

**Abnormal Vaginal Bleeding
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
1. Bayer SR, DeCherney AH. Clinical manifestations and treatment of dysfunctional uterine bleeding. <i>JAMA</i> . 1993; 269(14):1823-1828.	Review/Other-Tx	N/A	To review treatment of dysfunctional uterine bleeding.	Goals of treatment are to stop acute bleeding, avert future episodes, and prevent long-term complications.	4
2. Sweet MG, Schmidt-Dalton TA, Weiss PM, Madsen KP. Evaluation and management of abnormal uterine bleeding in premenopausal women. <i>Am Fam Physician</i> . 2012; 85(1):35-43.	Review/Other-Tx	N/A	Review evaluation and management of abnormal uterine bleeding in premenopausal women.	TVUS or SIS may be used to evaluate menorrhagia. The levonorgestrel-releasing intrauterine system is an effective treatment for menorrhagia. Oral progesterone for 21 days per month and nonsteroidal anti-inflammatory drugs are also effective. Tranexamic acid is approved by the FDA for the treatment of ovulatory bleeding, but is expensive. When clear structural causes are identified or medical management is ineffective, polypectomy, fibroidectomy, uterine artery embolization, and endometrial ablation may be considered. Hysterectomy is the most definitive treatment.	4
3. National Cancer Institute. <i>Comprehensive Cancer Information</i> . http://seer.cancer.gov/statfacts/html/ovary.html . Accessed November 27, 2012.	Review/Other-Tx	N/A	A report on US cancer statistics and cancer surveillance methods.	The report includes information on incidence, prevalence and survival from specific geographic areas representing 28% of the U.S. population and cancer mortality for the entire country.	4
4. Dimitraki M, Tsikouras P, Bouchlariotou S, et al. Clinical evaluation of women with PMB. Is it always necessary an endometrial biopsy to be performed? A review of the literature. <i>Arch Gynecol Obstet</i> . 2011; 283(2):261-266.	Review/Other-Dx	N/A	To examine available literature on the diagnostic evaluation of postmenopausal women with vaginal bleeding, accentuating the most important aspects on this topic: the accuracy of US and endometrial biopsy in predicting endometrial hyperplasia and endometrial carcinoma.	In the last decades, there has been an explosion of publications indicating that US may be useful in predicting endometrial pathology. Since advanced endometrial carcinoma has been known to occur in cases without noticeable endometrial thickness on US, the clinician should beware of the diagnostic evaluation of postmenopausal women with vaginal bleeding.	4
5. Doubilet PM. Diagnosis of abnormal uterine bleeding with imaging. <i>Menopause</i> . 2011; 18(4):421-424.	Review/Other-Dx	N/A	The authors present two clinical algorithms: the "ultrasound-first" approach and the "biopsy-first" approach.	Either of the two algorithms is an acceptable approach to the use of US and/or endometrial biopsy in women with postmenopausal bleeding.	4

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6. Hofmeister FJ. Endometrial biopsy: another look. <i>Am J Obstet Gynecol.</i> 1974; 118(6):773-777.	Review/Other-Dx	20,677 total biopsies from 1949- 1973: 3,011 biopsies from 1967-1973	To examine role of endometrial biopsy for early diagnosis and treatment.	For the 3,011 biopsies, absolute detection rate by endometrial biopsy was 1.1%. Endometrial malignancies were detected 40 times with a detection rate of 1.3%. Papanicolaou smear or symptoms are added. Asymptomatic and unsuspected carcinoma was found in 15% of these 40 cases. Cervical and vaginal pool Papanicolaou smear revealed a clue in 45% of these 40 cases. It was positive in 205, atypical and suspicious in 25% and negative in 47% of these cases. For the 20,677 biopsies, endometrial malignancies were detected 187 times. Detection rate of 0.9% for malignancy of the endometrium was established. Of these, a total of 32 were asymptomatic and unsuspected (17%). Of the 187, the Papanicolaou smear was atypical or positive in 50 instances (26%).	4
7. Smith-Bindman R, Weiss E, Feldstein V. How thick is too thick? When endometrial thickness should prompt biopsy in postmenopausal women without vaginal bleeding. <i>Ultrasound Obstet Gynecol.</i> 2004; 24(5):558-565.	Review/Other-Dx	Theoretical cohort of postmenopausal women aged ≥ 50 years	To determine an endometrial thickness threshold that should prompt biopsy in a postmenopausal woman without vaginal bleeding.	In a postmenopausal woman without vaginal bleeding, if the endometrium measures >11 mm a biopsy should be considered as the risk of cancer is 6.7%, while if the endometrium measures ≤ 11 mm a biopsy is not needed as the risk of cancer is extremely low.	4
8. ACOG practice bulletin: management of anovulatory bleeding. <i>Int J Gynaecol Obstet.</i> 2001; 72(3):263-271.	Review/Other-Tx	N/A	To provide management guidelines for treatment of anovulatory bleeding based on best available evidence.	Treatment of choice for anovulatory bleeding is medical therapy with oral contraceptives. Cyclic progestins are also effective. Endometrial ablation is recommended for women who have failed medical therapy and do not desire future childbearing. Endometrial ablation is an efficient and cost-effective alternative treatment for anovulatory bleeding, although it may be definitive therapy.	4

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9. Farquhar C, Ekeroma A, Furness S, Arroll B. A systematic review of transvaginal ultrasonography, sonohysterography and hysteroscopy for the investigation of abnormal uterine bleeding in premenopausal women. <i>Acta Obstet Gynecol. Scand.</i> 2003; 82(6):493-504.	Review/Other-Dx	19 studies	Systematic review to determine the accuracy of TVUS, sonohysterography and diagnostic hysteroscopy for examining abnormal uterine bleeding in premenopausal women.	A positive test result with sonohysterography diagnosed submucous fibroids with a pooled likelihood ratio of 29.7 (17.8, 49.6). A positive test result with hysteroscopy diagnosed submucous fibroids with a pooled likelihood ratio of 29.4 (13.4, 65.3), and any intrauterine pathology with a pooled likelihood ratio of 7.7 (4.3, 13.7). A negative test result with hysteroscopy for diagnosing any intrauterine pathology had a pooled likelihood ratio of 0.07 (0.04, 0.15). All three diagnostic tests were moderately accurate in detecting intrauterine pathology. However, sonohysterography and hysteroscopy performed better than TVUS in detecting submucous fibroids.	4
10. Epstein E, Ramirez A, Skoog L, Valentin L. Dilatation and curettage fails to detect most focal lesions in the uterine cavity in women with postmenopausal bleeding. <i>Acta Obstet Gynecol. Scand.</i> 2001; 80(12):1131-1136.	Observational-Dx	105 women	Prospective study to determine the prevalence of focally growing lesions in the uterine cavity in women with postmenopausal bleeding and endometrium ≥ 5 mm and the extent to which such lesions can be correctly diagnosed by D&C.	80% (84/105) of the women had pathology in the uterine cavity, and 98% (82/84) of the pathological lesions manifested a focal growth pattern at hysteroscopy. In 87% of the women with focal lesions in the uterine cavity, the whole or parts of the lesion remained in situ after D&C. D&C missed 58% (25/43) of polyps, 50% (5/10) of hyperplasias, 60% (3/5) of complex atypical hyperplasias, and 11% (2/19) of endometrial cancers. The agreement between the D&C diagnosis and the final diagnosis was excellent (94%) in women without focally growing lesions at hysteroscopy.	2
11. Yarandi F, Izadi-Mood N, Eftekhar Z, Shojaei H, Sarmadi S. Diagnostic accuracy of dilatation and curettage for abnormal uterine bleeding. <i>J Obstet Gynaecol. Res.</i> 2010; 36(5):1049-1052.	Observational-Dx	311 patients	To compare the histological findings of D&C with those on subsequent hysterectomy in patients with abnormal uterine bleeding.	The mean age of our patients was 46.6 years. In 164/311 patients (52.7%), D&C failed to detect intrauterine disorders subsequently found at hysterectomy. The sensitivity was 30.2%, the specificity was 72.3%, the PPV was 77.1%, and the NPV was 25.1%. The accuracy was 40.5% overall. D&C is an inadequate diagnostic tool for uterine focal lesions, but the accuracy of D&C in the detection of endometrial hyperplasia and carcinoma is relatively high (92.1%).	3

