# Evaluation of the Routine Use of Pelvic MRI in Women Presenting With Symptomatic Uterine Fibroids: When Is Pelvic MRI Useful?

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**Background:** Pelvic ultrasound (US) diagnosis of uterine fibroids may overlook coexisting gynecological conditions that contribute to women's symptoms.

**Purpose:** To determine the added value of pelvic MRI for women diagnosed with symptomatic fibroids by US, and to identify clinical factors associated with additional MRI findings.

Study Type: Retrospective observational study.

**Population:** In all, 367 consecutive women with fibroids diagnosed by US and referred to our multidisciplinary fibroid center between 2013–2017.

**Field Strength/Sequence:** All patients had both pelvic US and MRI prior to their consultations. MRIs were performed at 1.5 T or 3 T and included multiplanar T<sub>2</sub>-weighted sequences, and precontrast and postcontrast T<sub>1</sub>-weighted imaging.

**Assessment:** Demographics, symptoms, uterine fibroid symptom severity scores, and health-related quality of life scores, as well as imaging findings were evaluated.

**Statistical Tests:** Patients were separated into two subgroups according to whether MRI provided additional findings to the initial US. Univariate and multivariate regression analyses were performed.

**Results:** Pelvic MRI provided additional information in 162 patients (44%; 95% confidence interval [CI] 39–49%). The most common significant findings were adenomyosis (22%), endometriosis (17%), and partially endocavitary fibroids (15%). Women with pelvic pain, health-related quality of life scores less than 30 out of 100, or multiple fibroids visualized on US had greater odds of additional MRI findings (odds ratio [OR] 1.68, 2.26, 1.63; P = 0.02, 0.004, 0.03, respectively), while nulliparous women had reduced odds (OR 0.55, P = 0.01). Patients with additional MRI findings were treated less often with uterine fibroid embolization (14% vs. 36%, P < 0.001) or MR-guided focused US (1% vs. 5%, P = 0.04), and more often with medical management (17% vs. 8%, P = 0.01).

**Data Conclusion:** Pelvic MRI revealed additional findings in more than 40% of women presenting with symptoms initially ascribed to fibroids by US. Further evaluation using MRI is particularly useful for parous women with pelvic pain, poor quality of life scores, and/or multiple fibroids.

Level of Evidence: 4
Technical Efficacy: Stage 3

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TERINE FIBROIDS are the most common solid tumor of the female pelvis, affecting 80% of women over the age of 50.1,2 Fibroids can severely impact a woman's health and quality of life, typically by causing abnormal uterine bleeding or urinary symptoms, such that up to 25% of women with fibroids pursue treatment. 1-3 Fibroids are the leading indication for elective hysterectomy in premenopausal women, contributing to an annual cost of treatment of fibroids in the United States estimated as high as 34.4 billion dollars. 4,5 In the past two decades, less invasive alternatives have become available, including hysteroscopic or laparoscopic myomectomy, uterine fibroid embolization (UFE), and magnetic resonance-guided focused ultrasound (MRgFUS). However, the choice of optimal treatment depends on fibroid features, such as size, number, location, and viability, as well as on the presence of concomitant gynecological conditions.<sup>6,7</sup>

Because of its low cost and ready availability, pelvic ultrasound (US) is advocated by many medical associations as the first imaging modality for the investigation of abnormal uterine bleeding and is often the only imaging performed in patients with suspected fibroids. Below However, US has limited sensitivity for conditions that often coexist with fibroids, such as adenomyosis and endometriosis, which can contribute to symptoms and alter treatment options. Prior studies have shown that magnetic resonance imaging (MRI) is more sensitive than US for detecting coexisting pathology and is better at characterizing fibroid features. These factors are particularly important when considering minimally invasive and uterine-sparing treatments.

At our institution, patients presenting with symptomatic uterine fibroids are seen in a multidisciplinary clinic, with MRI routinely obtained prior to consultation. The primary purpose of this study was to determine the added diagnostic value of pelvic MRI in women referred to our multidisciplinary clinic with presumed fibroids based only on pelvic US. Our secondary purpose was to identify factors associated with the presence of additional information provided by MRI.

## **Materials and Methods**

# Study Design and Subjects

This retrospective observational study was approved by our Institutional Review Board and informed consent was waived.

Our study included 568 consecutive women with a diagnosis of symptomatic uterine fibroids who were referred to our multidisciplinary fibroid center from April 2013 to July 2017. Patients were referred by their primary care physician or gynecologist (223/367; 61%), or self-referred (144/367; 39%) for abnormal uterine bleeding, pelvic pain, and/or bulk-related symptoms, such as urinary frequency, or sensation of pelvic pressure.

In all, 119 patients without prior pelvic US imaging or report available for review were excluded from this study. An additional 82 patients with greater than a year between US and MRI exams were also excluded, due to concern that any additional findings seen on MRI could have developed in the interval (Fig. 1).

Demographics for the remaining 367 women are summarized in Table 1.

