Trendelenburg position. During the procedures, adhesiolysis was implemented for mobilization of the rectum and sigmoid colon in cases of pelvic adhesions. Ureters were dissected at the level of the uterine arteries. Limited tubular resection in a mesosparing manner close to the bowel was used to preserve the branches of the inferior hypogastric plexus (133).

During the complete intra-abdominal NOSE procedure, after skeletonization and isolation of the affected rectum, the rectum was tied off laparoscopically proximally and distally to the DE nodule with a nonabsorbable suture (Dafilon 0; B Braun AG, Meslungen, Germany). A laparoscopic atraumatic temporary intestinal clamp (Aesculap, Tuttlingen, Germany) was placed to decrease the chance of fecal spillage, cephalad to the resection line. A transverse colostomy was performed in healthy tissue using a harmonic scalpel to deliver the anvil from a circular stapler (Proximatew ILS CDH 29, Ethicon Endo-Surgery), introduced through the anus using a sterile laparoscopic camera sleeve (folded laparoscopic camera sleeve; 3M, St Paul, MN, USA). With the use of a camera sleeve for anvil introduction into the abdominal cavity, the possibility of peritoneal cavity contamination was reduced (93, 133).

A completely transected specimen was extracted transrectally through the camera sleeve in a specimen retrieval bag. The proximal part of the anastomosis was created by suturing the anvil in place with the purse string of a monofilament laparoscopic suture (PDS 2.0; Ethicon, Inc., Cincinnati, OH, USA). The intestinal clamp was removed. The distal rectum was closed by using an endoscopic linear stapler. End-to-end anastomosis was performed by using a circular stapler (133).

With conventional segmental bowel resection, dissection was continued towards the pelvic floor distally to the affected segment. The rectum was then skeletonized using a vessel-sealing device (Harmonic Scalpel ACE; Ethicon Endo-Surgery, Cincinnati, OH) laterally and anteriorly, entering the rectovaginal septum and preserving the posterior wall of the vagina. The distal rectum was closed using an endoscopic linear stapler (Echelon Flex Endopath, Ethicon Endo-Surgery). The mobilized rectum with the specimen was retrieved through a small suprapubic incision. The anvil of a conventional circular stapler was introduced into the proximal colon following the placement of a purse-string suture (PDS 2.0; Ethicon, Inc., Cincinnati, OH, USA). Circular stapled colorectal end-to-end anastomosis was then performed (Proximatew ILS CDH 29) (133).

At the end of both procedures, extensive saline irrigation was performed, and the integrity of the suture line at the distal rectum was verified using the Michelin test. A drain was conventionally left in place in the pouch of Douglas (79, 93).

The perioperative care was similar in patients from both arms of the study, as the participants received the same medication and nursing technique (133).

LTADE was performed using transanal staplers (semicircular staplers) or directly through the vagina in cases of vaginal infiltration. The procedure began with rectal shaving. If the anterior rectal wall at the shaved site remained infiltrated, it felt rigid and thickened during palpation with a laparoscopic probe. In these instances, complete treatment was achieved through full-thickness disk excision using a concomitant transanal approach. The colorectal surgeon utilized the Contour Transtar (Ethicon Endo-Surgery) stapler when the shaved area was located less than 7 cm above the anus. The thinner and softer the shaved rectal wall, the larger the diameter of the rectal patch that could be excised with the transanal stapler (79).

4. Results

4.1. Demographic data

A total of 91 patients were enrolled in the study between September 30, 2019, and December 31, 2020, at University Hospital, with 42 randomly assigned to the NC arm and 49 assigned to the CLR arm. One patient was lost to follow-up (Figure 2) (133).

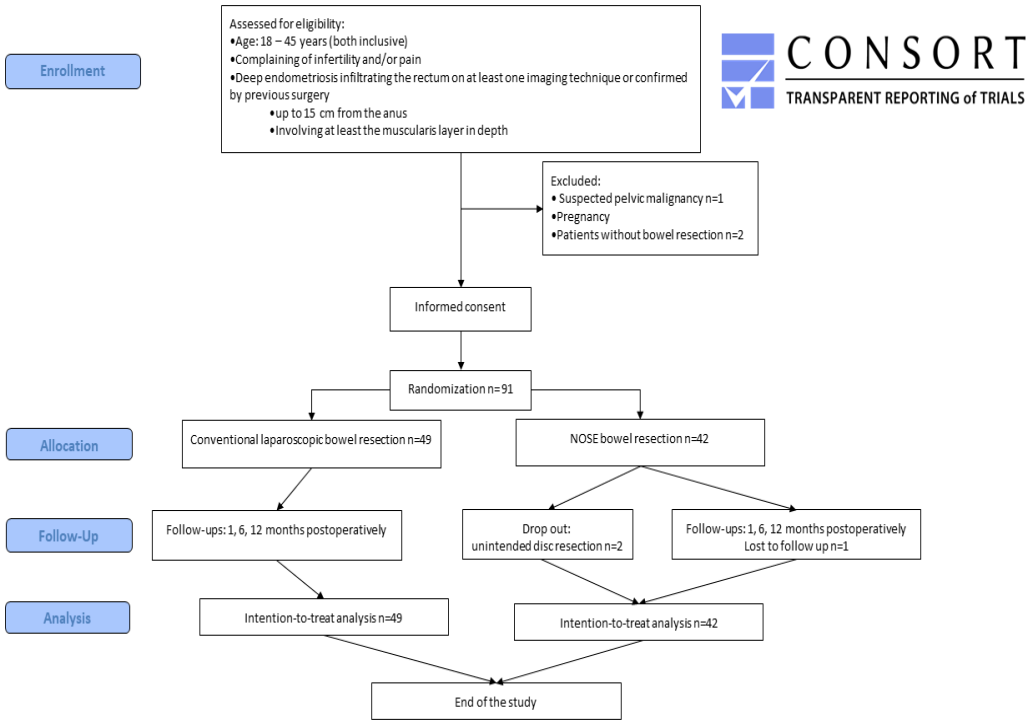

Figure 2. Flow diagram (CONSORT 2010) (145) for study of patients who underwent NOSE or conventional laparoscopic segmental resection for rectal DE (133).

Demographic and clinical characteristics of the participants are shown in Table 1. The mean age of the patients in the NC and CLR groups was 35±5 and 34±5 years, respectively. All the patients had one or more pain or intestinal symptoms. Twenty-six patients in the NC group (63.4%) and 35 patients in the CLR group (71.4%) had undergone one or more previous surgeries for endometriosis, excluding colorectal procedures (133).

Table 1.:Demographic data. **Data are n(%) and mean ±SD (133)**

Patients' baseline characteristics	NOSE (n=42)	Conventional (n=49)
Age (years)	35±5	34±5
BMI (kg/m2)	21±3	23±4
ASA score		
I.	29 (70.7%)	32 (65.3%)
II.	12 (29.3%)	17 (34.7%)
Infertility	14 (34.1%)	20 (40.8%)
Previous surgeries for endometriosis		
NO surgery	15 (36.6%)	14 (28.6%)
1 surgery	17 (41.5%)	17 (34.7%)
2 or more surgeries	9 (21.9%)	18 (36.7%)
Type of previous surgeries		
No of patients with previous surgeries	26 (63.4%)	35 (71.4%)
Previous laparoscopy	23 (56.1%)	32 (65.3%)
Previous laparotomy	7 (17.1%)	12 (24.4%)
Previous pregnancy/delivery		
Pregnancy	12 (29.3%)	12 (24.4%)
Delivery	9 (21.9%)	5 (10.2%)

Between October 2009 and December 2018, a total of 1,494 patients (RUH, n = 831; SU, n = 407; HJGWH, n = 256) underwent surgery for bowel endometriosis. Among these patients, 211 were diagnosed with low colorectal deep infiltrating endometriosis (DE) and underwent either NVSSR (n = 140) or LTADE (n = 71). Data from 205 consecutive patients were available for final analysis, with a median follow-up period of 46 ± 11 months. The prevalence of preoperative infertility was significantly higher in the NVSSR group compared to those undergoing LTADE (P < .001). However, no differences were observed in pain symptoms, except for dyspareunia. The mean age was 29.9 ± 4.2 years for LTADE and 32.6 ± 4.9 years for NVSSR (76). The patients' characteristics are found in Table 2 (79).

Table 2.: Patient characteristics (79)
Mann-Whitney *U* and Pearson chi-squared tests were used.

	LTADE		NVSSR		
	n	**%**	**n**	**%**	
Characteristics	**66**	**32.2**	**139**	**67.8**	***P* value**
Age (y), mean ± SD	29.9 ± 4.2		32.6 ± 4.9		<.000
BMI (kg/m2), mean ± SD	23.3 ± 4.6		24.1 ± 3.9		.42
Obstetrical history					
Parity, mean ± SD	0.25 ± 0.64		0.30 ± 0.58		.51
Gravidity, mean ± SD	0.53 + 0.93		0.44 + 0.83		.304
Previous gynecological surgeries					
Laparotomies	3	4.5	19	13.7	.001
Laporoscopies					
1	17	25.8	45	32.4	.31
≥ 2	10	15.2	23	16.5	.879
Preoperative subfertility	18	27.3	82	59.0	<.000
Preoperative cyclic symptoms					
Dysmenorrhea	66	100	136	97.8	.241
Intensity of dysmenorrhea (VAS > 4)	63	95.5	131	94.2	.81
Dyspareunia	63	95.4	110	79.1	.007
Intensity of dyspareunia (VAS > 4)	41	63.6	83	59.7	.34
Dyschezia	51	77.2	84	60.4	.045
Intensity of dyschezia (VAS > 4)	36	54.5	71	51	.507

4.2. Intraoperative findings

Table 3 presents intraoperative findings. The anatomical distribution of the DE lesion sites was similar in both groups. There was no difference in the length of hospital stay between the NC and CLR groups (5,3±3 days in the NC group versus 5,7±2 days in the CLR group). All cases were confirmed by histological examination. The intraoperative classification of endometriosis was performed according to the rASRM and ENZIAN classification systems during all procedures (37, 146), see Tables 3 and 4 (133).

Table 3.:Intraoperative findings. **Data are n(%) and mean ±SD (133)**

		NOSE (n=42)	Conventional (n=49)	p value
Operative time (min)		139±97	147±76	0.7
Hospital stay (day)		5.3±3	5.7±2	0.2
Blood loss (ml)		22±16	24±22	0.4
Localisation of deep nodules of the digestive tract				
	rectum	34 (82.9%)	42 (85.7%)	0.3
	sigmoid/rectum junction	5 (12.2%)	7 (14.3%)	0.5
	sigmoid	9 (21.9%)	7 (14.3%)	0.09
	sigmoid and appendix	2 (4.8%)	2 (4.0%)	0.6
	ileum	0 (0.0%)	6 (12.2%)	0.03
	coecum	2 (4.8%)	6 (12.2%)	0.2
Segmental resection of ileum/coecum		2 (4.8%)	12 (24.4%)	0.7
Appendectomy		2 (4.8%)	2 (4.0%)	0.1
Omental/Mesorectal flap		3 (7.3%)	2 (4.0%)	0.9
Protective colostomy		0 (0.0%)	1 (2.0%)	0.6
Diameter of largest rectal nodule (mm)		27±3.8	29±2.5	0.5
Deepest infiltration of the rectum				
	mucosa	5 (12.2%)	2 (4.0%)	0.5
	submucosa	8 (19.5%)	6 (12.2%)	0.9
	muscularis	28 (68.3%)	41 (83.8%)	0.2
Height of the lowest nodule (from the anal verge)				
	below 7cm	19 (46.3%)	20 (40.8%)	0.8
	above 7cm	22 (53.7%)	29 (59.2%)	0.6
Length of the removed bowel segment (mm)		67±2.7	83±3.8	0.06
ASRM score		51±24	47±17	0.8
Concomitant management of				
	ovarian endometrioma	12 (29.3%)	15 (30.6%)	0.5
	bladder nodule	11 (26.8%)	10 (20.4%)	0.3
	rectovaginal space DE	30 (73.2%)	43 (87.7%)	0.2
	vaginal inflitration	14 (34.1%)	19(38.7%)	0.4
	peritoneal disease	39(95.1%)	47 (95.9%)	0.3
	ureteral DE	0 (0.0%)	7 (14.3%)	0.02
EFI score		4.8±2.1	5.2±1.8	0.3
Patency of Fallopian tubes				
	Unilateral occulusion	4 (9.8%)	15 (30.6%)	0.007
	Bilateral occlusion	20 (48.7%)	18 (36.7%)	0.2
	Patent	17 (41.5%)	16 (32.7%)	0.1

Table 4.:Intraoperative findings. **Data are n(%) (133)**

ENZIAN	**NOSE (n=42)**	**Conventional (n=49)**	**p value**
Compartment A	30 (73.2%)	43 (87.7%)	0.1
Compartment B	15 (36.6%)	12 (24.4%)	0.9
Compartment C	42 (100%)	49 (100%)	n.a
Compartment FA	27 (65.9%)	25 (51.0%)	0.8
Compartment FB	11 (26.8%)	10 (20.4%)	0.3
Compartment FU	0 (0.0%)	7 (14.3%)	0.02
Compartment FI	13 (31.7%)	21 (42.9%)	0.7
Compartment FO	1 (2.4%)	3 (6.1%)	0.9

In our retrospective, international, multicenter cohort analysis, the anatomical distribution of endometriotic DE lesion sites was similar in both groups. The length of the resected bowel section ranged from 5 to 19 cm, with an average length of 8 cm (±6 cm) in the NVSSR cases. Most patients had endometriosis present in areas outside the colorectal region. The frequency of extra-colonic localization of endometriotic lesions was comparable between both groups, with the most common sites being the rectovaginal septum, pelvic peritoneum, bladder, ureters, and ovaries (79).

In the LTADE and NVSSR groups, 57 out of 66 patients (86%) and 111 out of 139 women (79%), respectively, required vaginal resection due to vaginal involvement (P = .391). There was no statistically significant difference in the duration of surgeries between the LTADE group and the NVSSR group, with recorded times of 218 minutes (±71.4) and 225 minutes (±71.4), respectively (P = .58). The mean revised American Fertility Society (rAFS) score was 53.4 ± 30.1 in the LTADE group and 67.2 ± 37.8 in the NVSSR group (79). See Table 5.

Table 5.: Intraoperative findings (79)
Comparison between the two surgical techniques using the Fisher exact, Pearson chi-squared and Mann-Whitney *U* tests.

