ABSTRACT

Transvaginal color and pulsed Doppler ultrasound depicts the endometrium in great details. The texture and thickness of the endometrium are indicators of endometrial development, while blood flow analysis may be used as a bioassay of the uterine receptivity. This method can non-invasively detect uterine anomalies, endometrial polyps, submucous leiomyomas, intruterine adhesions and other uterine causes that can lead to poor reproductive performance. Vascularization of the uterine tumors, if used together with analysis of morphology and size, can increase our accuracy in differentiation between uterine sarcoma and leiomyoma. It seems that the multiparameter sonographic approach, which includes morphology and size depicted by transvaginal ultrasonography and color flow imaging with pulsed Doppler analysis of neovascular signals, can help in diagnosis of uterine sarcoma in high-risk groups such as postmenopausal patients with a rapidly enlarging uterus. Therefore, serial measurements are recommended for evaluation of the myometrial density, follow-up of the tumoral growth, and detection of the impedance to blood flow. Only such complex observations can lead to proper diagnosis of these rare tumors with unpredictable prognosis. The application of transvaginal color Doppler to the postmenopausal population for screening of endometrial carcinoma may be a viable option if combined with ovarian screening in the same scan. In this way, the capital costs would be shared, and an oncological preventive medicine for women could be created. The use of this technique could also result in a reduction in dilatation and curettage operations with considerable saving of both the potential risks and economic costs of the operation.

**Key words:** endometrial lesions, myometrial tumors, transvaginal sonography, transvaginal color Doppler

INTRODUCTION

The aim of this review is to investigate the role of color Doppler and three-dimensional ultrasound in the evaluation of the uterine lesions. Morphological and vascular criteria assessed by different forms of ultrasound are listed for each type of the uterine lesion.

The uterus lies in the middle of the pelvis with its long axis perpendicularly to the ultrasound probe. Using two-dimensional ultrasound the examination of the uterine lesions is limited to transverse and sagittal planes, which give an inadequate view of the uterus and uterine pathology. Three-dimensional ultrasound provides simultaneous display of coronal, sagittal, and transverse planes. Volume data can be viewed using a standard anatomic orientation demonstrating entire volume and continuity of curved structures in a single image. More accurate evaluation of numerous sections through the studied organ becomes possible due to not limited number and the orientation of reformatted planes. When three perpendicular planes are simultaneously displayed on the screen, sagittal plane is chosen for volume measurements, while the other two planes are used to ensure that the entire pathology is included in the measurement. Surface rendering mode allows exploration of the outer or inner contour of the lesion, while “niche aspect” presents detection and analysis of the selected sections of the uterine lesion. Three-dimensional ultrasound offers improved visualization of the lesions, more accurate volume estimation, retrospective review of stored data, assessment of tumor invasion, and using rendered images it can identify more accurately location of abnormalities needing surgical intervention.

Three dimensional sonohysterography is very useful in the evaluation of the uterine cavity and is more useful than hysterosonography by two-dimensional transvaginal ultrasound in cases of submucous myomas and polyps.
The three-dimensional power Doppler system improves the information available on normal and abnormal (tumoral) vascularity, enabling visualization of the overlapping vessels and assessment of their relationship to other vessels or surrounding tissue. Power Doppler ultrasound compared to standard color Doppler has the advantage of more sensitivity to low velocity flow overcoming the angle dependence and aliasing. Using contrast agents it is possible to enhance the 3-D power Doppler examination rate of small vessels.

In this chapter we will compare findings of uterine lesions assessed with conventional B-mode and transvaginal color Doppler ultrasound on one side and three-dimensional and power Doppler ultrasound on the other.

