Endometrial Lesions and Doppler

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ABSTRACT
Centrally placed in the uterus, the endometrium covers the cavity of the uterus. It changes in structure and thickness with growing age and also in different phases of the menstrual cycle. The later changes are dependent chiefly on estrogen and progesterone. Transvaginal ultrasound is the modality of choice for its assessment. Endometrial pathologies may be inflammatory, may be due to an abnormal response to hormones, or may be benign or malignant neoplasms. The endometrium has a typical vascular pattern during different phases of the menstrual cycle and also has a typical branching pattern specific to different pathologies. Doppler therefore plays a very important role in understanding and evaluating the physiological changes as well as for the differential diagnosis of endometrial pathologies. 3D ultrasound with 3D power Doppler helps for a better understanding of the endometrial pathologies.

Keywords: Endometritis, Endometrial hyperplasia, Endometrial malignancy, Polyps.

Donald School Journal of Ultrasound in Obstetrics and Gynecology (2019): 10.5005/jp-journals-10009-10009-1593

INTRODUCTION
Endometrium is central in the uterus. It outlines the potential cavity of the uterus. It has a cell-rich connective tissue composed of a superficial functional layer and an inner basal layer (Fig. 1). It is the most dynamic anatomical structure in the uterus. In response to the hormonal changes during the menstrual cycle, the functional layer of the endometrium sheds off completely during menstruation, then grows gradually during the proliferative phase under the effect of estrogen, gets compacted when exposed to progesterone, and then—again under the effect of progesterone and estrogen in the luteal phase—grows to maximum till the mid-luteal phase and then again starts regressing in a nonconception cycle to break through during menstruation (Fig. 2). Endometrium also has different appearances from neonatal life to menopause.

Endometrium is best evaluated on a transvaginal scan, but a prior abdominal scan is recommended for evaluation of the pelvic anatomy.1 Doppler must be used for the assessment of the vascularity. 3D ultrasound is useful for the evaluation of the coronal plane and is a modality with a proved ability for the assessment of the endometriomyometrial junction.

Endometrial thickness is measured from the outer margin of the hyperechoic line to the outer margin of the hyperechoic line, at the broadest part of the endometrium, perpendicular to the central line of the endometrium (Fig. 3).

Endometrial pathologies may be inflammatory, may be due to abnormal response to hormones, or may be benign or malignant neoplasms. But before initiating the discussion on the endometrial lesions and their vascular patterns, it is essential to get acquainted with the standard terminology used worldwide. This is described under the international endometrial tumor analysis (IETA) consensus.2 It can be used to describe the endometrial appearance on the B-mode ultrasound, sonohysterography, and Doppler. There are specific terms used for the description of each aspect of the endometrium. Figures 4 to 8 illustrate the appearances and the legends narrate the terms to be used.

INFLAMMATORY LESIONS
The endometrium is easily susceptible to infections because of its possibly easy access to infections through the vagina and cervix. An inflammation of the endometrium may be related to pregnancy or to PID. An inflammation related to pregnancy–postpartum endometritis is more florid and may present with fever, pain, bleeding (secondary hemorrhage), and a foul-smelling lochia.

Chronic endometritis may be due to retained products of conception, but may also be due to tuberculosis, intrauterine contraceptive devices, or neoplastic masses such as an endometrial carcinoma or a submucous fibroid. Patients with an acute and chronic inflammation will present differently. Patients with the acute endometritis may complain of a bad odour in the menstrual discharge. At times, it may also present as menorrhagia or...

Fig. 1: Diagrammatic demonstration of the layers of the uterine wall
metrorrhagia, often associated with an acute pelvic pain. In contrast, patients with the chronic endometritis will more commonly present with a scanty bleeding or amenorrhea.

**Acute Endometritis**

The acute inflammatory process leads to edema and hyperemia due to neoangiogenesis. Edema includes the endometrium and also the subendometrial tissue due to its close anatomical vicinity. However, the subendometrial layer is also likely to be affected because it is this layer that hosts the dilated spiral vessels, the parent vessels of the endometrial vessels. Extravasation of the fluid from these dilated vessels may also be the cause of edema in the subendometrial layer.

