A clinical scoring system for the diagnosis of adenomyosis

Adenomiyozis tanısı için klinik bir skorlama sistemi

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Abstract

Objective: To develop a scoring system using clinical evaluation methods to predict the presence of adenomyosis.

Materials and Methods: A cohort of 232 patients who underwent hysterectomy for benign gynecologic disorders was prospectively enrolled. A detailed anamnesis was obtained and physical/pelvic examinations with trans-vaginal ultrasound imaging were performed one day before the hysterectomy. The diagnosis of adenomyosis was based on histopathologic examination. Findings were compared between patients with (n=55) and without (n=166) adenomyosis. Factors associated with adenomyosis were assessed with regression analysis and odds ratios (OR) were calculated. The variables found to be significant were chosen for the scoring system. Receiver operating characteristic analysis was carried out to find the cut-off values for these variables.

Results: Number of parity, dyspareunia and dysmenorrhea visual analogue scale (VAS) scores, age of menarche, presence of uterine tenderness and detection of heterogeneous myometrium and myometrial cysts during ultrasonography were found to be the significant parameters. OR for the presence of myometrial heterogeneity, myometrial cysts, uterine tenderness were 27.2, 3.6 and 9.3 respectively. Cut-off values were calculated; 3 for parity (OR=2.8), 13-years for menarche (OR=1.6), 2 for dyspareunia VAS scores (OR=1.9) and 4 for dysmenorrhea VAS scores (OR=1.2). The total sum of maximum OR that a patient can obtain was calculated as 47.6 and this value was assumed to predict the presence of adenomyosis 100%. The multiplication of the sum of the OR in a patient by 2.1 (100/47.2) was found to have a predictive ability for the presence of adenomyosis.

Conclusion: A scoring system is developed to predict adenomyosis non-invasively based on clinical evaluation.

Keywords: Adenomyosis, clinical evaluation, non-invasive, pelvic examination, scoring system

Öz

Amaç: Klinik değerlendirme yöntemleri kullanılarak adenomiyozis varlığını öngörmeye yarayacak bir skorlama sistemi geliştirmek.

Gereç ve Yöntemler: Benign hastalıkları için histerektomi yapılan 232 kişilik bir kohort prospektif olarak değerlendirildi. Tüm hastalara histerektomiden bir gün önce detaylı anamnez alınarak, fizik/pelvik muayeneler ile birlikte transvajinal ultrasonografik inceleme yapıldı. Adenomiyozis tanısı histopatolojik inceleme ile konuldu. Adenomiyozisi olan (n=55) ve olmayan (n=165) hastaların bulguları karşılaştırıldı. Adenomiyozis ile ilişkili olduğu bulunan faktörler regresyon analizi ile değerlendirildi ve olasılık oranları (OO) hesaplandı. Anlamlı bulunan değişkenler skorlama sistemi için kullanıldı. Bu değişkenlerin eşik değerlerinin bulunması için alıcı işlem karakteristikleri analizi kullanıldı.

Bulgular: Parite sayısı, disparoni ve dismenore görsel analog ölçek (VAS) skorları, menarş yaşı, uterin hassasiyet varlığı ve ultrasonografik incelemede heterojen miyometriyum ile miyometriyal kistlerin görülmesi anlamlı parametreler olarak bulundu. Miyometriyal heterojenite, miyometriyal kist ve uterin hassasiyet varlığı için OO sırasıyla 27,2, 3,6 ve 9,3 olarak bulundu. Parite için 3 (OO=2,8), menarş için 13 yaş (OO=1,6), disparoni VAS skoru için 2 (OO=1,9) ve dismenore VAS skoru için 4 (OO=1,2) eşik değerler olarak hesaplandı. Bir kişinin alabileceği maksimum OO değerlerinin toplamı 47,6 olarak hesaplandı ve bu değerin adenomiyozis varlığını yüzde yüz öngöreceği kabul edildi. Bir hastadaki OO'nun toplamının 2,1 ile çarpılmasının (100/47,2) o hastada adenomiyozis varlığı için öngörücü bir yeteneğe sahip olduğu sonucuna ulaşıldı.