	LTADE		NVSSR		
	n	**%**	**n**	**%**	
	66	**32.2**	**139**	**67.8**	***P* value**
Operative time (min), mean ± SD	218.6 ± 71.4		225.5 ± 96.1		.58
Surgical approach					
Laparotomy	0	0.0	4	2.9	.05
Laparoscopy	66	100	135	97.1	.673
Revised rAFS score, mean ± SD	53.4 ± 30.1		67.2 ± 37.8		
rAFS stage I	0	0.0	1	0.7	.49
rAFS stage II	11	16.7	9	6.5	.022
rAFS stage III	6	9.1	18	12.9	.42
rAFS stage IV	49	74.2	111	79.9	.364
Rectal DE lesion size					
10-29 mm	12	18.1	38	27.4	.154
>30 mm	54	81.9	101	72.6	
Rectovaginal endometriosis	65	98.4	131	94.2	.391
Ovarian endometriosis	41	62.1	103	74.1	.137
Temporary diverting stoma					
Ileostomy	2	3.0	4	2.9	.37
Colostomy	49	72.2	45	32.3	<.001
Additional surgical digestive procedures					
Sigmoid colon resection	11	16.6	0	0	.000
Appendectomy	4	6.0	10	7.1	.462
Vaginal opening/resection	57	86.3	111	79.8	.37
Urinary tract procedures					
Resection of bladder DE	8	12.1	22	15.8	.54
Ureteral resection and reanastomosis	6	9.0	24	17.2	.071
Ureteral neoimplantation	1	1.5	3	2.1	.316

4.3. Postoperative scores

There was no statistically significant difference in the change in LARS, GIQLI, EHP30, and VAS scores between the NOSE and conventional treatment groups 12 months after surgery when compared to preoperative values (T3 minus baseline). See Table 6.

The results of follow-up assessments for each time point (T0, T1, T2, and T3) are depicted in Table 7, 8, 9 (133).

Table 6.:Clinical assessment 12 months after surgery. T0: preoperative, T3:12 months after surgery (133).
Mann-Whitney U test was used.

		NOSE (n=42)	Conventional (n=49)	p value
LARS delta T3-T0		-5,93±10,58	-6,80±11,50	0.923
Min-max		-24-18	-34-16	
GIQLI delta T3-T0		18,03±19,51	15,07±20,75	0.654
Min-max		-10-70	-27-70	
EHP30 delta T3-T0				
	Pain	-23,01±23,85	-21,21±22,18	0.666
	Min-max	-70,45-25	-63,64-18,18	
	Emotional well-being	-26,21±24,08	-23,00±24,97	0.356
	Min-max	-70,83-41,67	-75-29,17	
	Control and powerlessness	-34,35±26,79	-29,77±27,89	0.375
	Min-max	-91,67-25	-87,50-29,17	
	Sexuality	-21,40±28,49	-29,90±31,75	0.900
	Min-max	-95-40	-90-60	
	Self Image	-24,18±26,07	-18,75±26,77	0.311
	Min-max	-91,67-8,33	-90-60	
	Social support	-20,79±25,56	-22,02±23,17	0.865
	Min-max	-75-30	-70-10	
VAS scores delta T3-T0	***Dysmenorrhea***	-2,41±3,94	-3,25±4,37	0.510
	Min-max	-9,65-6,78	-10-6,21	
	Chronic pelvic pain	-4,29±3,50	-3,27±4,10	0.331
	Min-max	-10-3,36	-10-7,11	
	Dyspareunia	-3,79±3,45	-3,42±3,91	0.903
	Min-max	-10-17	-10-8,3	
	Dysuria	-0,52±1,58	-0,16±2,04	0.270
	Min-max	-8-1,73	-6-8,08	
	Dyschezia	-2,99±3,54	-3,60±4,27	0.281
	Min-max	-10-4,90	-10-7,75	

Table 7.:Pre- and postoperative assessment of functional and quality of life outcomes in each timepoint after NOSE colectomy.
Mann-Whitney U test was used.

Questionnaires	NOSE (n=42)							
	T0		T1		T2		T3	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
LARS	22.2	11.7	26.36	9.09	17.79	9.66	16.33	14.18
GIQLI	96.17	16.07	99.88	19.28	111.44	14.64	112.13	16.8
EHP 30								
Pain	31.7	26.3	17.95	16.48	8.31	13.88	6	9.2
Emotional well-being	43.4	23.4	19.79	15.35	19.00	20.09	17.4	15.8
Control and powerlessness	45.9	26.5	15.21	17.44	13.01	16.65	11.4	16.2
Self Image	37	26.5	26.46	23.86	16.67	21.41	12.6	15
Social support	24.3	24.6	19.48	24.43	7.16	12.28	5.1	9.1
Sexuality	36.1	34.9	13.33	18.39	17.42	26.07	12.3	20.5
VAS scores								
Dysmenorrhea	4	1.9	3	2.8	2	2.8	3	2.1
Chronic pelvic pain	6	5.2	2	3.1	2	2.4	3	2.2
Dyspareunia	6	4.2	1	1.9	1	2.6	3	3.1
Dysuria	3	5.8	2	2.4	1	1.2	1	1.7
Dyschezia	6	4.4	2	2.4	1	2.4	3	2.1

Table 8.:Pre- and postoperative assessment of functional and quality of life outcomes at each timepoint after conventional laparoscopic bowel resection.
Mann-Whitney U test was used.

Questionnaires	Conventional (n=49)							
	T0		T1		T2		T3	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
LARS	21.41	10.2	21.88	11.30	17.12	11.45	17.9	11.18
GIQLI	95.44	23.11	102.06	19.77	110.76	16.78	111.39	18.48
EHP 30								
Pain	30.8	25.5	21.52	19.59	7.88	14.83	10.2	14.2
Emotional well-being	38.9	25.5	16.58	15.06	17.60	18.29	16.6	17.7
Control and powerlessness	41.1	31.9	18.20	21.00	10.54	16.30	12.2	16.5
Self Image	37	31.8	22.96	21.21	14.80	20.29	18	23.9
Social support	31.6	31	22.64	29.41	8.21	17.28	6.9	14.4
Sexuality	43.9	34.5	12.40	20.01	17.78	23.10	19.1	25.3
VAS scores								
Dysmenorrhea	5	5.1	3	3.3	1	2.2	4	3.1
Chronic pelvic pain	7	3.3	3	3.0	2	2.7	2	2.3
Dyspareunia	6	4.5	1	1.4	1	1.9	3	2.5
Dysuria	2	5.8	2	3.0	1	1.3	1	2.8
Dyschezia	5	4.7	2	3.3	1	2.7	2	1.7

Table 9.:Pre- and postoperative assessment of functional and quality of life outcomes at each timepoint after conventional laparoscopic bowel resection and NOSE colectomy

Questionnaires	NOSE vs Conventional			
	T0 vs T0	T1 vs T1	T2 vs T2	T3 vs T3
	p value	p value	p value	p value
LARS	0.799	0.051	0.826	0.339
GIQLI	0.914	0.776	0.960	0.473
EHP 30				
Pain	0.678	0.575	0.398	0.150
Emotional well-being	0.389	0.286	0.803	0.925
Control and powerlessness	0.552	0.771	0.384	0.767
Self Image	0.763	0.487	0.519	0.845
Social support	0.431	0.924	0.952	0.971
Sexuality	0.353	0.547	0.590	0.195
VAS scores				
Dysmenorrhea	0.455	0.471	0.374	0.777
Chronic pelvic pain	0.791	0.702	0.912	0.286
Dyspareunia	0.851	0.188	0.766	0.612
Dysuria	0.700	0.950	0.964	0.443
Dyschezia	0.167	0.466	0.607	0.473

4.3.1. LARS

The LARS scores (see Table 10, 12) did not reveal significant differences 12 months after the operation compared to the baseline values in both groups (NC: T0=22.2±11.7, T3=16.33±14.18, p=0.87; CLR: T0=21.41±10.2, T3=17.90±11.1, p=0.934) (133).

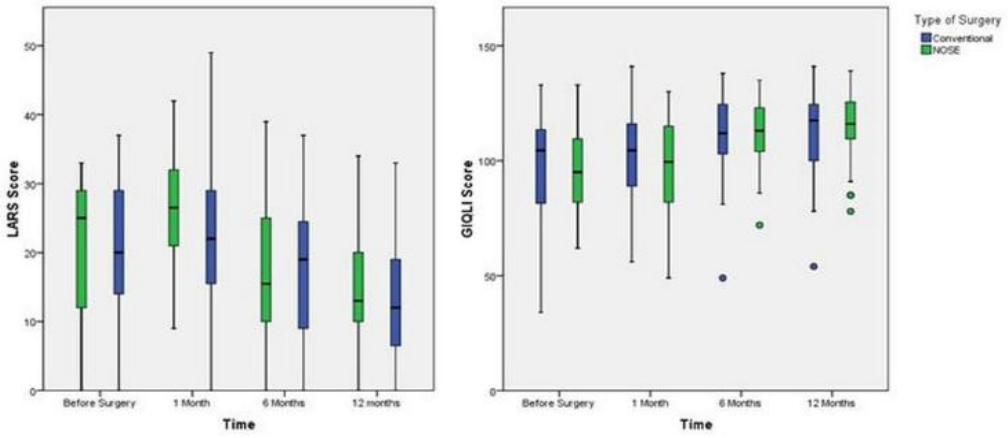

Figure 3. presents pre-, and postoperative GIQLI and LARS scores. Blue column: Conventional surgery, green column: NOSE surgery (133).

Table 10.: Preoperative and postoperative assessment of digestive function and quality of life after NOSE surgery (133).
T0: preoperative, T3: 12 months after surgery. Mann-Whitney U test was used.

Questionnaires	NOSE (n=42)				
	T0		T3		p value
	Mean	SD	Mean	SD	
LARS	22.2	11.7	16.33	14.18	0.87
GIQLI	96.17	16.07	112.13	16.8	0.001
EHP 30					
Pain	31.7	26.3	6	9.2	0.001
Emotional well-being	43.4	23.4	17.4	15.8	0.001
Control and powerlessness	45.9	26.5	11.4	16.2	0.016
Self Image	37	26.5	12.6	15	0.001
Social support	24.3	24.6	5.1	9.1	0.000
Sexuality	36.1	34.9	12.3	20.5	0.043
VAS scores					
Dysmenorrhea	4	1.9	3	2.1	0.03
Chronic pelvic pain	6	5.2	3	2.2	0.004
Dyspareunia	6	4.2	3	3.1	0.0001
Dysuria	3	5.8	1	1.7	0.04
Dyschezia	6	4.4	3	2.1	0.0003

In our retrospective multicenter cohort study, there was no statistically significant difference in the incidence of LARS between patients undergoing LTADE and those treated with NVSSR, with rates of 31.7% and 37.9%, respectively (P = 0.4). The prevalence of major LARS in the LTADE group was recorded at 16.7%, which is comparable to the 12.2% observed in the NVSSR group (P = 0.6). Furthermore, the occurrence of major LARS was positively associated with the use of protective colostomy (P = 0.02) (79). See Table 11.

Table 11.: Bowel function after laparoscopic-transanal disk excision and nerve- and vessel-sparing segmental resection (79)
Comparison between the two surgical techniques using the Fisher's exact and Pearson chi-squared tests.
LARS score, range 0-42: 0-20, no LARS; 21-29, minor LARS; 30-42, major LARS.

	LTADE		**NVSSR**		
	n	**%**	**n**	**%**	
	66	**32.2**	**139**	**67.8**	***P* value**
Do you ever have occasions when you cannot control your flatus (wind)?					
No, never	26	39.3	72	52.2	.056
Yes, less than once per week	18	27.2	30	21.5	
Yes, at least once per week	22	33.3	37	26.6	
Do you ever have any accidental leakage of liquid stool?					
No, never	55	83.3	122	87.7	.118
Yes, less than once per week	8	12.1	12	8.6	
Yes, at least once per week	3	4.6	5	3.7	
How often do you open your bowels?					
More than 7 times per day (24 h)	1	1.5	5	3.5	.23
4-7 times per day (24 h)	2	3	20	14.3	
1-3 times per day (24 h)	31	46.9	67	48.2	
Less than once per day (24 h)	32	48.4	47	33.8	
Do you ever have to open your bowels again within 1 h of the last bowel opening?					
No, never	30	45.4	39	28	.071
Yes, less than once per week	16	24.2	54	38.8	
Yes, at least once per week	20	30.4	46	33.1	
Do you ever have such a strong urge to open your bowels that you have to rush to the toilet?					
No, never	33	50	57	41	.068
Yes, less than once per week	22	33.3	56	40.2	
Yes, at least once per week	11	16.6	26	18.7	
LARS score					
No LARS	41	62.1	95	68.3	.6
Minor LARS	14	21.2	27	19.4	
Major LARS	11	16.7	17	12.2	
LARS score, median	19		20		

4.3.2. EHP30

The EHP30 scores (see Tables 10 and 12) significantly improved 12 months after the operation compared to the preoperative values in both groups. The overall GIQLI,

EHP30, and LARS scores did not reveal significant differences between the two arms 12 months after surgery (133).

