



Total Laparoscopic Hysterectomy in Patients with Deep Infiltrative Endometriosis: How Different is it, or should be, from the Standard Procedure?

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Abstract

Endometriosis including deep infiltrative disease affects mainly women of reproductive age. The majority of these women requiring surgery are treated with fertility-sparing procedures. Hysterectomy is reserved for patients with advanced endometriosis and severe pain symptoms and those with recurrences, for whom the open approach is the usual choice. For patients with deep endometriosis total laparoscopic hysterectomy may represent a safe and valid option providing that a more extended operation in comparison with standard laparoscopic hysterectomy is practiced, to address also deep nodules. Important prerequisites for a surgeon to undertake such procedures are thorough knowledge of pelvic retroperitoneal anatomy, advanced laparoscopic skills, and experience in pelvic radical surgery. This procedure should aim for a complete removal of all deep lesions using a multi-disciplinary approach when necessary. Incomplete surgery is associated with an increased risk of postmenopausal anatomic relapse, recurrence of pain symptoms, and postmenopausal complications. Hormone replacement therapy after hysterectomy and ovarian conservation are among the most important risk factors for recurrence and re-operation. There is also a theoretical risk of a malignancy developing in residual deep lesions that is difficult to quantify.

Introduction

Endometriosis is considered a disease of reproductive years. Surgery remains the treatment of choice for many patients with endometriosis and in particular those with endometriomas and deep infiltrative disease. For young women who wish to preserve their fertility, surgery should aim at radical excision of the endometriotic lesions and conservation of the uterus and ovaries [1,2].

Hysterectomy with or without oophorectomy is reserved for women who have completed their family and present with severe disease, and/or recurrence (-es) after previous attempts to treat endometriosis with fertility-sparing surgery. Many of these patients have undergone multiple open and/or laparoscopic procedures, and the majority complain of severe pain symptoms [3,4]. The open approach is the usual choice for women with endometriosis scheduled for radical surgery. The fear of extensive adhesions due to previous procedures, the marked inflammation and anatomical distortion that accompanies severe disease, and in particular the lack of experience in radical extirpative laparoscopic surgery are among the reasons for this practice [5,6].

Deep Infiltrative Endometriosis (DIE) represents one of the most challenging indications for hysterectomy, especially when recurrent [7]. Patients with DIE commonly complain of severe pain symptoms and many have significant involvement of non-gynecological organs such as the bowel and the urinary tract that requires attention per se. Standard hysterectomy with bilateral adnexectomy may be adequate treatment for most benign gynecologic pathologies but may prove inadequate in the case of DIE [8].

What is the target population for hysterectomy in the DIE group?

Patients with endometriosis including those with DIE that undergo hysterectomy are commonly younger compared with those treated with the same procedure for other indications. Uccella S et al. [9], comparing patients with endometriosis treated with total laparoscopic hysterectomy (TLH) with those treated with TLH for other benign indications found a mean age difference of 2 years (42 vs. 44, $p < 0.001$) [9]. This age difference observed also in other studies may have important implications on the need for Hormone Replacement Therapy (HRT) and the risk of recurrence in postmenopausal years [10].

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Another common characteristic of these patients is the frequent history of previous abdominal surgeries both open and laparoscopic, the majority of these to treat endometriosis [9,11]. This past history forms a challenging and dangerous operative environment for any subsequent surgery due to the increased risk of dense adhesions involving not only the peritoneal cavity but also the retroperitoneum, especially when previous inadequate retroperitoneal surgery had been performed to treat DIE. The majority of patients with DIE to be treated with radical surgery invariably complain of CPP symptoms [12]. Pain relief represents the most important aspect of a patient's decision to undergo a radical procedure. Therefore, planning of surgery should take into consideration adequate management of pain, not only the achievement of surgical menopause.

