ULTRASOUND

Tumor Vascular Pattern and Blood Flow Impedance in the Differential Diagnosis of Leiomyoma and Adenomyosis by Color Doppler Sonography[1]

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Purpose: *Our objective was to evaluate the differences between leiomyoma and adenomyosis by color Doppler sonography with new criteria.*
Methods: *A total of 78 patients with symptomatic uterine nodularities who were sonographically suspected to have leiomyoma or adenomyosis without other coexisting pathologic conditions was enrolled in the study. All patients underwent transvaginal color Doppler sonography (7.0-MHz vaginal probe) or transabdominal color Doppler sonography (5.0 MHz) during the early follicular phase. The morphology, tumor vascular pattern, and blood flow impedance of the uterine tumors were measured. All of the patients underwent surgery and the pathologic reports were used as references.*
Results: *The mean age was not statistically significant in patients with adenomyosis versus leiomyoma ($P > 0.05$). The morphologic criteria for adenomyosis and leiomyoma by sonography detected 79% of adenomyosis and 84% of leiomyoma. Adenomyosis had 87% randomly scattered vessels or intratumoral signals and 88% of leiomyomas showed peripheral scattered vessels or outer feeding vessels. Eighty-two percent of adenomyoses had a pulsitility index (PI) of arteries within or around uterine tumors >1.17 and 84% of leiomyomas had a PI ≤ 1.17. The reliability test of tumor vascular pattern and blood flow impedance were better than that of using morphological criteria alone.*
Conclusions: *With the aid of color Doppler sonography, tumor vascular pattern and blood flow impedance of the arteries within or around uterine tumors could more accurately diagnose adenomyosis and leiomyoma in addition to the morphologic criteria on transvaginal sonography.*

KEY WORDS: adenomyosis; blood flow impedance; color Doppler sonography; leiomyoma; tumor vascular pattern.

INTRODUCTION

Leiomyoma and adenomyosis are two common diseases that affect women of reproductive age. Although different in nature, both have a certain degree of detrimental effect on fecundity, especially adenomyosis. Several methods have been designed to diagnose adenomyosis with varying success (1).

Hysterosalpingography (HSG) and transabdominal sonography (TAS) lack specificity for diagnosing adenomyosis (1). Recently, the diagnosis of adenomyosis, adenomyoma, and leiomyoma by transvaginal sonography (TVS) has been reported by Fedele *et al.* with an acceptable accuracy (2,3). Although the emerging data have shown that magnetic resonance imaging (MRI) has a higher sensitivity and specificity (4), the medical costs of general application of MRI for this purpose are high. Moreover, a study has demonstrated that TVS was as accurate as MRI in the diagnosis of adenomyosis (5).

The recent availability of color Doppler sonography (CDS) has provided the gynecologist with a sophisti-

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cated method of investigating uterine morphologic and physiologic features. With the aid of pulsed Doppler sonography and CDS, recording of vascular patterns and measurement of changes in blood flow resistance and flow velocity can be easily achieved in addition to TVS. Although some investigators have reported their findings (6–8), to our knowledge, the use of CDS and color Doppler energy in differentiating the presence of adenomyosis and leiomyoma has not yet been well discussed. The purpose of this study was to evaluate the potential of CDS in the differential diagnosis of adenomyosis and leiomyoma in patients with a clinically enlarged uterus by new criteria.

