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Ultrasound Obstet Gynecol 2019; **53**: 576–582
Published online in Wiley Online Library (wileyonlinelibrary.com). **DOI:** 10.1002/uog.19096

Opinion

Sonographic classification and reporting system for diagnosing adenomyosis

T. VAN DEN BOSCH[1#], A. M. DE BRUIJN[2#], R. A. DE LEEUW[2], M. DUEHOLM[3], C. EXACOUSTOS[4], L. VALENTIN[5], T. BOURNE[1,6], D. TIMMERMAN[1] and J. A. F. HUIRNE[2*]

[1]*Department of Obstetrics and Gynecology, University Hospitals KU Leuven, Leuven, Belgium;* [2]*Department of Obstetrics and Gynecology, Amsterdam Reproduction and Development Research Institute, Amsterdam University Medical Centers, VUMC, Amsterdam, The Netherlands;* [3]*Department of Obstetrics and Gynecology, Aarhus University Hospital, Aarhus, Denmark;* [4]*Department of Biomedicine and Prevention, Obstetrics and Gynecological Clinic, University of Rome 'Tor Vergata', Rome, Italy;* [5]*Department of Obstetrics and Gynecology, Skåne University Hospital Malmö, Lund University, Malmö, Sweden;* [6]*Queen Charlotte's & Chelsea Hospital, Imperial College, London, UK*
**Correspondence. (e-mail: j.huirne@vumc.nl)*
T.V.d.B. and A.M.d.B. are joint first authors.

Introduction

In 2015, the international Morphological Uterus Sonographic Assessment (MUSA) group published a consensus on which terminology to use when describing myometrial lesions seen on ultrasonography[1]. The use of MUSA terminology to describe ultrasound images of fibroids, including their location according to the International Federation of Gynecology and Obstetrics (FIGO), is relatively straightforward to implement[2,3]. However, even though the MUSA consensus statement suggests which terms should be used to describe ultrasound images of adenomyosis, it does not provide guidelines on how to classify morphological types or the extent of adenomyosis[1].

We propose a uniform reporting system for ultrasound findings of adenomyosis. The opinion presented herein is based on a thorough discussion among all authors, including a Delphi procedure (Appendix S1). Images and videos of cases typical of the different morphological variations of adenomyosis were used in the debates.

Ultrasonography as a (single) diagnostic tool

The gold standard for the diagnosis of adenomyosis is histological examination of a hysterectomy specimen. Because only a small, selected group of women undergo hysterectomy, an accurate estimation of the prevalence of the disease cannot be established[4]. The introduction of imaging techniques such as transvaginal sonography and magnetic resonance imaging (MRI) has allowed non-invasive diagnosis of adenomyosis[5–8]. Ultrasound imaging is widely available in an office setting, is relatively inexpensive, requires no preparation, has no contraindications and is relatively accurate in expert hands, making it the imaging modality of choice in gynecology[7]. Although adenomyosis is usually diagnosed in women between 40 and 60 years of age, it is also described in younger women, in whom any surgery performed on the uterus might adversely affect child-bearing[9]. The treatment of choice for adenomyosis is primarily hormonal (e.g. levonorgestrel intrauterine device; oral progestins)[10]. Patient management is often based on ultrasound diagnosis alone. This highlights the importance of a uniform, reproducible and clinically relevant reporting system for ultrasound findings of adenomyosis. Uniform reporting also facilitates studies on the prevalence, etiology and clinical implications of adenomyosis and on the effectiveness of therapies.

Pathogenesis of adenomyosis

There are various theories about the pathogenesis of adenomyosis. It is commonly thought to originate from direct contact between the endometrium and the underlying myometrium, which allows the formation of ectopic endometrial glands and stroma. However, the precise pathophysiological pathway is not known. Reported risk factors for adenomyosis include multiparity[11,12] and previous uterine surgery[13–16] (curettage and Cesarean delivery), suggesting a possible role of damage to the endometrial–myometrial junction. Such damage allowing the growth of ectopic endometrial glands and stroma into the myometrium may explain ultrasound findings of subendometrial lines and buds with expansion to hyperechogenic islands in the myometrium (Figure 1)[1].