NORMAL UTERUS

Two-dimensional ultrasound imaging of the uterus is limited due to the movement of the transducer allowing sagittal and transverse planes through the uterus. Three-dimensional sonography permits multiplanar display of all three perpendicular sections: coronal, sagittal, and transverse plane. The coronal plane of the uterus enables to visualize both horns of the endometrium and the cervix at the same time. The normal uterus is usually presented by a convex shape of the endometrium and myometrium in the fundus. Blood vessels of the uterus and endometrium can be detected by color and power Doppler ultrasound where endometrium and myometrium constitute an anatomical and functional unit. Uterine arteries branch off the internal iliac arteries. Ultrasonically, they look like hyperechoic structures running along the cervix and the isthmic part of the uterus. Arcuate arteries are tortuotic anechoic structures that spread through myometrium. Radial arteries penetrate vertically the myometrial layers of smooth muscle cells. Spiral arteries supply stratum functional of endometrium. Their shape and size change during menstrual cycle and they shed during menstruation together with the glandular tissue. During pregnancy, these arteries become uteroplacental decidual arteries. Basal arterioles supply endometrial stratum basale. They do not change during menstrual cycle. Color Doppler research has determined that every blood vessel in the body has its own typical waveform. This waveform changes under the influence of hormones, ischemia, internal or external vasoactive factors. The vessels in genital tract undergo cyclic changes dictated by the hormonal cycle. During the menstrual phase, due to hormonal deprivation and alterations in the spiral arteriolar system, spiral arterioles undergo increased coiling and cause a circulatory stasis which lead to tissue ischemia. Vasocostriction of the spiral arterioles and necrosis of their walls result in bleeding. Anechoic areas that are sometimes visualized indicate endometrial breakdown. Later on, a mixed appearance with anechoic area (indicating blood) and hyperechoic parts (exfoliated endometrium and clots) can be observed. During the late menstrual phase, the endometrium appears sonographically as a thin, single-line, slightly irregular echogenic interface. In this phase, the uterine artery shows high resistance index. In the early follicular phase, the endometrium is imaged as a hyperechoic line with endometrial thickness of less than 5 mm, but is not always possible to visualize the endometrial-myometrial junction. As the ovulation approaches, the glands become numerous and the expected endometrial thickness is about 10 mm. A triple-line endometrium is typical of the periovulatory phase. The hyperechoic echo that represents the endometrial-myometrial junction becomes more prominent and does not produce posterior enhancement. The central echogenic interface probably represents refluxed mucus. Doppler velocimetry of the spiral arteries shows progressive diminution of resistance indices. Secretory phase is characterized by hyperechoic and homogenous endometrium with a loss of the triple-line morphology and surrounding anechoic halo. During this phase of the cycle the ultrasonographic image of the endometrium shows increased echogenicity with respect to the myometrium. The interface of the myometrium with the endometrium is still visible as a hypoechoic zone. Maximum echogenicity is seen in the mid-luteal phase, when the endometrium appears homogenously hyperechoic. Posterior enhancement is a sonographic characteristic of this phase. Doppler velocimetry demonstrates further decrease of the vascular resistance in uterine and spiral arteries being the lowest in the mid-luteal phase.

Since changes in the texture and volume of the endometrium can be precisely observed using three-dimensional ultrasound, and retrospectively reviewed or consulted with colleagues, this method may become a method of choice for scanning endometrial pathology in multitude of clinical conditions.
ENDOMETRIAL POLyps

Endometrial polyps develop as solitary or multiple, soft, sessile and penduculated tumors containing hyperplastic endometrium (1, 2). Clinically, asymptomatic or symptoms like infertility, bleeding, infection, endometritis or pain are usually present in patients with endometrial polyps. Ultrasonographic appearance of endometrial polyps is best imaged during the early proliferative phase of the menstrual cycle or during the secretory phase after injection of a negative contrast medium into the uterine cavity. The vascularization of polyps is supported by already existing vessels originating from terminal branches of the uterine arteries assessed by transvaginal color Doppler ultrasound. It is possible to identify flow in regularly separated vessels and analyze the velocity of blood flow through them. The resistance index is moderate, usually higher than 0.45 (1, 3). Infection or necrosis of polyps may lower the impedance to blood flow (RImin=0.37). The importance of endometrial polyps lies in the fact that marked reduction in blood flow impedance noted on the periphery and/or within the endometrial polyps may lead an inexperienced ultrasonographer to a false positive diagnosis of endometrial malignancy.

Tamoxifen is a non-steroidal antiestrogen that is widely used in the hormonal therapy of breast cancer. However, the weak estrogen-like effect that tamoxifen has on the endometrium is a cause of great concern. Patients using tamoxifen should, therefore, be monitored at regular intervals, since several studies have described cases of endometrial cancer associated with this therapy. A wide spectrum of pathological uterine findings has been described in association with long-term tamoxifen therapy at a dose of 20 mg/day (4). These findings include epithelial metaplasia, simple and atypical hyperplasia, endometrial polyps and endometrial carcinoma (5). Endometrial changes are characterized sonographically by abnormal endometrial thickening and non-homogeneous hyperechogenicity, with multiple, small cystic structures. At least three studies have indicated that tamoxifen treatment in postmenopausal breast cancer patients is associated with a high incidence of endometrial polyps (6-8). Achiron and colleagues (7) found that a peculiar endometrial honeycomb appearance, manifested on gray-scale transvaginal sonography, occurred in 44% of this population, and was associated with the same high incidence (40%) of endometrial polyps. The effect of tamoxifen on endometrial blood flow is less evaluated. Achiron and his group described blood flow changes in the endometrial and subendometrial regions. In asymptomatic postmenopausal patients receiving tamoxifen whose endometrial thickness was less than 5 mm, increased endometrial blood flow with significant reduction of the resistance index compared to untreated, control menopausal women was reported. Another study by the same authors (5) found that women with thick endometrium, and particularly those with endometrial polyps, presented a significantly lower RI, compared to those with thin endometrium (mean RI of 0.39 versus 0.79). The RI values returned to normal following resection of the endometrial polyps, thus supporting a benign transitory effect of long-term tamoxifen therapy on the endometrium.

