

Asymptomatic Simple Ovarian Cyst in Postmenopausal Women: Syndrome of 'Visible Ovary'

Ivica Zalud, Raydeen Busse, Biserka Funduk Kurjak

ABSTRACT

Simple cysts of the ovary are quite common, with a prevalence of 5 to 17%. Advances in the technology of ultrasound and the increasing frequency of use of TVS has made it all the more important to have knowledge of the natural history of simple asymptomatic postmenopausal cysts. Previously, due to the paucity of data, postmenopausal women with asymptomatic simple cysts were managed much too aggressively. Current available data suggest a more conservative approach with serial ultrasounds, Doppler evaluation and CA-125 levels. Further studies are needed in order to have definitive guidelines for the gynecologic practitioner.

Keywords: Cysts of the ovary, Serial ultrasound, Doppler evaluation, CA-125 levels.

How to cite this article: Zalud I, Busse R, Kurjak BF. Asymptomatic Simple Ovarian Cyst in Postmenopausal Women: Syndrome of 'Visible Ovary'. *Donald School J Ultrasound Obstet Gynecol* 2013;7(2):182-186.

Source of support: Nil

Conflict of interest: None declared

INTRODUCTION

The performance of high-resolution ultrasound in the postmenopausal female is becoming more commonplace in modern medicine. The old adage of the 'postmenopausal palpable ovary syndrome' as described by H Barber et al in 1971¹ requiring surgical management is no longer the sole issue in determining a normal or abnormal postmenopausal ovary. The new adage is 'the visible ovary syndrome' and the issues surrounding the management of these findings.

Ovarian cancer deaths are the leading cause of gynecological malignancy mortality in the United States causing more than 16,000 deaths projected in 2004.² About 1 in every 57 women in the United States will develop ovarian cancer; and most cases occur in women over the age of 50. It is well-known that the overall 5-year survival rate is 39%.³ This lends particular importance to the need to know the natural history and prevalence of simple ovarian cysts in the postmenopausal state and how it relates to ovarian carcinoma, if at all. Our ignorance has led to an aggressive approach when an ovarian cyst is detected. It is also well-known that the majority of ovarian cancers, especially in older women, are diagnosed in the advanced stage and that the survival rate is the highest for stage I disease. This chapter covers the most up-to-date and best evidence on this challenge of the simple ovarian cyst seen in the postmenopausal patient.

NATURAL HISTORY OF THE POSTMENOPAUSAL OVARY

The menopausal ovary gets lighter and smaller as atrophy of the graafian follicles and ova take place. Ultrasound studies looking at the mean normal size of a postmenopausal ovary shows that overall, the size should not exceed $2 \times 3 \times 4$ cm. Ovarian volume studies also done show that normal postmenopausal ovarian volumes range from 2.5 to 4.33 cu mm.⁴

There are a few studies that have looked at the prevalence of simple ovarian cysts in asymptomatic postmenopausal women. The general consensus is 5 to 17% (Table 1).⁵ Wolf et al⁶ performed transabdominal (TAS) and transvaginal sonography (TVS) on 149 unselected, self-referred asymptomatic female volunteers aged 50 years or older who were at least 1 year postmenopausal and had at least one ovary. Unilocular cysts ranged from 0.4 to 4.7 cm in diameter in 22 (14.8%) women. Conway et al⁷ performed TVS on 1769 asymptomatic postmenopausal women and found 116 (6.6%) simple ovarian cysts less than 5 cm in diameter. Andolf and Jorgensen⁸ performed TAS on 534 postmenopausal women and found simple ovarian cysts ranging from 2 to 8 cm in size in 30 (5.6%) of them. Aubert et al⁹ performed TVS on 622 asymptomatic postmenopausal women and found simple unilocular cysts between 1 and 5 cm in diameter in 36 (5.7%). Bailey et al¹⁰ performed TVS on 7705 asymptomatic postmenopausal women and found unilocular ovarian cystic tumors in 256 (3.3%) of them. Of these, 231 (3%) of the cysts were 5 cm or less in diameter, and 25 were 5 to 10 cm in diameter.⁵

Additional circumstances in which asymptomatic postmenopausal women have gynecological ultrasounds are during tamoxifen use and postmenopausal hormone therapy. Kazandi et al¹¹ found that ovarian cysts are a common

