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New Sonographic Classification of Adenomyosis: Do Type and Degree of Adenomyosis Correlate to Severity of Symptoms?

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ABSTRACT **Study Objective:** To correlate the type and degree of adenomyosis, scored through a new system based on the features of transvaginal sonography, to patients' symptoms and fertility.

Design: This is a multicenter, observational, prospective study.

Setting: Two endometriosis tertiary referral centers (University of Rome "Tor Vergata" and University of Siena).

Patients: A total of 108 patients with ultrasonographic signs of adenomyosis.

Interventions: A new ultrasonographic scoring system designed to assess the severity and the extent of uterine adenomyosis was used to stage the disease in correlation with the clinical symptoms. Menstrual uterine bleeding was assessed by a pictorial blood loss analysis chart, painful symptoms were evaluated using a visual analog scale, and infertility factors were considered.

Measurements and Main Results: A total of 108 patients with ultrasonographic signs of adenomyosis (mean age \pm standard deviation, 37.7 ± 7.7 years) were classified according to the proposed scoring system. Women with ultrasound diagnosis of diffuse adenomyosis were older ($p = .04$) and had heavier menstrual bleeding ($p = .04$) than women with focal disease; however, no statistically significant differences were found regarding the presence and severity of dyspareunia and dysmenorrhea. Higher values of menstrual bleeding were found for severe diffuse adenomyosis, with the highest values being found in those with adenomyomas. In patients trying to conceive, the presence of ultrasound findings of focal disease was associated with a higher percentage of infertility than in those with diffuse disease, and the focal involvement of the junctional zone showed a higher percentage of at least 1 miscarriage than in those with diffuse adenomyosis.

Conclusion: The ultrasonographic evaluation of the type and extension of adenomyosis in the myometrium seems to be important in correlation to the severity of symptoms and infertility. *Journal of Minimally Invasive Gynecology* (2020) 27, 1308–1315. © 2019 AAGL. All rights reserved.

Keywords: Adenomyosis; Transvaginal ultrasound; Classification; Heavy menstrual bleeding; Pain

Adenomyosis is a frequent benign gynecologic disease, defined by the presence of endometrial glands and stroma within the myometrium, associated with the hypertrophy of the smooth muscle. Adenomyosis may involve different sites of myometrium or most of the uterine wall, ranging

from focal to diffuse adenomyosis. It can also present as a nodular lesion forming an adenomyoma [1].

The real prevalence of adenomyosis is difficult to accurately assess owing to the requirement of histologic confirmation after a clinical diagnosis, which is based on the patient's symptoms and results of imaging studies. Its prevalence has been reported to range from 5% to 70% in hysterectomy specimens [2–6]. However, the study of prevalence through histologic diagnosis presents a large selection bias because of the advanced age of and clinical symptoms observed in patients undergoing hysterectomy. Moreover, a study highlighted the variability in the histologic diagnosis of adenomyosis from center to center and among pathologists [7].

The authors declare that they have no conflict of interest.

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Certainly, it becomes more difficult to ascertain prevalence when various diagnostic criteria are used during imaging assessment in patients, with or without symptoms, not undergoing surgery.

Transvaginal sonography (TVS) has recently been used for the noninvasive diagnosis of adenomyosis and to study its prevalence [1,8–10]. When TVS is performed by dedicated sonographers, it shows high accuracy in detecting this pathology [11–13].

Adenomyosis seems to be associated with endometriosis [14,15]. Surely, both conditions share pathogenesis and symptoms such as dysmenorrhea, heavy menstrual bleeding, infertility, dyspareunia, and chronic pelvic pain [14,16–18].

Some authors suggest that the severity of symptoms and the clinical features correlate with the extent and depth of adenomyosis [18–21]. So far, however, the only classification proposed for the extension of the disease is based on the histologic findings after surgery and not on imaging. Because adenomyosis often results in poorly defined lesions, possibly disseminated in different parts of the myometrium, it is difficult to express its severity in quantitative terms.

Through TVS, it is possible to assess the characteristics of adenomyosis. Therefore, recently we have proposed a scoring system [22] that grades the type of adenomyosis and its extension inside the uterus.

To the best of our knowledge, there are no prospective studies using noninvasive techniques to assess the link between type and degree of adenomyosis and the severity of clinical symptoms.

