# **ARTICLE IN PRESS**

Best Practice & Research Clinical Obstetrics and Gynaecology xxx (2018) 1-9

Contents lists available at ScienceDirect



Best Practice & Research Clinical Obstetrics and Gynaecology



journal homepage: www.elsevier.com/locate/bpobgyn

1

# Ultrasound diagnosis of endometriosis and adenomyosis: State of the art

Thierry Van den Bosch, MD, PhD<sup>\*</sup>, Dominique Van Schoubroeck, MD, PhD

Department of Obstetrics and Gynecology, University Hospital K.U. Leuven, Herestraat 49, 3000, Leuven, Belgium

Keywords: Adenomyosis Endometriosis Deep infiltrating endometriosis Ultrasonography Transvaginal ultrasonography Diagnosis

## ABSTRACT

Transvaginal ultrasonography has become the primary test in the diagnosis of pelvic endometriosis and adenomyosis. A review of the literature on the diagnostic accuracy of ultrasonography in pelvic endometriosis and adenomyosis, as well as a comparison with magnetic resonance imaging, will be presented. Criteria for diagnosis of an endometrioma according to robust prospective data together with guidelines as to adequate reporting of the location of deep infiltrating endometriosis will be given. The sonographic features of adenomyosis and a uterine fibroid are reviewed. The available data in the literature on ultrasound diagnosis of pelvic endometriosis and adenomyosis, their clinical relevance, and their limitations are discussed.

© 2018 Published by Elsevier Ltd.

## Introduction

Both endometriosis and adenomyosis are characterized by the presence of ectopic endometrial tissue, outside and inside the uterus, respectively. Endometriosis and adenomyosis often occur simultaneously. This paper on the ultrasound diagnosis of endometriosis and adenomyosis will focus on practical guidelines for the ultrasound examiner, as well as on the diagnostic accuracy of ultrasonography, as compared with magnetic resonance imaging (MRI) or histology.

\* Corresponding author.

*E-mail addresses:* thierry.vandenbosch@uzleuven.be (T. Van den Bosch), dominique.vanschoubroeck@uzleuven.be (D. Van Schoubroeck).

https://doi.org/10.1016/j.bpobgyn.2018.01.013 1521-6934/© 2018 Published by Elsevier Ltd.

# **ARTICLE IN PRESS**

### Endometriosis

Endometriosis is defined as the presence of endometrial tissue outside the uterus. It can be superficial, involving the peritoneum of the pelvic organs/abdominal wall including the diaphragm or the surface of the ovary. It may cause ovarian cysts (endometrioma) or it may extend beyond the peritoneum and deeply infiltrate the bladder, the bowel wall, and the structures surrounding the uterus (e.g., uterosacral ligaments) or be extra-abdominal (e.g., abdominal wall) [1]. Endometriosis affects between 5% and 45% of women of reproductive age [2]. The main challenges of imaging for endometriosis are the detection of nonovarian disease and the evaluation of the extension of the disease into pelvic structures [3].

The principal role of ultrasonography in the diagnosis of endometriosis is to tailor the management of patients. A correct mapping of endometriotic lesions may alert the surgeon on the presence of lesions that are not readily visible at laparoscopy (e.g., rectovaginal septum or vaginal wall nodules). In particular, the exact localization and extent of deep infiltrating endometriosis (DIE) is of importance in the planning of the type and degree of difficulty of a surgical procedure. For instance, in case of bowel wall infiltration or involvement of the ureter, extensive surgery is to be anticipated and the woman is to be informed accordingly. Preoperative imaging is also of value in the estimation of the operation time and the duration of the hospital stay.

Superficial peritoneal endometrioses such as peritoneal blebs and "gunshot" lesions are too small to be detected at ultrasound examination. At most, site-specific tenderness or reduced organ sliding during vaginal scanning may give a hint as to the presence of active peritoneal endometriosis, adhesions, or fibrosis. Site-specific tenderness, reduced ovarian mobility, and the presence of loculated peritoneal fluid in the pelvis are called "soft markers" for pelvic pathology, including superficial endometriosis [4].

An ovarian endometriotic cyst or endometrioma is often easy to diagnose at ultrasonography. In premenopausal women, a typical endometrioma is a cystic lesion with a ground glass echogenicity. The lesion may count from one to four locules but does not contain any solid parts. In a series of 713 endometriomas, more than half were unilocular cysts with ground glass echogenicity of the cyst content [5]. Color Doppler may help in the differential diagnosis between an endometrioma, a cystic corpus luteum, and a malignant lesion [3]. A corpus luteum typically presents with marked circular flow, while the presence of vessels within papillations raises the suspicion for malignancy. After menopause, ovarian cystic or solid cystic masses with a ground glass appearance have a high risk of malignancy [5]. Ovarian malignancy may mimic an endometriotic cyst in menopausal women. A malignancy may develop in an endometrioma. Especially, the presence of papillations with detectable blood flow in an ovarian cyst should alarm the clinician and is an indication for further investigation. The tumor marker CA125 is rarely helpful in the differential diagnosis between a benign endometrioma and a malignant ovarian mass in a woman of reproductive age because CA125 levels are often increased in women with endometriosis. In pregnant women, endometriomas decidualize leading to rounded, sometimes highly vascularized papillary projection with smooth contours within a solid-cystic ovarian lesion with ground glass or low-level echogenicity of the cystic content [6].