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12. Dijkhuizen FP, Mol BW, Brolmann HA, Heintz AP. Cost-effectiveness of the use of transvaginal sonography in the evaluation of postmenopausal bleeding. <i>Maturitas</i> . 2003; 45(4):275-282.	Review/Other-Dx	N/A	Performed a decision analysis to assess the cost-effectiveness of TVUS in the diagnostic workup of women with postmenopausal bleeding.	Most cost-effective strategies were the strategy with endometrial biopsy and the strategy with TVUS followed by endometrial biopsy in case of an increased endometrial thickness. The strategy starting with endometrial biopsy was the most cost-effective when the prevalence of endometrial carcinoma was $\geq 15.3\%$. The strategy with TVUS and endometrial biopsy was the most cost-effective for women in which the prevalence of endometrial carcinoma was lower. In these strategies, a cut-off level for abnormality of 9 mm resulted in lowest cost per life-year gained.	4
13. Dubinsky TJ. Value of sonography in the diagnosis of abnormal vaginal bleeding. <i>J Clin Ultrasound</i> . 2004; 32(7):348-353.	Review/Other-Dx	N/A	Review article to determine whether US or biopsy is more effective in evaluating women with abnormal vaginal bleeding.	Endometrial biopsy and TVUS have equal sensitivities for carcinoma, but US is far more effective in diagnosing benign disease.	4
14. Hulka CA, Hall DA, McCarthy K, Simeone JF. Endometrial polyps, hyperplasia, and carcinoma in postmenopausal women: differentiation with endovaginal sonography. <i>Radiology</i> . 1994; 191(3):755-758.	Observational-Dx	68 women	Retrospective study to determine whether endometrial hyperplasia, polyps, and carcinoma can be differentiated on the basis of their US appearance. Pathologic and US findings were correlated.	30 sonograms showed hyperechoic endometria in women with hyperplasia (n=8), polyps (n=4), polyps and hyperplasia (n=2), or atrophy, proliferative change, mild atypia, or normal endometria (n=16); 27 sonograms showed cystic spaces in women with polyps (n=21), carcinoma (n=1), polyps and hyperplasia (n=2), or atrophy (n=3); and 11 sonograms showed heterogeneous endometria in women with endometrial carcinoma (n=7), atrophy (n=2), proliferative endometrium (n=1), or secretory endometrium (n=1). Cystic spaces were predictive of polyps ($P=1.19 \times 10^{-10}$).	3
15. Smith P, Bakos O, Heimer G, Ulmsten U. Transvaginal ultrasound for identifying endometrial abnormality. <i>Acta Obstet Gynecol. Scand</i> . 1991; 70(7-8):591-594.	Observational-Dx	96 patients	To evaluate the endometrium in patients referred for D&C with TVUS. The US display was correlated to the histopathologic diagnosis.	In 45 patients with postmenopausal bleeding, the sensitivity of US in diagnosing endometrial pathology was 100% and the specificity was 61%. PPV and NPV were 39% and 100%, respectively. In 51 premenopausal women, the sensitivity in diagnosing endometrial pathology was 67% and the specificity 75%. PPV and NPV were 14% and 97%, respectively.	2

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16. Smith-Bindman R, Kerlikowske K, Feldstein VA, et al. Endovaginal ultrasound to exclude endometrial cancer and other endometrial abnormalities. <i>JAMA</i> . 1998; 280(17):1510-1517.	Review/Other-Dx	35 articles; 5,892 women	To determine accuracy of EVUS in detecting endometrial disease in postmenopausal women with vaginal bleeding according to hormone replacement use.	In women not using hormone replacement therapy, 593 (8%) with normal histological findings had an abnormal EVUS result (specificity, 92%; 95% CI, 90%-94%), whereas 1,544 (23%) using hormone replacement therapy had an abnormal EVUS result (specificity, 77%; 95% CI, 75%-79%). EVUS has a high sensitivity.	4
17. Delisle MF, Villeneuve M, Boulvain M. Measurement of endometrial thickness with transvaginal ultrasonography: is it reproducible? <i>J Ultrasound Med</i> . 1998; 17(8):481-484; quiz 485-486.	Observational-Dx	55 patients	To assess the intraobserver and interobserver variability of TVUS measurement of endometrial thickness, two investigators independently evaluated two successive measurements. Each observer was blinded to his or her own and to the other's results.	Intraobserver kappa values (agreement on endometrium ≤ 5 mm and > 5 mm) were 0.70 and 0.81, respectively; the interobserver kappa value was 0.74. TVUS measurement of endometrial thickness has excellent intraobserver and good interobserver agreement.	4
18. Dueholm M, Lundorf E, Olesen F. Imaging techniques for evaluation of the uterine cavity and endometrium in premenopausal patients before minimally invasive surgery. <i>Obstet Gynecol. Surv</i> 2002; 57(6):388-403.	Review/Other-Dx	N/A	Literature review that compares the diagnostic effectiveness and accuracy of TVUS hysterosonographic examination, hysteroscopy, and MRI in abnormalities of the uterine cavity and endometrium in premenopausal patients referred to surgery and women with abnormal uterine bleeding.	TVUS should be a first choice modality for experienced clinicians, but should be supplemented by other techniques. Hysterosonographic examination or hysteroscopy performed by experienced clinicians should be used as supplements to TVUS for exclusion of polyps. MRI can be recommended as the first choice modality for exact evaluation of submucous myoma uterine in-growth before advanced minimal invasive treatment of myomas.	4
19. Gull B, Karlsson B, Milsom I, Granberg S. Can ultrasound replace dilation and curettage? A longitudinal evaluation of postmenopausal bleeding and transvaginal sonographic measurement of the endometrium as predictors of endometrial cancer. <i>Am J Obstet Gynecol</i> . 2003; 188(2):401-408.	Observational-Dx	339 women	To evaluate postmenopausal bleeding and TVUS measurement of endometrial thickness as predictors of endometrial cancer and atypical hyperplasia in women whose cases were followed for ≥ 10 years after referral for postmenopausal bleeding.	Reliability of endometrial thickness as a diagnostic test for endometrial cancer was: sensitivity, 100%; specificity, 60%; PPV, 25%; and NPV, 100%. The incidence of endometrial cancer or atypical hyperplasia in women with an intact uterus whose cases had been followed for ≥ 10 years was 5.8% (15/257 women) compared with 22.7% (15/66 women) in women who had ≤ 1 episode of recurrent bleeding. TVUS scanning is an excellent tool to determine whether further investigation with curettage or some form of endometrial biopsy is necessary.	3