The aim of this study was to correlate the type and degree of adenomyosis to symptoms and fertility through a new scoring system [22] based on the features of TVS.

Materials and Methods

This is a multicenter, prospective, observational study conducted in 2 tertiary referral university hospitals (“Tor Vergata” University Hospital, Department of Biomedicine and Prevention; “Santa Maria alle Scotte” University Hospital, Department of Molecular and Developmental Medicine) between January 2017 and March 2018. The study was approved by the local research ethics committee.

A total group of 148 women aged between 29 and 46 years old referred to our center for pelvic pain were included in the study and divided in 2 groups based on the presence of sonographic signs of adenomyosis, according to previous studies [1,13,22]. Inclusion criteria were premenopausal status, availability to perform transvaginal ultrasound, and no hormonal therapy, whereas exclusion criteria were an ongoing pregnancy, a gynecologic malignant disease, and the presence of more than 3 uterine myomas. A total of 108 women with ultrasound diagnosis of adenomyosis were finally enrolled in the study, and 40 patients without any sonographic signs of myometrial pathology were excluded from the analysis.

All patients underwent a detailed ultrasound evaluation of the uterus in which type and extension of adenomyosis were classified according to a previously published study [22].

Furthermore, demographic data and detailed medical history were recorded before the TVS scan, and the presence of painful symptoms (including dysmenorrhea, dyspareunia, dyschezia, and dysuria) of heavy menstrual bleeding and/or infertility was evaluated.

Historic Information

A complete medical, surgical, and obstetric history including women’s age, body mass index (kg/m^2), age at menarche, gravidity and parity (number of all previous pregnancies: spontaneous pregnancy loss and/or live births), and the mode of delivery were recorded. Infertility was defined as no pregnancy after 12 months of unprotected intercourse.

Patients were also asked about any medication they were taking including the use of analgesics for the treatment of painful periods. The presence of the following painful symptoms was noted: dysmenorrhea, dyspareunia, dysuria, dyschezia, and chronic pelvic pain. Symptom intensity was evaluated through the visual analog scale (VAS) system, using a 10-cm line with the extreme points 0 and 10 corresponding to “no pain” and “maximum pain,” respectively. Severe symptoms were considered if VAS score was equal to or more than 5. Furthermore, the presence of heavy menstrual bleeding was investigated. Women were asked about the frequency and duration of menstrual periods and about any episodes of intermenstrual bleeding. To obtain an objective evaluation regarding the amount of menstrual loss, a pictorial blood loss analysis chart (PBAC) was used. The PBAC provides a score that depends on the number of tampons or sanitary towels used during the menstrual cycle and on the degree to which each item is soiled. The PBAC score has been shown to have a high specificity and sensitivity when used as a diagnostic test for objective menstrual bleeding [23], and a PBAC score of more than 100 is consistent with heavy menstrual bleeding.

Ultrasound Examination

All transvaginal ultrasound examinations were performed by 2 experienced sonographers (C.E. and L.L.) using a 4- to 9-MHz probe with a three-dimensional (3D) capability (Voluson E6; GE Medical Systems, Zipf, Austria). The 2 sonographers were blinded to the patient’s clinical symptoms, and the clinical examination was performed after the ultrasound. Briefly, a conventional two-dimensional (2D) ultrasound with gray scale and power Doppler for assessment of the pelvis was performed. First, we carefully evaluated the uterus, the myometrium, and the endometrium. The myometrium was systematically examined for the presence of any abnormalities. A 2D examination was followed by the acquisition of 3D volume of the uterus

with and without power Doppler. Thereafter, the scan examined the adnexa, the pouch of Douglas, and the other pelvic organs (bladder, rectum, rectosigmoid junction, ureters) and sites (posterior, lateral and anterior parametria, rectovaginal septum, vesicouterine pouch, uterosacral ligaments), looking for features of endometriosis according to a previous ultrasound mapping system [24]. Women were considered affected by endometriosis if an ovarian endometrioma or deep endometriotic nodules were detected at the ultrasound evaluation. Adhesions of the anterior and posterior compartments were suspected by the presence or absence of the “sliding sign” and the pain induced during the examination was recorded, carefully mapping all painful sites (“tenderness-guided” ultrasonography) [25].