MATERIALS AND METHODS

A total of 78 patients (age range, 28 to 52 years; mean, 39.9 ± 4.6 years) with symptomatic uterine nodularities who were sonographically suspected to have leiomyoma or adenomyosis without other coexisting pathologic conditions and scheduled for indicative surgeries were enrolled in this prospective study. In these patients, the possibility of endometrial polyps, endometrial cancer, and cervical cancer had already been excluded by hysteroscopy, colposcopy, and fractional dilatation and curettage prior to CDS and surgeries. Surgery was performed within 2 weeks of color Doppler sonography. The indications for surgery in our study were sonographically proven uterine nodularities with the following clinical findings: a history of infertility (n = 28), persistent hypermenorrhea (n = 15), continued dysmenorrhea (n = 23), and compression symptoms or pain associated with a mass lesion (n = 12). Histopathologic diagnoses were made by means of hysterectomy, myomectomy, adenomyomectomy, and biopsy specimens obtained from surgery. The pathologist (K.-F.L.) was blinded to the sonography findings. Criteria used for the pathologic diagnosis of adenomyosis included the presence of endometrial glands and/or stroma more than one high-power field deeper than the endometrial–myometrial junction. Adenomyoma was diagnosed when a circumscribed nodular aggregate of smooth muscle and endometrial glands was found together with compensatory hypertrophy of the myometrium surrounding the site of ectopic endometrium (3). Leiomyoma was diagnosed when the major constituents were smooth muscle cells forming discrete tumors sharply demarcated from the surrounding myometrium by a pseudocapsule of light areolar tissue or compressed myometrial tissues.

The patients further underwent CDS (Acuson 120XP/10, Mountainview, CA) by one operator (C.-H.C.) after the previous sonographic scanning. All patients were asked to fast overnight to reduce the bowel artifacts and to void before each examination. The transvaginal route was used first; if complete exploration of the whole uterus could not be achieved, the transabdominal route with a distended bladder was then adopted. Transvaginal ultrasound with an appropriately focused 7.0-MHz sector probe was performed first to evaluate morphologic characters and then pulsed and color Doppler imaging (TV-CDS; 5.0 MHz) was applied for evaluation of the tumor vascular pattern and blood flow impedance in 71 patients. Transabdominal ultrasound with a pulsed and color Doppler probe (TA-CDS; 5.0 MHz) was performed in six patients. For all examinations, the smallest possible field of view (FOV) was used to depict the whole myometrium optimally. The intraobserver variation for the measurement of blood flow impedance of the vessels around or within the uterine tumors ranged from 10% to 18%.

All subjects were imaged between 0700 and 0900 during the early follicular phase of their menstrual cycle (days 3–5). Morphologic criteria of adenomyosis and adenomyoma under sonography included one or more heterogeneous myometrial areas not encapsulated and within round anechoic areas 1 to 3 mm in diameter (2) and dishomogeneous circumscribed areas in the myometrium with indistinct margins and containing anechoic lacunae of varying diameters (3). Well-defined margins, heterogeneous structure, and variable echogenecity (3) were used as the morphologic criteria of leiomyoma on sonography. The criteria of the vascular pattern for leiomyoma we used were that (a) multiple peripherally located vessels surrounded the uterine tumor or outer feeding vessels and (b) when only a few vessels surrounded the tumor, these vessels were longer than 1 cm. As opposed to leiomyoma, the criteria for adenomyosis were that (a) randomly scattered vessels were present in the heterogeneous myometrial area or intratumoral sigals on CDS, (b) for focal adenomyosis, the intratumoral signals usually presented without peripherally located vessels, and (c) if peripheral vessels were present, they were less than 1 cm. Moreover, at least different observations of optimal waveforms were measured in both vascular patterns at different vessels. Only the lowest pulsitility index (PI), resisting index (RI), and highest time-averaged maximum velocity (TAMXV) of each tumor were recorded on the color prints in the study.

The pathologic findings were compared with those obtained from ultrasound. The sensitivity, specificity, positive predictive value, and negative predictive value were calculated (9). ANOVA test was used to compare the blood flow impedance between two groups. $P < 0.05$ was considered statistically significant.

