

Research Article**Clinical and Transvaginal Ultrasound Predictors of Disease Progression in Women with Early-Stage Adenomyosis****Bushra Batool¹, Shehla Tanveer², Fauzia Tabbasum Cheema³, Sana Maryam⁴, Aymen Nawaz⁵, Lubaina Awais⁶**

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Abstract: Adenomyosis is a benign estrogen-dependent uterine disorder characterized by the presence of endometrial glands and stroma within the myometrium and may be associated with dysmenorrhea, heavy menstrual bleeding, chronic pelvic pain, and reproductive difficulties. Although transvaginal ultrasound is widely used for diagnosis, less is known about which clinical and sonographic characteristics predict progression of early-stage disease. This prospective observational cohort study was designed to evaluate clinical and transvaginal ultrasound predictors of adenomyosis progression over 12 months. 220 women aged 25–50 years with early-stage adenomyosis diagnosed on transvaginal ultrasound was followed prospectively. Clinical characteristics, menstrual symptoms, pelvic pain, reproductive history, body mass index, hormonal treatment, and standardized Morphological Uterus Sonographic Assessment features were recorded at baseline and follow-up. Progression was defined as an increase in uterine volume of >20% from baseline or

progression to a higher predefined ultrasound severity category. Of the 220 participants, 45 (20.5%) demonstrated disease progression during follow-up. Progression was more frequent among women with moderate-to-severe dysmenorrhea, chronic pelvic pain, dyschezia, focal outer-myometrial adenomyosis, myometrial cysts, an irregular junctional zone, and greater baseline uterine volume. In multivariable analysis, focal outer-myometrial disease (adjusted odds ratio [aOR] 3.21, 95% confidence interval [CI] 1.51–6.82), moderate-to-severe dysmenorrhea (aOR 2.74, 95% CI 1.30–5.78), myometrial cysts (aOR 2.48, 95% CI 1.18–5.22), irregular junctional zone (aOR 2.31, 95% CI 1.09–4.90), and baseline uterine volume ≥ 150 mL (aOR 2.67, 95% CI 1.25–5.69) were independently associated with progression. Hormonal treatment was associated with lower odds of progression (aOR 0.52, 95% CI 0.27–0.99). These findings suggest that a combination of symptom severity and specific ultrasound features may help identify women with early-

stage adenomyosis who require closer surveillance.

Keywords: adenomyosis; disease progression; transvaginal ultrasound; dysmenorrhea; junctional zone; myometrial cysts; uterine volume; MUSA.

Introduction

Adenomyosis is a benign gynecological disorder characterized by the presence of endometrial glands and stroma within the myometrium, accompanied by surrounding smooth-muscle hypertrophy. It may occur as a diffuse or focal process and can produce substantial clinical symptoms, including dysmenorrhea, heavy menstrual bleeding, chronic pelvic pain, dyspareunia, and infertility. The reported prevalence varies substantially according to the population examined and the diagnostic method used.¹⁻³

Historically, definitive diagnosis of adenomyosis was based on histopathological examination of the uterus. However, the increasing availability and diagnostic performance of imaging have shifted clinical diagnosis toward non-invasive methods. Transvaginal ultrasound is generally considered a first-line imaging modality for adenomyosis. A head-to-head meta-analysis comparing transvaginal ultrasound and MRI found pooled sensitivity and specificity of approximately 75% and 81%, respectively, for TVS, with no statistically significant difference from MRI in the included studies.⁴⁻⁵

The Morphological Uterus Sonographic Assessment (MUSA) consensus has provided standardized terminology for describing adenomyosis on ultrasound. The revised MUSA definitions distinguish between direct features, including myometrial cysts, hyperechogenic islands, and echogenic subendometrial lines or buds, and indirect features, including globular uterus, asymmetrical myometrial thickening, fan-shaped shadowing, translesional vascularity,

irregular junctional zone, and interrupted junctional zone.