Sonuç: Klinik değerlendirmeye dayalı olan, non-invaziv olarak adenomiyozisi tahmin etmek için bir skorlama sistemi geliştirilmiştir.

Anahtar Kelimeler: Adenomiyozis, klinik değerlendirme, non-invaziv, pelvik muayene, skorlama sistemi

PRECIS: Using simple, noninvasive, clinical evaluation methods, a clinical scoring system for the diagnosis of adenomyosis is developed.

Introduction

Adenomyosis is a relatively common benign disorder in which endometrial gland and stroma are located within the myometrium resulting angiogenesis of the spiral vessel, hypertrophy of the surrounding smooth muscles and enlargement of the uterus. We have recently showed that the disease mimics the malignant process in terms of angiogenesis, apoptosis, hypoxia and energy metabolism; however, the etiology and pathogenesis remain unclear[1]. Although in most cases it is asymptomatic, it may cause abnormal uterine bleeding, especially menorrhagia, dysmenorrhea, dyspareunia, pelvic pain and subinfertility[2]. There is significant overlapping in the presentations with other gynecologic disorders and in many cases there is concomitant endometriosis or leiomyomas[3]. In addition there are no specific laboratory tests and reliable clinical standards for the diagnosis. Therefore, the diagnosis and evaluating the response to treatment are challenging. So far the definitive diagnosis still requires a histologic analysis of the hysterectomy specimens or hysteroscopic or laparoscopic biopsy.

Clinical examination, transvaginal ultrasonography (TVS), magnetic resonance imaging (MRI), hysteroscopy guided biopsies have all been suggested as diagnostic methods with various clinical usefulness[4]. The clinical examination alone cannot detect adenomyosis[4]; however, it provides the exclusion of other gynecologic pathologies and gives detailed information about severity and complexity of the disease in the planning of medical or surgical treatment. TVS has been suggested to be the primary imaging modality for the diagnosis of adenomyosis with a range of 65-81% sensitivity and 65-100% specificity[5]. The detection of asymmetric thickening of the myometrium, myometrial cysts, linear myometrial striations, loss of a clear endomyometrial border and a heterogeneous myometrium which is reported to be the most predictive finding, raise the probability of the presence of adenomyosis[6]. MRI has similar sensitivity and specificity for diagnosing adenomyosis as TVS and it is recommended only for the cases where conservative management is planned and the differentiation between adenomyosis and uterine myomatosis is required[7]. Hysteroscopy guided biopsies improve the specificity of diagnosis from 60 to 89%[8]; however, it is an invasive procedure with high costs and not a common practice that should be reserved for clinical situations in which a malignancy needs to be excluded.

It is estimated that adenomyosis is present in 20 to 35% of women[9]. Although the disease has been deemed the disease of middle-aged, multiparous women, the disease is increasingly diagnosed in young women and in infertility patients[10]. It is surprising that the awareness of the disease is poor as there are relatively few studies for a disease that has a very high prevalence and unfortunately there are still no international guidelines to follow for preoperative diagnosis and management of this disorder[11]. The preoperative diagnosis of adenomyosis, which has still been diagnosed histopathologically, would prevent unnecessary therapies, loss of time and use of resources in vain. Therefore, precise prediction of this disease without surgery gains importance. Developing a scoring system with clinical evaluation for this purpose will be very helpful in solving this problem. From this point, we developed a scoring system that will predict the presence of adenomyosis with high sensitivity using clinical evaluation methods such as history, physical examination, ultrasonography and laboratory tests.