RESULTS

Of the 78 patients enrolled in our study, 31 casses underwent myomectomy, 30 cases had hysterectomy, 14 cases received adenomyomectomy, and 3 cases were biopsied by surgery. Forty-two cases had leiomyoma(s) only. Thirty-one cases had adenomyosis only (including the three cases of adenomyoma), three patients had both adenomyosis and leiomyoma, and two cases had no pathologic diagnosis when using the histopathologic report as the standard of reference. The mean age among patients with adenomyosis was 40.1 ± 3.9 years, compared to 39.9 ± 5.3 years among patients with leiomyoma ($P > 0.05$). Transvaginal sonography with morphologic criteria correctly diagnosed the presence of adenomyosis in 27 patients (31 of 39 adenomyosis lesions [79%], a single lesion in 29 patients, and two lesions in 5 patients at pathology) and the absence in 35 patients (true negative). There were nine false-positives and seven false-negatives, resulting in a sensitivity of 79%, a specificity of 80%, a positive predictive value of 75%, and a negative predictive value of 83%. Regarding leiomyoma, sonography with morphological criteria depicted the presence of leiomyoma in 37 patients and excluded it in 26 (true negative). There were seven false-positives and eight false-negatives, therefore, yielding a sensitivity of 82%, a specificity of 79%, a positive predictive value of 84%, and a negative predictive value of 77% (Table I). A total of 68 lesions of leiomyoma was identified by the pathologist, and the sonographer correctly diagnosed 57 lesions (84%). The 11 lesions that had been omitted by sonography were mainly smaller than 2 cm and located in the fundus. There were single lesions in 27 patients, two lesions in 10 patients, and three lesions in 7 patients.

In 34 patients with adenomyosis, 30 cases were found to have randomly scattered vessels within uterine tumor or intratumoral signals on CDS (Fig. 1) and 41 cases were excluded (true negative). There were three false-positives and four false-negatives. The sensitivity was 88%, the specificity 93%, the positive predictive value 91%, and the negative predictive value 91%. A total of 39 cases was found to have outer

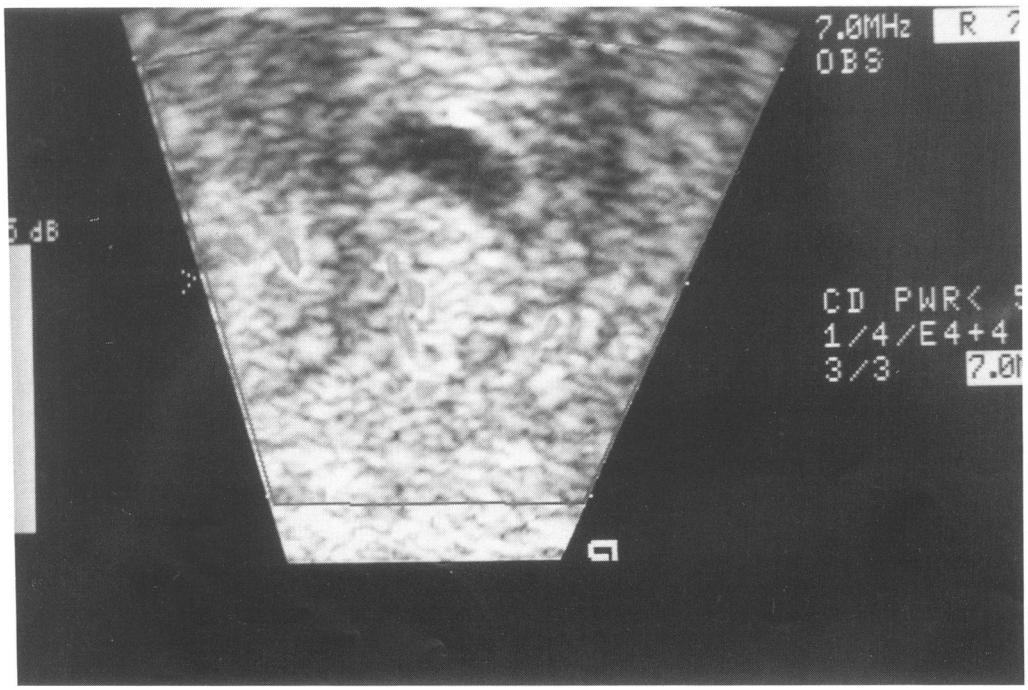

Fig. 1. Randomly scattered vessels or intratumoral signals with a characteristic myometrial cyst in adenomyosis was shown by color Doppler energy.