**Ultrasound Findings**

Edema leads to an irregularly increased thickness of the endometrio–myometrial junctional zone (JZ) (Fig. 9). Endometrial...
edema may appear as an increased thickness of the endometrium with a homogeneous texture. It may have a ground-glass-like echogenicity and, both because of its echogenicity similar to that of the normal myometrium and because of irregularity of the JZ, it may be difficult to distinguish the endometrium from the myometrium. There may be a fluid in the endometrial cavity that is turbid (blood/pus) (Fig. 10). If it is due to a foreign body such as a guaze or retained products of conception, one may see heterogeneous shadows in the cavity. If it is postpartum, a subinvlouted uterus is seen, which appears bulky and vascular. In the presence of anaerobic infections, air may be seen in the endometrial cavity as bright-scattered echoes.

If associated with PID, adnexa will also present signs of inflammation such as free fluid (Fig. 11), hydrosalpinx, or oophoritis. The neoangiogenesis of inflammation is documented on the ultrasound as increased vascularity in the endometrium. These vessels typically have a larger diameter than the normal spiral vessels and also have a low-resistance (RI < 0.5) blood flow.
The vascular distribution may be heterogeneous due to a nonuniform involvement of the endometrium in the inflammatory process. However, interestingly, the low-resistance blood flow in the endometrium cannot always be used as a diagnostic criterion for diagnosis of the acute inflammatory process. This is so because it is known that normally also during the preovulatory and the secretory phase, there is physiological neoangiogenesis in the endometrium with development of low-resistance blood vessels. Therefore, this...
sign can be used only in a phase of the cycle when normally the endometrium is avascular or has a high-resistance blood flow. This phase is called the early proliferative phase.

A thickened endometrium also cannot be used as "the" diagnostic criterion for an acute inflammation in preovulatory and secretory phases for reasons described earlier. Though a thickened irregular endometriomyometrial junction can be used a strong supportive sign for inflammatory reaction.

**Chronic Endometritis**

The chronic inflammatory process instead results into fibrosis, compromising the normal endometrial tissue. This does not allow the endometrium to grow in thickness under estrogen or progesterone stimulation. This means that the endometrium remains thin even during the preovulatory and the secretory phases when it should otherwise grow in thickness. It is important to clarify here that normally the endometrium is also thin and avascular or has scanty vascularity in the early proliferative phase. Similar to the acute endometritis, even the chronic endometritis shows an irregular endometriom–myometrial junction and this may help suspect chronic endometritis in the early proliferative endometrium (Fig. 12).

Normally the endometrium shows vascularity, reaching the inner layers of the endometrium in the preovulatory and secretory phases with a vascular resistance index (RI) of <0.6 and <0.5, respectively. As a result of chronic inflammation, the endometrium shows scanty high-resistance vascularity. The vascular abundance and resistance may vary according to the severity of the inflammation.

**Tuberculous Endometritis**

One of the most commonly found, feared of, and difficult-to-treat infection in the developing countries is tuberculosis. In the acute state of the disease, it is not possible to differentiate other infections from tuberculosis. The ultrasound shows an irregular endometriom–myometrial junction and thickening at times. Sometimes one may find a fairly normal-looking endometrium in patients with tuberculosis. However, typically, acute tubercular endometritis does not show a low-resistance blood flow. This may be so because tuberculosis commonly affects end-arteries.