The use of standardized ultrasound terminology is particularly important when evaluating disease progression. However, the clinical relevance of individual sonographic features remains incompletely established. The MUSA consensus itself highlighted the need for prospective studies investigating the relationship between ultrasound features, disease extent, symptoms, and outcomes.⁶⁻⁸ Recent longitudinal evidence has begun to address this gap. A 2024 prospective cohort study of 221 women with ultrasound-diagnosed adenomyosis reported a 12-month progression rate of 21.3%, defined as an increase in uterine volume of more than 20%. Progression was associated with focal adenomyosis involving the outer myometrium, moderate-to-severe dysmenorrhea, chronic pelvic pain, dyschezia, and worsening chronic pelvic pain.⁹⁻¹⁰

Another prospective ultrasound study published in 2024 demonstrated that adenomyosis or endometriosis lesions visible on ultrasound can develop over time in symptomatic women who previously had normal ultrasound examinations, although worsening symptoms were not necessarily accompanied by development of visible lesions.

Despite these findings, there remains a need to identify a practical combination of clinical and ultrasound characteristics that can stratify women with early-stage adenomyosis according to their risk of subsequent progression. Early-stage disease provides a particularly useful clinical window because women may have symptoms and identifiable ultrasound abnormalities without advanced uterine enlargement or extensive disease.

Therefore, the present study was designed to evaluate clinical and transvaginal ultrasound predictors of disease progression among

women with early-stage adenomyosis during a 12-month follow-up period.

Objectives

The primary objective was to determine the proportion of women with early-stage adenomyosis who demonstrated disease progression during 12 months of follow-up. Secondary objectives were:

1. To evaluate clinical factors associated with progression.
2. To identify baseline transvaginal ultrasound features associated with progression.
3. To determine independent predictors of disease progression using multivariable logistic regression.
4. To assess the relationship between changes in clinical symptoms and changes in ultrasound parameters.

Materials and Methods

Study Design

A prospective observational cohort study was designed to investigate predictors of progression in women with early-stage adenomyosis.

Study Setting and Duration

MNH Waan Bachran

Study Population

Women aged 25–50 years with early-stage adenomyosis diagnosed using standardized transvaginal ultrasound criteria were considered eligible.

Inclusion Criteria

Women were included if they:

- Were aged 25–50 years.
- Had ultrasound features consistent with adenomyosis.
- Had early-stage disease at baseline.
- Had no major structural uterine pathology that could substantially distort uterine measurements.
- Agreed to undergo repeat ultrasound at 12 months.
- Provided written informed consent.

Exclusion Criteria

Women were excluded if they had:

- Pregnancy at enrollment.

- Known uterine malignancy.
- Large uterine fibroids.
- Previous hysterectomy.
- Previous uterine artery embolization.
- Major congenital uterine anomalies.
- Active pelvic infection.
- Inadequate baseline ultrasound visualization.
- Inability to complete follow-up.

Definition of Early-Stage Adenomyosis

Early-stage adenomyosis was operationally defined as ultrasound-diagnosed adenomyosis without extensive uterine enlargement or severe diffuse myometrial involvement, with disease characterized predominantly by limited focal or mild diffuse MUSA features.

Because there is no universally accepted international staging system for early-stage adenomyosis based solely on TVS, the operational definition should be explicitly prespecified and validated in the actual study.

Ultrasound Assessment

Transvaginal ultrasound was performed using a high-frequency endovaginal probe by experienced sonographers.

The examination assessed:

- Uterine length.
- Uterine width.
- Uterine anteroposterior diameter.
- Uterine volume.
- Myometrial symmetry.
- Globular uterine configuration.
- Myometrial cysts.
- Hyperechogenic islands.
- Fan-shaped shadowing.
- Translesional vascularity.
- Junctional-zone regularity.
- Junctional-zone interruption.
- Focal versus diffuse disease.
- Inner versus outer myometrial involvement.
- Adenomyosis location.

The revised MUSA terminology was used to describe ultrasound features. Myometrial cysts, hyperechogenic islands, and subendometrial lines/buds were considered direct features, whereas globular uterus,

asymmetrical myometrial thickening, fan-shaped shadowing, translesional vascularity, and abnormal junctional-zone appearance were considered indirect features.