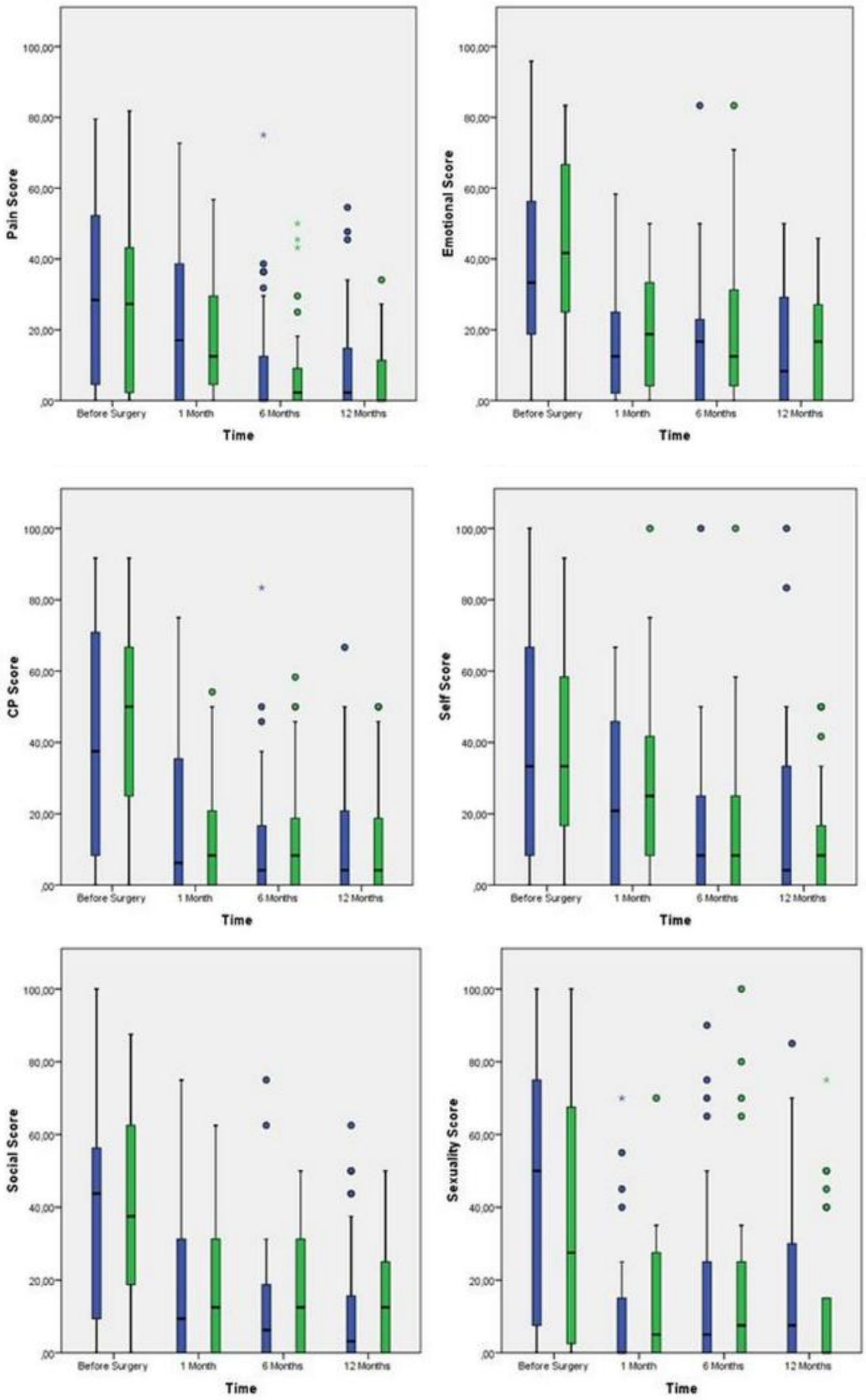

Figure 4. presents pre-, and postoperative EHP30 scores scores. Blue column: Conventional surgery, green column: NOSE surgery (133).

4.3.3. GIQLI

GIQLI (see Table 10, 12) significantly improved 12 months after the operation compared with the baseline values in both groups NC: T0=96.17±16.07, T3=112.13±16.8, p=0.001, and CLR: T0=95.44±23.1, T3=111.39±18.4, p=0.002 (133).

Table 12.:Preoperative and postoperative assessment of digestive function and quality of life after conventional surgery (133).
T0: preoperative, T3: 12 months after surgery. Mann-Whitney U test was used.

Questionnaires	Conventional (n=49)				
	T0		T3		p value
	Mean	SD	Mean	SD	
LARS	21.41	10.2	17.9	11.18	0.934
GIQLI	95.44	23.11	111.39	18.48	0.002
EHP 30					
Pain	30.8	25.5	10.2	14.2	0.001
Emotional well-being	38.9	25.5	16.6	17.7	0.01
Control and powerlessness	41.1	31.9	12.2	16.5	0.014
Self Image	37	31.8	18	23.9	0.000
Social support	31.6	31	6.9	14.4	0.000
Sexuality	43.9	34.5	19.1	25.3	0.003
VAS scores					
Dysmenorrhea	5	5.1	4	3.1	0.24
Chronic pelvic pain	7	3.3	2	2.3	0.0001
Dyspareunia	6	4.5	3	2.5	0.0001
Dysuria	2	5.8	1	2.8	0.27
Dyschezia	5	4.7	2	1.7	0.0001

4.3.4. VAS

Regarding pain symptoms, the chronic pelvic pain, dyspareunia, and dyschezia VAS scores were significantly improved in both groups compared with the baseline scores one year after surgery (chronic pelvic pain: NC T0=6±5.2, T3=3±2.2, p=0.004; CLR: T0=7±3.3, T3=2±2.3, p=0.0001; dyspareunia: NC T0=6±4.2, T3=3±3.1; p=0.0001; CLR: T0=6±4.5, T3=3±2.5, p=0.0001; dyschezia: NC T0=6±4.4, T3=3±2.1, p=0.0003; CLR: T0=5±4.7, T3=2±1.7, p=0.0001). We found statistically significant decreases in the intensity of dysmenorrhea (T0=4±1.9, T3=3±2.1, p=0.03) and dysuria (T0=3±5.8, T3=1±1.7, p=0.04) after one year of follow-up in the NC group (133). See Tables 10 and 12.

4.4. Infertility assessment

During the 14±2.6 months of follow-up, 22 patients with active child wishes achieved pregnancy in the NC arm (21%) and 14 in the CLR arm (29%) (p=0.867). Two (4%) and

two (5%) conceived spontaneously. Seven (NC group, 18%) and seven (CLR group, 14%) live births were reported in both groups (133).

4.5. Postoperative complications

When comparing the NC and CLR groups concerning the rates of grade I and II postoperative complications, no statistically significant difference was found. According to the Clavien-Dindo classification, we observed two severe (grade III or higher) complications (2.27%): one anastomotic leakage in the NC group and one rectovaginal fistula in the CLR group (146). These were managed with a covering ileostoma repair. Intestinal continuity was restored within three months (133). The postoperative complications are depicted in Table 13.

Table 13.:Postoperative surgical complications (133).
Data are n(%). Fisher exact test has been executed.

Complications according to Clavien-Dindo classification		NOSE (n=42)	Conventional (n=49)	p value
I.	Bladder atony (max 7 days)	5 (11.9%)	4 (8.1%)	0.739
	Fever	4 (9.52%)	3 (6.1%)	0.705
	Clostridium difficile infection	4 (9.52%)	3 (6.1%)	0.705
II.	Rectal bleeding	2 (4.76%)	2 (4.1%)	n.a
	Ileus	0 (0.0%)	1 (2.0%)	n.a
III.	Anastomotic leakage	1 (2.38%)	0 (0.0%)	n.a
	Rectovaginal fistula	0 (0.0%)	1 (2.0%)	n.a
IV.		0 (0.0%)	0 (0.0%)	n.a.

In our multicenter cohort study, according to the Clavien-Dindo classification, we observed an overall severe complication rate (grade IIIb or higher) of 28.6% among 205 patients. Anastomotic leakage was noted in 2 out of 139 (1.4%) patients in the NVSSR group, while none occurred in the LTADE group (P = 0.3) (79). However, there was a significantly higher incidence of rectovaginal fistulae in the LTADE group (10.6%) compared to the NVSSR group (3.6%, P = 0.04). When comparing the LTADE and NVSSR groups regarding the rates of grade I postoperative complications, we found no statistically significant difference (P =0.55). Additionally, a case of bowel stenosis was reported in the LTADE group following a concomitant segmental sigmoid resection at the level of the anastomosis of the sigmoid colon, which was not associated with the large rectal disk excision (79). Data are shown in Table 14.

Table 14.: Postoperative complications according to Clavien-Dindo (79)
Comparison between the two surgical techniques using the Fisher exact test

	LTADE		NVSSR		
	n	**%**	**n**	**%**	
Clavien-Dindo complications	**66**	**32.2**	**139**	**67.8**	***P* value**
Grade I	3	4.5	7	5.03	.098
Grade II					
Bladder atony after 7 d requiring self-catheterization	11	16.7	9	6.49	.001
Grade III-IV					
Rectovaginal fistula	7	10.6	5	3.6	.04
Stenosis of rectal lumen, requiring additional procedure	1	1.5	0	0	.14
Anastomosis leakage	0	0	2	1.4	.3
Pelvic abscess	6	9	3	2.1	.007
Pyosalpinx	0	0	1	0.7	.5
Stenosis of the ureteral anastomosis	0	0	1	0.7	.5
Ureteral fistula	0	0	1	0.7	.5

5. Discussion

To the best of our knowledge, this is the first prospective randomized study on bowel function, quality of life, and pain outcomes of two different specimen extraction techniques for the surgical treatment of recto-sigmoidal DE (133).

We observed no statistically significant difference in the occurrence of LARS and GIQLI scores in our cohort of patients who underwent either the NOSE technique or the conventional nerve- and vessel-sparing bowel resection after one year of follow-up. We found no evidence confirming the superiority of the NOSE technique over conventional laparoscopic segmental resection in terms of bowel function and quality of life (133).

The complex of symptoms consisting of incontinence due to flatus and/or feces, constipation, and frequent bowel movements is referred to as LARS. However, little is known about the exact cause of LARS. Several studies have addressed the symptoms of LARS, but significant variability exists in the reporting of outcomes after anterior resection (133, 147).

Riiskjaer et al., in their prospective observational study (78), reported a significant increase in the frequency of defecation one year after surgery, probably as a result of decreased reservoir capacity. The mean overall LARS score was not significantly different 1 year after surgery. Most patients had minor/major LARS, both before and after surgery. Our study assessed the occurrence of LARS both pre- and postoperatively and found no statistical difference between the extent of LARS before and after surgery in the investigated cohort of women (133).

In the prospective cohort trial by Hudelist et al. comparing segmental and disc resection, they did not observe significant differences in long-term functional outcomes regarding minor or major LARS ($p=0.48$ and $p=0.66$, respectively) (72). These findings are in line with those previously reported by our group (79). In agreement with recent findings (75, 78), we would like to emphasize that impaired bowel function alone should not be an indication for bowel surgery (133).

In the present study, GIQLI scores were comparable in both groups and showed a statistically significant improvement over time from the baseline values until 1 year after surgery in the NC group ($p=0.001$) and CLR group ($p=0.002$). This is consistent with Roman et al. (75), who observed improved and comparable GIQLI-scores one year after anterior segmental resection compared to disc excision.

Similar to previously published data (47, 72, 75, 79, 148), our results confirm that radical excision of colorectal DE improves the quality of life and lowers pain scores (133).

As secondary outcomes, we assessed the occurrence of major surgical complications, time to recovery, and length of hospitalization. Our data correlate with previously reported data (93, 148); however, we could not confirm the shorter hospital stay and lower postoperative pain scores after NOSE colectomy in our cohort of patients (133).

Recently, a meta-analysis by Liu et al. reported that the incidence of anastomotic leakage for the NOSE group was 3.6% compared to 5% in the conventional laparoscopic group (102). Another meta-analysis by Ma et al. showed that laparoscopic resection with NOSE resulted in fewer postoperative complications (100). From the pooled data of the two meta-analyses, the incidence of anastomotic leakage was not significantly different between the two groups. Thus, we conclude that laparoscopic colorectal surgery with NOSE is as safe as conventional laparoscopic surgery. Previous studies have reported faster gastrointestinal recovery, less post-operative pain, and shorter hospital stays following laparoscopic colorectal surgery with NOSE (85, 93, 98). The results of two recently published meta-analyses also suggested that the NOSE group had less post-operative pain and shorter hospital stays than the conventional laparoscopic anterior resection group (100-102). In the aforementioned meta-analyses, the use of the NOSE technique was clearly associated with a shorter hospital stay, less postoperative pain, and fewer perioperative complications, although this was not confirmed in our study (133).

In agreement with recent findings(75, 78), we would like to underline the fact that impaired bowel function alone should not be an indication for bowel surgery since we noted the presence of different degrees of LARS in the majority of our patients preoperatively and the LARS scores did not significantly change after surgery (133).

Keane et al. recently defined LARS using a robust methodology that includes multiple stakeholders. This innovative approach suggested that both symptoms and consequences are important priorities in LARS (149). These important priorities may lead to better identification of patients who experience bowel dysfunction and offer a better perception of LARS in the future. Moreover, further research is needed to elucidate the underlying mechanism of the presence of LARS before colorectal resection (133).

In the present study, the difference between specimen extraction techniques after colorectal resection for DE had no effect on the functional/surgical outcome or quality of life.

The wider implication of our study is that NOSE colectomy offers the same benefits regarding bowel function, amelioration of pain symptoms, and quality of life as conventional laparoscopic anterior resection. Furthermore, after both procedures, the occurrence of LARS was lower than that previously reported (78, 116), and was similar to our recently published multicentric data (79, 133).

As all surgeries were performed by the same surgical team, it is less likely that unbalanced patient enrollment significantly affected the outcomes.

An obvious study limitation was our lack of blinding; however, this was not feasible because of the clinical nature of our study. The simple randomization method used in our study represents another limitation because it resulted in unequal study groups.

We report no imprecision in patient selection or detection, but a potential source of attrition bias in our data occurred in one case (loss to follow-up) exclusively in the NOSE group (133).

In our retrospective multicenter cohort analysis, we presented the first study comparing the outcomes of two surgical approaches for treating endometriosis (DE) infiltrating the low rectum (within 7 cm of the anal verge). While different rates of rectovaginal fistula development were observed, the techniques appear comparable in terms of other major complications and the occurrence of Low Anterior Resection Syndrome (LARS). In addition to the established benefits of surgical intervention for DE with associated colorectal involvement—such as alleviation of pain symptoms and improved pregnancy rates (65) for both spontaneous and assisted reproductive techniques—there is a risk of significant complications. Therefore, understanding the potential risk factors that may exacerbate surgery-related complications is critical, given that endometriosis is a benign, non-life-threatening condition, in contrast to cancer surgery. Consequently, various studies have sought to assess the pros and cons of conservative techniques, such as rectal shaving and discoid resection, alongside more radical options like segmental bowel resection, which is typically performed in a more extensive manner for rectal cancer (79).

It should be noted that there is currently no consensus or evidence regarding the optimal approach for performing segmental resection for rectal deep endometriosis. Various adaptations, including autonomic nerve preservation and the maintenance of nerves, mesorectal fat, and vessels, have been described and may provide benefits related to both

short- and long-term complications associated with bowel surgery. Our observations highlight the significant risk of major complications within this patient population, with an overall complication rate of 28.6%. This statistic must be taken into consideration when deciding on surgical treatment for low-lying rectovaginal deep endometriosis (DE). Although we found no differences in the occurrence of anastomotic leakage, patients who underwent LTADE demonstrated significantly higher rates of rectovaginal fistulae compared to those who had NVSSR (10.6% vs. 3.6%), despite a similar incidence of concomitant vaginal resection in both groups (79).

Nonetheless, due to the non-randomized and retrospective design of this study, caution should be exercised in interpreting these differences. Additionally, patients undergoing LTADE typically present with large rectal lesions (greater than 3 cm) and anastomotic heights between 4 and 5 cm, which may further elevate the risk of fistula formation. Importantly, we found no significant difference in the occurrence of LARS between patients who underwent LTADE and those who underwent NVSSR. One might speculate that the preservational effects of LTADE and NVSSR on autonomic nerve supply and large and small vessel perfusion could be comparable. When considering LARS, it is essential to acknowledge that digestive complaints may also be present before surgery in women with extensive rectal DE (78). Furthermore, large DE lesions affecting the parametrium can impact both bladder and rectal function by irritating the inferior hypogastric plexus. According to Riiskjaer et al., a significant proportion (73.5%) of patients reported experiencing symptoms consistent with minor or major LARS post-surgery; however, this was also evident prior to the surgical intervention (78).

