First International Consensus Report on Adnexal Masses

Management Recommendations

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Supplemental material online at wileyonlinelibrary.com/journal/jum

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We thank Kathi Minton, MA, RDMS, RDCS, for dedication and support in aid of preparation of this consensus statement. This work was supported by an unrestricted education grant from the Endowment for Education and Research of the American Institute of Ultrasound in Medicine to support consensus conference meeting costs.

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Abbreviations

IOTA, International Ovarian Tumor Analysis; MRI, magnetic resonance imaging

doi:10.1002/jum.14197

The First International Consensus Conference on Adnexal Masses was convened to thoroughly examine the state of the science and to formulate recommendations for clinical assessment and management. The panel included representatives of societies in the fields of gynecology, gynecologic oncology, radiology, and pathology and clinicians from Europe, Canada, and the United States. In the United States, there are approximately 9.1 surgeries per malignancy compared to the European International Ovarian Tumor Analysis center trials, with only 2.3 (oncology centers) and 5.9 (other centers) reported surgeries per malignancy, suggesting that there is room to improve our preoperative assessments. The American College of Obstetricians and Gynecologists Practice Bulletin on "Management of Adnexal Masses," reaffirmed in 2015 (*Obstet Gynecol* 2007; 110:201–214), still states, "With the exception of simple cysts on a transvaginal ultrasound finding, most pelvic masses in postmenopausal women will require surgical intervention." The panel concluded that patients would benefit not only from a more conservative approach to many benign adnexal masses but also from optimization of physician referral patterns to a gynecologic oncologist in cases of suspected ovarian malignancies. A number of next-step options were offered to aid in management of cases with sonographically indeterminate adnexal masses. This process would provide an opportunity to improve risk stratification for indeterminate masses via the provision of alternatives, including but not limited to evidence-based risk-assessment algorithms and referral to an "expert sonologist" or to a gynecologic oncologist. The panel believed that these efforts to improve clinical management and preoperative triage patterns would ultimately improve patient care.

Key Words—adnexal masses; consensus statement; gynecologic oncology; gynecologic ultrasound

An international multidisciplinary panel of experts was convened to thoroughly examine the state of the science relative to asymptomatic adnexal masses and to formulate recommendations for clinical assessment and management. It was hoped that these recommendations might promote more conservative management for benign disease and optimize referrals to gynecologic oncologists in cases of suspected ovarian malignancies. It is estimated that 200,000[1,2] women in the United States undergo surgery for a pelvic mass, yet only 21,290[3] women are ultimately found to have ovarian cancer. Furthermore, we note that in the Unites States, there are approximately 9.1 surgeries per malignancy[1] compared to the

European International Ovarian Tumor Analysis (IOTA) center trials, with only 2.3 (oncology centers) and 5.9 (other centers) reported surgeries per malignancy,[4] suggesting that there is room to improve our preoperative assessments. The American College of Obstetricians and Gynecologists Practice Bulletin on "Management of Adnexal Masses," reaffirmed in 2015, states "With the exception of simple cysts on a transvaginal ultrasound finding, most pelvic masses in postmenopausal women will require surgical intervention."[5] Surgical exploration of benign lesions is not without potential consequences, with reported complication rates ranging from 2% to 15%.[6,7] When malignancy is suspected, survival outcomes are improved if surgery and treatment are performed by a gynecologic oncologist.[8] Surprisingly, only 33% of women with ovarian cancer benefit from a preoperative referral to a gynecologic oncologist[9]; thus, better use of gynecologic oncology can improve treatment outcomes. The group acknowledged that although expert sonographic adnexal evaluation can correctly characterize most benign or malignant adnexal masses,[10] sonography is often performed and interpreted by practitioners with varying levels of expertise. This recognition provided an opportunity to improve risk stratification via the provision of alternatives, including but not limited to evidence-based risk-assessment algorithms and referral to an "expert sonologist" or to a gynecologic-oncologist. The panel believed that these efforts to improve clinical risk stratification and triage patterns would ultimately improve patient care.

Methods and Conference Preparation

The cochairs of the conference (S.R.G. and P.G.) invited the following societies to sponsor a representative of their choosing: American College of Obstetricians and Gynecologists, Society of Obstetricians and Gynecologists of Canada, International Society of Ultrasound in Obstetrics and Gynecology, American College of Radiology, Canadian Association of Radiology, Society of Radiologists in Ultrasound, Society of Gynecologic Oncology, Gynecologic Oncology Canada, and IOTA. Each society agreed to send a representative (supplemental Table A) to a consensus conference held in New York City November 9–10, 2014. The panel comprised 4 gynecologists (United States, Canada, and Europe), 2 gynecologic oncologists (United States and Canada), 1 research PhD with a focus on gynecologic oncology (United States), 5 radiologists (United States and Canada), and 1 pathologist (United States). The goal was to achieve the first international consensus document that would be based on expert input from practicing gynecologists, gynecologic oncologists, imaging specialists, and their respective societies. Key articles within each area of discussion were precirculated to the panel. Day 1 discussion topics included the role of the general gynecologist, the role of the gynecologic oncologist, and the role of imaging, as well as the pathogenesis of ovarian cancer, seminal prior consensus documents,[10] and serum biomarkers and risk assessment algorithms, with an emphasis on the work of the European IOTA group. Discussion was limited to women with sonographically detected adnexal masses of ovarian origin. In the evening, a subset of panelists discussed preliminary consensus statements (S.R.G., D.L., P.G., D.T., F.R.U., and E.P.), which were collated and presented the following day (S.R.G. and P.G.) for further discussion and revision by the entire group of panelists. After the conference, these initial consensus statements were circulated for approval and subsequently expanded into this consensus document. Recommendations were primarily based on published evidence, with consensus opinion used secondarily in some considerations.

Role of the General Gynecologist

General gynecologists are often the first to discover an adnexal mass and are on the front line for management decisions. In this capacity, the generalist makes assessments about whether surgery or monitoring is required. The foremost consideration is the risk of malignancy, although fertility and the effects of surgery on hormonal status are also important. To make this important individual decision, the physician relies on a combination of imaging, the patient's history, physical examination, and laboratory tests to form a recommendation. The imperative step in this process is to rule out ovarian cancer, a disease with high mortality. Hence, it is important to triage patients, giving weight to the preoperative suspicion of cancer. In the absence of a surgical intervention, the general gynecologist will often be responsible for determining appropriate follow-up.

Approach to Adnexal Masses Discovered Incidentally on Sonography

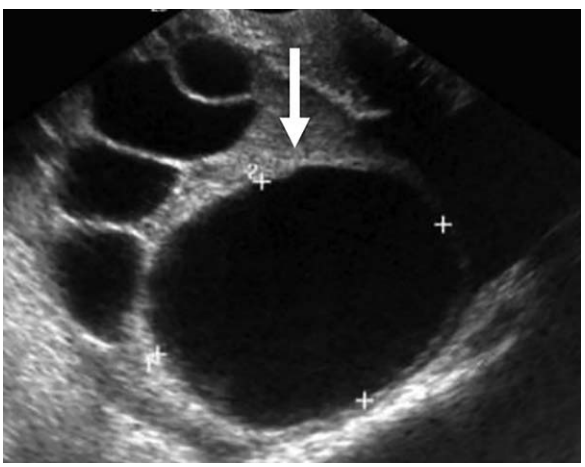
In North America, most sonographically confirmed adnexal masses undergo subjective evaluation without

standardized terminology or risk stratification. In Europe, standardized terminology matched to images and reported via evidence-based risk algorithms is gaining in popularity.[11,12]

Approach 1: Simple Risk Assessment Stratification Profile Based on Pattern Recognition

Although expert sonologists can correctly characterize most benign or malignant adnexal masses,[10] imaging is often performed and interpreted by practitioners with varying levels of expertise and confidence. Thus, providing a simple risk assessment stratification profile may help improve triage patterns. It is based on the recognition that what may be confidently interpreted as "almost certainly benign" or "almost certainly malignant" in the hands of one examiner may well be "indeterminate" for another (supplemental Table B). Almost certainly benign lesions are those that have a "classic appearance" that can benefit from conservative management, often with serial follow-up sonography. Pattern recognition of sonographic morphologic characteristics with color Doppler flow assessment can accurately diagnose most adnexal masses.[10] These include the classic appearance of a unilocular or simple cyst, a hemorrhagic cyst, endometrioma, a dermoid, or a fibroma. Familiarity with these classic appearances via pattern recognition can improve triage into the almost certainly benign category (Figures 1–5). Detailed descriptions of these classic appearances have been previously published.[10,11] If surgery is indicated, gynecologic oncology need not be involved.