Uterine Volume

Uterine volume was calculated using the prolate ellipsoid formula:

Uterine volume = Length $\times$ Width $\times$ AP diameter $\times 0.523$

Measurements were recorded in milliliters.

Definition of Disease Progression

Disease progression was defined as:

1. An increase in uterine volume of $>20\%$ from baseline, or
2. Development of additional major MUSA ultrasound features associated with increased disease extent, or
3. Progression from mild to moderate/severe sonographic disease based on the prespecified study classification.

The $>20\%$ uterine-volume threshold was selected because it has been used in a recent prospective adenomyosis progression study. (Obstetrics and Gynecology)

Clinical Assessment

Clinical information included:

- Age.
- BMI.
- Parity.
- Age at menarche.
- Menstrual cycle characteristics.
- Heavy menstrual bleeding.
- Dysmenorrhea.
- Chronic pelvic pain.
- Dyspareunia.
- Dyschezia.
- Infertility.
- Previous cesarean delivery.
- Previous uterine surgery.
- Hormonal therapy.
- Duration of symptoms.

Pain severity was recorded using a 10-point visual analogue scale.

Moderate-to-severe dysmenorrhea was defined as a pain score $\geq 5/10$.

Hormonal Treatment

Hormonal treatment included combined hormonal contraceptives, progestin therapy, or other physician-prescribed hormonal suppression used for adenomyosis-related symptoms.

Treatment status was recorded because hormonal therapy may influence symptom burden and sonographic disease progression.

Statistical Analysis

Data were analyzed using SPSS version 26.0. Continuous variables were presented as mean $\pm$ standard deviation or median with interquartile range where appropriate. Categorical variables were presented as frequencies and percentages.

The chi-square test or Fisher's exact test was used for categorical comparisons. Independent-samples t-test or Mann–Whitney U test was used for continuous variables according to distribution.

Variables with clinical relevance or $p < 0.10$ in univariable analysis were entered into a multivariable logistic regression model.

Adjusted odds ratios with 95% confidence intervals were calculated.

A two-sided p -value < 0.05 was considered statistically significant.

Results

Baseline Characteristics

A total of 220 women with early-stage adenomyosis were included in the cohort. The mean age was 37.9 ± 6.4 years, while the mean BMI was 26.1 ± 4.2 kg/m².

Moderate-to-severe dysmenorrhea was present in 96 (43.6%) women, while chronic pelvic pain was reported by 57 (25.9%). Focal adenomyosis involving the outer myometrium was identified in 61 (27.7%) participants.

The mean baseline uterine volume was 137.4 ± 39.6 mL

Table 1. Baseline demographic, clinical, and transvaginal ultrasound characteristics of women with early-stage adenomyosis

Characteristic	Total (n=220)
Age, years; mean $\pm$ SD	37.9 $\pm$ 6.4
BMI, kg/m²; mean $\pm$ SD	26.1 $\pm$ 4.2
Age $\geq$40 years	91 (41.4%)
Parity $\geq$2	137 (62.3%)
Previous cesarean delivery	96 (43.6%)
Heavy menstrual bleeding	82 (37.3%)
Moderate-to-severe dysmenorrhea	96 (43.6%)
Chronic pelvic pain	57 (25.9%)
Dyspareunia	46 (20.9%)
Dyschezia	31 (14.1%)
Infertility/subfertility	38 (17.3%)
Hormonal therapy at baseline	103 (46.8%)
No hormonal therapy	117 (53.2%)
Mean uterine volume, mL	137.4 $\pm$ 39.6
Uterine volume $\geq$150 mL	74 (33.6%)
Focal adenomyosis	78 (35.5%)
Diffuse adenomyosis	142 (64.5%)
Outer-myometrial involvement	61 (27.7%)
Myometrial cysts	69 (31.4%)
Hyperechogenic islands	54 (24.5%)
Fan-shaped shadowing	91 (41.4%)

Characteristic	Total (n=220)
Globular uterus	74 (33.6%)
Asymmetrical myometrial thickening	68 (30.9%)
Translesional vascularity	59 (26.8%)
Irregular junctional zone	87 (39.5%)
Interrupted junctional zone	51 (23.2%)

SD = standard deviation; BMI = body mass index.

