American College of Radiology
ACR Appropriateness Criteria®
Abnormal Uterine Bleeding

Variant: 1   Abnormal uterine bleeding. Initial imaging.

Procedure	Appropriateness Category	Relative Radiation Level
US duplex Doppler pelvis	Usually Appropriate	O
US pelvis transabdominal	Usually Appropriate	O
US pelvis transvaginal	Usually Appropriate	O
US sonohysterography	May Be Appropriate (Disagreement)	O
MRI pelvis without and with IV contrast	Usually Not Appropriate	O
MRI pelvis without IV contrast	Usually Not Appropriate	O
CT pelvis with IV contrast	Usually Not Appropriate	☢☢☢
CT pelvis without IV contrast	Usually Not Appropriate	☢☢☢
CT pelvis without and with IV contrast	Usually Not Appropriate	☢☢☢☢

Variant: 2   Abnormal uterine bleeding. Follow-up imaging when original ultrasound is inconclusive or further imaging characterization is needed.

Procedure	Appropriateness Category	Relative Radiation Level
US sonohysterography	Usually Appropriate	O
MRI pelvis without and with IV contrast	Usually Appropriate	O
US duplex Doppler pelvis	May Be Appropriate (Disagreement)	O
US pelvis transabdominal	May Be Appropriate (Disagreement)	O
US pelvis transvaginal	May Be Appropriate (Disagreement)	O
MRI pelvis without IV contrast	May Be Appropriate (Disagreement)	O
CT pelvis with IV contrast	Usually Not Appropriate	☢☢☢
CT pelvis without IV contrast	Usually Not Appropriate	☢☢☢
CT pelvis without and with IV contrast	Usually Not Appropriate	☢☢☢☢

Variant: 3   Abnormal uterine bleeding. Follow-up imaging when surveillance is appropriate given findings from the initial ultrasound.

Procedure	Appropriateness Category	Relative Radiation Level
US duplex Doppler pelvis	Usually Appropriate	O
US pelvis transabdominal	Usually Appropriate	O
US pelvis transvaginal	Usually Appropriate	O
US sonohysterography	Usually Appropriate	O
MRI pelvis without and with IV contrast	Usually Appropriate	O
MRI pelvis without IV contrast	May Be Appropriate	O
CT pelvis with IV contrast	Usually Not Appropriate	☢☢☢
CT pelvis without IV contrast	Usually Not Appropriate	☢☢☢
CT pelvis without and with IV contrast	Usually Not Appropriate	☢☢☢☢

Panel Members

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Summary of Literature Review

Introduction/Background

Introduction/Background

At least one-third of women can be expected to experience abnormal uterine bleeding (AUB) at some time in their lives [1]. AUB is defined as bleeding from the uterus that is abnormal in regularity, volume, frequency, or duration and occurs in the absence of pregnancy [2]. Causes of AUB can be partitioned into structural and nonstructural etiologies. Structural causes of AUB include endometrial polyps, adenomyosis, leiomyoma, malignancy (endometrial or myometrial), and endometrial hyperplasia. Nonstructural causes include coagulopathies, ovulatory dysfunction, primary endometrial disorders (such as molecular deficiencies in the regulation of endometrial hemostasis), iatrogenic etiologies (including exogenous gonadal steroids and intrauterine devices), and other causes not otherwise classified [1,2]. Because the nonstructural causes of AUB cannot be assessed with imaging, these will not be further discussed in this document. On the other hand, the structural causes can be diagnosed with imaging. In premenopausal women, polyps, adenomyosis, and leiomyoma are the common structural sources of AUB [3]. Although postmenopausal bleeding may be due to structural causes such as polyps or endometrial hyperplasia, endometrial cancer is the most serious etiology and is thus the main focus of the evaluation of the workup of AUB in the postmenopausal population [3-5]. The workup of a woman with abnormal bleeding begins with a thorough history, physical examination, and appropriate laboratory tests and may include imaging to primarily assess for structural abnormalities and help triage and manage both reproductive age and postmenopausal women with AUB [3,5-7]. Endometrial sampling may be considered in patients with AUB who have an increased risk for endometrial cancer due to obesity, chronic anovulation, family history, or age irrespective of imaging findings. AUB during pregnancy is beyond the scope of this document and is addressed in the ACR Appropriateness Criteria® topic on "First Trimester Vaginal Bleeding" [8] and the ACR Appropriateness Criteria® topic on "Second and Third Trimester Bleeding" [9].