Recurrence of disease may or may not accompany recurrence of symptoms. Commonly recurrence of endometriosis and DIE in particular, is located in the area previously treated [8,13]. In such cases radical excision of DIE lesions represents a challenging but important part of surgery planning. Such surgery may involve resection of non-gynecological organs and a multi-disciplinary approach may become necessary [14,15]. Frequently patients with DIE have co-existing pathologies such as fibroids and adenomyosis that represent the main indication for hysterectomy [16-19]. Addressing these pathologies laparoscopically is not made easier by the presence of DIE. There may be important technical issues including inadequate uterine mobility, reduced space for maneuvers, increased blood loss and increased risk of complications.

Preparation for surgery

The preoperative approach in patients with DIE scheduled for laparoscopic hysterectomy is largely dictated by the disease itself. A detailed symptom analysis and especially of pain symptoms is of paramount importance to investigate the possibility of involvement of non-gynecological organs. A thorough clinical and pelvic examination assisted by the appropriate for the case imaging tools (TVS, TRS, MRI, barium enema, IVP), and Para-clinical examinations (recto-sigmoidoscopy, cystoscopy) will give important information on the size, location, and geometry of the DIE lesion (-s), and involvement of adjacent anatomical structures [20]. We have found the ENZIAN scoring system a very important tool, not only for the preoperative staging of DIE, but also for surgery planning [21].

In cases that are of high risk to require bowel or urinary tract resections, a colorectal surgeon and an urologist skilled in advanced laparoscopic surgery should be consulted in advance [15,22]. A multi-disciplinary approach in these complicated cases is of paramount importance to reduce complications during a particularly lengthy operation, and avoid medico-legal implications. In addition to this, a signed detailed informed consent form should be obtained in all cases.

For bowel preparation a standard protocol is followed in our practice. A residual-free diet is prescribed for 4-7 days prior to surgery, depending on the case. Patients at a high risk of bowel resection are also prepared the eve of surgery with bowel irrigation. Nevertheless, it should be mentioned that the benefits of bowel preparation in cases undergoing elective bowel surgery are debatable [23]. Another important issue of preoperative preparation is the availability of adequate theatre time. When TLH in DIE cases aims at removing radically the endometriotic lesions, it is significantly longer in comparison with the standard procedure [12,24]. Resection of non-gynecological organs will probably be associated with longer

operation times [25].

Instrumentation

In comparison to standard TLH that can be performed with basic mainly reusable laparoscopic equipment (scissors, grasping forceps, standard bipolar, needle holders, suction-irrigation canula), TLH in the context of DIE is considerably different in the sense that extensive retroperitoneal dissections may require an array of more sophisticated instruments. Regarding uterine manipulation, apart for the Clermont-Ferrand manipulator we routinely use in our standard TLH cases, for DIE cases uterine manipulation may vary during the procedure to improve ergonomics, increase space, and facilitate nodule resection (Valtchev manipulator, uterine sounds). Advanced hemostatic tools including ultrasonic shears and advanced bipolar technology may become necessary in difficult dissections. Vascular clip applicators and a bowel manipulator are important for DIE surgery to mention only instruments used by the gynecologist.

Important operative considerations in DIE cases treated with TLH

The technique of pelvic dissection to radically excise deep endometriotic lesions has been described in detail by several authors [26-30]. In this section an effort will be made to highlight the most important aspects of DIE surgery adapted to TLH.

Common steps with standard TLH

DIE again dictates the operative approach. The target should be the radical removal of all endometriotic lesions. There are some common steps with standard TLH that target a clear operative field and maximum uterine mobility. As many of these patients have undergone previous (sometimes multiple) surgeries, they invariably present with extensive adhesions, that combine with adhesions caused by endometriosis itself. Such adhesions are frequently dense, firm and vascular, and involve bowel, uterus and adnexa, obliterating at various degrees the pouch of Douglas. In recurrent DIE the situation may be even worse, as any previous attempt to develop the retroperitoneal spaces may cause dense adhesions that make future dissections difficult and risky. This part of the procedure may be unexpectedly long and cumbersome.