#### **US and MRI Evaluation**

All patients underwent transvaginal pelvic US and pelvic MRI prior to the clinic visit with a team comprised of a minimally invasive gynecologic surgeon and interventional and diagnostic radiologists at our multidisciplinary fibroid center. US and MRI were performed wherever it was most convenient for patients, which included imaging centers across the United States. All MRI protocols included multiplanar T2-weighted sequences and precontrast T1-weighted imaging in either the sagittal or axial plane; 94% (345/367) included postcontrast T<sub>1</sub>-weighted fat-saturated sequences. All MR images were subsequently uploaded to our institution's picture archiving and communication system (PACS) and reviewed by a fellowship-trained, academic radiologist with 12 years of experience in abdominal and pelvic MRI (P.G.). MRIs were reviewed prior to the consultation, with the radiologist blinded to the patient's demographics, presenting symptoms, and prior US results. This interpretation was then incorporated into each patient's clinical note created during her appointment. Our retrospective analysis compared the report of this prospective MRI interpretation with the results of a retrospective review of the US images, performed by two radiologists (A.F. and K.V., with 3 and 5 years of experience, respectively). In order to assess the generalizability of the above MR and US imaging reviews, interreader agreement was determined for each of two randomly selected and separate subsets of the US and MRI exams independently reviewed by three fellowship-trained radiologists (K.V., P.G., and S.V., with 5, 12, and 16 years of experience, respectively).

## Data Collection

A retrospective review of the patient electronic medical records and imaging was performed (R.S., A.F., and K.V.). Collected data included demographics, presenting symptoms, hormonal medications, obstetrical history, uterine fibroid symptom severity scores, and health-related quality of life (UFS-QoL) scores, US and MRI findings, and treatment.

Briefly, the UFS-QoL is a validated questionnaire comprised of two parts: the UFS score, used to evaluate symptoms such as abnormal uterine bleeding and urinary frequency common in women with fibroids, with higher scores indicating more severe symptoms, and the QoL score, which measures the impact of these symptoms on anxiety level, ability to engage in activities, energy/mood, control, self-consciousness, and sexual function, with lower scores indicating a poorer quality of life. <sup>14</sup>

MRI data included number, location, and viability/enhancement of fibroids, and the presence of additional diagnoses. Location of fibroids included partially endocavitary fibroids, defined as submucosal fibroids with greater than 50% surface area in contact with the endometrial cavity. <sup>15,16</sup>

For the purposes of our study, relevant additional MRI findings were those that could 1) potentially contribute to the presenting symptoms, including adenomyosis, endometriosis, or endometrial polyps, <sup>17–21</sup> or 2) affect clinical outcome, such as the presence of

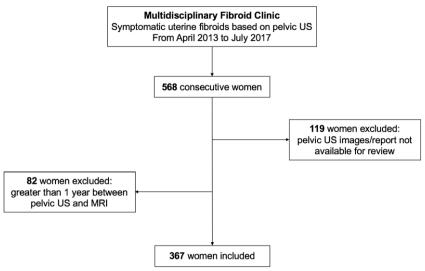


FIGURE 1: Flowchart of study population selection. Exclusion criteria included patients without prior pelvic US imaging or report available for review and patients with greater than a year between US and MRI exams.

partially endocavitary fibroids or nonenhancing fibroids. Specifically, polyps and endocavitary fibroids are approachable hysteroscopically and may be expelled if treated by UFE. Nonenhancing fibroids are already devascularized and are not expected to respond to MRgFUS or UFE. 22,23 In the absence of surgical pathologic results, MRI findings were used as the reference standard.

## Statistical Analysis

Our study population was separated into two subgroups according to whether MRI provided additional findings to the initial US diagnoses. Percent agreement for each finding among the three readers was calculated using Gwet's AC.<sup>24</sup> A consensus reading among the three readers was also calculated for each finding and compared to the original report. In cases of perfect agreement, no statistics were calculated. Differences between groups with and without additional MRI findings in continuous/ordinal variables were tested by the two-tailed Wilcoxon rank-sum test. Differences between groups in categorical variables were tested by Fisher's exact test. Univariate logistic regression analyses were conducted to evaluate patient characteristics and US imaging that were associated with additional MRI findings. Correlations among the clinical factors were estimated by Kendall's tau-b for binary factors and Spearman rank correlation for continuous ones. Variables with strong correlation, as defined by correlation coefficient r > 0.60, were excluded from the multivariate analysis. Variables with P < 0.05 were included in a multivariate logistic regression of noncorrelated factors. Sensitivity and specificity were calculated for each factor associated with additional MRI findings. Additional univariate and multivariate analyses were performed on subgroups of patients with the most common additional diagnoses to find more specific clinical factors. A P value cutoff level of less than 0.05 was considered significant. All data were analyzed using STATA Release 15.1 (StataCorp, College Station, TX).

#### Results

# **US and MRI Findings**

While nearly all patients (366/367; 99.7%) were diagnosed with fibroids by pelvic US, adenomyosis was found only in

nine patients (2.4%), endometriosis in seven patients (1.9%), and an endometrial polyp in one patient (0.3%). Twenty-two women were found to have partially endocavitary fibroids (6.0%).