Special Imaging Considerations

There are limitations to transvaginal ultrasound (TVUS), and it is not possible to assess the uterus in all women with AUB [10,11]. The position of the uterus, patient body habitus, and presence of uterine pathology, such as adenomyosis and leiomyomas, can all cause incomplete visualization of portions of the uterus and endometrium. In women with AUB, the main differential includes both endometrial causes (eg, endometrial cancer, hyperplasia, polyp, or endometrial atrophy) and myometrial causes (eg, leiomyomas, leiomyosarcomas, or adenomyosis). If the endometrium cannot be completely evaluated by ultrasound (US), endometrial sampling should be considered based upon each patient's risk factors for endometrial cancer [10]. MRI can also be considered for the assessment of the endometrium. Even in the presence of leiomyomas and adenomyosis, MRI can visualize the endometrium because of its multiplanar capability and excellent tissue contrast

resolution [12,13] when US cannot.

Although pelvic MRI protocols may vary somewhat between institutions, we specifically note that the addition of a diffusion-weighted imaging sequence is important in the MRI examination of the uterus in women with AUB. Diffusion-weighted imaging has been shown to improve the sensitivity and specificity of MRI for the accurate diagnosis of uterine pathology [14-16]. This has been most extensively studied in endometrial cancer; however, there is ongoing research in using diffusion-weighted imaging for differentiating leiomyosarcomas from benign leiomyomas [16-23]. MR angiography may be incorporated into the MRI protocol in the preprocedural workup of leiomyomas prior to uterine artery embolization because the vascular anatomy serves as a road map for the interventional radiologist [24,25].

In the initial assessment of leiomyomas and other uterine pathologies, 3-D US may also be considered, because this technique has the potential to help with spatial assessment and treatment planning [26]. Research is ongoing to determine the clinical accuracy of 3-D US compared with 2-D US alone [27-29]. Three-dimensional US may increase the confidence of the diagnosis and be helpful when communicating with the referring physician on the location and size of uterine pathology [30,31].

US elastography measures tissue stiffness. Small studies have shown that, in combination with routine 2-D US, strain, elastography may increase the diagnostic accuracy of US in differentiating endometrial polyps from submucosal leiomyomas [32] and differentiating leiomyomas from adenomyosis [33].

Initial Imaging Definition

Initial imaging is defined as imaging at the beginning of the care episode for the medical condition defined by the variant. More than one procedure can be considered usually appropriate in the initial imaging evaluation when:

- There are procedures that are equivalent alternatives (ie, only one procedure will be ordered to provide the clinical information to effectively manage the patient's care)

OR

- There are complementary procedures (ie, more than one procedure is ordered as a set or simultaneously wherein each procedure provides unique clinical information to effectively manage the patient's care).

Discussion of Procedures by Variant

Variant 1: Abnormal uterine bleeding. Initial imaging.

Variant 1: Abnormal uterine bleeding. Initial imaging.
A. CT Pelvis

To our knowledge, there is no relevant literature to support the use of CT pelvis in the initial imaging evaluation of AUB.

Variant 1: Abnormal uterine bleeding. Initial imaging.

B. MRI Pelvis

To our knowledge, there is no relevant literature to support the use of MRI pelvis in the initial imaging evaluation of AUB.

Variant 1: Abnormal uterine bleeding. Initial imaging.
C. US Duplex Doppler Pelvis

Although it is rated as a separate imaging procedure per ACR methodology, this document considers Doppler imaging to be a standard component of pelvic US. Color and spectral Doppler are routinely used in pelvic US examinations to evaluate internal vascularity of pelvic findings and distinguish fluid from vascular soft-tissue.