DIE has been defined as the presence of endometrial glands and stroma infiltrating more than 5 mm in the subperitoneal tissue [7,8]. The prevalence of DIE is estimated to be 1-2% [7]. Deep endometriosis typically presents as a single nodule in the vesicouterine fold or in the lower 20 cm of the bowel. Deep endometriosis is often associated with severe pain. It has been suggested to be a cofactor in infertility [7]. On sonographic appearance, it has been reported as "hypoechoic linear thickening or nodules/ masses with or without regular contours" [9,10]. The use of systematic and "tenderness-guided" transvaginal ultrasonography (TVUS) [4,9] optimizes the detection of DIE.

The anterior compartment involves the detection of bladder wall endometriosis. The distal part of the ureters up to the level of the fossae ovaricae can be evaluated during transvaginal scanning, while the upper part of the ureters and the kidneys can be assessed transabdominally. The presence of hydronephrosis suggests ureter stenosis. The systematic evaluation of the posterior compartment includes the meticulous visualization of the vaginal wall including the vaginal fornices, rectovaginal septum, the uterosacral ligaments, the anterior rectal wall, and the lower part of the anterior sigmoid wall. The use of extra gel in the vagina or within the probe cover may create an accoustic window and

3

optimize the ultrasound image of retrocervical deep endometriotic nodules [11]. The sliding of the uterus against the rectum allows for the detection of the pouch of Douglas adhesions or obliteration [12]. Retrocervical DIE involving both the posterior vaginal fornix and the anterior rectal wall have been described as diabolo-like or hourglass-shaped lesions [13,14].

TVUS has become the primary diagnostic tool in the diagnosis of deep infiltrating pelvic endometriosis. In the majority of cases, TVUS will give enough information to the surgeon allowing for adequate preoperative planning without the need for MRI [15]. Compared to MRI, TVUS is widely available in gynecologic outpatient clinics, well tolerated, less time-consuming, and less expensive [16].

In a systematic review, Guerriero et al. [17] compared the diagnostic accuracy of TVUS and MRI in pelvic DIE. Studies from 1989 till 2016 in which patients underwent both techniques were considered, and six studies have been selected, including 424 women. The diagnostic accuracy for DIE was evaluated for three locations: the rectosigmoid, the rectovaginal septum, and the uterosacral ligament. They showed that the overall diagnostic performance was similar for both techniques. For DIE in the recto-sigmoid, the pooled sensitivity for MRI and TVUS was 0.85 (95% CI, 0.78–0.90) and 0.85 (95% CI, 0.68–0.94), respectively, while the pooled specificity was 0.95 (95% CI, 0.83–0.99) and 0.96 (95% CI, 0.68–0.94), respectively. For DIE in the rectovaginal septum, the pooled sensitivity for MRI and TVUS was 0.85 (95% CI, 0.78–0.90) and 0.85 (95% CI, 0.68–0.94), respectively. For DIE in the rectovaginal septum, the pooled sensitivity for MRI and TVUS was 0.95 (95% CI, 0.83–0.99) and 0.96 (95% CI, 0.68–0.94), respectively. For DIE in the rectovaginal septum, the pooled sensitivity for MRI and TVUS was 0.95 (95% CI, 0.83–0.99) and 0.96 (95% CI, 0.68–0.94), respectively. For DIE in the uterosacral ligaments, the pooled sensitivity for MRI and TVUS was 0.70 (95% CI, 0.55–0.82) and 0.67 (95% CI, 0.55–0.77), respectively, while the pooled specificity was 0.93 (95% CI, 0.87–0.97) and 0.86 (95% CI, 0.73–0.93), respectively.

Nisenblat et al. [18] performed a Cochrane review on the diagnostic accuracy of imaging modalities for the diagnosis of pelvic superficial endometriosis, ovarian endometriosis, and DIE using surgical diagnosis as a reference standard, including 49 studies involving 4807 women. Neither TVUS nor MRI met the criteria of diagnostic accuracy for a replacement or triage test for detecting pelvic endometriosis. The sensitivity and specificity for diagnosis of endometrioma by TVUS were 0.93 (95% CI, 0.87–0.99) and 0.96 (95% CI, 0.92–0.99), respectively, versus 0.95 (95% CI, 0.90–1.00) and 0.91 (95% CI, 0.86–0.97), respectively, for MRI. For DIE, the sensitivity and specificity were 0.79 (95% CI, 0.69–0.89) and 0.94 (95% CI, 0.88–1.00), respectively, for TVUS, versus 0.94 (95% CI, 0.90–0.97) and 0.77 (95% CI, 0.44–1.00), respectively, for MRI.

Hudelist et al. [19] reviewed the literature from 1966 till 2010 on the diagnostic value of TVUS for bowel endometriosis, including 10 studies involving 1106 patients. The pooled estimates of sensitivities and specificities were 91% and 98%, respectively.

Guerriero et al. [20] reviewed the literature from 1989 till 2014 evaluating the diagnostic accuracy of TVUS in the detection of DIE in the uterosacral ligaments, rectovaginal septum, vagina, and bladder. Eleven studies, including 1583 patients, were included in the meta-analysis. Overall, the sensitivity was fair but the specificity was high. In the diagnosis of DIE in the uterosacral ligaments, the overall pooled sensitivity and specificity of TVUS were 53% (95% CI, 35–70%) and 93% (95% CI, 83–97%), respectively; for DIE in the rectovaginal septum, the overall pooled sensitivity and specificity were 49% (95% CI, 36–62%) and 98% (95% CI, 95–99%), respectively; and for vaginal DIE, the overall pooled sensitivity and specificity were 58% (95% CI, 40–74%) and 96% (95% CI, 87–99%), respectively.