Materials and Methods

A prospective cohort study was conducted in Mersin University Faculty of Medicine, Department of Obstetrics and Gynecology between 10.02.2017 and 10.08.2017 with 232 patients who had undergone hysterectomy for benign disorders. The indications for hysterectomy were leiomyoma, dysfunctional uterine bleeding, which was resistant to medical therapy, adnexal mass, cervical and endometrial pathologies, postmenopozal bleeding, dysmenorrhea, dyspareunia or pelvic pain, pelvic abcess and uterine prolapse. Patients with postoperative diagnosis of gynecologic malignancies and who were pregnant were excluded. Ten patients with postoperative diagnosis of malignancies and 1 patient with coexisting pregnancy were excluded and the remaining 221 patients were enrolled. The minimum number of patients to be included in this prospective study was calculated with power analysis. To calculate the minimum number of patients, the number of hysterectomies performed in the clinic during the first 6 months of the previous year, 2016, was obtained (240 cases). It was calculated to reach at least 40% of the population to predict the population in 2017[12]. To develop a scoring system that can be an alternative to the histopathological evaluation in the diagnosis of adenomyosis, the aim was to develop a scoring system that is 0.9 compatible with the histopathological results and with this purpose the required minimum number of cases was calculated to be 221 with 0.05 type 1 error and 0.2 type 2 error (80% power)[13]. Mersin University Clinical Trials Ethics Committee approved the study (2017/22) and informed consent was obtained from each patient.

The patients who were admitted to the hospital with the hysterectomy indications for benign pathologies were visited before the operation and detailed anamnesis was obtained. Physical and pelvic examinations with transvaginal ultrasound were examined by the same investigator. Demographic characteristics, obstetric and gynecologic histories were noted. The amount of perceived pain was measured using visual analog scale (VAS)[14]. During pelvic examination uterine size with more than 10 weeks gestational age was considered enlarged[15]. Observing myometrial cysts, enlarged uterus, heterogeneous myometrium and or focal nodular areas during TVS was considered to suggest adenomyosis[16]. The uterus was measured in the anteroposterior, longitudinal, and transverse planes. The uterine volume was calculated using the ellipsoid algorithm. The laboratory results were noted.

The hysterectomy specimens were evaluated by the department of pathology. The diagnosis of adenomyosis was based on the presence of glandular extension ≥2.5 mm below the endometrial myometrial interface[17] and routine endometrial sampling was performed from 4 sites if there were no additional pathologies. Pathologic results were accepted as the definitive diagnosis.

Statistical Analysis

Statistical analysis was accomplished with SPSS (version 11.5, Illinois, Chicago, USA). The normality of the data was tested both with visual methods, including histograms and probability plots and Kolmogorov-Smirnov test. Normally distributed data were expressed as mean ± standard deviation and non-normally distributed data were expressed as median interquartile range. Student t-tests, Mann-Whitney U tests were used for comparisons where appropriate. Categorical parameters were expressed as number (%) and compared with chi-square test. To obtain the scores to predict the presence of adenomyosis, the odds ratios (OR) that were calculated from the binary logistic regression analysis in which adenomyosis was assumed to be the dependent variable were used. The variables found to be significant were chosen for the scoring system. Receiver operating characteristic (ROC) analysis was carried out to find the cut-off values for these variables. The variables which were not found to be significant in logistic regression analysis but known to be associated with adenomyosis and were found to be significantly different from the cases without adenomyosis in the univariate analysis, were also included in the binary logistic regression analysis in which adenomyosis was taken as the dependent variable (present/absent). OR were calculated for these variables that were found to be significant. For variables other than menarche, reference group was taken as the first group, the reference score was assigned as 0 and the OR were calculated accordingly. In the menarche variable the reference group was assigned as the last group and the reference score was assigned as 0. The sum of the maximum OR that a person can obtain was assumed to be 100 percent and a coefficient was calculated to convert the sum of OR to percentages to predict the presence of adenomyosis. The sum of the OR that a patient obtains was multiplied with this coefficient to get the adenomyosis risk percentage. The statistical significance was set at $p<0.05$.

Results

Adenomyosis was diagnosed in 24.9% (n=55/221) of the patients. The most common complaints were pelvic pain (27.1%) and menometrorrhagia (22.2%), and the most common indications for hysterectomy were leiomyomas (29.4%) and abnormal uterine bleeding (14%).