US duplex Doppler evaluation of the vascularity of the endometrium can help identify vessels within endometrial polyps or cancer, or the lack of vascularity in the normal endometrium [30]. Visualization of a vascular pedicle during transvaginal color Doppler imaging has a specificity of 62% to 98% and a negative predictive value of 50% to 94% for the detection of endometrial polyps [34-36].

Currently, investigations are ongoing to evaluate whether color Doppler patterns can differentiate endometrial polyps from endometrial cancer [4,34,37]. The addition of Doppler may improve the sensitivity, specificity, and positive predictive value of US for the diagnosis of adenomyosis [38]. To our knowledge, there is no relevant literature that has assessed vascularity of leiomyomas and leiomyosarcomas in order to differentiate these two entities.

Variant 1: Abnormal uterine bleeding. Initial imaging.
D. US Pelvis Transabdominal

A combined transabdominal and transvaginal approach is typically used for pelvic US imaging. Transabdominal US is most helpful in the case of a significantly enlarged uterus or uterine tumor, in which the limited field-of-view of TVUS cannot image all portions of the uterus or uterine tumor.

Variant 1: Abnormal uterine bleeding. Initial imaging.
E. US Pelvis Transvaginal

TVUS should be combined with transabdominal US whenever possible in order to fully assess the pelvic structures. Combining the anatomic overview provided by the transabdominal approach with the greater spatial and contrast resolution of transvaginal imaging will allow for more complete assessment of the pelvis. TVUS is able to detect both benign endometrial or myometrial pathologies such as endometrial hyperplasia, polyps, adenomyosis, or leiomyomas [39-41]. In the setting of postmenopausal bleeding, TVUS is considered the first-line screening test for endometrial cancer [5,42]. An endometrial thickness of ≤4 mm in a postmenopausal woman conveys a negative predictive value for cancer of nearly 100% [5,10,43-45]. Although TVUS is sensitive for the evaluation of endometrial thickness, it cannot reliably determine the etiology of endometrial thickening [4]. Therefore, particularly in postmenopausal women, a thickened endometrium (≥5 mm) generally prompts evaluation by endometrial tissue sampling [10]. In premenopausal women, normal endometrial thickness varies with the phase of the menstrual cycle. Many studies have shown that the thickness of the endometrium in premenopausal women is not an indicator of endometrial pathology, and even if the thickness is <5 mm, endometrial polyps or other endometrial pathology may be present [43]. There is no validated absolute upper limit cutoff for endometrial thickness in premenopausal women [46]. For both postmenopausal and premenopausal women, abnormal echogenicity and texture of the endometrium has been

correlated with significant underlying uterine pathology [5,44,45].

Leiomyomas and adenomyosis are other structural causes of AUB. In a meta-analysis of 14 studies including 1,898 women who had US for uterine pathology, the pooled sensitivity and specificity for TVUS for the diagnosis of adenomyosis were 82.5% and 84.6%, respectively [41]. However, detection of adenomyosis at TVUS may be limited if there is coexisting uterine pathology, such as leiomyomas. In one study, the sensitivity and specificity of TVUS for diagnosing adenomyosis in patients with and without leiomyomas were 33.3% and 78% and 97.8% and 97.1%, respectively [47].

Variant 1: Abnormal uterine bleeding. Initial imaging.
F. US Sonohysterography

US sonohysterography, also referred to as hysterosonography, can be used in the setting of AUB, particularly if the initial TVUS demonstrates a focal endometrial abnormality [48]. The technique involves transcervical injection of sterile fluid, such as saline, in combination with routine TVUS [10,49]. Although some authors describe transcervical injection of gel [37], sterile saline is currently the accepted standard endometrial contrast agent [49]. The literature supports the use of US sonohysterography as an examination to further characterize endometrial observations on TVUS [48-51].

Variant 2: Abnormal uterine bleeding. Follow-up imaging when original ultrasound is inconclusive or further imaging characterization is needed.

Variant 2: Abnormal uterine bleeding. Follow-up imaging when original ultrasound is inconclusive or further imaging characterization is needed.
A. CT Pelvis

To our knowledge, there is no relevant literature to support the use of CT pelvis for the reassessment or follow up imaging of AUB.