Guerriero et al. [21] reviewed the literature from 1989 till 2014, more specifically on the diagnostic accuracy of TVUS in the detection of rectosigmoid endometriosis. They selected 19 studies including 2639 patients. The overall pooled sensitivity and specificity were 91% (95% CI, 85–94%) and 97% (95% CI, 95–98%), respectively.

The lack of free movement of the pelvic organs while pushing gently on the uterus and ovaries suggests adhesions or endometriosis [22]. Reid et al. [12] evaluated inter-/intra-observer agreement and diagnostic accuracy in the prediction of the pouch of Douglas obliteration at offline analysis of two-dimensional videos using the dynamic real-time TVUS "sliding sign" technique. Among gynecologic ultrasound specialists, the Cohen's kappa reflecting the intraobserver agreement for the interpretation of the "sliding sign" and the prediction of the pouch of Douglas obliteration ranged from 0.71 to 0.95 and 0.67–1.0, respectively, indicating substantial agreement. The ranges for sensitivity and specificity for gynecologic ultrasound specialists were 92.9–100 and 90.9–100, respectively.

Nisenblat et al. [23] performed a Cochrane review on the diagnostic accuracy of combinations of different noninvasive testing modalities for ovarian, peritoneal, or DIE. Eleven studies that included 1339 patients were deemed eligible. In the diagnosis of rectal endometriosis, the combination of vaginal examination and TVUS had a sensitivity and specificity of 0.96 (95% CI, 0.86–0.99) and 0.98 (95% CI, 0.94–1.00), respectively; for obliterated pouch of Douglas, a sensitivity of 0.87 (95% CI, 0.69–0.96) and a specificity of 0.98 (95% CI, 0.95–1.00); for vaginal wall endometriosis, a sensitivity of 0.82 (95% CI, 0.60–0.95) and a specificity of 0.99 (95% CI, 0.97–1.0), respectively, and for rectovaginal septum endometriosis, a sensitivity of 0.88 (95% CI, 0.47–1.00) and a specificity of 0.99 (95% CI, 0.96–1.00), respectively. For endometrioma, TVUS and serum CA-125 (cutoff  $\geq$ 35 U/ml) had a sensitivity of 0.52 (95% CI, 0.33–0.71) and a specificity 0.97 (95% CI, 0.90–1.00).

Magnetic resonance and ultrasonography have a similar diagnostic accuracy for endometriosis [2]. A better awareness of DIE as well as improved technology might improve detection rates. The main limitation of ultrasonography is the detection of lesions located above the rectosigmoid junction. Transvaginal scanning has a limited field-of-view while transabdominal ultrasonography has a low detection rate for upper bowel lesions [2].

Medeiros et al. [24] in a meta-analysis on the accuracy of pelvic MRI in the diagnosis of DIE, including 20 studies (1819 women) between 1990 and 2013, reported a pooled sensitivity and specificity of 0.83 and 0.90, respectively, for all sites; 0.64 and 0.98, respectively, for bladder DIE; 0.84 and 0.97, respectively, for intestinal lesions; 0.89 and 0.94, respectively, for the pouch of Douglas DIE; 0.83 and 0.88, respectively, for the rectosigmoid; 0.77 and 0.95, respectively, for the rectovaginal DIE; 0.85 and 0.80, respectively, for the uterosacral ligaments; and 0.82 and 0.82, respectively, for vaginal lesions.

#### Adenomyosis

Adenomyosis is defined as the presence of ectopic endometrial tissue within the myometrium. The prevalence based on hysterectomy pathology reports ranges from 5% to 70% [25-28]. This discrepancy in prevalence can be attributed to the various diagnostic classifications, different patients' populations, differences in tissue sample sizes, and possible pathologist bias [29–33]. In a prospective observational study on 985 consecutive women undergoing TVUS examination [34], adenomyosis was present in 20.9% (95% CI, 18.5–23.6%). On multivariate analysis, the prevalence of adenomyosis was significantly associated with women's age, gravidity, and pelvic endometriosis (p < 0.001). In a cross-sectional study on 3D ultrasound in 1015 patients undergoing artificial reproductive technology (ART) [35], the prevalence of adenomyosis was 24.4%. In Puente's series [35], the ultrasound criteria for adenomyosis were presence of a globular uterine configuration, myometrial anterior-posterior asymmetry, heterogeneous myometrial echotexture, poor definition of the junctional zone, and subendometrial cysts. The prevalence was higher in women with a history of recurrent pregnancy loss (38.2%; p < 0.005) and previous ART failure (34.7%; p < 0.0001). Adenomyosis was associated with endometriosis in 35.1%. In a smaller series of 121 women undergoing ultrasound scanning before operative laparoscopy for DIE, almost half of women (49%) showed concomitant adenomyosis [36]. Compared to those women with only DIE, those with associated DIE and adenomyosis had more complaints of dysmenorrhea (p = 0.0019), dyspareunia (p = 0.004), and abnormal uterine bleeding (p = 0.001).

Following ultrasonographic features have been associated with adenomyosis: an irregular or interrupted junctional zone, subendometrial lines and buds, echogenic islands within the myometrium, myometrial cysts, presence of fan-shaped shadowing, uterine wall asymmetry, translesional vascularity, and/or a globally enlarged uterus [37–39]. However, the above-mentioned ultrasound features are not pathognomonic for adenomyosis. Myometrial cysts may, for example, undergo cystic degeneration in fibroids or secondary to tamoxifen use. Fan-shaped shadowing is also seen in fibroids owing to the presence of calcifications and/or cysts. An interrupted junctional zone is also typical for FIGO 1, 2, or 3 fibroids or in case of (early) myometrial invasion in endometrial cancer. Endometrial malignancy may be associated with an irregular ill-defined junctional zone as well.

