Differences in the Sonographic Features of Adenomyosis and Concurrent Endometriosis Compared to Isolated Adenomyosis

A MUSA Criteria Analysis

Ran Matot, MD, Ophir Blickstein, MD, Gideon Leibner, MD, Uval Bar-Peled, MD, Adi Borovich, MD, Yossi Geron, MD, Yinon Gilboa, MD, Haim Krissi, MD, Sharon Perlman, MD

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Address correspondence to Ran Matot, Ze'ev Jabotinsky Street 39, Petah Tikva 4941492, Israel.

E-mail: ran.matoth@gmail.com

Abbreviations

DIE, deep infiltrating endometriosis; ESHRE, European Society of Human Reproduction and Embryology; MUSA, Morphological Uterus Sonographic Assessment; TIAR, tissue injury and repair; TVS, transvaginal ultrasound

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Objective—To examine whether the co-occurrence of endometriosis affects the sonographic features of adenomyosis based on the revised Morphological Uterus Sonographic Assessment (MUSA) criteria.

Methods—This prospective cohort study utilized data from a tertiary referral center collected between 2010 and 2022. Non-pregnant women aged 20–53 years who presented with symptoms potentially related to adenomyosis and underwent pelvic ultrasound scans were included. Diagnoses were based on the revised MUSA criteria, which distinguish between direct features (endometrial cysts, hyperechogenic islands, echogenic sub-endometrial lines, and buds) and indirect features (globular shape of the uterus, asymmetrical uterine wall thickening, irregular junctional zone, fan-shaped shadowing, translesional vascularity, and interrupted junctional zone). Patients were categorized into 2 groups: 1) concurrent adenomyosis and endometriosis and 2) isolated adenomyosis. Demographic and clinical characteristics were retrospectively collected.

Results—Ninety-four patients were diagnosed with adenomyosis. Of these, 24 (27%) had concurrent endometriosis, while 70 had isolated adenomyosis. The most frequent sonographic features were globular uterine configuration (52%), myometrial cysts (44%), and asymmetrical myometrial thickening (33%). The isolated adenomyosis group had a higher proportion of direct features (29%) and both direct and indirect features (33%) compared to the concurrent group, which predominantly exhibited indirect features (71%) ($P < .05$). Direct features of myometrial cysts were significantly more frequent in the isolated adenomyosis group (51%) compared to the concurrent group (21%, $P = .01$).

Conclusions—Utilizing the revised MUSA criteria revealed significant differences in the sonographic features of adenomyosis in symptomatic patients with concurrent endometriosis compared to isolated adenomyosis. This highlights the necessity for standardized diagnostic methods and enhances understanding of the complex relationship between adenomyosis and endometriosis, underscoring the importance of accurate diagnosis in clinical practice.

Key Words—adenomyosis; endometriosis; gynecological imaging; MUSA criteria; transvaginal ultrasound

Adenomyosis is a benign gynecological disease affecting approximately 20 percent of women of reproductive age,

with a key characteristic of ectopic endometrial tissue within the myometrium.[1] This disease is frequently called "enigmatic" as the pathophysiology remains unknown, and several theories have been suggested. Among these theories, 1 revolves around an invagination of the endometrial basalis layer via a tissue injury and repair ("TIAR") process, while the other depicts a process of metaplasia of displaced embryonic pluripotent cells or differentiation of adult stem cells.[2,3]

Adenomyosis is characterized by a broad clinical spectrum, ranging from asymptomatic patients diagnosed incidentally to women suffering from severe dysmenorrhea, menorrhagia, chronic pelvic pain, fertility issues, and impaired quality of life.[4] Some studies suggest that up to 82% of symptomatic women required hysterectomy and 37% were given chronic pain medications.[5]

While the gold standard for diagnosing adenomyosis is the histological inspection of specimens obtained following hysterectomies,[6,7] 2D transvaginal ultrasonography is widely accepted as the first-line diagnostic tool for the diagnosis of superficial, deep and ovarian endometriosis holding an overall sensitivity of 65–81% and an overall specificity of 65–100%.[8–11]