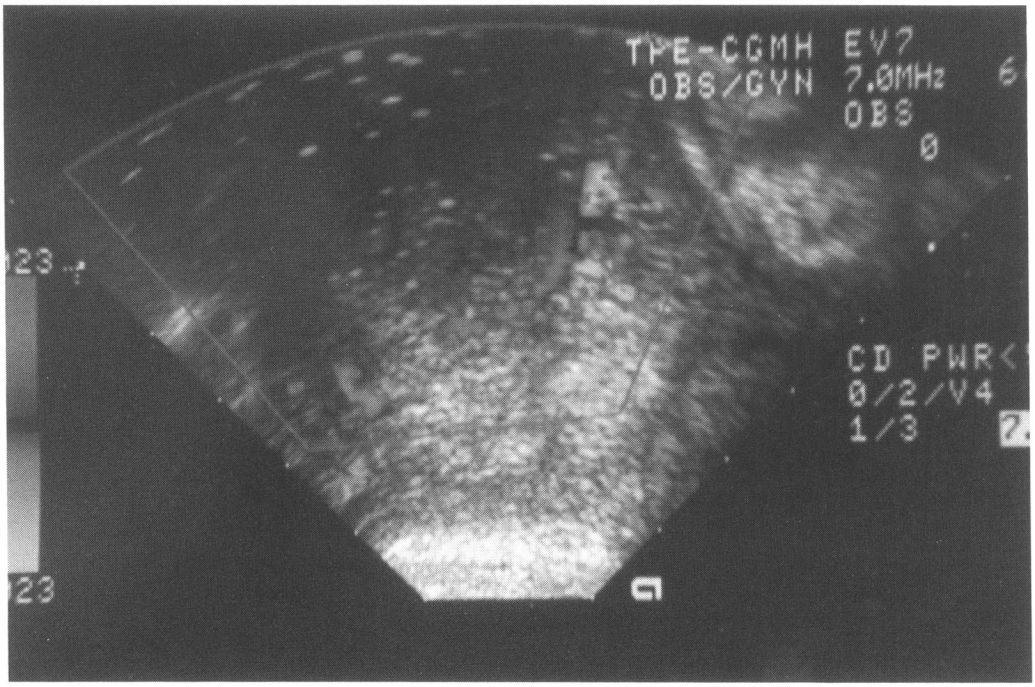

Fig. 2. Peripherally located vessels or outer feeding vessels around the leiomyoma were shown by TV-CDS.

feeding vessels on CDS (Fig. 2) of 45 patients with leiomyoma and 30 cases were absent (true negatives). Six cases were false-negatives and three cases false-positives. Thus, a sensitivity of 87%, a specificity of 91%, a positive predictive value of 93%, and a negative predictive value of 84% were noted (Table I).

All the parameters of blood flow impedance (PI, RI, and TAMXV) of arteries within or around the uterine tumors revealed a statistically significant difference between the two groups, especially the PI (Table II). The PI and RI tended to be lower for leiomyoma (PI mean, 1.00 ± 0.25; range, 0.55 to 1.81; RI mean, 0.63 ± 0.10; range, 0.43 to 0.85), as opposed to adenomyosis (PI mean, 1.52 ± 0.36; range, 1.0 to 2.61; RI mean, 0.76 ± 0.07; range, 0.6 to 0.88) (both P's < 0.0001). The TAMXV of outer feeding vessels of leiomyoma (mean, 10.0 ± 4.5 cm/sec; range, 4 to 28 cm/sec) was higher than that of intratumoreal vessels of adenomyosis (mean, 6.5 ± 3.3 cm/sec; range, 3 to 21 cm/sec)($P < 0.0001$) (Figs. 3 and 4). Using a cutoff value of PI >1.17 (approaching the median number of PI of all enrolled patients) resulted in a sensitivity of 82%, a specificity of 84%, a positive predictive value of 80%, and a negative predictive value of 86% for adenomyosis. Using a cutoff value of PI ≤1.17, there was a sensitivity of 84%, a specificity of 82%,

Table I. The Reliability Tests of Sensitivity, Specificity, Positive Predictive Value, and Negative Predictive Value with Each Criterion[a]

	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)
Adenomyosis				
Morphology	79	80	75	83
Blood flow impedance (PI of tumors >1.17)	82	84	80	86 tumor vascular
Pattern (intratumoral signals)	88	93	91	91
Leiomyoma				
Morphology	82	79	84	77
Blood flow impedance (PI of tumors ≤1.17)	84	82	86	80 tumor vascular
Pattern (outer feeding vessels)	87	91	93	84

[a] Tumor vascular pattern and blood flow impedance had a higher accuracy than morphology.

