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Imaging in gynecology

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Abstract

This chapter summarizes the diagnostic performance (sensitivity, specificity, positive and negative likelihood ratios) of ultrasound, computer tomography, and magnetic resonance imaging in the diagnosis of various gynecological diseases and tumors. Positron emission tomography is not discussed. Imaging in infertility, in the diagnosis of Mullerian duct anomalies and in gynecological oncology (staging of gynecological cancers, diagnosis of recurrence of gynecological cancer, diagnosis of trophoblastic tumors) is not dealt with.

Ultrasound is the first line imaging method for discrimination between viable intrauterine pregnancy, miscarriage and tubal pregnancy in women with bleeding and/or pain in early pregnancy, for discrimination between benign and malignant adnexal masses and for making a specific diagnosis in adnexal tumors (e.g., dermoid cyst, endometrioma, hemaorrhagic corpus luteum, ectetera), for diagnosing intracavitary uterine pathology in women with bleeding problems, and for confirming or refuting pelvic pathology in women with pelvic pain. Magnetic resonance imaging may have a role as a secondary test in the diagnosis of adenomyosis, ‘deep endometriosis‘ (e.g., endometriosis in the rectovaginal septum or in the utero-sacral ligaments), and in the diagnosis of extremely rare types of ectopic pregnancy (e.g., in the spleen, liver or retroperitoneum).

Key words (MESH):Ultrasonography, Magnetic Resonance Imaging, Diagnostic Imaging, Pelvis, Gynecology

Introduction

The basis for making a correct diagnosis in women with gynecological problems is anamnesis and clinical examination. To confirm or refute a diagnosis suspected on the basis of these, clinicians often add imaging methods. To the best of my knowledge there are no randomized trials that have tried to answer the question whether adding one or other imaging method to anamnesis and clinical examination eventually affects the health of the patient, or has other effects, e.g., on the rate of correct diagnosis before institution of treatment or on the time taken to arrive at a correct diagnosis. The lack of randomized trials is probably explained either by it being obvious that adding imaging to clinical examination has positive effects, or by difficulties with conducting a randomized trial, e.g., because of difficulties with defining relevant outcome measures or difficulties caused by the need for life-long follow-up. On the other hand, clinical information improves test reading accuracy [1].

Because there are no randomized trials assessing the effects of using imaging methods in women with gynecological problems, in this chapter I will focus on the reported sensitivity, specificity and likelihood ratios of imaging methods used in gynecology. Likelihood ratios indicate by how much a given test results will raise or lower the pretest probability of the target disorder. They reflect very well the clinical usefulness of a diagnostic test. Likelihood ratios > 10 or < 0.1 generate large and often conclusive changes from pre-test to post-test odds of the outcome, likelihood ratios of 5 – 10 or 0.1 – 0.2 generate moderate changes from pre-test to post-test odds, likelihood ratios of 2 – 5 or 0.2 – 0.5 generate only small changes from pre-test to post-test odds, and likelihood ratios of 1 – 2 or 0.5 –1 do not change probabilities to any important degree [2]. I will add comments on the likely effect (not proven in randomized trials) of using imaging

methods in clinical practice. I will not deal with imaging in gynecological oncology (staging of gynecological cancers, diagnosis of recurrence of gynecological cancer, diagnosis of trophoblastic tumors), imaging in infertility or in the diagnosis of Mullerian duct anomalies.

It is important to bear in mind that when it comes to diagnostic imaging methods it is not only the definition of an abnormal imaging result, the skill of the examiner or reader, and the quality of the equipment used that will determine the performance of the method but also the population studied. For example, if a study population of adnexal masses contains only masses that are easy to classify with an imaging method, sensitivity and specificity will be high, whereas if the study population contains only masses that are difficult to classify, sensitivity and specificity will be low; and in a study population comprising only of cases with advanced disease, the imaging method is likely to perform better than in a population comprising only of cases with mild disease.

Questions to be answered and literature sources are shown in Box 1.

Box 1

Questions and literature sources for imaging methods in gynecology

Question components

Population: women with gynecological problems

Interventions: imaging methods used to facilitate correct diagnosis (ultrasound, computer tomography, magnetic resonance imaging)

Outcomes: comparison with gold standard where available (sensitivity, specificity, likelihood ratios)

Comments: possible effects on rate of correct diagnosis, time to correct diagnosis, and patient health in a short and long term perspective

Study designs: primary studies, systematic reviews, meta-analyses

Literature sources

Electronic databases: MEDLINE

Manual search: reference lists of original articles and review articles

Bleeding and/or pain in early pregnancy

A woman who presents with bleeding and/or pain in the first trimester may have one of the following four diagnoses: normal intrauterine pregnancy, failed intrauterine pregnancy, ectopic pregnancy, or trophoblastic disease. In most cases, anamnesis and clinical examination will not immediately yield a correct diagnosis. In a series of 772 consecutive women presenting with threatened abortion <28 gestational weeks the diagnosis suggested by the clinician on the basis of anamnesis and clinical examination agreed with the true diagnosis in only 75% of cases (576 of 772 cases, Kappa 0.57), whereas the diagnosis suggested after the clinician had added a transvaginal ultrasound examination agreed with the true diagnosis in 98% of cases (757 of 772 cases, Kappa 0.96) [3]. Ultrasound has become a very valuable – not to say indispensable – diagnostic tool in the management of women with early pregnancy complications. That, in skilled hands, ultrasound diagnosis is quicker and more accurate than diagnosis without ultrasound is so obvious, that it requires no further confirmation in randomized trials.

The first question to be answered in a woman with bleeding and/or pain in early pregnancy is if the pregnancy is intrauterine or ectopic. In appropriately trained hands, a single transvaginal ultrasound examination can correctly confirm the presence of an intrauterine or ectopic

pregnancy in 90% of cases [4, 5]. In a prospective study of 6621 consecutive women with an early pregnancy, 85% of whom presented with pain and/or bleeding, tubal pregnancy was correctly diagnosed with transvaginal ultrasound with a sensitivity 91% and a specificity of 99.9%[5]. The sensitivity and specificity of transvaginal ultrasound with regard to tubal pregnancy are shown in Table 1 [5-9]. The table shows that transvaginal ultrasound is an excellent method for confirming or excluding tubal pregnancy, but sensitivity and specificity are likely to depend highly on the skill of the examiner and on the quality of the ultrasound equipment used.

