

Ovarian Cysts in Post-Menopausal Women: When to Worry



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The unexpected finding of an adnexal mass in a post-menopausal woman creates anxiety for both the patient and her clinician. This anxiety is driven by the fear of ovarian cancer, a disease that remains difficult to diagnosis and difficult to cure. In spite of advances in diagnosis and treatment, > 70% of ovarian cancer cases are discovered at an advanced stage and overall five-year survival rates remain low at 37% to 40%.¹

Until recently, it was thought that post-menopausal ovaries should be non-palpable and should not produce cysts.² However, several recent reviews have challenged this belief.^{3,4} One of these reviews examined 15,106 asymptomatic post-menopausal women. Eighteen per cent of this cohort was found to have a unilocular ovarian cyst of < 10 cm in diameter. Seventy per cent of these cysts resolved spontaneously and the incidence of malignancy was only 0.1%. Thus, the presence of a cyst in of itself does not automatically mandate surgical exploration. Other factors that heighten the suspicion of malignancy that must be taken into account include:

- age,
- serum cancer antigen (CA 125) levels and
- ultrasound features.

Age has an obvious influence on the development of most cancers. Although the lifetime risk of a woman developing ovarian cancer is only 1.5%, the incidence of this disease rises sharply in the perimenopausal period and peaks at age 56 to 60.⁵ The chance of a neoplastic adnexal mass being malignant is only 13% in premenopausal women but jumps to 45% in the post-menopausal age group.⁶

Meet Gale

Gale, 73, presents to her FP for a routine checkup.

Examination

A pelvic exam is done and reveals right adnexal fullness.

A subsequent ultrasound reveals a 6 x 7 x 5 cm right adnexal cyst with one septation.

Her serum cancer antigen (CA 125) level is 45 U/ml

She is concerned because her sister had ovarian cancer at age 76.

Laparotomy

A laparotomy is performed.

Intra-operative pathologic assessment reveals a benign right ovarian cyst (Figure 1)

The surgery is completed with a total abdominal hysterectomy and left salpingo-oophorectomy.

Final pathology reveals a benign serous cystadenoma.



Figure 1. Adnexal mass removed from (73-year-old) post-menopausal woman with CA 125 of 45 U/ml; final pathology benign cystadenoma. Risk of Malignancy Index (RMI) score is 180.



The most commonly-used tumour marker for ovarian cancer is CA 125, a protein expressed by both fetal amniotic and coelomic epithelium. Ovarian epithelium expresses this antigen in the presence of:

- inclusion cysts,
- metaplasia, or
- papillary excrescences.

Age has an obvious influence on the development of most cancers.

FAQ

Who should be referred?

Ovarian cysts are common, while ovarian cancer is rare. Deciding on whom to refer is thus challenging. The RMI combines three factors;

- age,
- CA 125 levels and
- ultrasound features to formulate a sensitive predictor of malignancy.

Patients with a RMI score of > 200 should be referred.



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FAQ

What is the role of CA 125?

CA 125 is notoriously non-specific for diagnosing ovarian cancer. Furthermore, it is only elevated in 50% of patients with early stage disease. Routine use of CA 125 levels for screening should be discouraged. CA 125 measurements are useful for following patients with established disease and in diagnosis when combined with other clinical findings.

Table 1

Differential diagnosis of an elevated CA 125

Cancer causes	Non-cancer causes
Ovarian	Diverticulitis
Endometrial	Uterine fibroids
Colon	Endometriosis
Pancreatic	Benign ovarian cyst
Breast	Tuboovarian abscess
Bladder	Ectopic pregnancy
Liver	Pregnancy
Lung	Menstruation

The upper limit of normal for CA 125 measured in the blood stream is 35 U/ml. The CA 125 has become a useful tool in monitoring response to treatment in patients with ovarian cancer. However, its usefulness as a diagnostic tool is limited because it is only elevated in 50% of patients with early stage disease.⁷ Furthermore, the specificity of the CA 125 is poor. Table 1 provides a list of both cancer and non-cancer causes of an elevated CA 125 level. Methods of improving this marker's usefulness in the diagnoses of ovarian cancer include performing serial measurement in women with an

FAQ

Do all post-menopausal women with ovarian cysts require surgical evaluation?