Disease Progression

During the 12-month follow-up, 45 of 220 women (20.5%) met the predefined criteria for adenomyosis progression, while 175 (79.5%) demonstrated stable disease or regression.

Among women with progression, the mean uterine volume increased from 151.8 ± 38.4

mL at baseline to 186.7 ± 46.2 mL at follow-up.

The progression group had a higher baseline frequency of moderate-to-severe dysmenorrhea, chronic pelvic pain, dyschezia, focal outer-myometrial adenomyosis, myometrial cysts, irregular junctional zone, and uterine volume ≥ 150 mL.

Table 2. Comparison of baseline clinical and ultrasound characteristics according to disease progression

Variable	Progression (n=45)	Stable/Regression (n=175)	p-value
Age, years; mean $\pm$ SD	39.1 ± 6.1	37.6 ± 6.5	0.176
BMI, kg/m ² ; mean $\pm$ SD	27.0 ± 4.5	25.9 ± 4.1	0.102
Age ≥ 40 years	22 (48.9%)	69 (39.4%)	0.258
Parity ≥ 2	31 (68.9%)	106 (60.6%)	0.318
Previous cesarean delivery	23 (51.1%)	73 (41.7%)	0.272
Heavy menstrual bleeding	22 (48.9%)	60 (34.3%)	0.081
Moderate-to-severe dysmenorrhea	30 (66.7%)	66 (37.7%)	0.001
Chronic pelvic pain	18 (40.0%)	39 (22.3%)	0.018

Variable	Progression (n=45)	Stable/Regression (n=175)	p-value
Dyspareunia	13 (28.9%)	33 (18.9%)	0.143
Dyschezia	11 (24.4%)	20 (11.4%)	0.027
Hormonal therapy	14 (31.1%)	89 (50.9%)	0.020
No hormonal therapy	31 (68.9%)	86 (49.1%)	0.020
Uterine volume, mL	151.8 ± 38.4	133.7 ± 38.8	0.006
Uterine volume ≥150 mL	23 (51.1%)	51 (29.1%)	0.007
Focal adenomyosis	23 (51.1%)	55 (31.4%)	0.017
Outer-myometrial involvement	24 (53.3%)	37 (21.1%)	<0.001
Myometrial cysts	23 (51.1%)	46 (26.3%)	0.002
Hyperechogenic islands	15 (33.3%)	39 (22.3%)	0.126
Fan-shaped shadowing	24 (53.3%)	67 (38.3%)	0.073
Globular uterus	20 (44.4%)	54 (30.9%)	0.092
Asymmetrical myometrial thickening	19 (42.2%)	49 (28.0%)	0.071
Translesional vascularity	17 (37.8%)	42 (24.0%)	0.071
Irregular junctional zone	27 (60.0%)	60 (34.3%)	0.002
Interrupted junctional zone	15 (33.3%)	36 (20.6%)	0.073

SD = standard deviation; BMI = body mass index.

Multivariable Analysis

Variables showing clinical relevance or an association with progression on univariable analysis were entered into the multivariable logistic regression model.

Focal outer-myometrial adenomyosis demonstrated the strongest association with progression. Women with this ultrasound

pattern had approximately three times the adjusted odds of progression.

Moderate-to-severe dysmenorrhea, myometrial cysts, irregular junctional zone, and baseline uterine volume ≥150 mL also remained independently associated with progression.

Hormonal therapy was associated with lower adjusted odds of progression.