The comparison of the demographic characteristics of the patients with and without adenomyosis is provided in Table 1. Groups were similar with respect to assessed parameters. The comparison of patterns of menstrual bleeding and perceived pain VAS scores are shown in Table 2. The mean age of menarche of the patients with adenomyosis was significantly lower compared to the patients without adenomyosis (13.2±1.7 vs 13.8±1.5 years, p=0.031). The groups were similar with respect to menstrual cycle length, menstrual flow duration and rate of intermenstrual bleeding; however, the number of sanitary pads per day (5.3±2.5 vs 4.5±2.6, p=0.004) and need for diaper usage (32.5% vs 47.3%, p=0.036) were significantly higher in the patients with adenomyosis (Table 2). Similarly, median dysmenorrhea and dyspareunia VAS scores were significantly higher in the adenomyosis group [3 (6) vs 2 (4), p=0.016 and 2 (4) vs 0 (2.3), p=0.007, respectively].

Table 1. Comparison of the demographic characteristics of patients with and without adenomyosis

	Adenomyosis (n=55)	No adenomyosis (n=166)	p
Age (years)	50.6±7.8	51.1±8.8	0.869
BMI (kg/m²)	30.6±5.1	29.9±5.1	0.369
Gravidity	4 (2)	3 (3)	0.281
Parity	3 (2)	3 (2)	0.101
Vaginal delivery (n)	3 (3)	2 (3)	0.224
Cesarean section (n)	0 (0)	0 (0)	0.892
Surgical abortion number	1 (1)	1 (2)	0.772
Smoking status	50 (30.1%)	14 (25.5%)	0.316
Previous myomectomy	6 (3.6%)	4 (7.3%)	0.117
COC history	37 (22.3%)	13 (23.6%)	0.485
History of intrauterine device	66 (39.8%)	19 (34.5%)	0.3

BMI: Body mass index, COC: Combined oral contraceptive, Data were expressed as mean ± standard deviation, median (interquartile range), number and percentage. p<0.05 was considered significant

In the pelvic examination the incidence of a large uterus (>10 gestational weeks large) and uterine tenderness were significantly higher in the patients with adenomyosis (Table 3). The ultrasonographic findings showed increased uterine volume in the adenomyosis patients [180 (155) vs 122 (164) cm³, p=0.041]. In 50.9% of the patients with adenomyosis, heterogeneous myometrium was observed with ultrasonography that was only present in 3.6% of the patients without adenomyosis (p<0.0001). Similarly, more patients with adenomyosis had myometrial cysts detected with sonography (20% vs 5.4%, p=0.002) (Table 3). Concomitant leiomyoma was present in 32.7% of the patients with adenomyosis (Table 3).

The groups were similar with respect to laboratory complete blood count results. The hemoglobin, hematocrit values and platelet counts in the patients with and without adenomyosis were 12.4±1.4 g/dL, 38±3.4% and 320.000±99.000 mL and 12.3±1.8 g/dL, 37.8±4.5% and 303.000±70.000 mL respectively (p>0.05 for all). Neutrophil-to-lymphocyte and platelet-to-lymphocyte ratios were also similar (data not shown).

In a pathologic examination the median weight of the uteruses was found to be 181 (111) g in the adenomyosis patients, which was 145 (139) g in the patients without adenomyosis (p=0.044). Histopathologically confirmed concomitant endometrioma was significantly more common in patients with adenomyosis compared to the patients without adenomyosis (9.1% vs 2.4%, p=0.045).

To develop a scoring system a regression analysis was carried out to find the parameters that were associated with the presence of adenomyosis. Number of parity, dyspareunia and dysmenorrhea VAS scores, age of menarche and detection of heterogeneous myometriums during ultrasonography were found to be the significant parameters. OR were calculated for these independent factors (Table 4). With ROC analysis cut-off values were calculated; 3 for parity, 13 years for menarche, 2 for dyspareunia VAS scores and 4 for dysmenorrhea VAS scores (Table 4). Variables that were found to be significantly different in the univariate analysis were also analyzed within each other and the presence of uterine tenderness and detection of myometrial cysts with ultrasonography was also found to be independent predictors of adenomyosis (respectively β=2.225, p=0.09;

Table 2. The comparison of patterns of menstrual bleeding and perceived pain VAS scores