Average time between US and MRI studies was  $91.5 \pm 103.7$  days (SD). MRI identified additional findings 162 patients (44.1%, 95% confidence interval [CI] 39-49%). Pelvic MRI provided additional information about fibroid characteristics, including fibroid number, location, and viability. MRI reported significantly more fibroids than US, with an average of 4.1  $\pm$  3.1 fibroids diagnosed on MRI, whereas only an average of 2.4  $\pm$  1.8 fibroids were described on US (P < 0.001). Pelvic MRI also revealed partially endocavitary fibroids in 54 patients (14.7%, 95% CI 11-29%) and nonenhancing fibroids in 10 patients (2.7%, 95% CI 1-5%) (Fig. 2). Furthermore, MRI found additional gynecologic diagnoses in 118 patients (32.2%, 95% CI 27-37%), including adenomyosis (21.8%, 95% CI 18-26%), endometriosis (17.2%, 95% CI 13-21%), and endometrial polyps (1.6%, 95% CI 1-4%) (Figs. 3-4). Nine patients (9/366; 2.5%, 95% CI 1-5%) diagnosed with fibroids on US were found to have focal adenomyosis without fibroids on MRI (Fig. 5).

Percent agreement for each finding among the three readers for US ranged from 88% for identification of partially endocavitary fibroids to 99% for the presence of fibroids. For MRI, agreement ranged from 93% for adenomyosis to 99% for fibroids. Agreement was also high when comparing the consensus reviewer interpretation for each US and MRI finding with the findings in the official report for each exam. Complete results are summarized in Table 2.

# Clinical Factors Associated With Additional MRI Findings

The results of the univariate and multivariate analyses are summarized in Table 3. Significantly increased likelihood of

Characteristics	Study population ( $n = 367$ )
Age, years (average $\pm$ SD)	$44.1 \pm 6.81$
BMI, kg/m $^2$ (average $\pm$ SD)	$26.2 \pm 6.47$
Nulligravidity, n	108/367 (29.4%)
Parity, $n$ (average $\pm$ SD)	$1.78 \pm 1.73$
History of cesarean-section, <i>n</i>	67/367 (18.3%)
Current oral contraceptive use, <i>n</i>	75/367 (20.4%)
Presenting symptoms	
Menorrhagia, n	246/367 (67.0%)
Menstrual irregularity, $n$	117/367 (31.9%)
Passage of clots, n	144/367 (39.2%)
Pelvic pain, n	135/367 (36.8%)
Dyspareunia, n	58/367 (15.8%)
Bulk-related symptoms, $n$	178/367 (48.5%)
UFS-QoL questionnaire	
UFS score, % (average $\pm$ SD)	$51.0 \pm 24.6$
QoL score, % (average $\pm$ SD)	$51.8 \pm 26.8$

additional MRI findings was observed in women presenting with pelvic pain (odds ratio [OR] 1.68, 95% CI 1.08–2.59, P=0.02) and with QoL scores below 30 out of 100 (OR 2.26, 95% CI 1.31–3.92, P=0.004). Visualization of more than one fibroid on US was significantly associated with additional MRI findings (OR 1.63, 95% CI 1.04–2.56, P=0.03). Conversely, nulligravid patients were significantly less likely to have additional findings (OR 0.55, 95% CI 0.34–0.88, P=0.01).

Although age greater than 45 years was found to be associated with additional MRI findings on univariate analysis (OR 1.71, 95% CI 1.13–2.59, P=0.01), this association was not significant on multivariate analysis (OR 1.55, 95% CI 1.00–2.40, P=0.051). Because of its correlation with other variables (irregular menses r=0.22, number of fibroids on US r=0.11, nulligravidity r=-0.24, and infertility r=-0.21, all P<0.05), we thus omitted age from the multivariate models. Similarly, UFS scores had a strong negative correlation with QoL scores (r=-0.77, P<0.001), which is expected due to the nature of the questionnaire, and so were omitted from multivariate analysis. No other variables met criteria for strong correlation.

## Sensitivity and Specificity of Clinical Factors

Sensitivity and specificity were computed for each clinical factor and the results are summarized in Table 4. Pelvic pain and QoL scores less than 30 out of 100 had high specificity for additional MRI findings (68.3% and 83.1%, 95% CI 61.4–74.6% and 76.6–88.5%, respectively). Multiple fibroids visualized on US and a history of pregnancy were observed to have high sensitivity for additional MRI findings (72.2% and 77.8%, 95% CI 64.7–79.0% and 70.6–83.9%, respectively).

# Clinical Factors Associated With Specific MRI Findings

Additional univariate and multivariate analyses were performed to evaluate for clinical factors associated with the three most common additional MRI findings: adenomyosis, endometriosis, and partially endocavitary fibroids (Table 5). Patients with pelvic pain and dyspareunia were found to have adenomyosis (OR 2.09 and 1.88, 95% CI 1.27–3.43 and 1.02–3.47, P = 0.004 and 0.04, respectively) and endometriosis (OR 3.11 and 2.08, 95% CI 1.72–5.61 and 1.04–4.19, P < 0.001 and 0.04, respectively) significantly more often. Menorrhagia (OR 5.17,

