

Sodoben pristop k diagnostiki žensk s sumom na pelvično endometriozo

Contemporary approach to diagnostics in women with suspected pelvic endometriosis

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Izvleček

Endometrijoza je pogosta kronična bolezen ženskega reproduktivnega sistema. Za njo je značilna prisotnost endometrijskega tkiva izven endometrija in miometrija. Simptomi, ki jih povzročajo, lahko pomembno vplivajo na nižjo kakovost življenja prizadetih žensk, po drugi strani pa lahko endometrijoza vpliva tudi na nižjo plodno sposobnost. Navkljub razvoju na področju konzervativnih medikamentoznih metod zdravljenja je operativna terapija pogosto sestavni del zdravljenja te bolezni. Včasih je veljalo, da je neinvazivna diagnoza endometrijoze mogoča samo kadar je ta prisotna na jajčnikih v obliki cist. Razvoj slikovnih metod v zadnjih desetletjih pa je pomembno spremenil pristop k diagnostiki in danes lahko globoko pelvično endometriozo diagno-

Abstract

Endometriosis is a common chronic female reproductive system disease, characterised by the presence of endometrial tissue outside the endometrium and myometrium. It can severely compromise quality of life and have an impact on fertility. Although advances in conservative medical treatment options have been made, surgery is often a necessary part of treatment for this insidious disease.

Historically, it was believed that only ovarian endometriosis could be diagnosed non-invasively by an ultrasound examination, while endometriosis at other locations could not be observed. With advances in imaging techniques over the last decades, this has changed dramatically and today deep pelvic endometriosis can be diagnosed non-invasively with

sticiramo z visoko senzitivnostjo in specifičnostjo neinvazivno. Namen našega pregleda literature je ocena doprinosa različnih diagnostičnih metod k diagnostiki endometrioze. Te vključujejo klinični pregled, laparoskopijo in neinvazivne slikovne metode, kot sta predvsem transvaginalni ultrazvok in magnetna resonanca.

Na podlagi podatkov, ki so na voljo, lahko zaključimo, da sodobna ultrazvočna tehnologija ob zadostnih izkušnjah omogoča visoko diagnostično natančnost v diagnostiki globoke pelvične endometrioze. Natančna ultrazvočna preiskava je metoda izbora za diagnostiko žensk s kronično pelvično bolečino in sumom na endometriozo.

high sensitivity and specificity. The aim of this review is to evaluate the contribution of clinical examination, laparoscopy, and non-invasive imaging techniques, mainly transvaginal ultrasound and magnetic resonance imaging, to diagnose deep pelvic endometriosis.

Evidence shows that transvaginal ultrasound with high-quality equipment in experienced hands offers high diagnostic accuracy for deep pelvic endometriosis diagnosis. Comprehensive ultrasound examination should be used as a first-line method of choice in diagnostics of women with suspected endometriosis and chronic pelvic pain.

INTRODUCTION

Pelvic endometriosis is a common female reproductive system disease that is defined by the presence of endometrial glands and stroma at anatomically ectopic locations. Its exact prevalence in the general population is unknown, but can be estimated to be about 6%–30% based on laparoscopic sterilization findings (1, 2). In women experiencing pelvic pain or infertility, the prevalence rises and is estimated to be between 30%–45% (3). The most commonly affected sites by endometriosis are the ovaries, uterosacral ligaments, and rectovaginal septum (4). Ultrasound has been shown to be accurate in diagnosing ovarian endometriomas, but other lesions have historically been considered virtually undetectable (5). Contrary to this belief, several studies in the last decade have shown that ultrasound in experienced hands is a reliable method to diagnose pelvic endometriosis (3). The reported accuracy is dependent on variations in examination technique, quality of ultrasound equipment, and experience of the operator.

Accurate non-invasive diagnostics are of utmost importance, since they are a prerequisite for further appropriate management of these patients. In particular, highly symptomatic women with deep infiltrating endometriosis (DIE) often need surgical treatment, although developments in medical therapy may offer new possibilities for conservative

management (6-8). Surgery for DIE is often challenging and insufficient preoperative preparation can lead to suboptimal surgical procedures during planned surgery, increasing complication rates and significantly worsening the long-term clinical outcome. On the other hand, endometriosis is increasingly managed medically and surgery can be avoided or delayed in a growing proportion of cases. In these cases, it is also important to correctly establish the diagnosis for further monitoring of the disease.