Figure 1. Almost certainly benign: the simple cyst (arrow). Features include a round or oval configuration, anechoic, smooth inner walls, no internal components, avascular, and posterior acoustic enhancement. In the premenopausal woman, a cyst of 3 cm of smaller is usually physiologic, representing follicles, whereas 3- to 5-cm cysts are typically physiologic functional cysts.



"Suspicious for malignancy" includes those features that should trigger concern for potential malignancy within an adnexal mass (supplemental Table C and Figures 6–9). We caution that none of these sonographic features should be given singular weight. The best way to evaluate these features is by incorporating them together with the clinical evaluation. Cases in this category should receive prompt referral to a gynecologic oncologist.

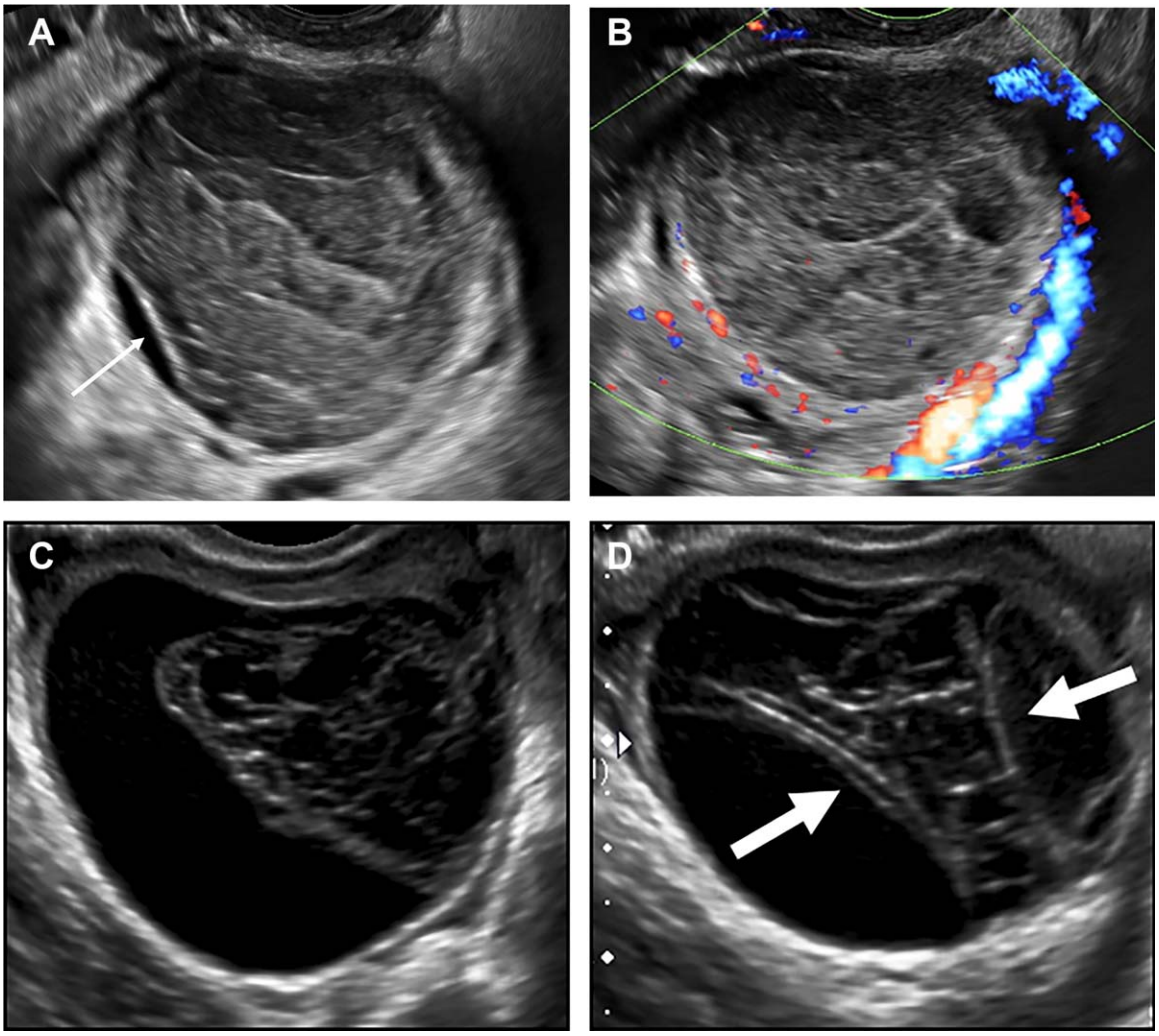
The indeterminate mass does not clearly fit either of the 2 previous categories: almost certainly benign and suspicious for malignancy. The panel agreed that rather than prompt immediate surgical exploration, indeterminate masses can be approached in a variety of appropriate "next steps." The decision of which to use will reside with the experience and comfort of the clinician, as well as the availability of resources.

Approach 2: Risk Prediction Models—Emphasis on IOTA Simple Rules

The IOTA group has developed a Simple Rules approach to the sonographic evaluation of an ovarian lesion. These Simple Rules were initially developed from a population of women who all had surgery for an adnexal mass to help less-experienced operators distinguish between benign and malignant adnexal masses.[13] These Simple Rules permit ultrasound practitioners of varying degrees of expertise and background to quickly use uniform terminology and arrive at similar results.[13] The IOTA Simple Rules are comprised of 5 features that are indicative of malignant lesions (M rules) and 5 features that are indicative of benign lesions (B rules). If 1 or more M features apply in the absence of a B feature, the mass is classified as malignant. If 1 or more B features apply in the absence of M features, the mass is classified as benign. If both M features and B features apply, or if no rule applies, the mass cannot be classified.[13] These features are summarized in supplemental Table D and graphically in Figures 10 and 11. In the original study, the rules could be applied in 76% (937 of 1233) of tumors, and in these, the masses were correctly classified as benign or malignant with sensitivity of 93% (259 of 278) and specificity of 90% (594 of 659). The positive and negative predictive values were 80% (259 of 324) and 97% (594 of 613), respectively. When

prospectively tested, the Simple Rules were applicable in 76% (386 of 507) of the tumors, where they had sensitivity of 95% (106 of 112), and specificity of 91% (249 of 274).[13] When the Simple Rules could not be applied (≈25% of cases), the recommendation was to refer the patient to an expert gynecologic sonologist or, alternatively, to label the tumor as "possibly malignant," since 40% of inconclusive masses classified by the Simple Rules proved to be malignant (62). The rules work best in tumors that are usually easily classifiable by pattern recognition (endometrioma, dermoid cysts, simple cysts, and advanced invasive malignancies) but less well in tumors that tend to be more difficult to classify on sonography (peritoneal cysts, abscesses, fibromas, rare