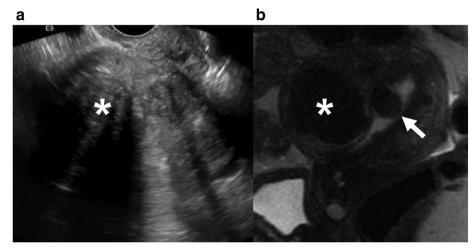


FIGURE 2: Images from a 45-year-old woman presenting with menometrorrhagia, passage of clots, and cramping. (a) Sagittal view of the uterus from a pelvic US demonstrating an enlarged uterus with multiple intramural fibroids with a large anterior fibroid (white asterisk) causing attenuation and poor acoustic penetration. (b) Sagittal T<sub>2</sub>-weighted single-shot fast spin echo image from a pelvic MRI performed 6 days after the US showing a myomatous uterus including the large anterior intramural fibroid (white asterisk) as well as an endocavitary fibroid (white arrow), which was likely responsible for the patient's symptoms. This endocavitary fibroid was amenable to hysteroscopic myomectomy.

95% CI 2.39–11.3, P < 0.001) and lack of bulk-related symptoms (OR 2.31, 95% CI 1.33–4.00, P = 0.003) were significantly associated with partially endocavitary fibroids.

Treatments in Women With and Without Additional MRI Findings

In the subgroup of patients for whom MRI did not reveal additional information, treatment was distributed among surgery in 37.0% (76/205), UFE in 36.1% (74/205), MRgFUS in 5.4% (11/205), medical management in 8.3% (17/205), and expectant management in 10.2% (21/205). Women with additional MRI findings were observed to be treated significantly less often with UFE (23/162; 14.2%, P < 0.001) and MRgFUS (2/162; 1.2%, P = 0.04), and significantly more

often with medications (28/162; 17.3%, P = 0.01) and expectant management (32/162; 19.8%, P = 0.01). Surgery was performed at similar rates in both groups (76/205; 37.0% vs. 55/162; 34.0%, P = 0.58).

# Discussion

Symptomatic uterine fibroids reduce the quality of life for many women and incur large societal costs.<sup>3,4</sup> With its easy accessibility, pelvic US usually represents the first—and often the only—imaging modality used to evaluate fibroids, but at the cost of lower sensitivity to certain fibroid characteristics and coexisting gynecologic conditions.

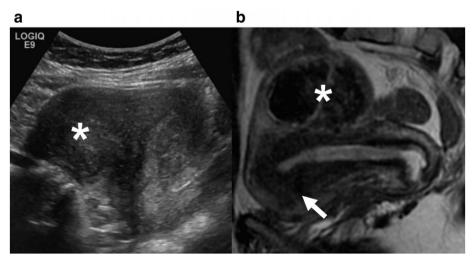


FIGURE 3: Images from a 50-year-old woman presenting with dysmenorrhea and menorrhagia. (a) Sagittal view of the uterus from a pelvic US demonstrating a posterior fundal uterine fibroid (white asterisk). (b) Sagittal T<sub>2</sub>-weighted single-shot fast spin echo image from a pelvic MRI performed 3 months after the US identified the previously seen posterior fundal fibroid (white asterisk), and revealed findings of adenomyosis, including a thickened junctional zone measuring 18 mm (white arrow). Adenomyosis commonly results in painful periods with heavy bleeding, whereas the intramural fibroid would not be expected to explain the patient's presenting symptoms.

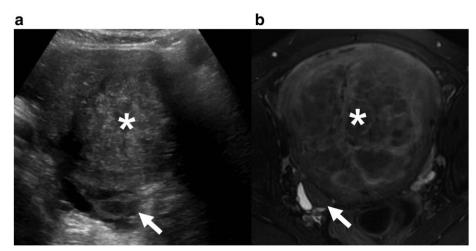


FIGURE 4: Images from a 43-year-old woman presenting with dysmenorrhea and menorrhagia. (a) Axial view of the uterus from a pelvic US demonstrating a dominant transmural uterine leiomyoma (white asterisk) and a reportedly normal right ovary (white arrow). (b) Axial fat-saturated T<sub>2</sub>-weighted fast spin echo image from a pelvic MRI performed 45 days after the US confirmed the presence of a large fibroid (white asterisk). The MRI also revealed a homogeneously T<sub>2</sub> hypointense lesion (white arrow) arising from the right ovary. The lesion demonstrated corresponding intrinsic T<sub>1</sub> hyperintensity and no enhancement (not shown), consistent with an endometrioma. Dysmenorrhea is more commonly associated with endometriosis rather than fibroids.

Compared to US alone, our study found that pelvic MRI provided additional findings in more than 40% of patients, affecting the diagnosis and adding information about the fibroid burden. Adenomyosis and endometriosis were the most common secondary diagnoses, and endocavitary location was the most common fibroid-related feature revealed by MRI. Our results were consistent with the previously published rates of co-conditions in patients with symptomatic uterine fibroids, specifically adenomyosis (36–50%) and endometriosis (12–20%). <sup>19,25–27</sup>

Although MRI offers better characterization of fibroid features and detection of coexisting gynecologic conditions, the routine use of pelvic MRI may not be feasible in clinical practices with restricted resources and limited availability of

MRI. Our study revealed that pelvic pain, a QoL score below 30 out of 100, and multiple fibroids visualized on US are associated with the presence of additional information on MRI.