Images were stored as 2D still images, 2D video clips, and 3D volumes. The sonographic diagnosis of adenomyosis was made when at least one of the following features of the disease was observed at the ultrasound examination:

- Globally enlarged uterus: the fundus of the uterus appears enlarged
- Asymmetrically enlarged uterus (1 uterine wall thicker than others) unrelated to leiomyoma
- Round cystic area within the myometrium surrounded by a hyperechoic halo
- Inhomogeneous, irregular myometrial echotexture in an indistinctly defined myometrial area with decreased or increased echogenicity; hyperechogenic islands; and subendometrial lines and buds
- Myometrial hypoechoic linear striations seen as a radiating pattern of thin acoustic shadows not arising from echogenic foci or leiomyoma (fan-shaped shadowing)
- Indistinct, fuzzy endometrial-myometrial border (ill-defined endometrial stripe)
- Presence of diffuse minimal vascularity seen as diffuse spread of small vessels within the myometrium
- Question mark sign [9], defined as when the corpus uterus is flexed backward, the fundus of uteri is facing the posterior pelvic compartment, and the cervix is directed frontally toward the urinary bladder

All these ultrasound features have been previously described, and there is a wide consensus that they are reliable morphologic markers of adenomyosis [1,11–13,22,26–29].

The type of adenomyosis was divided into focal, diffuse, or adenomyomas according to the TVS features described in a previous study [22]. Focal adenomyosis is classified when typical ultrasonographic adenomyotic signs are circumscribed in aggregates and surrounded by normal myometrium, whereas diffuse adenomyosis is classified when typical alterations at TVS spread throughout the myometrium [30–33]. Adenomyomas are a subgroup of focal adenomyosis surrounded by hypertrophic myometrium.

In our analysis, we considered focal and diffuse adenomyosis of the outer and inner myometrium junctional zone (JZ) separately.

The ultrasound detection of each type of adenomyotic lesion in the external myometrium and in the JZ was classified in 4 grades according to the parameters published in a previous study [22]. Through the use of uterine drawings, the previously published adenomyosis extension score (using the same criteria) was simplified to help clarify it and make it easier to apply to all sonographers as shown in Fig. 1. Briefly, as previously described [22], we considered 4 degrees of extension for each type of disease considered: diffuse and focal adenomyosis (of inner and outer myometrium) and adenomyoma. For diffuse adenomyosis of the outer myometrium, degree is assigned according to the thickness of the uterine wall (> or <20 or 30 mm) and number of the uterine walls affected (anterior, posterior lateral left or right). For diffuse adenomyosis of the inner myometrium, thickness of the JZ and length of the infiltrated JZ tract was considered in the 4 degrees. Focal adenomyosis of the inner and outer myometrium was assigned a degree according to the largest diameter of the focal lesion and the number of foci. Similarly, adenomyomas were divided in 4 degrees according to size (largest diameter 20, 30, 40, >40) and number of adenomyomas. A score from 1 to 4 was attributed to each degree of disease considered. Then, the ultrasound extent of the disease was calculated through the sum of the scores obtained and classified in 3 groups: mild (ranged, 1–3), moderate (4–6), and severe (≥ 7) adenomyosis.

Patients’ characteristics, severity of symptoms, and uterine menstrual bleeding were correlated to the type of adenomyosis and score. Finally, the extent of adenomyosis, which was classified as mild, moderate, or severe, was correlated to the severity of symptoms, uterine menstrual bleeding, presence of pelvic endometriosis (ovarian and deep infiltrating), and infertility.

Statistical Analysis

Statistical analysis was undertaken using the Statistical Package for the Social Sciences (SPSS v.15.0; SPSS, Inc., Chicago, IL). All continuous variables were expressed in terms of mean \pm standard deviation, whereas categorical variables were expressed in terms of frequency and percentage.