Chronic tuberculous endometritis, though like other chronic inflammatory endometritis, shows persistently a thin endometrium with an irregular junctional zone; it also presents with certain features...
that are much more commonly seen in the tubercular infection when compared to other infections (Fig. 13). The most consistent is a vertical orientation of the interstitial part of the tube (Fig. 14). Fluid collection may be seen in the endometrium, but typically the inner layer of the endometrium appears hyperechoic with an irregular endometrio–myometrial junction and no vascularity beyond the junctional zone (Fig. 15). Endometrial, myometrial, and endometrio–myometrial junctional zone calcifications may be seen (Fig. 16). Endometrial scarring and synchieae occur due to healing with fibrosis (Fig. 17). Tuberculous endometritis may also at times present as multiple micropolyps in the endometrium (Fig. 18). Tuberculosis may also affect the myometrium and cause myometrial cysts. Though, like endometrium, the myometrium also is typically hypovascular.

**Abnormal Response to Hormones**

As described earlier in this paper, it is known that the endometrium has a changing morphology throughout the menstrual cycle. It is the receptor organ for estrogen and progesterone. For the normal menstrual cycle, an alternate predominance of estrogen and progesterone is essential. Moreover, it is the withdrawal of both that leads to a breakthrough of the endometrium. A break in this hormonal cycle may lead to abnormalities in the endometrium or even an abnormal response of the endometrium to the normal hormonal changes may lead to pathologies of the endometrium.

It is due to a persistent estrogen exposure that the endometrium keeps on growing to a thickness beyond physiological limits. The cutoff is mentioned as 15 mm in literature, but we have observed the endometrium growing to 18 mm thickness in some patients with a normal endometrial morphology. Apart from the thickness, the endometrium changes its morphology in the presence of persistent estrogen exposure. Under the influence of rising estrogen levels, the endometrium changes its morphology from a single-line to a multilayered endometrium. With rising estrogen levels, the endometrium changes its morphology from a multilayered pattern to a homogeneous endometrium. This is due to the proliferation of endometrial glands. Persistently high levels of estrogen leads to the endometrial hyperplasia due to an
increased endometrial-gland-to-stroma ratio. A mildly hyperechoic endometrium with multiple well-defined round anechoic areas is the typical ultrasound appearance. These anechoic areas are the hyperplastic glands. Patients with the endometrial hyperplasia is present with a period of amenorrhea followed by spotting. As is known, the endometrium has glandular and stromal components. The abundance of anechoic areas in the thickened endometrium indicates that it is predominantly a glandular hyperplasia (Fig. 19), and if it has a chiefly solid look with only few anechoic areas, it is predominantly a stromal hyperplasia (Fig. 20). The endometrial hyperplasia may show a polypoid endometrium at times. This shows an irregular central line on the B mode and a polypoid endometrium on sonohysterography. The endometriomyometrial junction is typically intact in the endometrial hyperplasia. The endometrial hyperplasia on Doppler shows regularly distributed blood vessels throughout the endometrium (Fig. 21). These blood vessels have a moderate resistance flow with RI: 0.60–0.70.

A persistent progesterone exposure leads to a compact hyperechoic endometrium, with an intact endometriomyometrial junctional zone. It is the hyperechogenicity that differentiates the hyperestrogenic endometrium from the hyperprogesteronic endometrium. On the Doppler, the endometrium that is hyperprogesteronic shows variable vascularity. Actually, the vascularity of the progesterone-exposed endometrium depends on the estrogen–progesterone ratio.

**ENDOMETRIAL METAPLASIA**

Apart from this, the endometrial hyperplasia may also be seen as an effect of tamoxifen. Hyperplastic endometrium is seen in the tamoxifen-exposed patients as well as those with the endometrial metaplasia. Tamoxifen is widely used for treating breast cancers and has a prooestrogenic effect on the endometrium. The endometrial metaplasia due to a tamoxifen exposure is about progressive changes in the endometrium when the patient is on tamoxifen therapy.

On the ultrasound, the endometrium shows different pictures at different stages of this progressive change. The changes seen are as follows:

- Echogenic endometrium with a good halo and homogeneous echopattern
- Echogenic endometrium, good boundaries with small echo-free cysts (Fig. 22)
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**Neoplastic Lesions**

**Polyps**

Endometrial polyps are solid projectile lesions of the endometrium. They are often diagnosed as an incidental finding. However, some patients may present with spotting and infertility.

