

Understanding the Endometrium at Menopause: Magnetic Resonance Imaging: A Radiologist's View

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Key aspect of imaging is to provide accurate anatomical piece of information regarding female genital organs and unique to female pelvis is the changes occurring cyclically and through the phases of cycle. Ultrasonography (USG) transabdominal/transvaginal (TVS) is the primary and most powerful versatile imaging modality to evaluate the female pelvis. It is the established standard of care in clinical practice with well-defined standardized terminologies to describe the abnormalities such as IEATA guidelines as detailed in the article in previous issue. A normal TVS sonogram in a postmenopausal patient has a high negative predictive value and

high overall accuracy rate with excellent pathologic correlation.

However, the modality has limitations with regard to the modality, disease, difficult anatomy, and complex lesions requiring further characterization before management decision is made. It is at this point that the role of magnetic resonance imaging (MRI) is undisputed and established, the strength of MRI is where the gray zone of ultrasound ends, it complements/adds to provide complete assessment with its excellent soft-tissue contrast and multiplanar capability. Advanced functional imaging parameters such as diffusion-weighted images (DWIs) with apparent diffusion coefficient (ADC) provide macroscopic histopathologic correlation of the lesion, thereby adding accuracy and specificity. Hence, multiparametric MRI including T2-weighted images (T2WIs) with diffusion-weighted images with ADC is helpful for differentiating the various endometrial lesions and establishing specific diagnoses and appropriate treatment.

The aim of this pictorial essay is to demonstrate the multiparametric MR imaging assessment of endometrial cavity in terms of technique, imaging protocol including recent advances, imaging appearances of normal, and various abnormalities of endometrial cavity where the clinical utility of MRI is undisputed and indispensable in patient care and management. Finally, a diagnostic algorithm of MR Imaging assessment in the clinical care is proposed.

The step-wise diagnostic evaluation in postmenopausal endometrium as practiced in clinical care is detailed in Box 1 with the role of imaging and nonimaging modalities outlined.^[1-4]

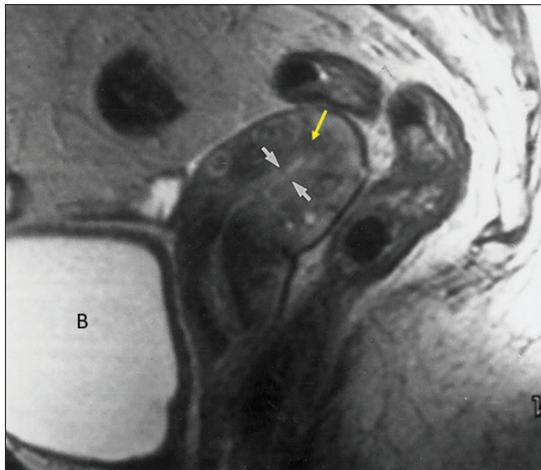


Figure 1: Normal postmenopausal endometrium: Sagittal T2-weighted magnetic resonance image obtained in a 60-year-old female 3 years after menopause reveals a small uterus with a normal, thin (<4-mm), hyperintense endometrium (solid arrows) and barely perceptible hypointense junction zone (yellow arrow). The zonal anatomy is best visualized during the reproductive years and may be poorly depicted or absent in prepubertal and postmenopausal women.^[5] Note that the uterine corpus has undergone some atrophy and is only slightly bulkier than the cervix. In late menopause, the uterine corpus is smaller than the cervix, and the uterine zonal anatomy may be difficult to appreciate. B = Bladder

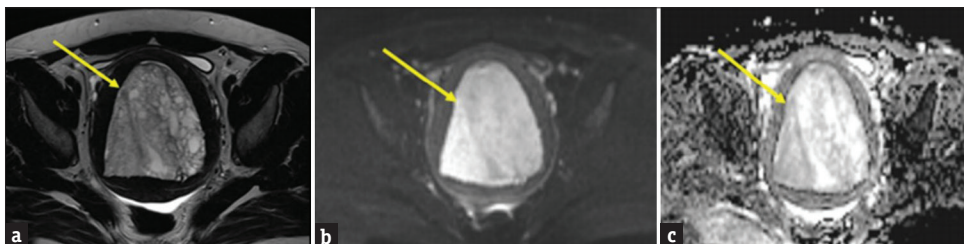


Figure 2: Endometrial hyperplasia in a 45-year-old female with: (a) Axial T2-weighted image demonstrating markedly distended endometrial cavity with smooth compressed junctional zone all around, internal morphology is smooth marginated Sol with multiple cysts of varying sizes showing predominant high T2 signal. (b) High b-value (b = 800) diffusion-weighted image shows high SI and (c) apparent diffusion coefficient map shows high SI (arrow) with values 1.7–2.1, which indicates no diffusion restriction