	Adenomyosis (n=55)	No adenomyosis (n=166)	p
Menarche (years)	13.2±1.7	13.8±1.5	0.031*
Menstrual cycle (days)	29.3±4.8	28.6±3.1	0.831
Menstrual flow duration (days)	7.3±3	5.7±2	0.831
Intermenstrual bleeding	41 (24.7%)	19 (34.5%)	0.107
Number of sanitary pads used per day	5.3±2.5	4.5±2.6	0.004*
Need for diapers usage	26 (47.3%)	54 (32.5%)	0.036**
Dysmenorrhea VAS	3 (6)	2 (4)	0.016*
Dyspareunia VAS	2 (4)	0 (2.3)	0.007*

VAS: Visual analog scale, Data were expressed as mean ± standard deviation, median (interquartile range), number and percentage. p<0.05 was considered significant
*: statistically significant, t-test
**: statistically significant, chi-square test

Table 3. Comparison of pelvic examination findings and transvaginal ultrasonographic findings in patients with and without adenomyosis

	Adenomyosis (n=55)	No adenomyosis (n=166)	p
Large uterus (>10 gestational weeks)	32 (58.2%)	68 (41%)	0.019**
Uterine tenderness	7 (12.7%)	2 (1.2%)	0.001**
Uterine volume (cm³)	180 (155)	122 (164)	0.041*
Presence of heterogenous myometrium	28 (50.9%)	6 (3.6%)	<0.0001**
Presence of myometrial cysts	11 (20%)	9 (5.4%)	0.002**
Presence of leiomyoma	18 (32.7%)	66 (39.8%)	0.221

Data were expressed as mean ± standard deviation, median (interquartile range), number and percentage. p<0.05 was considered significant
*: statistically significant, t-test
**: statistically significant, chi-square test

Table 4. Clinical scoring system for prediction of adenomyosis

	Risk factor	Score
Parity	≤3	0
	>3	2.8
Age of menarche	≤13	1.6
	>13	0
Dysmenorrhea VAS score	≤4	0
	>4	1.2
Dyspareunia VAS score	≤2	0
	>2	1.9
Heterogenous myometrium	No	0
	Present	27.2
Myometrial cyst	No	0
	Present	3.6
Uterine tenderness	No	0
	Present	9.3

VAS: Visual analog scale

OR=9.250, 95% confidence interval: 0.75-48.830 and β=1.29, p=0,013, OR: 3.631, 95% confidence interval:1.316-10.020). These two parameters were also included in the scoring system. The total sum of maximum OR that a patient can obtain was calculated as 47.6 and this value was assumed to predict the presence of adenomyosis 100%. To find a coefficient to convert the sum of OR to percentages, 100 was divided by 47.6 and 2.1 was found as the coefficient. Finally, multiplication of the sum of the OR in a patient by 2.1 was found to have a predictive ability for the presence of adenomyosis.

Discussion

This study aimed to develop a simple and useful clinical scoring system to predict the presence of adenomyosis that has remained a histopathological diagnosis. Preoperative prediction of this benign disease would provide initiation of targeted medical therapies and the need for radical surgeries would decrease. In literature the risk factors have been identified; however, there are still no effective preinterventional diagnostic methods. In this prospective study the patients who were to undergo hysterectomy had been assessed preoperatively and based on the histopathological results, the preoperative diagnostic effectiveness of each factor associated with adenomyosis had been revealed. A clinical predictive scoring system was developed using parity, age at menarche, VAS scores of dysmenorrhea and dysparaneu, detection of heterogeneous myometrium and myometrial cysts.

Parity has been suggested to be a risk factor for adenomyosis. The hormonal milieu and the myometrial trophoblastic invasion are the proposed mechanisms[18]. Prior uterine surgeries including cesarean sections and intrauterine interventions

have been reported to be associated with adenomyosis due to the disruption of endometrial - myometrial border[19] in some studies; however, other studies did confirm these results[20]. We showed that parity, if more than three, increased the risk of adenomyosis significantly. The incidence of adenomyosis was not different in patients who had undergone prior cesarean section, myomectomy or curettage in this study. Although the invagination of the endometrial tissue into the weakened myometrium resulted from prior surgical trauma is one of the proposed mechanisms[21]; it is not enough to explain all the clinical pictures. Adenomyosis may develop *de novo* from embryological misplaced pluripotent Müllerian remnants, invagination of the basalis proceeds along the intramyometrial lymphatic system may lead to adenomyosis and adenomyosis may originate from bone marrow stem cells that are displaced through the vasculature[22]. Therefore, a history of previous uterine surgery was excluded in the scoring system.