Most adenomyosis lesions are ill defined, but some may be well defined and are called adenomyomas. Although some adenomyosis lesions are apparently focal on ultrasound scan or macroscopic examination, the ectopic endometrial tissue is often more diffusely present within the myometrium on

5

histological examination [29]. Most myometrial cysts are located completely in the myometrium, but incidentally a communication between the endometrial cavity and the adenomyotic cyst may be observed during contrast sonohysterography [40].

The differential diagnosis between adenomyosis and uterine fibroids is important in the management, especially while contemplating medical treatment or surgical options [41,42]. A fibroid grows and pushes the adjacent myometrium away. Although the myometrium may be compressed and look thinned, it is able to recover after myomectomy without loss of healthy myometrial tissue. On the contrary, in adenomyosis, the ectopic endometrial tissue penetrates between the myometrial cells without compressing the myometrium, as endometrial tissue is amid the myometrial tissue. Resection of adenomyosis may result in a substantial loss of myometrium. Although the differential diagnosis between an adenomyoma and a fibroid with cystic degeneration may be difficult to make using ultrasonography, the difference between a typical fibroid and diffuse adenomyosis is often straightforward. A fibroid is typically a well-defined round lesion, whereas most adenomyosis lesions are ill defined. The echogenicity of fibroids varies widely from uniform hypo-, iso-, or hyperechogenic to nonuniform with mixed echogenicity and/or strong calcifications. The presence of endometrial tissue and/or fluid-filled glandular structures (cysts) within the myometrium in women with adenomyosis causes the heterogeneous cystic ultrasound appearance of the uterine wall.

It is important to stress the lack of well-designed prospective data on the value of the different features described in the literature, in terms of diagnostic importance and clinical relevance. It is generally believed that the more features are detected, the more likely the diagnosis of adenomyosis. However, the importance of each of the features and clinical symptoms of pain or uterine bleeding is not known. The therapeutical implications should therefore be considered with caution.

Although TVUS is the first choice imaging modality in the diagnosis of adenomyosis, MRI may add information and increase diagnostic performance in difficult cases, e.g., with coexistence of lesions such as fibroids. Although adenomyosis is located within the myometrium and is thus not visible on hysteroscopy, incidentally an adenomyosis lesion may protrude in the uterine cavity and be seen at hysteroscopy [43].

In earlier times, TVUS was not considered reliable in the evaluation of the junctional zone [44]. With the emergence of newer ultrasound technologies in the past decade, including high-frequency probes, three-dimensional (3D) ultrasonography, and volume contrast imaging (VCI), the junctional zone can reliably be evaluated nowadays [45].

In a prospective observational study on 205 nulligravid women between age 18 and 30 years, a regular spontaneous menstrual cycle, and no history of gynecologic pathology, the prevalence of diffuse adenomyosis was 34% [46]. The sonographic features for diffuse adenomyosis included a heterogeneous myometrium; hypoechoic striation in the myometrium; myometrial anechoic lacunae or cysts; asymmetrical myometrial thickening of the uterine walls with the presence of straight vessels, extending into the hypertrophic myometrium on power Doppler examination; and a maximal junctional zone thickness (JZmax)  $\geq$  8 mm or a difference between the maximal and minimal JZ thickness (JZdiff)  $\geq$  4 mm on 3D-TVUS. The most common sonographic feature was an asymmetric myometrial thickening of the uterine walls. There was a significant association between diffuse adenomyosis, as diagnosed on ultrasonography, and dysmenorrhea (p = 0.005) and abnormal uterine bleeding (p = 0.03). Women with diffuse adenomyosis were reported to have a thicker junctional zone: JZmax (6.38 ± 2.30 mm, P < 0.001) and JZdiff (4.33 ± 1.99 mm, p < 0.001).

According the literature, the accuracy of TVUS in detecting adenomyosis ranges widely. However, the published accuracy figures should be interpreted with caution because the reference tests used, being either histology or MRI, have their own diagnostic limitations.

Exacoustos et al. [47] studied a series of 72 premenopausal patients who underwent 2D- and 3D-TVUS before hysterectomy for benign indications. The prevalence of adenomyosis on histology was 44% patients. For 2D-TVUS and 3D-TVUS, the overall sensitivity was 75% and 91%, respectively, and the overall specificity was 90% and 88%. The most specific (98%) ultrasound feature on 2D-TVUS for adenomyosis was the presence of myometrial cysts and the most sensitive feature (88%) was a heterogeneous myometrium. On 3D-TVUS, both the JZdiff  $\geq$ 4 mm and JZ infiltration and distortion had high sensitivity (88%).

Andres et al. [48] published a systematic review on the accuracy of 2D- and 3D-TVUS. Screening the literature from the past 10 years, they included 8 studies. For 2D-ultrasonography, pooled sensitivity and specificity for the diagnosis of adenomyosis for all combined imaging characteristics was 83.8% and 63.9%, respectively. The highest sensitivity (86.0%) for a single 2D-ultrasound feature was heterogeneous myometrium. For 3D-ultrasonography, pooled sensitivity and specificity for all combined imaging characteristics was 88.9% and 56.0%, respectively. The highest pooled sensitivity (86%) and specificity (56.0%) for a single feature was for poor definition of the junctional zone.