A recent study by Juul et al. (150) found that major LARS (scores >30) are prevalent in the general population, affecting approximately 9.9% to 17.2% of individuals, including women aged 20-45. Therefore, it is essential to consider normative data for LARS when interpreting results from studies assessing bowel function following rectal surgery for DE. One significant limitation of our study is the absence of preoperative assessments of LARS within our cohort. Additionally, the retrospective design of our study poses a challenge; however, this may be mitigated by prospectively established electronic databases for data collection. While colonic adaptation over approximately 12 months may improve bowel function, a recent meta-analysis confirms that a notable portion of patients continue to experience ongoing issues in the mid and long term. According to Croese et al., (151) the etiology of LARS is complex and likely multifactorial. Impaired anal sphincter function has been observed in patients after low anterior resection, which

may result from both direct injury to the anal sphincter and damage to its innervation. Further research is necessary to investigate follow-up LARS (79).

6. Conclusion

Our data demonstrated that both NOSE and conventional laparoscopic colectomy are safe methods for the surgical treatment of colorectal DE. The occurrence of long-term bowel dysfunction does not appear to be related to a specific surgical technique. The external validity of our outcomes must be investigated in multicenter prospective randomized trials in a larger cohort of patients (133).

The findings of this retrospective multicenter cohort study emphasize the importance of being aware of the surgical risks and potential complications associated with low rectal full-thickness resections, whether performed using conservative or segmental resection techniques. These procedures should only be conducted in tertiary referral centers by well-trained multidisciplinary teams with significant expertise in surgery for deep endometriosis and in managing postoperative complications. Furthermore, long-term bowel dysfunction does not appear to be associated with a specific surgical technique (79).

7. Summary

The conventional laparoscopic approach for the surgical management of deep endometriosis (DE) infiltrating the rectum ensures improved digestive functional outcomes and quality of life. The natural orifice specimen extraction (NOSE) technique for treating colorectal DE can significantly accelerate postoperative recovery, reduce the duration of hospital stay, and result in less postoperative pain and fewer complications (133). However, short- and mid-term solid data on gastrointestinal function following conventional laparoscopic segmental bowel resection (CLR) compared with NOSE-colectomy (NC) for DE are sparse (133). There is increasing evidence that intermediate and long-term bowel dysfunction may arise as a result of radical surgery for deep endometriosis (DE) of the rectum. Numerous studies have indicated that functional outcomes may be more favorable with conservative surgical approaches, specifically, the excision of endometriotic tissue while preserving the luminal structure of the rectal wall, compared to traditional segmental resection techniques for DE, particularly when performed for low DE (79).

Our randomized, open-label, two-arm, parallel-group controlled trial indicates that no significant differences were observed in the NC and CLR groups' postoperative LARS scores, VAS, EHP30, and GIQLI. LARS scores did not reveal significant differences 12 months postoperatively compared to the preoperative values in both groups. GIQLI scores, pain symptoms, and quality of life scores improved significantly 12 months after the operation compared with baseline values in the CLR and NC groups (133).

We found no statistically significant difference between the incidence of LARS (31.7% and 37.9%, respectively) among patients operated by LTADE when compared with NVSSR (P = 0.4). A higher rate of severe complications was observed in women undergoing LTADE (19.7%) when compared with patients with NVSSR (9.0%, P = 0.029) (79).

According to our results, NC is a feasible, effective, and safe surgical approach for treating patients with rectal DE. Our study did not show a statistically significant difference between CLR and NC techniques in mid-term digestive and pain outcomes (133). The incidence of low anterior resection syndrome does not appear to be higher following nerve- and vessel-sparing segmental resection compared to more conservative surgical approaches, such as laparoscopic transanal disc excision, in patients undergoing rectal surgery for low deep infiltrating endometriosis (79).

8. References

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10. Acknowledgements

I am grateful to my supervisor, Dr. Attila Bokor, for always making time for consultations despite his many other responsibilities. His guidance has been extremely helpful, and I am truly thankful for the opportunity to be a part of his research group.

I would like to thank Professor Nándor Ács for his support in obtaining my PhD degree.

I am deeply grateful to Dr. Péter Lukovich for setting me on my scientific path.

I would like to express my gratitude to all the staff at the Department of Obstetrics and Gynecology, Semmelweis University, who tirelessly assisted with patient recruitment and postoperative care, making our study possible despite their demanding clinical duties.

Finally, I am profoundly grateful to my family for their unwavering support throughout my professional journey.

Randomised controlled trial

INTERNATIONAL JOURNAL OF SURGERY

OPEN

Laparoscopic natural orifice specimen extraction colectomy versus conventional laparoscopic colorectal resection in patients with rectal endometriosis: a randomized, controlled trial

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Background: The conventional laparoscopic approach for the surgical management of deep endometriosis (DE) infiltrating the rectum appears to ensure improved digestive functional outcomes. The natural orifice specimen extraction (NOSE) technique for the treatment of colorectal DE can significantly accelerate postoperative recovery; however, data on gastrointestinal function following conventional laparoscopic segmental bowel resection (CLR) compared with NOSE colectomy (NC) for DE are sparse.

Materials and methods: Between 30 September 2019 and 31 December 2020, a randomized, open-label, two-arm, parallel-group controlled trial with women aged 18–45 years was conducted at University Hospital. Ninety-nine patients were randomized to CLR or NC, with DE infiltrating at least the muscular layer, at least 50% of the circumference of the bowel, up to 15 cm from the anal verge, exhibiting pain and bowel symptoms and/or infertility. The primary endpoint was bowel function, represented by low anterior resection syndrome (LARS). Secondary parameters included the Endometriosis Health Profile 30 (EHP30), Gastrointestinal Quality of Life Index (GIQLI), Visual Analog Scale (VAS) scores preoperatively and at set times (1 and 6 months, 1 year) following surgery.

Results: No significant differences were observed in the postoperative LARS scores, VAS, EHP30, and GIQLI between the NC and CLR groups. LARS scores did not reveal significant differences 12 months postoperatively compared to the preoperative values in both groups (CLR group $P = 0.93$ versus NC group, $P = 0.87$). GIQLI scores were significantly improved 12 months after the operation compared with baseline values in the CLR group ($P = 0.002$) and NC group ($P = 0.001$). Pain symptoms and quality of life scores significantly improved 12 months postoperatively in both groups.

Conclusions: NC is a feasible surgical approach for treating patients with rectal DE. Our study did not show a statistically significant difference between CLR and NC techniques in mid-term digestive and pain outcomes.

Keywords: colorectal endometriosis, endometriosis health profile 30, gastrointestinal quality of life index, low anterior resection syndrome, natural orifice specimen extraction

Introduction

Colorectal endometriosis is observed in up to 3–37% of women with a known diagnosis of endometriosis[1,2], and is most commonly located in the rectum or sigmoid colon[3]. Although bowel endometriosis may be entirely asymptomatic, colorectal deep endometriosis (DE) commonly affects health-related quality of life[3–7].

Laparoscopic surgery is the most widely accepted surgical approach in cases of bowel involvement[8–10], but the optimal type of resection remains unresolved[11–14].

Surgical specimen removal after segmental bowel resection can either be accomplished by minilaparotomy or by the natural

HIGHLIGHTS

- Both natural orifice specimen extraction colectomy and conventional laparoscopic colorectal resection equally improve the functional outcomes and the quality of life of patients with deep infiltrating rectal endometriosis.
- Pain symptoms and quality of life were significantly improved 12 months postoperatively compared to the preoperative values in both groups.
- Impaired bowel function alone should not be an indication for the surgical treatment of colorectal endometriosis.

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Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

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International Journal of Surgery (2023) 109:4018–4026

Received 13 June 2023; Accepted 21 August 2023

Supplemental Digital Content is available for this article. Direct URL citations are provided in the HTML and PDF versions of this article on the journal's website, www.lww.com/international-journal-of-surgery.

Published online 14 September 2023

http://dx.doi.org/10.1097/JS9.0000000000000728

orifice extraction technique[15–18]. According to previously published systematic reviews and meta-analyses, the natural orifice specimen extraction (NOSE) procedure is safe, may significantly reduce the duration of hospital stay, accelerate postoperative recovery with a better cosmetic outcome, results in lower postoperative pain, and complication rates[19–21]. Several studies have demonstrated a significant drop in pain scores and amelioration of impaired sexual functioning in women following the surgical resection of colorectal endometriosis; nevertheless, long-term, prospectively collected data on gastrointestinal well-being after segmental bowel resection for DE in a large cohort of patients are sparse[11,22–25].

The primary objective of this study was to report the short-term and medium-term outcomes of bowel function as reflected by the Low Anterior Resection Syndrome (LARS) score[26].

Our secondary outcomes assessed Visual Analog Scale (VAS) scores, Gastrointestinal Quality of Life Index (GIQLI)[27,28], Endometriosis Health Profile 30 (EHP30)[29,30], rate of complications, length of hospital stay, and recovery after NOSE versus conventional nerve and vessel spearing – colectomy for colorectal endometriosis.

Material and methods

This study was designed in accordance with the Declaration of Helsinki and approved by the Institutional Ethical and Review Board of the University for the protection of human subjects (no.: 58723-4/2016/EKU) on 8 December 2016.

We conducted a single-center, randomized, open-label, two-arm, parallel-group controlled trial to assess functional outcomes and endometriosis-related pain changes in women undergoing NOSE colectomy (NC) or conventional laparoscopic resection (CLR) for the management of colorectal DE between 30 September 2019 and 31 December 2020, at University Hospital. The secondary outcomes included complication rates and fertility outcomes. The mean follow-up time was 14 ± 2.6 months.

Inclusion criteria were being clinically diagnosed (by at least one imaging technique or via a previous surgery) as having intestinal deep infiltrating endometriosis up to 15 cm from the anus, involving at least the muscular layer in depth, and at least 50% of the recto-sigmoideal circumference in case of patients complaining of pain and/or infertility, and age 18–45 years. Ongoing pregnancy and suspected malignancy were excluded. Written informed consent was obtained from all patients before randomization.

All selected women underwent clinical examination by a gynecologist experienced in colorectal surgery for endometriosis, as well as a transvaginal ultrasound examination. Transvaginal sonography was performed to assess whether the rectum was involved, and to estimate the depth of rectal wall infiltration according to the IDEA protocol[31]. In case of parametrial involvement a pelvic MRI was also performed. All the surgeries were performed by the same surgical team.

This work has been reported in line with the Consolidated Standards of Reporting Trials (CONSORT, Supplemental Digital Content 1, http://links.lww.com/JS9/A991) Guidelines (Fig. 1)[32].

Theory/calculation

Questionnaires

Patients were asked to complete baseline questionnaires including questions about pelvic organ function, pelvic pain, and quality of life related to endometriosis using the VAS (dysmenorrhea, dyspareunia, dyschezia, dysuria, and chronic pelvic pain), EHP30 (pain, control and powerlessness, emotional well-being, social support, self-image, sexuality)[29,30], the GIQLI[27,28], and the LARS[26] score to assess bowel function preoperatively (T0), and at 30 days (T1), 6 months (T2), and 1 year (T3) postoperatively.

Infertility assessement

The endometriosis fertility index[33] was calculated for each procedure. The clinical pregnancy rates were calculated during the first postoperative year.

Randomization

Assigning patients to NOSE or conventional colorectal resection was based on a randomization list using a simple randomization method. To determine the allocation sequence, computer-based coin flipping (http://www.random.org) was carried out by a staff member with no clinical involvement in the study. Randomization started after the patient had completed all baseline assessments and provided written consent to be enrolled in the trial. Patients were analyzed within the group to which they were allocated, irrespective of whether they had experienced the intended intervention (intention-to-treat analysis).

Blinding in our study was not feasible.

Statistical analysis

The study data were evaluated using descriptive statistical methods such as average, median, range frequency, and distribution. Variables were tested for normality using the Kolmogorov–Smirnov–Lilliefors and the Shapiro–Wilk tests; skewness and kurtosis were also examined. Groups of values without a normal distribution were compared using the Mann–Whitney *U* test, Kruskal–Wallis test, Fisher's exact test, or Wilcoxon signed-rank test. Where the distribution allowed, an independent samples *t*-test was used for continuous variables. The evolution of quality of life and digestive symptoms was tested based on the records at 12 months.

All tests were two-sided, and $P < 0.05$ was accepted as a significant difference. Statistical analyses were performed using IBM SPSS version 17 (IBM Corp.).

Sample size calculations

Based on the results of our previously published[22], multicenter, retrospective study on the data of 205 patients with low rectal endometriosis undergoing laparoscopic surgery, we ascertained that in our center, the mean LARS scores were 29 ± 12 in the CLR group and 21 ± 9 in the NC group at one year postoperatively. In our present study, the randomized case selection enabled us to build a cohort where at least 80% statistical power was set as the target. LARS is the key characteristic/measure of a technique's outcome, supporting the power calculation performed (https://clincalc.com/Stats/SampleSize.aspx) using our previous data. To detect low anterior resection syndrome using the LARS score as a continuous variable by assessing two independent study groups

with a mean of 29 ± 12 for the CLR group and 21 ± 9 for the NC group, a sample size of 70 patients was required with 80% power at 0.05 alpha. Based on our previous experience, we predicted a drop-out/loss to follow-up rate of 22%; therefore, our final sample size was 91 patients.

Surgical procedures

The primary objective of surgery was to achieve visibly complete elimination of all endometriotic lesions, regardless of the technique used. The team included two gynecological surgeons with extensive experience in endometriosis surgery. Nerve-sparing and vessel-sparing techniques were used to preserve the inferior hypogastric plexus, hypogastric nerves, and splanchnic nerves on at least one side.

All patients were placed in the modified dorsal lithotomy position. Pneumoperitoneum was induced by inserting a Veress needle (Karl Storz, Tuttlingen, Germany) into the umbilicus. A 4-port approach was used. Subsequently, the patient was placed in the steep Trendelenburg position. During the procedures, adhesiolysis was implemented for mobilization of the rectum and sigmoid colon in cases of pelvic adhesions. The ureters were dissected at the level of the uterine arteries. Limited tubular resection in a mesosparing manner close to the bowel was used to preserve the branches of the inferior hypogastric plexus.