On the other hand, Kishi *et al.*[17] reported infiltration of endometriosis from outside the uterus, with disruption of the serosa and infiltration of the external myometrium inducing another subtype of adenomyosis. Extrauterine adenomyosis has also been reported, for example in the rectovaginal septum[18]. Other theories involve infolding of endometrium which then penetrates into the myometrium, basement membrane damage through single nucleotide polymorphisms, and initiation/progression of adenomyosis modulated by vascular factors and estrogen receptors[18–20].

Histology of adenomyosis

The histologic diagnosis of adenomyosis is made by observing the presence of endometrial stroma and glands in the myometrium. However, there is no consensus among pathologists, and various

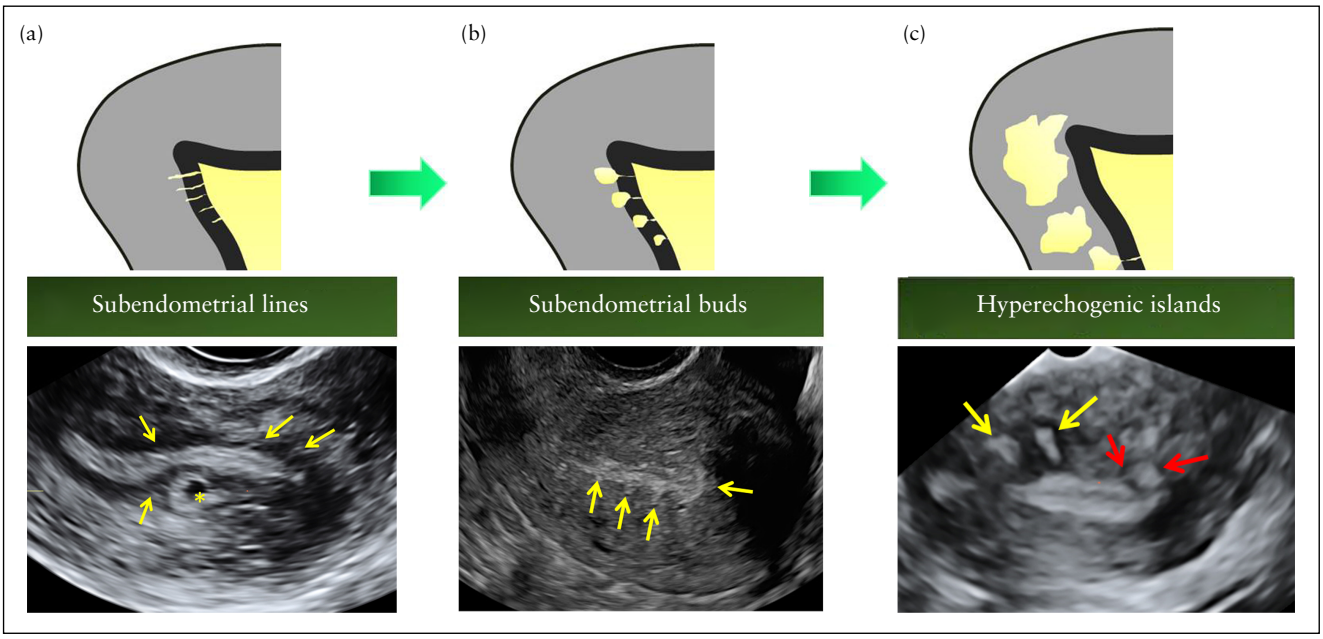

Figure 1 Ultrasound findings compatible with growth of endometrium into myometrium. (a) Subendometrial lines: tiny echogenic lines (yellow arrows); some cross junctional zone (JZ) and are in contact with small myometrial cyst with typical echogenic rim (*). (b) Subendometrial buds: echogenic lines/buds (yellow arrows) crossing JZ. (c) Echogenic islands (yellow arrows); some have hypoechogenic halo. Red arrows indicate tiny echogenic lines in contact with echogenic bud/island.

histopathological definitions have been reported, including: (1) disruption of the normal boundary between the endometrium and myometrium[21,22], (2) presence of ectopic endometrium that is basal-type non-secretory tissue with a direct connection to the basalis layer[5], (3) myometrial invasion by endometrium >4 mm below the basalis layer[23], (4) myometrial invasion by endometrium >2.5 mm below the basalis layer[5], (5) endometrial invasion to $>25\%$ of the thickness of the uterine musculature, as measured from the endometrial–myometrial junction[18]. On histology, adenomyosis is classified as focal if there are circumscribed nodular aggregates of endometrial glands and stroma surrounded by normal myometrium, and diffuse if there are endometrial glands and stroma distributed diffusely throughout the myometrium[24]. Adenomyomas are a subgroup of focal adenomyosis surrounded by hypertrophic myometrium[25]. Different histological disease severity classifications have been suggested, but without international consensus[17,26–30].