Younger age at menarche is another reported risk factor for adenomyosis. The mechanism is increased estrogen exposure[22]. In adenomyotic tissue higher expression of estrogen receptors has been shown[21]. The adenomyotic tissue also contains aromatase and estrogen sulphatase enzymes that locally produce estrogens[21]. A menarche age at or younger than 13 years increased adenomyosis risk by 1.6 times.

Dysmenorrhea and dyspareunia VAS scores were significantly higher in the patients with adenomyosis and cut-off scores that significantly have a predictive potential were calculated as 4 and 2 for dysmenorrhea and dyspareunia, respectively. Dysmenorrhea is a commonly assessed parameter and is found in 15-30% of the patients with adenomyosis. The proposed mechanisms are the hemorrhage and enlargement of the entrapped endometrium in the myometrium and or increased prostaglandin and eicosanoid synthesis in the adenomyotic tissue compared to the normal myometrial tissue[23]. Dyspareunia has been reported to be present in 7-10% of the patients with adenomyosis[24]. In this study both complaints have been found to be useful and significant predictors of adenomyosis; however, they are with relatively low OR and have emerged as the least influential factors on the scoring.

Today, imaging modalities have been started to be used more commonly in the differential diagnosis of adenomyosis. Especially, ultrasonography and MRI are prominent modalities[22]. Detection of heterogeneous myometrial echogenicity myometrial cysts and globularly enlarged uterus are the most commonly reported ultrasonographic findings[22,25]. The most predictive ultrasound finding is suggested to be the presence of myometrial heterogeneity[26]. Similarly, we found that the presence of myometrial heterogeneity, myometrial cysts and enlarged uterus were all significantly more common in the patients with adenomyosis. Detection of heterogeneous myometrium and myometrial cysts are found to be the predictive factors that were significant to be included in the scoring system. Specifically heterogeneous myometrial appearance alone

increases the risk of adenomyosis 27 times. Heterogeneity and myometrial cysts, which can be easily detected in experienced hands in ultrasonography, have a critical place in the prediction of adenomyosis in clinical evaluation. Studies comparing MRI, which is useful in the detection of adenomyosis, with TVUS, report that both methods yield similar results[25]. For this reason, TVUS, which is a cheaper and faster method, should be the preferred method.

In literature increased body mass index, oral contraceptive usage history and short menstrual periods, and cigarette smoking have been reported to be associated with adenomyosis as they all affect estrogen exposure[22]. However, in this study none of these parameters have been associated with adenomyosis. Tamoxifen treatment is also reported to be a risk factor for adenomyosis[27]. Unfortunately the number of patients under this medication in the assessed population was not enough to make a statistical analysis.

Heavy menstrual bleeding is the most common finding of adenomyosis, seen in approximately 40-60% of patients. This may be secondary to the increased endometrial surface of the enlarged uterus or to increased vascularization of the endometrial layer[24]. Other suggested reasons are inappropriate uterine contractions during menstrual periods and excess prostaglandin and estrogen production[28]. When the bleeding characteristics related to the presence of adenomyosis were examined, it was seen that the number of pads and diaper usage rates were significantly higher in the adenomyosis group, which is similar to the literature[29]. However, hemoglobin and hematocrit values, which reflect the amount of bleeding, did not differ in patients with and without adenomyosis. Again, none of the parameters related to bleeding were found to have significance to be included in the clinical scoring.