In 2015, the MUSA (Morphological Uterus Sonographic Assessment) statement was published, encompassing the terms, definitions, and measurements for describing myometrial features and lesions with transvaginal ultrasound (TVS). This statement mentions the following features as typical for adenomyosis: asymmetrical myometrial wall thickening, myometrial cysts, myometrial hyperechoic islands, fan-shaped shadowing, echogenic subendometrial lines and buds, translesional vascularity within the myometrium, irregular junctional zone, and interrupted junctional zone.[12]

A few years later, a new consensus regarding diagnosing adenomyosis using TVS was established and referred to as the "revised MUSA criteria."[13] Among the main changes accepted, a distinction was made between direct and indirect features of adenomyosis. Direct features suggested the actual presence of ectopic endometrial tissue in the myometrium (cysts, hyperechogenic islands, echogenic sub-endometrial lines, and buds), while indirect features imply the presence of ectopic endometrial tissue in the myometrium by depicting the secondary changes they create (globular shape of the uterus, asymmetrical uterine wall thickening, irregular junctional zone, fan-shaped shadowing, translesional vascularity, and interrupted junctional zone). The revised MUSA criteria were accepted internationally and have been used ever since.

The relationship between adenomyosis and endometriosis and the actual coexistence of these diseases have been the subject of vigorous research.[14–18] Both conditions originate from the displacement of endometrial cells[3,19] and are characterized by the presence of oligoclonal endometrial glandular epithelial cells. Due to somatic mutations, these cells may implant on peritoneal surfaces or become entrapped in the myometrium, leading to endometriosis and adenomyosis.[20,21]

Genetic analysis of endometriosis and adenomyosis epithelial cells revealed an increased incidence of Kirsten Rat Sarcoma Viral Oncogene Homolog (KRAS) mutations, which promote cell survival and growth, highlighting a shared molecular basis for their pathogenesis.[22,23] Additionally, both endometrial and adenomyotic stromal cells exhibit similar epigenetic abnormalities that affect steroid receptor expression, contributing to excessive estrogen production and progesterone resistance. This hormonal imbalance is crucial for the persistence and symptomatology of both conditions.[23]

We hypothesized that isolated adenomyosis and concurrent adenomyosis with endometriosis would present with different sonographic features according to MUSA criteria. This study aimed to examine whether the co-occurrence of endometriosis affects the sonographic features of adenomyosis based on the revised MUSA criteria.

Materials and Methods

This retrospective cohort study utilized collected data from a tertiary referral center between 2010 and 2022. The study included non-pregnant women who underwent targeted pelvic ultrasound scans due to symptoms potentially indicative of adenomyosis, such as menorrhagia, dysmenorrhea, dyspareunia, chronic pelvic pain, and infertility.

Several accredited gynecologists with expertise in gynecological imaging performed the pelvic targeted scans. For this study, all examinations were reviewed by an independent reviewer according to established diagnostic criteria for adenomyosis. The reviewer was blinded to the demographic and clinical data. This methodological approach aimed to minimize bias and increase the reliability of the imaging assessments.

The ultrasound scans were performed using commercial Voluson 730, E6/E8/E10 (GE Healthcare, Zipf, Austria) ultrasound machines equipped with high-resolution transvaginal probes. Women diagnosed with adenomyosis based on the revised MUSA criteria were included in the study.[12,13]

To ensure thorough visualization and accurate diagnoses, a systematic approach was employed using high-resolution TVS. The probe was moved systematically through the uterus and adnexa in sagittal and transverse planes. Uterine morphology was assessed for features such as an enlarged or globular shape and asymmetry in myometrial wall thickness. Myometrial changes, including a heterogeneous echotexture, myometrial cysts, and hyperechoic striations, were identified and correlated with the revised MUSA criteria. Junctional zone abnormalities, including thickening and ill-defined borders, were also evaluated. Doppler imaging was used to identify vascular patterns within the myometrium, particularly in areas suspected of adenomyosis. For concurrent endometriosis, ovarian evaluations focused on detecting endometriomas characterized by their ground-glass echogenicity, thick walls, and absent internal vascularity. Additionally, hypoechoic nodules and thickened uterosacral ligaments suggestive of deep infiltrating endometriosis (DIE) were examined in the pouch of Douglas and surrounding pelvic structures.