If an intrauterine gestational sac is found at transvaginal ultrasound examination in a woman with bleeding and/or pain in early pregnancy the following questions arise: Is there a living embryo/fetus? If there is a living embryo/fetus, how likely is it that the pregnancy will end in miscarriage? Some ultrasound findings have been suggested to exclude normal pregnancy: intrauterine gestational sac with a mean diameter of ≥ 8 mm but without a visible yolk sac [10], intrauterine gestational sac with a mean diameter of ≥ 16 mm but without a visible embryo with a heart beat [10], embryo with crown rump length of ≥4mm but with no heart beat [11]. The sensitivity and specificity with regard to failed early pregnancy of various ultrasound findings that have been suggested to be diagnostic of non-viability are shown in Table 2 [10-15]. The sensitivity and specificity will depend on the skill of the ultrasound examiner, the quality of the ultrasound equipment and any presence of technical problems, e.g., large uterine fibromas obscuring the view of the uterine cavity. If there is the slightest uncertainty about the viability of the pregnancy, a diagnosis of pregnancy failure must not be made. Instead, the ultrasound examination should be repeated to assess the development of the pregnancy. Indeed, pregnancies fulfilling the above criteria of non-viability have resulted in live births [16]. Logistic regression

models have been constructed to predict pregnancy outcome in intrauterine pregnancies with gestational sacs <16 mm or < 20 mm without a visible embryo [17, 18], but these risk calculation models have not been tested prospectively.

Ultrasound examination can also be used to estimate the risk of miscarriage in pregnant women with bleeding but where the embryo/fetus has a beating heart at ultrasound examination. Falco et al [19] constructed a logistic regression model containing information on gestational sac diameter, crown-rump length and embryonic/fetal heart rate. The model had an area under the receiver operating characteristic (ROC) curve of 0.79. Using a risk cut-off of 6% it predicted miscarriage with a sensitivity of 83% and a specificity of 71%, corresponding to a positive likelihood ratio of 2.9 and a negative likelihood ratio of 0.2. This shows that the model was not a very good diagnostic test. It has not been tested prospectively. A logistic regression model including ultrasound variables to predict the risk of demise of living embryos/fetuses has also been constructed for asymptomatic pregnant women who conceived in an assisted reproduction technology program. Using that model it seemed to be possible to predict miscarriage with a sensitivity of approximately 75% and a specificity of approximately 95%, corresponding to a positive likelihood ratio of approximately 15 and a negative likelihood ratio of approximately 0.3. This model, too, has not been prospectively cross-validated [20].

There are several reviews reporting on the accuracy of ultrasound examination in the diagnosis of early pregnancy failure [21-23].

Ultrasound diagnosis provides a basis for individually tailored treatment of women with spontaneous abortion or ectopic pregnancy, i.e., expectant management, medical treatment, or

surgery [24-32]. Protocols for managing women with pregnancies with unknown location at ultrasound examination have also been developed [33-35].

Computer tomography (CT) is contraindicated in early pregnancy. Magnetic resonance imaging (MRI) can be used, but it plays no important role in the management of women with bleeding and pain in early pregnancy, because most diagnostic problems can be solved using ultrasound. MRI may contribute to the diagnosis of extremely rare pregnancy complications, e.g., ectopic pregnancy in spleen [36], liver [37], or retroperitoneum [38]. I have seen no reports on the sensitivity and specificity of MRI in the diagnosis of miscarriage or ectopic pregnancy.

Postmenopausal bleeding

Approximately 10% of women with postmenopausal bleeding have endometrial cancer [39]. Before the introduction of ultrasound examination virtually all women with postmenopausal bleeding underwent dilatation and curettage (D&C) to confirm or exclude the diagnosis of endometrial cancer. However, there is strong scientific evidence that a transvaginal ultrasound examination with measurement of endometrial thickness can reliably discriminate between women with high and low risk of endometrial cancer. According to a meta-analysis [39], 96% of women with endometrial cancer have endometrial thickness ≥5mm (sensitivity 96%) vs. 8 % of those without cancer and not on hormone replacement therapy (specificity 92%) and vs. 23% of those without cancer and on hormone replacement therapy (specificity 77%). This means that a postmenopausal woman with vaginal bleeding not on hormone replacement therapy and a 10% pretest probability of endometrial cancer has a probability of cancer of 1% if her endometrium measures ≤ 4mm at a transvaginal ultrasound examination. Management protocols have been developed where women with postmenopausal bleeding are primarily examined with transvaginal

ultrasound and where only those with endometrium ≥ 5mm undergo further investigations including saline infusion sonography (see below) or diagnostic hysteroscopy and endometrial sampling by one or the other method [40]. Such an approach does seem to be both safe [41] and cost-effective [42].

A different approach to using a simple endometrial thickness cutoff to classify a woman as being at high or low risk of endometrial cancer would be to use multiple logistic regression models including both clinical variables (e.g., age, use of hormone replacement therapy, parity, body mass index) and ultrasound variables (e.g., endometrial thickness, endometrial internal echogenicity, regularity of the endometrial-myometrial border, and possibly Doppler findings, see below) to calculate the individual risk of malignancy for each woman. Such models have been developed [43, 44] [45, 46], but none of these models has been validated prospectively in populations other than those where the models were created.

According to a meta-analysis of 24 studies, where all but two studies comprised both pre-and postmenopausal women, saline infusion sonography (infusion of sterile saline into the uterine cavity during scanning) makes it possible to detect focally growing lesions in the uterine cavity with a sensitivity of 95% and a specificity of 88% (positive and negative likelihood ratios 8 and 0.06) [47]. Agreement between office saline infusion sonography and hysteroscopy in general anesthesia with regard to detecting focal lesions in the uterine cavity is excellent in women with postmenopausal bleeding, disagreement between the two methods occurring in only three of 75 women in one study [48]. Most endometrial pathology in women with postmenopausal bleeding manifests a focal growth pattern at hysteroscopy, the likelihood of endometrial pathology increasing if focal lesions are seen in the cavity and decreasing if none are seen [49]. Many focal

lesions will not be removed or only partially removed at a blind D&C or endometrial biopsy [49-52].Therefore, it has been suggested that women with postmenopausal bleeding and an endometrium measuring ≥ 5mm at transvaginal ultrasound examination should undergo saline infusion sonography (as an alternative to diagnostic hysteroscopy), and that women with focal lesions at saline infusion sonography should undergo hysteroscopic resection of the focal lesions (not only blind endometrial sampling by D&C or a simple outpatient sampling device), whereas it would suffice to submit women with no focal lesions in the uterine cavity to blind endometrial sampling . In a randomized crossover study comprising consecutive asymptomatic postmenopausal women, most women preferred saline infusion sonography to office hysteroscopy [53].