Box 1: The step wise diagnostic evaluation in post-menopausal endometrium as practiced in clinical care

Heterogeneous endometrial pathologies → postmenopausal bleeding → needs to be discriminated to navigate the treatment process

First diagnostic step

TVS Most efficient first step diagnostic method with high sensitivity and low specificity^[1]

Timing of evaluation: Beginning/end of a cycle of treatment, the reason being endometrium is thickest prior to progestin exposure and thinnest after progestin phase

Standard US TAS/TVS examination as described by the IETA guidelines. This includes quantitative/qualitative assessment of endometrium including color Doppler assessment as a part of routine assessment

Normal postmenopausal endometrium <5 mm smooth without focal thickening ±3 mm if on cyclic estrogen + progestin therapy

Abnormal >8 mm

Second diagnostic step

Biopsy recommended

Difficult situations where biopsy not feasible, or biopsy confirmed malignancy as a part of Risk assessment prior to surgical planning

Third diagnostic/Prerisk stratification step

MRI with its superior soft-tissue contrast and multiplanar capability plays A KEY ROLE IN EVALUATION

Multiparametric MRI is utilizing different pulse sequences to add specificity, accuracy to the heterogeneous pathologies by adding tissue characterization and functional information^[2]

Conventional sequences show significant overlap between hyperplasia, polyps and carcinoma endometrium

Advanced sequences DWI with ADC can detect, differentiate endometrial cancer from normal endometrium and benign lesions

In carcinoma endometrium it provides prognostic marker information regarding depth of myometrial invasion, cervical involvement and lymph node status there by adding value to the FIGO staging^[3]

Contrast enhanced MRI/dynamic contrast can be substituted by the combination of T2W with DWI and ADC in view of better diagnostic performance plus obviating the risk of MRI contrast in compromised renal functions in postmenopausal females^[4]

TAS: Transabdominal, TVS: Transvaginal, US: Ultrasound, MRI: Magnetic resonance imaging, DWI: Diffusion-weighted images, ADC: Apparent diffusion coefficient, T2W: T2-weighted

WHEN TO REFER FOR MAGNETIC RESONANCE IMAGING?

- When dedicated TVUS protocol is not feasible:(Unmarried)
- Pitfalls and potential mimickers on US for specificity
- Suboptimal evaluation in difficult anatomy/coexistent pathologies add to US prior to surgical management
- Difficult to obtain histologic samples, thereby allowing differentiation of various diseases and Establishment of specific diagnoses for many diseases
- HPE confirmed malignancies as a part of risk assessment before surgery.

WHAT TO LOOK IN MAGNETIC RESONANCE IMAGING? MULTIPARAMETRIC MAGNETIC RESONANCE IMAGING WITH ADVANCES SEQUENCES (T2/T1/FATSAT T1-WEIGHTED/SWI) AND FUNCTIONAL SEQUENCES (DIFFUSION-WEIGHTED IMAGE AND APPARENT DIFFUSION COEFFICIENT)

Characterization of the abnormality/morphological assessment/evaluation of extent using conventional

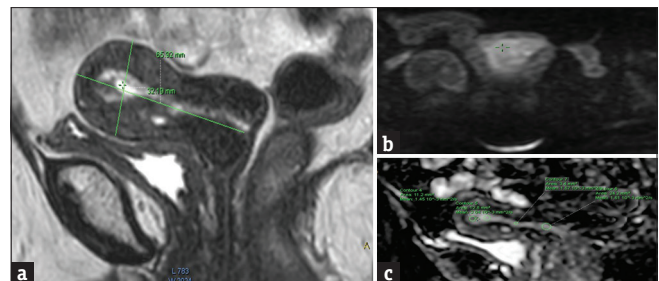


Figure 3: Endometrial polyp in a 50-year-old perimenopausal woman shows representative magnetic resonance imaging findings in a majority of our cases. (a) T2-weighted image in sagittal plane shows a polyp with slightly low signal intensity compared with normal endometrium. There is low signal intensity central fibrous cores (yellow arrow) and small high signal intensity intratumoral cyst (blue arrow). (b) diffusion-weighted image with b value of 1000s/mm² in the sagittal plane at the same level as in A shows a polyp with low signal intensity compared with endometrium. (c) Apparent diffusion coefficient reveals a value of 1.4 in the fibrous core and 1.6–2.0 in the polyp and intratumoral cyst

sequences with T2W being the standard, Additional sequences being T1W, T1FATSAT, SWI.