Magnetic resonance imaging (MRI) is one of the non-invasive techniques available for a complete pelvic examination for the presence of endometriosis. However, the method is complex, time consuming, costly, and, therefore, today considered not appropriate for initial evaluation of women presenting with pelvic pain. Hence, a recent development of transvaginal ultrasound (TVUS) has provided a non-invasive and reliable means of diagnostics in women with suspected pelvic endometriosis. Unfortunately, there is significant inconsistency in the way diagnostics in women with suspected endometriosis are approached and how the results are reported. Different clinicians use different terms when describing the same anatomical locations and this ultimately creates confusion in the field. Hence, an attempt towards standardisation in reporting has been made in a

recently published consensus by a group of experts dealing with endometriosis (9). This review aims to provide recent available evidence that should guide clinicians in their decisions on

HISTORY AND CLINICAL EXAMINATION

The first basic method used when evaluating women with suspected endometriosis has always been accurate clinical history and pelvic examination. Comprehensive clinical history with emphasis on the patient's symptoms is essential to plan further investigations. The history should include an accurate report about the incidence and quality of symptoms (dysmenorrhea, dyspareunia, dysuria, dyschezia, chronic pelvic pain, haematuria, and cyclic rectal bleeding), family history of endometriosis, and previous surgical procedures. It should be mentioned that several authors have shown that severity of symptoms poorly correlates with the severity of endometriotic lesions. The predictive value of these symptoms for diagnosing endometriosis is thus uncertain (3, 10). Presentation with more than one symptom increases the chance of endometriosis (3). However, in a significant proportion of cases endometriosis can also be asymptomatic (11-13).

The next step involves a physical examination. However, the reliability of pelvic examination has remained low and the patient may present with no abnormal physical findings (3). The diagnosis is most commonly suspected in cases of painful palpation or nodules present in the posterior fornix (Figure 1). It can also present with thickening of uterosacral ligaments and cervical displacement, palpable adnexal mass, painful uterine manipulation, and cervical stenosis (10). Physical examination findings enable a clinician to plan for a more specific diagnostic approach and contribute to faster diagnosis of endometriosis. Here, the clinician's experience is crucial (3). Clinical examination is an important part of preoperative assessment despite the poorly defined relationship between severity of the symptoms and clinical stage of the disease according to the American Fertility Society (14). A retrospective study has shown

that clinical pelvic examination for rectosigmoid and retrocervical endometriosis sites has a sensitivity of only 72% and 68% and specificity of 54% and 46%, respectively (15, 16).



Figure 1. Endometriosis of the posterior vaginal fornix seen as dark nodules on vaginal inspection.

MAGNETIC RESONANCE IMAGING

MRI is not useful for the diagnosis of superficial peritoneal endometriosis (3) and should not be used as a primary diagnostic tool when endometriosis is suspected (17). It enables direct identification of ectopic endometrial deposits and local anatomy distortions, which occur in the presence of endometriosis (18). The intensity of endometriotic implants is usually the same as in a normal endometrium. However, hyperintensity or hypointensity in T1 and T2 images may be present (10). MRI sensitivity for diagnosis of ovarian endometriosis is low since other pathologies present similarly on MRI images (10).

MRI is more useful for the diagnosis of moderate and severe disease (10). In these cases, accurate preoperative planning is important for lowering the risk of surgical complications (10, 18). DIE is defined as an invasion of endometrial tissue more than 5 mm below the peritoneum (18). MRI is helpful for evaluating the extent of the disease involving the

bowel, bladder, and ureters according to the ESHRE (European Society for Human Reproduction and Embryology) guidelines and recently published NICE (National Institute for Health and Care Excellence) recommendations (3, 17). It is not universally used in the diagnostic process. The use of MRI should be decided on an individual basis according to the ESHRE guidelines (3).