Figure 2. Almost certainly benign: the hemorrhagic cyst in the premenopausal woman. Classic features include a fine reticular pattern composed of interdigitating fibrinous strands, which do not traverse the entirety of the cystic lesion. Typically, this appearance represents bleeding into a follicle after ovulation. The hemorrhagic components are always avascular, although a peripheral rim of vascularity is common with a hemorrhagic corpus luteum. Evolution over time, including clot retraction with the development of concave margins and a progressive decrease in size, help confirm the diagnosis. **A**, Hemorrhagic ovarian cyst with heterogeneous internal echoes (arrow), which, over time, will organize and resorb. Note the reticular or fishnet appearance with retractile margins associated with hemorrhagic contents. **B**, Addition of color Doppler assessment of blood flow. Note that the rim of increased peripheral vascularity in association with avascular internal contents is typical of a hemorrhagic corpus luteum. **C**, Different hemorrhagic ovarian cyst only partially filled with hemorrhage, represented by a fine lacy network of interdigitating fibrinous strands. **D**, By rotating the transducer on the hemorrhagic ovarian cyst shown in **C**, the typical retractile concave margins (arrows) of and evolving clot can be shown.

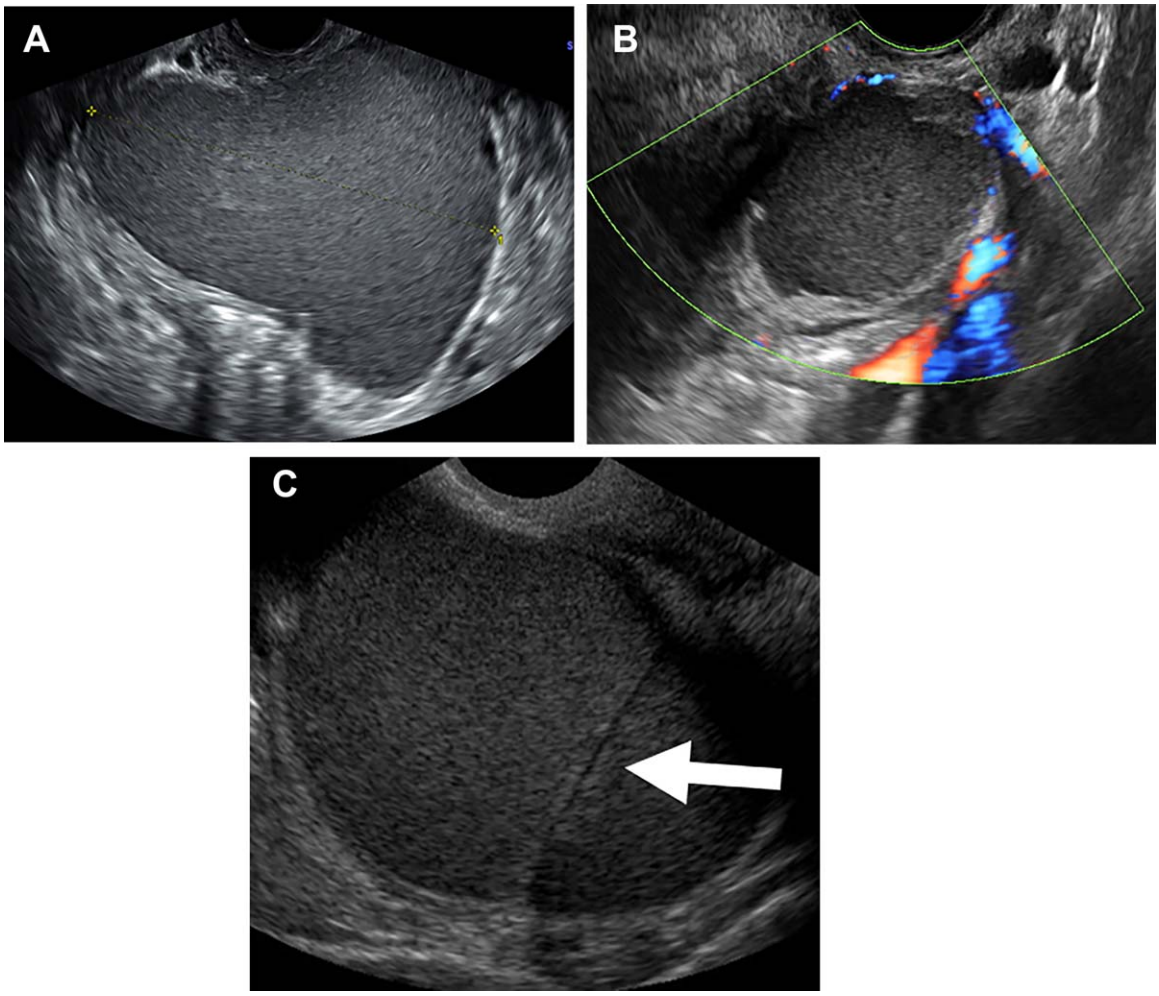


benign tumors, stage I borderline tumors, and stage I primary invasive tumors).[14]

Malignant Potential of Simple and Unilocular Cysts

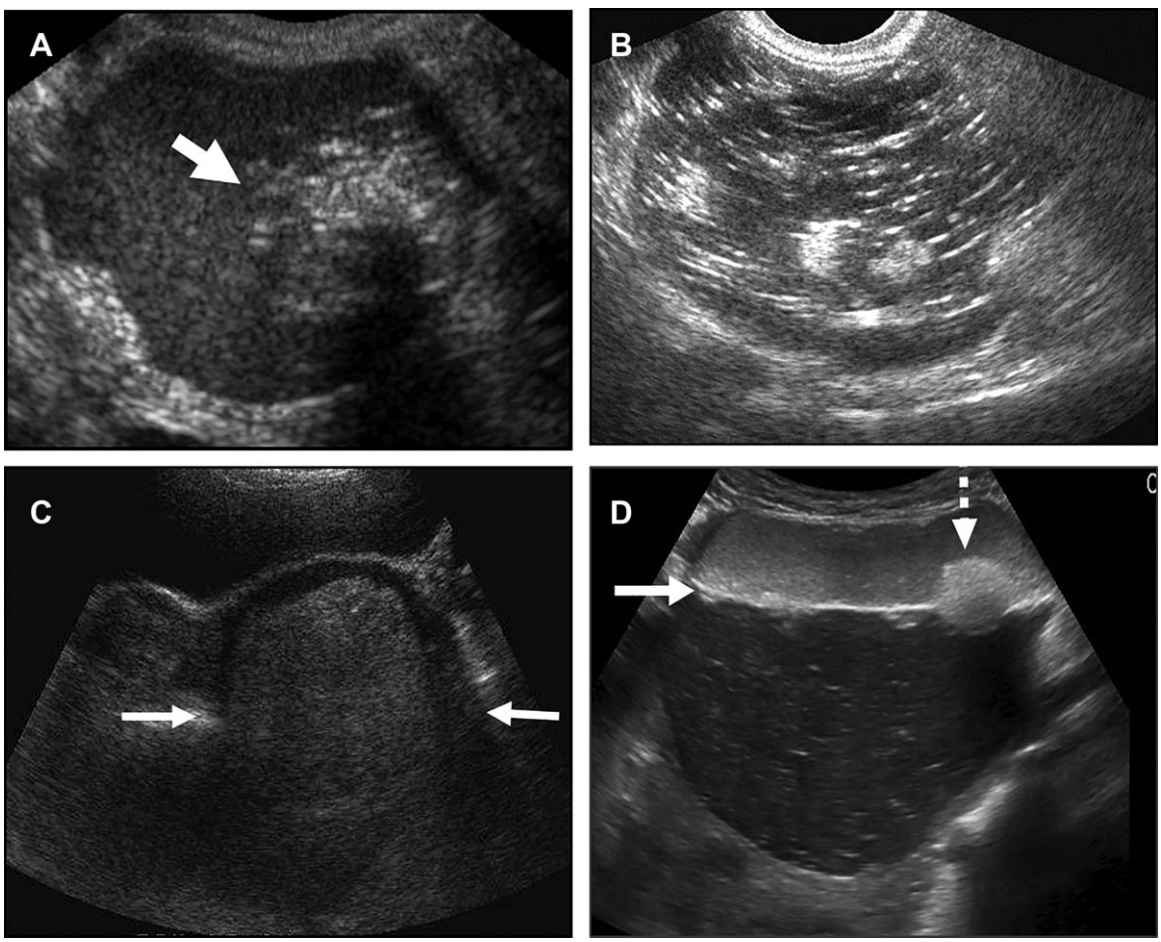
A simple cyst is defined as anechoic round or oval lesion, whereas a unilocular cyst may contain incomplete thin septations, solid wall irregularities of less than 3 mm in height, or internal echoes.[11] Most simple-appearing cysts resolve spontaneously, but within the persistent group with larger lesions, as many as one-half to two-thirds are serous cystadenomas.[15,16] Studies that focus on the origin of high-grade serous cancers or tumors early in their natural history[17] have identified a fallopian tube origin,[6,18] whereas there is no documented relationship that confirms the transformation of a serous cystadenoma into a high-grade serous carcinoma.[16] Molecular studies are also supportive of the finding that serous cystadenomas do not transform into high-grade serous carcinomas.[1,19] Thus, the long-term risk of malignancy after a diagnosis of serous cystadenoma is considered similar

