

The Prognostic Significance of Transvaginal Ultrasound for Adenomyosis: Association with Histopathology

Original
Article

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ABSTRACT

Background: Presence of ectopic endometrial glands and stroma within the myometrium, as well as adjacent myometrium hypertrophy and hyperplasia, define adenomyosis. There was no agreement on the currently used diagnostic criteria.

Objectives: To assess the diagnostic precision of different transvaginal sonographic markers for diagnosing adenomyosis by contrasting them with the gold standard histopathological findings.

Patients and Methods: In this prospective study, transvaginal sonography was performed preoperatively for 104 women scheduled for hysterectomy. If any of the following sonographic characteristics were observed, adenomyosis diagnosis was made: indistinct endometrial-myometrial junction definition, subendometrial echogenic linear striations, subendometrial myometrial cysts, asymmetrical thickness of the posterior and anterior myometrial walls, a globular-shaped uterus, or heterogeneous myometrial echotexture. The sonographic features were contrasted with the histopathological results.

Results: For adenomyosis diagnosis, the sensitivity, specificity, negative (NPV) and positive (PPV) predictive values, and overall transvaginal US accuracy were 85.7%, 70%, 80%, 77.8%, and 79.2%, respectively. The greatest accuracy for the adenomyosis diagnosis was observed in a globular-configured regularly enlarged uterus, ill-defined endomyometrial junction, and heterogeneous myometrium. Heterogeneous myometrium was the most prevalent finding in patients with adenomyosis (45/61 patients), but it exhibited a low level of specificity. The sonographic feature with the highest PPV (88.89%) for the adenomyosis diagnosis was the subendometrial linear striations presence, which was more specific (95.35%).

Conclusion: The globular enlarged uterus, ill-defined endomyometrial junction, and heterogeneous myometrium on transvaginal US helps the adenomyosis diagnosis. The diagnostic accuracy of subendometrial linear striations is the greatest among the transvaginal US diagnostic adenomyosis findings.

Key Words: Adenomyosis, histopathology, transvaginal ultrasound.

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INTRODUCTION

The term "adenomyosis" refers to existence of ectopic endometrial glands and stroma within the myometrium, with surrounding adjacent myometrium hyperplasia and hypertrophy. The cause of adenomyosis is not well comprehended. Several explanations have been proposed, such as the absence of the basement membrane at the endometrial-myometrial interface that permits endometrial tissue to proliferate into the myometrium. Adenomyosis usually presents as a generalized process, but it might also present as a focal lesion within the myometrium^[1].

In transvaginal ultrasound (US) imaging, subendometrial linear striations are the most accurate indicator, showing a positive predictive value (PPV) of 80%, and a specificity of 96% for adenomyosis diagnosis^[2].

Regarding the identification of an irregular junctional zone on the coronal plane, Ahmadi and Haghghi^[3] determined that the PPV was 95% and the accuracy of 3D-TVS was 80% in diagnosing adenomyosis. 3D-TVS offer a thorough and complete examination of the uterus, enhancing adenomyosis assessment in the office as a primary diagnostic method.

A thorough understanding of the histopathologic characteristics of the disease is crucial for its diagnosis and classification^[4].

We aimed to assess the diagnostic precision of different transvaginal sonographic findings for diagnosing adenomyosis by contrasting them with the histopathological findings as the gold standard. Additionally, it aimed to identify the most informative sonographic characteristic for diagnosing adenomyosis.

PATIENTS AND METHODS

A prospective study was performed at Obstetrics and Gynecology Department, Faculty of Medicine, Menoufia University. One hundred four women scheduled for hysterectomy during the period from March 2022 to September 2023 were included in the current study. Participants underwent preoperative transvaginal US examination and postoperative histopathological examination to confirm the adenomyosis diagnosis.

The Institutional Review Board of the Faculty of Medicine, Menoufia University, approved the study protocol. All participants provided written informed consents.

Inclusion criteria

- Patients are typically aged 40-60 years old with any of the following clinical presentations: chronic pelvic pain, or abnormal uterine bleeding (menorrhagia, irregular bleeding, poly-menorrhea).
- Adenomyosis is suggested by 2D ultrasonography.
- The junction zone should be visible on imaging. It represents the inner myometrium.
- A bulky uterus (larger than a 10-week gestational size) with no prior histologic investigation.