LAPAROSCOPY

Today, laparoscopic exploration with histopathological examination of suspicious lesions is still considered to be the gold standard for diagnosis of endometriosis (Figure 2) (10). However, there is scarce evidence regarding the diagnostic value of laparoscopy in diagnosing endometriosis (3). Endometriosis can be excluded with a high accuracy in patients with symptoms and signs suggestive of endometriosis if no lesions are identified during laparoscopy (3, 19). It is superior to laparotomy as endometriotic implants can be magnified for visualization (20). On the other hand, positive laparoscopy has a limited diagnostic value when no histologic examination of lesions is made (19). It is therefore recommended to obtain tissue for histopathologic examination in cases of

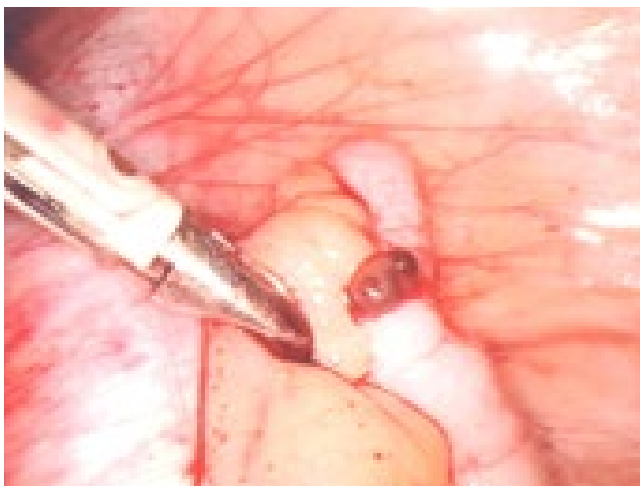


Figure 2a. Endometriosis of the appendix visualised at diagnostic laparoscopy.



Figure 2b. Endometriosis infiltrating abdominal wall seen at laparotomy.

positive laparoscopy (3). Positive histology confirms the diagnosis, but negative histology does not exclude it (3).

The value of laparoscopy in diagnosing endometriosis depends on the skills and knowledge of the clinician (3). The limited value of negative histology can be attributed in part to the limited skills of the clinician and low quality of the obtained samples (3). Retroperitoneal and vaginal endometriosis can be missed during laparoscopy and preoperative clinical examination of the pelvis, which is preferably made during anaesthesia that is required prior to laparoscopy (3, 17). Anatomical structures, including the uterus, adnexa, peritoneum of the Douglas space, vesico-uterine fold, ovarian fossae, pararectal space, rectum, sigmoid, caecum, appendix, and diaphragm, should be carefully examined during laparoscopy as suggested by the ESHRE guidelines (3). Some clinicians suggest that when a patient is undergoing surgery for ovarian endometrioma or deep infiltrating endometriosis, tissue for histological examination should be obtained to exclude malignancy (21). This is based on the data that ovarian endometriosis can very rarely (0.3%–0.8%) pose a risk of malignancy (21).

ULTRASOUND

Ultrasound is generally accepted as a first-line method of examination for endometriosis because of its availability, diagnostic accuracy, and relatively low cost. Developments in ultrasound technology have allowed for better visualisation of minor anatomical pathologies, which has contributed to significantly better capabilities to diagnose DIE in the last decade. However, there is a significant lack in standardisation of consensual terminology describing appearance and location of endometriotic lesions (9).

The examination should include meticulous evaluation of the uterus, ovaries, uterosacral ligaments, rectovaginal septum, rectosigmoid colon, urinary bladder, pelvic ureters, and pelvic peritoneum. Ovarian endometriosis is most commonly observed, which is also easiest to diagnose. Deep endometriotic lesions are most frequently located in the posterior compartment involving the uterus, uterosacral ligaments, vagina, rectovaginal septum, rectosigmoid colon, and pouch of Douglas (POD). These tend to be more challenging to diagnose compared to ovarian endometriosis. Hence, sonographic accuracy should be analysed according to specific endometriotic lesion locations.

Pelvic screening should be systematic and include posterior, anterior, and lateral compartments. Endometriotic lesions generally appear as hypo- or isoechoic solid nodules, which vary in size and may have regular or irregular contours. A transabdominal scan should be systematically used to screen for ureteral involvement and consequent hydronephrosis. This is especially important, since hydronephrosis can be asymptomatic and lead to an irreversible compromise of the kidney function. It is important to have a good knowledge of the pathophysiological background in endometriosis and be aware of the sites that are commonly affected by endometriosis. Deep endometriosis most often affects the posterior compartment, involving the isthmic part of the uterus, uterosacral ligaments, vagina, rectovaginal septum, POD, and rectosigmoid colon. Anterior

compartment with vesico-uterine pouch, bladder, and round ligaments are less frequently involved. Rarely, parametria, ureters, and lateral pelvic wall are involved in the disease. Hence, an ultrasound examination with the aim to map endometriosis should include a detailed examination of all of these regions. Additionally, the presence of 'soft markers' (site-specific tenderness and mobility of pelvic organs) should be noted.