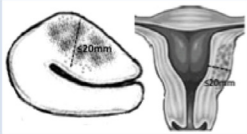
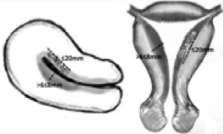
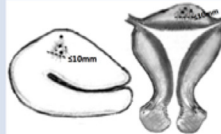


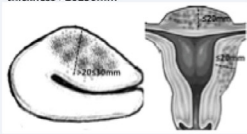
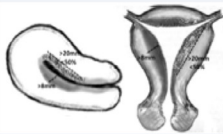
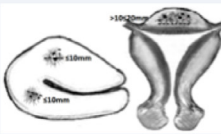


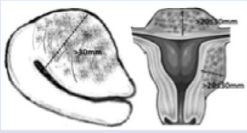

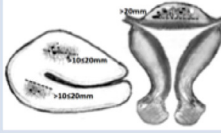


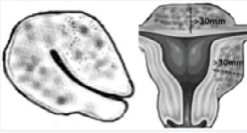



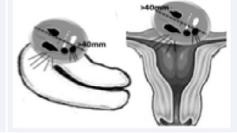
A PBAC score of ≥ 100 was estimated to be consistent with heavy menstrual bleeding. Severe symptoms were considered if VAS score was equal to or more than 5.

Prevalence of symptoms and percentage related to the single type and score of adenomyosis were calculated. Prevalence of pelvic endometriotic lesions at TVS evaluation was evaluated.

Two analyses were performed using predetermined combinations of predictor variables: (1) correlation between single ultrasound types of adenomyosis and their extension inside the myometrium and patients’ symptoms, infertility, miscarriage, and age; and (2) correlation between the total adenomyosis score and the patients’ symptoms, infertility, miscarriage, and age.

Fig. 1

Ultrasound score system used to classify the severity of adenomyosis [20].

SCORE	DIFFUSE ADENOMYOSIS OF THE OUTER MYOMETRIUM	DIFFUSE ADENOMYOSIS OF THE INNER MYOMETRIUM OR JUNCTIONAL ZONE (JZ)	FOCAL ADENOMYOSIS OF THE OUTER MYOMETRIUM	FOCAL ADENOMYOSIS OF THE INNER MYOMETRIUM OR (JZ)	ADENOMYOMA
1	<ul style="list-style-type: none"> •1 myometrial wall involvement with myometrial wall thickness ≤ 20mm 	<ul style="list-style-type: none"> •maximum JZ thickness > 6mm •diffuse infiltration of the JZ ≤ 20mm in length 	<ul style="list-style-type: none"> •1 focal intramyometrial lesion ≤ 10mm 	<ul style="list-style-type: none"> •1 focal lesion of the JZ by hyperechoic tissue or cystic areas ≤ 10mm 	<ul style="list-style-type: none"> •1 adenomyoma with the largest diameter ≤ 20mm 
2	<ul style="list-style-type: none"> •2 myometrial wall involvement with wall thickness ≤ 20mm •1 myometrial wall involvement with wall thickness > 20 to ≤ 30mm 	<ul style="list-style-type: none"> •maximum JZ thickness > 8 mm •diffuse infiltration of the JZ > 20mm in length or $\leq 50\%$ of the uterus 	<ul style="list-style-type: none"> •≥ 2 focal intramyometrial lesions ≤ 10mm •1 focal intramyometrial lesions > 10 to ≤ 20mm 	<ul style="list-style-type: none"> • ≥ 2 focal lesions of the JZ ≤ 10mm • 1 focal lesion of the JZ > 10 to ≤ 20mm 	<ul style="list-style-type: none"> •2 adenomyomas with the largest diameter ≤ 20mm •1 adenomyoma with the largest diameter > 20 to ≤ 30mm 
3	<ul style="list-style-type: none"> •1 myometrial wall involvement with wall thickness > 30mm •2 myometrial wall involvement with wall thickness > 20 to ≤ 30mm 	<ul style="list-style-type: none"> •diffuse infiltration of the JZ $> 50\%$ to $\leq 80\%$ of the uterus 	<ul style="list-style-type: none"> •≥ 2 focal intramyometrial lesions > 10 to ≤ 20mm •1 focal intramyometrial lesion > 20mm 	<ul style="list-style-type: none"> • ≥ 2 focal lesions of the JZ > 10 to ≤ 20mm • 1 focal lesion of the JZ > 20mm 	<ul style="list-style-type: none"> •2 adenomyomas with the largest diameter > 20 to ≤ 30mm •1 adenomyoma with the largest diameter > 30 to ≤ 40mm 
4	<ul style="list-style-type: none"> •2 myometrial wall involvement with wall thickness > 30mm •all the uterus involvements with globally enlarged uterus 	<ul style="list-style-type: none"> •80% to total infiltration of the JZ 	<ul style="list-style-type: none"> •≥ 2 focal intramyometrial lesion > 20mm • ≥ 3 focal intramyometrial lesions 	<ul style="list-style-type: none"> • ≥ 2 focal lesions of the JZ > 20mm • ≥ 3 focal lesions of the JZ 	<ul style="list-style-type: none"> •≥ 3 adenomyomas •1 adenomyoma with the largest diameter > 40mm 

The characteristics between adenomyosis groups were compared using chi-square tests for categorical variables and independent samples *t* tests or Mann-Whitney U tests as appropriate for continuous data. Fisher exact test was used to compare the prevalence, and $p < .05$ was considered statistically significant.