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20. Moodley M, Roberts C. Clinical pathway for the evaluation of postmenopausal bleeding with an emphasis on endometrial cancer detection. <i>J Obstet Gynaecol.</i> 2004; 24(7):736-741.	Review/Other-Dx	N/A	Review the clinical pathway for the evaluation of postmenopausal bleeding with emphasis on endometrial cancer detection.	Based on a literature review, the evidence favors a conservative approach if the endometrial thickness is <4 mm, unless there are risk factors. All patients with endometrial thickness 4 mm should have outpatient endometrial sampling. If this is unsuccessful, then outpatient hysteroscopy with directed biopsy or inpatient hysteroscopy is favored.	4
21. Shi AA, Lee SI. Radiological reasoning: algorithmic workup of abnormal vaginal bleeding with endovaginal sonography and sonohysterography. <i>AJR Am J Roentgenol.</i> 2008; 191(6 Suppl):S68-73.	Review/Other-Dx	2 patients	Two cases are presented: a premenopausal woman presenting with vaginal bleeding and a postmenopausal woman taking tamoxifen who has abnormal findings on EVUS.	EVUS is used to identify mural abnormalities such as fibroids and adenomyosis and to screen for thickened endometria that require nonfocal biopsy for the diagnosis of cancer or hyperplasia. Sonohysterography serves as a triage tool to detect focal abnormalities of the endometrial cavity, such as endometrial polyps or subendometrial fibroids, thereby identifying those women who require more invasive workup with hysteroscopy.	4
22. Gupta JK, Chien PF, Voit D, Clark TJ, Khan KS. Ultrasonographic endometrial thickness for diagnosing endometrial pathology in women with postmenopausal bleeding: a meta-analysis. <i>Acta Obstet Gynecol. Scand.</i> 2002; 81(9):799-816.	Review/Other-Dx	57 studies with 9,031 patients	Meta-analysis to determine the diagnostic accuracy of endometrial thickness measurement by pelvic US for diagnosing endometrial pathology in women with postmenopausal bleeding.	4 mm (9 studies) and 5 mm (21 studies) were the common cut-offs. 4/21 studies used the ≤5 mm cut-off level, which had the best-quality criteria. For the 4 studies, a positive test result raised the probability of carcinoma from 14.0% (95% CI, 13.3-14.7) to 31.3% (95% CI, 26.1-36.3), while a negative test reduced it to 2.5% (95% CI, 0.9-6.4). US measurement of endometrial thickness alone, using the best-quality studies cannot be used to accurately rule. However, a negative result at ≤5 mm cut-off level measuring both endometrial layers in the presence of endometrial pathology rules out endometrial pathology with good certainty.	4

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23. Karlsson B, Granberg S, Wikland M, et al. Transvaginal ultrasonography of the endometrium in women with postmenopausal bleeding--a Nordic multicenter study. <i>Am J Obstet Gynecol.</i> 1995; 172(5):1488-1494.	Observational-Dx	1,168 women: 351 receiving hormonal replacement therapy; 165 receiving estriol; and 186 receiving systemic hormone replacement therapy with sequential estrogen-progestin therapy	Multicenter study to determine whether measurement of endometrial thickness with TVUS can be used to exclude endometrial abnormality in women with postmenopausal bleeding.	In women with atrophic endometrium the mean endometrial thickness was 3.9 +/- 2.5 mm. The corresponding figures for women with endometrial cancer were 21.1 +/- 11.8 mm. The risk of finding pathologic endometrium at curettage when the endometrium is \leq 4 mm as measured by TVUS is 5.5%.	3
24. Goldstein RB, Bree RL, Benson CB, et al. Evaluation of the woman with postmenopausal bleeding: Society of Radiologists in Ultrasound-Sponsored Consensus Conference statement. <i>J Ultrasound Med.</i> 2001; 20(10):1025-1036.	Review/Other-Dx	N/A	A panel of physicians met to discuss the role of US in women with postmenopausal bleeding.	Panelists agreed that either TVUS or endometrial biopsy could be used safely and effectively as the first diagnostic step. Whether US or endometrial biopsy is used initially depends on the physician's assessment of patient risk, the nature of the physician's practice, and the availability of high-quality US, and patient preference.	4
25. ACOG Committee Opinion No. 426: The role of transvaginal ultrasonography in the evaluation of postmenopausal bleeding. <i>Obstet Gynecol.</i> 2009; 113(2 Pt 1):462-464.	Review/Other-Dx	N/A	To examine role of TVUS in the evaluation of postmenopausal bleeding.	TVUS can be useful in the triage of patients in whom endometrial sampling was performed but tissue was insufficient for diagnosis.	4

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26. Dreisler E, Sorensen SS, Ibsen PH, Lose G. Value of endometrial thickness measurement for diagnosing focal intrauterine pathology in women without abnormal uterine bleeding. <i>Ultrasound Obstet Gynecol.</i> 2009; 33(3):344-348.	Observational-Dx	686 women (429 pre- and 257 postmenopausal)	To assess the diagnostic value of TVUS measurement of endometrial thickness for diagnosing focal intrauterine pathology in women without abnormal uterine bleeding. Histology report was gold standard.	375 women underwent full evaluation and were included in the final analysis (217 premenopausal and 158 postmenopausal). Focal intrauterine pathology was confirmed in 41 women (35 with polyps, 5 with submucosal myomas and one with polypoidal growing cancer). For premenopausal women, the AUC was 0.79 (95% CI, 0.68-0.89) and for postmenopausal women it was 0.84 (95% CI, 0.76-0.92). For premenopausal women, the best negative likelihood ratio (0.11) was obtained at an endometrial thickness of 5.2 mm, with a NPV of 99% and PPV of 10%. For postmenopausal women the best negative likelihood ratio (0.08) was obtained at an endometrial thickness of 2.8 mm, with a NPV of 99% and a PPV of 26%. In women without abnormal uterine bleeding, TVUS measurement of endometrial thickness is a poor diagnostic test, but is apparently efficacious in excluding focal intrauterine pathology, especially in postmenopausal women. The 4-5 mm threshold conventionally used to exclude endometrial malignancy in women with postmenopausal bleeding is not transferable to women without abnormal uterine bleeding for excluding focal intrauterine pathology.	3
27. Ozdemir S, Celik C, Gezginc K, Kiresi D, Esen H. Evaluation of endometrial thickness with transvaginal ultrasonography and histopathology in premenopausal women with abnormal vaginal bleeding. <i>Arch Gynecol Obstet.</i> 2010; 282(4):395-399.	Observational-Dx	144 women	To examine cut-off value of the endometrial thickness by TVUS and to detect the accuracy of preoperative Pipelle biopsy in premenopausal women with abnormal vaginal bleeding.	113 (78.4%) women had normal and 31 (21.6%) had abnormal endometrium. With endometrial thickness of 8 mm, sensitivity was 83.6%, specificity 56.4% and NPV 95.6%. Accuracy rate of preoperative Pipelle biopsy was 94.7% in 57 women.	2
28. McLucas B. Diagnosis, imaging and anatomical classification of uterine fibroids. <i>Best Pract Res Clin Obstet Gynaecol.</i> 2008; 22(4):627-642.	Review/Other-Dx	N/A	Review diagnosis, imaging and anatomical classification of uterine leiomyomata.	US is commonly used and least expensive option, and is a preferred choice for detecting of myomata. MRI is an excellent technique for the precise mapping of myomata, but is expensive and access may be limited. Imaging helps in the selection of therapy.	4