Uterus and adnexa

First, the uterus should be visualised in detail, specifically to search for signs of adenomyosis, which is commonly associated with the presence of endometriosis (22). Next, the adnexa should be inspected. The presence of endometriomas should be noted along with their measurements in three orthogonal planes and their echographic characteristics (Figure 3A). Large ovarian endometriomas are especially frequently associated with other endometriotic lesions, such as adhesions and DIE. This is also the reason that endometriomas are less prone to torsion compared to other benign

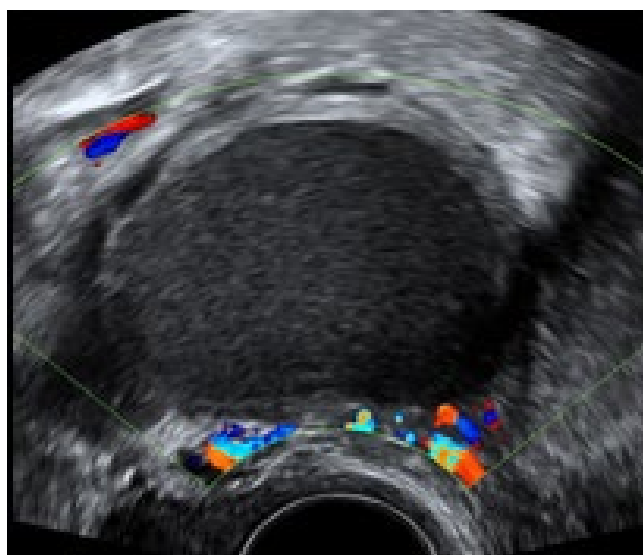


Figure 3a. Typical appearance of ovarian endometrioma. Ovarian endometrioma with 'ground-glass' appearance.

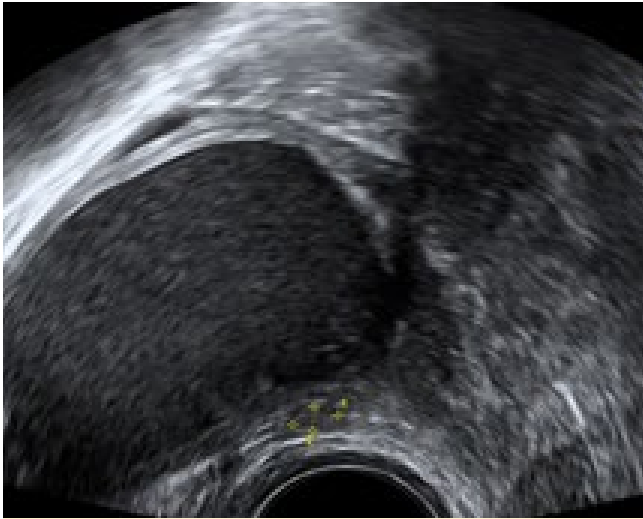


Figure 3b. Typical appearance of ovarian endometrioma. With large ovarian endometriomas, endometriotic nodules on the surface of the ovary with surrounding adhesions are frequently visible.

ovarian cysts (Figure 3B). During pregnancy, endometriomas tend to undergo a decidualisation, which can lead to confusion with malignancy (23). Simultaneous visualisation of other endometriosis signs may facilitate a correct diagnosis and avoid unnecessary surgery and concerns.

The presence of soft markers, such as site-specific tenderness and fixed ovaries, increases the likelihood of superficial endometriosis and adhesions (24, 25). By applying pressure transabdominally to the uterus and the ovaries, one can evaluate the mobility of pelvic organs. Hence, ovarian mobility in relation to the ovarian fossa, pelvic sidewall, uterus, uterosacral ligaments, and surrounding bowels can be assessed. If there is any free fluid, occasionally peritoneal pseudocysts may form inside the pelvic adhesions. Fallopian tubes are frequently involved in endometriosis and in these cases the normal tubal physiology is distorted, endometriotic foci may occlude the tube, and hydrosalpinges may form. Another soft marker useful in search for endometriosis is the sliding sign of the POD (26, 27). This is a sign that is easy to learn and is useful indirect evidence of adhesion presence. Gentle pressure is applied to the cervix with a transvaginal probe to establish whether the rectum

