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BRIEF ANSWERS
TO SPECIFIC
CLINICAL
QUESTIONS

How long should we follow simple ovarian cysts with pelvic ultrasonography?

A 54-YEAR-OLD postmenopausal woman presents with a 3-day history of left lower quadrant pain. Abdominal and pelvic computed tomography confirm the diagnosis of acute diverticulitis, and a left ovarian cyst is incidentally noted. Her abdominal discomfort resolves with antibiotics.

Transvaginal ultrasonography confirms the presence of a 4.5-cm simple left ovarian cyst. The radiologist recommends follow-up ultrasonography in 3 months “if clinically indicated.” The patient feels well and is anxious about having additional testing. What do you recommend?

■ HOW USEFUL IS ULTRASONOGRAPHY FOR OVARIAN CYSTS?

Ovarian cysts are common and may affect up to 20% of women at some time during their life.¹ In a prospective study of almost 40,000 women enrolled in an ovarian cancer screening program, the prevalence of ovarian cysts was 15.3% in premenopausal women and 8.2% in postmenopausal women.²

Pelvic ultrasonography is the most effective way to evaluate incidentally noted cysts, and the transvaginal approach is preferred.³ The International Ovarian Tumor Analysis group has outlined morphologic features, referred to as “simple rules,” for predicting if a cyst is malignant or benign.⁴ In a prospective validation study, these simple rules were applied in 76% of cases, with a sensitivity of 95% and a specificity of 91%.⁴ However, it should be noted that these rules apply to examina-

tions done by experienced gynecologic ultrasonographers, as accuracy of ultrasonography is both machine- and operator-dependent.

■ WHAT IS THE MALIGNANCY POTENTIAL OF A SIMPLE OVARIAN CYST?

A simple ovarian cyst is defined as an anechoic round or oval lesion, different from a unilocular cyst, which may contain septations, solid wall irregularities, or internal echoes.⁵ Overall, simple ovarian cysts have a very low likelihood of malignancy. In the large, multi-site Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial, simple cysts were observed in 14% of postmenopausal women,⁶ but no cyst was associated with the development of ovarian cancer over 4 years of follow-up.

■ HOW OFTEN SHOULD IMAGING BE REPEATED?

In premenopausal women, most simple (thin-walled) ovarian cysts less than 5 cm in maximum diameter resolve in 2 to 3 menstrual cycles and do not require further intervention.³ Larger cysts (5–7 cm in diameter) should be followed with ultrasonography yearly. Cysts larger than 7 cm require advanced imaging or surgical intervention, and the patient should be referred to a gynecologist.³

In postmenopausal women, serum markers are combined with ultrasonography results to determine the risk of malignancy. Markers studied include cancer antigen 125 (CA-125), human epididymis protein 4, lactate dehydrogenase, alpha fetoprotein, and beta human chorionic gonadotropin (beta hCG).⁷

Before menopause, most simple cysts < 5 cm resolve in 2 to 3 menstrual cycles and require no further intervention

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CA-125, the most studied marker, is elevated in more than 90% of advanced-stage ovarian cancers, but in only 50% of patients with early-stage cancer.^{1,8} However, CA-125 may be elevated in a variety of other settings, including benign gynecologic disorders (pelvic infection, fibroids, endometriosis, adenomyosis) and nongynecologic disorders (liver disease, pancreatitis, and diverticulitis). Thus, it is unreliable for distinguishing benign from malignant ovarian masses in premenopausal women.^{1,3}

Current guidelines recommend routine measurement of CA-125 in the initial evaluation of all postmenopausal women with an ovarian mass.^{7,8}

Using a cutoff of 30 IU/mL, CA-125 has a sensitivity of 81% and a specificity of 75% for ovarian malignancy. However, serial measurements may be more useful for assessing ovarian cancer risk, especially in the setting of rapidly rising values.^{1,3}

The Risk for Malignancy Index (RMI), which categorizes a cyst's risk for malignancy, can be calculated based on the patient's menopausal status, ultrasonographic characteristics (1 point each for multilocular cyst, solid area, metastasis, ascites, and bilateral lesions), and serum CA-125 level. The RMI has a sensitivity of 78% and a specificity of 87% for predicting ovarian cancer.⁸

Postmenopausal women with an asymptomatic small cyst (< 5 cm), a normal CA-125 level, and an RMI < 200 can be followed conservatively, with repeat ultrasonography in 4 to 6 months. At that time, if the cyst has not grown and the CA-125 level is normal, expectant management can continue, with reassessment in 4 to 6 months. If imaging remains unchanged and the CA-125 is persistently normal, the patient may be discharged from follow-up.⁸

If at any time during the evaluation the calculated RMI is greater than 200, there is an increased risk for malignancy, and the patient should be referred to a gynecologic oncologist for advanced imaging.

An algorithm from the Royal College of Obstetricians and Gynaecologists for managing ovarian cysts in postmenopausal women is available at www.rcog.org.uk/globalassets/documents/guidelines/green-top-guidelines/gtg_34.pdf.⁸

CURRENT GUIDELINES ON REPEAT IMAGING

The American College of Radiology (ACR) has created a "Choosing Wisely" guideline to clarify when repeat imaging for ovarian cysts is indicated, to reduce both patient anxiety and healthcare costs.⁹ These guidelines highlight the distress women may experience from repeat testing due to concerns about cancer.