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29. Meredith SM, Sanchez-Ramos L, Kaunitz AM. Diagnostic accuracy of transvaginal sonography for the diagnosis of adenomyosis: systematic review and metaanalysis. <i>Am J Obstet Gynecol.</i> 2009; 201(1):107 e101-106.	Review/Other-Dx	14 trials with 1,895 aggregate participants	To critically appraise the diagnostic accuracy of TVUS for diagnosing adenomyosis.	TVUS predicted adenomyosis with a likelihood ratio of 4.67 (95% CI, 3.13-6.17). The overall prevalence of adenomyosis was 27.9% (95% CI, 25.5-30.3). The probability of adenomyosis with an abnormal TVUS was 66.2% (95% CI, 61.6- 70.6). The probability of adenomyosis with a normal TVUS was 9.1% (95% CI, 7.3-11.1).	4
30. Bazot M, Cortez A, Darai E, et al. Ultrasonography compared with magnetic resonance imaging for the diagnosis of adenomyosis: correlation with histopathology. <i>Hum Reprod.</i> 2001; 16(11):2427-2433.	Observational-Dx	120 consecutive patients	To prospectively compare the accuracy of TAUS and TVUS and MRI for the diagnosis of adenomyosis, and to correlate imaging with histological findings. Results of these examinations were interpreted blindly to histopathological findings.	Sensitivity, specificity, PPV and NPV values of TAUS and TVUS were 32.5% and 65.0%, 95.0% and 97.5%, 76.4% and 92.8%, and 73.8% and 88.8% respectively. Sensitivity, specificity, PPV and NPV values of MRI were 77.5%, 92.5%, 83.8% and 89.2% respectively. No difference in accuracy was found between TVUS and MRI, but sensitivity was lower with US in women with associated myomas. TVUS is as efficient as MRI for the diagnosis of adenomyosis in women without myoma, while MRI could be recommended for women with associated leiomyoma.	2
31. Goldstein SR. Use of ultrasonohysterography for triage of perimenopausal patients with unexplained uterine bleeding. <i>Am J Obstet Gynecol.</i> 1994; 170(2):565-570.	Review/Other-Dx	21 women	Prospective study to evaluate the use of fluid instillation to enhance vaginal probe US examination of the endometrium in perimenopausal patients with unexplained uterine bleeding.	Endometrial fluid instillation to enhance vaginal US in perimenopausal women can reliably distinguish between patients with minimal tissue whose bleeding may be of anovulatory origin and best treated with hormonal therapy and those patients with significant amounts and type of tissue in need of formal curettage. Also, polyps may be distinguished from submucous myomas, which allows appropriate preoperative triage for operative hysteroscopy when indicated and eliminates the need for diagnostic hysteroscopy.	4

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32. Werbrouck E, Veldman J, Luts J, et al. Detection of endometrial pathology using saline infusion sonography versus gel instillation sonography: a prospective cohort study. <i>Fertil Steril.</i> 2011; 95(1):285-288.	Observational-Dx	804 patients	To compare SIS with GIS in terms of feasibility and diagnostic accuracy.	The technical failure rate (difference between proportions and CI) was 5.0% for SIS vs 1.8% for GIS, respectively (3.21; [0.69-5.95]). Failure due to inadequate distension was 1.5% vs 0.3% for SIS and GIS, respectively (1.25; [-0.16-2.99]). Pathology was diagnosed in 180 patients (49%) of the SIS group vs 147 patients of the GIS group (40.2%) (8.88; [1.69-15.95]). The sensitivity was 77.8% and 85.0%, respectively (NS). The NPV was 79.1% for SIS and 88.6% for GIS (9.54; [2.17-16.89]).	3
33. Van Den Bosch T, Van Schoubroeck D, Luts J, et al. Effect of gel-instillation sonography on Doppler ultrasound findings in endometrial polyps. <i>Ultrasound Obstet Gynecol.</i> 2011; 38(3):355-359.	Observational-Dx	25 women	To evaluate if GIS affects the power Doppler signal in patients with endometrial polyps.	At unenhanced US a pedicle artery was seen in 27%-46% of cases, whereas, after gel infusion the examiners reported a pedicle artery in 30%-46% of cases (Exact McNemar's test P-values ranged from 0.50 to 1.00). The level of agreement between unenhanced US and GIS ranged from 59% to 91% (Cohen's kappa values ranged from 0.17 to 0.79). There was no tendency for a pedicle artery to be identified less often at GIS than before gel instillation.	2
34. de Kroon CD, de Bock GH, Dieben SW, Jansen FW. Saline contrast hysterosonography in abnormal uterine bleeding: a systematic review and meta-analysis. <i>BJOG.</i> 2003; 110(10):938-947.	Review/Other-Dx	24 studies 2,278 procedures	Systematic review and meta-analysis of diagnostic studies to assess the diagnostic accuracy of saline contrast hysterosonography in the evaluation of the uterine cavity in women complaining of abnormal uterine bleeding.	Overall success rate of saline contrast hysterosonography was 93% (95% CI, 92%-94%). The feasibility of saline contrast hysterosonography in postmenopausal women (success rate 86.5%, 95% CI, 83.2-89.8) is significantly lower (P<0.01) compared with premenopausal women (success rate 95%, 95% CI, 94%-96%).	4
35. van Dongen H, de Kroon CD, Jacobi CE, Trimpos JB, Jansen FW. Diagnostic hysteroscopy in abnormal uterine bleeding: a systematic review and meta-analysis. <i>BJOG.</i> 2007; 114(6):664-675.	Review/Other-Dx	17 studies with 4,208 procedures	Systematic review and meta-analysis of studies to assess the accuracy and feasibility of diagnostic hysteroscopy in the evaluation of intrauterine abnormalities in women with abnormal uterine bleeding.	Pooled likelihood ratios of all studies were 6.5 (95% CI, 4.1-10.4) and 0.08 (95% CI, 0.07-0.10), changing the pre-test probability of 0.46 to post-test probabilities of 0.85 (95% CI, 0.78-0.90) and 0.07 (0.06-0.08) for positive and negative results respectively. Subgroup analyses gave similar results. The overall success rate of diagnostic hysteroscopy was estimated at 96.9% (SD 5.2%, range 83-100%). Study shows diagnostic hysteroscopy is both accurate and feasible in the diagnosis of intrauterine abnormalities.	4

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36. Laifer-Narin S, Ragavendra N, Parmenter EK, Grant EG. False-normal appearance of the endometrium on conventional transvaginal sonography: comparison with saline hysterosonography. <i>AJR Am J Roentgenol.</i> 2002; 178(1):129-133.	Observational-Dx	180 patients	To assess the utility of transvaginal saline hysterosonography in patients presenting with a normal-appearing endometrium on conventional TVUS. Endometrial appearance on conventional TVUS was compared with that of uterine cavity on saline hysterosonography.	Saline hysterosonography showed abnormalities in 114 patients. 16 (14%) of 114 patients showed abnormalities (polyps and submucosal leiomyomas) on saline hysterosonography despite normal-appearing endometria on conventional TVUS. Conventional TVUS does not appear to be a screening procedure of sufficient diagnostic value in the symptomatic patient with abnormal vaginal bleeding. In patients presenting with the chief complaint of abnormal vaginal bleeding, diagnostic evaluation with a saline hysterosonogram may be warranted despite normal findings on a TVUS.	3
37. Erdem M, Bilgin U, Bozkurt N, Erdem A. Comparison of transvaginal ultrasonography and saline infusion sonohysterography in evaluating the endometrial cavity in pre- and postmenopausal women with abnormal uterine bleeding. <i>Menopause.</i> 2007; 14(5):846-852.	Observational-Dx	100 premenopausal and 33 postmenopausal women	Prospective study to compare the diagnostic accuracy of TVUS and SIS of the endometrial cavity in pre- and postmenopausal women with abnormal uterine bleeding.	When TVUS and SIS findings were compared with pathological results, the sensitivity and specificity of TVUS in diagnosing endometrial pathologies were 83% and 70.6%, respectively, whereas the sensitivity and specificity of SIS were 97.7% and 82.4%, respectively. The sensitivity and specificity of SIS in the diagnosis of endometrial polyps were 100% and 91.8%, respectively, and in the diagnosis of fibroids were 95% and 100%, respectively. SIS is more accurate than TVUS alone in the evaluation of the endometrial cavity in women with abnormal uterine bleeding.	2