Table II. ANOVA of Blood Flow Impedance of Arteries Within or Around Uterine Tumors Between Adenomyosis and Leiomyoma.

	Adenomyosis (n = 34)	Leiomyoma (n = 45)	P value
Pulsitility index (PI)	1.52 ± 0.36	1.00 ± 0.25	<0.0001*
Resisting index (RI)	0.76 ± 0.07	0.63 ± 0.25	<0.0001
TAMXV (cm/sec)	6.5 ± 3.3	10.0 ± 4.5	<0.0001

* The P values of PI, RI, and TAMXV were 1.2E-10, 5.8E-09, and 3.2E-04, respectively. The PI was more significant than the RI and TAMXV among the Doppler indices.

a positive predictive value of 86%, and a negative predictive value of 80% for leiomyoma (Table I).

DISCUSSION

The differences between adenomyosis and leiomyoma was of critical importance in the decision of which treatment or surgery should be performed on patients of reproductive age or with infertility from a practical point of view. Because adenomyosis per se is not a treatable disease by conservative surgery, such a distinction could avoid unnecessary operation and benefit patients with leiomyoma. Several studies have shown promising results of the conception rate among infertility patients following myomectomy (10,11). However, difficulties of differentiation between leiomyoma and adenomyosis still exist.

Symptoms associated with adenomyosis or leiomyoma, including dysmenorrhea, abnormal menstrual cycles, lower abdominal pain, and infertility (12,13), were not specific enough to be used as diagnostic criteria. Many methods such as HSG, TAS, TVS, and MRI were included in previous studies that were done in an effort to diagnose adenomyosis nonsurgically (1). The use of HSG (cavitary lesions, spiculated patterns, and lollipop-like diverticuli on hysterograms) or TAS (5- to 7-mm cystic spaces that disrupted the normal echo patterns of the uterus) has been proven to be less effective due to its lack of diagnostic sensitivity and specificity (1,14–16). TVS has been proven to be a helpful tool in diagnosing diffuse adenomyosis, adenomyoma, and leiomyoma (2–5,17). The criteria for adenomyosis on TVS in previous reports and our data have yielded a sensitivity varying from 80% to 89%, a specificity of 74% to 98%, a positive predictive value of 71% to 81%, and a negative predictive value of 73% to 98.6% (2,3,5,17). The criteria for leiomyoma on TVS have yielded a sensitivity varying from 82% to 99%, a specificity of 79% to 96%, a positive predictive value of 83% to 91%, and a negative predictive value