In a systematic review of papers published up to 2010, Champaneria et al. [49] included 23 articles, involving 2312 women. The selected studies reported data on ultrasound and/or MRI, with the reference standard for a definitive diagnosis being histology of hysterectomy specimen. Both TVUS and MRI showed high levels of accuracy for the diagnosis of adenomyosis. The pooled sensitivity for TVUS was 72% (95% CI, 65–79%), and the specificity was 81% (95% CI, 77–85%), whereas MRI had a pooled sensitivity of 77% (95% CI, 67–85%) and a specificity of 89% (95% CI, 84–92%). This illustrates that, in older series, MRI had a slightly better diagnostic accuracy as compared to TVUS.

In a retrospective series of 213 consecutive patients scheduled for hysterectomy undergoing preoperative TVUS [50], the prevalence of adenomyosis was 40%. The diagnosis of adenomyosis was based on the presence of one or more of the following sonographic features: a globular uterine configuration, poor definition of the junctional zone, sub-endometrial echogenic linear striations, myometrial anterior—posterior asymmetry, myometrial cysts, and a heterogeneous myometrial echotexture. The sensitivity and specificity of TVUS for the diagnosis of adenomyosis were 87% and 60%, respectively. The presence of subendometrial linear striations had the highest diagnostic accuracy for adenomyosis.

In a prospective study on 70 consecutive patients undergoing TVUS before hysterectomy [51], the prevalence of adenomyosis was 37%. Adenomyosis was defined as the presence of at least one of the following sonographic features: heterogeneous myometrial echotexture, globular-appearing uterus, asymmetrical thickness of the anteroposterior wall of the myometrium, subendometrial myometrial cysts, subendometrial echogenic linear striations, or poor definition of the endometrial–myometrial junction. The sensitivity and specificity of TVUS for the diagnosis of adenomyosis were 80.8% and 61.4%, respectively. A regularly enlarged uterus with a globular appearance, subendometrial echogenic linear striations, and myometrial cysts were the features with the highest accuracy for the diagnosis of adenomyosis. The presence of subendometrial linear striations was the most specific sonographic feature (95.5%).

In 2009, Meredith et al. [52] reported a systematic review on the diagnostic accuracy of TVUS for adenomyosis. They included 14 studies (involving 1895 women) between 1966 and 2007. The overall prevalence of adenomyosis was 27.9% (95% CI, 25.5–30.3). The probability of adenomyosis with an abnormal TVUS was 66.2% (95% CI, 61.6–70.6). The probability of adenomyosis with a normal TVUS was 9.1% (95% CI, 7.3–11.1). Given the inclusion of very old studies, back in times where high-frequency ultrasonography and 3D-scanning were not available yet, the overall accuracy figures cannot be considered relevant today. This is also illustrated in the review by Levgur [53] including papers published from 1949 to 2005, reporting a range for sensitivity for diagnosis of adenomyosis by TVUS between 50% and 87%.

In a small series on 30 consecutive women with suspected adenomyosis, elastosonography suggested a higher degree of softness in the adenomyotic area compared with the surrounding uterine tissue [54].

Eisenberg et al. [55], in a retrospective case-control study in 154 women, showed a higher prevalence of adenomyosis in women with endometriosis compared with healthy controls. The diagnosis of endometriosis was made by laparoscopy, and the diagnosis of adenomyosis by TVUS. The ultrasonographic signs were asymmetrical myometrial thickening, linear striations, myometrial cysts, hyperechoic islands, irregular endometrial–myometrial junction, parallel shadowing, and localized adenomyomas. Women who had five of more sonographic signs had a threefold risk for infertility (OR = 3.2, 95% Cl, 1.3-8.2).

Adenomyosis has been associated with silent uterine rupture [56–58], while endometriosis has been reported to be associated with spontaneous hemoperitoneum in pregnancy (SHiP). SHiP is a serious acute complication with high rates of adverse outcome [59–62].

The most common cancer associated with ectopic endometrium is the endometrioid adenocarcinoma. Other subtypes such as a clear cell carcinoma are very rare [63]. Cancer arising from adenomyotic foci may remain undetectable by hysteroscopy and endometrial sampling as long as the tumor does not involve the eutopic endometrium [64].

## Summary

Real-time dynamic TVUS is the first test in the diagnosis of both endometriosis and adenomyosis. Site-specific tenderness, the absence of organ sliding, and the visualization of typical sonographic features will lead to lesion detection. Both a high-end ultrasound machine and a high level of expertise will optimize diagnostic accuracy [3].

In most cases, TVUS will enable an accurate diagnosis of ovarian endometriosis (endometrioma); pouch of Douglas obliteration; DIE of the anterior- (bladder wall), posterior- (rectovaginal septum, rectum, and rectosigmoid), and lateral- (uterosacral ligaments and ureters) compartment, as well as of adenomyosis. Accurate detection of DIE is crucial to triage those patients in whom surgery is indicated. Appropriate mapping of DIE lesions is essential in the planning of endometriosis surgery, especially by anticipating the need for extensive bowel, ureter, or bladder surgery. The correct diagnosis of adenomyosis, and more specifically, the differentiation between adenomyosis and uterine fibroids has important therapeutic implications. Whereas a well-performed myomectomy is associated with limited myometrial damage, resection of adenomyosis is much more likely to cause extensive injury of the myometrium.

The published diagnostic accuracy figures should be interpreted with caution: the reference test (e.g., histology of a hysterectomy specimen) is not infallible and may be associated with false-negative results, the index test used may be outdated (e.g., in systematic reviews including papers published more than 5 or 10 years ago), and the expertise and awareness of the examiner may vary widely (for TVUS as well as MRI).

#### **Conflict of interest statement**

None.