Exclusion criteria

- GnRH analog or hormonal treatment administered within the recent three months before the hysterectomy.
- History of minimally invasive treatment for endometrial conditions (e.g. endometrial resection, or endometrial ablation).

All participants underwent comprehensive history-taking, general, pelvic, and abdominal examination and routine preoperative laboratory investigations, such as complete blood picture, coagulation profile, fasting blood sugar, kidney and liver function tests.

Transvaginal US

All participants were asked to empty their bladder, and transvaginal sonography was performed using a high-frequency (4/7 MHz) endovaginal probe (Voluson 730 Pro machine, GE Healthcare, Austria). Both sagittal and coronal planes were used for measuring the subendometrial halo thickness, endometrial-myometrial junction, endometrial thickness, and uterine size^[5].

Common features^[6,7]

1. Globular uterine enlargement, typically of length up to 12 cm, which is not attributable to the existence of leiomyomata.
2. Cystic anechoic lakes or spaces in the myometrium: vary in size and can be distributed throughout the myometrial tissue.
3. Subendometrial echogenic linear striations
4. Heterogeneous echo texture: The myometrium is not homogeneous, and there are signs of architectural disturbance.
5. Obscured endometrial/myometrial border due to myometrium invasion by the glands.
6. Transition zone Thickening: This layer encircles the endometrial layer and appears as a hypoechoic halo. It has been demonstrated that adenomyosis is connected with a thickness of 12 mm or more.

Uncommon features

A localized mass within the myometrium, known as focal adenomyosis. Two types of focal adenomyosis are known to exist: adenomyosis that is restricted to a single uterine wall and the circumscribed form of adenomyosis.

The distinction between focal adenomyosis and leiomyoma is crucial because focal adenomyosis is frequently confused with leiomyoma^[8,9]. The most prevalent adenomyosis type is the diffuse form. The focal form is rarer and causes diagnostic difficulties on both MRI and TVS^[10].

Histopathological examination

Microscopic and gross histopathological investigations were conducted by the same pathologist, who was blinded to the sonographic data. Specimens were oriented using a fixed marker placed on the anterior uterine wall. Associated pathological abnormalities, macroscopic morphology, and uterine weight are recorded. The maximal thicknesses of the wall of the uterine were measured at the left, right, fundal, posterior, and anterior locations. Any associated pathological abnormalities were documented^[11].

Histopathological adenomyosis diagnosis was made according to the ectopic endometrial glands and/or stroma existence, accompanied by smooth-muscle hyperplasia and hypertrophy situated 2.5 mm beyond the endometrial-myometrial junction^[12].

Sample size calculation

An earlier study detected that in the adenomyosis diagnosis, the sensitivity of heterogeneous myometrium found by TVUS was 80.8%,^[13]. As the prevalence of adenomyosis histology among hysterectomies demonstrated by a previous Indian study was 10.7%^[14]. Therefore, the sample size required to investigate the results of the current study with a significant $P < 0.05$ is determined, and a drop-out rate of 10% is added. Consequently, a minimum of 104 women need to be recruited for the research.

Statistical analysis

The data were collected, tabulated, and imported into the statistical software for social science (SPSS v 19). Absolute frequencies (number) and relative frequencies (percentage) were used to present categorical qualitative variables, while continuous quantitative variables, were presented as the mean \pm SD (and range). The validity of the screening tests (TVS) was evaluated regarding specificity, sensitivity, accuracy, PPV and negative predictive value (NPV).

True Negative (TN) / (TN+ False Negative (FN)) = NPV.

True Positive (TP)/ (TP+ False positive (FP)) = PPV.

TP / (TP+FN) = Sensitivity.

TN / (TN + FP) = Specificity.

TP+FP+FN+TN/grand total = Accuracy.