Endometriosis was diagnosed by imaging lesions at a minimum of 1 site, including ovaries, vagina and fornix, urinary bladder, ureterovesical region, rectovaginal septum, uterosacral ligaments, rectosigmoid colon, and cul-de-sac.[14] Participants with Mullerian malformations and uterine fibroids were excluded. Baseline demographic data and clinical characteristics were collected from the computerized medical records system.

The study population was divided into 2 groups: a study group of women with concurrent adenomyosis and endometriosis and a control group of women with adenomyosis without endometriosis) isolated adenomyosis(. The sonographic characteristics of adenomyosis according to the revised MUSA criteria were compared between the groups.

Statistical Analysis

Continuous variables were expressed as means and standard deviations, while categorical variables were presented as numbers and percentages. One-way ANOVA tests were used for continuous variables, and chi-square or Fisher's exact tests were applied for categorical variables as appropriate. A *P*-value of <.05 was considered statistically significant. All analyses were performed using RStudio version 0.04.2024.

Ethical Approval\Informed Consent

The study was approved by the ethics committee of Rabin Medical Center and institutional review board approval. The approval is for conducting a study with existing data, is retrospective, and thus does not require informed consent.

Results

During the study period, 710 patients underwent targeted sonographic examination for symptoms suggestive of adenomyosis. Ninety-four women were diagnosed with adenomyosis based on the MUSA criteria. Of these, 24 women (26%) had concurrent adenomyosis and endometriosis (of whom 9 were diagnosed with DIE), and 70 had isolated adenomyosis.

Table 1 displays the demographic data of the study population. There were no statistically significant differences regarding maternal age, weight, smoking status, parity, and uterine surgical interventions, including past cesarean sections or curettage. Figure 1 presents the sonographic features of the control and study groups based on the MUSA criteria.

The most frequent sonographic features for diagnosing adenomyosis were indirect signs such as globular uterine configuration (52%) and asymmetrical myometrial thickening (33%), along with the direct feature of myometrial cysts (44%). For the whole cohort, 55% of patients exhibited 1 diagnostic feature, 34% exhibited 2, and 11% exhibited 3 sonographic diagnostic features, as outlined in Table 2. No

Table 1. Demographic and Clinical Characteristics of the Study Cohort

Characteristic	Overall, (n = 94)	Isolated Adenomyosis (n = 70)	Concurrent Adenomyosis and Endometriosis (n = 24)	*P*-value[a]
Age (years), mean (SD)	39.2 (6.5)	39.5 (6.8)	38.5 (5.4)	0.5
Weight (kg), mean (SD)	69 (13)	68 (13)	74 (11)	0.3
Smoker, n (%)	7 (7.4)	5 (7.1)	2 (8.3)	>0.9
Parity, mean (SD)	2.64 (1.72)	2.79 (1.86)	2.21 (1.14)	0.2
Gravidity, mean (SD)	3.66 (2.16)	3.89 (2.31)	3.00 (1.50)	0.083
Previous CS, n (%)	45 (48)	35 (50)	10 (42)	0.48
Past curettage, n (%)	29 (31)	24 (34)	5 (21)	0.218

[a]Chi-square test or 1-way ANOVA; *P*-value for differences across group.

significant differences regarding the number of diagnostic features based on the MUSA criteria were demonstrated between the groups ($P = .2$).

Within the study group of concurrent adenomyosis and endometriosis, the most common features were the indirect signs of globular uterine configuration (58%) and asymmetrical thickening (33%). In contrast, within the control group of isolated adenomyosis, the most common feature was the direct sign of myometrial cysts (51%), followed closely by the indirect feature of globular uterine configuration (50%). Figures 2 and 3 provide visual examples of direct and indirect features illustrating the differences in sonographic presentations.

An analysis using the revised MUSA criteria revealed distinct sonographic differences between patients with isolated adenomyosis and those with concurrent endometriosis (Table 3).