Results

The study included 108 women with an ultrasound evidence of adenomyosis. Demographics, clinical characteristics, and symptoms are shown in [Table 1](#). Deep endometriosis was detected in 40% of women with adenomyosis, whereas an ovarian endometriotic lesion was identified in 15% of cases. More than half (55%) of the infertile patients had a history of at least 1 miscarriage in the previous 2 years. The correlation of each type of adenomyosis with patients' age, menstrual bleeding, and painful symptoms is shown in [Table 2](#). Each type of adenomyosis was also evaluated according the scoring system ([Fig. 1](#)) and divided into 4 subgroups.

Different ultrasound types of adenomyosis are coexistent: diffuse adenomyosis of the outer myometrium and of the JZ are associated in 51% of cases (55/108). Focal adenomyosis of the JZ occurs together with focal adenomyosis of the outer myometrium in 31% of cases (33/108). Diffuse adenomyosis of the JZ and adenomyomas are associated in 17% of cases (18/108), whereas focal and diffuse adenomyosis coexist in only 6% of women (6/108).

Compared with women with focal disease (of the outer myometrium and JZ), women with diffuse adenomyosis (of the outer myometrium and JZ) are significantly older and showed heavier menstrual bleeding ($p = .04$), but no differences were observed regarding the presence and severity of dyspareunia and dysmenorrhea. Moreover, women with adenomyomas were older and showed higher severity of heavy menstrual bleeding than women with focal disease, whereas the severity of dysmenorrhea was found to be lower than that in women with focal disease of the outer myometrium.

Table 1

Patients' characteristics and the symptoms of the study population (N = 108)	
Patient demographics and characteristics	Study group
Age, yrs	37.7 ± 7.7
BMI	22.4 ± 4.3
Gravidity	0.43 ± 0.8
Parity	0.21 ± 0.5
Amount of menstrual bleeding with PBAC	248.3 ± 201.8
Heavy menstrual bleeding, PBAC ≥ 100	91 (84.2)
Dysmenorrhea VAS score	6.0 ± 3.6
Severe dysmenorrhea, VAS score ≥ 5	78 (72.2)
Dyspareunia VAS score	3.2 ± 3.7
Severe dyspareunia, VAS score ≥ 5	43 (39.8)
Infertility (of 70 women trying to conceive)	39 (55.7)
Miscarriage (of 70 women trying to conceive)	24 (34.3)
Endometrioma	17 (15.7)
Deep endometriosis	43 (39.8)

BMI = body mass index; PBAC = pictorial blood loss analysis chart; VAS = visual analog scale.
Values are given in mean ± standard deviation or number (%).

During the analysis of the single ultrasonographic type of adenomyosis according to the score, which reflects the extension of the disease inside the uterus, we only observed a difference in age and PBAC mean score between scores 1 and 4 for diffuse adenomyosis of the outer myometrium and between score 1 and 3 for focal disease. Patients with low score for diffuse and focal adenomyosis showed a younger age. Mean dysmenorrhea VAS score was significantly higher in patients with a score of 4 for diffuse adenomyosis than in those with a score of 1 for the same type and a score of 4 for adenomyoma.

In patients trying to conceive, the presence of ultrasound findings of focal disease was associated with a higher percentage of infertility than in those with diffuse disease (Table 3). In addition, women with focal disease affecting the JZ showed a higher rate of at least 1 miscarriage than did women affected by diffuse adenomyosis. Regarding the association between adenomyosis and endometriosis, women with moderate and severe adenomyosis showed a statistically significant association with endometriosis compared with those with mild adenomyosis.