Various research teams have tried to refine the diagnosis of endometrial pathology by assessing the ultrasound morphology of the endometrium (e.g., regular or irregular endometrial-myometrial border, homogenous or inhomogenous internal endometrial echogenicity, hyperechoic lines surrounding the endometrial complex, echogenicity similar to that of myometrium) [54-61]. When sonomorphological criteria similar to those suggested in references 54 -60 were applied prospectively to 105 consecutive women with postmenopausal bleeding and endometrial thickness ≥ 5mm, the sensitivity and specificity with regard to endometrial polyp were 49% and 81% (positive and negative likelihood ratio 3 and 0.6), with regard to malignancy 60% and 90% (positive and negative likelihood ratio 6 and 0.4), and with regard to submucuous myoma 30% and 97% (positive and negative likelihood ratio 10 and 0.7). The sensitivity and specificity of hysteroscopy in general anesthesia in the same cohort of women were 81% and 94% for endometrial polyp (positive and negative likelihood ratio 14 and 0.2), 84% and 85% for endometrial cancer (positive and negative likelihood ratio 6 and 0.2) and 67% and 97% for

submucuous myoma (positive and negative likelihood ratio 22 and 0.3). This shows that in this particular cohort of women with postmenopausal bleeding, hysteroscopy was superior to transvaginal ultrasound examination with regard to the diagnosis of polyps and submucuous myomas, whereas the performance was similar with regard to endometrial cancer. Saline infusion sonography was successful in 78 of the105 women. It had a sensitivity and specificity with regard to endometrial polyp of 79% and 76% (positive and negative likelihood ratio 2.3 and 0.3), with regard to endometrial cancer 44% and 94% (positive and negative likelihood ratio 7 and 0.6), and with regard to submucuous myoma of 80% and 99% (positive and negative likelihood ratio 80 and 0.2). Both at saline infusion sonography and at hysteroscopy benign polyps were confused with endometrial cancer and vice versa [48].This shows that neither saline infusion sonography nor hysteroscopy can reliably discriminate between benign and malignant focal lesions in the uterine cavity in women with postmenopausal bleeding.

Concerns have been raised that saline infusion sonography and hysteroscopy might lead to intraperitoneal dissemination of malignant cells in women with endometrial cancer. It seems that a small risk of malignant cell dissemination exists in patients with endometrial carcinoma who undergo saline infusion sonography [62]. On the other hand, 5-year survival has been reported to be the same in women with early endometrial cancer who have undergone hystesteroscopy before laparotomy as in those who have not undergone preoperative hysteroscopy [63].

Attempts have been made to discriminate between various types of endometrial pathology by studying the vascularity of the uterus or endometrium using color- power- or spectral Doppler ultrasound [46, 64-68]. In one study, analysis of the color content of the endometrial scan contributed to the diagnosis of endometrial cancer in women with postmenopausal bleeding [46],

but the role of Doppler ultrasound examination in the diagnosis of endometrial pathology in women with postmenopausal bleeding is not yet clear.

There are no publications on the use of ultrasound contrast as a diagnostic tool in women with postmenopausal bleeding. MRI and CT have no role in the primary investigation of women with postmenopausal bleeding, even though both methods can been used for staging of endometrial cancer [69] and for diagnosis of recurrence of endometrial cancer.

Transvaginal ultrasound examination enables reliable discrimination between women with postmenopausal bleeding at high and low risk of endometrial cancer. This makes it possible to tailor management to each individual woman.

Bleeding disturbances before the menopause

Common causes of bleeding disturbances in non-pregnant women before the menopause are hormonal dysfunction (e.g., anovulatory bleeding), hormonal treatment (e.g., contraceptive pills), intrauterine contraceptive devices, and infections. None of these causes can be definitely established by using an imaging method. Imaging methods can only be used to confirm or refute an anatomical abnormality, e.g., a submucuous myoma, an endometrial polyp, or adenomyosis. These may or may not be the cause of the bleeding problem. Endometrial cancer is an uncommon cause of bleeding disturbance in women before the menopause. A review of the diagnostic accuracy of transvaginal ultrasound, saline infusion sonography, hysteroscopy and MRI with regard to abnormalities in the uterine cavity in premenopausal women has been published by Dueholm et al [70].

Two appropriately designed studies (hysterectomy as gold standard, blinded examiners) compared the diagnostic accuracy with regard to uterine cavity abnormalities of various imaging methods in premenopausal women [71, 72]. In one of the studies, MRI was found to be superior to transvaginal sonography, saline infusion sonography and hysteroscopy for correct determination of the exact ingrowth of submucuous myomas into the uterine cavity [71]. Other results of the two studies are summarized in Table 3. They show that saline infusion sonography is a good method for showing/excluding pathology in the uterine cavity in premenopausal women.

The problem is, that even if one finds a submucuous myomas or an endometrial polyp in the uterine cavity of a premenopausal woman with bleeding problems, one cannot be sure that these are the cause of the abnormal bleeding. Endometrial polyps are common (10%) in asymptomatic women, and submucuous myomas are also not uncommon (3%) (data from a population study presented at the World Congress of the International Society of Ultrasound in Obstetrics and Gynecology in 2003 by Dr E Dreisler, Denmark). One randomized controlled trial compared various methods of assessing the endometrium with regard to performance, patient acceptability, and cost-effectiveness, the assssment being done in three groups of women, i.e., women with postmenopausal bleeding, women ≥ 40 years old with abnormal bleeding, and women <40 years old with abnormal bleeding [73]. There is no unequivocal evidence whether the most efficient way of managing women with abnormal bleeding before the menopause would be to use an imaging method as a first line investigation or if it would be to use an imaging methods only when there is a strong clinical suspicion of an anatomical abnormality causing the bleeding.