During the complete intra-abdominal NOSE procedure, after skeletonization and isolation of the affected rectum, the rectum was tied off laparoscopically proximally and distally to the DE nodule with a nonabsorbable suture (Dafilon 0; B Braun AG). A laparoscopic atraumatic temporary intestinal clamp (Aesculap) was placed to decrease the chance of fecal spillage, cephalad to the resection line. A transverse colostomy was performed in healthy tissue using a harmonic scalpel to deliver the anvil from a circular stapler (Proximatew ILS CDH 29, Ethicon Endo-Surgery) introduced through the anus using a sterile laparoscopic camera sleeve (folded laparoscopic camera sleeve; 3M, St Paul). With the use of a camera sleeve for anvil introduction into the abdominal cavity, the possibility of peritoneal cavity contamination was reduced[18].

A completely transected specimen was extracted transrectally through the camera sleeve in a specimen retrieval bag. The proximal part of the anastomosis was created by suturing the anvil in place with the purse-string of a monofilament laparoscopic suture (PDS 2.0; Ethicon, Inc.). The intestinal clamp was removed. The distal rectum was closed by using an endoscopic linear stapler. End-to-end anastomosis was performed by using a circular stapler.

With conventional segmental bowel resection, dissection was continued towards the pelvic floor distally to the affected segment. The rectum was then skeletonized using a vessel-sealing device (Harmonic Scalpel ACE; Ethicon Endo-Surgery) laterally and anteriorly, entering the rectovaginal septum and preserving the posterior wall of the vagina. The distal rectum was closed using an endoscopic linear stapler (Echelon Flex Endopath, Ethicon Endo-Surgery). The mobilized rectum with the specimen was retrieved through a small suprapubic incision. The anvil of a conventional circular stapler was introduced into the proximal colon following the placement of a purse-string suture (PDS 2.0; Ethicon, Inc.). Circular stapled colorectal end-to-end anastomosis was then performed (Proximatew ILS CDH 29).

At the end of both procedures, extensive saline irrigation was performed, and the integrity of the suture line at the distal rectum was verified using the Michelin test. A drain was conventionally left in place in the pouch of Douglas[18,22].

The perioperative care was similar in patients from both arms of the study as the participants received the same medication and nursing technique.

Outcomes

The primary outcome of our study was to test whether the NOSE colectomy technique offered any advantage in terms of functional outcomes and quality of life when compared to conventional laparoscopic bowel resection. As secondary outcomes, the complication rates, time to recovery, and impact on fertility of both procedures were assessed.

Results

A total of 91 patients were enrolled in the study between 30 September 2019 and 31 December 2020, at the University Hospital, with 42 randomly assigned to the NC arm and 49 assigned to the CLR arm. One patient was lost to follow-up (Fig. 1).

The demographic and clinical characteristics of the participants are shown in Table 1. The mean age of the patients in the NC and CLR groups was 35 ± 5 and 34 ± 5 years, respectively. All the patients had one or more pain or intestinal symptoms. Twenty-six patients in the NC group (63.4%) and 35 patients in the CLR group (71.4%) had undergone one or more previous surgeries for endometriosis, excluding colorectal procedures.

Tables 2 and 3 present intraoperative findings and postoperative complications, respectively. The anatomical distribution of the endometriotic DE lesion sites was similar in both groups. There was no difference in the length of hospital stay between the NC and CLR groups (5,3 ± 3 days in the NC group versus 5,7 ± 2 days in the CLR group). All cases were confirmed by histological examination.

The intraoperative classification of endometriosis was performed according to the rASRM and ENZIAN classification systems during all procedures[34,35], see Table 2.

When comparing the NC and CLR groups with regard to the rates of grade I and II postoperative complications, no statistically significant difference was found. According to the Clavien–Dindo classification, we observed two severe (grade III or higher) complications (2.27%): one anastomotic leakage in the NC group and one rectovaginal fistula in the CLR group[36]. These were managed with a covering ileostoma repair. Intestinal continuity was restored within three months.

Table 4 shows preinterventional and postinterventional values of GIQLI, EHP30, LARS, and VAS scores, which were comparable between the two arms. The LARS scores did not reveal significant differences 12 months after the operation compared to the baseline values in both groups (NC: T0 = 22.2 ± 11.7, T3 = 16.33 ± 14.18, $P = 0.87$; CLR: T0 = 21.41 ± 10.2, T3 = 17.90 ± 11.1, $P = 0.934$). GIQLI significantly improved 12 months after the operation compared with the baseline values in both groups NC: T0 = 96.17 ± 16.07, T3 = 112.13 ± 16.8, $P = 0.001$ and CLR: T0 = 95.44 ± 23.1, T3 = 111.39 ± 18.4, $P = 0.002$.

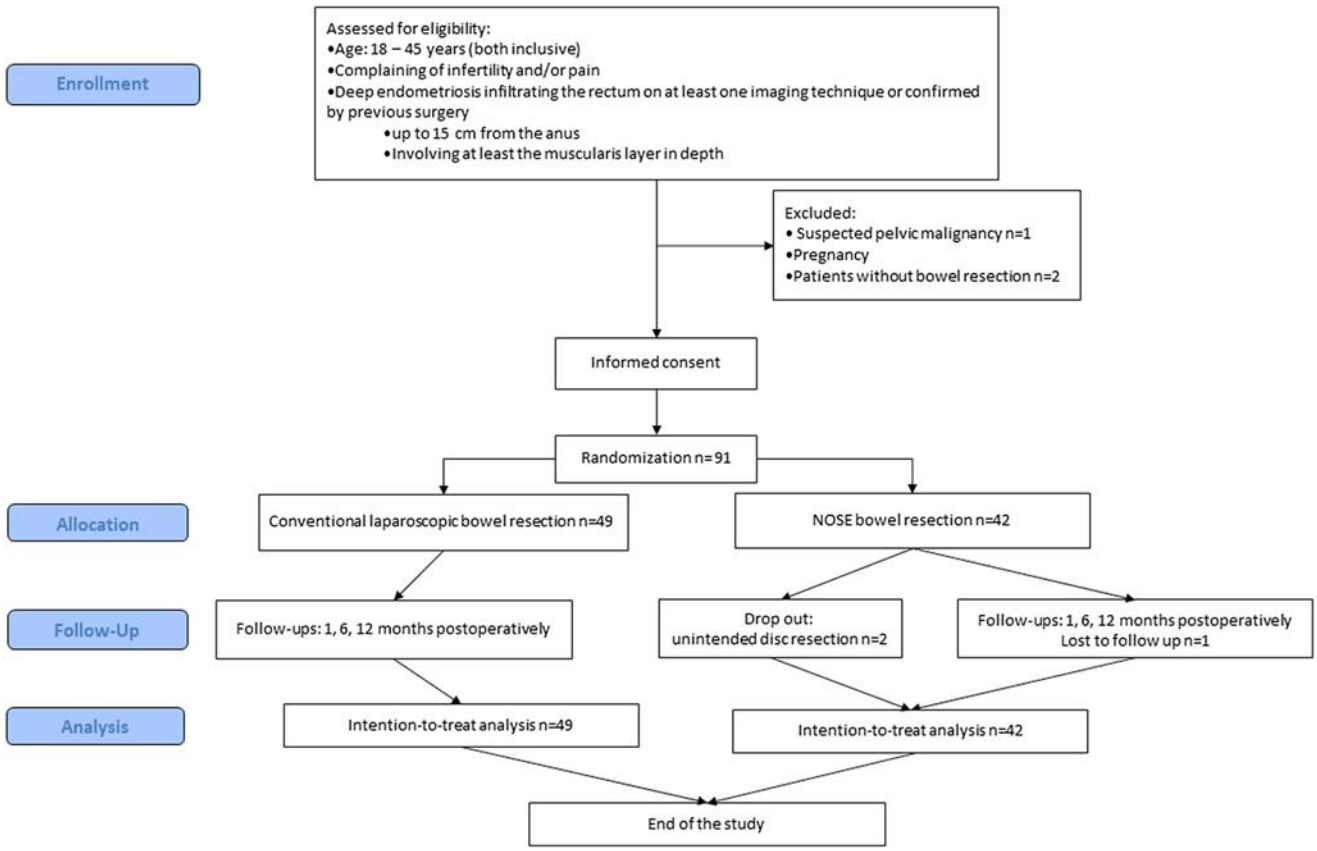

Figure 1. Flow diagram (CONSORT 2010) for study of patients, who underwent NOSE or conventional laparoscopic segmental resection for rectal DE.

The EHP30 scores significantly improved 12 months after the operation compared to the preoperative values in both groups. The overall GIQLI, EHP30, and LARS scores did not reveal significant differences between the two arms 12 months after surgery.

Table 1

Demographic data.

Patients' baseline characteristics	NOSE ($n=42$)	Conventional ($n=49$)
Age (years)	35 ± 5	34 ± 5
BMI (kg/m^2)	21 ± 3	23 ± 4
ASA score		
I	29 (70.7%)	32 (65.3%)
II	12 (29.3%)	17 (34.7%)
Infertility	14 (34.1%)	20 (40.8%)
Previous surgeries for endometriosis		
NO surgery	15 (36.6%)	14 (28.6%)
1 surgery	17 (41.5%)	17 (34.7%)
2 or more surgeries	9 (21.9%)	18 (36.7%)
Type of previous surgeries		
No of patients with previous surgeries	26 (63.4%)	35 (71.4%)
Previous laparoscopy	23 (56.1%)	32 (65.3%)
Previous laparotomy	7 (17.1%)	12 (24.4%)
Previous pregnancy/delivery		
Pregnancy	12 (29.3%)	12 (24.4%)
Delivery	9 (21.9%)	5 (10.2%)

Data are *n* (%) and mean ± SD.

ASA, American Society of Anaesthesiologists score; NOSE, Natural Orifice Specimen Extraction.

Figure 2 presents preoperative, and postoperative EHP30 scores, GIQLI and LARS scores.

Regarding pain symptoms, the chronic pelvic pain, dyspareunia, and dyschezia VAS scores were significantly improved in both groups compared with the baseline scores 1 year after surgery (chronic pelvic pain: NC T0 = 6 ± 5.2, T3 = 3 ± 2.2, $P=0.004$; CLR: T0 = 7 ± 3.3, T3 = 2 ± 2.3, $P=0.0001$; dyspareunia: NC T0 = 6 ± 4.2, T3 = 3 ± 3.1; $P=0.0001$; CLR: T0 = 6 ± 4.5, T3 = 3 ± 2.5, $P=0.0001$; dyschezia: NC T0 = 6 ± 4.4, T3 = 3 ± 2.1, $P=0.0003$; CLR: T0 = 5 ± 4.7, T3 = 2 ± 1.7, $P=0.0001$). We found statistically significant decreases in the intensity of dysmenorrhea (T0 = 4 ± 1.9, T3 = 3 ± 2.1, $P=0.03$) and dysuria (T0 = 3 ± 5.8, T3 = 1 ± 1.7, $P=0.04$) after 1 year of follow-up in the NC group.

There was no statistically significant difference in the change in LARS, GIQLI, EHP30, and VAS scores between the NOSE and conventional treatment groups 12 months after surgery when compared to preoperative values (T3 minus baseline) see Table 5.

The results of follow-up assessments for each time point (T0, T1, T2, and T3) are depicted in Supplementary Table 1 (Supplemental Digital Content 2, http://links.lww.com/JS9/A992).

During the 14 ± 2.6 months of follow-up, 22 patients with active child wishes achieved pregnancy: 8 in the NC arm (21%) and 14 in the CLR arm (29%) ($P=0.867$). Among them, two (4%) and two (5%) conceived spontaneously. Seven (NC group, 18%) and seven (CLR group, 14%) live births were reported in both groups.

Table 2

Intraoperative findings.

	NOSE ($n=42$)	Conventional ($n=49$)	P
Operative time (min)	139 ± 97	147 ± 76	0.7
Hospital stay (day)	5.3 ± 3	5.7 ± 2	0.2
Blood loss (ml)	22 ± 16	24 ± 22	0.4
Localization of deep nodules of the digestive tract			
rectum	34 (82.9%)	42 (85.7%)	0.3
sigmoid/rectum junction	5 (12.2%)	7 (14.3%)	0.5
sigmoid	9 (21.9%)	7 (14.3%)	0.09
sigmoid and appendix	2 (4.8%)	2 (4.0%)	0.6
ileum	0 (0.0%)	6 (12.2%)	0.03
coecum	2 (4.8%)	6 (12.2%)	0.2
Segmental resection of ileum/coecum	2 (4.8%)	12 (24.4%)	0.7
Appendectomy	2 (4.8%)	2 (4.0%)	0.1
Omental/Mesorectal flap	3 (7.3%)	2 (4.0%)	0.9
Protective colostomy	0 (0.0%)	1 (2.0%)	0.6
Diameter of largest rectal nodule (mm)	27 ± 3.8	29 ± 2.5	0.5
Deepest infiltration of the rectum			
mucosa	5 (12.2%)	2 (4.0%)	0.5
submucosa	8 (19.5%)	6 (12.2%)	0.9
muscularis	28 (68.3%)	41 (83.8%)	0.2
Height of the lowest nodule (from the anal verge)			
below 7cm	19 (46.3%)	20 (40.8%)	0.8
above 7cm	22 (53.7%)	29 (59.2%)	0.6
Length of the removed bowel segment (mm)	67 ± 2.7	83 ± 3.8	0.06
ASRM score	51 ± 24	47 ± 17	0.8
ENZIAN			
Compartment A	30 (73.2%)	43 (87.7%)	0.1
Compartment B	15 (36.6%)	12 (24.4%)	0.9
Compartment C	42 (100%)	49 (100%)	n.a
Compartment FA	27 (65.9%)	25 (51.0%)	0.8
Compartment FB	11 (26.8%)	10 (20.4%)	0.3
Compartment FU	0 (0.0%)	7 (14.3%)	0.02
Compartment FI	13 (31.7%)	21 (42.9%)	0.7
Compartment FO	1 (2.4%)	3 (6.1%)	0.9
Concomitant management of			
ovarian endometrioma	12 (29.3%)	15 (30.6%)	0.5
bladder nodule	11 (26.8%)	10 (20.4%)	0.3
rectovaginal space DE	30 (73.2%)	43 (87.7%)	0.2
vaginal infiltration	14 (34.1%)	19 (38.7%)	0.4
peritoneal disease	39 (95.1%)	47 (95.9%)	0.3
ureteral DE	0 (0.0%)	7 (14.3%)	0.02
EFI score	4.8 ± 2.1	5.2 ± 1.8	0.3
Patency of fallopian tubes			
Unilateral occlusion	4 (9.8%)	15 (30.6%)	0.007
Bilateral occlusion	20 (48.7%)	18 (36.7%)	0.2
Patent	17 (41.5%)	16 (32.7%)	0.1

Data are *n*(%) and mean ± SD.