Three simple maneuvers to increase uterine mobility are the division of the round ligaments, the extensive opening of the anterior leaf of the broad ligament, and the division of the vesico-uterine fold for posterior nodules, or the posterior leaf of the broad ligament for bladder nodules. This will facilitate subsequent dissection of involved compartments.

Define the 1st operative target

There are three options regarding TLH in DIE: a) To excise the DIE lesion first, b) To perform hysterectomy first and subsequently address the nodule and c) To remove the uterus and disease en block. We believe that there are certain points favoring the 1st approach: 1) the uterine manipulation facilitates dissection of the retroperitoneal spaces, making identification of correct surgical planes easier 2) vital structures (ureter, vessels, nerves) are easier to identify, dissect and preserve, 3) complications are easier to detect and manage (bleeding, organ injuries), 4) tailoring of vaginal excision and reconstruction (when necessary) is more precise. Furthermore, en block resection especially of large nodules may be more difficult due to space and ergonomics limitations.

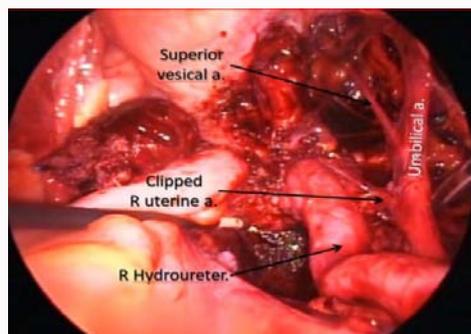


Figure 1: Medial and lateral development of pelvic spaces in a patient with DIE and hydronephrosis.

Temporary suspension of adnexa and bowel

This common maneuver in DIE surgery is also important during TLH when the nodule is to be attacked first. Adnexa are invariably suspended after being completely mobilized. When an oophorectomy is planned, this can be performed as an early step to improve visibility of the underlying structures. The bowel is not systematically suspended, but there are cases in which this maneuver may temporarily prove useful.

Dissection of ureters

This part of the procedure is invariably necessary when TLH is performed in DIE cases. Frequently the ureter is adhered to a diseased peritoneum of the ovarian fossa or involved by the disease process, and an ureterolysis is necessary at least up to the ureteric channel. Whereas in conservative DIE surgery a medial approach to dissect the ureter is usually adequate, in TLH and especially when large nodules are involved a combined approach (lateral+medial) is probably more appropriate and safer taking into account the radicality of the procedure (Figure 1). Nodule location and geometry are equally important with poster lateral nodules requiring more extensive dissections of the ureter. In the case of bladder nodules distal dissection of the ureters may become necessary.

Development of retroperitoneal spaces

It is clear that safe TLH in the context of DIE is impossible without mastering retroperitoneal anatomy. Dissection should follow a radical hysterectomy type of approach, with the additional difficulty of infiltration of the retroperitoneal spaces by the disease. Development of any particular retroperitoneal space may become necessary at any phase of this procedure, when radical excision of the nodule remains the target. Dissection should proceed from healthy to diseased, with an effort to circumscribe the nodule following the planes developed by the gas. Creation of pseudo-spaces and fluid irrigation should be avoided. Again previous retroperitoneal dissections and inadequate surgeries for DIE increase dramatically the risk of complications.

Demanding and risky adnexectomy

Adnexectomy in such cases should not be taken lightly. Several patients may have undergone previous ovarian surgeries for endometriomas, and may even have recurrent ovarian disease. The pelvic peritoneum is invariably diseased and frequently distorted and the ureters densely adhered to the ovaries. The difficulty to separately identify the ureter from the infundibulopelvic ligament is another strong argument to follow a lateral approach to perform adnexectomy as part of the TLH.