On the ultrasound, these are seen as solid echogenic lesions in the endometrial cavity, in between the endometrial lines. Polyps can be diagnosed on the B-mode scan and are best visible in the periovulatory phase of the menstrual cycle. The endometrium in this phase is multilayered, with the intervening area being hypoechoic.

Against this background, these solid soft tissue lesions stand out as echogenic round or ovalish lesions with smooth margins (Fig. 24). In the early proliferative phase, before endometrium becomes multilayered, a polyp is only seen to deshape the endometrial cavity. Though at times if there is a fluid in the endometrial cavity, it may help as a negative contrast media and show the polyp as a solid soft-tissue projectile lesion in the cavity (Fig. 25). However, we would prefer not to use the menstrual period as a scanning time for endometrial lesions, as there is a strong possibility to misinterpret blood or blood products as endometrial lesions. Blood clots may appear as solid echogenic structures in the endometrial cavity. Pedunculated fibroids also move up and down in the endometrial cavity with peristalsis like blood clots. In the secretory phase, the endometrium is hyperechoic and obscures the visibility of the polyp.

Polyps may vary in size from very small ones, which may be difficult to visualize on the ultrasound, to large ones, which may mimic a thickening of the entire endometrium, like in hyperplasia or malignancy (Fig. 26). When the endometrial cavity fills up, it is a thin slit of the fluid between the solid lesion and the endometrial hyperechoic line that excludes the possibility of an endometrial hyperplasia and favors that of a polyp (Fig. 27). Very small polyps

- Echogenic nonhomogeneous, small cystic structures, blurred boundaries
- Echogenic nonhomogeneous endometrium, blurred boundaries, interrupted halo (Fig. 23)
- This last one is the nonreversible stage to endometrial malignancy.

On the Doppler, a high-velocity, low-resistance flow is seen, where RI may be as low as 0.39. The lower the resistance, the higher is the risk of atypia and malignancy.

**Fig. 21:** Cystic glandular hyperplasia on a power Doppler showing scanty endometrial vascularity

**Fig. 22:** Endometrium showing a well-defined round anechoic lesion-endometrial cyst of an endometrial metaplasia

**Fig. 23:** Echogenic nonhomogeneous endometrium, blurred boundaries, and interrupted halo-tamoxifen effect

**Fig. 24:** A B-mode ultrasound image of an endometrial polyp (arrow)
may be isoechoic or mildly hyperechoic to the endometrium and sometimes can barely be seen on the B-mode ultrasound. Sometimes polyps may show tiny anechoic cystic areas due to dilated endometrial glands. This may be seen in the polyps in patients on tamoxifen therapy also. The diagnostic clue to such a polyp is an abnormal curve in the central line of the endometrium (Fig. 28). Polyps may be pedunculated or sessile. Polyps may often be multiple (Fig. 29).

In spite of this huge variability in types of polyps and their appearances on ultrasound, its typical vascular supply is diagnostic. The polyp has a characteristic blood supply by a single feeding vessel or by a maximum of two vessels very closely placed (pedicular vessels esp. in sessile polyps). Even when there are multiple polyps, each one has an individual single feeding vessel. Interestingly when polyps are seen in the cervix, even these show a similar vascular pattern (Fig. 30). Polyps being benign lesions, the feeding vessels have a high resistance flow (RI about 0.6). However, with resistance index (RI) <0.45, atypia may be suspected in these polyps. Infection, necrosis, or atypia in the polyp leads to a heterogeneous echogenicity on the B mode and the Doppler shows an abundant branching of the vessels inside the polyp mass.

The adenomyomatous polyp also shows an abundant branching of the blood vessels (Fig. 31) inside the polyp mass, but the RI of these vessels is almost always >0.5. The vascular pattern has a high accuracy for a differential diagnosis of endometrial lesions.