Figure 3. Almost certainly benign: Endometriomas. Classic features include a background of homogeneous low-level echoes in an avascular thick-walled cystic mass. They are commonly multilocular, and the locules may have varying levels of echogenicity. Occasionally, hyperechoic wall foci are present, increasing the specificity of the diagnosis. Not all adnexal masses with low-level echoes are endometriomas; thus, it is important to ensure that the lesion is avascular with smooth septations and no solid elements. **A**, Classic appearance of an endometrioma. Note the homogeneous "ground glass" appearance in association with the posterior wall acoustic enhancement typical of a fluid-filled structure. **B**, The addition of color Doppler sonography shows no internal vascularity. **C**, Multilocular (arrow) endometrioma with homogeneous low-level echoes. **D**, Unilocular endometrioma with hyperechoic wall foci (arrows).



to that of the general population. Modesitt et al[17] reported on 15,106 women at least 50 years of age in an ovarian screening program to study the natural history of unilocular cysts smaller 10 cm managed conservatively. Of these, 2763 (18%) had a diagnosis of unilocular cysts smaller than 10 cm, and repeated transvaginal sonography was performed at 4 to 6 weeks on these patients. Almost 70% resolved spontaneously and two-thirds within 3 months. Of note, 52% of 117 persistent cystic masses that were removed were serous cystadenomas, and none were malignant or borderline. Ultimately, invasive cancer was diagnosed in 10 patients, of whom 7 developed a solid component on follow-up; 2 had resolved before a cancer developed; and in 1, cancer developed in the contralateral ovary. Thus, no woman with an isolated simple cyst smaller than 10 cm developed ovarian cancer, supporting the concept that simple cysts are not precursors to invasive ovarian carcinoma. In a similar vein, over 4 years of transvaginal sonographic screening for the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial, Greenlee et al[20] found simple cysts in 14% of women older than 55 years, with 54% of these simple cysts persisting at 1 year. Women with 1 or more simple cysts at their first sonographic screen were not at a significantly increased risk for the subsequent development of invasive ovarian cancer. Of

Figure 4. Almost certainly benign: dermoid cyst or mature cystic teratoma. Classic features on sonography include the following: **A**, Regional bright echogenic nodule with acoustic shadowing, also referred to as a Rokitansky nodule (arrow). **B**, Dermoid mesh: echogenic interdigitating lines and dots representing hair in sebum. **C**, Echogenic mass with strong acoustic shadowing, which may obscure the back wall of a large mass, giving rise to the descriptor "tip of the iceberg" sign (arrows).**D**, A Fat-fluid level and dermoid ball are less common signs but highly specific. The fat-fluid sign (solid arrow) represents the echogenic layer of fat floating on the hypoechoic fluid within the dermoid cyst. The dermoid ball (dashed arrow) is a rounded ball of fat, which is echogenic with acoustic shadowing floating within the dermoid cyst. These may be single or multiple.



note, 15% of women with a false-positive result who underwent surgery had a major complication. Thus, one could conclude that although simple cysts do not increase the risk of subsequent ovarian cancer, their excision may increase morbidity secondary to a major surgery–associated complication. More recently, Sharma et al[21] and Jacobs et al[22] from the UK Collaborative Trial of Ovarian Cancer Screening studied 48,053 postmenopausal women, of whom 2531 had unilocular cysts.[11] Within 3 years of the first scan, 5 of these patients developed a borderline tumor, and 4 developed type 2 epithelial ovarian cancers (high-grade serous cystadenocarcinoma), suggesting that the risk of associated malignancy with unilocular cysts was 0.35% (9 of 2531). The authors commented that "there was a change in morphology in these unilocular cysts that went on to develop epithelial ovarian cancer." It is unclear whether these cysts were miscategorized initially as unilocular, or

Figure 5. Almost certainly benign: fibroma. The classic appearance is a solid hypoechoic mass with strong acoustic shadowing (arrows). At times, the appearance may be confused with a fibroid lesion; however, that is related to the ovary, rather than the uterus. They tend to have minimal vascularity when interrogated with color Doppler sonography. **A**, Small ovarian fibroma, clearly intraovarian, with a crescent of ovarian tissue surrounding it (arrow) and a hypoechoic appearance with acoustic shadowing. **B**, Larger ovarian fibroma with a typical hypoechoic appearance (arrows) and strong acoustic shadowing. No rim of ovarian tissue is identified; thus, it is more challenging to diagnose confidently.