Imaging methods used to diagnose uterine myoma, adenomyoma, and leiomyosarcoma

Ultrasound and MRI can be used to diagnose uterine myomas. Differential diagnoses are adenomyoma, benign solid ovarian tumors, e.g. ovarian fibroma / fibrothecoma (in case of myoma on a stalk) and leiomyosarcoma [74]. Most myomas have a very typical appearance at ultrasound examination [74, 75]. Using the 'refractory shadowing pattern' in 222 pelvic masses, myomas were diagnosed using transvaginal ultrasound with a sensitivity of 87% and a specificity of 89%. This corresponds to a positive likelihood ratio of 8 and a negative likelihood ratio of 0.15. In a study comparing ultrasound with MRI, transvaginal ultrasound and MRI had similar ability to diagnose uterine myomas, the sensitivity, specificity, positive and negative likelihood ratio for ultrasound being 99%, 91 %, 11 and 0.01 vs. 99%, 86%, 7 and 0.13 for MRI [76]. MRI was superior to ultrasound for determining the exact location of myomas, particularly in large uteri with more than four myomas [76]. Neither ultrasound nor MRI seems to be able to reliably discriminate between uterine leiomyoma and leiomyosarcoma [77-79]. Transvaginal ultrasound can distinguish myomas from adenomyomas (Table 4)[80-82], but I have found no publication describing the sensitivity and specificity of MRI with regard to adenomyoma.

Adenomyosis can be fairly confidently diagnosed using transvaginal ultrasound or MRI (Table 5)[83-91]. For both methods the diagnostic performance varies enormously between studies. I have seen no publications on the diagnostic performance of CT with regard to adenomyosis.

Palpable pelvic mass

A pelvic mass may be found in a woman presenting with gynecological complaints, in which case it may or may not be related to her symptoms. It may also be an incidental finding in a woman with no gynecological problems. Whatever the case, a pelvic mass usually raises anxiety,

because it may be a malignancy. Therefore, imaging methods – particularly ultrasound – are often used to help make a correct diagnosis, so that appropriate treatment can be chosen.

Ultrasound examination in skilled hands is an excellent tool for distinguishing benign from malignant adnexal masses [92, 93]. It may also be used to make a specific diagnosis, e.g., dermoid cyst, endometrioma, hydrosalpinx, etcetera [94]. Experienced ultrasound examiners usually use "pattern recognition", i.e., subjective evaluation of the gray scale ultrasound image (sometimes supplemented by color- power- or spectral Doppler ultrasound) to make a diagnosis of an adnexal mass [94]. Ultrasound morphology of various types of adnexal pathology is described in reference [74] and the diagnostic value of adding Doppler ultrasound to gray scale imaging is thoroughly discussed in reference [95]. The sensitivity and specificity of pattern recognition both with regard to malignancy and specific diagnoses are shown in Table 6 [94, 96-109]. A meta-analysis describing the diagnostic accuracy of transvaginal ultrasound specifically for the diagnosis of endometriomas has been published [110].

In studies where pattern recognition was compared to other ultrasound methods (Lerner score [111], risk of malignancy index [112], the Tailor risk calculation model [113], the Timmerman risk calculation model [114] and the mathematical risk calculation models designed in the International Ovarian Tumor Analysis (IOTA) study [115]), pattern recognition was superior to the other methods for distinguishing benign from malignant adnexal masses (Table 7)[115-117]. Because the diagnostic performance of pattern recognition improves with experience[93], scoring systems or logistic regression models to calculate an individual risk of malignancy might work better for less experienced ultrasound examiners. However, whether this is indeed the case has not been studied. Some of the risk calculation models (the Timmerman model [114], the Tailor

model[113]) and scoring systems (the Sassone score [118], the Lerner score [111], the De Priest score [119]) did not perform very well when they were tested prospectively [116, 117, 120, 121]. The IOTA models [115] and the Ferrazzi score[120] have not yet been prospectively cross-validated.

Two studies have examined the contribution of three dimensional (3D) power Doppler ultrasound examination to a correct diagnosis of an adnexal mass. One of them found 3D power Doppler to improve sensitivity and specificity with regard to malignancy [122], the other did not [123]. The possibility to use ultrasound contrast for evaluating adnexal masses has been discussed in two publications [124, 125], but there are not yet any published studies describing the clinical usefulness of using ultrasound contrast.

Not all adnexal masses are easily classified as benign or malignant using pattern recognition. Borderline tumors, papillary cystadeno(fibro)mas and struma ovarii are particularly difficult to classify [126]. For these ‘difficult tumors‘ another diagnostic method would be needed, but currently a method capable of distinguishing benign from malignant ‘difficult masses‘ is lacking. Another diagnostic problem is to distinguish borderline epithelial ovarian malignancies from stage I epithelial ovarian cancers. It does not seem to be possible to distinguish these two entities using either ultrasound, CT or MRI [127, 128].

Ultrasound has been found to be as good as or superior to CT for discrimination between different types of pelvic tumor [109, 129]. MRI has also been used to characterize different types of adnexal tumor in the female pelvis [130-136]. MRI can recognize specific types of tissue, e.g., blood (endometriomas, haemorrhagic cysts), fat (dermoid cysts), and fibrous tissue (fibromas)

[136]. The value of adding CT or MRI to ultrasound imaging in 'indeterminate ovarian masses' was studied in a meta-analysis. The results showed that MRI was superior to CT [137]. In another study, MRI was found to be superior to ultrasound for discriminating between benign and malignant adnexal masses, because it was associated with fewer false positive results [138]. However, in that study it was mainly haemorrhagic cysts, endometriomas and dermoid cysts that comprised the false positive ultrasound results. Therefore, the skill of the ultrasound examiner must be questioned, because in the hands of a skilled ultrasound examiner hemorrhagic cysts, endometriomas and dermoid cysts very rarely cause diagnostic problems, see Table 6.