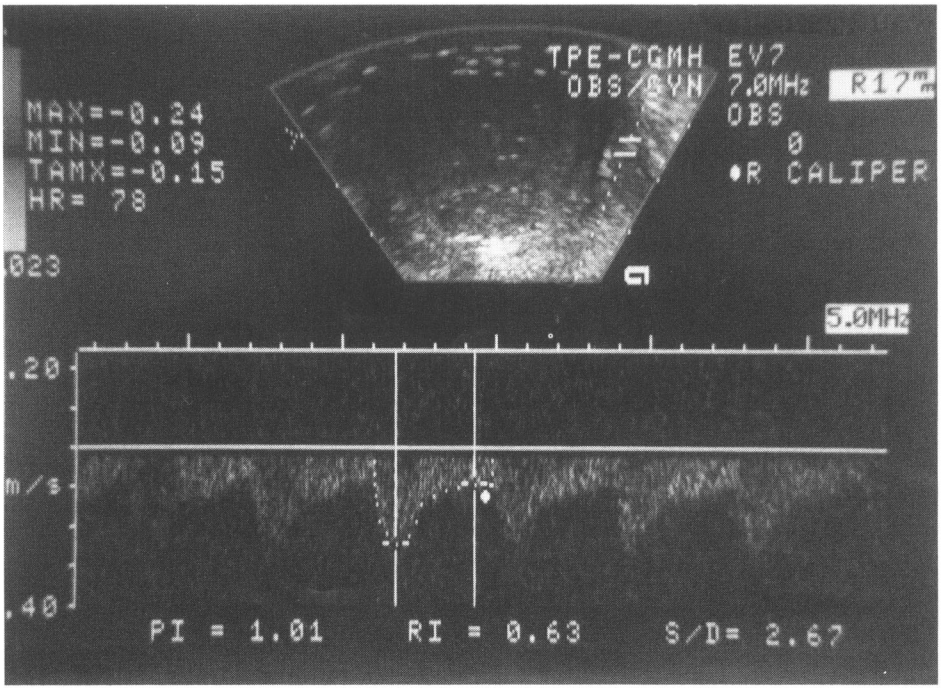

Fig. 3. The picture revealed that leiomyoma had a lower PI and RI and a higher TAMXV of outer feeding vessels than adenomyosis (by TV-CDS).

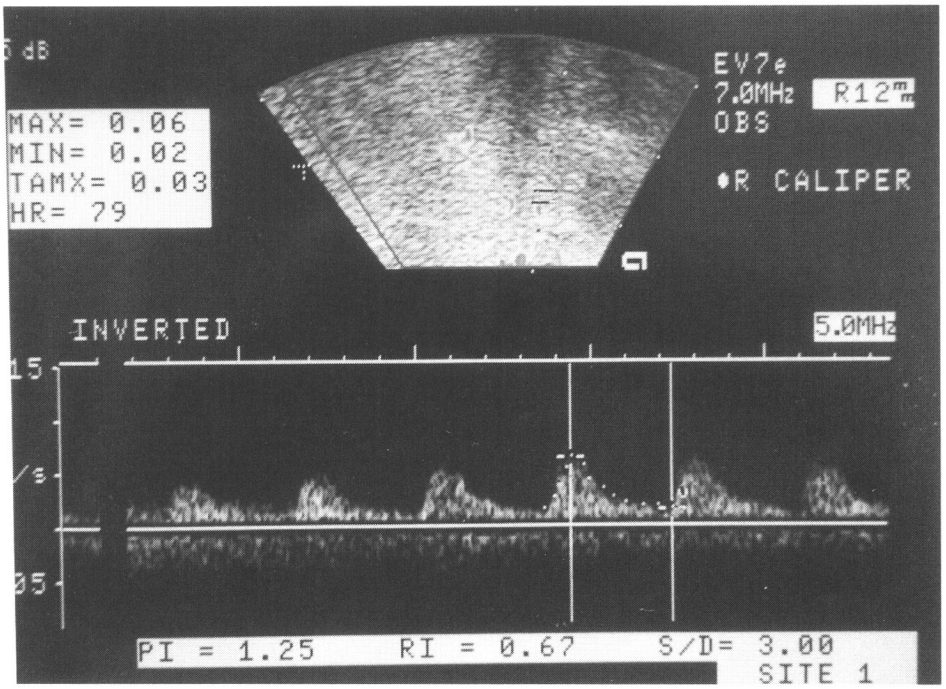

Fig. 4. Adenomyosis had a higher PI and RI and a lower TAMXV of intratumoral vessels than those of outer feeding vessels of leiomyoma (by color Doppler energy).

of 77% to 98% (3,18; our data). Although the results were acceptable, the differential diagnosis was difficult when the scanned uterine tumors showed an identical echotexture in cases of huge leiomyoma or adenomyosis, degenerated leiomyoma, coexisting leiomyoma and adenomyosis, or adenomyomas on TVS. Besides, the limited scanning distance of TVS made scanning of the entire uterus difficult in some cases.