Functional Sequences (DWI and ADC): values provide a diagnostic differentiation between benign and malignant endometrial lesions without any overlapping. In addition, provides prognostic marker information such as depth of invasion and lymph node status.

DWI together with ADC measurement can be used for diagnostic purposes in conditions of difficult endometrial biopsy or curettage due to the presence of endometrial atrophy, adhesions, and the requirement of anesthesia in postmenopausal patients.

NORMAL UTERINE ANATOMY AND ENDOMETRIAL CAVITY

The normal postmenopausal endometrium has

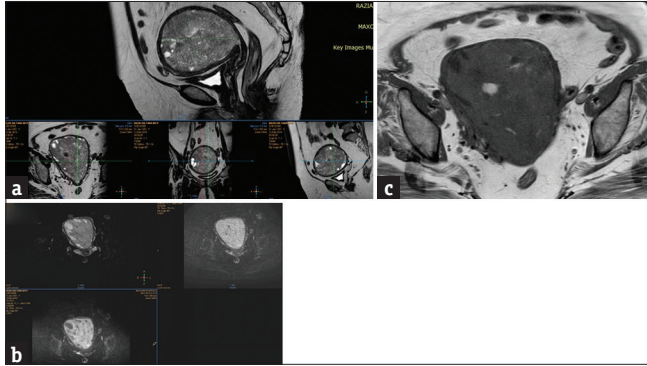


Figure 4: Giant endometrial Polyp: Multiplanar T2-weighted image. (a) Sagittal images delineated markedly distended endometrial cavity with smooth compressed uterine myometrium all around and normal cervical canal confirming that it developed within the uterine cavity positioned centrally, signal predominantly showing T2 shine through on diffusion-weighted image. (b) Apparent diffusion coefficient value within the high signal diffusion-weighted image mass was 1.3–1.4 and within the cyst was 2.1–2.3. On plain T1-weighted images (c) reveal the mass mainly isointense on plain T1 images with intratumoral cysts along the periphery and central hemorrhagic areas (hyperintense on T1W, hypointense on T2-weighted, Blue arrows). Ultrasound examination (not shown) revealed a 86 mm mass within the uterus with some central vessels at Doppler examination

hyperintense signal on T2-weighted MR images and should be no more than 5 mm thick with smooth uniform margins.^[5] T1-weighted images show poor contrast distinction between the endometrium and myometrium [Figure 1].

ENDOMETRIAL HYPERPLASIA

Classically, endometrial hyperplasia affects the entire endometrium and results in widening of the endometrium [Figure 2]. On imaging, endometrial hyperplasia appears mostly as diffuse smooth endometrial thickening.^[2] It shows similar SI of the endometrium on T2WI and small cystic components. On DWI, it shows low SI with high ADC values above 1.1, which is an important point in differentiating it from malignancy, which shows high SI with low ADC due to relatively high cellularity [Figure 2].^[4]

ENDOMETRIAL POLYPS

Histologically, polyps contain mixture of three elements in varying degrees: stroma of dense fibrous core, thick-walled vascular channels, and endometrial glands with endometrial glands forming predominant part of the lesion [Figure 3].^[2,6]

GIANT ENDOMETRIAL POLYP

Polyps greater than 4 cm are called giant polyps [Figure 4]. The Morphostructural features of the polyp parallel the histology with gross appearance being well-circumscribed margins with shape mass like/endometrial thickening distending the cavity Box 2.

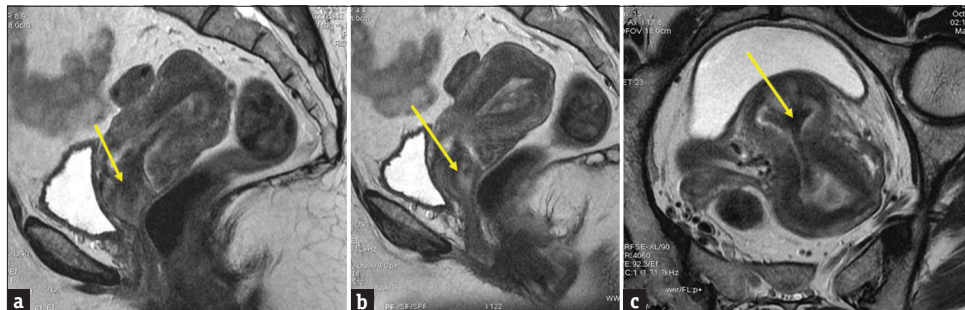


Figure 5: A 49-year-old female presenting with pain and PV bleeding with endometrial polypoidal SOL: Sagittal (a and b) and Coronal T2-weighted images (c) through uterine axis reveal a long narrow pedicle from the fundus, leading to 3.8-cm sized polypoid lesion (yellow arrow) coursing through the endometrial cavity and distending cervical canal, with low signal intensity (SI) on T2, diffusion-weighted image low signal with low apparent diffusion coefficient values (T2 Dark Phenomena)