The data from Goldstein et al. (9) suggest that the objective assessment of blood flow impedance (resistance index, pulsatility index) in endometrial polyps and the size of these polyps cannot replace surgical removal and pathologic evaluation to predict histologic type. Patients with nonfunctional polyps were older and less likely to have vaginal bleeding. Perez-Medina et al. (10) evaluated the efficacy of color Doppler exploration for assessing atypia inside endometrial polyps (polyp stalk). Thirty-five polyps (out of 106) with sonographic indications of atypia were pathologically confirmed. Sonographic indications of atypia inside 16 polyps were not confirmed. Three non-questionable endometrial polyps had atypia inside them. They conclude that low Doppler resistance (RI<0.50) is highly predictive of atypia inside endometrial polyps.

Three-dimensional hysterosonography can better visualize the uterine cavity and the endometrial thickness than with transvaginal sonography, transvaginal sonohysterography, transvaginal color Doppler, or hysteroscopy according to Bonilla-Musoles et al (11). Using the multiplanar views polypoid structures can be nicely visualized, allowing for the optimal plane to present their pedicle. Surface rendering mode can suppress undesirable echoes allowing seeing the polypoid structure in continuity with the endometrial lining (12).

Gruboec et al. (13) performed the measurements of endometrial thickness assessed by conventional 2-D ultrasound and endometrial volume assessed with three-dimensional ultrasound in symptomatic postmenopausal patients and they compared the results. The endometrial thickness was similar in patients with endometrial hyperplasia and polyps, but the endometrial volume in hyperplasia was significantly higher than the volume
in patients with polyps. In conclusion, the difference between endometrial hyperplasia and polyps cannot be detected by the measurement of endometrial thickness, but with 3-D volume measurement. Polyps are localized thickenings of the endometrium not affecting the whole of the uterine cavity, and therefore their volume is much smaller, while the maximum thickness is similar to that of hyperplasia. The volume measurement is performed using longitudinal plane delineating the whole of the uterine cavity in a number of parallel longitudinal sections 1-2 mm apart. Then, the endometrial volume is calculated automatically by the in-built computer software program.

**INTRAUTERINE SYNECHIAE (ADHESIONS)**

Destruction of the basal layer of the endometrium may result in scarring and development of bands of scar tissue (synechiae) in the uterine cavity. This damage of endometrium may occur as a result of a too vigorous curettage of an advanced pregnancy. Tuberculosis may also cause uterine adhesions. Menstrual pattern is characterized by amenorrhea or hypomenorrhea. Ultrasound scan of a patient with Asherman’s syndrome shows a mixed picture: in some parts of uterine cavity no endometrium can be visualized, and in others the endometrium appears normal. If there are adhesions in the uterine cavity, they are visualized as hyperechoic bridges. Intrauterine adhesions do not display increased vascularity on color Doppler examination. They are better visualized during menstruation when intracavitary fluid outlines them. The second option is sonohysterography. Sonohysterography performed with 3-D ultrasound has several advantages over that with conventional 2-D ultrasound. It gives more accurate information about the location of abnormalities which is very important for preoperative assessment and distinguishing pathologies. Furthermore, the uterus is for shorter time distended compared to the time necessary for 2-D exams which results in better patients’ acceptance. However, according to Momtaz et al. (14) in cases of intrauterine adhesions, the use of echogenic contrast media (e.g. Echovist, Schering) is more accurate than saline-contrast 3-D sonohysterography. Intrauterine synechiae can be accurately visualized on both multiplanar and rendered imaging traversing the uterine cavity (12). Weinraub et al. (12) concluded that surface rendering in cases of equivocal signals confirmed their presence, appearance, actual size, volume, and relationship to the surrounding structures.

Three-dimensional ultrasound is helpful in delineation of intracavitary adhesions and determination of their location which assists in surgical planning. In the cases of bridging adhesions, the degree of cavity obliteration is accurately assessed. Similarly, this technique is beneficial for differentiation between small polyps and adhesions.

**ADENOMYOSIS**

Adenomyosis of the uterus is a condition in which clusters of endometrial tissue in grow into the myometrium. It may be localized close to endometrium, or it may extend through the myometrium and serosa. Adenomyosis affects 20% of women, mainly multiparous. The uterus can be normal-sized or enlarged with symptoms such as dysmenorrhea, pelvic pain and menometrorrhagia. Two-dimensional ultrasound findings include “Swiss cheese” appearance of the myometrium due to areas of hemorrhage and clots within the muscle). Disordered echogenicity of the middle layer of the myometrium is usually present in severe cases. Sometimes the uterus is generally hypoechoic, with the large cysts rarely seen. Using hysterosonography contrast medium penetrates the myometrium. Color Doppler characteristics present increased vascularity by moderate vascular resistance within the myometrium (RI=0.56±0.12), while the RI of the uterine arteries show a decreased value compared to controls (15). Statistically significant differences exist between adenomyosis and uterine malignancies in both RI and maximum velocity. However, no significant difference was noted between adenomyosis and myoma in the RI but a slight difference was observed in the maximum velocity (16).