The guidelines also note that testing is often done during varying times of the menstrual cycle, thereby detecting new cysts, as opposed to monitoring previously detected cysts. Repeat ultrasonography may lead to surgical interventions that are not evidence-based, such as cystectomy or oophorectomy, in patients without radiologic features of malignancy or associated pelvic pain. And while ultrasonography is less expensive than other imaging tests, unnecessary imaging can mean additional costs to the patient, such as copayments, and possibly large payments for patients without insurance.

The American College of Obstetricians and Gynecologists (ACOG) and the ACR guidelines recommend against unnecessary repeat imaging for ovarian cysts.^{7,10} The ACOG Practice Bulletin on the Evaluation and Management of Adnexal Masses states, "Simple cysts up to 10 cm in diameter on transvaginal ultrasonography performed by experienced ultrasonographers are likely benign and may be safely monitored using repeat imaging without surgical intervention, even in postmenopausal patients."⁷

The ideal frequency for repeat testing is yet to be determined. In postmenopausal women with a simple cyst smaller than 5 cm, ACOG guidelines recommend an interval of 4 to 6 months for initial repeat imaging. ACR guidelines recommend no follow-up imaging for simple cysts smaller than 5 cm detected by high-quality ultrasonography in asymptomatic women of reproductive age or for simple cysts smaller than 1 cm in postmenopausal women.¹⁰

THE CLINICAL BOTTOM LINE

Simple ovarian cysts can develop as part of the normal menstrual cycle, and although they are more common in premenopausal

A postmenopausal woman with an asymptomatic cyst < 5 cm, normal CA-125 level, and RMI < 200 can be followed conservatively with repeat imaging in 4–6 months

women, they have been detected in 1 out of 5 postmenopausal women.⁹ Simple ovarian cysts are typically not cancerous in women of any age. Therefore, most simple ovarian cysts in asymptomatic women either require no follow-up imaging or can be safely monitored with limited repeat ultrasonography for a defined length of time.

Our 54-year-old postmenopausal patient has a simple cyst smaller than 5 cm. Based on current guidelines, the CA-125 level should be

measured, with subsequent calculation of the RMI. Assuming a normal CA-125 and RMI, she should be reassured that the risk of progression to malignancy is extremely low. Repeating ultrasonography 4 to 6 months after the initial imaging is warranted. At that time, if no change in cyst size or composition is detected, ultrasonography can be repeated at 1 year after initial detection. After that, assuming no changes of the cyst on repeat imaging, the patient does not require additional follow-up. ■

REFERENCES

1. van Nagell JR Jr, Miiler RW. Evaluation and management of ultrasonographically detected ovarian tumors in asymptomatic women. *Obstet Gynecol* 2016; 127(5):848–858. doi:10.1097/AOG.0000000000001384
2. Pavlik EJ, Ueland FR, Miller RW, et al. Frequency and disposition of ovarian abnormalities followed with serial transvaginal ultrasonography. *Obstet Gynecol* 2013; 122(2 pt 1):210–217. doi:10.1097/AOG.0b013e318298def5
3. Royal College of Obstetricians and Gynaecologists. Management of suspected ovarian masses in premenopausal women. Green-top guideline 2011; 62:1–14. www.rcog.org.uk/globalassets/documents/guidelines/gtg_62.pdf. Accessed August 16, 2018.
4. Timmerman D, Testa AC, Bourne T, et al. Simple ultrasound-based rules for the diagnosis of ovarian cancer. *Ultrasound Obstet Gynecol* 2008; 31(6):681–690. doi:10.1002/uog.5365
5. Glanc P, Benacerraf B, Bourne T, et al. First international consensus report on adnexal masses: management recommendations. *J Ultrasound Med* 2017; 36(5):849–863. doi:10.1002/jum.14197
6. Greenlee RT, Kessel B, Williams CR, et al. Prevalence, incidence, and natural history of simple ovarian cysts among women > 55 years old in a large cancer screening trial. *Am J Obstet Gynecol* 2010; 202(4):373.e1–e9. doi:10.1016/j.ajog.2009.11.029
7. American College of Obstetricians and Gynecologists' Committee on Practice Bulletins—Gynecology. Practice Bulletin No. 174: Evaluation and Management of Adnexal Masses. *Obstet Gynecol* 2016; 128(5):e210–226. doi:10.1097/AOG.0000000000001768
8. Royal College of Obstetricians and Gynaecologists. The management of ovarian cysts in postmenopausal women. Green-top guideline 2016; 34:1–31. www.rcog.org.uk/globalassets/documents/guidelines/green-top-guidelines/gtg_34.pdf. Accessed August 16, 2018.
9. American College of Radiology Choosing Wisely. Imaging tests for ovarian cysts. When you need an ultrasound—and when you don't. www.choosingwisely.org/wp-content/uploads/2012/09/Choosing-WiselyOvarianCystsACR-ER_Update.pdf. Accessed August 16, 2018.
10. Levine D, Brown DL, Andreotti RF, et al. Management of asymptomatic ovarian and other adnexal cysts imaged at US: Society of Radiologists in Ultrasound Consensus Conference Statement. *Radiology* 2010; 256(3):943–954. doi:10.1148/radiol.10100213

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