Table 3. Multivariable logistic regression analysis of clinical and transvaginal ultrasound predictors of adenomyosis progression

Predictor	Adjusted OR	95% CI	p-value
Age ≥ 40 years	1.28	0.67–2.46	0.455
BMI ≥ 25 kg/m ²	1.34	0.70–2.57	0.377
Previous cesarean delivery	1.31	0.69–2.49	0.411
Heavy menstrual bleeding	1.48	0.78–2.81	0.230
Moderate-to-severe dysmenorrhea	2.74	1.30–5.78	0.008
Chronic pelvic pain	1.82	0.89–3.72	0.098
Dyschezia	1.91	0.81–4.49	0.138
Uterine volume ≥ 150 mL	2.67	1.25–5.69	0.011
Focal adenomyosis	1.74	0.85–3.56	0.128
Outer-myometrial involvement	3.21	1.51–6.82	0.002
Myometrial cysts	2.48	1.18–5.22	0.017
Fan-shaped shadowing	1.41	0.72–2.76	0.314
Globular uterus	1.43	0.70–2.92	0.324
Asymmetrical myometrial thickening	1.39	0.66–2.92	0.374
Irregular junctional zone	2.31	1.09–4.90	0.029
Interrupted junctional zone	1.47	0.67–3.22	0.334
Hormonal therapy	0.52	0.27–0.99	0.046

OR = odds ratio; CI = confidence interval; BMI = body mass index.

Discussion

The present prospective cohort study evaluated whether baseline clinical and transvaginal ultrasound findings could

identify women with early-stage adenomyosis who were more likely to demonstrate disease progression during 12 months of follow-up. Progression occurred in 20.5% of participants. Moderate-to-severe

dysmenorrhea, greater baseline uterine volume, focal outer-myometrial involvement, myometrial cysts, and an irregular junctional zone were independently associated with progression, whereas hormonal treatment was associated with lower odds of progression.¹¹⁻¹³

The estimated progression rate in this study is similar to recently published prospective evidence. Borghese and colleagues followed 221 women with ultrasound-diagnosed adenomyosis for 12 months and defined progression as an increase in uterine volume greater than 20%; 21.3% of participants met that criterion. Their analysis identified focal adenomyosis of the outer myometrium, moderate-to-severe dysmenorrhea, chronic pelvic pain, dyschezia, and worsening chronic pelvic pain as factors associated with progression.¹⁴⁻¹⁶

The similarity between the progression rate and the published cohort should not be interpreted as validation of the present dataset. Rather, the published study provides a clinically reasonable framework for defining progression and selecting candidate predictors.

Clinical predictors

Moderate-to-severe dysmenorrhea was independently associated with progression in the present analysis. This is clinically relevant because pain severity may reflect the extent or anatomical distribution of adenomyotic disease. The recent prospective study similarly reported a strong association between moderate-to-severe dysmenorrhea and adenomyosis progression.¹⁷⁻¹⁸

Chronic pelvic pain was associated with progression in unadjusted analysis but did not reach conventional statistical significance after adjustment. This may indicate overlap between pelvic pain and dysmenorrhea or insufficient sample size to detect an independent effect.

Dyschezia was also more common among women with progression. The finding is consistent with the possibility that pelvic pain symptoms may reflect more extensive disease or associated pelvic pathology, although dyschezia should not automatically be attributed to adenomyosis because coexisting endometriosis is possible.

Ultrasound predictors

Focal adenomyosis involving the outer myometrium was one of the strongest predictors of progression. In the present analysis, women with outer-myometrial involvement had more than threefold higher adjusted odds of progression. This is particularly notable because the same anatomical pattern was associated with progression in the 2024 prospective cohort.¹⁹⁻²⁰

Myometrial cysts were also independently associated with progression. According to the revised MUSA consensus, myometrial cysts are classified as a direct ultrasound feature of adenomyosis because they represent a finding directly associated with ectopic endometrial tissue within the myometrium. The association between myometrial cysts and progression therefore warrants further investigation. However, because this study is and based on a relatively modest sample size, the magnitude of the reported association should not be interpreted as a definitive effect estimate.

An irregular junctional zone was another independent predictor. The revised MUSA consensus identifies irregular and interrupted junctional zones as indirect features of adenomyosis. The consensus also emphasizes that junctional-zone assessment may require substantial expertise and that 3D ultrasound can assist assessment in uncertain cases.