Scans of cases with isolated adenomyosis revealed a significantly higher proportion of direct (29%) and both direct and indirect (33%) features compared to the concurrent adenomyosis and endometriosis group, which predominantly exhibited indirect features (71%) $P < .05$. Specifically, myometrial cysts were significantly more frequent in the isolated adenomyosis group (51% versus 21%; $P < .01$, Figure 1).

Figure 1. Distribution of sonographic features of adenomyosis in the study cohort based on the MUSA criteria.

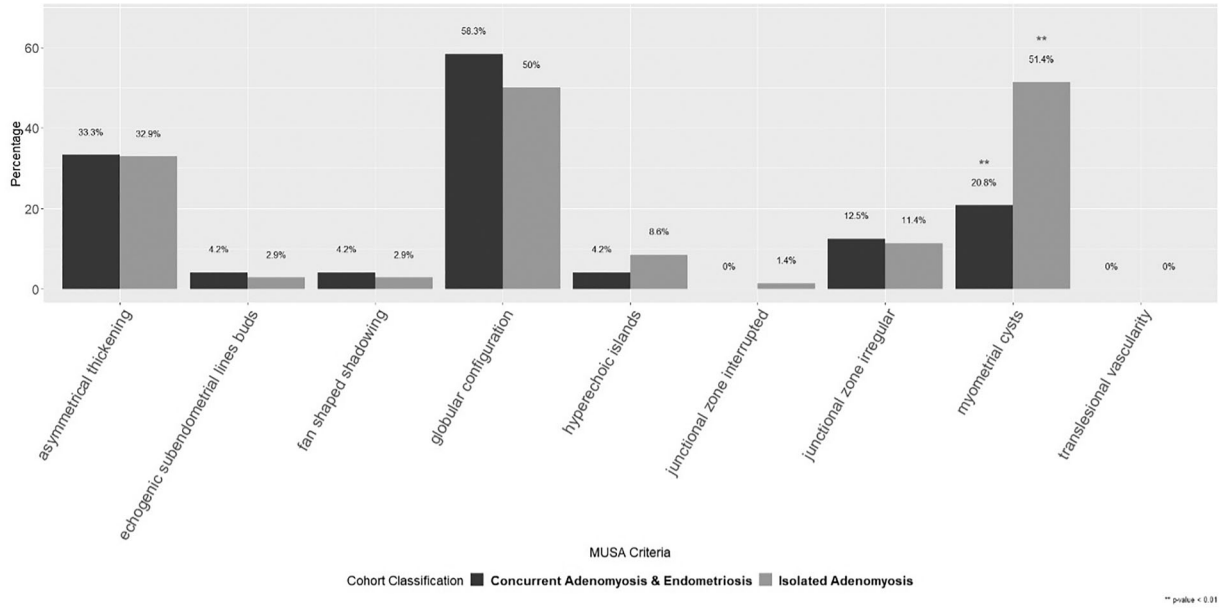
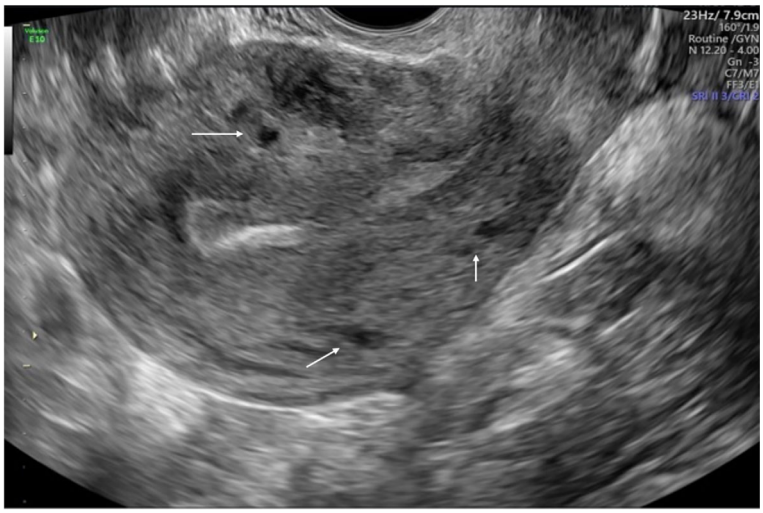