High quality ultrasound is the imaging method of choice in the differential diagnosis of adnexal masses in most cases. It is simpler, cheaper, and quicker than both CT and MRI, it is readily available and safe, and in skilled hands it will yield a correct diagnosis in most cases (Table 6). A reliable diagnosis makes it possible to choose optimal treatment.

Pelvic pain

Acute pelvic pain

There are a number of acutely painful conditions where an ultrasound examination, particularly a transvaginal ultrasound examination, can contribute to a correct diagnosis: ovarian cysts and tumors (although they do not always cause pain), torsion of the adnexa, and pelvic inflammatory disease, PID, (pyosalpinx, tubo-ovarian abscess, early salpingitis).

The sensitivity and specificity of ultrasound with regard to different types of adnexal masses are presented in Table 6.

Ultrasound findings typical of pelvic inflammatory disease have been described by Timor-Tritsch et al [139] and by Molander et al [140]. The sensitivity and specificity of ultrasound with regard to PID are shown in Table 8 [141-144]. The variable results may be explained by differences in stage of inflammation, ultrasound criteria of PID, skill of the examiner, and quality of the ultrasound systems used.

Even though there are many studies describing features typical of adnexal torsion at ultrasound examination [145-150], CT and MRI [151, 152], there is only one study reporting data that enables calculation of sensitivity and specificity with regard to adnexal torsion: in a study of 65 women with clinical suspicion of adnexal torsion, abnormal color Doppler findings in an adnexal mass predicted torsion (n =15) with a sensitivity of 100% and a specificity of 98% [153].

Chronic pelvic pain

There is no agreed definition of chronic pelvic pain and there is much controversy about what may cause it [154]. Some believe that peritoneal endometriosis and pelvic adhesions cause chronic pelvic pain [155]. Adenomyosis may also be associated with pelvic pain. Imaging methods to diagnose adenomyosis have been described above (Table 5). Okaro et al [156] invented the ultrasound term ‘soft marker‘ to indicate pelvic pathology in women with chronic pelvic pain, the ‘soft markers‘ being presence of immobile ovaries and/or site specific tenderness and/or loculated pelvic fluid at transvaginal ultrasound examination. They found these soft markers to indicate significant pelvic pathology with a positive likelihood ratio of 1.9 and a negative likelihood ratio of 0.2. i.e., the absence of soft markers substantially decreased the likelihood of finding pelvic pathology at laparoscopy. Possibly, the use of soft markers could reduce the number of unnecessary laparoscopies performed in women with chronic pelvic pain,

but the results of Okaro et al would nee to be reproduced by others before being universally adopted.

Endometriosis

I know of no study that has compared clinical examination to imaging methods with regard to diagnosing peritoneal endometriosis. Clinical examination alone does not seem to be a good method for detecting peritoneal endometriosis [157]. The sensitivity and specificity of ultrasound and MRI with regard to various forms of peritoneal endometriosis are shown in Table 9 [158-167]. Results are extremely variable. One study found ultrasound staging of pelvic endometriosis to agree with laparoscopic staging in 82% of cases [168]. I have found no studies reporting the diagnostic performance of CT for the diagnosis of peritoneal endometriosis.

Pelvic adhesions

There are few publications describing the diagnostic accuracy of various imaging methods in the diagnosis of pelvic adhesions. Guerriero and colleagues determined the sensitivity and specificity of various ultrasound findings (blurred margins of the ovary, fixed ovary, distance between ultrasound probe and ovary) and various combinations of ultrasound findings and clinical findings with regard to laparoscopically diagnosed pelvic adhesions in women with risk factors for pelvic adhesions [169]. They also constructed a logistic regression model to calculate the likelihood of pelvic adhesions, but they did not report the sensitivity and specificity of the model, and to the best of my knowledge it has not been tested prospectively. Most ultrasound findings and their combinations changed the odds of pelvic adhesions only little (positive likelihood ratios ranging from 2.6to 6.1, and negative likelihood ratios ranging from 0.4 to 0.7). Ubaldi and co-workers found poor definition of pelvic structures at transvaginal ultrasound examination to

predict pelvic adhesions at laparoscopy with a sensitivity of 61% and a specificity of 98% (positive likelihood ratio 30.5, negative likelihood ratio of 0.6) [170]. The results of Guerriero et al and Ubaldi et al point in the same direction: ultrasound findings suggestive of pelvic adhesions substantially increase the risk of adhesions, but absence of suspicious ultrasound findings does not decrease the risk very much. Three-dimensional ultrasound combined with analysis of serum Ca 125 has been reported to have a sensitivity of 90% and a specificity of 100 % for the diagnosis of pelvic adhesions (negative likelihood ratio of 0.1) [171], whereas MRI has been reported to have a sensitivity of 73% and a specificity of 87% (positive likelihood ratio 6, negative likelihood ratio of 0.3) [172]. I have found no reports on the diagnostic performance of CT for the diagnosis of pelvic adhesions.

Summary

Ultrasound is the first line imaging method in the differential diagnosis of most gynecological diseases and tumors. It can diagnose tubal pregnancy with a sensitivity of 91% and a specificity of 99.9%, it can diagnose malignancy in an adnexal mass with a sensitivity of 88% and a specificity of 96%, it can discriminate between benign and malignant endometrium in women with postmenopausal bleeding not on hormone replacement therapy of with a sensitivity of 96% and a specificity of 92%, it can diagnose adenomyosis with a sensitivity of 87% and a specificity of 96%, which is similar to the sensitivity and specificity reported for MRI. Ultrasound may also be used in the diagnosis of pelvic inflammatory disease, the finding of a thick walled fluid filled tube at ultrasound examination having been found to have a sensitivity of 85% and a specificity of 100%. Transvaginal or transrectal ultrasound can be used to diagnose endometriosis in the recto-vaginal septum and utero-sacral ligaments, but MRI may be an as good or even better

imaging method for these entities. The role of 3D ultrasound and ultrasound contrast is not yet clear.

Practice points

Bleeding and pain in early pregnancy

- Ultrasound signs of early pregnancy failure have been described (mean gestational sac diameter ≥ 8mm but no visible yolk sac, mean gestational sac diameter ≥ 16 mm but no visible embryo with heart beat, embryo ≥ 5mm without heart beat), but none of these signs completely exclude a viable pregnancy
- If there is the slightest uncertainty about the viability of an early pregnancy (for example because of a technically difficult examination), a diagnosis of pregnancy failure must not be made. Instead, the ultrasound examination should be repeated to assess the development of the pregnancy.