The ultrasound characteristics of adenomyosis reflect the histological features. Different morphological types, seen on ultrasound examination or histological examination, may reflect different stages in the development of the disease, and may have different clinical significance with respect to symptomatology, fertility, obstetric outcome and therapeutic options. Clearly, there is a need for an internationally accepted, uniform classification of adenomyosis that, preferably, can be achieved using ultrasound.

Reporting adenomyosis

Seven items should be assessed when examining and describing a uterus with adenomyosis.

Presence

First, the myometrium should be classified as normal or as abnormal, and, in the latter case, according to whether it manifests signs of adenomyosis, myoma or sarcoma, using MUSA terminology[1]. Other myometrial lesions to be considered in the differential diagnosis are accessory cavitated uterine masses, also reported as juvenile cystic adenomyoma, and postoperative uterine scarring, including focal loss of myometrium and fistulae[31]. MUSA features typical of a uterus with adenomyosis include an enlarged globular uterus, asymmetrical thickening of the myometrium, myometrial cysts, echogenic subendometrial lines and buds, hyperechogenic islands, fan-shaped shadowing, an irregular or interrupted junctional zone and translesional vascularity on color Doppler ultrasound examination (Figure 2)[1]. The definitions of these features can be found in the MUSA Consensus Opinion[1].

Location

The location of the adenomyosis should be described as anterior, posterior, lateral left, lateral right or fundal. To determine the exact location, the uterus should be examined in both sagittal and transverse planes. The additional value of three-dimensional ultrasound to examine the coronal plane of the uterus needs to be established in future studies.

Differentiation (focal/diffuse)

In each location, it should be determined whether the adenomyosis is focal or diffuse, by estimating

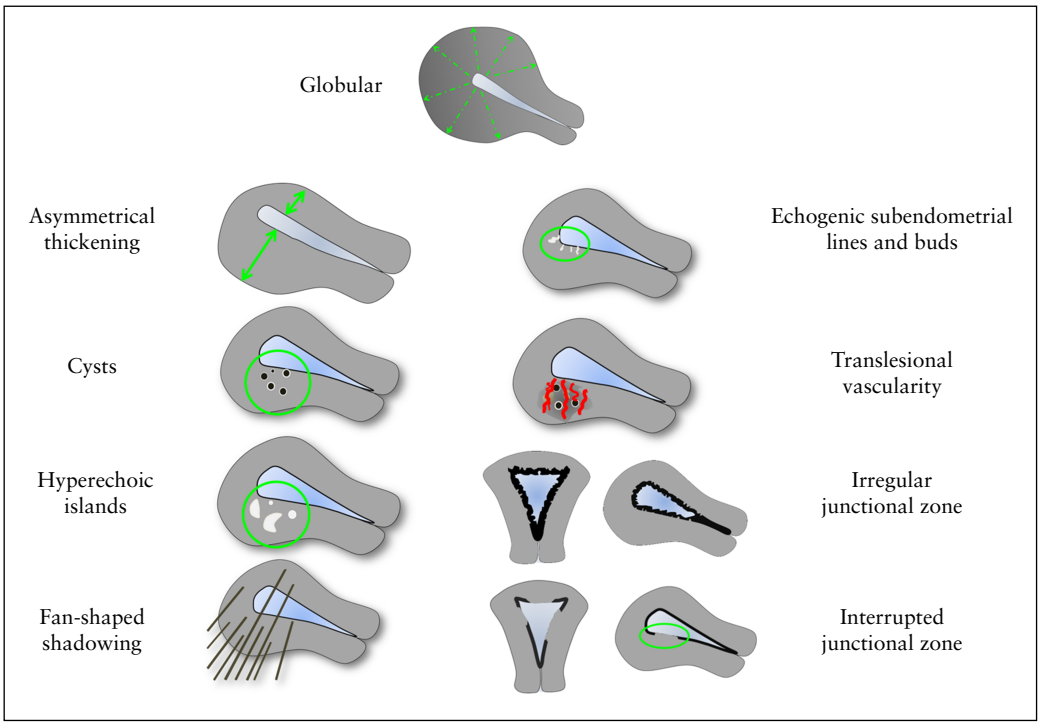

Figure 2 Morphological Uterus Sonographic Assessment (MUSA) criteria for diagnosis of adenomyosis. Adapted from Van den Bosch *et al.*[1].