A comparison between MRI and TVS has been discussed recently. Whether MRI was superior to TVS in diagnosing adenomyosis remained controversial due to the limited number of cases and the conflicting reports in the literature. Ascher *et al.* reported that MRI was significantly better ($P < 0.02$) than TVS in the diagnosis of adenomyosis in a prospective study of 20 cases (4). However, a prospective report with double-blind comparison between MRI and TVS by Reinhold *et al.* showed that the application of TVS in diagnosing adenomyosis was as good as that of MRI. The sensitivity and specificity were 89% for TVS and 86% for MRI. The positive predictive value was 71% for TVS and 65% for MRI. The negative predictive value was 96% for TVS and 95% for MRI (5). Furthermore, the medical cost and time-consuming procedures of MRI have made it impossible to use as a screening examination in practice. Therefore, TVS still could be a useful screening method to detect adenomyosis and leiomyoma.

The use of CDS has provided investigators new parameters such as blood flow impedance and power imaging, in addition to gray-scale ultrasonography. In the present study, TV-CDS could offer better resolution and more detailed information than TA-CDS, whereas TA-CDS has the advantage of scanning the uterus completely. Hirai *et al.* have demonstrated the possibility of using color techniques to diagnose adenomyosis and leiomyoma with characteristic vascular patterns, adenomyosis having intratumoral signals and 91% of leiomyomas showing one or two outer feeding arteries around the tumor (6). However, further discussion of the intratumoral signals of adenomyosis has not been given. We found that 30 of 34 cases of adenomyosis (88%) had intratumoral signals and 87% of leiomyomas had outer feeding vessels in the study. The sensitivity was 88%, the specificity 93%, the positive predictive value 91%, and the negative predictive value 91% for adenomyosis, and the sensitivity 87%, the specificity 91%, the positive predictive value 93%, and the negative predictive value 84% for leiomyoma, both with characteristic vascularity. The reliability was better than that using morphologic criteria alone. However, several studies have indicated that a small tumor

size and uterine contractions could affect the visualization of blood flow of leiomyoma (7,19).

Several studies have shown the relationships between blood flow impedance and uterine tumors, although some were contradictive (6–8,19–23). Hirai *et al.* found that pulsed and color Doppler analysis revealed no statistically significant difference between adenomyosis and leiomyoma with respect to RI and peak systolic velocity (V_{max}) (6). Sladkevicius *et al.* reported the PI of arteries in the wall and core of myomas (mean, 0.8 and 0.67, respectively) and concluded that Doppler measurement of blood flow velocity in tumor arteries did not add substantial information to the differential diagnosis between myomas and benign or malignant solid ovarian tumors (20). Recently, Alatas *et al.* reported that none of the uterine arteries Doppler indices could differentiate the myomatous uterus from the normal uterus (21). However, Kurjak *et al.* have shown that increased blood velocity and decreased RI and PI in both uterine arteries occurred in patients with uterine fibroids (22). Sladkevicius *et al.* conclude that uterine myomas substantially affect blood flow velocity in the uterine arteries and that PI values <1.0 are common in uterine myomas (23). Moreover, Huang *et al.* demonstrated that intratumoral PI values (mean, 0.88; range, 0.2550–1.533) showed a negative correlation with the sizes of myomas (8). In the present study, PI of the arteries within or around the uterine tumor was more powerful than RI and TAMXV among the Doppler indices. Adenomyosis had higher intratumoral PI and RI and lower TAMXV values than those of outer feeding vessels of leiomyoma. Using a PI of intratumoral arteries >1.17 as the criterion for adenomyosis resulted in a sensitivity of 82%, a specificity of 84%, a positive predictive value of 80%, and a negative predictive value of 86%. Using a cutoff value of the PI of outer feeding vessels ≤ 1.17, there was a sensitivity of 84%, a specificity of 82%, a positive predictive value of 86%, and a negative predictive value of 80% for leiomyoma. Using the PI of arteries within or around uterine tumors had a better accuracy than using morphologic criteria alone.

CONCLUSIONS

In summary, in addition to the morphological criteria from TVS, the tumor vascular pattern and blood flow impedance of uterine tumors detected by CDS could increase the accuracy of diagnosing adenomyosis and leiomyoma. Recently, the application of three-dimensional color Doppler energy showed the tumor vascular patterns in a three-dimensional manner that was more clear and more comprehensive to the investigators. The differential diagnosis between adenomyosis and leiomyoma might be easier with three-dimensional reconstructed ultrasound angiography using the characteristic vascular pattern.

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