A potential explanation for the first factor is that patients with fibroids alone are not expected to present with pelvic pain as a predominant symptom and are likely to have additional diagnoses, such as adenomyosis and endometriosis, that account for their symptoms. <sup>28,29</sup> Second, women with QoL scores below 30 out of 100 may be more likely to have additional conditions causing symptoms that may compound with their fibroid-related symptoms and result in lower QoL scores. Third, our observation that MRI was more sensitive

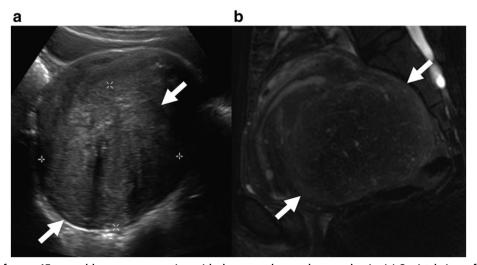


FIGURE 5: Images from a 45-year-old woman presenting with dysmenorrhea and menorrhagia. (a) Sagittal view of the uterus from a pelvic US demonstrating a large posterior uterine body mass diagnosed as a leiomyoma (white arrows). (b) Sagittal T<sub>2</sub>-weighted single-shot fast spin echo image from a pelvic MRI performed 25 days after the US revealing a T<sub>2</sub> hypointense posterior uterine body mass that contained numerous small T<sub>2</sub> hyperintense cysts and was separate from the junctional zone, consistent with an adenomyoma (white arrows). The clinical presentation was more consistent with adenomyosis rather than an intramural fibroid.

TABLE 2. Interreader Agreement and Consensus Reader Agreement With Official Report for US and MRI Findings

		Interreader agreement			Consensus reader agreement with official report	
		Agreement			Agreement	
US Finding	Prevalence	Number	Percent (95% CI)	Gwet's AC (95% CI)	Percent (95% CI)	Gwet's AC (95% CI)
Fibroid	~99%	47/48	99% (96–99%)	0.99 (0.96–0.99)	100%	_
Partially endocavitary fibroid	~10%	39/48	88% (80–95%)	0.85 (0.74–0.96)	88% (78–97%)	0.85 (0.71–0.98)
Adenomyosis	-3%	44/48	94% (89–99%)	0.94 (0.88–0.99)	94% (87–99%)	0.93 (0.85–0.99)
Endometriosis	~1%	46/48	97% (93–99%)	0.97 (0.93–0.99)	100%	_
Endometrial polyp	-2%	47/48	99% (96–99%)	0.99 (0.96–0.99)	100%	_

		Inter-reader agreement		reement	Consensus reader agreement with official report	
		Agreement			Agreement	
MRI finding	Prevalence	Number	Percent (95% CI)	Gwet's AC (95% CI)	Percent (95% CI)	Gwet's AC (95% CI)
Fibroid	~92%	49/50	99% (96–99%)	0.98 (0.95–0.99)	98% (94–97%)	0.98 (0.93–0.99)
Partially endocavitary fibroid	-33%	45/50	93% (88–99%)	0.88 (0.77–0.96)	88% (79–97%)	0.78 (0.61–0.96)
Adenomyosis	-31%	45/50	93% (88–99%)	0.88 (0.78–0.99)	94% (87–99%)	0.93 (0.85–0.99)
Endometriosis	~15%	47/50	96% (91–99%)	0.95 (0.88–0.99)	96% (90–99%)	0.95 (0.87–0.99)
Endometrial polyp	~2%	48/50	97% (94–99%)	0.97 (0.93–0.99)	100%	_

to other diagnoses when multiple fibroids were visualized on US could reflect that the fibroids obscured these additional findings on US. The presence of multiple fibroids can increase the attenuation of the US beam and reduce sensitivity. <sup>6,30,31</sup>

Our multivariate analyses also found that nulligravidity was inversely related with additional MRI findings. Gravidity is a known risk factor for adenomyosis, the most common additional MRI diagnosis in our study. 32,33 A theory is that pregnancy disrupts the junctional zone, allowing endometrial glands to penetrate into the myometrium and leading to

adenomyosis.<sup>34,35</sup> This could explain the inverse relationship between nulligravidity and additional MRI findings in our study.

When calculating sensitivity and specificity of these clinical factors, our results showed that multiple fibroids visualized on US and gravidity had higher sensitivity for additional MRI findings, whereas pelvic pain and QoL scores less than 30 out of 100 had higher specificity for additional MRI findings. This indicates that, when considering pelvic MRI in previously pregnant patients and/or those with more than one fibroid visualized on US, we are more likely to capture the

TABLE 3. Multivariate Regression Analysis Evaluating Patient and Fibroid Characteristics That Are Associated With Additional MRI Findings