Box 2: The morphological structural features of the polyp

Morphology	Internal structure	Signal intensity		
		T2W	DWI	ADC
Well circumscribed margins	Fibrous core	Slightly low	Low	High (mean 1.78±0.27)
Mass like	Intratumoral cysts			
Diffuse endometrial thickening	Foci of hemorrhage			

T2W: T2-weighted, DWI: Diffusion-weighted images, ADC: Apparent diffusion coefficient

SUBMUCOUS FIBROIDS AND DEGENERATED FIBROID POLYP PROJECTING INTO CAVITY LEIOMYOMA

On MRI, leiomyoma appears as well-circumscribed

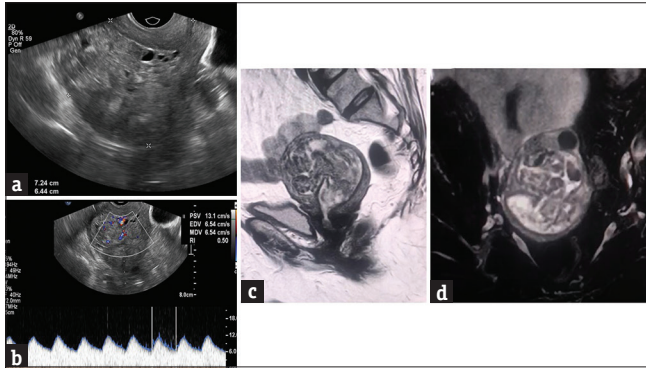


Figure 6: Degenerated leiomyoma prolapsing into the endometrial cavity: Ultrasound is commonly the first examination to be performed, but it has limitations in the characterization of masses. This is why magnetic resonance imaging is helpful in such cases. (a and b) TVS and color Doppler images reveal thick endometrium with Swiss cheese appearance with vascularity not typical pedicle pattern of endometrial polyp and the margins of endometrial cavity are ill defined anteriorly (yellow circle). (c and d) Sagittal and oblique axial T2-weighted images reveal submucosal anterior wall leiomyoma with degeneration prolapsing into the endometrial cavity (orange dashed line) occupying the fundus and body with defect in the continuity of the junctional zone anteriorly (Blue arrow). Seedling intramural anterior wall myoma present in upper body (Red arrow). diffusion-weighted image showed low signal on high B value with apparent diffusion coefficient values 1.6–1.7, suggesting no restricted diffusion-weighted image (T2 SHINE THROUGH): HPE: Degenerated leiomyoma prolapsing into endometrial cavity

mass, and the submucosal type appears as a polypoid mass protruding into the uterine cavity. Typically, it shows homogenous low SI on T2WI without diffusion restriction [Figure 5]. Atypical benign leiomyomas can be differentiated from malignant masses based on T2W with DWI and ADC characteristics. High DWI signal greater than that in endometrium, and ADC less than or equal to $0.905 \times 10^{-3} \text{ mm}^2/\text{s}$ is predictive for malignancy,^[7] in contrast, a global or focal area of low T2 signal intensity and a low or an intermediate DWI signal less than that in endometrium are seen in atypical leiomyomas [Figure 6].^[7]

ADENOMYOMAS

Adenomyomas that manifest as polypoid masses protruding either into the endometrial cavity or outside the uterine surface are called polypoid adenomyomas (PAs). It is benign mixed epithelial and mesenchymal tumor composed of a variable number of endometrial glands and endometrial-type stroma surrounded by smooth muscle. They typically develop in the lower segment of the uterine corpus but may occasionally develop in the upper corpus or fundus.^[8] Submucosal PAs usually occur in premenopausal females, and abnormal vaginal bleeding is the most commonly associated symptom.