In some cases, transonic areas may not represent adenomyosis, but prominent vessels, or other conditions which give rise to hyperemia. Lee et al. (17) performed the study which confirmed the superiority of 3-D power Doppler sonography compared to transvaginal color Doppler ultrasound in the detection of flow in the areas of adenomyosis. Women with a provisional diagnosis of adenomyosis, listed for hysterectomy were studied. Gray scale ultrasound was first used to screen for the presence of adenomyosis using predetermined ultrasound criteria. Then 3-D power Doppler sonography
of adenomyotic areas was performed. Ultrasound findings such as distribution of vessels and pattern of flow in adenomyotic foci were compared with histological results. The same method was used for tracing regular vessels’ course in this abnormality. Using 3-D PDS the authors were able to demonstrate the perfusion in adenomyotic foci as well as the vessels’ distribution and their branching pattern.

ENDOMETRIAL HYPERPLASIA

The endometrial thickness in postmenopausal women is no more than a thin line of 1-3 mm. Abnormal endometrial thickness may be detected in some benign uterine conditions, as well as in the endometrial malignancy. Endometrial thickness greater than 14 mm in premenopausal and greater than 5 mm in postmenopausal women should be further investigated (1). Using B-mode transvaginal sonography alone it is not possible to distinguish endometrial hyperplasia from carcinoma. More accurate diagnosis of endometrial pathology can be obtained by color and pulsed Doppler sonography (2, 3). Color Doppler findings characteristically for endometrial hyperplasia include peripheral distribution of the regularly separated vessels with resistance index significantly higher (mean RI=0.55±0.05) than in carcinoma (mean RI=0.42±0.02) (18). However, reliable differentiation between endometrial hyperplasia and carcinoma is not possible due to an overlap in the endometrial thickness measurements, as well as to controversial results of blood flow measurements assessed by transvaginal color Doppler ultrasound. Since there is a positive correlation between arterial blood flow impedance and number of years from menopause (19), one can estimate the risk of uterine malignancy in postmenopausal patients with decreased vascular resistance.

Emoto et al. (20) examined the usefulness of transvaginal color Doppler ultrasound in differentiating between endometrial hyperplasia and endometrial carcinoma and in predicting tumor spread in patients with carcinoma. No significant difference was found in the mean value of endometrial thickness between patients with hyperplasia (n = 18 patients; 16.2 mm +/- 15.9 mm) and patients with carcinoma (n = 53 patients; 18.7 mm +/- 17.1 mm). Intratumoral blood flow was detected in significant number of patients who had endometrial carcinoma (71.7% 38 of 53 patients) compared with patients who had endometrial hyperplasia (5.6%; 1 of 18 patients; P < 0.0001). Thus, no patients with hyperplasia showed any blood flow in the endometrial lesions, transvaginal color Doppler may be more useful in differentiating between endometrial hyperplasia and carcinoma than measuring endometrial thickness by transvaginal gray-scale sonography. For patients with carcinoma, the detection of intratumoral blood flow may be helpful in distinguishing between low-grade and high-grade tumors and predicting myometrial invasion. However, intratumoral blood flow analysis using RI, PI, or PSV may not be useful for predicting tumor spread before surgery.

Jarvela et al. (21) evaluated the possible hemodynamic changes in uterine blood flow using transvaginal color Doppler ultrasonography after thermal balloon endometrial ablation therapy. Thermal balloon endometrial ablation therapy induces a rise in uterine blood flow impedance, but not until 6 months after the treatment. The rise in impedance may be due to fibrosis in the uterine cavity which thermal balloon therapy has been shown to produce.

More recently, with the aid of three-dimensional ultrasound, endometrial volume measurements became possible. According to Gruboeck et al. (13), endometrial volume was successfully measured in 94.2% of patients, while in others the presence of anterior uterine wall myomas caused acoustic shadowing on 3-D records. The volume of the endometrium was measured by delineating the uterine cavity on parallel longitudinal sections 1-2 mm apart. The sections were added together using in-built computer software to calculate the volume. The endometrial volume was significantly lower in patients with benign pathology such as hyperplasia (mean 8.0 ml, SD 7.81 ml) than in patients with endometrial carcinoma (mean 39.0 ml, SD 34.16 ml). Normal endometrial volume in this study was 0.9 ml (SD 1.72 ml).