ASRM, American Society of Reproductive Medicine; DE, deep endometriosis; EFI, Endometriosis Fertility Index; NOSE, Natural Orifice Specimen Extraction.

Table 3

Postoperative surgical complications.

	NOSE ($n=42$)	Conventional ($n=49$)	P
Complications according to Clavien–Dindo classification			
I			
Bladder atony (max 7 days)	5 (11.9%)	4 (8.1%)	0.739
Fever	4 (9.52%)	3 (6.1%)	0.705
Clostridium difficile infection	4 (9.52%)	3 (6.1%)	0.705
II			
Rectal bleeding	2 (4.76%)	2 (4.1%)	n.a
Ileus	0 (0.0%)	1 (2.0%)	n.a
III			
Anastomotic leakage	1 (2.38%)	0 (0.0%)	n.a
Rectovaginal fistula	0 (0.0%)	1 (2.0%)	n.a
IV	0 (0.0%)	0 (0.0%)	n.a.

Data are *n*(%).

NOSE, Natural Orifice Specimen Extraction.

Fisher Exact test has been executed.

Discussion

To the best of our knowledge, this is the first prospective randomized study on bowel function, quality of life, and pain outcomes of two different specimen extraction techniques for the surgical treatment of recto-sigmoideal DE.

We observed no statistically significant difference in the occurrence of LARS and GIQLI scores in our cohort of patients who underwent either the NOSE-technique or the conventional nerve and vessel-sparing bowel resection after one year of follow-up. We found no evidence confirming the superiority of the NOSE-technique technique over conventional laparoscopic segmental resection in terms of bowel function and quality of life.

The complex of symptoms consisting of incontinence due to flatus and/or feces, constipation, and frequent bowel movements is referred to as LARS. However, little is known about the exact cause of LARS. Several studies have addressed the symptoms of LARS, but significant variability exists in the reporting of outcomes after anterior resection[37].

Riiskjaer *et al.*[25], in their prospective observational study, reported a significant increase in the frequency of defecation one year after surgery, probably as a result of decreased reservoir capacity. The mean overall LARS score was not significantly different 1 year after surgery. Most patients had minor/major LARS, both before and after surgery. Our study assessed the occurrence of LARS both preoperatively and postoperatively, and found no statistical difference between the extent of LARS before and after surgery in the investigated cohort of women.

In the prospective cohort trial by Hudelist *et al.*[11] comparing segmental and disk resection, they did not observe significant differences in long-term functional outcomes regarding minor or major LARS ($P=0.48$ and $P=0.66$, respectively). These findings are in line with those previously reported by our group[22]. In agreement with recent findings[13,25], we would like to emphasize that impaired bowel function alone should not be an indication for bowel surgery.

In the present study, GIQLI scores were comparable in both groups and showed a statistically significant improvement over time from the baseline values until 1 year after surgery in the NC group ($P=0.001$) and CLR group ($P=0.002$) groups. This is consistent with Roman *et al.*[13], who observed improved and comparable GIQLI scores one year after anterior segmental resection compared to disk excision.

Similar to previously published data[11,13,22,38,39] our results confirm that radical excision of colorectal DE improves the quality of life and lowers pain scores.

As secondary outcomes, we assessed the occurrence of major surgical complications, time to recovery, and length of hospitalization. Our data correlate with previously reported data[18,39]; however, we could not confirm the shorter hospital stay and

Table 4

Preoperative and postoperative assessment of digestive function and quality of life.

	NOSE ($n=42$)					Conventional ($n=49$)				
	T0		T3			T0		T3		
Questionnaires	**Mean**	**SD**	**Mean**	**SD**	***P***	**Mean**	**SD**	**Mean**	**SD**	***P***
LARS	22.2	11.7	16.33	14.18	0.87	21.41	10.2	17.9	11.18	0.934
GIQLI	96.17	16.07	112.13	16.8	0.001	95.44	23.11	111.39	18.48	0.002
EHP30										
Pain	31.7	26.3	6	9.2	0.001	30.8	25.5	10.2	14.2	0.001
Emotional well-being	43.4	23.4	17.4	15.8	0.001	38.9	25.5	16.6	17.7	0.01
Control and powerlessness	45.9	26.5	11.4	16.2	0.016	41.1	31.9	12.2	16.5	0.014
Self-Image	37	26.5	12.6	15	0.001	37	31.8	18	23.9	0.000
Social suppose	24.3	24.6	5.1	9.1	0.000	31.6	31	6.9	14.4	0.000
Sexuality	36.1	34.9	12.3	20.5	0.043	43.9	34.5	19.1	25.3	0.003
VAS scores										
Dysmenorrhea	4	1.9	3	2.1	0.03	5	5.1	4	3.1	0.24
Chronic pelvic pain	6	5.2	3	2.2	0.004	7	3.3	2	2.3	0.0001
Dyspareunia	6	4.2	3	3.1	0.0001	6	4.5	3	2.5	0.0001
Dysuria	3	5.8	1	1.7	0.04	2	5.8	1	2.8	0.27
Dyschezia	6	4.4	3	2.1	0.0003	5	4.7	2	1.7	0.0001

EHP30, Endometriosis Health Profile 30; GIQLI, Gastrointestinal Quality of Life Index; LARS, Low Anterior Resection Syndrome; NOSE, Natural Orifice Specimen Extraction; T0, preoperative; T3, 12 months after surgery; VAS, Visual Analogue Scale.
Mann–Whitney *U* test was used.

lower postoperative pain scores after NOSE colectomy in our cohort of patients.

Recently, a meta-analysis by Liu *et al*.[40] reported the incidence of anastomotic leakage for the NOSE group was 3.6 compared to 5% in the conventional laparoscopic group. Another meta-analysis by Ma *et al*.[20] showed that laparoscopic resection with NOSE resulted in fewer postoperative complications. From the pooled data of the two meta-analyses, the incidence of anastomotic leakage was not significantly different between the two groups. Thus, we conclude that laparoscopic colorectal surgery with NOSE is as safe as conventional laparoscopic surgery. Previous studies have reported faster gastrointestinal recovery, less postoperative pain, and a shorter hospital stays following laparoscopic colorectal surgery with NOSE[18,19,41]. The results of two recently published meta-analyses also suggested that the NOSE group had less postoperative pain and shorter hospital stay than the conventional laparoscopic anterior resection group[20,21,40]. In the aforementioned meta-analyses, the use of

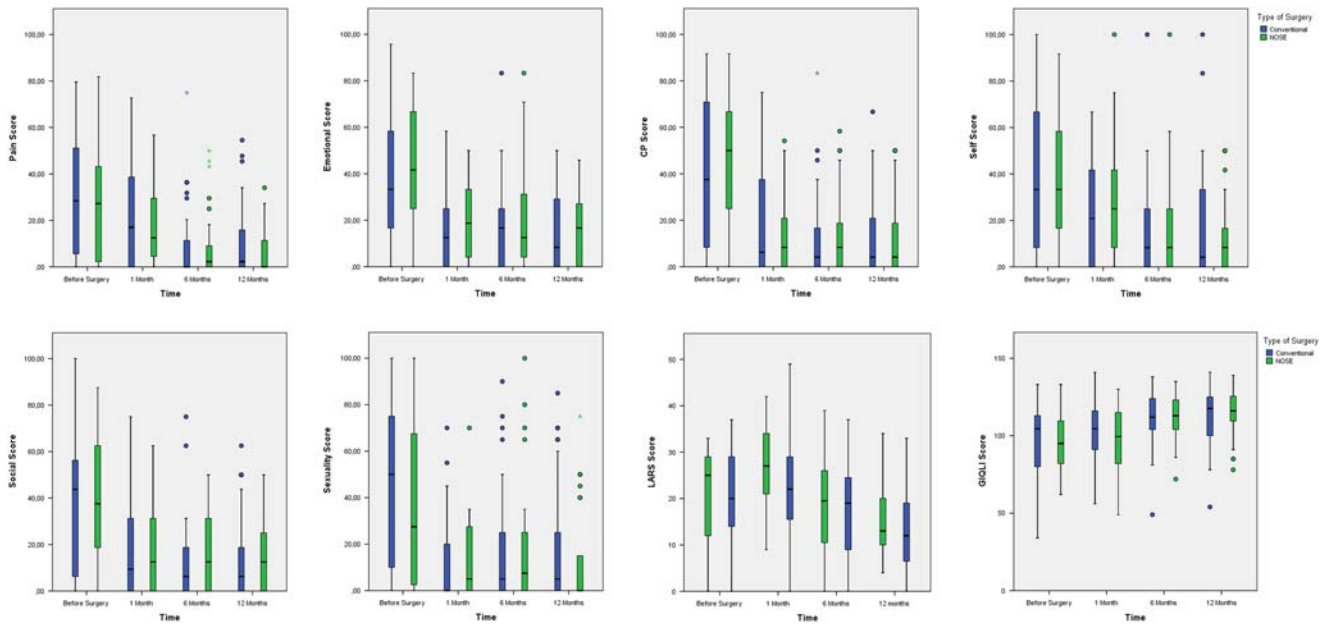

Figure 2. Endometriosis Health Profile 30 scales (pain, emotional well-being, control and powerlessness-CP, self-image, social support, sexuality), LARS (Low Anterior Resection Syndrome) score and GIQLI (Gastrointestinal Quality of life Index) score in conventional and NOSE surgery groups preoperatively, 1 month, 6 months, and 1 year after the surgery.

Table 5

Clinical assessment 12 months after surgery.

	NOSE ($n=42$)	Conventional ($n=49$)	P
LARS delta T3-T0	−5.93 ± 10.58	−6.80 ± 11.50	0.923
Min–max	−24–18	−34–16	
GIQLI delta T3-T0	18.03 ± 19.51	15.07 ± 20.75	0.654
Min–max	−10–70	−27–70	
EHP30 delta T3-T0			
Pain	−23.01 ± 23.85	−21.21 ± 22.18	0.666
Min–max	−70.45–25	−63.64–18.18	
Emotional well-being	−26.21 ± 24.08	−23.00 ± 24.97	0.356
Min–max	−70.83-41.67	−75-29.17	
Control and powerlessness	−34.35 ± 26.79	−29.77 ± 27.89	0.375
Min–max	−91.67-25	−87.50-29.17	
Sexuality	−21.40 ± 28.49	−29.90 ± 31.75	0.900
Min–max	−95-40	−90–60	
Self-Image	−24.18 ± 26.07	−18.75 ± 26.77	0.311
Min–max	−91.67–8.33	−90–60	
Social support	−20.79 ± 25.56	−22.02 ± 23.17	0.865
Min–max	−75–30	−70–10	
VAS scores delta T3-T0			
Dysmenorrhea	−2.41 ± 3.94	−3.25 ± 4.37	0.510
Min–max	−9.65-6.78	−10-6.21	
Chronic pelvic pain	−4.29 ± 3.50	−3.27 ± 4.10	0.331
Min–max	−10–3.36	−10–7.11	
Dyspareunia	−3.79 ± 3.45	−3.42 ± 3.91	0.903
Min–max	−10-17	−10-8.3	
Dysuria	−0.52 ± 1.58	−0.16 ± 2.04	0.270
Min–max	−8–1.73	−6–8.08	
Dyschezia	−2.99 ± 3.54	−3.60 ± 4.27	0.281
Min–max	−10–4.90	−10–7.75	

EHP30, Endometriosis Health Profile 30; GIQLI, Gastrointestinal Quality of Life Index; LARS, Low Anterior Resection Syndrome; NOSE, Natural Orifice Specimen Extraction; T0, preoperative; T3, 12 months after surgery; VAS, Visual Analog Scale.
Mann–Whitney *U* test was executed.

the NOSE-technique was clearly associated with a shorter hospital stay, less postoperative pain, and fewer perioperative complications, although this was not confirmed in our study.

In agreement with recent findings[13,25] we would like to underline the fact that impaired bowel function alone should not be an indication for bowel surgery since we noted the presence of different degrees of LARS in the majority of our patients preoperatively and the LARS scores did not significantly change after surgery.

Keane *et al*. recently defined LARS using a robust methodology that includes multiple stakeholders. This innovative approach suggested that both symptoms and consequences are important priorities in LARS[42]. These important priorities may lead to better identification of patients who experience bowel dysfunction and offer a better perception of LARS in the future. Moreover, further research is needed to elucidate the underlying mechanism of the presence of LARS before colorectal resection.

In the present study, the difference between specimen extraction techniques after colorectal resection for DE had no effect on the functional/surgical outcome or quality of life.

The wider implication of our study is that NOSE colectomy offers the same benefits regarding bowel function, amelioration of pain symptoms, and quality of life as conventional laparoscopic anterior resection. Furthermore, after both procedures, the occurrence of LARS was lower than that previously reported[23,25], and was similar to our recently published multicentric data[22].

As all surgeries were performed by the same surgical team, it is less likely that unbalanced patient enrollment significantly affected the outcomes.

An obvious study limitation was our lack of blinding; however, this was not feasible because of the clinical nature of our study. The simple randomization method used in our study represents another limitation, because it resulted in unequal study groups.

We report no imprecision in patient selection or detection, but a potential source of attrition bias in our data occurred in one case (loss to follow-up) exclusively in the NOSE group.

Conclusion

Our data demonstrated that both NOSE and conventional laparoscopic colectomy are safe methods for the surgical treatment of colorectal DE. The occurrence of long-term bowel dysfunction does not appear to be related to a specific surgical technique. The external validity of our outcomes must be investigated in multicenter prospective randomized trials in a larger cohort of patients.

Ethical approval

This study was approved by the Institutional Ethical and Review Board of Semmelweis University for the protection of human subjects (no.: 58723-4/2016/EKU) on 8 December 2016.

Consent

Written informed consent was obtained from the patient for publication and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Sources of funding

None.

Author contribution

N.D.: study concept and design, acquisition of data, analysis and interpretation of data, manuscript drafting, and critical discussion; G.M.: study concept and design, analysis and interpretation of data, manuscript drafting, and critical discussion; N.C.S., R.B.: acquisition of data, manuscript drafting, and critical discussion; G.H: analysis and interpretation of data, manuscript drafting, and critical discussion; N.Á.: manuscript drafting and critical discussion; A.B.: study concept and design, acquisition of data, analysis and interpretation of data, manuscript drafting, and critical discussion.

Conflicts of interest disclosure

All authors declare that no conflict of interest or financial ties to disclosure.

Research registration unique identifying number (UIN)

ClinicalTrials.gov ID:NCT04109378. https://clinicaltrials.gov/ct2/show/NCT04109378?term=NCT04109378&draw=2&rank=1.