Morphologically, PAs are epicentered in the junctional zone with myometrial invasion and cystic foci of varying

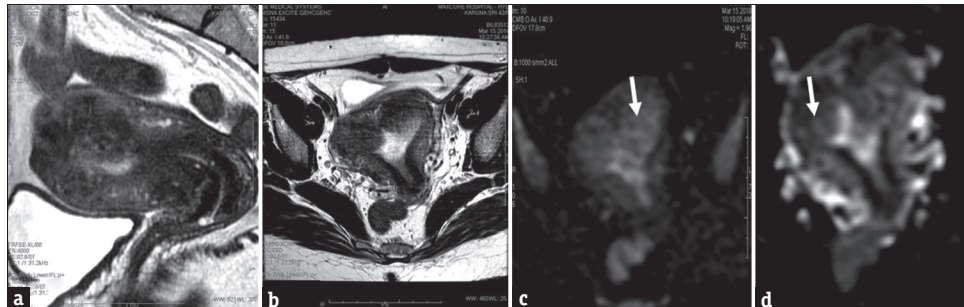


Figure 7: (a) Sagittal T2- and (b) axial T2-weighted images show submucosal mass projecting into the cavity with hyperintense small cystic components (yellow arrows). (c) diffusion-weighted image and (d) apparent diffusion coefficient show T2 dark phenomenon with projection of junctional zone into the endometrial cavity with nodular morphology and ill-defined borders (white arrows): polypoid adenomyoma

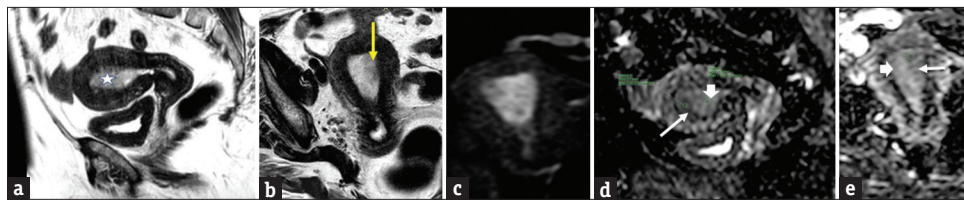


Figure 8: Stage 1A endometrial cancer in a 52-year-old female. (a) Sagittal T2-weighted magnetic resonance image shows distension of the endometrial cavity by an intermediate-signal-intensity tumor (*). (b) Axial oblique T2-weighted magnetic resonance image shows the intermediate signal intensity tumor (yellow arrow) within the hyperintense endometrial cavity along left lateral aspect. The junctional zone is well delineated, with no evidence of invasion. (c) diffusion-weighted image shows restricted diffusion-weighted image and with focal decreased apparent diffusion coefficient (d and e) within this area (0.8–0.9, white arrow) suggesting area of neoplastic changes. ACD within rest of the endometrial cavity is (1.3–1.4 arrow head)

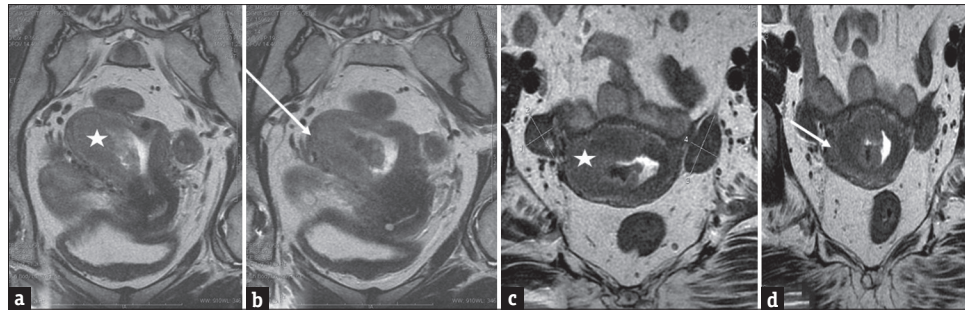


Figure 9: Stage 1B endometrial cancer in a 53-year-old female. (a and b) Coronal oblique T2-weighted magnetic resonance images demonstrates a tumor (*) with invasion of the myometrium and poor tumor-to-myometrium contrast (arrow). (c and d) Axial T2-weighted magnetic resonance image shows a large iso- to hypointense endometrial tumor (*) with poor tumor-to-myometrium contrast (arrow) and invasion of the outer half of the myometrium (short arrow)