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38. Hann LE, Gretz EM, Bach AM, Francis SM. Sonohysterography for evaluation of the endometrium in women treated with tamoxifen. <i>AJR Am J Roentgenol.</i> 2001; 177(2):337-342.	Observational-Dx	50 sonohysterograms obtained in 48 women	To compare endometrial biopsy and sonohysterography for evaluation of the endometrium in tamoxifen-treated women in a retrospective review.	Sonohysterography revealed 31 endometrial polyps (62%), 6 thickened endometria (12%), 5 normal endometria (10%), and 4 subendometrial cysts (8%). Surgery was avoided when 7 sonohysterograms (14%) revealed normal endometria or subendometrial cysts. In the group with histopathologic correlation, 23/28 polyps were confirmed and 2/5 thickened endometria were shown to represent endometrial hyperplasia. 12 (63%) of 19 sonohysterograms with prior normal endometrial biopsy findings had abnormalities on sonohysterography, including 10 polyps and 2 thickened endometria.	3
39. Markovitch O, Tepper R, Aviram R, Fishman A, Shapira J, Cohen I. The value of sonohysterography in the prediction of endometrial pathologies in asymptomatic postmenopausal breast cancer tamoxifen-treated patients. <i>Gynecol Oncol</i> 2004; 94(3):754-759.	Observational-Dx	85 patients who had TVUS endometrial thickness of ≥8 mm followed by hysteroscopy and endometrial histological findings	To assess the value of sonohysterography in identifying endometrial pathologies in asymptomatic postmenopausal tamoxifen-treated patients by evaluating its performance characteristics.	ROC curve analysis of intrauterine mass revealed 5 mm as the best accurate cutoff value for the diagnosis of endometrial pathologies, with a sensitivity of 74.1%, specificity of 93.0%, PPV of 88.3% and NPV of 84.2%. Sonohysterography improves the accuracy of diagnosis of intrauterine mass in asymptomatic postmenopausal tamoxifen-treated patients. The size of the intrauterine mass correlates with the severity of the endometrial pathology.	3
40. Abou-Salem N, Elmazny A, El-Sherbiny W. Value of 3-dimensional sonohysterography for detection of intrauterine lesions in women with abnormal uterine bleeding. <i>J Minim Invasive Gynecol.</i> 2010; 17(2):200-204.	Observational-Dx	50 perimenopausal and 20 postmenopausal women	To compare 2D sonohysterography and 3D sonohysterography with saline solution infusion vs diagnostic hysteroscopy for investigation of intrauterine lesions in perimenopausal and postmenopausal women with abnormal uterine bleeding.	For 2D sonohysterography, sensitivity, specificity, PPV, NPV, overall accuracy, likelihood ratio for a positive result, and likelihood ratio for a negative result were 79%, 72%, 89%, 54%, 76%, 2.82, and 0.29, respectively, and for 3D sonohysterography, were 92%, 89%, 96%, 80%, 91%, 8.36, and 0.09, respectively; and for diagnostic hysteroscopy, were 94%, 89%, 96%, 84%, 93%, 8.55, and 0.07, respectively. Thus, 3D sonohysterography was superior to 2D sonohysterography (P=.02) and comparable to diagnostic hysteroscopy (P=.75) for diagnosis of intrauterine lesions.	3

**Abnormal Vaginal Bleeding
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
41. Terry S, Banks E, Harris K, Duvivier R, Dar P. Comparison of 3-dimensional with 2-dimensional saline infusion sonohysterograms for the evaluation of intrauterine abnormalities. <i>J Clin Ultrasound</i> . 2009; 37(5):258-262.	Observational-Dx	125 patients	To compare 3D SIS with 2D SIS using hysteroscopy and histologic diagnosis as the gold standard.	Of 804 patients that had SIS, 125 patients met the inclusion criteria. Patient median age was 48 (range 19-82). Also, 77 patients were premenopausal, and 48 patients were postmenopausal. Furthermore, 43 patients had 2D SIS and 82 patients had 3D SIS. 3D SIS was found to correlate with hysteroscopic findings more often than 2D SIS (P<0.05). A trend for higher specificity of 3D SIS with the different uterine pathologies was seen, but it did not reach statistical significance. No difference in sensitivity of 3D SIS compared with 2D SIS was found for all pathologic diagnoses.	3
42. Coleman BG, Arger PH, Grumbach K, et al. Transvaginal and transabdominal sonography: prospective comparison. <i>Radiology</i> . 1988; 168(3):639-643.	Observational-Dx	230 exams (126 pelvic, 104 pregnancy) 215 patients	To prospectively compare TVUS and TAUS.	TVUS scanning was significantly better than TAUS scanning in the visualization of gestational sac contents (P<.005), detection of fetal heart motion (P<.001), and evaluation of the endometrial canal in the retroverted or retroflexed uterus (P<.001). TVUS scanning was significantly better than TAUS scanning in visualization of the ovaries in patients with uterine leiomyomas (P<.005) but not significantly better in perimenopausal and postmenopausal patients (P>.05).	3
43. Timmerman D, Verguts J, Konstantinovic ML, et al. The pedicle artery sign based on sonography with color Doppler imaging can replace second-stage tests in women with abnormal vaginal bleeding. <i>Ultrasound Obstet Gynecol</i> . 2003; 22(2):166-171.	Observational-Dx	3,099 patients	Prospective observational study to determine accuracy of pedicle artery test in detecting endometrial polyps.	Of the 3,099 women, no gold standard was available in 2,230. Only 28/199 patients who were test-positive did not have a gold standard. In the 869 patients in whom a gold standard was available, 182 had one or more endometrial polyps. The pedicle artery test had an apparent sensitivity for detection of endometrial polyps of 76.4%, specificity of 95.3%, PPV of 81.3%, and NPV of 93.8%. When extending the test to the prediction of any focal intracavitary pathology the PPV was 94.2%.	3