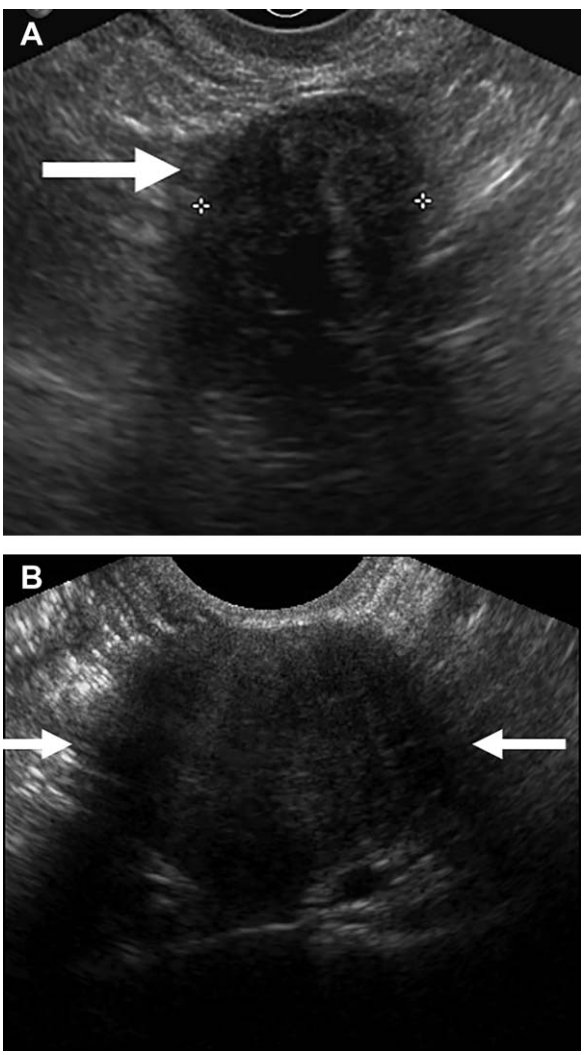
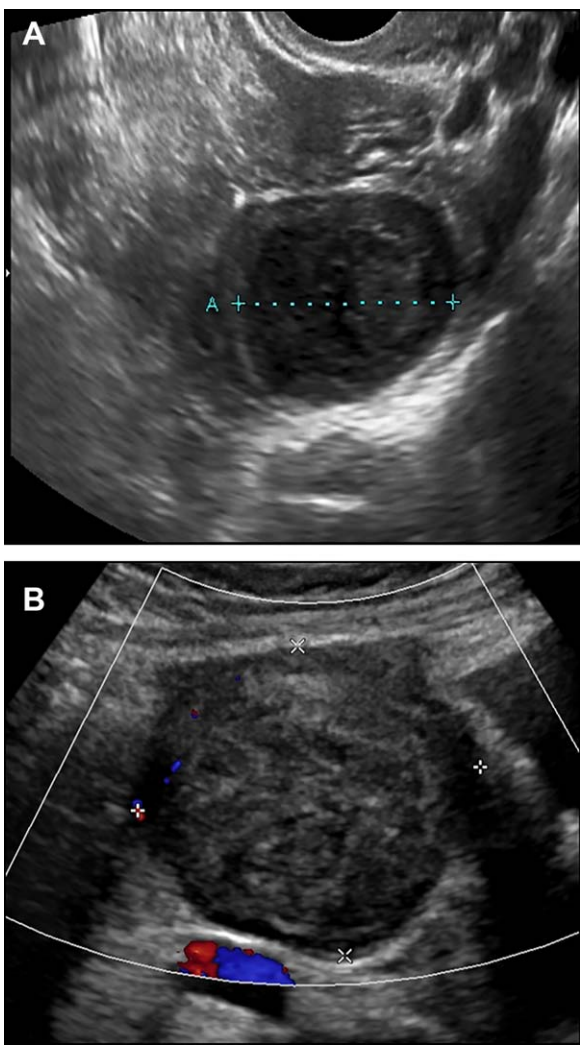


Figure 6. Suspicious for malignancy: solid mass with interim growth. **A**, Solid mass measuring 3 cm. **B**, Solid mass measuring 5.5 cm showing interim growth within 8 months.



whether they truly underwent some morphologic change. Regardless, this underscores 2 very important points: (1) simple or unilocular cysts do not need immediate surgical intervention; and (2) follow-up scans at an interval are appropriate to detect the very small number of cysts (<0.4%) that were either difficult to evaluate initially or might undergo morphologic changes.

Malignant Potential of Cysts With Septations, Papillary Projections, and Other Internal Contents

True septations extend in continuity across a cyst and should be evaluated with regard to number, thickness, and regularity. A single thin (≤3 mm) septation is considered a benign finding.[23] In a screening study that evaluated 2870 cystic masses that had 1 or more septations but no papillary projection or solid elements, 38.8% of the cysts resolved spontaneously, albeit over a period as long as 12 months. Of the 128 that were surgically excised within the first 3 months, most were serous or mucinous cystadenomas, with 1 borderline tumor and no ovarian cancers, suggesting that even multiseptated cysts without solid elements are associated with a very low risk of malignancy.[10,11,23] A common definition of a papillary projection is any protrusion of solid tissue into a cyst cavity with a height of 3 mm or greater.[13] Cysts with 1 or a few small papillary projections that are less than 3 mm are likely to be benign; however, if papillary projections of any size involve greater than 50% of the inner cyst wall, or are 4 or more in number, malignancy is more likely.[11] Short-term follow-up may be appropriate for patients with unilocular cysts that contain 1 or a few small solid avascular papillary projections. A benign mucinous ovarian cystadenoma is typically thin walled, large, and with multiple locules of low-level echogenicity. Sparse literature exists on their natural history; however, some publications have suggested that malignant transformation can occur but typically over a long period.[24,25] Borderline mucinous ovarian tumors are generally at least 10 cm with more than 10 locules.[26] Thus, sonographic surveillance may still be appropriate in smaller cysts with fewer locules.

Figure 7. Suspicious for malignancy: solid vascular component. The large solid nodule within an otherwise simple cyst shows internal central vascularity on color Doppler sonography.

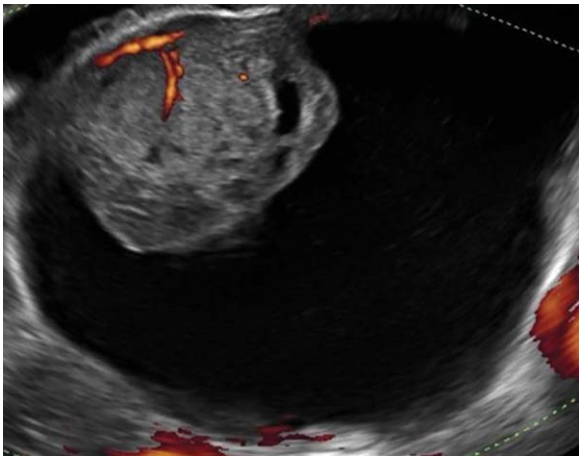
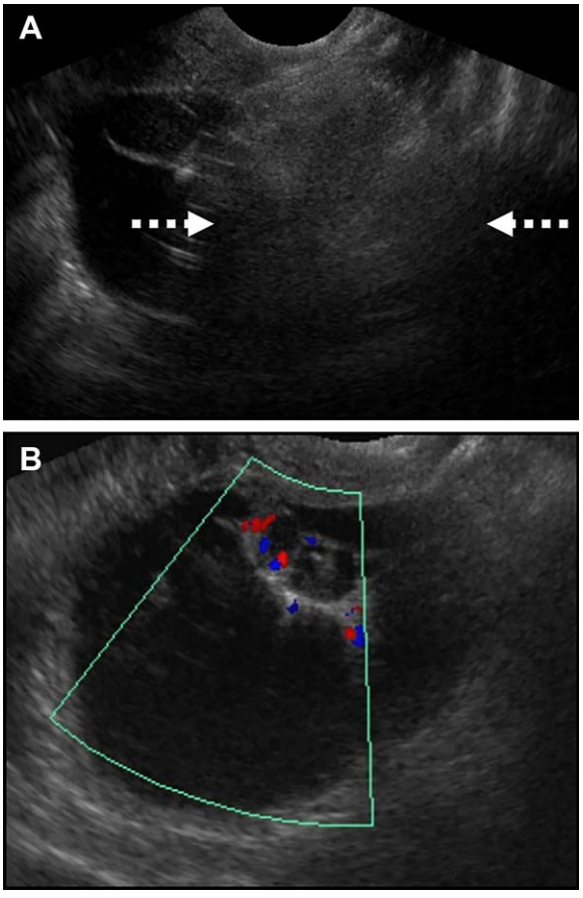
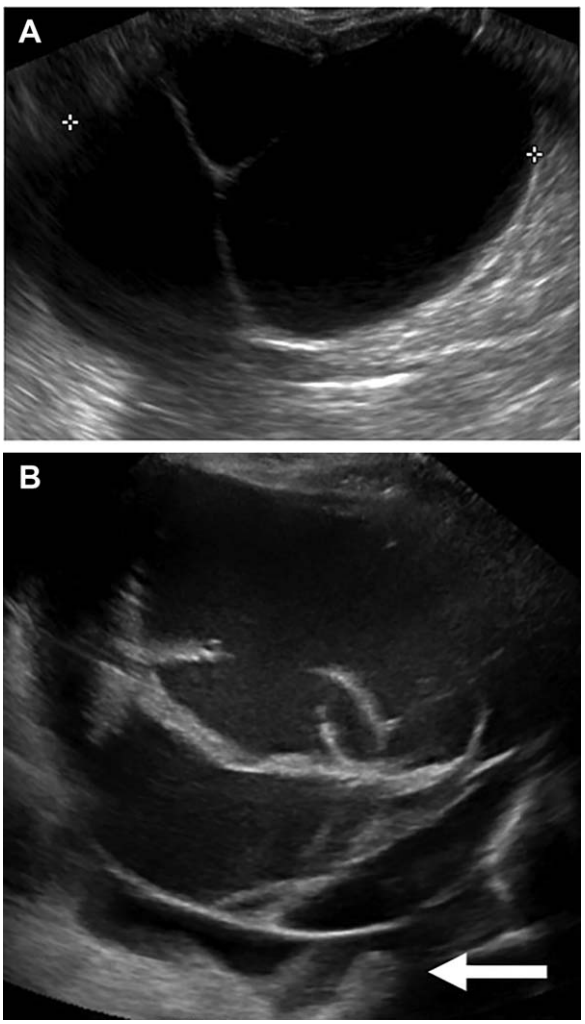