Single vessel pattern has a sensitivity of 81.2%, specificity of 88.2%, positive predictive value of 92.9%, and negative predictive value of 71.4% for the diagnosis of polyps. According to another study, the single feeding vessel (pedicle artery) has a sensitivity of 76.4%, specificity of 95.3%, positive predictive value of 81.3%, and negative predictive value of 91.3% for the diagnosis of polyps. Large polyps also have characteristic single feeding vessel, whereas hyperplastic endometrium shows uniformly distributed multiple vessels, as discussed earlier and malignant endometrial growth shows heterogeneously distributed, increased vascular density (Fig. 32), with vessels of asymmetrical caliber.

Apart from the Doppler, sonohysterography is useful for the diagnosis and differential diagnosis of endometrial lesions. It is a simple, almost painless procedure and does not require any analgesia or anesthesia. It can be used with the Doppler or with the 3D ultrasound. One can use a dedicated sonohysterography catheter for the procedure but we prefer to use Foley’s catheter 6–8 Fr. (ext. diam. 1.6 mm, int. diam. 1.1 mm). The catheter is introduced into the cervix, with the balloon in the cervical canal. The balloon...
is distended with 1.5–2 mL of normal saline or distilled water. After fixing the balloon, 5–7 mL of normal saline is slowly introduced in the endometrial cavity with a 10–20 mL syringe. While filling the endometrial cavity with the saline, the speculum and anterior retractor that are used earlier to visualize the cervix and facilitate the introduction of the probe are removed from the vagina and the probe is introduced to observe the endometrial cavity as it is being filled up with the saline. As the saline fills up and the endometrial cavity distends, the solid lesions of the endometrium can be clearly visualized in the endometrial cavity. Once the cavity is distended and the lesion is visualized, either a B-mode sweep in sagittal and axial planes can be taken and stored or a 3D volume of the uterus can be taken. One can also use the Doppler after the endometrial cavity is filled with the saline for a differential diagnosis of endometrial lesions.

Endometrial Fibroids
Fibroids are benign neoplasms originating from the myometrium. However, some of these distort the endometrium and some may be pedunculated and grow in the endometrium. These pedunculated fibroids may mimic polyps and the differential diagnosis may at times be difficult. Intra-endometrial fibroids also have the same morphology as the other fibroids. This means that these are also hypoechoic to the myometrium. In the periovulatory phase, the endometrium is typically hypoechoic to the myometrium and the fibroids appear isoechoic to this and difficult to diagnose except for an abnormal endometrial contour. Though on the B mode also these fibroids can be seen in the secretory phase of the menstrual cycle, that is hypechoic and acts as a contrast for hypoechoic fibroid (Fig. 33).

The Doppler can be a diagnostic technique in these cases as fibroids typically show peripheral vascularity (Fig. 34), unlike the single feeding vessel in a polyp.
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Fibroid Polyp
This is a confusing and very loosely used term. Large polyps are often termed as fibroid polyps. Though true, fibroid polyps on pathology may have a combination of myometrial and endometrial tissue and may be difficult to correctly diagnose on imaging. A typical fibroid polyp on the B mode or on 3D sectional planes may show a broad base and continuity of the myometrial interface may be seen towards the polyp wall (Fig. 35). It has a heterogeneous echogenicity. On the Doppler, unlike fibroid, this lesion typically shows a feeding pedicle but usually this pedicle has multiple vessels. Abundant branching may be seen and this may be mistaken for atypia in the lesion. Upon tracing these feeding vessels, continuity is seen from the myometrial radial vessels rather than from the spiral vessels, which are feeders to the endometrium (Fig. 36).

Endometrial Synechiae
These are typically avascular lesions of the endometrium. It is known that synechiae occur as a result of a surgical insult or inflammation finally leading to fibrosis. Patients with this condition are present with severe oligomenorrhea or amenorrhea. These appear as soft tissue strands across the endometrial cavity on the B mode ultrasound, but are often not seen on the ultrasound; instead, it only appears as a thin endometrium. Their echogenicity may vary depending on the firmness, thickness, or calcifications of the synechiae. Sonohysterography may be a more helpful technique for investigating these cases (Fig. 37).