Abnormal Vaginal Bleeding
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
44. Cil AP, Tulunay G, Kose MF, Haberal A. Power Doppler properties of endometrial polyps and submucosal fibroids: a preliminary observational study in women with known intracavitary lesions. <i>Ultrasound Obstet Gynecol.</i> 2010; 35(2):233-237.	Observational-Dx	49 patients; 32 with endometrial polyps and 17 with submucosal fibroids	To compare power Doppler flow mapping characteristics of endometrial polyps and submucosal fibroids and analyze whether two different power Doppler characteristics, single-vessel pattern and rim-like vessel pattern, can help to differentiate these focal endometrial lesions.	Included in the final analysis were 49 patients with histological confirmation of the type of endometrial lesion: 32 with endometrial polyps and 17 with submucosal fibroids. Power Doppler signals were observed in 47 of these; they were not observed in 2 patients with endometrial polyps. Of the 32 with endometrial polyps, 26 (81.3%) endometrial polyps showed a single-vessel pattern, 3 (9.4%) showed a multiple-vessel pattern and one (3.1%) showed a scattered-vessel pattern. Of the 17 with submucosal fibroids, 12 (70.6%) showed a rim-like vessel pattern, 3 (17.6%) showed a multiple-vessel pattern and 2 (11.8%) showed a single-vessel pattern. Single-vessel pattern was associated with 2 false-positive cases, but there were no false-positive cases for rim-like vessel pattern. The sensitivity, specificity and PPV and NPV for single-vessel pattern in diagnosing endometrial polyps were 81.2%, 88.2%, 92.9% and 71.4% and for rim-like pattern in diagnosing submucosal fibroids they were 70.6%, 100%, 100% and 86.5%, respectively.	3
45. Bezircioglu I, Baloglu A, Cetinkaya B, Yigit S, Oziz E. The diagnostic value of the Doppler ultrasonography in distinguishing the endometrial malignancies in women with postmenopausal bleeding. <i>Arch Gynecol Obstet.</i> 2012; 285(5):1369-1374.	Observational-Dx	106 women	To investigate the diagnostic value of blood flow measurements in endometrial, myometrial and uterine vasculature by transvaginal Doppler US in the differentiation of the neoplastic endometrial pathologies in women with postmenopausal bleeding.	Endometrial malignancy was diagnosed in 24 of the patients (22.7%). Endometrial thickness was found to be higher in the patients with malign histopathology compared with the patients of benign histopathology. Statistically, uterine artery PI, RI, radial artery PI, spiral artery PI, and RI were also significantly lower in patients with malign histopathology. According to ROC curve analysis the endometrial thickness of 5 mm, uterine artery PI of 1.450, uterine artery RI of 0.715, radial artery PI of 1.060, and radial artery RI of 0.645 were defined as the cut-off points. In multivariate regression model, only uterine artery PI was identified as independent determinant of malignant endometrium.	3

**Abnormal Vaginal Bleeding
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
46. Merce LT, Alcazar JL, Lopez C, et al. Clinical usefulness of 3-dimensional sonography and power Doppler angiography for diagnosis of endometrial carcinoma. <i>J Ultrasound Med.</i> 2007; 26(10):1279-1287.	Observational-Dx	84 women	To assess whether endometrial volume and 3D power Doppler indices can discriminate between hyperplasia and endometrial carcinoma and can predict extension of the endometrial carcinoma.	The endometrial volume and 3D power Doppler indices (vascularization index, flow index, and vascularization-flow index) were significantly higher in endometrial carcinoma than endometrial hyperplasia, whereas the intratumoral RI was significantly lower (P<.05). A vascularization-flow index of 2.07 was the best cutoff for predicting endometrial carcinoma, with sensitivity of 76.5% and specificity of 80.8%. No significant differences were noticed for endometrial thickness. The endometrial vascularization index was significantly higher when the tumor stage was greater than I. All the 3D power Doppler indices were significantly higher when the carcinoma infiltrated more than 50% of the myometrium. The intratumoral RI was significantly lower in cases with a high histologic grade, myometrial infiltration of more than 50%, and lymph node metastases.	3
47. Andreotti RF, Fleischer AC, Mason LE, Jr. Three-dimensional sonography of the endometrium and adjacent myometrium: preliminary observations. <i>J Ultrasound Med.</i> 2006; 25(10):1313-1319.	Review/Other-Dx	90 patients	To characterize the types of additional information that can be obtained in patients undergoing pelvic sonography with routine 2D as well 3D reconstructed images in the coronal plane.	Additional findings were obtained on the coronal view in 28 studies (30.8%). No additional findings were obtained in 63 studies (69.2%). Normal endometrial and myometrial findings were obtained by conventional 2D imaging in 42/91 patients. Of this group, additional findings were shown in 2 (5%) patients. 49/91 patients had abnormal findings by 2D imaging. Additional information was obtained in 26 (53%) of these patients. Added information included uterine anomalies, better definition of the endometrium, more accurate delineation and location of endometrial polyps, location of leiomyomas, visualization of cystic areas within the myometrium, and confirmation of the location of intrauterine devices.	4

**Abnormal Vaginal Bleeding
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
48. Lev-Toaff AS, Pinheiro LW, Bega G, Kurtz AB, Goldberg BB. Three-dimensional multiplanar sonohysterography: comparison with conventional two-dimensional sonohysterography and X-ray hysterosalpingography. <i>J Ultrasound Med.</i> 2001; 20(4):295-306.	Observational-Dx	20 women	Compare findings to assess the value of transvaginal sonohysterography and 3D multiplanar US to optimize assessment of the uterus.	In 9 (69%) of 13 comparisons between 3D sonohysterography and 2D sonohysterography and in 11 (92%) of 12 comparisons between 3D sonohysterography and X-ray hysterosalpingography, 3D sonohysterography was advantageous. The coronal plane was most useful for displaying the relationship between lesions and the uterine cavity. 3D sonohysterography provided additional information compared with standard accepted techniques in the vast majority of women.	3
49. Benacerraf BR, Shipp TD, Bromley B. Which patients benefit from a 3D reconstructed coronal view of the uterus added to standard routine 2D pelvic sonography? <i>AJR Am J Roentgenol.</i> 2008; 190(3):626-629.	Observational-Dx	66 consecutive patients had standard 2D pelvic US followed by 3D US	To evaluate whether 3D reconstructed coronal view of the uterus provides added benefit to standard gynecologic US.	3D coronal views of the uterus added value to the 2D scan in 16 (24%) of the 66 patients. 3D coronal view of the uterus is a valuable adjunct to a 2D pelvic scan, particularly in patients presenting with infertility or suspected endometrial lesions. In addition, the coronal view is helpful in patients with an endometrium ≥ 5 mm.	3
50. Alcazar JL, Galvan R. Three-dimensional power Doppler ultrasound scanning for the prediction of endometrial cancer in women with postmenopausal bleeding and thickened endometrium. <i>Am J Obstet Gynecol.</i> 2009; 200(1):44 e41-46.	Observational-Dx	99 postmenopausal women	Prospective observational study to evaluate the role of 3D-PDA to discriminate between benign and malignant endometrial disease in women with postmenopausal bleeding and thickened endometrium.	Histologic diagnoses were endometrial cancer (44 cases), hyperplasia (13 cases), polyp (23 cases), cystic atrophy (14 cases), and submucous myoma (5 cases). Endometrial volume, vascularity index, and vascularity-flow index were significantly higher in malignant vs benign conditions. ROC analysis revealed that vascularity index was the best parameter for the prediction of endometrial cancer. Findings show that 3D-PDA may be useful for the prediction of endometrial cancer in women with postmenopausal bleeding and thickened endometrium at baseline US.	3