	Additional MRI findings					
Factors	Univariate a	nalysis	Multivariate analysis*			
	OR (95% CI)	P value	OR (95% CI)	P value		
Age ≥ 45	1.71 (1.13–2.59)	0.01	1.55 (1.00–2.40)	0.051		
BMI ≥ 25	1.07 (0.71–1.62)	0.73	_	_		
Nulligravidity	0.53 (0.33-0.84)	0.007	0.55 (0.34–0.88)	0.01		
Infertility	0.95 (0.39–2.30)	0.90	_	_		
History of cesarean-section	0.97 (0.57–1.65)	0.90	_	_		
Current oral contraceptive use	0.76 (0.42–1.39)	0.37	_	_		
Menorrhagia	1.45 (0.93–2.27)	0.10	_	_		
Irregular menses	0.87 (0.55–1.37)	0.55	_	_		
Passage of clots	0.97 (0.63–1.50)	0.90	_	_		
Pelvic pain	1.64 (1.07–2.51)	0.02	1.68 (1.08–2.59)	0.02		
Bulk symptoms	0.68 (0.45–1.03)	0.07	_	_		
Dyspareunia	1.12 (0.64–1.97)	0.69	_	_		
UFS scores						
0–20.0	Reference	Reference	Reference	referenc		
20.1–40.0	1.01 (0.41–2.49)	0.99	_	_		
40.1–60.0	1.27 (0.55–2.92)	0.58	_	_		
60.1-80.0	1.94 (0.81–4.64)	0.14	_	_		
80.1–100	2.62 (0.99–6.99)	0.05	_	_		
QoL scores						
Quartiles						
0-30.0	3.43 (1.76–6.69)	<0.001	_	_		
30.1–51.0	1.31 (0.68–2.53)	0.43	_	_		
51.1–74.0	Reference	Reference	_	_		
74.1–100.0	1.56 (0.81–3.02)	0.18	_	_		
QoL ≥ 30	Reference	Reference	Reference	referenc		
QoL < 30	2.68 (1.57–4.56)	<0.001	2.26 (1.31–3.92)	0.004		
Number of fibroids on US						
1	Reference	Reference	Reference	referenc		
More than 1	1.66 (1.07–2.59)	0.02	1.63 (1.04–2.56)	0.03		

<sup>\*</sup>Given that QoL data were missing in 59 patients (16.1%), separate multivariate analyses were performed for patients with and without missing data. Factors that were significant on multivariate analysis of all patients remained significant when limiting the analysis to patients with QoL score. Patients with and without QoL scores were similar, except that patients without QoL scores were less likely to be nulligravid (15% vs. 32%, P = 0.008) and less likely to present with pain (22% vs. 40%, P = 0.012).

BMI = body mass index; CI = confidence interval; MRI = magnetic resonance imaging; OR = odds ratio; QoL = health-related quality of life; UFS = uterine fibroid symptom; US = ultrasound.

TABLE 4. Sensitivity and Specificity of Clinical Factors				
Factors	Sensitivity (95% CI)	Specificity (95% CI)		
Pelvic pain	43.2% (35.5–51.2%)	68.3% (61.4–74.6%)		
Nulligravidity*	77.8% (70.6–83.9%)	35.1% (28.6–42.1%)		
QoL < 30 out of 100	35.2% (27.4–43.7%)	83.1% (76.6–88.5%)		
More than 1 fibroid on US	72.2% (64.7–79.0%)	39.0% (32.3–46.1%)		
*Inverse relationship.  CI = confidence interval; QoL = health-related quality of life; US = ultrasound.				

majority of patients with potential additional findings, which is not surprising since these are common clinical variables in the general female population. However, these factors are not very specific and thus not likely to be useful for clinical decision making. Conversely, women with pelvic pain and/or severe decrease in QoL have a greater likelihood of having additional findings on their MRI, such as adenomyosis and endometriosis. These factors, although more specific, are less sensitive, since not all patients with additional MRI findings present in the same way.

When multivariate analyses were performed on subgroups of women with adenomyosis, endometriosis, and partially endocavitary fibroids, additional clinical factors were found that were more specific. Endometriosis and adenomyosis were significantly associated with dyspareunia and pelvic pain. Endometriotic foci can deposit on the pelvic peritoneum, and the resulting inflammatory response may lead to dyspareunia. The presence of menorrhagia, rather than bulk-related symptoms, was a specific factor associated with partially endocavitary fibroids. This finding is not surprising

since, given their close proximity to the endometrium, endocavitary fibroids may alter the integrity and function of the endometrium and cause more bleeding symptoms than intramural and subserosal fibroids which, when symptomatic, are frequently associated with more bulk-related symptoms. 38,39

In the subgroup of patients with additional MRI findings, UFE and MRgFUS were performed less often, whereas medical and expectant management were used more often. This is likely because UFE and MRgFUS are not as effective when adenomyosis or endometriosis are also present. <sup>12,40</sup> In certain circumstances, partially endocavitary fibroids are better treated by hysteroscopic myomectomy, which avoids the potential risk of expulsion after UFE. <sup>15,16</sup> Also, nonenhancing fibroids would not be expected to respond to UFE or MRgFUS. <sup>22,23</sup> Thus, medical and expectant management can be more appropriate uterine-sparing treatment options in women with these findings.