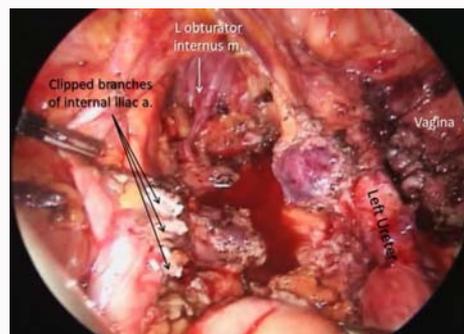


Figure 2: Division of branches of the left iliac artery and vein in a DIE case during TLH and left radical parametrectomy.

Dissection and clipping of branches of internal iliac vessels

During TLH for DIE it may be useful to dissect and clip branches of the internal iliac vessels. This will reduce the total amount of blood loss and it is definitely necessary in cases with perivascular infiltration by the disease (Figure 2). Additionally, clipping and division of uterine arteries and veins will facilitate distal ureterolysis. In cases with previous dissection of the retroperitoneal spaces and dense retroperitoneal adhesions, selective lymphadenectomy may help to achieve identification and complete dissection of vascular structures.

Nerve sparing a key step to preserve function

Unlike standard TLH for other benign indications, where a nerve sparing technique is usually irrelevant, in cases with DIE the lesion may expand to areas with dense autonomic innervation, and in common with conservative DIE surgery, these structures should be respected. This may not be possible in all cases as deep endometriosis may infiltrate nerves, but an effort for pelvic nerve sparing should always be made, with at least unilateral preservation (Figure 3). Frequently this effort may prove difficult and time-consuming, and the surgeon should always try to keep balance between radicality of DIE excision and preservation of organ function (bladder, bowel, and vagina).

Bowel endometriosis: TLH a case for more conservative surgery?

Taking into account the fore-coming surgical menopause in patients treated with TLH and bilateral salpingo-oophorectomy (BSO), maybe there is a case in this group to treat bowel endometriosis with more conservative surgery avoiding bowel resection. Our practice is to initially attempt in all cases bowel shaving, using the classic

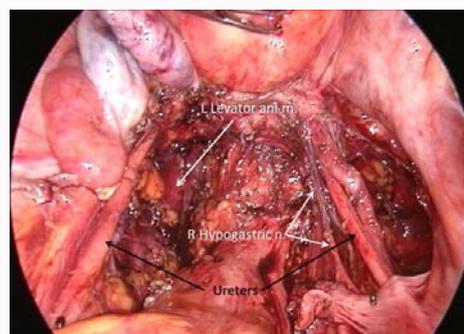


Figure 3: Unilateral sparing of pelvic autonomic innervations in a case with bilateral involvement of the uterosacral ligaments by DIE nodules.



Figure 4: Tailoring vaginal excision using the reverse technique of bowel shaving.

and reverse techniques plus nodule bisection in those with large nodules (Figure 4), keeping discoid resection an option for a thin and ischemic anterior wall. This practice is supported by evidence from trials on fertility-sparing DIE surgery [31,32,33]. Of course exceptions that require a bowel resection still remain i.e. patients with bowel stenosis, or extensive organ involvement both in length or circumference [29,34]. In such cases a multidisciplinary approach is preferred, with the trans-vaginal technique of bowel extraction being more practicable, with the vagina open [35]. Prior nodule excision (better development of spaces) and hysterectomy will provide more space for maneuvers. Suture lines in such cases should be protected and isolated (omental flap).

Surgical menopause and incomplete DIE surgery: Does it matter?