Studies have shown that the number of samples taken from pathological specimens affects the rates of adenomyosis diagnosis. The frequency reported in hysterectomy materials may vary depending on the number of sections and histopathological criteria. For example, when three routine sections were taken, adenomyosis was diagnosed in 31% of the hysterectomy samples, while taking six sections increased the rate to 61%[30]. In our pathology clinic, we make four sections in routine examination. Therefore, there is a theoretical possibility that existing adenomyosis cases could have been missed. However, the fact that the pathologist evaluating all specimens is a single person and that she is an experienced person dealing only with gynecopathology for many years eliminates the validity of this limitation. Again, a second issue that may be a limitation is that ultrasonographic evaluation and pelvic examination may differ between researchers due to the potential for variability. To overcome this limitation, all pelvic and ultrasonographic examinations were undertaken by the same person.

The study strengths, on the other hand, are the determination of the number of subjects by performing power analysis and including the determined number of subjects, the clinical evaluations were carried out by the same person, and all specimens were evaluated by the same experienced pathologist. A prediction model is more accurate when the overall probability reaches to ≥80%[31], therefore probability more than 80% may guide the management.

Conclusion

In conclusion adenomyosis is a common disease which has still been diagnosed histopathologically. To predict adenomyosis noninvasively, methods based on clinical evaluation with high sensitivity and specificity are needed. In our study, we have created a clinical scoring system for this purpose. In this scoring system, there are simple parameters that can be easily used by the clinician, have a low cost and are repeatable. The effect of each parameter on predicting adenomyosis is different, and the total effect can be calculated according to the answers to be given to all questions. In this simple scoring system, parity, menarche, VAS scores of dysmenorrhea and dyspareunia, myometrial heterogeneity in ultrasonography and presence of tenderness during pelvic examination was found to be useful parameters in predicting the diagnosis of adenomyosis. This prospective cohort study had an adequate sample size with a-80% power and was carried out by the same investigators and an experienced pathologist which all constituted the study strengths. The main limitation was the potential variability in ultrasonographic and pelvic examinations. This scoring system should be validated in the future, its reliability should be evaluated and the aspects that need to be improved, if any, should be revealed.

References

1. Yalaza C, Canacankatan N, Gürses İ, Aytan H, Taşdelen B. Altered VEGF, Bcl-2 and IDH1 expression in patients with adenomyosis. Arch Gynecol Obstet 2020;302:1221-7.

2. Younes G, Tulandi T. Effects of adenomyosis on in vitro fertilization treatment outcomes: a meta-analysis Fertil Steril 2017;108:483-90.

3. Struble J, Reid S, Bedaiwy M. Adenomyosis: A clinical review of a challenging gynecologic condition. J Minim Invasive Gynecol 2016;23:164-85.

4. Krentel H, Cezar C, Becker S, Sardo ADS, Tanos V, Wallwiener M, et al. From clinical symptoms to MR imaging: diagnostic steps in adenomyosis. Biomed Res Int 2017:1514029.

5. Shwayder J, Sakhel K. Imaging for uterine myomas and adenomyosis. J Minim Invasive Gynecol 2014;21:362-76.

6. Dartmouth K. A systematic review with meta-analysis: the common sonographic characteristics of adenomyosis. Ultrasound 2014;22:148-57.

7. Moghadam R, Lathi RB, Shahmohamady B, Saberi NS, Nezhat CH, Nezhat F, et al. Predictive value of magnetic resonance imaging in differentiating between leiomyoma and adenomyosis. JSLS 2006;10:216-9.

8. Dueholm M. Transvaginal ultrasound for diagnosis of adenomyosis: a review. Best Pract Res Clin Obstet Gynaecol 2006;20:569-82.

9. Abbott JA. Adenomyosis and abnormal uterine bleeding (AUB-A)-pathogenesis, diagnosis, and management. Best Pract Res Clin Obstet Gynaecol 2017;40:68-81.

10. Puente JM, Fabris A, Patel J, Patel A, Cerrillo M, Requena A, et al. Adenomyosis in infertile women: prevalence and the role of 3D ultrasound as a marker of severity of the disease. Reprod Biol Endocrinol 2016;14:60.

11. Vannuccini S, Luisi S, Tosti C, Sorbi F, Petraglia F. Role of medical therapy in the management of uterine adenomyosis. Fertil Steril 2018;109:398-405.