The main limitation of our study is the absence of histopathologic correlation as a "gold standard." Many patients in our population with adenomyosis and endometriosis

TABLE 5. Multivariate Regression Analysis Evaluating Patient and Fibroid Characteristics That Are Associated With
Additional MRI Diagnoses of Adenomyosis, Endometriosis, and Partially Endocavitary Fibroids

MRI findings	Factors	OR (95% CI)	P value
Adenomyosis	Pelvic pain	2.09 (1.27–3.43)	0.004
	Dyspareunia	1.88 (1.02–3.47)	0.04
Endometriosis	Pelvic pain	3.11 (1.72–5.61)	< 0.001
	Dyspareunia	2.08 (1.04–4.19)	0.04
Partially endocavitary fibroid	Bulk symptoms*	2.31 (1.33–4.00)	0.003
	Menorrhagia	5.17 (2.39–11.3)	<0.001

<sup>\*</sup>Inverse relationship.

CI = confidence interval; MRI = magnetic resonance imaging; OR = odds ratio.

underwent medical management, and pathologic confirmation was not available. This reflects current practice, especially with the recent trend towards cost containment. Another potential limitation of our study is the lack of standardized imaging technique, since the studies were obtained at multiple centers using variable equipment and scanning parameters. MRI protocols all included multiplanar T2-weighted imaging; the addition (or not) of contrast-enhanced imaging was the most common variable. Having the same reader review all the scans in our study was done to ensure internal consistency. A third potential limitation is referral bias, since we are a tertiary care hospital with a multidisciplinary fibroid center. Many patients were seeking a second opinion or were referred by their gynecologists and may be more likely to have coexisting conditions not addressed in their original treatment.

In conclusion, our study found that the use of pelvic MRI provides better characterization of fibroids and better detection of coexisting gynecologic conditions in women presenting with symptoms initially ascribed to uterine fibroids by US. These additional findings may alter management in women seeking minimally invasive treatment options. When there are resource constraints, further evaluation with pelvic MRI is likely to be most relevant for parous patients who present with pelvic pain, a QoL score below 30 out of 100, and/or multiple fibroids on a pelvic US examination.

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## References

- Baird DD, Dunson DB, Hill MC, Cousins D, Schectman JM. High cumulative incidence of uterine leiomyoma in black and white women: ultrasound evidence. Am J Obstet Gynecol 2003;188:100–107.
- Buttram VCJ, Reiter RC. Uterine leiomyomata: Etiology, symptomatology, and management. Fertil Steril 1981;36:433–445.
- Soliman AM, Margolis MK, Castelli-Haley J, Fuldeore MJ, Owens CD, Coyne KS. Impact of uterine fibroid symptoms on health-related quality of life of US women: Evidence from a cross-sectional survey. Curr Med Res Opin 2017;33:1971–1978.
- Cardozo ER, Clark AD, Banks NK, Henne MB, Stegmann BJ, Segars JH. The estimated annual cost of uterine leiomyomata in the United States. Am J Obstet Gynecol 2012;206:211.e211-219.
- Carlson KJ, Nichols DH, Schiff I. Indications for hysterectomy. N Engl J Med 1993;328:856–860.
- Battista C, Capriglione S, Guzzo F, et al. The challenge of preoperative identification of uterine myomas: Is ultrasound trustworthy? A prospective cohort study. Arch Gynecol Obstet 2016;293:1235–1241.