**Abnormal Vaginal Bleeding
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
51. Odeh M, Vainerovsky I, Grinin V, Kais M, Ophir E, Bornstein J. Three-dimensional endometrial volume and 3-dimensional power Doppler analysis in predicting endometrial carcinoma and hyperplasia. <i>Gynecol Oncol.</i> 2007; 106(2):348-353.	Observational-Dx	56 women with post-menopausal and 89 with peri-menopausal bleeding	To evaluate the accuracy of endometrial volume measurement and 3D-PDA in the diagnosis of endometrial carcinoma and endometrial hyperplasia in women with post- and peri-menopausal bleeding.	90 women (62%) had normal histology, 26 (17.9%) had an endometrial polyp, 18 (12.5%) hyperplasia and 11 (7.6%) had endometrial carcinoma. Mean endometrial thickness was 11 mm and 15.5 mm in the normal and pathologic groups respectively (P<0.005). The mean endometrial volume was 6.87 cc and 15.5 cc in the 2 groups respectively (P<0.001). The vascularity index was 2.27% and 2.95% in the 2 groups respectively (P=0.022). The flow index was 18.6 and 23.6 in the 2 groups respectively (P=0.014). The vascularity flow index was 0.68 and 0.89 in the 2 groups respectively (P=0.018). Using ROC the area under the curve was 0.698, 0.728, 0.621, 0.631, and 0.625 for endometrial thickness, endometrial volume, vascularity index, flow index and vascularity flow index respectively. The best predictor of endometrial carcinoma was an endometrial volume of 3.56 cc or more (sensitivity 93.1%, specificity 36.2%).	3
52. Rossi A, Forzano L, Romanello I, Fachechi G, Marchesoni D. Assessment of endometrial volume and vascularization using transvaginal 3D power Doppler angiography in women with postmenopausal bleeding. <i>Int J Gynaecol Obstet.</i> 2012; 119(1):14-17.	Observational-Dx	48 women	To compare the usefulness of 3D-PDA and endometrial thickness measurement by 2D Doppler US in the distinction of benign from malignant disease in postmenopausal women with abnormal uterine bleeding and an endometrial thickness greater than 4.5mm.	The histologic findings were normal or benign for 38 women (79%) and malignant for 10 (21%). All vascular indices were significantly higher in the group with malignancies except for the vascularization flow index. There were no differences in the values obtained using the 9 degrees or the 30 degrees angle. ROCs curves were traced for all indices. The vascularity index had the best area under the curve (0.78), 77.8% sensitivity, and 82.6% specificity. The areas under the curve were smaller for the shell than for the endometrium.	3

**Abnormal Vaginal Bleeding
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
53. Stamatopoulos CP, Mikos T, Grimbizis GF, et al. Value of magnetic resonance imaging in diagnosis of adenomyosis and myomas of the uterus. <i>J Minim Invasive Gynecol.</i> 2012; 19(5):620-626.	Observational-Dx	153 women	To estimate the diagnostic performance of MRI in detection of myomas and adenomyosis of the uterus.	The sensitivity, specificity, PPV, and NPV of MRI for the diagnosis of uterine pathology was calculated using histologic findings as the standard criterion for final diagnosis. ROCs curves were constructed to describe the diagnostic performance of MRI. In the diagnosis of myomas, MRI demonstrated sensitivity of 94.1%, specificity of 68.7%, PPV of 95.7%, and NPV of 61.1%. In the diagnosis of adenomyosis, MRI demonstrated sensitivity of 46.1%, specificity of 99.1%, PPV of 92.3%, and NPV of 88.5%. The AUC for the diagnostic performance of MRI in the detection of myomas and adenomyosis was 0.81 and 0.73, respectively. Uterine sarcoma was diagnosed in 5 patients; in these cases, MRI demonstrated sensitivity of 60.0%, specificity of 99.2%, PPV of 75.0%, and NPV of 98.4%. The AUC for MRI in the diagnosis of uterine sarcomas was 0.80.	2
54. Costa-Paiva L, Godoy CE, Jr., Antunes A, Jr., Caseiro JD, Arthuso M, Pinto-Neto AM. Risk of malignancy in endometrial polyps in premenopausal and postmenopausal women according to clinicopathologic characteristics. <i>Menopause.</i> 2011;18(12):1278-1282.	Review/Other-Dx	870 women	To evaluate the prevalence of endometrial premalignant and malignant polyps in premenopausal and postmenopausal women, as well as the clinical, US, and hysteroscopic factors associated with malignancy.	The mean (SD) age of the women was 57.5 (10.6) years. Of these women, 76.4% were postmenopausal. Women were diagnosed with benign lesions in 95.8% of cases. Premalignant polyps accounted for 1.6% of the total number of cases. Malignant polyps represented 2.5% of the total sample. Postmenopausal bleeding and age greater than 60 years were the only factors that remained associated with a higher risk of malignancy with a prevalence ratio of 3.67 (95% CI, 1.69–7.97) and 1.5 (95% CI, 1.01–1.09), respectively.	4

**Abnormal Vaginal Bleeding
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
55. Grasel RP, Outwater EK, Siegelman ES, Capuzzi D, Parker L, Hussain SM. Endometrial polyps: MR imaging features and distinction from endometrial carcinoma. <i>Radiology</i> . 2000; 214(1):47-52.	Observational-Dx	35 patients with surgically proved endometrial polyp /3 independent readers	To determine the MRI characteristics of endometrial polyps and the accuracy of MRI in distinguishing endometrial polyps from endometrial carcinomas in a case-control blinded study.	Central fibrous core (low signal intensity on T2-weighted images) and intratumoral cysts (high signal intensity on T2-weighted images) were seen more frequently in endometrial polyps than in carcinomas; myometrial invasion and necrosis showed high predictive value for carcinomas. The readers' responses showed a mean sensitivity of 79%, specificity of 89%, accuracy of 86%, PPV of 82%, and NPV of 88% for diagnosis of carcinoma. MRI can help to distinguish most polyps from endometrial carcinomas on the basis of morphologic features.	3
56. Beddy P, Moyle P, Kataoka M, et al. Evaluation of depth of myometrial invasion and overall staging in endometrial cancer: comparison of diffusion-weighted and dynamic contrast-enhanced MR imaging. <i>Radiology</i> . 2012; 262(2):530-537.	Observational-Dx	48 women	To compare the diagnostic performance of DWI MRI with that of dynamic contrast material-enhanced MRI in evaluating the depth of myometrial invasion and overall stage in patients with endometrial cancer.	For assessing the depth of myometrial invasion, diagnostic accuracy, sensitivity, and specificity, respectively, were as follows: DWI MRI-reader 1, 90%, 84%, and 100%; reader 2, 85%, 84%, and 88%; dynamic contrast-enhanced MRI-reader 1, 71%, 61%, and 88%; reader 2, 79%, 77%, and 82%. The improvement in diagnostic accuracy for reader 1 was significant (P=.035). For myometrial invasion, kappa values were 0.75 with DWI MRI and 0.26 with dynamic contrast-enhanced MRI. There was no association between inaccurate assessment of myometrial invasion and standard pitfalls with DWI MRI. Readers 1 and 2 correctly staged more patients by using DWI MRI (39 and 38 patients, respectively) than by using dynamic contrast-enhanced MRI (29 and 30 patients, respectively) (P<.05). For overall stage, kappa values were 0.74 with DWI MRI and 0.22 with dynamic contrast-enhanced MRI.	2