Figure 8. Suspicious for malignancy: internal vascularity within a mature cystic teratoma. **A**, Large mass with features of a dermoid lesion, including the dermoid mesh pattern (interdigitating echogenic lines and dots; solid arrow) and the tip of the iceberg sign (echogenic mass with strong acoustic shadowing obscuring the posterior border; dashed arrow). **B**, In the superior portion of the lesion is a vascular solid component. It is important to meticulously interrogate the entire lesion to ensure that there are no suspicious features of malignancy.



Mature cystic teratomas and endometriomas have a low association with malignancy, typically less than 0.8%.[27] Therefore, just as with mucinous cysts, it is prudent to follow these over time to assess for morphologic changes, in particular, looking for lesions that show rapid growth or develop solid vascular elements. There is an increased risk of malignant transformation in larger endometriomas (>9 cm) and older women (>45 years).[28] Overall, there is no definitive data to indicate that early surgical treatment of endometriotic implants is associated with a reduced risk of malignancy.

Figure 9. Suspicious for malignancy: thickened irregular septations. A few smooth septations are not concerning for malignant disease; however, if there are multiple (>10) or irregularly thickened and vascular septations, they are concerning for malignancy. **A**, Cyst with several smooth thin septations on a background of low-level echoes. When persistent, these likely represent benign serous or mucinous cystadenoma. **B**, A large (>10 cm) cystic lesion with multiple septations (>10) of varying thickness, with low-level echoes, is suspicious for malignancy. Note mural wall nodules (arrow).



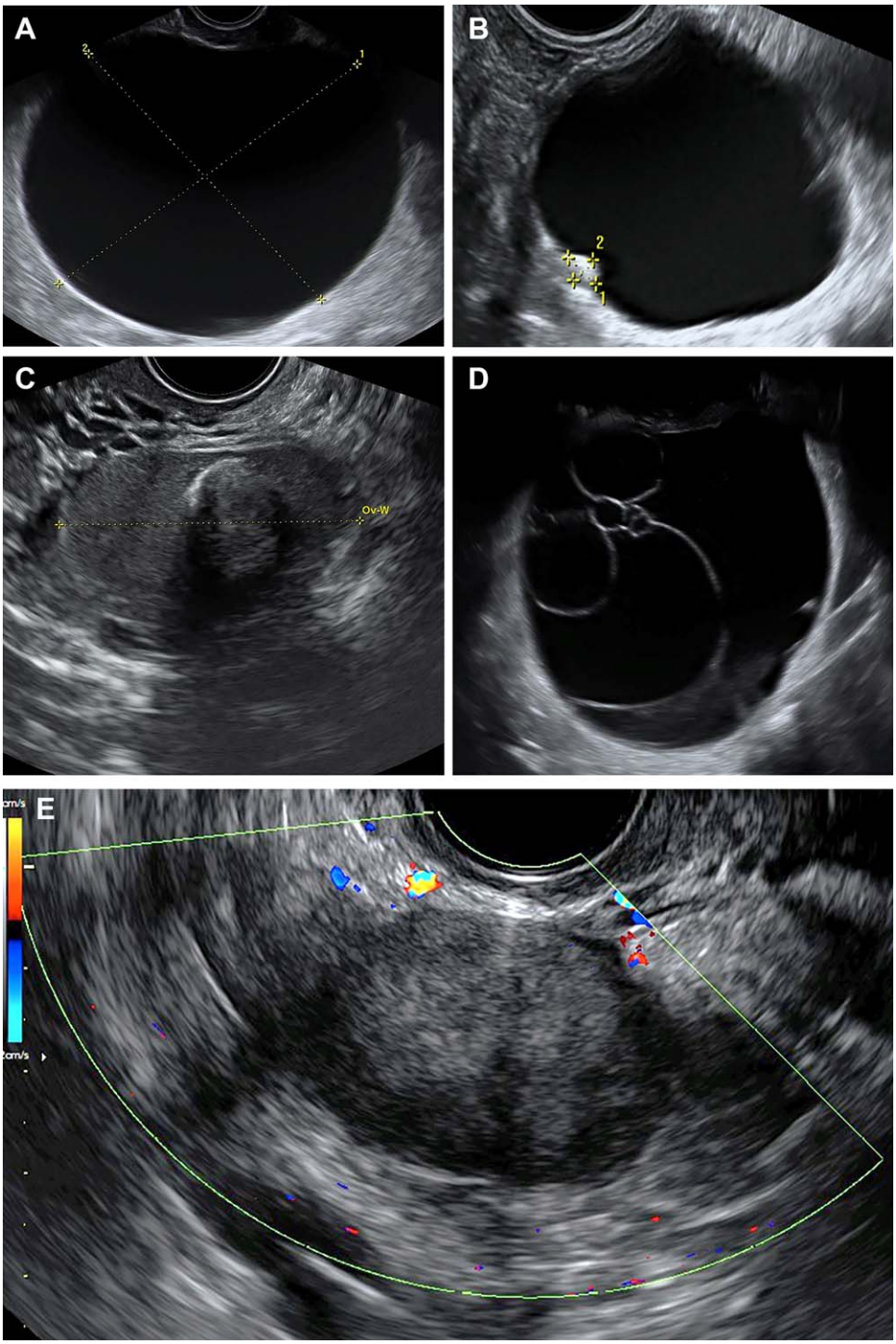
Solid Masses With or Without Vascularity

A unilocular or multilocular cystic mass with solid elements or a predominantly solid (>80%) ovarian mass has an increased risk of being a borderline tumor or epithelial ovarian cancer.[17,21] Up to 5% to 10% of all ovarian tumors are metastatic; however, most have a known history of primary carcinoma. Although mostly solid or solid masses have typically been considered hallmarks of potential malignancy, common benign solid masses such as pedunculated fibroids and ovarian fibrothecomas also occur. A pedunculated fibroid is identified by its classic sonographic appearance of a hypoechoic solid mass with a connection to the uterus. Fibrothecomatous ovarian masses account for approximately 5% of ovarian neoplasms. Their classic sonographic appearance is a hypoechoic mass with acoustic shadowing. Fibromas may be associated with ascites and pleural effusions, termed Meigs syndrome. Thecomas may secrete estrogen, resulting in endometrial changes, bleeding, or both. The fibrothecoma group can be challenging to diagnose accurately on sonography and often have atypical, cystic, or vascular features; in these cases, adjunctive magnetic resonance imaging (MRI) may be helpful to define their fibrous nature.[29,30] Accurate diagnosis is important so that their benign nature is correctly interpreted. Caution is recommended in this diagnosis, as in a study based on IOTA terms and definitions, a small but real false-negative rate for malignancy[31] was identified when a sonographic diagnosis of fibroma was given.