Our group reported on the use of 3-D power Doppler sonography in patients with endometrial hyperplasia (21). We were able to demonstrate regularly separated vessels at the periphery of the examined endometrium. Bonilla-Musoles et al. suggest that in patients on hormone replacement therapy or tamoxifen, 3-D sonohysterography allowed for differentiation of normal proliferative from hyperplastic endometrium (11).
ENDOMETRIAL CARCINOMA

Endometrial carcinoma is the most common gynecological malignancy in many countries with the reported incidence of about 10% in postmenopausal patients presenting uterine bleeding. Early transabdominal sonographic investigations have demonstrated that increased endometrial thickness is associated with endometrial neoplasms in postmenopausal women, but the quality of transabdominal sonographic images is affected by obesity, retroversion of the uterus, and an unfilled bladder, factors that do not influence transvaginal sonographic visualization of the endometrium. Ultrasound findings assessed by conventional B-mode sonography include increased endometrial thickness >5 mm in postmenopausal women or >8 mm in perimenopausal women, hyperechoic endometrium, free fluid in the cul-de-sac, intrauterine fluid or possible invasion in patients with disrupted endometrial-subendometrial layer. In addition, color and pulsed Doppler improves diagnostic accuracy, because the endometrial carcinoma shows abnormal blood flow due to tumor angiogenesis (22). Endometrial blood flow is absent in normal, atrophic and most cases of endometrial hyperplasia, while, according to our investigation (18) in 91% of the cases of endometrial carcinoma areas of neovascularization were demonstrated as intratumoral or peritumoral (Figure 1). Neovascular signals from the central parts of the lesion demonstrate low vascular resistance (RI=0.42±0.02), while increased vascularity signals surrounding the lesion are suspected for invasion. If the myometrial vessels are invaded, low vascular resistance is detected due to incomplete or absent membrane and leaky structure.

Conventional 2-D ultrasound measurements of endometrial thickness have disadvantages in distinguishing patients with benign and malignant endometrial pathology due to varying thickness, and interference of other pathology like polyps or hypoplasia.

In distinguishing cancer from benign pathology endometrial volume measurements assessed by 3-D ultrasound seems to be more helpful. Gruboeck et al. (13) compared endometrial thickness and volume in patients with postmenopausal bleeding and examined the value of each parameter in differentiating between benign and malignant endometrial pathology. Each patient underwent three-dimensional ultrasonography for the measurement of endometrial thickness and volume. The results were compared to the histological diagnosis after endometrial biopsy or dilatation and curettage. The mean endometrial thickness in patients with endometrial cancer was 29.5 mm (SD 12.59) and the mean volume was 39.0 ml (SD 34.16). The optimal cut-off value of endometrial thickness for the diagnosis of cancer was 15 mm, with the test sensitivity of 83.3% and positive predictive value of 54.4%. With a cut-off level of 13 ml, the diagnosis of cancer was made with the sensitivity of 100%. One false-positive result in a patient with hyperplasia gave a specificity of 98.8% and positive predictive value of 91.7%. According to Gruboeck et al. (13) the endometrial volume was significantly higher in patients with carcinoma than those with benign lesions. The measurements of endometrial volume were superior to that of endometrial thickness as a diagnostic test for the detection of endometrial cancer in symptomatic postmenopausal women. Increasing volume size is associated with the severity or higher grade of the endometrial carcinoma, and also with progressive myometrial invasion. The depth of myometrial invasion showed positive correlation with both endometrial thickness and volume. Only patients with tumor volume larger than 25 ml had evidence of pelvic node involvement at operation.

Bonilla et al. (11) suggest that 3-D hysterosonography allowed for better visualization of myometrial invasion, playing a significant role in staging malignant tumors in the future. Using simultaneous display of the transverse plane with 3-D ultrasound it is possible to detect infiltration of cervical or endometrial carcinoma into the bladder or rectum.

In our study (23), apart from endometrial volume, other 3-D sonographic and power Doppler criteria for the
diagnosis of endometrial malignancy included suben- 
dometrial hallo, irregularity, presence of the intracavi-
tary fluid, chaotic vessel’s architecture and branching 
pattern (Table 1). In patients with endometrial carci-
noma, mean endometrial volume was 37.0±31.8 ml 
(Table 2). The endometrial volume in hyperplasia had 
the mean value of 7.8±7.60 ml and was significantly 
higher than the volume in patients with polyps (mean 
2.63±2.12 ml). In patients with normal or atrophic 
enodemtrial the mean value was 0.8±1.51 ml. Suben-
dometrial hallo was regular in all patients with benign 
enodemtrial pathology, whereas 8 out of 12 patients with 
enodemtrial carcinoma had irregular endometrial-my-
ometrial border. Intracavitary fluid was present in 4 pa-
tients with benign endometrial lesions and in 5 patients 
with endometrial malignancy. Dichotomous branching 
and randomly dispersed vessels were detected in 91.67 
% of the patients with endometrial carcinoma, while 
single vessel arrangement and regular branching were 
typical for benign lesions. Three-dimensional PDS ac-
curately detected structural abnormalities of the malig-
nant tumor vessels such as microaneurysms, arterio-
venous shunts, tumoral lakes, elongation and coiling. 
Combining morphological and power Doppler criteria,
the diagnosis of endometrial carcinoma had a sensitiv-
ity of 91.67 %. One false positive result was obtained 
in a patient with endometrial hyperplasia and one false 
negative in a patient with endometrial carcinoma re-
ceiving tamoxifen therapy. In this case endometrial le-
sion demonstrated regularly separated peripheral ves-
sels was falsely interpreted as hyperplasia. 
Kupesic et al. (24) performed staging of endometrial 
carcinoma by 3-D power Doppler. The objective of this 
study was to evaluate the accuracy of three-dimensional 
power Doppler in determining the depth of myometrial 
invasion in patients with proved adenocarcinoma of the 
enodemtrium, relative to the amount of myometrial in-
vation measured in hystopathological analysis (Table 
3). Thirty-four patients with hystologically proved ade-
nocarcinoma of the endometrium were analyzed. Deep 