the relative proportions of the lesion and the surrounding normal myometrium on a sagittal section through the uterus where the adenomyotic lesion appears to be at its largest (Figure 3). We propose that an adenomyotic lesion should be defined as focal if $>25\%$ of the circumference of the lesion is surrounded by normal myometrium. Adenomyosis is classified as diffuse if $<25\%$ of the lesion is surrounded by normal myometrium. If it is difficult to differentiate focal from diffuse adenomyosis, the lesion should be reported as diffuse. If there is both diffuse and focal adenomyosis in different locations in the uterus, this should be classified as 'mixed-type adenomyosis'. Futures studies are needed to determine the value of using the transverse and/or coronal planes for discriminating between focal and diffuse adenomyosis. When focal adenomyosis is demarcated distinctly and surrounded by hypertrophic myometrium, it is called an adenomyoma[8] (Figure 3).

Cystic/non-cystic

Adenomyosis should be classified as cystic or non-cystic (Figure 4). Presence of cysts should be reported for all types of adenomyosis (focal, diffuse, mixed-type and adenomyoma). Adenomyosis is defined as cystic in the presence of measurable myometrial cysts, i.e. with largest diameter ≥ 2 mm. Cystic fluid is usually anechoic or of low-level echogenicity, and cysts may be surrounded by an echogenic rim. It is sufficient to measure the largest diameter of the largest cyst only, and whether the rim is echogenic should be recorded.

Uterine layer involvement

We propose that involvement of the uterine layers, not only the junctional zone but also the other layers of the myometrium and serosa, should be evaluated, and speculate that the number and type of layers involved might depend on the etiology of adenomyosis and be associated with the clinical presentation. Adenomyosis may involve one or more of three uterine layers: the junctional zone (the inner myometrium, also called the subendometrial layer, consisting of longitudinal and circular, closely packed, smooth-muscle fibers); the middle myometrium (the myometrium between the vascular arcade and the junctional zone, consisting of crisscrossing muscle fibers); and the outer myometrium (the subserosal layer, i.e. the layer between the serosa and the vascular arcade)[17,28,32–34] (Figure 5). If the outer myometrium is involved, the serosal layer may be intact or interrupted. To help identify serosal involvement of adenomyosis, the presence of sliding of or fixed viscera[32] (bowels) against the uterus should always be recorded. Discussion of ultrasound examination with regard to concomitant superficial or deep endometriosis[35] is beyond the scope of this Opinion.

Involvement of one of the three layers is recorded as Type 1, 2 or 3, as appropriate (Figure 5). If more than one layer is involved, the type is recorded and described, for example, as Type 1–2, Type 2–3 or Type 1–3.

To differentiate between involvement of the subserosal layer and middle myometrial layer, it may help to use color Doppler and estimate the location in relation to the vascular arcade. Future studies are needed to

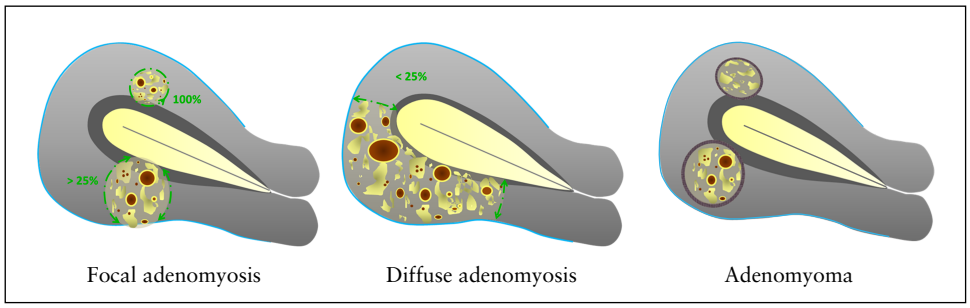

Figure 3 Differentiation between focal and diffuse adenomyosis and adenomyoma. Diagrams are color-coded as follows: endometrium is yellow, junctional zone (inner myometrium) is dark gray, myometrium (middle myometrium and outer myometrium) is gray and serosa is blue. Adenomyosis is focal if > 25% of circumference of lesion is surrounded by normal myometrium (i.e. sum of green dotted lines must represent > 25% of circumference of lesion), provided that < 25% of myometrium of corpus uteri is involved.