There are several theoretical risks and considerations regarding incomplete DIE surgery after TLH: a) Anatomic recurrence in the post menopause, b) recurrence of symptoms, even in the absence of identifiable relapse of disease, c) the possible effect of hormone replacement therapy on remaining lesions, d) the risk of DIE-related postmenopausal complications, e) the risk of malignancy, developing in residual DIE.

a) Postmenopausal recurrence of DIE

Recurrence of endometriosis though rare in menopause has been reported by several authors [36-38]. It is estimated that postmenopausal endometriosis affects 2% to 4% of the female population, but it is difficult to define the exact incidence as many patients complaining of symptoms suggestive of a relapse, do not undergo laparoscopic evaluation [36]. The key suggested mechanism involves excessive hormonal stimulation of residual or microscopic disease of various sources: adrenal androgen to estrogen conversion in fat in obese patients, ectopic local estrogen production in residual endometriotic lesions with operation of autocrine and paracrine pathways, estrogen-producing ovarian tumors, hormone replacement therapy, and phytoestrogens. Of all the above, administration of HRT seems to have the most consistent role in the development or awakening of postmenopausal endometriosis [38].

b) Recurrence of pain symptoms

Severe chronic pelvic pain is a most frequent indication for both conservative and radical surgery in DIE. Pain recurrence may or may not relate to anatomic relapse of disease, taking into account that severe endometriosis represents a chronic inflammatory condition [39]. Incomplete surgery, ovarian conservation, and postoperative administration of HRT are among the most important factors for

postmenopausal recurrence of pain [40,41].

Fedele L et al. [12], compared two groups of patients with DIE undergoing hysterectomy. In the first group they performed a standard extrafascial procedure and in the second a modified radical hysterectomy with excision of all DIE lesions. All their patients received postoperative HRT. After 48 months of follow-up 30% of patients in the former group reported pain recurrence compared with 0% of cases treated with radical surgery [12].

Similarly, Vignali M et al. [13], in a retrospective study on 150 patients with DIE has shown that incomplete initial surgery is the principal risk factor for re-operation with a Relative Risk (RR) of 21.9. This group has also demonstrated that in re-operated patients the recurrence was sited at exactly the same position where the lesion was found during the initial surgery [13]. This has been also the observation of Taylor and Williams, who reported a RR of 2.54 to find a recurrence in the same area of the initial lesion, compared with other adjacent or distal locations [42].

It has also been shown that ovarian conservation during hysterectomy performed for endometriosis is related to an increased risk of pain recurrence compared with BSO. Namnoum A et al. [43], in a retrospective study of patients treated with hysterectomy for endometriosis compared those managed with ovarian conservation with those in whom BSO was performed. In the former group, 62% developed a symptomatic recurrence and 31% were re-operated, compared with 10% and 3.7%, respectively, of patients in the BSO group. They found a 6.1 RR of pain recurrence and an 8.1 RR of re-operation in the ovarian conservation group [43].

Shakiba K et al. [44], in their retrospective study compared patients undergoing hysterectomy and BSO for endometriosis, with those treated with hysterectomy and unilateral or bilateral conservation of the ovaries, regarding their reoperation-free survival. After a 7 years follow-up, 91.7% of patients in the BSO group did not have further surgery compared with 75.3% of the unilateral and 48.9% of the bilateral ovarian conservation group [44].

c) The potential effects of HRT

Administration of HRT in patients with endometriosis undergoing surgical castration is still a matter of debate. Many patients with endometriosis entering menopause are younger than the average hysterectomy population, and the need for HRT administration to avoid postmenopausal estrogen deprivation morbidity may become more urgent than in other groups. So far, the risk of recurrence of disease or pain symptoms in patients with endometriosis under HRT has not been clearly defined.

Al KadriH et al., in their 2009 Cochrane review concluded that there is currently no evidence that HRT administration (either a combination of estrogen/progestogen-E/P, or tibolone) in patients undergoing surgical menopause is associated with an increased risk of aggravation of pain symptoms due to endometriosis [45].