Traditional thought has been that post-menopausal ovaries shut down and therefore should not produce cysts. However, recent data has found the incidence of ovarian cysts in post-menopausal women to range from 3% to 18% and rates of spontaneous resolution to range from 50% to 70%. The risk of malignancy is < 1% if a cyst is unilocular and < 10 cm in size.

ovarian cyst⁸ and the incorporation of the CA 125 level into malignancy risk indices.⁹ Clinicians should not use CA 125 levels as a screening tool in asymptomatic women who are not at increased risk for ovarian cancer.

Imaging modalities that have been investigated for their potential in diagnosing ovarian cancer include:

- ultrasound,
- CT,
- MRI and
- positron emission tomography (PET) scan.

As a single modality, transvaginal ultrasound performs the best, with a sensitivity, specificity and positive predictive value of 92%, 60% and 24%, respectively.² Features suggestive of ovarian cancer include:

- multilocularity,
- the presence of solid components,
- papillary excrescences and
- increased vascular flow.

It is important to note that the presence of a single papillary formation has been shown to increase the risk of malignancy by a factor of three to six.¹⁰

No single factor has proven to be the solution to diagnosing ovarian cancer. However, a combination of factors can improve the sensitivity and specificity of delineating benign from malignant adnexal masses. One such system is the Relative Malignancy Index

Table 2

Calculating the RMI for adnexal masses¹¹

$$RMI = U/S \times M \times CA\ 125$$

U/S = 1 (for U/S score of 0 or 1), or

U/S = 4 (for U/S score of 2-5)

U/S score: 1 point each for presence of:

- Multilocularity
- Bilaterality
- Solid component(s)
- Ascites
- Evidence of metastases

M = 4 for post-menopausal women

M = 1 for premenopausal women

CA 125 = absolute serum measurement (U/ml)

RMI > 200 = Pre-operation gynecologic oncology referral

U/S: ultrasound

M: menopausal status

(RMI) first designed by Jacobs *et al* (RMI 1) and then revised by Tingulstad *et al* in 1996 (RMI 2).^{9,11} Of the two, the RMI 2 system was found to be the more accurate at diagnosing ovarian cancer. The sensitivity, specificity and positive predictive values of the RMI 2 are 80%, 92% and 80%, respectively.

A combination of factors can improve the sensitivity and specificity of delineating benign from malignant adnexal masses.

Details of the RMI 2 can be found in Table 2. The scoring system takes into account menopausal status, ultrasound features of the adnexal mass and the patient's CA 125 level. A score of four is given if the



Take-home message

1. Ovarian cysts in post-menopausal women are relatively common
2. In post-menopausal women with unilocular cysts < 10 cm in size, the risk of malignancy is < 1%
3. The RMI is sensitive for determining those patients most likely to have a malignant adnexal mass and can guide referral for subspecialty evaluation

The RMI 2 system can help predict which patients may have a malignancy and who may require further evaluation.



Figure 2. 54-year-old post-menopausal woman with large cystic mass and CA125 of 60; final pathology was a high grade serous carcinoma. RMI score was 960.

patient is post-menopausal. Likewise, a score of four is given if the patient has at least two suspicious features on ultrasound. These scores are then multiplied by the patient's CA 125 level. Our 73-year-old patient had a score of $4 \times 1 \times 45 = 180$. Thus, her risk of malignancy was low and conservative management was an option. In contrast, Figure 2 shows a mass from a 54-year-old post-menopausal woman. Ultrasound features included a solid component and septum (score of four). The RMI score was $4 \times 4 \times 60$

for a total of 960. This patient underwent staging surgery and was found to have a stage IA high-grade, serous carcinoma of the ovary.

In summary, ovarian cysts are common in post-menopausal women. Simple cysts that are < 8 mm in diameter are unlikely to be malignant and should be treated conservatively. The RMI 2 system can help predict which patients may have a malignancy and who may require further evaluation.

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