Postmenopausal bleeding

- Measurement of endometrial thickness is a simple and accurate method for estimating the risk of endometrial malignancy, endometrial thickness ≤ 4mm indicating low risk and endometrial thickness ≥ 5 mm indicating high risk
- Endometrial morphology at grey scale ultrasound examination with or without saline infusion cannot reliably discriminate between benign and malignant endometrial lesions
- The role of 3D ultrasound, color- power- or spectral-Doppler ultrasound with regard to predicting endometrial malignancy is uncertain

Pelvic masses

- The ‘refractory shadowing pattern‘ (‘stripes‘) is typical of uterine leiomyomas at ultrasound examination
- The presence of both solid components and irregularity in an adnexal mass at ultrasound examination makes malignancy likely
- Neither ultrasound nor CT nor MRI can reliably discriminate between an epithelial borderline ovarian tumor and a stage I epithelial ovarian cancer
- The role of 3D ultrasound and ultrasound contrast in the differential diagnosis of adnexal masses is uncertain

Pelvic pain

- Neither ultrasound (not even Doppler ultrasound) nor CT nor MRI can reliably exclude adnexal torsion in a woman with acute pelvic pain
- Neither ultrasound nor CT nor MRI can reliably exclude pelvic adhesions
- The reported diagnostic performance of ultrasound and MRI for the diagnosis of ‘deep endometriosis‘ varies considerably between studies, and it is not possible to recommend one method over the other
- The diagnostic performance of ultrasound and MRI with regard to adenomyosis is probably similar

Research agenda

- The clinical value of 3D ultrasound examination (including 3D hydrosonography and 3D power Doppler) in gynecology needs to be determined
- The role of ultrasound contrast in gynecology needs to be determined

- Better multiple logistic regression models to estimate the risk of endometrial malignancy in women with postmenopausal bleeding need to be developed and tested prospectively
- Grey scale and Doppler ultrasound characteristics of various types of endometrial pathology need to be defined
- The clinical significance of the presence of focal lesions in the uterine cavity at ultrasound examination in asymptomatic women of fertile age needs to be determined
- Imaging features (or other diagnostic methods) that can confidently discriminate between borderline ovarian tumors and stage I invasive ovarian tumors need to be defined
- Ultrasound features that can confidently discriminate between benign, borderline, and invasive ovarian tumors with papillary projections need to be defined

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Table 1. Sensitivity and specificity of ultrasound in the diagnosis of tubal pregnancy (gold standard is surgery +/-histology)

Author	Number of women	Study population characteristics	Prevalence of ectopics	TAS or TVS	Sens, %	Spec, %	LR+	LR-
Condous -05[5]	6621	Consecutive in EPU, 85% symptomatic	2.3% (152)	TVS	91	99.9	910	0.09
Shalev -98[9]	840	Clinical suspicion of ectopic	45% (380)	TVS	87	94	14	0.13
Kaplan -96[8]	439	Consecutive in ED All symptomatic	13% (56)	TAS+/- TVS	69	99	69	0.31
Hopp -95[7]	184	Clinical suspicion of ectopic	56% (103)	TVS	96	88	8	0.05

cont.

Table 1. Continued

Author	Number of women	Study population characteristics	Prevalence of ectopics	TAS or TVS	Sens, %	Spec, %	LR+	LR-
Brown -94[6]	2216	Mixed populations Meta-analysis	25% (565)	TVS	84	98.9	76	0.16

TAS, transabdominal sonography; TVS, transvaginal sonography; Sens, Sensitivity; Spec, Specificity; LR+, positive likelihood ratio; LR-, negative likelihood ratio; EPU, early pregnancy unit; ED, emergency department

Table 2. Sensitivity and specificity of ultrasound findings with regard to early pregnancy failure

Author	Number of women	Ultrasound sign	Sens, %	Spec, %	LR+	LR-
Levi -88[10]	62	MSD ≥ 8mm, no yolk sac	67	100	-	0.33
		MSD ≥ 16mm, no embryo	50	100	-	0.50
		MSD ≥ 16mm, no embryo OR embryo with no heart beat	100	100	-	-
Brown -90[12]	217	CRL ≥ 5mm, no heart beat	?	100	-	-
Levi -90[13]	71	CRL ≥ 4mm, no heart beat	65	88	5	0.40
Goldstein -92[11]	96	CRL ≥ 4mm, no heart beat	54	100	-	0.46

Cont.

Table 2. Continued

Author	Number of women	Ultrasound sign	Sens, %	Spec, %	LR+	LR-
Tongsong -94[15]	211	MSD ≥13mm, no yolk sac	73	100	-	0.27
		MSD ≥17mm, no embryo	50	100	-	0.50
Schouwink -00[14]	424	MSD ≥ 16mm, no yolk sac	41	98	21	0.60
		MSD ≥ 16mm, no heart beat	82	100	-	0.18
		MSD ≥ 16mm, no yolk sac AND no heart beat	27	100	-	0.73

Sens, Sensitivity; Spec, Specificity; LR+, positive likelihood ratio; LR-, negative likelihood ratio; MSD, mean gestational sac diameter; CRL, crown-rump-length

Table 3. Sensitivity and specificity of various imaging methods with regard to intracavitary uterine pathology in premenopausal women

Author	N	Pathology (n)	Imaging method	Outcome	Sens, %	Spec, %	LR+	LR-	Comment
Dijkhuisen -00[72]	50	any (n = 23), myoma* (n =13) polyp (n = 10)	TVS successful SIS	Any pathology	61 100	96 92	16 12.5	0.4 -	SIS failed in 8%
			TVS successful SIS	Myoma	62 82	95 100	12 -	0.4 0.3	
			TVS successful SIS	Polyp	40 90	100 95	- 18	0.6 0.1	

Cont.