glides freely in relation to the posterior aspect of the cervix and posterior vaginal wall. If this is the case, the sliding sign is considered positive. The examiner can also place a free hand on the lower abdomen and apply pressure to see whether the anterior bowel glides freely in relation to the posterior aspect of the uterus. When both sliding signs are positive (posterior aspect of the cervix and the uterus), the POD is reported as not obliterated (9). If at least one of these locations is positive for the gliding sign, the POD is considered to be obliterated with adhesions. While POD obliteration is not a direct sign of endometriosis, it is frequently associated with severe DIE and especially with rectosigmoid endometriosis. In this setting, the sliding sign is highly relevant. Meta-analysis report pooled sensitivities and specificities of the sliding sign for obliteration of POD are 52.3%–83.0% and 91.7%–97.0%, respectively (28, 29).

Posterior compartment

Normal uterosacral ligaments are usually not visible on an ultrasound, except in the rare cases when surrounding fluid is present. In this case, they may present as thin regular hyperechoic strands. They are a common site for endometriosis implantation and in this case they appear as regular or irregular linear echogenic thickening (Figure 4). They are visible below the isthmic uterine part medial to the uterine artery in the longitudinal view of the uterus. Meta-analyses have been published analysing ultrasound diagnostic accuracy in visualisation of uterosacral endometriosis (30, 31).

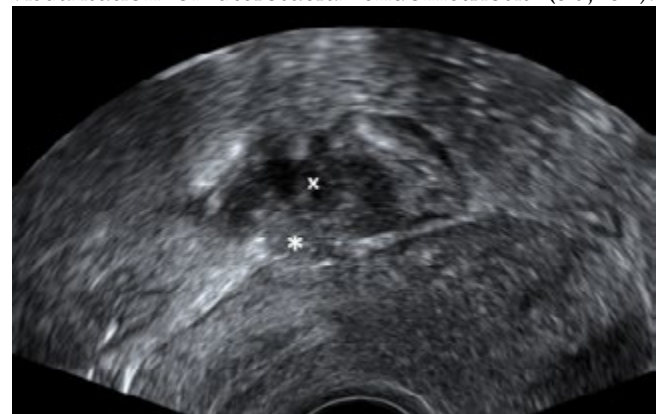


Figure 4. Endometriotic nodule in the uterosacral ligament (*) with adhesions to the rectosigmoid colon, where also an endometriotic nodule is seen (x).

The reported pooled sensitivities and specificities were 53%–64% and 93%–97%, respectively. This indicates that uterosacral endometriosis is difficult to diagnose and requires a very high level of ultrasound experience. The diagnostic accuracy is not improved if rectal endoscopic sonography is used (30, 32).

Although there is some inconsistency in the definition of rectovaginal septum endometriosis, recent consensus suggested that it should be diagnosed when

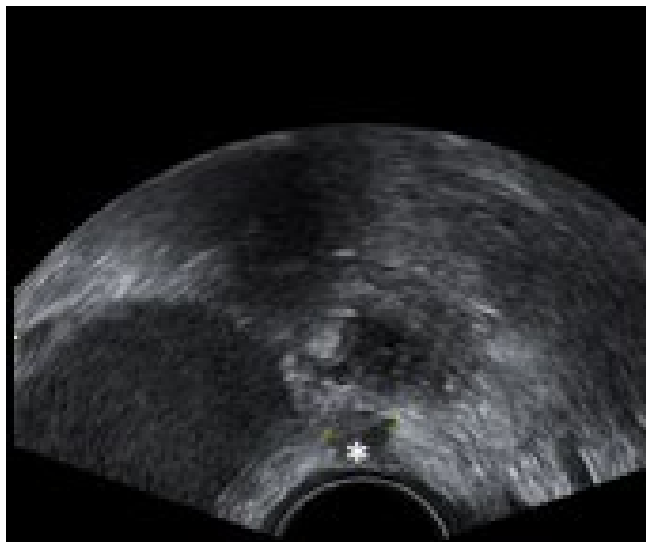


Figure 5a. Endometriosis of the rectovaginal septum. Endometriosis of the rectovaginal septum (*) with adherent ovary containing an endometrioma.



Figure 5b. Endometriosis of the rectovaginal septum. Endometriotic nodule (*) in the rectovaginal septum.