#### **Practice Points**

- An endometrioma presents in the premenopause as a cystic lesion (one to four locules) with ground glass appearance without any solid parts.
- TVUS gives sufficient preoperative information as to the presence and location of DIE.
- Differentiating between adenomyosis and a fibroid is of clinical importance.

#### **Research agenda**

- Prediction of the depth of invasion of the bowel wall in deep infiltrating endometriosis.
- The relative relevance of the sonographic features in the diagnosis of adenomyosis.
- The extent of adenomyosis according to ultrasound scan versus histology.
- The association of sonographic appearance and clinical symptoms in adenomyosis.

Please cite this article in press as: Van den Bosch T, Van Schoubroeck D, Ultrasound diagnosis of endometriosis and adenomyosis: State of the art, Best Practice & Research Clinical Obstetrics and Gynaecology (2018), https://doi.org/10.1016/j.bpobgyn.2018.01.013

7

# **ARTICLE IN PRESS**

T. Van den Bosch, D. Van Schoubroeck / Best Practice & Research Clinical Obstetrics and Gynaecology xxx (2018) 1–9

#### References

- Cacciato Insilla A, Granai M, Gallippi G, Giusti P, Giusti S, Guadagni S, et al. Deep endometriosis with pericolic lymph node involvement: a case report and literature review. World J Gastroenterol 2014;20:6675–9.
- [2] Exacoustos C, Manganaro L, Zupi E. Imaging for the evaluation of endometriosis and adenomyosis. Best Pract Res Clin Obstet Gynaecol 2014;28:655–81.
- [3] Exacoustos C, Zupi E, Piccione E. Ultrasound imaging for ovarian and deep infiltrating endometriosis. Semin Reprod Med 2017;35:5–24.
- [4] Okaro E, Condous G, Khalid A, Timmerman D, Ameye L, Huffel SV, et al. The use of ultrasound-based 'soft markers' for the prediction of pelvic pathology in women with chronic pelvic pain—can we reduce the need for laparoscopy? BJOG 2006; 113:251–6.
- [5] Van Holsbeke C, Van Calster B, Guerriero S, Savelli L, Paladini D, Lissoni AA, et al. Endometriomas: their ultrasound characteristics. Ultrasound Obstet Gynecol 2010;35:730–40.
- [6] Mascilini F, Moruzzi C, Giansiracusa C, Guastafierro F, Savelli L, De Meis L, et al. Imaging in gynecological disease. 10: clinical and ultrasound characteristics of decidualized endometriomas surgically removed during pregnancy. Ultrasound Obstet Gynecol 2014;44:354–60.
- [7] Koninckx PR, Ussia A, Adamyan L, Wattiez A, Donnez J. Deep endometriosis: definition, diagnosis, and treatment. Fertil Steril 2012;98:564–71.
- [8] Guerriero S, Condous G, van den Bosch T, Valentin L, Leone FP, Van Schoubroeck D, et al. Systematic approach to sonographic evaluation of the pelvis in women with suspected endometriosis, including terms, definitions and measurements: a consensus opinion from the International Deep Endometriosis Analysis (IDEA) group. Ultrasound Obstet Gynecol 2016; 48:318–32.
- [9] Guerriero S, Ajossa S, Gerada M, Virgilio B, Angioni S, Melis GB. Diagnostic value of transvaginal 'tenderness-guided' ultrasonography for the prediction of location of deep endometriosis. Hum Reprod 2008;23:2452–7.
- [10] Coccia ME, Rizzello F. Ultrasonographic staging: a new staging system for deep endometriosis. Ann N Y Acad Sci 2011; 1221:61–9.
- [11] Guerriero S, Ajossa S, Gerada M, D'Aquila M, Piras B, Melis GB. "Tenderness-guided" transvaginal ultrasonography: a new method for the detection of deep endometriosis in patients with chronic pelvic pain. Fertil Steril 2007;88:1293–7.
- [12] Reid S, Condous G. Transvaginal sonographic sliding sign: accurate prediction of pouch of Douglas obliteration. Ultrasound Obstet Gynecol 2013;41:605–7.
- [13] Donnez J, Pirard C, Smets M, Jadoul P, Squifflet J. Surgical management of endometriosis. Best Pract Res Clin Obstet Gynaecol 2004;18:329-48.