Variant 2: Abnormal uterine bleeding. Follow-up imaging when original ultrasound is inconclusive or further imaging characterization is needed.
B. MRI Pelvis

When MRI is performed, the use of a gadolinium-based intravenous (IV) contrast agent is preferred. Please refer to the ACR *Manual on Contrast Media* for additional information [52]. The inclusion of diffusion-weighted sequences should also be strongly considered.

When the uterus is incompletely visualized by US or findings are indeterminate, MRI can be considered because of its multiplanar capabilities and excellent tissue contrast and resolution in the pelvis. MRI can display the endometrium, even in the setting of leiomyomas and adenomyosis, features which may obscure the endometrium on US. MRI can identify malignant uterine pathology with sensitivity and specificity up to 79% and 89%, respectively, for endometrial cancer and 100% and 100%, respectively, for leiomyosarcomas [17,53] and can differentiate benign endometrial pathologies (hyperplasia and polyps) from endometrial cancer [12-14,53]. An abnormal signal on diffusion-weighted images and irregularity of the endometrial-myometrial interface were the most helpful MRI features in differentiating benign from malignant pathologies, with area under the curve of 0.89 [14]. Please refer to the ACR Appropriateness Criteria[®] topic on "Pretreatment Evaluation and Follow-Up of Endometrial Cancer" [54] for additional information.

In the case of assessing leiomyomas prior to treatment, MRI has been shown to have increased sensitivity and specificity for location and size, in addition to helping exclude the coexistence of a leiomyosarcoma [12,16,17,20,21]. MRI has a sensitivity of approximately 78% and specificity of nearly 93% for the diagnosis of adenomyosis, and it can be used in the reassessment of women with AUB to exclude adenomyosis [13,55].

Variant 2: Abnormal uterine bleeding. Follow-up imaging when original ultrasound is inconclusive or further imaging characterization is needed.
C. US Duplex Doppler Pelvis

Although it is rated as a separate imaging procedure per ACR methodology, this document considers Doppler imaging to be a standard component of pelvic US. US duplex Doppler evaluation of the vascularity of the endometrium can help identify vessels within endometrial polyps or cancer [30,56]. Currently, there are no definitive studies demonstrating whether Doppler can differentiate between benign and malignant endometrial lesions; however, research is ongoing [37,56,57].

US duplex Doppler evaluation of leiomyomas and adenomyosis can be performed; however, there are no definitive studies demonstrating Doppler can differentiate between these two entities [58].

Variant 2: Abnormal uterine bleeding. Follow-up imaging when original ultrasound is inconclusive or further imaging characterization is needed.
D. US Pelvis Transabdominal

A combined transabdominal and transvaginal approach is most appropriate for pelvic US imaging. Transabdominal US is most helpful in the case of an enlarged uterus or uterine tumor, in which the limited field-of-view of TVUS cannot image all portions of the uterus or uterine tumor.

Variant 2: Abnormal uterine bleeding. Follow-up imaging when original ultrasound is inconclusive or further imaging characterization is needed.
E. US Pelvis Transvaginal

If the initial imaging and clinical evaluation (eg, endometrial sampling) of women with AUB are negative, endometrial cancer in these women is extremely unlikely [10]. Nonetheless, repeat TVUS can be performed to reassess the endometrium, because endometrial cancers may be missed on initial imaging or endometrial sampling [59]. If on repeat imaging, the endometrium remains <4 mm in a postmenopausal woman, the negative predictive value for cancer is nearly 100% [10].

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US sonohysterography, also referred to as hysterosonography, can be used in the setting of AUB, particularly if the initial TVUS demonstrates a focal endometrial abnormality [48]. The technique involves transcervical injection of sterile fluid, such as saline, in combination with routine TVUS [10,49]. Although some authors describe transcervical injection of gel [37], sterile saline is currently the accepted standard endometrial contrast agent [49].