Table 4 reports patients' age, menstrual bleeding, pain symptoms, contemporary presence of and infertility based on the 3 degrees of uterine involvement by adenomyosis. The sum of the single score of each type of adenomyosis (i.e., adenomyosis total score) determined these 3 categories: mild, moderate, and severe. There was a statistically significant difference between severe and mild disease regarding age, but not for any other features. With regard to miscarriage, there was a tendency, although not significant, toward a higher percentage in patients with severe adenomyosis than in those with mild adenomyosis.

Discussion

The aim of this study was to find a correlation between the TVS evaluation of type and severity of adenomyosis and painful symptoms, amount of uterine bleeding, and infertility.

The correlation between amount of histopathology features and clinical manifestations has been clarified in previous studies performed on uterine specimens obtained from hysterectomies. These studies showed no increase in the number of adenomyotic foci in women with heavy menstrual bleeding but confirmed direct correlation of foci number with severe dysmenorrhea [5,34,35]. Bird et al [5] reported that dysmenorrhea was present in 4.3% of women whose uterus had histologically defined grade I penetration, and in 42.4% and 83.3% of women with grade II and grade III penetration, respectively. Furthermore, Levгур et al [35] found that heavy menstrual bleeding was also related to the depth of the adenomyotic foci within the myometrium.

On the basis of these findings, there was the belief of a direct correlation between the extent of histopathologic features and clinical manifestations with the consequent hypothesis of a causal relationship between the number and depth of the adenomyotic foci and specific symptoms.

However, several authors did not show significant differences in the prevalence of adenomyosis among women with or without a history of heavy menstrual bleeding [4,36–38]. Unfortunately, all these studies showed a great bias, because they were conducted on the uteri of patients who were scheduled for hysterectomy for severe symptoms, mostly of older age, and had no desire for pregnancy.

The TVS diagnosis of adenomyosis through specific features showed an accuracy up to 91% [22]. TVS is a highly tolerable examination, and owing to its reduced invasiveness, it could be performed in all patients, including younger patients with fewer symptoms and a desire for pregnancy.

Therefore, TVS gave us the ability to evaluate the real impact of adenomyosis on specific symptoms. Previous studies have reported a correlation between the ultrasound features of adenomyosis and specific symptoms including infertility [18,20,21]; however, no correlation was ever demonstrated between the severity of symptoms and the type and extent of adenomyosis within the uterus.

We found that ultrasound features of diffuse adenomyosis were more frequent in older women with heavy menstrual bleeding compared with those with focal disease. We also observed a higher percentage of infertility and miscarriage in focal adenomyosis of the outer myometrium and the JZ, respectively. These findings could lead us to believe that different types and depth of adenomyosis (in terms of localization in the outer or inner myometrium) have an impact on symptoms and fertility.

We also demonstrated that severe diffuse adenomyosis is correlated to severe dysmenorrhea and heavy menstrual bleeding. However, we were not able to find any other

Table 2

Correlation of adenomyosis classified in different forms (diffuse, focal, and adenomyoma), location inside the myometrium (outer and JZ), and extension inside the uterus scored in 4 points according to symptoms