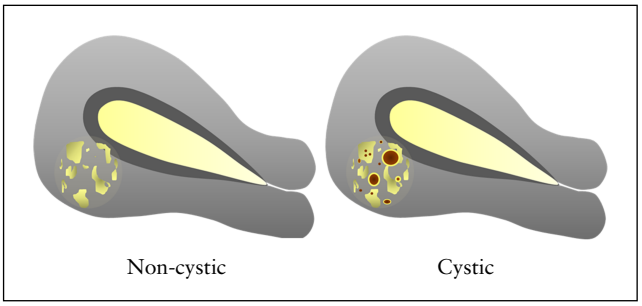

Figure 4 Cystic and non-cystic focal adenomyosis.

determine whether it is feasible to differentiate between the three muscle layers, and if there is any clinical value in differentiating between the middle and outer myometrium.

Extent

The extent of the disease should be assessed subjectively, based on the estimated proportion of the uterine corpus that is affected by adenomyosis, and classified as: mild (< 25% affected); moderate (25–50% affected); or severe (> 50% affected). If there are adenomyotic lesions in different locations, the sum of volumes of the different lesions should be estimated when describing the extent of the disease. The estimated extent of the disease might not be associated with the type or severity of symptoms, but may be useful for research purposes.

Size of lesion

The largest diameter of the adenomyosis lesion(s) should be measured. In clinical situations, this should be done in the plane of the largest diameter of the largest lesion. In the research setting, we advise measurement of the largest diameter of each focal lesion. In the case of a diffuse lesion, the myometrial wall thickness should be measured and the site involved noted. Future studies are needed to estimate the additional value of assessing lesion size in all three orthogonal planes.

Summary and perspective

We propose a consensus-based practical classification of adenomyosis, on the basis of ultrasound findings (Figure 6), that consists of: (1) identification of the presence of adenomyosis, using the MUSA criteria[1]; (2) determination of location of the adenomyosis; (3) differentiation between focal and diffuse disease; (4) discrimination between cystic and non-cystic lesion; (5) determination of myometrial layer involvement; (6) classification of disease extent as mild, moderate or severe; (7) measurement of size of lesion. Cycle day and current hormonal use should always be recorded. Several examples of classification are given in Table 1.

Although this consensus was developed using MUSA terms and definitions, we have proposed some changes. For example, using the original MUSA terminology, an 'ill-defined lesion' may be localized or diffuse, the latter being a lesion involving at least 50% of the total uterine volume[1]. We suggest reporting adenomyosis as focal or diffuse in each location. For example, it should be possible to report focal adenomyosis in the anterior wall and diffuse adenomyosis in the posterior wall, using the definition of focal disease outlined above. A second slight adjustment is the specification of the myometrial layer involved.

This classification should facilitate consistent reporting of adenomyosis, but it needs to be validated and refined in future studies. For example, the feasibility and reproducibility of the differentiation between the middle and outer myometrial layers using power Doppler needs to be assessed. Likewise, the additional value of the use of transverse and/or coronal planes (the latter using three-dimensional ultrasound) for the assessment of location, extent and size of adenomyotic lesions needs to be investigated further. Research is also needed to assess the accuracy of ultrasound examination in the diagnosis of focal *vs* diffuse adenomyosis. In a prospective case series assessing uterine lesions in hysterectomy specimens, some adenomyosis lesions appeared to be much more extensive than was suspected at ultrasonography or on macroscopic examination[36]. The possibility of diffuse disease not being detected at ultrasound examination