Endometrial Malignancies
Endometrial malignancy is the fourth commonest malignancy in the United States. Its incidence in Asian countries and New Zealand is 1.5–2.5 times higher than that in the European countries. The increased rates of endometrial cancer may be related to obesity, failing fertility, and an increased lifespan. Endometrial malignancy may present with varied menstrual disturbances.

Endometrial malignancy on the ultrasound may have variable appearances depending on its stage. However, still heterogeneous echogenicity is a consistent finding (Fig. 38). Depending on the extent of the disease, there may be focal/diffuse thickening of the endometrium. Premenopausal women with an endometrial
thickness of more than 15 mm, as mentioned in the literature and postmenopausal patients having a thickness of more than 5 mm with bleeding disorders may be suspected of having endometrial malignancy. Though an endometrial thickness of up to 15–16 mm may often be seen in the secretory phase in patients especially on fertility treatment. Endometrial thickness of <4 mm has a 100% negative predictive value for the endometrial cancer. Interestingly the endometrial echogenicity varies according to the stage and grade of the disease. Stage 1A cancers are hyperechoic or isoechoic, whereas stage 1B and above have a mixed echogenicity or are hypoechoic. Well or moderately differentiated (grades I–II) tumors are hyperechoic, compared to grade III, and more widespread lesions that are hypoechoic or heterogeneous. Though irregular endometrial surface is another diagnostic criterion for the diagnosis of the endometrial malignancy (Fig. 39), this can be best appreciated by sonohysterography. However, if malignancy is suspected either clinically or on the ultrasound, sonohysterography is not preferred for the risk of its peritoneal spread and seeding.

At times, a fluid
may be seen in the endometrial cavity. When the endometrial malignancy grows beyond the endometrial margins, it leads to irregularity of the subendometrial halo (endometriomyometrial junctional zone). Irregular endometrial margin has a positive likelihood ratio of 10 for endometrial malignancy.12

On the Doppler, it typically shows heterogeneously distributed dense vascularity with a low-resistance flow in the premenopausal women with endometrial malignancy, but in the early endometrial carcinoma in perimenopausal women, moderate intratumoral resistance may be seen (Fig. 40A). The vascular pattern is of multifocal origin, dispersed vessels, or a single vessel with abundant branching (Fig. 40B). In patients with endometrial malignancy, the uterine artery resistance is also low with uterine artery PI < 1.45 and radial artery PI < 1.06.13 Typically the malignant neoangiogenesis shows a chaotic vascular branching pattern with microaneurysms, arteriovenous shunts, elongation, and coiling (Fig. 40B). These are appreciated best on the 3D power Doppler angiography.

Combining morphological and 3D PD criteria, the sensitivity for endometrial carcinoma is 91.67%.14 3D ultrasound also plays an important role in diagnosing the extension of the endometrial carcinoma into the myometrium (Fig. 41A). 3D ultrasound can calculate the tumor volume accurately and an increasing volume of the endometrium suggests a higher grade endometrial carcinoma and also myometrial invasion.15 A volume larger than 25 mL has a high chance of pelvic node involvement at surgery. 3D hysterosonography with a transverse plane picture may also show bladder or rectal infiltration. 3DPD is efficient for the diagnosis of deep invasion with sensitivity 100%, specificity 94.44%, PPV 83.33%, and NPV 100%. The vascular pattern is seen to penetrate into the myometrium (Fig. 41B). Higher stages of the tumor show a lower resistance index, a higher velocity and a higher micro-vessel density (VI).16

**Conclusion**

Transvaginal ultrasound is the modality of choice for assessment of the endometrium and diagnosis of endometrial pathologies. Doppler is an essential addition for the differential diagnosis of these pathologies because of the specific vascular patterns of different endometrial pathologies. Sonohysterography and 3D US plays an important role in the demonstration of endometrial lesions. 3D power Doppler is especially important for the diagnosis, assessment of the extent, and the followup of malignant lesions.

**References**