| Table 1 Three-dimensional sonographic and power Doppler criteria for the diagnosis of endometrial malignancy (From reference 23, with permission) |
|---------------------------------|-----------------|
| 3-D sonographic and pozer Doppler criteria | Score |
| Endometrial volume | < 13 ml | 0 |
| 13 ml | 2 |
| Subendometrial hallo | Regular | 0 |
| Disturbed | 2 |
| Intracavitary fluid | Absent | 0 |
| Present | 1 |
| Vessel's architecture | Linear vessel arrangement | 0 |
| Chaotic vessel arrangement | 2 |
| Branching pattern | Simple | 0 |
| Complex | 2 |
| **TOTAL SCORE** | | |

Table 2 Volume and vascularity of the endometrial lesions (N=57) obtained by 3-D PDS (From reference 23, with permission)

<table>
<thead>
<tr>
<th>HISTOPATHOLOGY</th>
<th>V (SD) ml</th>
<th>Regular endometrial hallo (%)</th>
<th>Intracavitary fluid (%)</th>
<th>Neovascular signals (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal and/or atrophic endometrium</td>
<td>10</td>
<td>0.8 (1.51)</td>
<td>100</td>
<td>20.00</td>
</tr>
<tr>
<td>Endometrial hyperplasia</td>
<td>27</td>
<td>7.82 (7.60)</td>
<td>100</td>
<td>37.00</td>
</tr>
<tr>
<td>Endometrial polyp</td>
<td>28</td>
<td>26.2 (2.12)</td>
<td>100</td>
<td>35.71</td>
</tr>
<tr>
<td>Endometrial carcinoma</td>
<td>12</td>
<td>37.0 (31.8)</td>
<td>66.67</td>
<td>41.67</td>
</tr>
</tbody>
</table>

myometrial invasion (>50 %) was present at postopera-
tive histology in 5/22 (22.73 %) women, while superfi-
cial was reported in 17/22 (77.23 %). Three-dimen-
sional power Doppler demonstrated a sensitivity of 100 
% (5/5) and a specificity of 94.44 % (17/18) for deep in-
vasion, with a positive predictive value (PPV) of 83.33 
% (5/6) and a negative predictive value (NPV) of 100 
% (17/17). In only one patient with adenomyosis, inva-
sion was overestimated by 3-D power Doppler. Data 
showed acceptable accuracy in determining the depth 
of myometrial invasion in patients with adenocarcino-
ma. Three-dimensional power Doppler can potentially 
detect lesions that require aggressive intervention and 
thus direct to proper treatment.

Lee et al. (25) evaluated the relationship between blood 
flow in the tumor assessed by color Doppler ultrasound, 
microvessel density immunohistochemically, and vas-
cular endothelial growth factor levels in endometrial 
carcinoma. Significantly lower RIs were noted in tu-
mors of stage II or greater (0.37 compared with 0.50, 
P <.001), of high histologic grade (grade 3) (0.34 com-
pared with 0.49, P = .004), with deep myometrial inva-
sion (one-half depth or greater) (0.39 compared with 
0.49, P =.002), with lymphovascular emboli (0.38 com-
pared with 0.49, P <.001), or with lymph node meta-

| Table 3 Invasion of endometrial carcinoma assessed with the aid of 3-D PDS (From reference 24, with permission) |
|-----------------|---------|---------|
| Invasion | 3-d pozer doppler | Pathhistology |
| Superficial * | 17 | 18 |
| Deep ** | 5 | 4 |

* Invasion into less than a half of the total myometrial thickness
** Invasion into more than a half of the myometrial thickness

Kupesic et al. US of uterine malignancies
sis (0.30 compared with 0.49, \(P < .001\)) compared with stage I tumors and tumors of histologic grade 1 or 2, with superficial myometrial invasion, without lymphovascular emboli, or with no lymph node metastasis. Increased vascular endothelial growth factor levels and microvessel density also were detected in tumors of stage II or greater, with lymphovascular emboli, or with lymph node metastasis. Resistance index, microvessel density, and vascular endothelial growth factor levels in the tumor showed linear correlations. Blood flow assessed by color Doppler ultrasound has histologic and biologic correlations with angiogenesis and vascular endothelial growth factor levels and might play an important role in predicting tumor progression and metastasis in endometrial carcinoma.