RESULTS

(Table 1) demonstrates that the study participants were between the ages of 40 to 60 years old, with an average age of 45 years. The most common complaint among the studied group was abnormal uterine bleeding (46.2%), followed by 32.6% of patients who reported both pain and bleeding, while 21.2% experienced pain only. Three-quarters of the studied patients (75%) had a vaginal delivery, while the remaining 25% underwent a cesarean section. Regarding histopathological findings, adenomyosis was found in 61/104 (58.65%) patients at the histological examination. Various other histopathological findings, with or without adenomyosis, were detected, the majority of participants had leiomyomas (66.3%), while 3.8% had endometrial hyperplasia, and 29.9% had only adenomyosis with no other histopathological results.

Table 1: Demographic & clinical characteristics of the studied population

Variable	Studied group (n = 104)
Age (years)	
Mean \pm SD	45 \pm 5.1
Range	40-60
Parity	
Primigravida	4 (3.8%)
1	0 (0%)
2	4 (3.8%)
3	35 (33.7%)
4	39 (37.5%)
5	17 (16.3%)
6	5 (4.9%)
Clinical presentations	
Abnormal uterine bleeding	48(46.2%)
Chronic pelvic pain	22(21.2%)
Both	34 (32.6%)
Mode of delivery	
Cesarean section	26(25%)
Vaginal delivery	78 (75%)
Other histological findings	
Leiomyoma	69(66.3%)
Endometrial hyperplasia	4(3.8%)
No other findings	31(29.9%)

In 65 of the 104 patients, transvaginal US was diagnostic of adenomyosis; however, 52 (80%) of these patients had a histopathological adenomyosis diagnosis (13 false positive diagnoses). Out of the 39 cases in which none of the transvaginal US diagnostic criteria for adenomyosis were observed, nine (23%) had a histopathological adenomyosis diagnosis (9 false negative diagnoses). Transvaginal US diagnosed adenomyosis in 52 of the 61 women who were histologically diagnosed. In comparison with the gold-standard histopathological test, transvaginal US also accurately detected 30 out of 43 patients without adenomyosis. The specificity, sensitivity, NPV and PPV predictive values of transvaginal US for the adenomyosis diagnosis were 70%,85.7%, 77.8% and 80% respectively. The overall transvaginal US accuracy was 79.2%. (Table 2).

Table 2: Concordance between histopathological adenomyosis diagnosis and preoperative transvaginal ultrasound examination

TVS	Histopathological adenomyosis diagnosis		Total
	Positive	Negative	
Positive	52	13	65
Negative	9	30	39
Total	61	43	104

Sensitivity: 85.7%

Specificity: 70%

Positive predictive value: 80%

Negative predictive value: 77.8%

Accuracy: 79.2%

Upon comparison of each sonographic diagnostic adenomyosis feature with the histopathological results, we found that myometrial heterogeneity, a regularly enlarged uterus, and an ill-defined endomyometrial junction had a greater statistical significance ($P < 0.01$) than myometrial anteroposterior asymmetry, subendometrial echogenic linear striations, and myometrial cysts (Table 3).

(Table 4) delineates the NPVs, PPVs, specificities, sensitivities, and each transvaginal sonographic finding accuracies. For adenomyosis, the most sensitive criterion (73.77%) and the one with the greatest NPV was myometrial heterogeneity. Even though the presence of subendometrial echogenic linear striations was the least prevalent ultrasound finding in adenomyosis patients (26.23%), this finding was the most specific criterion (95.35%) and had the greatest PPV (88.89%).

Table 3: Concordance between histopathological adenomyosis diagnosis and each diagnostic finding of transvaginal ultrasound examination

US findings	Histopathological adenomyosis diagnosis		Chi-Square test	P-value
	Yes (n=61)	No (n=43)		
Globular configuration				
Yes	42 (68.85%)	12 (27.91%)	16.9	<0.001**
No	19 (31.15%)	31 (72.09%)		
Myometrial antero-posterior asymmetry				
Yes	40 (65.57%)	16 (37.21%)	8.17	0.004*
No	21 (34.4%)	27 (62.79%)		
Identification of endomyometrial junction				
Yes	36 (59.02%)	7 (16.28%)	18.99	<0.001**
No	25 (54.1%)	36 (83.72%)		
Subendometrial echogenic linear striations				
Yes	16 (26.23%)	2 (4.65%)	8.21	0.004*
No	45 (73.77%)	41 (95.35%)		
Myometrial cysts				
Yes	30 (49.18%)	9 (20.93%)	8.59	0.003*
No	31 (50.82%)	34 (79.07%)		
Heterogeneous myometrium				
Yes	45 (73.77%)	16 (37.21%)	13.9	<0.001**
No	16 (26.23%)	27 (62.79%)		