Adenomyosis (N = 108)	Age, yrs	Menstrual bleeding PBAC	Dysmenorrhea VAS score	Dyspareunia VAS score
Diffuse outer myometrium (n = 60)	38.8 ± 7.2*	279.2 ± 233*	5.6 ± 3.8	3.0 ± 3.7
Score 1 (n = 16)	34.8 ± 7.3 [†]	200.7 ± 128.2 [†]	5.3 ± 2.3 [†]	5.3 ± 2.3
Score 2 (n = 19)	38.7 ± 7.5	190.6 ± 94.5	4.4 ± 4.2	2.3 ± 3.6
Score 3 (n = 9)	42.1 ± 5.2	283.7 ± 140.8	5.9 ± 3.0	3.0 ± 4.1
Score 4 (n = 16)	41.1 ± 6.4 [†]	427.2 ± 338.2 [†]	7.5 ± 3.1 ^{†,‡}	3.0 ± 3.6
Diffuse inner myometrium (JZ), (n = 91)	38.7 ± 7.2	249.5 ± 193.5	5.9 ± 3.7	3.1 ± 3.8
Score 1 (n = 19)	37.5 ± 7.3	208.5 ± 115.1	5.6 ± 3.5	2.8 ± 3.8
Score 2 (n = 21)	37.7 ± 8.9	233.0 ± 160.9	6.4 ± 3.5	4 ± 3.6
Score 3 (n = 16)	40.4 ± 5.9	248.0 ± 176.9	6.4 ± 3.4	2.9 ± 3.6
Score 4 (n = 35)	39.1 ± 6.7	282.4 ± 246.7	5.7 ± 4.1	2.9 ± 4.0
Focal outer myometrium (n = 42)	35.5 ± 7.5* [§]	194.7 ± 119.5*	6.8 ± 2.9 [§]	3.5 ± 3.8
Score 1 (n = 6)	31.3 ± 6.8	157.7 ± 82.7	5.5 ± 4.4	3.3 ± 3.8
Score 2 (n = 23)	34.2 ± 7.9	185.5 ± 133.2	6.3 ± 2.9	3.9 ± 3.8
Score 3 (n = 12)	38.8 ± 4.6	232.7 ± 109.9	8.4 ± 1.5	2.3 ± 3.9
Score 4 (n = 1)	50	256	9	7
Focal inner myometrium (JZ) (n = 30)	35.2 ± 7.1* [§]	175.4 ± 98.5*	5.9 ± 3.6	3.6 ± 3.9
Score 1 (n = 15)	33 ± 4.8	150.5 ± 68.2	6.6 ± 3.0	5.0 ± 3.9
Score 2 (n = 12)	34 ± 4.5	239.9 ± 115.1	4.7 ± 3.7	2.0 ± 3.7
Score 3 (n = 3)	37.0 ± 4.3	156.7 ± 83.3	6.7 ± 5.8	2.3 ± 2.5
Score 4 (n = 0)				
Adenomyoma (n = 21)	40.8 ± 7.6 [¶]	243.3 ± 163.7	4.5 ± 4.1 [§]	2.2 ± 3.3
Score 1 (n = 7)	39.8 ± 4.8 [¶]	170.7 ± 74.2	4.4 ± 4.1	2.7 ± 3.9
Score 2 (n = 4)	37.5 ± 8.8	239.7 ± 143.8	6.7 ± 3.7	1.5 ± 1.7
Score 3 (n = 6)	40.5 ± 10.9	339.7 ± 235.0	5.5 ± 4.4	2.5 ± 3.9
Score 4 (n = 4)	46.0 ± 2.9 [¶]	229.2 ± 153.9	1.0 ± 2.0 [‡]	1.7 ± 3.5

JZ = junctional zone; PBAC = pictorial blood loss analysis chart; VAS = visual analog scale.

Values are mean ± standard deviation.

* p < .05 diffuse vs focal adenomyosis.

[†] p < .05 score 1 vs score 4 of diffuse adenomyosis.

[‡] p < .05 score 4 diffuse adenomyosis vs score 4 adenomyoma.

[§] p < .05 adenomyoma vs focal adenomyosis.

^{||} p < .05 score 1 vs score 3 of focal adenomyosis.

[¶] p < .05 score 1 vs score 4 of adenomyoma.

correlation to symptoms when classifying the extension of the diseases inside the uterus as mild, moderate, and severe.

This is in contrast with the results previously reported by Naftalin et al [21,39], in which there was a correlation between ultrasound severity of adenomyosis, menstrual pain, and heavy bleeding. Nevertheless, in these studies, adenomyosis was not distinguished in regard to type (focal and diffuse) or in regard to its extension inside the myometrial layers, but only according to the number of ultrasound features to evaluate the severity of the disease. Assessing the severity of adenomyosis based only on the number of sonographic characteristics could lead to false results: in some cases, a small focal lesion could show multiple ultrasound features of adenomyosis and vice versa.

The absence of a direct correlation between the ultrasound extension of adenomyosis within the uterus and the severity of symptoms was also observed in this study; this could be partially explained by the presence of other coexisting conditions such as endometriosis, rather than the

adenomyosis per se. Otherwise, we could hypothesize that this condition is very similar to pelvic endometriosis, where often the severity of the disease is not related to the severity of symptoms. Moreover, small endometriotic lesions may cause a lot of pain, whereas sometimes, deep nodules are completely asymptomatic.