The literature supports the use of US sonohysterography as an examination to further characterize endometrial observations on TVUS [48-51]. US sonohysterography can help distinguish between leiomyomas and endometrial polyps with pooled accuracies of 97% [51]. With the sonohysterographic features of an intact myometrial-endometrial interface, a single vessel, an

acute angle with the endometrium, and a homogenous echogenicity, the likelihood ratio of an endometrial polyp is optimized, whereas the combined features of absent endometrial-myometrial interface, arborized vascular pattern, obtuse angle with the endometrium, and a heterogeneous echogenicity maximizes the likelihood ratio of an intracavitary or submucosal leiomyoma [50].

Despite its ability to differentiate polyps and leiomyomata, sonohysterography cannot distinguish between benign endometrial pathology and endometrial cancer with a high degree of certainty, and endometrial sampling or direct visualization with hysteroscopy is recommended in women with suspected endometrial pathology [10,50,51]. In the setting of focal endometrial pathology, an accurate description of the location of the abnormality may direct hysteroscopic resection.

US sonohysterography is helpful to distinguish between focal or diffuse pathology in the setting of a postmenopausal woman with AUB and a thickened endometrium on TVUS [58]. However, US sonohysterography cannot distinguish between benign endometrial pathology and endometrial cancer with a high degree of certainty, and endometrial sampling or direct visualization with hysteroscopy is recommended in women with suspected endometrial pathology [10]. Additionally, US sonohysterography can confirm the diagnosis of endometrial atrophy. Although sonohysterography could be considered in the setting of a previously inconclusive US, there is no current evidence confirming this approach is helpful if the endometrium could not be visualized on conventional TVUS [28].

Variant 3: Abnormal uterine bleeding. Follow-up imaging when surveillance is appropriate given findings from the initial ultrasound.

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In the case of assessing leiomyomas prior to treatment or for potential growth, MRI has been shown to have increased sensitivity and specificity for location and size, in addition to helping

exclude the coexistence of a leiomyosarcoma [12,16,17,20,21]. MRI has a sensitivity of approximately 78% and specificity of nearly 93% for the diagnosis of adenomyosis, and it can be used in the reassessment of women with AUB to exclude adenomyosis [13,55].

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If the initial imaging and clinical evaluation (eg, endometrial sampling) of women with AUB are negative, endometrial cancer in these women is extremely unlikely [10]. Nonetheless, repeat TVUS can be performed to reassess the endometrium, because endometrial cancers may be missed on initial imaging or endometrial sampling [59]. If on repeat imaging, the endometrium remains <4 mm in a postmenopausal woman, the negative predictive value for cancer is nearly 100% [10].

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interface, arborized vascular pattern, obtuse angle with the endometrium, and a heterogeneous echogenicity maximizes the likelihood ratio of an intracavitary or submucosal leiomyoma [50].

Despite its ability to differentiate polyps and leiomyomata, sonohysterography cannot distinguish between benign endometrial pathology and endometrial cancer with a high degree of certainty, and endometrial sampling or direct visualization with hysteroscopy is recommended in women with suspected endometrial pathology [10,50,51]. In the setting of focal endometrial pathology, an accurate description of the location of the abnormality may direct hysteroscopic resection.

US sonohysterography is highly sensitive for endometrial lesions and can be used in the follow-up setting to assess for the presence and growth of endometrial pathology [60]. Additionally, US sonohysterography is helpful to distinguish between focal or diffuse pathology in the setting of a postmenopausal woman with AUB and a thickened endometrium on TVUS [58]. However, US sonohysterography cannot distinguish between benign endometrial pathology and endometrial cancer with a high degree of certainty, and endometrial sampling or direct visualization with hysteroscopy is recommended in women with suspected endometrial pathology [10].