- [14] Del Frate C, Girometti R, Pittino M, Del Frate G, Bazzocchi M, Zuiani C. Deep retroperitoneal pelvic endometriosis: MR imaging appearance with laparoscopic correlation. Radiographics 2006;26:1705–18.
- [15] Turocy JM, Benacerraf BR. Transvaginal sonography in the diagnosis of deep infiltrating endometriosis: a review. J Clin Ultrasound 2017;45:313–8.
- [16] Hoyos LR, Benacerraf B, Puscheck EE. Imaging in endometriosis and adenomyosis. Clin Obstet Gynecol 2017;60:27–37.
- [17] Guerriero S, Saba L, Pascual MA, Ajossa S, Rodriguez I, Mais V, et al. Transvaginal ultrasound (TVS) versus Magnetic Resonance (MR) for diagnosing deep infiltrating endometriosis: a systematic review and meta-analysis. Ultrasound Obstet Gynecol 2017 Nov 20. https://doi.org/10.1002/uog.18961.
- [18] Nisenblat V, Bossuyt PM, Farquhar C, Johnson N, Hull ML. Imaging modalities for the non-invasive diagnosis of endometriosis. Cochrane Database Syst Rev 2016 Feb 26;2. CD009591.
- [19] Hudelist G, English J, Thomas AE, Tinelli A, Singer CF, Keckstein J. Diagnostic accuracy of transvaginal ultrasound for noninvasive diagnosis of bowel endometriosis: systematic review and meta-analysis. Ultrasound Obstet Gynecol 2011;37: 257–63.
- [20] Guerriero S, Ajossa S, Minguez JA, Jurado M, Mais V, Melis GB, et al. Accuracy of transvaginal ultrasound for diagnosis of deep endometriosis in uterosacral ligaments, rectovaginal septum, vagina and bladder: systematic review and metaanalysis. Ultrasound Obstet Gynecol 2015;46:534–45.
- [21] Guerriero S, Ajossa S, Orozco R, Perniciano M, Jurado M, Melis GB, et al. Accuracy of transvaginal ultrasound for diagnosis of deep endometriosis in the rectosigmoid: systematic review and meta-analysis. Ultrasound Obstet Gynecol 2016;47: 281–9.
- [22] Groszmann YS, Benacerraf BR. Complete evaluation of anatomy and morphology of the infertile patient in a single visit; the modern infertility pelvic ultrasound examination. Fertil Steril 2016;105:1381–93.
- [23] Nisenblat V, Prentice L, Bossuyt PM, Farquhar C, Hull ML, Johnson N. Combination of the non-invasive tests for the diagnosis of endometriosis. Cochrane Database Syst Rev 2016 Jul 13;7. CD012281.
- [24] Medeiros LR, Rosa MI, Silva BR, Reis ME, Simon CS, Dondossola ER, et al. Accuracy of magnetic resonance in deeply infiltrating endometriosis: a systematic review and meta-analysis. Arch Gynecol Obstet 2015;291:611–21.
- [25] Devlieger R, D'Hooghe T, Timmerman D. Uterine adenomyosis in the infertility clinic. Hum Reprod Update 2003;9:139–47.
  [26] Tomassetti C, Meuleman C, Timmerman D, D'Hooghe T. Adenomyosis and subfertility: evidence of association and causation. Semin Reprod Med 2013;31:101–8.
- [27] Struble J, Reid S, Bedaiwy MA. Adenomyosis: a clinical review of a challenging gynecologic Condition. J Minim Invasive Gynecol 2016;1(23):164-85.
- [28] Shrestha A, Shrestha R, Sedhai LB, Pandit U. Adenomyosis at hysterectomy: prevalence, patient characteristics, clinical profile and histopatholgical findings. Kathmandu Univ Med J 2012;10:53–6.
- [29] Vandermeulen L, Cornelis A, Kjaergaard Rasmussen C, Timmerman D, Van den Bosch T. Guiding histological assessment of uterine lesions using 3D in vitro ultrasonography and stereotaxis. Facts Views Vis Obgyn 2017;9:77–84.
- [30] Garcia L, Isaacson K. Adenomyosis: review of the literature. J Minim Invasive Gynecol 2011;18:428–37.
- [31] Azziz R. Adenomyosis: current perspectives. Obstet Gynecol Clin N Am 1989;16:221–35.
- [32] Bergholt T, Bergholt T, Eriksen L, Berendt N, Jacobsen M, Hertz JB. Prevalence and risk factors of adenomyosis at hysterectomy. Human Reprod 2001;16:2418–21.