Table 1: Prevalence of simple ovarian cysts in asymptomatic postmenopausal women

<i>Authors</i>	<i>Number of women</i>	<i>Number of cysts</i>	<i>Percentage of women with cysts</i>
Wolf et al ⁶	149	22	14.8
Conway et al ⁷	1769	116	6.6
Andolf and Jorgensen ⁸	534	30	5.6
Aubert et al ⁹	622	36	5.7
Bailey et al ¹⁰	7705	256	3.3

finding in postmenopausal breast cancer patients on tamoxifen with an incidence of 13.2% (5/38) and Seoud et al¹² found an incidence of ovarian cysts to be 25% (18/72). In 1997, Bar-Hava et al¹³ found that hormone replacement therapy is associated with a reduced prevalence of ovarian cysts (only) in the early postmenopause.

The natural history of simple ovarian cysts that are followed by serial ultrasounds and possibly other test methods have been described by numerous authors since 1986. Valentin et al¹⁴ followed 134 patients with 160 cysts, 121 (76%) were unilocular and were followed at 3, 6 and 12 months. There was spontaneous resolution in 29% of patients and new cyst formation in 13%. There was no change in 49% and no malignancies detected in any cyst from 3 to 80 mm in diameter. The authors stated that women in whom cysts disappeared or developed were younger and had passed the menopause more recently than those in whom findings remained unchanged. They also stated that the cysts in the older women with more stable ultrasound findings are more likely to have been inclusion cysts or neoplastic cysts.

Bailey et al¹⁰ found unilocular cystic tumors less than 10 cm in diameter (90% less than 5 cm) in 256/7705 (3.3%) of patients and 125 (49%) resolved spontaneously and 131 (51%) persisted. Forty-five of these patients had surgical removal of the tumors and notably, there were no cases of ovarian carcinoma in this group. Kroon and Andolf¹⁵ followed 83 postmenopausal women with small completely anechoic, thin-walled cysts less than 5 cm, 43 underwent surgery and 32 underwent serial observation (8 were lost to follow-up). There were no ovarian cancers identified and 12 out of 32 cysts underwent spontaneous resolution. Levine¹⁶ did a study on 184 asymptomatic postmenopausal women and found 37 simple cysts and of these, 53% resolved spontaneously and out of 6 surgical interventions, there was 1 malignancy in a cyst that developed septations and an abnormal Doppler study.

Modesitt et al¹⁷ followed 15,106 asymptomatic women from 1987 to 2002 who were at least 50 years old. They found 2763 (18%) with 3259 (16.5%) unilocular ovarian cyst less than 10 cm in diameter. 2261 (69.4%) of these cysts resolved spontaneously, 537 (16.5%) developed a septum, 189 (5.8%) developed a solid area, and 220 (6.8%) persisted as an unilocular lesion. During this time, 27 women received a diagnosis of ovarian cancer, and 10 had been previously diagnosed with simple ovarian cysts. All ten of these women, however, developed another morphologic abnormality, experienced resolution of the cyst before developing cancer, or developed cancer in the contralateral ovary. No woman with an isolated unilocular cystic ovarian tumor had developed ovarian cancer in this population. Their

conclusion was that the risk of malignancy in unilocular ovarian cystic tumors less than 10 cm in diameter in women 50 years old or older is extremely low. The majority will resolve spontaneously. Shushan et al¹⁸ in 1996 also noted that ovarian cysts are a common side effect of tamoxifen and most of these cysts disappear after tamoxifen treatment is abandoned. Cohen et al¹⁹ found 9.6% of 322 postmenopausal women with breast carcinoma under treatment with tamoxifen had simple ovarian cysts and that there was a statistically significant decrease in cyst size over long-term follow-up.

PATHOLOGY OF SIMPLE CYSTS

A few studies have looked at the pathology of surgically removed simple ovarian cysts. In the Bailey study of 45 women who underwent oophorectomy, 32 (71%) had benign serous cystadenomas. Additional diagnoses were paratubal and paraovarian cysts, endometriotic cysts, mucinous cystadenomas, hydrosalpinx and peritoneal cyst in descending frequency.¹⁰ Goldstein et al²⁰ had similar results of 28 women who had undergone oophorectomy for simple ovarian cysts; 16 (57%) were serous cysts; and in descending order of frequency, hydrosalpinges, paraovarian cysts, endometriotic cyst and mucinous cyst. Rodriguez et al²¹ reported 3 out of 7 serous inclusion cysts, 2 paraovarian cysts, one mucinous inclusion cyst and one benign epithelial cyst. Conway et al⁷ found 67% of cysts removed from 18 women were benign serous cystadenomas. Hall and McCarthy²² found 10 simple cysts out of 13 postmenopausal cysts ranging in size from 1.5 to 10 cm: 7 were benign serous cysts, one was a hydrosalpinx and four were benign cystadenomas.