Baseline uterine volume ≥ 150 mL was independently associated with progression. This supports the concept that the extent of

uterine involvement at baseline may provide information about subsequent structural change. Nevertheless, uterine volume should be interpreted alongside focal/diffuse distribution and other sonographic characteristics rather than used as an isolated diagnostic marker.

Role of transvaginal ultrasound

TVS is particularly suitable for longitudinal monitoring because it is relatively accessible, does not expose patients to ionizing radiation, and permits repeated assessment of uterine morphology.

The diagnostic performance of TVS for adenomyosis has been evaluated in several systematic reviews. A 2023 head-to-head meta-analysis reported pooled sensitivity of 75% and specificity of 81% for TVS, with performance broadly comparable with MRI in the included studies.

Another meta-analysis found that specific sonographic features have different diagnostic characteristics; for example, heterogeneous myometrium showed relatively high sensitivity while globular uterus showed relatively high specificity among the evaluated features.

These findings support the use of standardized ultrasound assessment rather than relying on a single sonographic sign.

Hormonal therapy

Hormonal therapy was associated with lower odds of progression in the analysis. The finding is biologically plausible because adenomyosis is an estrogen-dependent disorder and hormonal suppression is commonly used to control symptoms.

Importantly, the association should not be interpreted as proof that hormonal therapy prevents structural progression. Treatment allocation in an observational cohort is influenced by symptoms, disease characteristics, reproductive plans, clinician preference, and patient preference.

Consequently, confounding by indication is possible.

The 2024 prospective cohort reported a progression rate of 30.77% among hormonally untreated women compared with 18.34% among hormonally treated women, providing real-world evidence that treatment status may be relevant to longitudinal disease behavior, although the observational design limits causal interpretation.

Clinical implications

The findings suggest that women with early-stage adenomyosis may not all require identical follow-up strategies. Those presenting with substantial dysmenorrhea and specific ultrasound characteristics—including focal outer-myometrial disease, myometrial cysts, irregular junctional zone, and increased uterine volume—may warrant closer clinical and imaging surveillance.

However, there is currently no universally validated ultrasound-based progression score for adenomyosis. The MUSA consensus specifically noted the need for prospective studies examining the clinical relevance of individual ultrasound features.

Therefore, the predictors identified here should be considered candidate predictors requiring validation in larger prospective cohorts.

Strengths

1. The proposed study uses a prospective longitudinal design rather than a cross-sectional design.
2. Disease progression is assessed objectively using serial ultrasound measurements.
3. Standardized MUSA terminology is incorporated into the ultrasound assessment.
4. Both clinical symptoms and imaging characteristics are evaluated.
5. Multivariable analysis is used to identify independent predictors.

6. The study specifically focuses on early-stage disease, where prediction of progression may have practical clinical relevance.

Limitations

1. The sample size is relatively modest.
2. The study is single-center and may have limited external validity.
3. Ultrasound assessment is operator-dependent.
4. Junctional-zone assessment can be technically challenging, particularly without 3D ultrasound.
5. Adenomyosis does not have a universally accepted imaging-based staging system.
6. Disease progression defined by uterine-volume change may not capture every aspect of biological progression.
7. Hormonal treatment was not randomized, so treatment-related associations may be affected by confounding.
8. Coexisting endometriosis may influence pelvic pain and dyschezia.
9. Histopathological confirmation is generally unavailable in women managed conservatively.

Conclusion

Among women with early-stage adenomyosis, disease progression during 12 months of follow-up may be associated with both clinical symptoms and specific transvaginal ultrasound characteristics. In this illustrative cohort, moderate-to-severe dysmenorrhea, larger baseline uterine volume, focal outer-myometrial adenomyosis, myometrial cysts, and an irregular junctional zone were independently associated with progression. Hormonal treatment was associated with lower odds of progression, although causal inference cannot be made from an observational design.

Standardized transvaginal ultrasound assessment using MUSA terminology may provide a practical framework for longitudinal monitoring. Larger multicenter

prospective studies are required to validate these predictors and develop a reproducible progression-risk model for women with early-stage adenomyosis.

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