Guarantor

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Data availability statement

Laparoscopic natural orifice specimen extraction (NOSE) colectomy versus conventional laparoscopic colorectal resection in patients with rectal endometriosis: a prospective randomized trial.

Provenance and peer review

Not commissioned, externally peer-reviewed.

Financial support and sponsorship

None.

Presentation

The study was partially presented at ESHRE 38th Annual Meeting; on 3–6 July 2022, Milan, Italy.

Acknowledgements

The authors would like to acknowledge the fundamental help of Endre Horváth and Dr. Birgit Senft (http://www.statistix.at) in the statistical analysis of the data.

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Received: 14 June 2020 | Revised: 11 October 2020 | Accepted: 3 November 2020

DOI: 10.1111/aogs.14046

ORIGINAL RESEARCH ARTICLE

AOGS Acta Obstetricia et Gynecologica Scandinavica

Low anterior resection syndrome following different surgical approaches for low rectal endometriosis: A retrospective multicenter study

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Abstract

Introduction: There is increasing evidence that intermediate and long-term bowel dysfunction may occur as a consequence of radical surgery for rectal deep endometriosis (DE). Typical symptoms include constipation, feeling of incomplete evacuation, clustering of stools, and urgency. This is described in the colorectal surgical literature as low anterior resection syndrome (LARS). Within this, several studies suggested that differences regarding functional outcomes could be favorable to more conservative surgical approaches, that is, excision of endometriotic tissue with preservation of the luminal structure of the rectal wall when compared with classical segmental resection techniques for DE, especially when performed for low DE.

Material and methods: A total of 211 patients undergoing rectal surgery for low DE (≤7 cm from the anal verge) in three different tertiary referral centers between October 2009 and December 2018 were retrospectively reviewed regarding major complications and LARS. From the 211 eligible patients, six women were excluded because of loss to follow-up. Finally, a total number of 205 patients were enrolled for the statistical analysis; 139 with nerve- and vessel-sparing segmental resection (NVSSR) and 66 operated for laparoscopic-transanal disk excision (LTADE) were included. Gastrointestinal functional outcomes of the two procedures were compared using the validated LARS questionnaire. The median follow-up time was 46 ± 11 months. As a secondary outcome, the surgical sequelae were examined.

Results: We found no statistically significant difference between the incidence of LARS (31.7% and 37.9%, respectively) among patients operated by LTADE when compared with NVSSR ($P = .4$). The occurrence of LARS was positively associated with the use of protective ileostomy or colostomy ($P = .02$). A higher rate of severe complications was observed in women undergoing LTADE (19.7%) when compared with patients with NVSSR (9.0%, $P = .029$).

Abbreviations: DE, deep infiltrating endometriosis; HJGWH, Center for Endometriosis, Department of Gynecology, Hospital St. John of God and Wilhelminen Hospital; LARS, low anterior resection syndrome; LTADE, laparoscopic-transanal disk excision; NVSSR, nerve- and vessel-sparing segmental resection; RUH, Department of Obstetrics and Gynecology, Rouen University Hospital; SU, Department of Obstetrics and Gynecology, Semmelweis University,.

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Conclusions: LARS is not more frequent after NVSSR when compared with a more conservative approach such as LTADE in patients undergoing rectal surgery for low DE. To confirm our findings prospective studies are required.

KEYWORDS

colorectal endometriosis, deep infiltrating endometriosis, laparoscopic surgery, low anterior resection syndrome, surgical complications

1 | INTRODUCTION

Deep infiltrating endometriosis (DE) represents the most severe form of endometriosis and is present in 20%-35% of all women suffering from the disease.[1] It is defined as the involvement of endometrial-like tissue with a depth of more than 5 mm.[2] Within this, intestinal lesions are observed in 3%-37% of patients with endometriosis.[3,4] In cases of colorectal DE, indications for surgical therapies may depend on the depth of infiltration, the size of the lesion, and the woman's quality of life.[5,6] Moreover, according to recently published data, the location of the lesion, that is, the distance from the anal verge, and therefore associated risks of surgical interventions, appears to be pivotal in planning the optimal surgical management.[5,6]

Several surgical procedures for the treatment of bowel endometriosis have been suggested and are a matter of constant debate. Conservative surgical techniques consist of shaving and disk resection procedures whereas disruption of the whole luminal structure of the bowel is accomplished in segmental resection, which is usually used for large and multifocal rectal DE.[5,7] Some authors suggest that conservative surgical treatment should be preferred to segmental resection, particularly for low rectal lesions, because of a possible increase of potential complications and postoperative bowel dysfunction.[8] A conservative surgical approach involving a laparoscopic-transrectal large full-thickness rectal disk excision employing a semicircular stapler was introduced to remove large nodules of low/mid rectum, the laparoscopic-transanal disk excision (LTADE) or so-called Rouen-technique.[9,10] However, a recent randomized controlled trial by Roman et al, including patients undergoing surgery for low, mid- and upper rectal DE lesions revealed no statistically significant differences regarding overall outcomes between LTADE and those who underwent anterior segmental resection.[10]

Although low anterior rectal resection and reanastomosis has been criticized for increasing the risk of complications when compared with discoid excision,[8,11] a variant involving limited resection of the bowel wall with preservation of all adjacent structures (autonomic pelvic plexus, rectal vascular supply, and mesorectal fat) described as nerve- and vessel-sparing limited segmental resection (NVSSR) may offer similar benefits regarding pain, fertility, and functional outcomes when compared with more conservative methods.[12,13]

Bryant et al assessed postoperative function of the pelvic organs after surgery for rectal cancer and defined the term low anterior resection syndrome (LARS).[14] In particular, altered bowel function has been shown to be associated with a decrease in quality of life.[15] To assess these possible sequelae, the LARS score has been implemented using a five-item scoring tool for measuring bowel function after restorative rectal oncologic surgery. Since its publication in 2012,[16] the score has been validated,[17] and used as an outcome measure in several scientific papers.[18,19]

Key message

Low anterior resection syndrome is not more frequent after nerve- and vessel-sparing segmental resection when compared with a more conservative approach such as laparoscopic transanal disk excision in patients undergoing rectal surgery for low deep infiltrating endometriosis.

In a recent meta-analysis[19] the prevalence of major LARS after low rectum resection was as high as 41% among patients treated for colorectal cancer. Although a lot is known about the incidence of LARS after colorectal cancer surgery, evidence concerning the use of LARS after colorectal resection for DE on the basis of symptoms and quality of life is scarce, especially for a high-risk patient group with low rectal resections resulting in anastomotic lines within 7 cm from the anus.[13,20,21] Hence, the aim of the present work was to compare two surgical approaches (LTADE and NVSSR) for full-thickness excision of rectal DE with an anastomotic height ≤7 cm distance from the anal verge with regards to the incidence of LARS, postoperative outcomes, and fertility results.

2 | MATERIAL AND METHODS

2.1 | Patient selection and preoperative workup

This study was designed as a retrospective international multicentric cohort study and contains all premenopausal women with DE of the lower rectum who were scheduled for surgical treatment of DE in three tertiary referral centers (Department of Obstetrics and Gynecology at Rouen University Hospital, Rouen, France [RUH]; Department of Obstetrics and Gynecology, Semmelweis University, Budapest, Hungary [SU], and Center for Endometriosis, Department of Gynecology, Hospital St. John of God and Wilhelminen Hospital

Vienna, Austria [HJGWH]) between October 2009 and December 2018.

In patients managed in Rouen, prospective recording of data concerning antecedents, clinical symptoms, findings of clinical and imagery examinations, surgical procedures, and postoperative outcomes was performed through the CIRENDO (North-West Inter Regional Female Cohort for Patients with Endometriosis) database (NCT02294825). This cohort serves as a basis of numerous projects and has led to several publications, focusing on various strategies of management and outcomes of ovarian colorectal endometriosis with different end points.

A total of 211 patients were eligible, six were excluded because of missing data or were lost to follow-up. In all, 205 patients were enrolled for the statistical analysis: 139 with NVSSR from the RUH (n = 52), SU (n = 50), and HJGWH (n = 37) and 66 patients operated at the RUH using the LTADE technique. Inclusion criteria were as follows: women aged between 18 and 45 years (both inclusive) complaining of endometriosis-related pain and/or infertility with DE infiltrating at least the muscular layer of the low rectum, up to 7 cm from the anal verge managed by either LTADE or NVSSR. Patients with diagnosed or suspected malignancy were excluded, as well as women who had undergone previous colorectal surgery or had a history of chronic inflammatory diseases of the gastrointestinal tract and/or chronic defecation dysfunction related to other factors such as birth trauma. Ongoing pregnancy was an exclusion criterion. Preoperative workup included a physical examination, transvaginal sonography, abdominal and pelvic MRI and in some cases at RUH, CT colonoscopy. When performed, transvaginal sonography examinations were carried out presurgically according to the IDEA protocol.[22]

2.2 | Surgical interventions and technique

Surgeries were all performed by a multidisciplinary team with the participation of the same gynecological and colorectal surgeon in each centre. Patients received antibiotic prophylaxis 30 minutes pre-operatively (2 × 1.5 g cefuroxime intravenously and 2 × 500 mg metronidazole intravenously) and a bowel preparation (two packs of laxatives containing sodium picosulfate and magnesium citrate) the day before surgery. Although mechanical bowel preparation is not generally recommended for laparoscopic colorectal resection, we administered bowel preparation to decrease the chance of anastomotic leakage and incisional surgical site infection.[23]

The goal of the surgical treatment in all institutions was to eliminate all macroscopically visible endometriotic foci and to preserve and/or enhance fertility. All surgeries were performed laparoscopically in a multidisciplinary set-up with the contribution of a gynecologist and a colorectal surgeon, and with the assistance of a urologist if needed; set-up was the same for all procedures. Patients were placed in a modified dorsal lithotomy position. The pneumoperitoneum was created by inserting a Veress needle in the umbilicus. A four-port approach was used: the first 10-mm port was inserted in the umbilicus. In cases of low rectum (4-7 cm from the anal verge) and vaginal nodules, special care was taken to preserve the branches of the inferior hypogastric plexus. During the NVSSR procedures we used a nerve "avoiding" technique with gentle pulling of the fibers laterally along with surgical instruments possessing minor lateral thermal effects. Furthermore, a limited tubular resection technique was performed in a meso-sparing manner close to the bowel in order to preserve the branches of the inferior hypogastric plexus, as described in detail previously as NVSSR.[12,13] The distal rectum was closed using a 45/60-mm endoscopic linear stapler (Echelon Flex Endopath Ethicon Endo-Surgery). End-to-end anastomosis was made using the circular stapler (Proximate ILS CDH 29; Ethicon Endo-Surgery). Air-leak testing was performed in all cases and a drain was placed in the pouch of Douglas.

LTADE was performed using transanal staplers (semicircular staplers) or directly through the vagina when opened to remove vaginal infiltration.[9] The procedure started by performing a rectal shaving. When the shaved area of the anterior rectal wall was still infiltrated, it appeared rigid and thickened under palpation with a laparoscopic probe. In these cases, a complete treatment was achieved by full-thickness disk excision, employing a concomitant transanal route.[10] The colorectal surgeon used the Contour Transtar (Ethicon Endo-Surgery) stapler when the shaved area was located less than 7 cm above the anus. The thinner and softer the shaved rectal wall was, the larger the diameter of the rectal patch that could be removed using the transanal stapler. When multiple nodules were revealed, the rectal nodule was managed using a conservative technique, whereas associated nodules of the colon, caecum or small bowel were treated separately, by shaving, disk excision or segmental resection.[24] Additional surgical procedures for non-colorectal manifestations of the disease were performed during the same procedure, such as cystectomy of ovarian endometriomas, excision of bladder DE nodules, ureterolysis or segmental ureteral resection/ureteric neoimplantation, excision of parametrium, and excision and/or ablation of peritoneal lesions. During the postoperative course, according to the ERAS (Enhanced Recovery After Surgery) protocols, we advised oral carbohydrate fluid intake on the first day after surgery.[25] On the second day we started a low-fiber diet, and the time to resume a normal diet was 3 to a maximum of 4 days. The criteria for hospital discharge in all cases were tolerance of a solid diet and passage of flatus and stool. Patients were asked to present for a postoperative check-up 4 weeks and 6 months after surgery. Postoperative evaluation of digestive function was assessed using the validated LARS at least 12 months after surgery. The analyzed items were: incontinence for flatus, incontinence for liquid stools, frequency, clustering, and urgency. The range (0-42) was divided into 0-20 (no LARS), 21-29 (minor LARS), and 30-42 (major LARS).[16] Early postoperative complications were recorded and categorized according to the Clavien-Dindo classification.[26]

2.3 | Statistical analyses

The study data were evaluated by descriptive statistical methods, such as average, median, range frequency, and distribution. Variables

were tested for normality using the Kolmogorov-Smirnov-Lilliefors and the Shapiro-Wilk tests; skewness and kurtosis were also examined. Groups of values without normal distribution were compared using the Mann-Whitney *U* test, Kruskal-Wallis test, Fisher's exact test, or Wilcoxon signed ranks test. Where the distribution allowed, Pearson chi-squared test was used for categorical variables and an independent samples t test regression model for continuous variables. All tests are two-sided and $P < .05$ was accepted as a significant difference. Statistical analysis was undertaken using IBM SPSS version 17 (IBM Corp., Armonk, NY, USA).

2.4 | Ethical approval

Data were retrieved retrospectively from a prospectively maintained electronic database used in all three included centers. Patient baseline characteristics, intraoperative findings, surgical procedures, and follow up were prospectively recorded in the North-West Inter Regional Female Cohort for Patients with Endometriosis (CIRENDO, 17 January 2019) database (NCT02294825) by a clinical research technician at the RUH. In the case of SU, the NOSERES database (NCT04109378) was used, and the TIE database was used in HSGWH. All databases and the study were approved by the local institutional ethical and review boards of RUH and SU for the protection of human subjects (nos 58723-4/2016/EKU [8 December 2016]; HSJGWH No:WSP-1-GYN and Barmherzige Brüder Ethikkommission [5 September 2017]).

3 | RESULTS

3.1 | Surgical findings and sequelae

From October 2009 until December 2018, a total of 1494 patients (RUH n = 831, SU n = 407, HJGWH n = 256) underwent surgery for bowel endometriosis. Out of the 1494 patients, 211 were diagnosed with low colorectal DE and underwent either NVSSR (n = 140) or LTADE (n = 71) and 205 consecutive patients had data available for final analysis. The median follow-up time was 46 ± 11 months. Further patient characteristics are depicted in Table 1. The prevalence of preoperative infertility was higher in the NVSSR group when compared with patients undergoing LTADE ($P < .001$), whereas no difference was found with regards to pain symptoms, except for dyspareunia.