- Friedman H, Vogelzang RL, Mendelson EB, Neiman HL, Cohen M. Endometriosis detection by US with laparoscopic correlation. Radiology 1985; 157:217–220.
- American College of Obstetricians and Gynecologists. ACOG Committee Opinion no. 557: Management of acute abnormal uterine bleeding in nonpregnant reproductive-aged women. Obstet Gynecol 2013;121: 891–896.
- Sweet MG, Schmidt-Dalton TA, Weiss PM, Madsen KP. Evaluation and management of abnormal uterine bleeding in premenopausal women. Am Fam Physician 2012;85:35–43.
- Bennett GL, Andreotti RF, Lee SI, et al. ACR appropriateness criteria(\*) on abnormal vaginal bleeding. J Am Coll Radiol 2011;8:460–468.
- Ascher SM, Arnold LL, Patt RH, et al. Adenomyosis: Prospective comparison of MR imaging and transvaginal sonography. Radiology 1994;190: 803–806.
- Spielmann AL, Keogh C, Forster BB, Martin ML, Machan LS. Comparison of MRI and sonography in the preliminary evaluation for fibroid embolization. AJR Am J Roentgenol 2006;187:1499–1504.
- Hottat N, Larrousse C, Anaf V, et al. Endometriosis: Contribution of 3.0-T pelvic MR imaging in preoperative assessment—Initial results. Radiology 2009;253:126–134.
- Spies JB, Coyne K, Guaou Guaou N, Boyle D, Skyrnarz-Murphy K, Gonzalves SM. The UFS-QOL, a new disease-specific symptom and health-related quality of life questionnaire for leiomyomata. Obstet Gynecol 2002;99:290–300.
- American Association of Gynecologic Laparoscopists (AAGL): Advancing Minimally Invasive Gynecology Worldwide. AAGL practice report: Practice guidelines for the diagnosis and management of submucous leiomyomas. J Minim Invasive Gynecol 2012;19:152–171.
- Verma SK, Bergin D, Gonsalves CF, Mitchell DG, Lev-Toaff AS, Parker L. Submucosal fibroids becoming endocavitary following uterine artery embolization: Risk assessment by MRI. AJR Am J Roentgenol 2008;190: 1220–1226.
- Novellas S, Chassang M, Delotte J, et al. MRI characteristics of the uterine junctional zone: From normal to the diagnosis of adenomyosis. AJR Am J Roentgenol 2011;196:1206–1213.
- 18. Siegelman ES, Oliver ER. MR imaging of endometriosis: Ten imaging pearls. Radiographics 2012;32:1675–1691.
- Hulka CA, Hall DA, McCarthy K, Simeone J. Sonographic findings in patients with adenomyosis: Can sonography assist in predicting extent of disease? AJR Am J Roentgenol 2002;179:379–383.
- Kamaya A, Yu PC, Lloyd CR, Chen BH, Desser TS, Maturen KE. Sonographic evaluation for endometrial polyps: The interrupted mucosa sign. J Ultrasound Med 2016;35:2381–2387.
- Grasel RP, Outwater EK, Siegelman ES, Capuzzi D, Parker L, Hussain SM. Endometrial polyps: MR imaging features and distinction from endometrial carcinoma. Radiology 2000;214:47–52.
- Nikolaidis P, Siddiqi AJ, Carr JC, et al. Incidence of nonviable leiomyomas on contrast material-enhanced pelvic MR imaging in patients referred for uterine artery embolization. J Vasc Intervent Radiol 2005;16: 1465–1471.
- Kirby JM, Burrows D, Haider E, Maizlin Z, Midia M. Utility of MRI before and after uterine fibroid embolization: Why to do it and what to look for. Cardiovasc Intervent Radiol 2011;34:705–716.
- 24. Gwet KL. Computing inter-rater reliability and its variance in the presence of high agreement. Br J Math Stat Psychol 2008;61:29–48.
- 25. Azziz R. Adenomyosis: Current perspectives. Obstet Gynecol Clin North Am 1989;16:221–235.
- Huang JQ, Lathi RB, Lemyre M, Rodriguez HE, Nezhat CH, Nezhat C. Coexistence of endometriosis in women with symptomatic leiomyomas. Fertil Steril 2010;94:720–723.
- 27. Uimari O, Järvelä I, Ryynänen M. Do symptomatic endometriosis and uterine fibroids appear together? J Hum Reprod Sci 2011;4:34–38.

- Stratton P, Berkley KJ. Chronic pelvic pain and endometriosis: Translational evidence of the relationship and implications. Hum Reprod Update 2011;17:327–346.
- Parker JD, Leondires M, Sinaii N, Premkumar A, Nieman LK, Stratton P. Persistence of dysmenorrhea and nonmenstrual pain after optimal endometriosis surgery may indicate adenomyosis. Fertil Steril 2006; 86:711–715.
- Fambrini M, Tondi F, Scarselli G, et al. Comparison of the number of uterine myomas detected by in-office transvaginal ultrasonography removed by laparotomic myomectomy: Preoperative work-up concerns. Clin Exp Obstet Gynecol 2009;36:97–101.
- Dueholm M, Lundorf E, Hansen ES, Sørensen JS, Ledertoug S, Olesen F. Magnetic resonance imaging and transvaginal ultrasonography for the diagnosis of adenomyosis. Fertil Steril 2001;76:588–594.
- Naftalin J, Hoo W, Pateman K, Mavrelos D, Holland T, Jurkovic D. How common is adenomyosis? A prospective study of prevalence using transvaginal ultrasound in a gynaecology clinic. Hum Reprod 2012;27:3432–3439.
- Vavilis D, Agorastos T, Tzafetas J, et al. Adenomyosis at hysterectomy: Prevalence and relationship to operative findings and reproductive and menstrual factors. Clin Exp Obstet Gynecol 1997;24:36–38.

- 34. Abbott JA. Adenomyosis and abnormal uterine bleeding (AUB-A)—Pathogenesis, diagnosis, and management. Best Pract Res Clin Obstet Gynaecol 2017;40:68–81.
- Struble J, Reid S, Bedaiwy M. Adenomyosis: A clinical review of a challenging gynecologic condition. J Minim Invasive Gynecol 2016;23: 164–185
- 36. Schliep KC, Mumford SL, Peterson CM, et al. Pain typology and incident endometriosis. Hum Reprod 2015;30:2427–2438.
- Bulletti C, Coccia ME, Battistoni S, Borini A. Endometriosis and infertility.
   J Assist Reprod Genet 2010;27:441–447.
- Puri K, Famuyide AO, Erwin PJ, Stewart EA, Laughlin-Tommaso SK. Submucosal fibroids and the relation to heavy menstrual bleeding and anemia. Am J Obstet Gynecol 2014;210:38.e31–37.
- Sulaiman S, Khaund A, McMillan N, Moss J, Lumsden MA. Uterine fibroids—do size and location determine menstrual blood loss? Eur J Obstet Gynecol Reprod Biol 2004;115:85–89.
- Tan N, McClure TD, Tarnay C, Johnson MT, Lu DS, Raman SS. Women seeking second opinion for symptomatic uterine leiomyoma: Role of comprehensive fibroid center. J Ther Ultrasound 2014;2:1–9.