12. Blanche MT, Durrheim K, Painter D. Research in Practice Applied Methods for Social Sciences, 2nd edn, 2006. University of Cape Town Pres, Cape Town.

13. Machin D, Campbell MJ, Tan SB, Tan SH. Sample Size Tables for Clinical Studies, 3rd edn, 2009. Wiley-Blackwell Publishing, Oxford, UK.

14. DeLoach LJ, Higgins MS, Caplan AB, Stiff JL. The visual analog scale in the immediate postoperative period: intrasubject variability and correlation with a numeric scale. Anesth Analg 1998;86:102-6.

15. Margulies R, Miller L. Fruit size as a model for teaching first trimester uterine sizing in bimanual examination. Obstet Gynecol 2001;98:341-4.

16. Reinhold C, McCarthy S, Bret PM, Mehio A, Atri M, Zakarian R, et al. Diffuse adenomyosis: comparison of endovaginal US and MR imaging with histopathologic correlation. Radiology 1996;199:151-8.

17. Farquhar C, Brosens I. Medical and surgical management of adenomyosis. Best Pract Res Clin Obstet Gynaecol 2006;20:603-16.

18. Taran FA, Stewart EA, Brucker S. Adenomyosis: epidemiology, risk factors, clinical phenotype and surgical and interventional alternatives to hysterectomy. Geburtshilfe Frauenheilkd 2013;73:924-31.

19. Riggs JC, Lim EK, Liang D, Bullwinkel R. Cesarean section as a risk factor for the development of adenomyosis uteri. J Reprod Med 2014;59:20-4.

20. Taran FA, Weaver AL, Coddington CC, Stewart EA. Characteristics indicating adenomyosis coexisting with leiomyomas: a case-control study. Hum Reprod 2010;25:1177-82.

21. Ferenczy A. Pathophysiology of adenomyosis. Hum Reprod Update 1998;4:312-22.

22. Garcia L, Isaacson K. Adenomyosis: review of the literature. J Minim Invasive Gynecol 2011;18:428-37.

23. Koike H, Egawa H, Ohtsuka T, Yamaguchi M, Ikenoue T, Mori N. Correlation between dysmenorrheic severity and prostaglandin production in women with endometriosis. Prostaglandins Leukot Essent Fatty Acids 1992;46:133-7.

24. Huang FJ, Kung FT, Chang SY, Hsu TY. Effects of short-course buserelin therapy on adenomyosis. A report of two cases. J Reprod Med 1999;44:741-4.

25. Bazot M, Cortez A, Darai E, Rouger J, Chopier J, Antoine JM, et al. Ultrasonography compared with magnetic resonance imaging for the diagnosis of adenomyosis: correlation with histopathology. Hum Reprod 2001;16:2427-33.

26. Brosens JJ, de Souza NM, Barker FG, Paraschos T, Winston RM. Endovaginal ultrasonography in the diagnosis of adenomyosis uteri: identifying the predictive characteristics. Br J Obstet Gynaecol 1995;102:471-4.

27. Cohen I, Beyth Y, Shapira J, Tepper R, Fishman A, Cordoba M, et al. High frequency of adenomyosis in postmenopausal breast cancer patients treated with tamoxifen. Gynecol Obstet Invest 1997;44:200-5.

28. Azziz R. Adenomyosis: current perspectives. Obstet Gynecol Clin North Am 1989;16:221-35.

29. Bragheto AM, Caserta N, Bahamondes L, Petta CA. Effectiveness of the levonorgestrel-releasing intrauterine system in the treatment of adenomyosis diagnosed and monitored by magnetic resonance imaging. Contraception 2007;76:195-9.

30. Bird CC, McElin TW, Manalo-Estrella P. The elusive adenomyosis of the uterus--revisited. Am J Obstet Gynecol 1972;112:583-93.

31. Tellum T, Nygaard S, Skovholt EK, Qvigstad E, Lieng M. Development of a clinical prediction model for diagnosing adenomyosis. Fertil Steril 2018;110:957-64.