Figure 10: Postmenopausal bleeding in an 85-year old women with poor/limited characterization on USG owing to large posterior wall myoma obscuring the endometrial cavity. (a and b) Sagittal, axial T2-weighted magnetic resonance image shows a large posterior wall intramural myoma showing variable predominantly low T2-weighted signal indenting along left posterior wall distorting the uterine cavity (*). Coexisting lesion seen in the endometrial cavity as focal sessile mass hypointense to the bright endometrium along anterior upper body on the left side (Yellow arrow, the depth of myometrial invasion is difficult to determine owing to poor tumor-to-myometrium contrast (White arrow). (c and d) On a sagittal diffusion-weighted magnetic resonance image ($b = 800$ s/mm) and axial apparent diffusion coefficient map, the tumor (*) has high signal intensity extending into the junctional zone (arrow) with the apparent diffusion coefficient values of 0.7–0.8. Here, the posterior wall leiomyoma demonstrated (T2-weighted variable signal, diffusion-weighted image low signal with apparent diffusion coefficient high values: Benign morphology). However, the endometrial cavity sessile lesion demonstrated T2 intermediate signal with diffusion-weighted image high and low apparent diffusion coefficient value: Restricted Diffusion suggesting malignant etiology: Final HPE revealed Stage 1B Grade 1 endometrial carcinoma involving up to 50% of uterine myometrium. This case illustrated the clinical utility of magnetic resonance imaging with diagnostic value of diffusion-weighted image and apparent diffusion coefficient in detecting and differentiating between benign and malignant lesions

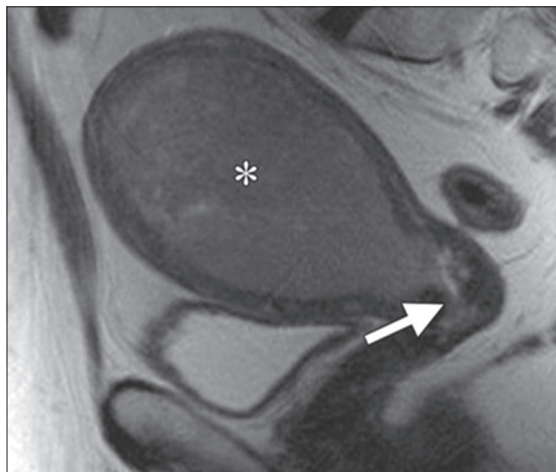


Figure 11: Stage II endometrial cancer in a 64-year-old female. (a) Sagittal T2-weighted magnetic resonance image shows the distention of the endometrial cavity by a tumor (*) that extends into the cervix (arrow). Signal intensity of the tumor is intermediate on T2-weighted with restricted diffusion showing apparent diffusion coefficient values of 0.8–0.9 (images not included here)

sizes and hemorrhagic components distinguishing it from endometrial polyps [Figure 7]. The ADC values overlap with benign causes with mean 1.1–1.3.

CARCINOMA ENDOMETRIUM

MRI plays a valuable role in evaluating endometrial carcinoma and differentiating it from benign lesions such as endometrial polyp or hyperplasia. The typical MRI findings are as follows: intermediate to low SI on T1WI, intermediate SI on T2WI compared with that of the myometrium, decreased or no contrast enhancement. Due to its high cellularity, endometrial carcinoma demonstrates diffusion restriction with high SI on DWI and low ADC value [Figures 8-14].

T2W imaging with DWI and ADC, dynamic contrast-enhanced MRI can give information about the tumor grade, depth of myometrial invasion, and lymph node status which are important for a surgeon to determine the method of treatment. [3,4]