Alcazar et al. (26) correlated intratumoral blood flow as assessed by transvaginal color Doppler ultrasound (resistance index and peak systolic velocity) with tumor histopathologic characteristics, tumor stage, and risk for recurrence in endometrial carcinoma. Significantly lower RI was found in tumors with the following characteristics: infiltrative growth pattern, grade 3, infiltrating greater than or equal to 50% of the myometrium, cervical involvement, lymph-vascular space invasion, lymph-node metastasis, stage greater than or equal to Ic, and high risk for recurrence. Significantly higher PSV was found in tumors that were grade 3, infiltrating greater than or equal to 50% of the myometrium, stage greater than or equal to Ic, and with a high risk for recurrence. Their data indicate that a correlation between intratumoral blood flow features and histopathological characteristics, tumor stage, and risk for recurrence exists in endometrial cancer.

Yaman et al. (27) evaluated the reproducibility of transvaginal three-dimensional (3D) endometrial volume measurement in patients with postmenopausal bleeding and compared the reproducibility of this technique to that of two-dimensional (2D) endometrial thickness measurement. Endometrial volume and thickness measurements by 3D and 2D ultrasound, respectively, show good reproducibility but the reproducibility of 3D ultrasound is better.

LEIOMYOMA

Leiomyomas are the most common tumors of the female pelvis and occur in 20-25% of women of reproductive age, arising from the smooth muscle and soft tissue of the uterine fundus and corpus, while 3% originate from cervix (28). Myomas are usually multiple and of various sizes. Intramural tumors are the most common, while the submucosal are the least common. If they extend outward, they become either pedunculated or subserosal (29). Symptoms of submucous leiomyomas include metrorrhagia, pelvic pain or infertility, whereas most subserosal leiomyomas are asymptomatic.

On the gray-scale ultrasound the uterine leiomyomas may be represented with uterine enlargement, distortion of the uterine contour, and varying echogenicity depending on the amount of connective or smooth muscle tissue.

Transvaginal color Doppler sonography demonstrates vascularization on the periphery of the myoma of uterine origin, with the RI of \(0.54 \pm 0.08\), allowing better delineation of the tumor. Blood vessels in the central part of the myoma in case of necrosis, inflammation or other degenerative changes demonstrate lower RI. Uterine arteries present lower impedance to blood flow in patients with myomas (RI=0.74±0.09) compared to normal (RI=0.84±0.09) (30).

Using simultaneous display of three perpendicular planes assessed by 3-D ultrasound demonstrates the accurate location of myomas, size, and its relationship to the endometrium that is very important in therapy planning. Patients receiving medical therapy such as gonadotropin-releasing hormone may be followed with serial 3-D ultrasound scans to estimate myoma size and effectiveness of the therapy. Hysterosonography by 3-D ultrasound is valuable in obtaining submucosal myomas (11, 12, 31, 32). Balen et al. (31) found that 3-D ultrasound and sonohysterography was useful in demonstrating the position of submucosal myomas. They studied both saline and a positive ultrasound contrast agent (Echovist) and found the positive contrast superior when looking at the cavity wall. Weinraub et al. (12) found that the negative contrast was better for evaluating the accurate contents of the uterine cavity delineating of the outer surface of lesions, whereas positive contrast only created a cast of the cavity.

One limitation of scanning the uterus with myomas by three-dimensional or two-dimensional ultrasound is due to a significant shadowing from calcification.

In our recent study (23) we evaluated myometrial lesions, morphology, volume, and vascularization with 3-D ultrasound and power Doppler sonography. The mean volume of the leiomyomas undergoing surgery was 78.52±51.8 ml. In 84.38%, 3-D power Doppler
detected regular vascularity at the periphery, while in cases of secondary degenerative lesions the findings were suggestive of neovascularity, irregular branching and chaotic vascular arrangement, because necrosis, inflammation and degeneration altered the leiomyoma vasculature. We concluded that because of the low positive predictive value of 16.67% this method should not be used for the evaluation of myometrial pathology, both benign and malignant.

**LEIOMYOSARCOMA**

Uterine sarcoma is a rare tumor, accounting for only 1-3% of all genital tract tumors and 3-7.4% of malignant tumors of the corpus uteri (33), characterized by early dissemination and poor prognosis for survival. Through the years, several questions regarding these tumors have remained unanswered, and a method for its early and correct diagnosis is still unknown. Furthermore, uterine sarcoma is expected to be more common in the near future, as gynecologists are more commonly using the conservative treatment of uterine myomas. Abnormal vaginal bleeding is the most common presenting symptom in patients with uterine sarcoma. Lower abdominal pain or pressure and a palpable abdominal mass are additional findings. An enlarged bulky uterus is palpated, and/or the tumor may be seen protruding through the cervix. Dilatation and curettage may be helpful in distinguishing benign from malignant pathology only if the tumor is submucosal. Clinically, a rapid increase in the size of a uterine tumor after the menopause arouses suspicion of sarcoma.