Table3. Continued

Author	N	Pathology (n)	Imaging method	Outcome	Sens, %	Spec, %	LR+	LR-	Comment
Dueholm -01[71]	106	any (n = 41),	TVS	Any pathology	69	83	4	0.4	SIS
failed									
		myoma* (n = 29)	SIS		83	90	8	0.2	in 4%,
		polyp (n = 12)**	Hysteroscopy		84	88	7	0.2	hysteroscopy
		hyperplasia (n = 3)**	MRI		76	92	9.5	0.3	failed in 3%
			TVS	Myoma	83	90	8	0.2	SIS failed
			SIS		90	89	8	0.1	in 4%,
			Hysteroscopy		82	87	6	0.2	hysteroscopy
			MRI		100	91	11	0.1	failed in 3%

Cont.

Table3. Continued

Author	N	Pathology (n)	Imaging method	Outcome	Sens, %	Spec, %	LR+	LR-	Comment

Sens, Sensitivity; Spec, Specificity; LR+, positive likelihood ratio; LR-, negative likelihood ratio; TVS, transvaginal sonography; SIS, saline infusion sonography; MRI, magnetic resonance imaging

*Submucuous myoma

**Sensitivity and specificity not reported for this outcome and not possible to calculate on the basis of the data published.

No method diagnosed hyperplasia, MRI missed 7 of 12 polyps.

Table 4. Sensitivity and specificity of transvaginal ultrasound with regard to uterine leiomyoma and adenomyoma

Author	N	Population	Outcome	Sens, %	Spec, %	LR+	LR-
Botsis -98[80]	206	Women scheduled for surgery for symptomatic uterine masses	Myoma (n = 111)	95	82	5	0.2
			Adenomyoma (n = 31)	82	83	5	0.1
Huang -95[81]	147	Women scheduled for surgery for symptomatic uterine masses	Myoma (n =110)	94	80	5	0.1
			Adenomyoma (n =30)	80	94	13	0.2
Fedele -92[82]	405	Women scheduled for surgery for symptomatic	Myoma (n = 922)	96	83	6	0.1

		uterine masses	Adenomyoma (n = 29)	87	98	6	0.1	Cont.

Table 4. Cont.

Author	N	Population	Outcome	Sens, %	Spec, %	LR+	LR-	

Sens, Sensitivity; Spec, Specificity; LR+, positive likelihood ratio; LR-, negative likelihood ratio

Table 5. Sensitivity and specificity of transvaginal ultrasound (TVS) and magnetic resonance imaging (MRI) with regard to adenomyosis

Author	N	Population	Prevalence, %	Imaging method	Sens, %	Spec, %	LR+	LR-
Bazot-02[90]	129	Women scheduled for HE	36	TVS	57	98	29	0.5
Reinold-95[85]	100	Women scheduled for HE	29	TVS	86	86	6	0.2
Fedele -92[83]	43	Women scheduled for HE	46	TVS	80	74	6	0.3
Atzori -96[89]	175	Women scheduled for HE	9	TVS	87	96	22	0.1
Vercellini -98[88]	102	Women scheduled for HE	29	TVS	83	67	2.5	0.3

Cont.

Table 5. Continued

Author	N	Population	Prevalence, %	Imaging method	Sens, %	Spec, %	LR+	LR-
Ascher -94[87]	20	Clinical suspicion of adenomyosis	85	TVS	53	67	2	0.7
				MRI	88	67	3	0.3
Reinold- 96[91]	119	Women scheduled for HE	24	TVS	89	89	8	0.1
				MRI	86	92	11	0.2
Bazot -01[84]	120	Women scheduled for HE	33	TVS	76	93	11	0.3
				MRI	78	93	11	0.2
Dueholm -01[86]	106	Women scheduled for HE	21	TVS	68	65	2	0.5

				MRI	70	86	5	0.3	Cont.

Table 5. Continued

Author	N	Population	Prevalence, %	Imaging method	Sens, %	Spec, %	LR+	LR-

Sens, Sensitivity; Spec, Specificity; LR+, positive likelihood ratio; LR-, negative likelihood ratio; TVS, transvaginal sonography; MRI, magnetic resonance imaging; HE, hysterectomy

Table 6. Sensitivity and specificity of subjective evaluation of the grey scale ultrasound image (‘pattern recognition‘) for discrimination between benign and malignant pelvic masses and for making a specific diagnosis

	My own series [94]		Other series [96 - 109]	
Diagnosis	Sensitivity	Specificity	Sensitivity	Specificity
Malignancy	88 (21/24)*	96 (143/149)	77 – 100	62 – 95
Dermoid cyst	90 (18/20)#	98 (150/153)	53 – 100	94 – 100
Endometrioma	92 (24/26)	97 (143/147)	43 – 84	89 – 100
Corpus luteum cyst	_	_	not reported	not reported
Hydro-, pyo-, or hemato-salpinx	100 (8/8)	100 (165/165)	83, 93	73, 90
Paraovarian or paratubal cyst	83 (5/6)¤	99 (166/167)	10 – 97	not reported
Peritoneal pseudocyst	100 (3/3)	99 (169/170)	not reported	not reported
Ovarian fibroma or	56 (5/9)	100 (164/164)	not reported	not reported

fibrothecoma

Myoma	86 (6/7)	99 (165/166)	93	98	Cont.

Table 1. Cont.

	My own series [94]		Other series [96 - 109]	
Diagnosis	Sensitivity	Specificity	Sensitivity	Specificity
Abscess	33 (1/3)	99 (169/170)	not reported	not reported

*All malignancies missed were borderline tumors; # No specific diagnosis was suggested in the two cases missed (false-negatives). The two cysts were seen to contain sonolucent fluid, a few septae, and minor solid components not resembling fat or hair; ¤ No specific diagnosis was suggested in the case missed (false-negative)

Table 7. Comparison of the diagnostic performance with regard to malignancy in adnexal masses of pattern recognition and other ultrasound methods (performance tested in the same population).