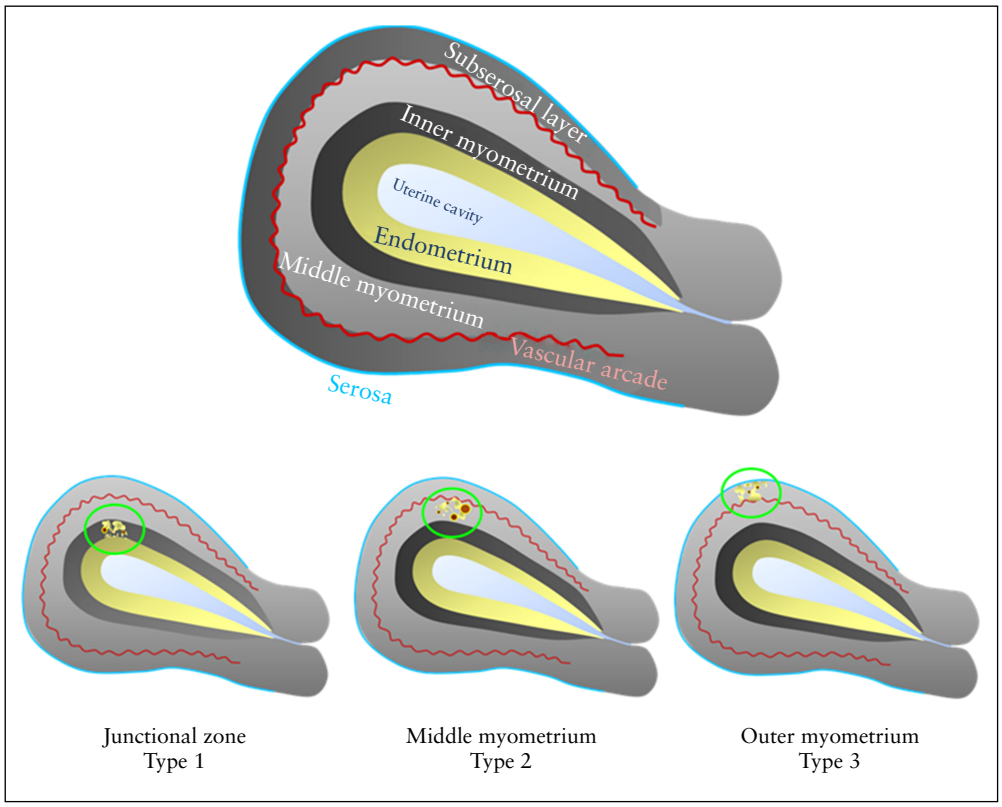

Figure 5 Uterine layer infiltration. Diagrams are color-coded as follows: endometrium is yellow, junctional zone (inner myometrium) is dark gray, middle myometrium, located between vascular arcade (red) and junctional zone, is gray; outer myometrium (subserosa), located between vascular arcade and serosa, is also gray and serosa is blue.