Ultrasonically leiomyosarcoma is presented as solid or solid-cystic structure, altering echogenicity of the myometrium. On transvaginal color Doppler, neovascularization of leiomyosarcoma is detected at the border or in the center of the tumor with high blood flow velocity and low impedance to blood flow (RI=0.37±0.03), with irregular, thin, randomly dispersed vessels (Fig.2). When cut-off value for RI of <0.40 was used, this method reached the sensitivity of 90.91%, specificity 99.82%, positive predictive value 71.43% and negative predictive value of 99.96% (34). Because of their rarity, uterine sarcomas are not suitable for screening. Transvaginal ultrasound can detect differences in myometrial tissue density, and therefore can be used for detection of uterine sarcoma, but because of low specificity this method is not appropriate as a screening procedure.

Szabo et al., (35) investigated uterine vascularity by color and pulsed Doppler in cases of uterine leiomyomas and uterine sarcomas, and determined the efficiency of uterine blood flow analysis in differentiating between them. The mean intratumoral resistance index (RI) and pulsatility index (PI) were significantly lower and the intratumoral peak systolic velocity (PSV) was significantly higher in patients with sarcomas than in patients with uterine leiomyomas. Marked reduction of RI and PI and increased PSV could be found in the leiomyoma cases which showed large size and/or necrotic, degenerative and inflammatory changes. When a cut-off value of 0.5 for the RI was considered, the detection rate for uterine sarcoma was 67% and the false-positive rate was 11.8%. These results suggest that the intratumoral RI detected by color and pulsed Doppler ultrasonography in themselves could be poor for the preoperative differential diagnosis of uterine sarcoma.

In our study (23), one patient with uterine leiomyosarcoma was examined with 3-D and power Doppler ultrasound. Enlarged volume of the tumor (97.2 ml) and irregular randomly vessels dispersed both in the central and peripheral parts of the tumor were obtained using this method. The diameters of these vessels were “uneven”, with numerous microaneurysms and stenosis. Because of the same problems mentioned in the paragraph about leiomyoma, low positive predictive value of 3-D PDS and small number of patients involved in the study, this technique is not acceptable for the evaluation of myometrial lesions.
CONCLUSIONS

Transvaginal sonography allows detailed analysis of the endometrial thickness and texture. Blood flow studies can be efficiently used to monitor endometrial development and to distinguish between benign and malignant uterine cavity lesions. It is hoped that color Doppler findings may help to reduce invasive procedures such as dilatation and curettage or hysteroscopy for detection of the uterine cavity lesions. This would decrease both the potential risks and the economic costs. Transvaginal color and pulsed Doppler sonography represents a non-invasive diagnostic tool that can be used repeatedly for assessing vascularity in endometrial lesions. The application of transvaginal color Doppler to the postmenopausal population for the screening of endometrial carcinoma may be a viable option if combined with ovarian screening in the same scan. In this way, the capital costs would be shared and oncological preventive medicine for women could be initiated. The use of this technique could also result in a reduction in dilatation and curettage operations, with considerable reduction of both the potential risks and the economic costs of the operation.

Assessment of vascularization of uterine tumors, if used together with analysis of morphology and size, can increase our accuracy in differentiating between uterine sarcoma and leiomyoma. However, it is unrealistic to expect Doppler studies to clarify confounding histological findings. It seems that the multiparameter sonographic approach, which includes morphology and size depicted by transvaginal ultrasonography and color flow imaging with pulsed Doppler analysis of neovascular signals, can help in the diagnosis of uterine sarcoma in high-risk groups such as postmenopausal patients with a rapidly enlarging uterus. Therefore, serial measurements are recommended for evaluation of myometrial density, follow-up of the tumoral growth and detection of the impedance to blood flow. Only such complex observations can lead to proper diagnosis of these rare tumors, which have an unpredictable prognosis. Three-dimensional and power Doppler ultrasound is a new diagnostic technique and its role in the assessment of uterine lesions has yet to be investigated. Three-dimensional ultrasound offers improved visualization of uterine lesions providing simultaneous display of coronal, sagittal, and transverse planes, displays entire volume demonstrating continuity of curved structures in a single image, offers more accurate volume estimation using a standard anatomic orientation, retrospective review of stored data, more complete viewing of pathology using rendered images identifying the location of abnormalities, and assessment of tumor invasion. Three-dimensional sonohysterography demonstrates the exact location of intrauterine pathology. It seems that 3-D power Doppler sonography has brought us a little closer to better understanding of malignant tumor angiogenesis. Interactive rotation of power Doppler rendered images provides improved visualization of the tumor vasculature. This method permits the ultrasonographer to view structures in three dimensions interactively, rather than having to assemble the sectional images in his/her mind. Contrast agents are another possibility for enhancing the three-dimensional power Doppler examination by increasing the detection rate of small vessels.

REFERENCES