A possible limitation of the present study could be that only 2 expert sonographers were recruited from specialized endometriosis centers. Although not uniformly accepted as standard of care, a strength of this study is the use of a sonographic diagnosis for adenomyosis, avoiding the need for histologic diagnosis, to assess the correlation with the symptomatology. Furthermore, this study investigates several important new issues. First, it attempts to provide a description differentiating the 3 types of the disease (diffuse, focal, and adenomyomas) using TVS. Second, these 3 types are divided according to the depth of involvement in the myometrial layers (external and internal myometrium), and third, the extension of the disease inside the whole uterus is

Table 3

Correlation of infertility and at least 1 miscarriage in the past 2 years with adenomyosis of different types (diffuse, focal, and adenomyoma), locations inside the myometrium (outer and JZ), and extension into the uterus scored in 4 points according to our scheme

Type of adenomyosis in women who try to conceive (Total n = 70)	Infertility, n (%)	Miscarriage, n (%)
Diffuse outer myometrium (n = 42)	22 (52)*	15 (36)*
Score 1 (n = 10)	8 (80)	5 (50)
Score 2 (n = 12)	5 (42)	3 (42)
Score 3 (n = 6)	2 (33)	2 (33)
Score 4 (n = 12)	7 (50)	5 (36)
Diffuse inner myometrium (JZ), (n = 62)	33 (53)	23 (37)
Score 1 (n = 10)	7 (70)	3 (30)
Score 2 (n = 13)	7 (54)	5 (38)
Score 3 (n = 13)	4 (31)	3 (23)
Score 4 (n = 26)	15 (58)	12 (46)
Focal outer myometrium (n = 22)	18 (82)*	9 (43)
Score 1 (n = 2)	2 (100)	1 (100)
Score 2 (n = 9)	8 (89)	3 (33)
Score 3 (n = 10)	7 (70)	5 (50)
Score 4 (n = 1)	1 (100)	0 (0)
Focal inner myometrium (JZ), (n = 16)	10 (62)	11 (69)*
Score 1 (n = 4)	3 (75)	2 (50)
Score 2 (n = 9)	5 (56)	6 (67)
Score 3 (n = 3)	2 (67)	3 (100)
Score 4 (n = 0)		
Adenomyoma (n = 19)	7 (37)	4 (21)
Score 1 (n = 7)	4 (57)	0
Score 2 (n = 4)	2 (50)	1 (25)
Score 3 (n = 4)	0	1(25)
Score 4 (n = 4)	1 (25)	2 (50)

JZ = junctional zone.

* p <.005 diffuse vs focal.

Table 4

Correlation of adenomyosis total score (sum of the single score of each type) with clinical symptoms and infertility

Adenomyosis total score (N = 108)	Age, yrs	Menstrual bleeding, PBAC	Dysmenorrhea, VAS score	Dyspareunia, VAS score	Women trying to conceive (n = 70)	Age, yrs	Infertility	Miscarriage
1–3 (mild), (n = 28)	34.9 ± 8.1*	195.7 ± 129.5	5.9 ± 3.6	3.2 ± 3.7	14	38.9 ± 6.3	8 (57)	2 (14)
4–6 (moderate), (n = 43)	36.2 ± 8.0*	263.1 ± 216.6	5.0 ± 3.1	5.0 ± 3.8	24	39 ± 8.3	14 (58)	8 (33)
≥7 (severe), (n = 37)	41.3 ± 5.5*	270.9 ± 225.5	6.1 ± 3.8	2.4 ± 3.7	32	41.3 ± 5.5	17 (53)	14 (44)

PBAC = pictorial blood loss analysis chart; VAS = visual analog scale.

Values are given in mean ± standard deviation or number (%).

* p <.05 moderate vs severe and mild vs severe.

assessed through a detailed schematic scoring system. In addition, we attempted to correlate these characteristics to the severity of symptoms. In our study, the evaluation of symptoms was not limited to investigating their presence or absence but was obtained using the VAS score and the PBAC score, allowing a quantitative assessment. Another major strength of the study was its prospective nature.

To conclude, we feel that TVS is able to assess the type and severity of adenomyosis inside the uterus. Our preliminary

data showed differences between focal and diffuse adenomyosis regarding age, menstrual bleeding, infertility, and miscarriage; however, we were not able to demonstrate a correlation between the severity of symptoms and the ultrasound extension of the disease (mild, moderate, and severe) within the uterus.

Further studies on a larger population could be useful to confirm our findings and to determine if this new TVS assessment scheme may be helpful in selecting and

evaluating the effectiveness of medical and surgical management, as well as the possible relationship between adenomyosis and infertility.

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