The average median and range of revised American Fertility Society scores of the patients are shown in Table 2. As presented, the anatomical distribution of endometriotic DE lesion sites was similar in both groups. The length of the resected bowel section varied from 5 to 19 cm with an average length of 8 cm (±6 cm) in NVSSR cases. Endometriosis was present in areas other than the colorectal region in most cases. As shown, the frequency of extra-colonic localization of endometriotic lesions was similar in both groups. Most commonly these were found in the rectovaginal septum, pelvic peritoneum, bladder, ureters, and ovaries (Table 2). In the LTADE and NVSSR groups, respectively, 57/66 patients (86%) and 111/139 women (79%) required vaginal resection because of vaginal involvement ($P = .391$). There was no statistically significant difference between the duration of surgeries in the LTADE group when compared with the NVSSR group: 218 minutes (±71.4) and 225 minutes (±71.4), respectively ($P = .58$).

TABLE 1 Patient characteristics

	LTADE		NVSSR		
	n	%	n	%	
Characteristics	**66**	**32.2**	**139**	**67.8**	***P* value[a]**
Age (y), mean ± SD	29.9 ± 4.2		32.6 ± 4.9		<.000
BMI (kg/m^2), mean ± SD	23.3 ± 4.6		24.1 ± 3.9		.42
Obstetrical history					
Parity, mean ± SD	0.25 ± 0.64		0.30 ± 0.58		.51
Gravidity, mean ± SD	0.53 + 0.93		0.44 + 0.83		.304
Previous gynecological surgeries					
Laparotomies	3	4.5	19	13.7	.001
Laparoscopies					
1	17	25.8	45	32.4	.31
≥2	10	15.2	23	16.5	.879
Preoperative subfertility	18	27.3	82	59.0	<.000
Preoperative cyclic symptoms					
Dysmenorrhea	66	100	136	97.8	.241
Intensity of dysmenorrhea (VAS > 4)	63	95.5	131	94.2	.81
Dyspareunia	63	95.4	110	79.1	.007
Intensity of dyspareunia (VAS > 4)	41	63.6	83	59.7	.34
Dyschezia	51	77.2	84	60.4	.045
Intensity of dyschezia (VAS > 4)	36	54.5	71	51	.507

Abbreviations: BMI, body mass index; LTADE, laparoscopic-transanal disk excision; NVSSR, nerve- and vessel-sparing segmental resection; VAS, visual analog scale.

[a]Mann-Whitney *U* and Pearson chi-squared tests.

According to the Clavien-Dindo classification, we observed a severe (grade IIIb or higher) overall complication rate of 28.6% in 205 patients. Anastomotic leakage occurred in 2 out of 139 (1.4%) patients in the NVSSR and in none of the LTADE group ($P = .3$). However, significantly more rectovaginal fistulae were observed in the LTADE group (10.6%) compared with NVSSR (3.6%, $P = .04$). When comparing the LTADE and NVSSR group with regards to rates of grade I postoperative complications we found no statistically significant difference ($P = .55$).

A case of bowel stenosis occurred in the group of patients operated using LTADE after a concomitant segmental sigmoid resection at the level of the anastomosis of the sigmoid colon and was not associated with the large rectal disk excision.

Further information is given in Table 3, and Table 4 shows postoperative rates of LARS in the respective cohorts. As demonstrated,

TABLE 2 Intraoperative findings

	LTADE		NVSSR		
	n	%	n	%	
	66	32.2	139	67.8	*P* value[a]
Operative time (min), mean ± SD	218.6 ± 71.4		225.5 ± 96.1		.58
Surgical approach					
Laparotomy	0	0.0	4	2.9	.05
Laparoscopy	66	100	135	97.1	.673
Revised rAFS score, mean ± SD	53.4 ± 30.1		67.2 ± 37.8		
rAFS stage I	0	0.0	1	0.7	.49
rAFS stage II	11	16.7	9	6.5	.022
rAFS stage III	6	9.1	18	12.9	.42
rAFS stage IV	49	74.2	111	79.9	.364
Rectal DE lesion size					
10-29 mm	12	18.1	38	27.4	.154
>30 mm	54	81.9	101	72.6	
Rectovaginal endometriosis	65	98.4	131	94.2	.391
Ovarian endometriosis	41	62.1	103	74.1	.137
Temporary diverting stoma					
Ileostomy	2	3.0	4	2.9	.37
Colostomy	49	72.2	45	32.3	<.001
Additional surgical digestive procedures					
Sigmoid colon resection	11	16.6	0	0	.000
Appendectomy	4	6.0	10	7.1	.462
Vaginal opening/resection	57	86.3	111	79.8	.37
Urinary tract procedures					
Resection of bladder DE	8	12.1	22	15.8	.54
Ureteral resection and reanastomosis	6	9.0	24	17.2	.071
Ureteral neoimplantation	1	1.5	3	2.1	.316

Abbreviations: DE, deep endometriosis; LTADE, laparoscopic-transanal disk excision; NVSSR, nerve- and vessel-sparing segmental resection; rAFS, revised American Fertility Society score.

[a]Comparison between the two surgical techniques using the Fisher exact, Pearson chi-squared and Mann-Whitney *U* tests.

no statistically significant difference between the incidence of the LARS (31.7% and 37.9%) was observed among patients undergoing LTADE when compared with women treated with NVSSR ($P = .4$). The prevalence of major LARS in the LTADE group was 16.7% with similar rates in NVSSR (12.2%, $P = .6$). The occurrence of major LARS was positively associated with the use of protective colostomy ($P = .02$).

4 | DISCUSSION

We report the first study comparing sequelae of two surgical approaches for treating DE infiltrating the low rectum (within 7 cm of the anal verge). Although different rates of rectovaginal fistula development were observed, the techniques appear to be comparable regarding other major complications and the development of LARS. In the light of the risk of rather high rates for major complications in the whole study cohort, it is a matter of debate whether and how to embark on surgical treatment in this special patient group exhibiting low rectovaginal DE.

Besides the proven benefits of surgical therapy for DE with additional colorectal involvement, such as reduction of pain symptoms and increases in spontaneous and assisted reproductive technique pregnancy rates,[27] it also confers the risk of major complications. Within this, knowledge of potential risk factors enhancing surgery-related complications is important, especially in light of the fact that endometriosis is a benign, non-life-threatening disease, which contrasts with cancer surgery. As a consequence, several studies have tried to evaluate the advantages and disadvantages of conservative, that is, rectal shaving and discoid resection techniques, as

TABLE 3 Postoperative complications according to Clavien-Dindo

	LTADE		NVSSR		
	n	%	n	%	
Clavien-Dindo complications	**66**	**32.2**	**139**	**67.8**	***P* value[a]**
Grade I	3	4.5	7	5.03	.098
Grade II					
Bladder atony after 7 d requiring self-catheterization	11	16.7	9	6.49	.001
Grade III-IV					
Rectovaginal fistula	7	10.6	5	3.6	.04
Stenosis of rectal lumen, requiring additional procedure	1	1.5	0	0	.14
Anastomosis leakage	0	0	2	1.4	.3
Pelvic abscess	6	9	3	2.1	.007
Pyosalpinx	0	0	1	0.7	.5
Stenosis of the ureteral anastomosis	0	0	1	0.7	.5
Ureteral fistula	0	0	1	0.7	.5

Abbreviations: LTADE, laparoscopic-transanal disk excision; NVSSR, nerve- and vessel-sparing segmental resection.

[a]Comparison between the two surgical techniques using the Fisher exact test.

well as more radical strategies like segmental bowel resection, which is also carried out for rectal cancer in a more extensive fashion.

Donnez et al recently reviewed the current evidence of the three surgical treatment options and suggested that conservative approaches must, whenever possible, be preferred to segmental resection because of the possible decrease in major complication rates, such as anastomotic leakage, rectovaginal fistula development, and long-term bladder catheterization.[8] Within this, it should be noted that there is no consensus, nor is there any evidence on how to ideally perform segmental resection for rectal DE because adaptations such as autonomic nerve preservation[28] and the preservation of nerves, mesorectal fat, and vessels[12,13] have been described and may confer benefits regarding short- and long-term problems related to bowel surgery. As already mentioned, the only prospective randomized controlled trial performed so far, by Roman et al,[10] comparing full-thickness discoid excision vs segmental resection in nodules infiltrating the rectum did not reveal a significant difference in major postoperative complications and occurrence of bowel dysfunction when assessed using standardized questionnaires. As the trial protocol had been written in 2009, the trial outcomes were not assessed using the LARS score, which was reported in the literature 3 years later.[16]

The results of the present work are in line with these findings and tried to elucidate the role of LTADE and NVSSR in a selected patient population prone to complications due to a low anastomotic height. Our observations underline the risk of major complications in this patient group with an overall complication rate of 28.6%, which necessarily needs to be taken into account when embarking on surgical treatment for low-lying rectovaginal DE. Although we observed no differences in occurrence of anastomotic leakage, patients undergoing LTADE exhibited significantly elevated rates of rectovaginal fistulae compared with NVSSR (10.6% vs 3.6%) with similar occurrence of concomitant vaginal resection in both groups. Nevertheless, because of the non-randomized and retrospective nature of this study, these differences must be interpreted with caution. Furthermore, patients undergoing LTADE usually exhibit large rectal lesions (above 3 cm) and anastomotic heights between 4 and 5 cm, which may further increase risk of fistula formation. Finally, we did not observe a difference in the occurrence of LARS between LTADE and NVSSR patients. One might postulate that the preservational effect of LTADE and NVSSR regarding autonomic nerve supply and large- and small-vessel perfusion may be similar. When looking at LARS, it generally needs to be taken into account that digestive complaints may also be present presurgically in women with extensive rectal DE.[20] Within this, large DE lesions affecting the parametrium may affect bladder and rectal function, through irritation of the inferior hypogastric plexus. According to Riiskjaer et al, a high number (73.5%) of the patients experienced symptoms equivalent to minor or major LARS after surgery; however, this was also the case before surgery.[20]

A recent study by Juul et al[18] found that major LARS (scores >30) were common (9.9%-17.2%) in the general population, even in the 20-45 years age group of female patients. Hence, normative data for LARS should be taken into account when interpreting LARS score results in studies evaluating bowel function after rectal surgery for DE.

One of the major limitations of our study is the lack of preoperative assessment of the LARS in our cohort. Ideally, the evaluation of digestive complaints should have been recorded both pre- and post-surgery, which was not accomplished for our study with LARS scores being introduced 3 years after 2009.

The other obvious limitation is the retrospective nature of our study, which may be balanced by the fact that the electronic databases that served as a basis of data collection were prospectively established.

TABLE 4 Bowel function after laparoscopic-transanal disk excision and nerve- and vessel-sparing segmental resection

	LTADE		NVSSR		
	n	%	n	%	*P* value[a]
	66	32.2	139	67.8	
Do you ever have occasions when you cannot control your flatus (wind)?					
No, never	26	39.3	72	52.2	.056
Yes, less than once per week	18	27.2	30	21.5	
Yes, at least once per week	22	33.3	37	26.6	
Do you ever have any accidental leakage of liquid stool?					
No, never	55	83.3	122	87.7	.118
Yes, less than once per week	8	12.1	12	8.6	
Yes, at least once per week	3	4.6	5	3.7	
How often do you open your bowels?					
More than 7 times per day (24 h)	1	1.5	5	3.5	.23
4-7 times per day (24 h)	2	3	20	14.3	
1-3 times per day (24 h)	31	46.9	67	48.2	
Less than once per day (24 h)	32	48.4	47	33.8	
Do you ever have to open your bowels again within 1 h of the last bowel opening?					
No, never	30	45.4	39	28	.071
Yes, less than once per week	16	24.2	54	38.8	
Yes, at least once per week	20	30.4	46	33.1	
Do you ever have such a strong urge to open your bowels that you have to rush to the toilet?					
No, never	33	50	57	41	.068
Yes, less than once per week	22	33.3	56	40.2	
Yes, at least once per week	11	16.6	26	18.7	
LARS score[b]					
No LARS	41	62.1	95	68.3	.6
Minor LARS	14	21.2	27	19.4	
Major LARS	11	16.7	17	12.2	
LARS score, median	19		20		

Abbreviations: LARS, low anterior resection syndrome; LTADE, laparoscopic-transanal disk excision; NVSSR, nerve- and vessel-sparing segmental resection.

[a]Comparison between the two surgical techniques using the Fisher's exact and Pearson chi-squared tests.

[b]LARS score, range 0-42: 0-20, no LARS; 21-29, minor LARS; 30-42, major LARS.

Whether LARS is directly associated with the application of protective stoma use as shown in the present work remains an open question. Changes in the intestinal microbiome in patients with endometriosis have been described,[29,30] and they may also occur because of the application of a diverting stoma. Whether this poses a risk for chronic bowel dysfunction needs to be elucidated in future studies.

Although colonic adaptation over a period of about 12 months may improve bowel function, a recent meta-analysis[31] confirms that a significant population of patients continue to suffer into the mid and long term. According to Croese et al,[31] the cause of LARS is complex and likely multifactorial. Impaired anal sphincter function has been identified in patients following low anterior resection, this could be a result of both direct injury to the anal sphincter as well as damage to its innervation. Further studies need to be conducted for follow-up LARS.

Very recently, Keane et al[15] had a first attempt to define LARS using robust methodology that included multiple stakeholders, including patients. This novel approach has identified that both symptoms and consequences are important priorities in LARS. Acknowledging this by transforming these important priorities into a new tool to measure LARS may enable better identification of patients who experience bowel dysfunction and more precise assessment of the severity of LARS in the future.

5 | CONCLUSION

Taken together, the results of the present work support the need for awareness of surgical risks and related complications in women undergoing low rectal full-thickness resections by either conservative or segmental resection techniques. These procedures should only be performed in tertiary referral centers by well-trained multidisciplinary teams with extensive experience in surgery for DE and the management of postoperative complications. Occurrence of long-term bowel dysfunction does not appear to be related to a specific surgical technique.

CONFLICT OF INTEREST

None.

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How to cite this article: Bokor A, Hudelist G, Dobó N, et al. Low anterior resection syndrome following different surgical approaches for low rectal endometriosis: A retrospective multicenter study. *Acta Obstet Gynecol Scand*. 2021;100:860–867. https://doi.org/10.1111/aogs.14046

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Licensed Content Author	Horace Roman, Jean-Jacques Tuech, Réka Brubel, et al
Licensed Content Date	Dec 19, 2020
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Licensed Content Issue	5
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Title of new work	Quality of life assessment after bowel resection performed for deep infiltrating colorectal endometriosis
Institution name	Semmelweis University Budapest, Hungary
Expected presentation date	Sep 2025
The Requesting Person / Organization to Appear on the License	Dr. Noémi Dobó Semmelweis University
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