Summary of Recommendations

- **Variant 1:** US duplex Doppler pelvis, US pelvis transvaginal, and US pelvis transabdominal are usually appropriate for the initial imaging of AUB. These procedures are complementary (ie, more than one procedure is ordered as a set or simultaneously where each procedure provides unique clinical information to effectively manage the patient's care.) The panel did not agree on recommending US sonohysterography for patients in this clinical scenario. There is insufficient medical literature to conclude whether or not these patients would benefit from this procedure. Imaging with US sonohysterography is controversial but may be appropriate.
- **Variant 2:** US sonohysterography and MRI pelvis without and with IV contrast are usually appropriate for the follow-up imaging of AUB when the original US is inconclusive or further imaging characterization is needed. These procedures are complementary (ie, more than one procedure is ordered as a set or simultaneously where each procedure provides unique clinical information to effectively manage the patient's care.) The panel did not agree on recommending MRI pelvis without IV contrast, US duplex Doppler pelvis, US pelvis transabdominal, and US pelvis transvaginal for patients in this clinical scenario. There is insufficient medical literature to conclude whether or not these patients would benefit from these procedures. Imaging with these procedures is controversial but may be appropriate.
- **Variant 3:** US pelvis transvaginal, US duplex Doppler pelvis, US pelvis transabdominal, US sonohysterography, and MRI pelvis without and with IV contrast are usually appropriate for the follow-up imaging of AUB when surveillance is appropriate given findings from the initial US. These procedures are complementary (ie, more than one procedure is ordered as a set or simultaneously where each procedure provides unique clinical information to effectively manage the patient's care.)

Supporting Documents

The evidence table, literature search, and appendix for this topic are available at https://acsearch.acr.org/list. The appendix includes the strength of evidence assessment and the

final rating round tabulations for each recommendation.

For additional information on the Appropriateness Criteria methodology and other supporting documents, please go to the ACR website at https://www.acr.org/Clinical-Resources/Clinical-Tools-and-Reference/Appropriateness-Criteria.

Appropriateness Category Names and Definitions

Appropriateness Category Name	Appropriateness Rating	Appropriateness Category Definition
Usually Appropriate	7, 8, or 9	The imaging procedure or treatment is indicated in the specified clinical scenarios at a favorable risk-benefit ratio for patients.
May Be Appropriate	4, 5, or 6	The imaging procedure or treatment may be indicated in the specified clinical scenarios as an alternative to imaging procedures or treatments with a more favorable risk-benefit ratio, or the risk-benefit ratio for patients is equivocal.
May Be Appropriate (Disagreement)	5	The individual ratings are too dispersed from the panel median. The different label provides transparency regarding the panel's recommendation. "May be appropriate" is the rating category and a rating of 5 is assigned.
Usually Not Appropriate	1, 2, or 3	The imaging procedure or treatment is unlikely to be indicated in the specified clinical scenarios, or the risk-benefit ratio for patients is likely to be unfavorable.

Relative Radiation Level Information

Potential adverse health effects associated with radiation exposure are an important factor to consider when selecting the appropriate imaging procedure. Because there is a wide range of radiation exposures associated with different diagnostic procedures, a relative radiation level (RRL) indication has been included for each imaging examination. The RRLs are based on effective dose, which is a radiation dose quantity that is used to estimate population total radiation risk associated with an imaging procedure. Patients in the pediatric age group are at inherently higher risk from exposure, because of both organ sensitivity and longer life expectancy (relevant to the long latency that appears to accompany radiation exposure). For these reasons, the RRL dose estimate ranges for pediatric examinations are lower as compared with those specified for adults (see Table below). Additional information regarding radiation dose assessment for imaging examinations can be found in the ACR Appropriateness Criteria[®] Radiation Dose Assessment Introduction document.

Relative Radiation Level Designations

Relative Radiation Level*	Adult Effective Dose Estimate Range	Pediatric Effective Dose Estimate Range
O	0 mSv	0 mSv
☢	<0.1 mSv	<0.03 mSv
☢☢	0.1-1 mSv	0.03-0.3 mSv
☢☢☢	1-10 mSv	0.3-3 mSv

| ☢☢☢☢ | 10-30 mSv | 3-10 mSv |
| ☢☢☢☢☢ | 30-100 mSv | 10-30 mSv |

*RRL assignments for some of the examinations cannot be made, because the actual patient doses in these procedures vary as a function of a number of factors (e.g., region of the body exposed to ionizing radiation, the imaging guidance that is used). The RRLs for these examinations are designated as "Varies."

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