Figure 5c. Endometriosis of the rectovaginal septum. Endometriotic nodule (*) in the rectovaginal septum with adherent normal ovary.

a nodule is found below the horizontal plane passing through the lower border of the posterior cervical lip (Figure 5) (9). Likely due to the discrepancies in the diagnostic criteria, the reported ultrasound pooled sensitivities and specificities for this entity range between 49%–88% and 98%–100%, respectively (30, 31).

Endometriotic involvement of the rectosigmoid bowel can be visualised well on an ultrasound. Generally, this appears as an irregular hypoechoic mass penetrating the intestinal wall. First, the muscularis propria layer of the bowel is affected and normal hypoechoic aspect of this layer is replaced by an abnormal tissue mass (Figure 4). Bowel can be affected at a single place or there may be multifocal lesions. TVUS pooled sensitivity and specificity for rectosigmoid colon endometriosis are reported to be 90% and 96%, respectively (30).

Anterior compartment

Investigation of the anterior compartment involves the vesico-uterine pouch, bladder, distal parts of the ureters, and round ligaments. The prevalence in these areas is relatively low, estimated to be only between 2.0% and 8.4% in women with endometriosis (33-

35). Bladder involvement in endometriosis can be suspected when a hypo-, isoechoic, or heterogeneous thickening is found within the bladder wall (Figure 6B). This usually contains numerous anechoic (bubble-like) areas indicative of endometriosis. Most frequently it is located in the posterior wall of the bladder or in the bladder dome. Diagnostic accuracy data are scarce, but reported sensitivities and specificities range between 41%–55% and 93.5–100%, respectively (29, 30). Endometriosis in the vesico-uterine pouch is characterised by hypo- or isoechoic nodules between the anterior wall of the



Figure 6a. Endometriosis in the anterior compartment: Endometriotic nodule (*) in the vesicouterine pouch.



Figure 6b. Endometriosis in the anterior compartment: Endometriotic nodule (*) of the bladder wall.

bladder and the anterior wall of the uterus (Figure 6A). During the diagnostic process, it is helpful to apply pressure with an ultrasound transducer to check for the sliding sign between the bladder and the uterus. The incidence of vesico-uterine endometriosis is low. Therefore, TVUS diagnostic accuracy data are scarce.

Lateral compartment

During lateral compartment examination, pelvic sections of the ureters should be routinely inspected. The diagnostic accuracy for endometriosis in this area has been reported to be high. This is of utmost importance, since obstruction can lead to deterioration of the kidney function. The ureters should be inspected at rest and during peristalsis. In one report, the diagnosis of ureteral endometriosis had a sensitivity and specificity of 92% and 100%, respectively (36).

DISCUSSION

The capabilities of non-invasive diagnostics of pelvic endometriosis have improved significantly in the last decade. For most deep endometriotic lesions, TVUS and MRI exhibit comparable sensitivities and specificities to laparoscopic examination, which is considered by most as the gold standard for diagnosis today. Non-invasiveness and diagnostic accuracy are the characteristics that render ultrasound an ideal first-line tool in the diagnostics of women with suspected pelvic endometriosis (37). In order to achieve a high diagnostic accuracy, ultrasound should be performed by experienced operators with special training in ultrasound diagnostics of endometriosis. The examination should include both the assessment of morphological features of pelvic organs as well as their mobility. Sufficient time should be allocated for the examination in order to ensure a thorough assessment. This generally takes significantly longer compared to assessment of other common gynaecologic conditions.

Before surgical treatment of deep endometriosis, a comprehensive mapping should be performed, which

can be achieved with an ultrasound. According to a study evaluating preoperative ultrasound mapping of endometriosis, there is a good correlation between preoperative findings and diagnosis during laparoscopy (35). This is of crucial importance when planning surgery in order to avoid unexpected complications (38). It also aids the surgeon in ensuring the availability of necessary staff, such as colorectal surgeons or urologists, when treatment of bowel or ureter disease is required. Preoperative underestimation of the DIE lesion severity increases the risk of incomplete excision, progression of the

disease, and possible need for multiple surgical procedures. On the other hand, accurate diagnosis is also important to monitor the disease if the patient decides on conservative management or when planning a subfertility treatment.

In conclusion, in light of recent advances in imaging techniques, ultrasound should be accepted as a first-line diagnostic technique for pelvic endometriosis. Efforts should be made to improve the quality of diagnostics and care offered to women suffering with this chronic and often progressing condition.

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