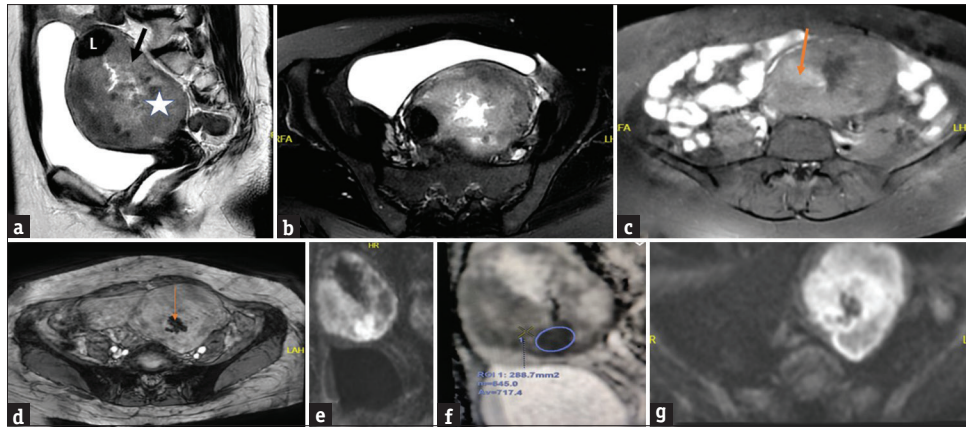


Figure 12: Stage 3 Stage IIIA endometrial cancer in a 65-year-old female: (a) Sagittal T2-weighted, (b) Axial T2-weighted, (c) T1FAT SAT, (d) SWI, (e-g) Sag and Axial DWI with apparent diffusion coefficient map: Sagittal T2-weighted ME image shows a large endometrial tumor (*). The depth of myometrial invasion is difficult to determine owing to poor tumor-to-myometrium contrast (arrow). (b) Axial oblique T2-weighted magnetic resonance image shows extension of the endometrial tumor (*) up to the serosa. The tumor is isointense relative to the adjacent myometrium. In addition, the uterus is distorted by two leiomyomas (L), whose presence is a commonly reported pitfall in staging. (c) T1FATSAT image reveals bright signal which shows corresponding blooming on SWI (arrow). (d) Suggestive of hemorrhage. (e and g) diffusion-weighted image reveals high signal with low apparent diffusion coefficient values of 0.5–0.6 (F): Restricted diffusion. HPE Mucinous adenocarcinoma

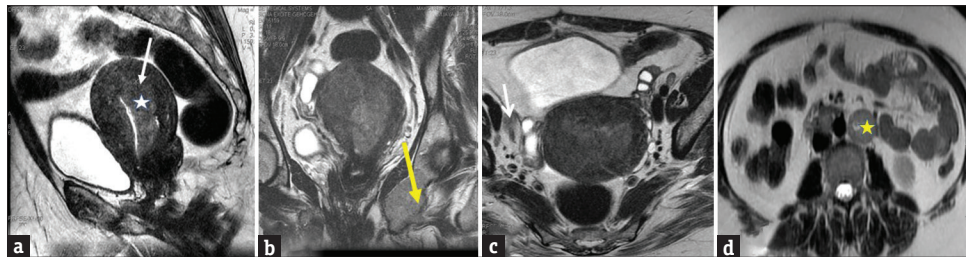


Figure 13: Stage IVB endometrial cancer in a 66-year-old female. (a) Sagittal T2-weighted magnetic resonance image shows a bulky endometrial tumor (*) with poor tumor-to-myometrium contrast (arrow). (b) On an Oblique coronal magnetic resonance image, the mass is extending and crossing the serosa and also there is bone marrow involvement of the left ischial tuberosity (yellow arrow) suggesting distant metastatic spread downstaging the tumor to IV B (c) On an Axial T2-weighted magnetic resonance image right external iliac lymph node seen (white arrow) (d) Sections through upper abdomen demonstrates Enlarged paraaortic and paracaval lymph nodes which are similar in signal intensity to the endometrial cavity mass (yellow star)

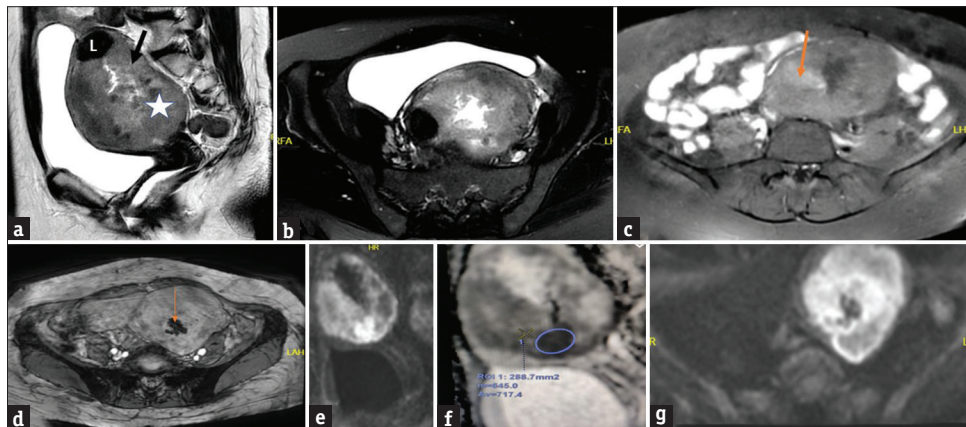
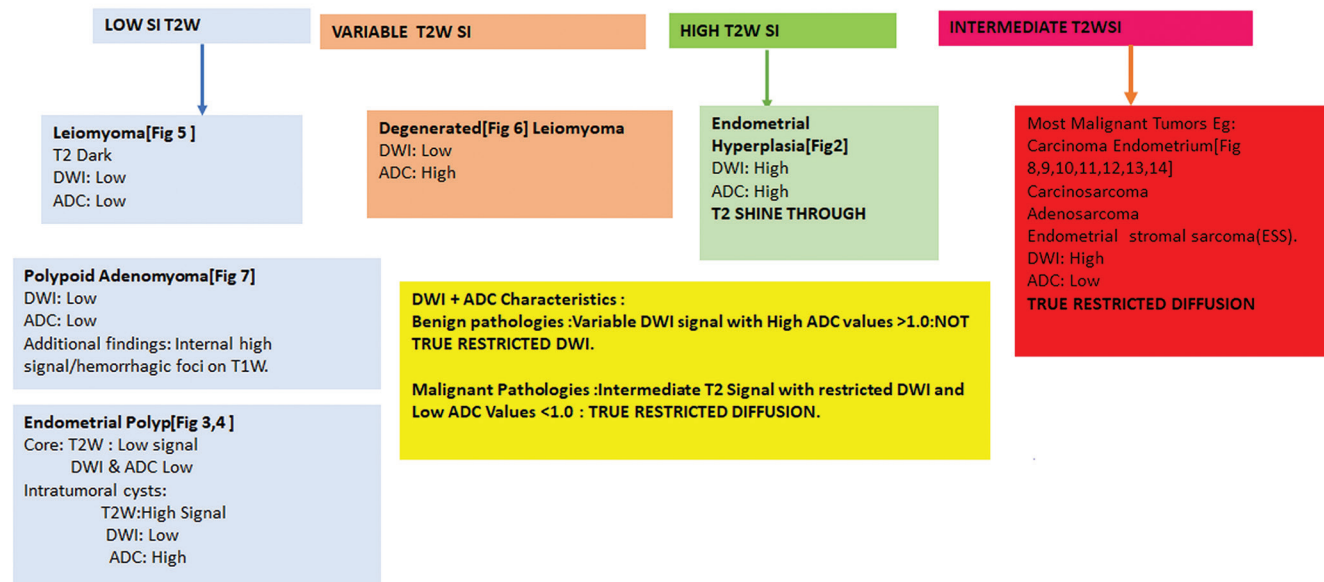