* Significant, ** highly significant

Table 4: Diagnostic accuracy of transvaginal ultrasound findings for the diagnosis of adenomyosis

	Sensitivity	Specificity	PPV	NPP	Accuracy
Globular configuration	68.85%	72.09%	77.785	62%	70.19%
Myometrial AP asymmetry	65.57%	62.79%	71.43%	56.25%	64.42%
Identification of endomyometrial junction	59.02%	83.72%	83.72%	59.02%	69.23%
Subendometrial echogenic linear striations	26.23%	95.35%	88.89%	47.67%	54.81%
Myometrial cysts	49.18%	79.07%	76.92%	52.31%	61.54%
Heterogeneous myometrium	73.77%	62.79%	73.77%	62.79%	69.23%

DISCUSSION

One hundred four women scheduled for hysterectomy were included in the current study. Participants underwent preoperative transvaginal US examination and postoperative histopathological examination to confirm adenomyosis diagnosis. This research objected to assess the diagnostic 2D transvaginal US precision for detecting adenomyosis, employing histopathology as the gold standard for comparison.

In this study, TVS accurately identified adenomyosis in 52 out of 61 patients (When compared to the gold-standard test; i.e., histopathological examination). The specificity, sensitivity, NPV and PPV and overall transvaginal US accuracy for adenomyosis diagnosis were 70%, 85.7%, 77.8%, 80%, and 79.2%, respectively.

These findings align positively with the results reported by Andres *et al.*^[15]. A comprehensive literature review from the past ten years was performed to assess the TVUS precision in diagnosing adenomyosis. For all combined

imaging properties, the analysis revealed a specificity of 56.0% and a sensitivity of 88.9%. For diagnosing adenomyosis using TVUS, a poorly defined junctional zone displayed the greatest specificity (56.0%) and the greatest sensitivity (86%).

Gaafar *et al.*^[16] assessed 100 cases who had TAH after undergoing a preoperative TVUS. The diagnostic ultrasonography precision was evaluated in comparison to uterine pathology. The sensitivity was 90% and specificity was 92.8% in premenopausal women with abnormal uterine hemorrhage. The diagnostic accuracy for adenomyosis was 92.42% overall, with 69.2% and 98.1% for the PPV and NPV, respectively.

Fifty-four symptomatic premenopausal women who had preoperative uterus TVS to assess changes to the JZ were included in a study by Luciano *et al.*^[17]. The US outcomes were contrasted with the histopathological results of the targeted biopsy specimens from the uterus. The findings displayed a sensitivity of 92% and specificity of 83%, with a total precision of 90% for the adenomyosis diagnosis.

One of our research's advantages is that, unlike Luciano *et al.*^[17], who focused on uterine biopsy specimens, our analysis encompassed only patients who had experienced a hysterectomy. As a result, we were able to rule out double pathology and produce more precise findings. However, one drawback of our research is that we were unable to identify the lesions' site.

Ahmadi and Haghighi^[3] investigated US application to evaluate the diagnostic precision of detecting a hazy, ill-defined, and irregular JZ on coronal plane. For diagnosing adenomyosis, they found that the accuracy and the PPV were 80% and 95%, respectively. However, the study had limitations, as it did not assess TVUS specificity or sensitivity in diagnosing adenomyosis.

We detected that a regularly globular configuration enlarged uterus, ill-defined endomyometrial junction and heterogeneous myometrium had the greatest accuracy for the adenomyosis diagnosis. The heterogeneous myometrium was the most prevalent finding in adenomyosis patients (45/61 patients), but it exhibited a low level of specificity. The most specific sonographic feature (95.35%) and the one with the greatest PPV (88.89%) for adenomyosis diagnosis was the presence of subendometrial linear striations.