Unfortunately conclusive data regarding safety of HRT administration in DIE patients especially after incomplete surgery do not exist. In a prospective study, Matorras R et al. [46] compared two groups of patients undergoing bilateral oophorectomy with or without hysterectomy for endometriosis. One group receiving an E/P combination was compared with a control group not receiving HRT. They demonstrated that conservation of the uterus and peritoneal involvement >3 cm were the most important risk factors

for recurrence of endometriosis (RR 11.8 and 8.1, respectively) [46]. Although their findings and suggestion to avoid HRT in patients with extensive peritoneal involvement cannot be extrapolated to include DIE cases, maybe for those with incomplete excision of DIE lesions HRT represents also a risk factor for recurrence.

Accordingly, no solid data exist so far on the relative safety of the different types of HRT in patients with DIE undergoing hysterectomy. In a small prospective study Fedele L et al. [12], reporting on only 21 patients who after incomplete surgery for endometriosis received either an E/P combination or tibolone, concluded that the later was associated with a reduced risk of pain relapse (9% vs. 40%), after 12 months of follow-up [47]. According to the report of Hickman T et al. [48], timing of HRT administration, i.e. immediately after surgery vs. 6 months' delay, was shown not to be important in relation to the risk of pain recurrence [48].

d) The potential risk of residual DIE-related postmenopausal complications

Although no large studies exist reporting on complications developing in postmenopausal patients with a history of deep endometriosis, there are many case reports or small series addressing this issue. A variety of complications have been reported involving several abdominal structures invaded by DIE. Postmenopausal recurrence of DIE apart from causing pain relapse may also result in bowel stenosis, ureteral obstruction, hydronephrosis with or without kidney loss, vascular obstruction requiring operative relief, and even upper abdominal complications involving the pancreas and spleen [49-52]. Many of such complications have in common postmenopausal administration of HRT, but in several others no such factor or other well defined mechanism was clearly identified. This fact on one hand outlines the value of case reports literature in medicine, but on the other makes evaluation of the real risk of unusual events related to a particular condition difficult.

e) The risk of malignant transformation of residual DIE lesions

In accordance with what was mentioned in relation to complications, there are several case reports of malignancies developing in residual DIE lesions during menopause. The majority of these neoplasms represent endometrioid adenocarcinomas, but other malignancies such as clear cell carcinomas and sarcomas have also been reported [53-56]. Several of these patients had received HRT during their postmenopausal years (commonly unopposed estrogen), but in others no clear mechanism of potential carcinogenesis has been elucidated, the disease occurring several years after hysterectomy [57]. Similarly, a history of incomplete DIE surgery was present in some women, whereas in a small minority no known history of premenopausal endometriosis existed prior to the diagnosis of malignancy [58].

Why is there scarcity of published data on radical laparoscopic extirpative surgery in DIE?

Hysterectomy is one of the most commonly performed surgical procedures in women. In the USA, more than 311.000 hysterectomies were performed in 2012 for a benign indication. Among those approximately 80.000 were performed to treat endometriosis, of which 22% were done laparoscopically [59,60]. Additionally, it has been estimated that 12% of patients with endometriosis will be treated with a hysterectomy [41]. Despite the large number of hysterectomies performed for endometriosis worldwide little has been published to address the specific issue of TLH in DIE patients.

The reasons for it are not difficult to imagine: radical laparoscopic surgery aiming to achieve at the time of hysterectomy complete removal of DIE lesions is a lengthy and dangerous procedure. It requires a radical hysterectomy type of approach with the added difficulty of retroperitoneal infiltration by the disease. Thorough knowledge of retroperitoneal anatomy and advanced laparoscopic skills are absolutely necessary to reduce the risk of complications that may sometimes be unpredictable in the long term. As with any type of DIE surgery, hysterectomy for DIE should be performed in tertiary referral centers with a multi-disciplinary approach.

Conclusion

TLH in patients with DIE is a demanding and risky procedure. It should aim at a complete excision of all DIE lesions. Residual disease despite surgical menopause may lead to persistence or recurrence of pain symptoms especially in patients receiving estrogen-only HRT, with a risk of serious postmenopausal complications. The true risk of malignant transformation of residual DIE is currently unknown.

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