Role of Doppler Sonography

Color or power Doppler sonography is recommended for the evaluation of most adnexal masses to determine the presence or absence of vascular flow within cystic or solid areas. In general, increased central vascularity correlates with increased malignant potential, whereas the absence of intratumoral vascularity has a high negative predictive value. The absence or presence of color Doppler flow cannot be used as an isolated feature to determine malignancy risk, since malignancy can occur without measurable flow. Importantly, spectral Doppler parameters alone do not effectively discriminate malignant from benign lesions.[10,32]

Figure 10. IOTA Simple Rules: benign features (B1–B5). **A**, B1 feature: unilocular cyst. By IOTA definitions, this category includes a cyst with thin, few, or incomplete septations or wall nodularity of less than 3 mm. There may be internal echoes. **B**, B2: presence of a solid component of less than 7 mm in largest diameter. **C**, B3: presence of acoustic shadowing. **D**, B4: smooth multilocular tumor with a largest diameter of less than 10 cm. **E**, B5: no detectable blood flow on Doppler examination.

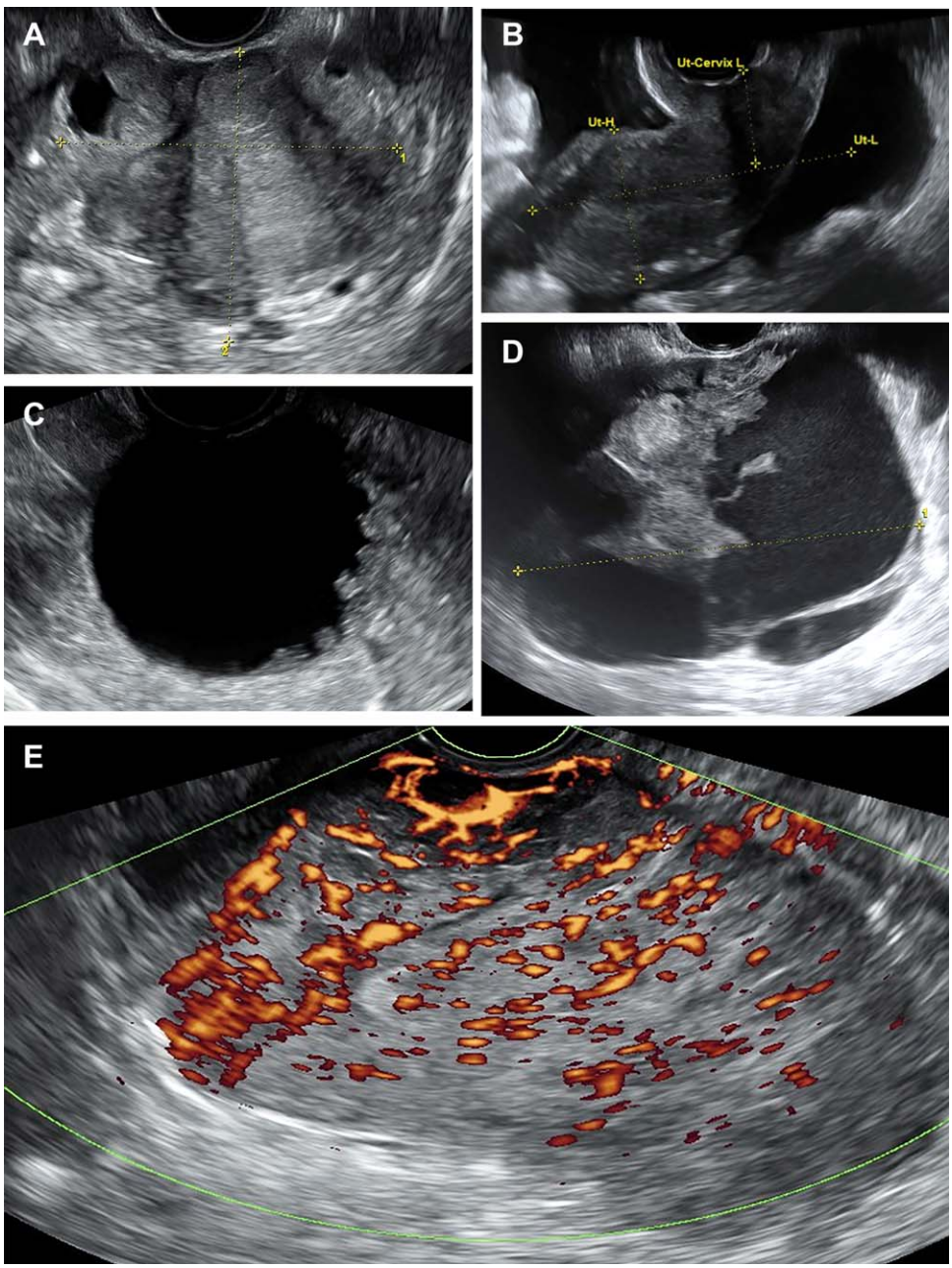


Indeterminate Masses: Next Steps

Role of Referral to an Expert Sonologist

Most reports indicate that in experienced hands, the discrimination between benign and malignant adnexal masses using sonography remains highly accurate, with sensitivity as high as 96.7%.[33] In addition, sonologists are able to make a correct specific diagnosis in 42% of cases.[14,34,35] Such expertise is not easily transferred from one person to another or from one center to another because sonography is operator and machine dependent.[36,37] Experienced ultrasound examiners take into

Figure 11. IOTA Simple Rules: malignant features (M1–M5). **A**, M1: irregular solid tumor. **B**, M2: presence of ascites. **C**, M3: at least 4 papillary structures within a cystic lesion. **D**, M4: irregular multilocular solid tumor with a largest diameter of 10 cm or greater. **E**, M5: very high color content on color Doppler examination.



account demographic, clinical, imaging, and Doppler characteristics in their evaluation while incorporating prior experiences into each evaluation. Thus, ultrasound expertise substantially affects the quality of subjective assessment.[34,37] Despite extensive research into various risk prediction models, subjective assessment in the hands of an expert remains as accurate as any technique for assessment of adnexal masses by sonography.[38] Thus, it is appropriate to consider referral to an expert gynecologic sonologist when faced with a challenging or indeterminate adnexal mass.