Exacoustos *et al.*^[7] conducted a study involving 72 premenopausal patients who were undergoing hysterectomy with a preoperative transvaginal sonographic junctional zone assessment, and a correlation with histopathology was performed. They found that a JZ thickness of ≥ 4 mm and JZ infiltration and distortion presence had the best overall accuracy and high sensitivity (88%) (85%

and 82%, respectively) for diagnosing adenomyosis. Additionally, these features demonstrated good specificity and sensitivity (88% and 91%) with an overall accuracy of 89%, indicating they provide a reliable approach for diagnosing adenomyosis.

Reinhold *et al.*^[18] examined 119 consecutive patients underwent hysterectomy. The MRI images and endovaginal US scans interpretations were carried out independently and without knowledge of each other's findings, following a double-blind approach. The study found that MR imaging had a specificity of 91%, sensitivity of 81%, NPV of 95% and PPV of 65%. Patients with and without proven adenomyosis had mean junctional zone (JZ) thicknesses on MR scans of 15.0 mm and 7.7 mm, respectively.

Hussein and El Refaey^[19] assessed the reliability of different transvaginal sonographic features for diagnosing adenomyosis by correlating them with histopathological outcomes. TV U/S accurately showed that adenomyosis was absent in 33 cases and present in 10 patients. There were 2 false negative and 5 false positive diagnoses. TVU/S demonstrated high accuracy for diagnosing adenomyosis, specificity, NPV, and but its PPV was low.

The variations in the primary diagnostic criteria selected are likely the cause of the variable accuracy of the ultrasound in the adenomyosis diagnosis. In the majority of studies, the primary diagnostic criterion for adenomyosis was myometrial heterogeneity, which has been associated with a smooth muscle hypertrophic to hyperplasia reaction^[20]. Bromley *et al.*^[21] confirmed that all patients with adenomyosis exhibited a mottled heterogeneous uterus, 95% had a globular uterus, 82% had small myometrial lucent areas, and 82% had an indistinct endometrial stripe, as per the findings of these previous studies. Nevertheless, Bazot *et al.*^[22] found that all adenomyosis patients had a mottled heterogeneous uterus, 82% had small myometrial lucent areas, 95% had a globular uterus, and 82% had an indistinct endometrial stripe, in accordance with these previous studies. Fedele *et al.*^[23] firstly reported that the myometrial anechoic lakes had a significant value in the adenomyosis diagnosis. They discovered that the sonographic specificity and sensitivity were 74% and 80%, respectively, in women who did not have leiomyoma or endometrial disease.

In the adenomyosis diagnosis, subendometrial echogenic nodules, subendometrial echogenic linear striations, and asymmetrical myometrial thickness exhibited the highest specificity and PPVs among all the sonographic features assessed by Atri *et al.*^[24]. Subendometrial linear striations exhibited the greatest specificity and PPV in our study, and we regard them as the most specific finding for differential diagnosis, despite the rarity of their detection in the US. This is consistent with the research conducted by Atri *et al.*^[24].

Several key limitations of using endovaginal US to diagnose adenomyosis should be emphasized. The procedure precision to diagnose adenomyosis could be significantly more reliant on the operator's skill & expertise compared to its use for other pelvic conditions, and the sonographic adenomyosis indicators can be subtle. Another limitation was the study population restriction to only women underwent hysterectomies, as well as the absence of exclusion of patients' with multiple or large myomas that distort the uterus and impede the evaluation of the surrounding myometrium. Thus the precise transvaginal US adenomyosis diagnosis was interfered by the most commonly encountered indication for hysterectomy, leiomyoma.

CONCLUSION

The presence of an enlarged uterus with a globular appearance, ill-defined endomyometrial junction, and heterogeneous myometrium on transvaginal US supports the adenomyosis diagnosis. Among the transvaginal US diagnostic adenomyosis findings, subendometrial linear striations have the greatest diagnostic accuracy.

CONFLICT OF INTERESTS

There are no conflicts of interest.

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