**Abnormal Vaginal Bleeding
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
57. Fujii S, Matsusue E, Kigawa J, et al. Diagnostic accuracy of the apparent diffusion coefficient in differentiating benign from malignant uterine endometrial cavity lesions: initial results. <i>Eur Radiol.</i> 2008; 18(2):384-389.	Observational-Dx	25 uterine endometrial cavity lesions in 25 female patients: endometrial carcinoma (n=11), carcinosarcoma (n=2), submucosal leiomyoma (n=8), and endometrial polyp (n=4)	Retrospective study to evaluate the diagnostic accuracy of ADC measurement in differentiating malignant from benign uterine endometrial cavity lesions.	Sensitivity, specificity, and accuracy were 84.6%, 100%, and 92%, respectively. ADC measurement can provide useful information in differentiating malignant from benign uterine endometrial cavity lesions.	3
58. Takeuchi M, Matsuzaki K, Nishitani H. Diffusion-weighted magnetic resonance imaging of endometrial cancer: differentiation from benign endometrial lesions and preoperative assessment of myometrial invasion. <i>Acta Radiol.</i> 2009; 50(8):947-953.	Observational-Dx	67 endometrial lesions (45 cancers and 22 benign lesions): 33 patients with endometrial cancer	To verify the feasibility of DWI MRI to distinguish benign and malignant endometrial lesions, and to evaluate myometrial invasion of endometrial cancer.	The ADC values (x10(-3) mm(2)/s) in cancer and benign lesions were 0.84 +/- 0.19 and 1.58 +/- 0.36, respectively (P<0.01). The staging accuracy (superficial or deep myometrial invasion) was 94% for DWI and 88% for gadolinium-enhanced T1-weighted images. Coexisting adenomyosis and infiltrative myometrial invasion caused staging errors on gadolinium-enhanced T1-weighted images, whereas DWI could demonstrate the tumor extent correctly.	3
59. Rechichi G, Galimberti S, Signorelli M, et al. Endometrial cancer: correlation of apparent diffusion coefficient with tumor grade, depth of myometrial invasion, and presence of lymph node metastases. <i>AJR Am J Roentgenol.</i> 2011; 197(1):256-262.	Observational-Dx	70 patients 36 controls	To investigate whether ADC values of endometrial cancer differ from those of normal endometrium and myometrium and whether they vary according to histologic tumor grade, the depth of myometrial invasion, or lymph node status.	The mean (+/- SD) ADC value (10(-3) mm(2)/s) of endometrial cancer (0.77 +/- 0.12) was significantly lower than that of normal endometrium (1.31 +/- 0.11, P<0.0001) and normal myometrium (1.52 +/- 0.21, P<0.0001), with no overlap between the two former distributions. There was no significant difference between ADC values of endometrial cancer tissue in patients with tumor grade 1 (0.79 +/- 0.08, n = 14), grade 2 (0.76 +/- 0.14, n = 40), or grade 3 (0.75 +/- 0.12, n = 16) (P=0.67); in patients with deep (0.77 +/- 0.13, n = 18) and those with superficial (0.76 +/- 0.12, n = 52) myometrial invasion (P=0.87); and in patients with (0.78 +/- 0.10, n = 6) and those without (0.75 +/- 0.14, n = 39) lymph node metastases (P=0.64).	1

**Abnormal Vaginal Bleeding
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
60. Grossman J, Ricci ZJ, Rozenblit A, Freeman K, Mazzariol F, Stein MW. Efficacy of contrast-enhanced CT in assessing the endometrium. <i>AJR Am J Roentgenol.</i> 2008; 191(3):664-669.	Observational-Dx	259 patients	Retrospective study to determine the efficacy of contrast-enhanced CT in detecting a thickened endometrium. TVUS used as the reference standard.	Overall sensitivity and specificity of CT in detecting the thickened endometrium was 53.1% and 93.5%, respectively, relative to TVUS. PPV and NPV were 66.7% and 89.1%, respectively. Routine pelvic CT correctly identifies a normal endometrium in most patients.	2
61. Yitta S, Hecht EM, Slywotzky CM, Bennett GL. Added value of multiplanar reformation in the multidetector CT evaluation of the female pelvis: a pictorial review. <i>Radiographics.</i> 2009; 29(7):1987-2003.	Review/Other-Dx	N/A	Review CT technique in the evaluation of the female pelvis. Also discuss and illustrate the MDCT appearance of the female pelvic anatomy as well as the imaging findings in a variety of benign and malignant conditions, with emphasis on the added value of MPR as an adjunct to conventional axial CT.	MDCT with MPR allows improved visualization of the normal anatomy and anatomic variants as well as greater diagnostic accuracy in the evaluation of the female pelvis. Although US and MRI remain the primary imaging modalities for the assessment of most female pelvic disorders, more accurate diagnosis of these disorders at MDCT may obviate additional imaging tests and allow more appropriate management.	4
62. Lerman H, Metser U, Grisaru D, Fishman A, Lievshitz G, Even-Sapir E. Normal and abnormal 18F-FDG endometrial and ovarian uptake in pre- and postmenopausal patients: assessment by PET/CT. <i>J Nucl Med.</i> 2004; 45(2):266-271.	Observational-Dx	285 consecutive female patients	To assess physiologic endometrial FDG uptake during the 4 phases of the menstrual cycle and to differentiate between physiologic and malignant endometrial uptake.	Increased ovarian FDG uptake was detected in 7 patients with ovarian cancer (9.1 +/- 4) and in 21 premenopausal patients without known ovarian malignancy (5.7 +/- 1.5, P<0.01), of whom 15 were at mid cycle and 3 reported oligomenorrhea. An ovarian SUV of 7.9 separated benign from malignant uptake with a sensitivity of 57% and a specificity of 95%. In premenopausal patients, normal endometrial uptake of FDG changes cyclically, increasing during the ovulatory and menstrual phases. Increased uptake in the endometrium adjacent to a cervical tumor does not necessarily reflect endometrial tumor invasion. Increased ovarian uptake in postmenopausal patients is associated with malignancy, whereas increased ovarian uptake may be functional in premenopausal patients.	3

Evidence Table Key

Study Quality Category Definitions

- *Category 1* The study is well-designed and accounts for common biases.
- *Category 2* The study is moderately well-designed and accounts for most common biases.
- *Category 3* There are important study design limitations.
- *Category 4* The study is not useful as primary evidence. The article may not be a clinical study or the study design is invalid, or conclusions are based on expert consensus. For example:
 - a) the study does not meet the criteria for or is not a hypothesis-based clinical study (e.g., a book chapter or case report or case series description);
 - b) the study may synthesize and draw conclusions about several studies such as a literature review article or book chapter but is not primary evidence;
 - c) the study is an expert opinion or consensus document.

Dx = Diagnostic

Tx = Treatment

Abbreviations Key

3D-PDA = 3-D power Doppler angiography

ADC = Apparent diffusion coefficient

AUC = Areas under the receiver operating characteristic curve

CI = Confidence interval

CT = Computed tomography

D&C = Dilatation and Curettage

DWI = Diffusion-weighted imaging

EVUS = Endovaginal ultrasound

FDG-PET = Fluorine-18-2-fluoro-2-deoxy-D-glucose-positron emission tomography

GIS = Gel instillation sonography

MDCT = Multidetector computed tomography

MPR = Multiplanar reformations

MRI = Magnetic resonance imaging

NPV = Negative predictive value

PET = Positron emission tomography

PI = Pulsatility index

PPV = Positive predictive value

RI = Resistive index

ROC = Receiver-operator characteristic

SD = Standard deviation

SIS = Saline infusion sonography

SUV = Standardized uptake value

TAUS = Transabdominal ultrasound

TVUS = Transvaginal ultrasound

US = Ultrasound