- [33] Bird CC, McElin TW, Manalo-Estrella P. The elusive adenomyosis of the uterus—revisited. Am J Obstet Gynecol 1972;112: 583–93.
- [34] Naftalin J, Hoo W, Pateman K, Mavrelos D, Holland T, Jurkovic D. How common is adenomyosis? A prospective study of prevalence using transvaginal ultrasound in a gynaecology clinic. Hum Reprod 2012;27:3432–9.
- [35] Puente JM, Fabris A, Patel J, Patel A, Cerrillo M, Requena A, et al. Adenomyosis in infertile women: prevalence and the role of 3D ultrasound as a marker of severity of the disease. Reprod Biol Endocrinol 2016;14:60.
- [36] Lazzeri L, Di Giovanni A, Exacoustos C, Tosti C, Pinzauti S, Malzoni M, et al. Preoperative and Postoperative clinical and transvaginal ultrasound findings of adenomyosis in patients with deep infiltrating endometriosis. Reprod Sci 2014;21: 1027–33.
- [37] Van den Bosch T, Dueholm M, Leone FP, Valentin L, Rasmussen CK, Votino A, et al. Terms, definitions and measurements to describe sonographic features of myometrium and uterine masses: a consensus opinion from the Morphological Uterus Sonographic Assessment (MUSA) group. Ultrasound Obstet Gynecol 2015;46:284–98.
- [38] Sakhel K, Abuhamad A. Sonography of adenomyosis. J Ultrasound Med 2012;31:805-8.
- [39] Valentini AL, Speca S, Gui B, Soglia G, Miccò M, Bonomo L. Adenomyosis: from the sign to the diagnosis. Imaging, diagnostic pitfalls and differential diagnosis: a pictorial review. Radiol Med 2011;116:1267–87.
- [40] Reeves MF, Goldstein RB, Jones KD. Communication of adenomyosis with the endometrial cavity: visualization with saline contrast sonohysterography. Ultrasound Obstet Gynecol 2010;36:115–9.
- [41] Alabiso G, Alio L, Arena S, Barbasetti di Prun A, Bergamini V, Berlanda N, et al. Adenomyosis: what the patient needs. J Minim Invasive Gynecol 2016;23:476–88.
- [42] Pontis A, D'Alterio MN, Pirarba S, de Angelis C, Tinelli R, Angioni S. Adenomyosis: a systematic review of medical treatment. Gynecol Endocrinol 2016;32:696–700.
- [43] Pontrelli G, Bounous VE, Scarperi S, Minelli L, Di Spiezio Sardo A, Florio P. Rare case of giant cystic adenomyoma mimicking a uterine malformation, diagnosed and treated by hysteroscopy. J Obstet Gynaecol Res 2015;41:1300–4.
- [44] Gordts S, Brosens JJ, Fusi L, Benagiano G, Brosens I. Uterine adenomyosis: a need for uniform terminology and consensus classification. Reprod Biomed Online 2008;17:244–8.
- [45] Votino A, Van den Bosch T, Installé AJ, Van Schoubroeck D, Kaijser J, Kacem Y, et al. Optimizing the ultrasound visualization of the endometrial-myometrial junction (EMJ). Facts Views Vis Obgyn 2015;7:60–3.
- [46] Pinzauti S, Lazzeri L, Tosti C, Centini G, Orlandini C, Luisi S, et al. Transvaginal sonographic features of diffuse adenomyosis in 18-30-year-old nulligravid women without endometriosis: association with symptoms. Ultrasound Obstet Gynecol 2015;46:730–6.
- [47] Exacoustos C, Brienza L, Di Giovanni A, Szabolcs B, Romanini ME, Zupi E, et al. Adenomyosis: three-dimensional sonographic findings of the junctional zone and correlation with histology. Ultrasound Obstet Gynecol 2011;37:471–9.
- [48] Andres MP, Borrelli GM, Ribeiro J, Baracat EC, Abrão MS, Kho RM. Transvaginal ultrasound for the diagnosis of adenomyosis: systematic review and meta-analysis. J Minim Invasive Gynecol 2018;25:257–64.
- [49] Champaneria R, Abedin P, Daniels J, Balogun M, Khan KS. Ultrasound scan and magnetic resonance imaging for the diagnosis of adenomyosis: systematic review comparing test accuracy. Acta Obstet Gynecol Scand 2010;89:1374–84.
- [50] Sun YL, Wang CB, Lee CY, Wun TH, Lin P, Lin YH, et al. Transvaginal sonographic criteria for the diagnosis of adenomyosis based on histopathologic correlation. Taiwan J Obstet Gynecol 2010;49:40–4.
- [51] Kepkep K, Tuncay YA, Göynümer G, Tutal E. Transvaginal sonography in the diagnosis of adenomyosis: which findings are most accurate? Ultrasound Obstet Gynecol 2007;30:341–5.
- [52] Meredith SM, Sanchez-Ramos L, Kaunitz AM. Diagnostic accuracy of transvaginal sonography for the diagnosis of adenomyosis: systematic review and metaanalysis. Am J Obstet Gynecol 2009;201:107. e1-6.
- [53] Levgur M. Diagnosis of adenomyosis: a review. J Reprod Med 2007;52:177–93.
- [54] Tessarolo M, Bonino L, Camanni M, Deltetto F. Elastosonography: a possible new tool for diagnosis of adenomyosis? Eur Radiol 2011;21:1546–52.
- [55] Eisenberg VH, Arbib N, Schiff E, Goldenberg M, Seidman DS, Soriano D. Sonographic signs of adenomyosis are prevalent in women undergoing surgery for endometriosis and may suggest a higher risk of infertility. BioMed Res Int 2017;2017: 8967803.
- [56] Indraccolo U, Iannicco A, Micucci G. A novel case of an adenomyosis-related uterine rupture in pregnancy. Clin Exp Obstet Gynecol 2015;42:810–1.
- [57] Nikolaou M, Kourea HP, Antonopoulos K, Geronatsiou K, Adonakis G, Decavalas G. Spontaneous uterine rupture in a primigravid woman in the early third trimester attributed to adenomyosis: a case report and review of the literature. J Obstet Gynaecol Res 2013;39:727–32.
- [58] Peng CR, Chen CP, Wang KG, Wang LK, Chen YY, Chen CY. Spontaneous rupture and massive hemoperitoneum from uterine leiomyomas and adenomyosis in a nongravid and unscarred uterus. Taiwan J Obstet Gynecol 2015;54:198–200.
- [59] Lier M, Malik RF, van Waesberghe J, Maas JW, van Rumpt-van de Geest DA, Coppus SF, et al. Spontaneous haemoperitoneum in pregnancy and endometriosis: a case series. BJOG 2017;124:306–12.
- [60] Lier MCI, Malik RF, Ket JCF, Lambalk CB, Brosens IA, Mijatovic V. Spontaneous hemoperitoneum in pregnancy (SHiP) and endometriosis - a systematic review of the recent literature. Eur J Obstet Gynecol Reprod Biol 2017;219:57–65.
- [61] Rafi J, Mahindrakar G, Mukhopadhyay D. Endometriosis nodule causing spontaneous haemoperitoneum in pregnancy: a case report and literature review. Case Rep Obstet Gynecol 2017;2017:3480287.
- [62] Van den Bosch T. Spontaneous haemoperitoneum in pregnancy (SHiP): take-home messages. BJOG 2017;124:313.
- [63] Baba A, Yamazoe S, Dogru M, Ogawa M, Takamatsu K, Miyauchi J. Clear cell adenocarcinoma arising from adenomyotic cyst: a case report and literature review. J Obstet Gynaecol Res 2016;42:217–23.
- [64] Boes AS, Tousseyn T, Vandenput I, Timmerman D, Vergote I, Moerman P, et al. Pitfall in the diagnosis of endometrial cancer: case report of an endometrioid adenocarcinoma arising from uterine adenomyosis. Eur J Gynaecol Oncol 2011;32: 431–4.