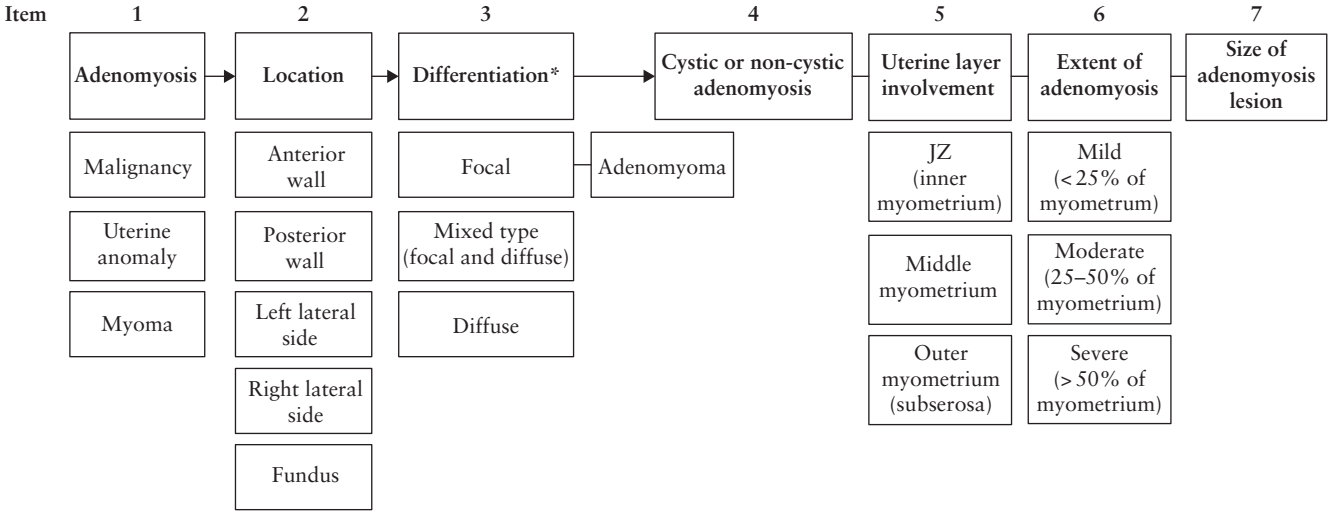

Figure 6 Classification and reporting guideline for ultrasonographic features of adenomyosis. *If in doubt, define as diffuse. JZ, junctional zone.

should be borne in mind when planning management of patients with adenomyosis and when planning studies.

Several recent studies have shown that the number of morphological features of adenomyosis is associated with clinical symptoms and success of fertility treatment[37–39]. However, more research is needed to evaluate the importance of different ultrasound features. In our clinical experience, some women with small lesions may present with severe symptoms of pain and uterine bleeding, whereas others with larger lesions may be asymptomatic. Clearly, the classification we have suggested cannot be used on its own to decide on treatment. The proposed classification might need to be amended after external validation and based on the results of future studies evaluating the relationships between ultrasound features, clinical symptoms, histological findings and possibly also MRI findings. There are still uncertainties regarding the clinical importance of myometrial cysts,

Table 1 Examples of classification and description of uteri with adenomyosis

Example	*Item 1: Presence of adenomyosis (yes/no)*	*Item 2: Location*	*Item 3: Differentiation (focal/diffuse)*	*Item 4: Cystic (yes/no)*	*Item 5: Uterine layer involvement (type)*	*Item 6: Extent of adenomyosis*	*Item 7: Size of lesion (max diam)*	*Description*
1	Yes	Anterior wall	> 25% of lesion surrounded by normal myometrium	Yes	Sliding viscera: yes JZ (inner myometrium) and middle myometrium (Type 1–2)	< 25% of total myometrium	2 cm	Focal Type-1–2 cystic adenomyosis in anterior wall Extent: mild Max diam: 2 cm
2	Yes	Posterior wall	Unclear	Yes	Sliding viscera: no JZ (inner myometrium), middle myometrium and outer myometrium (subserosa) (Type 1–3)	25–50% of total myometrium	3 cm	Diffuse Type-1–3 cystic adenomyosis in posterior wall Extent: moderate Max diam: 3 cm
3	Yes	Anterior wall	< 25% of lesion surrounded by normal myometrium	No	JZ (inner myometrium) and middle myometrium (Type 1–2)	> 50% of total myometrium	7 cm	Diffuse Type-1–2 adenomyosis in anterior wall Extent: severe Max diam: 7 cm
Mixed type								
4	Yes	Anterior wall	Adenomyoma	Yes	Type 1–2	Mild < 25%	3 cm	Mixed-type cystic adenomyosis: Type-1–2 adenomyoma in anterior wall and Type-3 focal adenomyosis in left lateral side Extent: mild Max diam: 1. Adenomyoma: 3 cm 2. Focal lesion: 2 cm
	Yes	Left lateral wall	Focal	Yes	Type 3	Mild < 25%	2 cm	
5	Yes	Left lateral wall	Focal	Yes	Type 2	Mild < 25%	4 cm	Mixed-type cystic adenomyosis: Type-2 focal adenomyosis in left lateral wall and diffuse Type-1–3 adenomyosis in anterior wall Extent: Severe Max diam: 1. Focal lesion: 4 cm 2. Diffuse lesion: 7 cm
	Yes	Anterior wall	Diffuse	Yes	Type 1–3	Severe > 50%	7 cm	

JZ, junctional zone; max diam, maximum diameter.

the relevance of discriminating between the uterine layers and the reliability of estimating disease extent. A study addressing the intra- and interobserver variability using the proposed reporting is also needed. Our suggested approach should be considered only as a first step towards an internationally accepted classification and reporting system.

Finally, we recognize that some aspects of the suggested reporting and classification system might require extensive ultrasound skills. After validation and optimization of this proposed classification, it would be reasonable to develop an e-learning program for less experienced ultrasonographers.

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Appendix S1 Consensus results