Author	Diagnostic method									
	Pattern recognition		Risk calculation		Lerner score		RMI		solid component = malignancy	
	Sens, %	Spec, %	Sens,%	Spec,%	Sens,%	Spec,%	Sens,%	Spec,%	Sens,%	Spec,%
Valentin -00[116]	83	97	_	_	92	64	_	_	96	63
Valentin -01[117]	83	91	71[1]	82	_	_	_	_		
	86	87	72[2]	68						

Cotinued

Table 7. Continued

Author	Diagnostic method									
	Pattern recognition		Risk calculation		Lerner score		RMI		solid component = malignancy	
	Sens, %	Spec, %	Sens,%	Spec,%	Sens,%	Spec,%	Sens,%	Spec,%	Sens,%	Spec,%
Timmerman -05[115]	86	92	93[3]	74	_	_	78	80	92	62
			90[4]	71						
			80[2]	81						
			63[1]	88						

RMI, risk of malignancy index; Sens, sensitivity; Spec, specificity; IOTA, international ovarian tumor analysis

[1]Tailor model[113], [2]Timmerman score[114], [3]IOTA model with 12 variables[115], [4] IOTA model with six variables[115]

Table 8. Sensitivity and specificity of imaging methods with regard to pelvic inflammatory disease

Author	N	Population	Prevalence %	Gold standard	Imaging method	Sens %	Spec %	LR+	LR-
Gaitan -02[143]	61	Non specific lower abdominal pain	51	Laparoscopy/ laparotomy, cultures, endometrial biopsy histopathology	Ultrasound	30	67	0.9	1.0
Boardman-97[142]	55	Signs of PID	35	Laparoscopy or culture	Ultrasound	32[1]	97	11	0.3
						42[2]	86	3	0.7
						32[3]	97	11	0.3
						37[4]	58	0.8	1.1

Cont.

Table 8. Continued

Author	N	Population	Prevalence %	Gold standard	Imaging method	Sens %	Spec %	LR+	LR-
Cacciatore- 02[141]	51	Lower abdominal pain	25	Plasma cell infiltration in endometrial biopsy	Ultrasound	85[5]	100	-	0.2
						100[6]	71	3	-
						77[7]	79	4	0.4
Tukeva -99 [142]	30	Clinical suspicion of PID	70	Laparoscopy	Ultrasound	81	78	4	0.2
					MRI	95	89	9	0.1

Sens, Sensitivity; Spec, Specificity; LR+, positive likelihood ratio; LR-, negative likelihood ratio; TVS, transvaginal sonography; PID, pelvic inflammatory disease; MRI, magnetic resonance imaging

[1] Visualization of fallopian tubes with or without fluid; [2] Multicystic ovary; [3] Visuaization of tubo-ovarian abscess

[4] Cul de sac fluid, [5]Visualization of thickened fluid filled tube; [6]Polycystic like ovaries; [7]Free fluid

Table 9. Sensitivity and specificity of various imaging methods with regard to "deep endometriosis"

Author	N	Population	Prevalence %	Gold standard	Localization of endometriosis	Imaging method	Sens %	Spec %	LR+	LR-
Bazot -04[160]	142	Clinical signs of endometriosis	58.5	Surgery, histology	Deep	TVS	79	95	16	0.2
					US-lig.	TVS	71	96	18	0.3
					Vagina	TVS	29	100	-	0.7
					RVS	TVS	29	99	29	0.7
					Bowel	TVS	87	97	29	0.1
					Bladder	TVS	71	100	-	0.3
Delpy –05[161]	30	Suspected endometriosis in RVS	87% RVS 73% US-lig	Surgery	RVS	AR-US	96	100	-	0.4

Cont.

Table 9. Continued

Author	N	Population	Prevalence %	Gold standard	Localization of endometriosis	Imaging method	Sens %	Spec %	LR+	LR-
Bazot-03[159]	30	Clinical signs of endometriosis	93%	Surgery, histology	US-lig.	TVS	75	63	3	0.4
						R-US	75	67	3	0.4
					Vaginal	TVS	25	100	-	0.8
						R-US	25	100	-	0.8
					Cul-de-sac	TVS	82	100	-	0.2
						R-US	45	100	-	0.6
					Rectosigmoid	TVS	95	100	-	0.5
						R-US	82	88	7	0.1

Cont.

Table 9. Continued

Author	N	Population	Prevalence %	Gold standard	Localization of endometriosis	Imaging method	Sens %	Spec %	LR+	LR-
Bazot-04[158]	195	Suspected pelvic endometriosis	63% deep endometriosis	Surgery, histology	Deep	MRI	90	91	10	0.1
					US-ligament	MRI	76	83	4	0.3
					Vagina	MRI	76	95	15	0.3
					RVS	MRI	80	98	40	0.2
					Rectosigmoid	MRI	88	98	44	0.1
Chapron -04[164]	81	Suspected deep endometriosis		Surgery	Infiltration of bowel wall	R-US	97	89	9	0.03
						MRI	77	98	39	0.2

Cont.

Table 9. Continued

Author	N	Population	Prevalence %	Gold standard	Localization of endometriosis	Imaging method	Sens %	Spec %	LR+	LR-
Fedele- 98[165]	140	Suspected endometriosis	24	Surgery, histology	RVS	R-US	97	96	24	0.03
					US-ligament	R-US	80	97	27	0.2
Abrao -04[162]	32	Susepcted RV endometriosis	82	Surgery	RVS	R-US	100	67	3	-
Dessole -031[163]	46	Suspected RV endometriosis	69.5	Surgery	RVS	TVS	44	50	0.9	1.3
						SVS	91	86	7	0.1
Takeuchi-05[167]	31	Suspected RV	71*	Surgery,	CDSO	MRI	91	78	4	0.1

	endometriosis	52**	histology	RVS	MRI	94	100	-	0.06

Cont.

Table 9. Continued

Author	N	Population	Prevalence %	Gold standard	Localization of endometriosis	Imaging method	Sens %	Spec %	LR+	LR-
Kataoka -05[166] 0.1	57	Suspected	53*	Surgery	E-ial implant	MRI	93	54	2	
		endometriosis			Adhesions	MRI	78	50	2	0.4
					CDSO	MRI	68	76	3	0.4

Sens, Sensitivity; Spec, Specificity; LR+, positive likelihood ratio; LR-, negative likelihood ratio; TVS, transvaginal sonography; MRI, magnetic resonance imaging; AR-US, anorectal ultrasound; R-US, rectal ultrasound;,US-lig, uterosacral ligament; RSV, rectovaginal septum; CDSO, cul-de-sac obliteration;E-ial , endometrial; *Cul-de-sac obliteration; **Deep infiltration