Table 2. Number of Sonographic Features of Adenomyosis Per Patient Based on the Morphological Uterus Sonographic Assessment (MUSA) Criteria

MUSA Criteria	Overall, (n = 94), n (%)	Isolated Adenomyosis (n = 70), n (%)	Concurrent Adenomyosis and Endometriosis (n = 24), n (%)	*P*-value[a]
Number of sonographic features				0.237
1	52 (55)	35 (50)	17 (71)	
2	32 (34)	27 (39)	5 (21)	
3+	10 (11)	8 (11)	2 (8.3)	

The numbers in the table represent the number of MUSA criteria features diagnosed in a single patient, characterizing adenomyosis. The features are categorized based on the study groups: isolated adenomyosis (control group) and adenomyosis with concurrent endometriosis (study group).
[a]Chi-square test or 1-way ANOVA; *P*-value for differences across group.

Figure 2. Isolated adenomyosis with direct features. Transvaginal ultrasound in a case of isolated adenomyosis demonstrating an anteverted uterus with myometrial cysts—a direct feature of adenomyosis (arrows).



Discussion

This study demonstrates significant differences in the sonographic features of adenomyosis and concurrent endometriosis compared to isolated adenomyosis. While the number of diagnostic features did not differ between the groups, direct features, specifically endometrial cysts within the myometrium, were significantly more prevalent in women with isolated adenomyosis than those with concurrent adenomyosis and endometriosis.

The rate of concurrent endometriosis in patients diagnosed with adenomyosis in our study (27%) was comparable to those described in former studies.[16] While both diagnoses are interrelated in their clinical, histological, and genetic characteristics, our imaging findings raise questions regarding the interrelation between endometriosis and adenomyosis features.

One hypothesis that may explain the significantly higher visualization of direct features in isolated adenomyosis is that the co-existence of endometriosis could alter the myometrium through cytokine release or other factors, thus preventing the development of direct features such as cysts on ultrasound. As this article focuses on the sonographic descriptions of these diseases, further examination of pathology specimens may reveal cellular-level changes, providing additional insight into this observation.

The gold standard for diagnosing adenomyosis is histopathology[24]; however, with the advanced age of

Figure 3. Isolated adenomyosis exhibiting both direct and indirect features. Transvaginal ultrasound in a case of isolated adenomyosis demonstrating a retroverted uterus with direct features of adenomyosis (hyperechogenic islands [*]) and indirect features (globular shaped uterus, asymmetrical uterine wall thickening, and irregular junctional zone [arrow]).

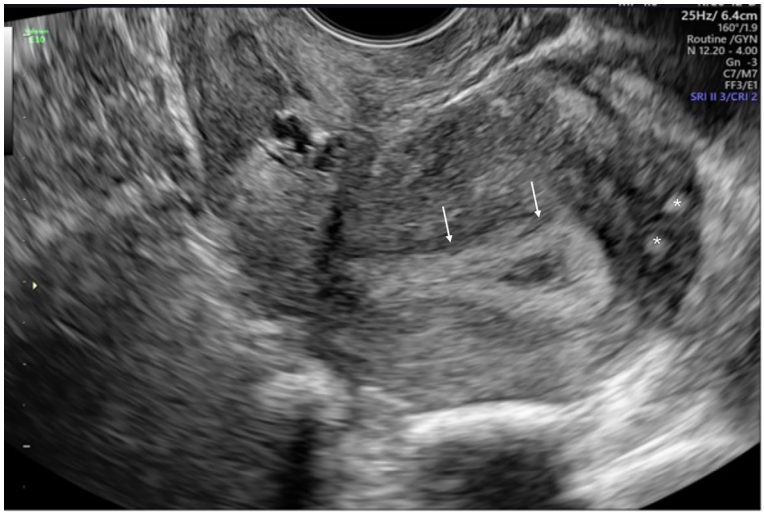


Table 3. Distribution of Sonographic Features of Adenomyosis in the Study Cohort Based on the Revised Morphological Uterus Sonographic Assessment (MUSA) Criteria