Role of Serial Sonography

Serial sonography has demonstrated that most adnexal masses will spontaneously resolve over time. In a recent report, Elder et al[39] demonstrated that serial sonography in 7104 women with ovarian tumors improves the prediction of ovarian malignancy while decreasing the number of operations performed for benign abnormalities. Thus, continuing surveillance with serial sonographic scans offers an opportunity to monitor ovarian lesions that are destined to resolve or remain stable, albeit along a variable timeline. A recent expert review suggested that low-risk abnormalities can undergo an initial 3-month follow-up, with those that remain stable or decreasing in size being examined every 12 months for 5 years.[40]

Role of Established Risk Prediction Models

A recent systematic review examining different risk prediction models recommended incorporating the use of the IOTA Simple Rules for preoperative characterization of ovarian masses, particularly in premenopausal women.[41] Recently, the IOTA group reported that the Simple Rules can use the number and type of features identified by sonographers to provide better individualized risk assessments of a given mass.[4]

Role of Referral for Serum Biomarkers

The role of serum biomarkers, whether in isolation or as part of an algorithm, is not yet clearly established. Cancer antigen 125 has low sensitivity in early-stage cancers and is elevated in many benign gynecologic and nongynecologic conditions, thus limiting its utility as a cancer-specific marker at initial diagnosis. The Risk of Malignancy Index score is the most widely used algorithm to assess high or low risk for malignancy, with a threshold value of 200 providing sensitivity of 78% and specificity of 87%.[42] In the United States, OVA1 and the Risk of Malignancy Algorithm are the only tests cleared by the US Food and Drug Administration for the preoperative evaluation of an ovarian tumor. The Risk of Malignancy Algorithm combines 2 biomarkers (cancer antigen 125 and human epididymal protein 4) into 2 separate logistic regression algorithms, depending on the patient's menopausal status.[43] Subjective assessment by an expert sonographer has been demonstrated to outperform Risk of Malignancy Algorithm in the group of difficult tumors.[38] OVA1 is a multivariate index assay, which in 2 trials published sensitivities of greater than 90% for early-stage cancer, highest for epithelial ovarian cancers[44,45]; however, specificities were relatively low.

Role of MRI

Magnetic resonance imaging is a consideration when the adnexal mass is not adequately characterized by sonography. Sonography followed by MRI for indeterminate masses decreases the risk of misdiagnosing a benign mass as malignant and increases the specificity of a benign diagnosis.[46] Benign lesions typically include mature teratomas with atypical imaging features or microscopic fat not recognizable on sonography, hemorrhagic lesions with blood clots mimicking solid tissue, and fibrous masses such as ovarian fibrothecomas and uterine leiomyomatas. Magnetic resonance imaging is also highly sensitive (96.6%) and specific (83.7%–94.0%) for the diagnosis of malignancy.[30,47] A recent meta-analysis concluded that MRI with contrast enhancement provides higher posttest probability of ovarian cancer confirmation[48] than sonography with Doppler imaging, computed tomography, or positron emission tomography for the examination of ovarian masses that are difficult to classify on sonography.

Role of Referral to a Gynecologic Oncologist When a Mass Is Indeterminate

When the initial evaluation is indeterminate, referral to a gynecologic oncologist, not necessarily for prompt surgical exploration but for use of the oncologist's expertise, is an appropriate next step. Referral will depend on a variety of factors (resources, confidence level of the initial physician, and local practice patterns).

Role of Referral to a Gynecologic Oncologist When a Mass Is Suspicious for Malignancy

Ovarian cancer is an aggressive gynecologic malignancy, with a 5-year survival rate of around 40%, accounting for approximately half of all deaths related to gynecologic malignancies.[1] The stage at diagnosis is the most

important predictor of survival[49]; however, it is well established that referral to a gynecologic oncologist leads to improved survival outcomes.[5,50] Improved survival is related to optimal surgical staging and debulking, adjuvant therapy, and use of alternative strategies (neoadjuvant, dose-dense, and intraperitoneal chemotherapy). Only 33% of women with ovarian cancers are referred to gynecologic oncologists.[9]

Discussion

The goal of this first international consensus panel was to evaluate the state of the science and to provide recommendations for proceeding when adnexal masses are discovered by sonography. The 2 approaches outlined here (pattern recognition and the Simple Rules risk prediction model) offer pathways to improve the initial assessment of adnexal masses for practitioners with varying levels of expertise for better distinguishing benign from malignant masses. This improved distinction should lead to a conservative management pathway for more abnormalities that are benign and the referral of more ovarian malignancies to gynecologic oncologists. A variety of next-step options to diagnosis can be used for indeterminate abnormalities (Table 1). Another outcome of the panel was the recognition of evidence-based risk algorithms, such as the Simple Rules provided by the IOTA group.

We thought it important to further disseminate this knowledge to a North American audience to be considered in the evaluation of adnexal masses, with the caveat that this process may sometimes miss early-stage malignancies and remains indeterminate in 23% of cases. By presenting these potential next steps, we hoped to decrease surgery on benign ovarian sonographic abnormalities that would either resolve or remain stable. Referrals to expert sonologists are underused in the United States relative to Europe, and the panel believed strongly that this approach should be a valid option for clinicians. A great deal of clinical information is drawn from large data sets, based primarily on cases that went to surgery or those identified via ovarian cancer screening trials. The next phase of the IOTA trials is anticipated to provide long-term evidence-based outcome data on a nonsurgical, nonscreened population. The panelists agreed that serial sonography was a beneficial strategy for many patients but did not come to an initial agreement on the exact length or timing of follow-up by serial sonography of probably benign or indeterminate lesions due to a paucity of evidence. Nonetheless, we have provided some suggested guidelines derived from previously published work[17,20,21,39,40,51,52] for probably benign masses. That simple and even unilocular cysts almost never contain malignancy needs to be understood by both patients and clinicians. We believe that the existence of a consensus document from a group of international experts who agree with watchful waiting from evidence-based literature will enable physicians to engage in discussions on surveillance, as nonurgent follow-up, in addition to surgery as appropriate for individual clinical situations.

Robust data exist showing improved cancer outcomes when initial surgery is performed by a gynecologic oncologist. Although the panel realizes that consultation with a gynecologic oncologist is not always possible, every attempt should be made to involve gynecologic oncology services when there is a high suspicion for ovarian malignancy. We anticipate that the published recommendations from this international multispecialty consensus

Table 1. Adnexal Mass Consensus Recommendations

Pelvic sonography should include the transvaginal approach with Doppler imaging as indicated.
Simple ovarian cysts are not precursor lesions to malignant ovarian cancer; however, it is crucial to perform a high-quality examination to ensure the absence of any solid/papillary structures before designating a cyst as a simple cyst. The risk of progression to malignancy is extremely low; thus, a degree of follow-up is prudent.
Real-time pattern recognition sonography in the hands of an experienced imager is currently the most accurate method of characterizing an ovarian mass.
Initial mass characterization could be performed either by pattern recognition or via a risk model such as the IOTA Simple Rules.
When an ovarian lesion is considered benign, the patient may be followed conservatively, or if indicated, surgery can be performed by a general gynecologist.
Serial sonography is a beneficial strategy, but there are limited prospective data to support an exact interval and duration.
Fewer surgical interventions may well result in an increase in sonographic surveillance.
When an ovarian lesion is considered indeterminate on initial sonography, and after appropriate clinical evaluation, a "second-step" evaluation may include: referral to an expert sonologist, serial sonography, application of established risk prediction models, correlation with serum biomarkers, correlation with MRI, or referral to a gynecologic oncologist for further evaluation.
Need to decrease surgery in benign conditions and to optimize referral patterns to gynecologic oncologists in cases of suspected ovarian malignancy.

panel will provide additional help for the gynecology community when choosing strategies of watchful waiting, second steps, and referral to a specialized gynecologic surgeon in the appropriate settings. The summary consensus comments of the panel can be reviewed in Table 1.

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