Figure 14: Stage 3 Stage IIIA endometrial cancer in a 65-year-old female: (a) Sagittal T2-weighted, (b) Axial T2-weighted. (c) T1FAT SAT. (d) SWI, (e-g) Sag and Axial DWI with apparent diffusion coefficient map: Sagittal T2-weighted ME image shows a large endometrial tumor (*). The depth of myometrial invasion is difficult to determine owing to poor tumor-to-myometrium contrast (arrow). (b) Axial oblique T2-weighted magnetic resonance image shows extension of the endometrial tumor (*) up to the serosa. The tumor is isointense relative to the adjacent myometrium. In addition, the uterus is distorted by two leiomyomas (L), whose presence is a commonly reported pitfall in staging. (c) T1FATSAT image reveals bright signal which shows corresponding blooming on SWI (arrow). (d) suggestive of hemorrhage. (e and g) diffusion-weighted image reveal high signal with low apparent diffusion coefficient values of 0.5–0.6. (f) Restricted diffusion. HPE Mucinous adenocarcinoma

BOX 3. DIAGNOSTIC ALGORITHM FOR ENDOMETRIAL LESIONS :MULTIPARAMETRIC MRI**T2W :Crucial for Anatomic Reference + DWI /ADC**

DWI: Diffusion-weighted images, ADC: Apparent diffusion coefficient, T2W: T2-weighted, ESS: Endometrial stromal sarcoma

In addition, MRI is indispensable in complex anatomy and coexisting lesions where the characterization of USG is suboptimal [Figure 10].

The standard imaging evaluation until recently was T2W and dynamic contrast enhancement (DCE) to stage the carcinoma.^[3,4] However the application of T2W with DWI and ADC values provides equal and superior results obviating the necessity to give contrast in the postmenopausal age group with compromised renal parameters.

Personal experience

DWI with ADC values in correlation with T2W imaging analysis can detect and differentiate between benign and malignant etiologies with high accuracy adding specificity to the clinical indication and justifying the role of multiparametric MRI in subset of patients where the biopsy is not feasible owing to comorbid conditions precluding anesthesia. In addition, the ADC values reflect the histological behavior of the tumor and correlated with grading with lower ADC values in high-grade lesions. However, there was a significant overlap between the ADC values across various malignant etiologies.

The MRI pictures are from Dr. Madhavi's collection and are copyrighted.

SUMMARY

Endometrial cavity lesions are heterogeneous and vary

from benign to malignant lesions. Diagnostic algorithm with multiparametric MRI findings of endometrial cavity lesions including T2WI and DWI [Box 3] is helpful for accurate diagnosis guiding formulation of a differential diagnosis to assist clinicians in determining appropriate treatment.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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