Revised MUSA Criteria	Overall (n = 94), n (%)	Isolated Adenomyosis (n = 70), n (%)	Concurrent Adenomyosis and Endometriosis (n = 24), n (%)	*P*-value[a]
Direct	23 (24)	20 (29)	3 (13)	0.023
Indirect	44 (47)	27 (39)	17 (71)	
Direct and indirect	27 (29)	23 (33)	4 (17)	

Direct: Myometrial cysts, hyperechogenic islands, echogenic sub-endometrial lines, and buds. Indirect: Globular shape of the uterus, asymmetrical uterine wall thickening, irregular junctional zone, fan-shaped shadowing, translesional vascularity, and interrupted junctional zone.
[a]Chi-square test or 1-way ANOVA; *P*-value for differences across groups.

women seeking fertility treatments and increased awareness of the consequences of adenomyosis on quality of life, there is a pressing need for non-invasive diagnostic methods. Consequently, extensive research has focused on the various imaging modalities' sensitivity, specificity, and accuracy. Studies indicate that the sensitivity and specificity of 2D TVS in diagnosing adenomyosis range from 72 to 87% and 60 to 90%, respectively.[9,25–28] While the application of 3D imaging for diagnosing adenomyosis has been explored in the literature,[9,25] we focused on the more commonly used and widely available 2D imaging in the present study. The advantage of this approach is that 2D imaging is accessible in most clinical settings, making it a practical option for routine diagnostics.

Several scholars have assessed the diagnostic characteristics of adenomyosis and concurrent endometriosis. Dior et al[17] found a significant diagnostic correlation between adenomyosis and the severity of endometriosis. They showed that patients with sonographic evidence of adenomyosis were more likely to have severe endometriosis, particularly stage IV, compared to those without such evidence (41% versus 9.8%, $P < .001$).

Chapron et al[29] explored the connection between magnetic resonance imaging (MRI) characteristics of adenomyosis and various endometriosis phenotypes. They found a notable link between focal adenomyosis in the outer myometrium and DIE. In contrast, Alborzi et al[15] reported no significant correlation

between adenomyosis subtypes (focal and diffuse) and specific endometriosis lesions.

To the best of our knowledge, this is the first study to utilize the MUSA and revised MUSA criteria[12,13] to explore the potential relationship between concurrent endometriosis and the sonographic features of adenomyosis. Although conducted as a retrospective analysis, using MUSA criteria and its updated version for diagnosis offers significant advantages. Implementing these consensus-based guidelines enhances standardization and validation, aligning with international standards, thereby improving ultrasonographic findings' credibility and reliability.

One of the main limitations of our study is the reliance on ultrasound findings for the diagnosis of endometriosis rather than the gold standard of histological confirmation via surgical sampling. Although transvaginal ultrasonography is a well-established, non-invasive diagnostic tool with significant sensitivity and specificity, it may not detect all cases, potentially leading to underdiagnosis. However, this diagnostic approach aligns with the European Society of Human Reproduction and Embryology (ESHRE) guideline,[30] which supports imaging-based diagnosis without requiring surgical or histological confirmation for symptomatic cases. This approach underscores the clinical utility of imaging in reducing diagnostic delays and minimizing the need for invasive procedures in appropriate patient populations. To address this limitation, future studies could benefit from incorporating histological verification to enhance diagnostic accuracy and validity.

Another limitation involves the potential variability in diagnostic accuracy across different clinical settings. Our study used high-quality imaging equipment, which may not be available in all environments, particularly in rural or smaller practices. This disparity in access to advanced ultrasound technology could affect the reproducibility of our findings, as diagnostic accuracy may vary in less-equipped settings, limiting the generalizability of the study's results.

Conclusion

Overall, our study highlights significant differences in the sonographic features of adenomyosis in symptomatic patients when it occurs concurrently with endometriosis compared to isolated adenomyosis. This research contributes to the broader investigation of the complex interplay between endometriosis and adenomyosis, suggesting that the spectrum of these conditions is more nuanced than previously understood. Our findings imply that these conditions may represent more than 2 distinct entities with varying etiologies potentially coexisting. Additionally, the study reinforces the value of ultrasound imaging in diagnosing and assessing these conditions. These insights pave the way for future research to improve diagnostic techniques and enhance our understanding of these interconnected diseases.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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