A more recent study by Ekerhovd et al²³ compared ultrasonographic and macroscopic appearances of the cysts with histopathologic diagnosis. The results for the postmenopausal population with cysts that were characterized either as echo-free, without solid parts or papillary formations showed 4 of 247 cysts (1.6%) proved to be borderline or malignant.

SONOGRAPHY

Simple cysts that are thin-walled, unilocular, with smooth walls are more likely to be benign than multiloculated cysts (Fig. 1). Most studies excluded cysts that were more than 5 cm in diameter even if they were simple. Findings suggestive for malignancy are: diameter more than 10 cm, multiple septations, thick septae, solid components, papillary projections, bilateralism, ascites/pelvic fluid and neovascularization (Table 2). These findings do not point toward conservative management but strongly point toward surgical exploration.⁵

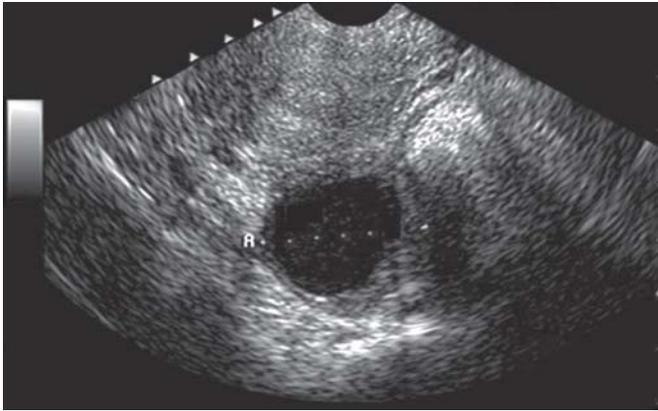


Fig. 1: A small simple cyst in postmenopausal ovary

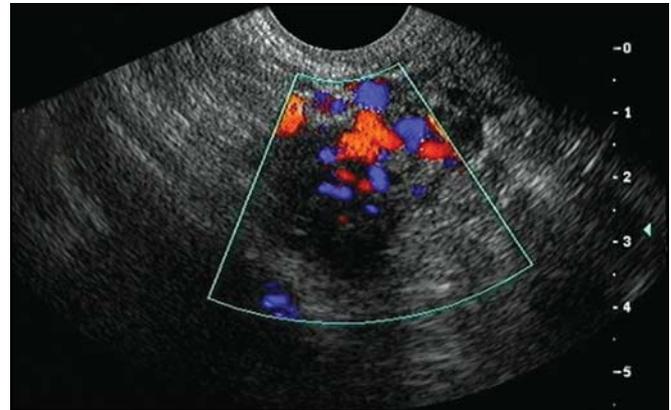


Fig. 2: Highly vascular ovary visualized by color Doppler

Table 2: Sonographic findings suggesting malignancy

- Diameter >10 cm
- Multiple septations
- Thick septae
- Solid components
- Papillary projections
- Bilaterality
- Ascites/pelvic fluid
- Neovascularization
- Doppler resistance index <0.4

Malignant tumors are frequently ‘vascular’ and Doppler waveform analysis can separate high vs low resistance vessels (Figs 2 and 3). Low resistance vessels tend to be new vessels; and new growth creates new vessels for nourishment. It is also known that solid tumors cannot grow more than 2 to 3 mm in diameter without neovascularization.²⁴ Color and pulsed Doppler sonography can reveal the vascularity of an adnexal mass; thus, it may help in determining which cysts are more likely to be malignant. Malignant neoplasms often have bizarre architecture and are often associated with a low-resistance, high-flow picture. Benign tumors usually have normal flow patterns, demonstrating a high-resistance type of flow.

Kurjak et al²⁵ examined 680 pre- and postmenopausal women with ovarian neoplasms and obtained a sensitivity of 96% and a specificity of 99% for distinguishing between benign and malignant neoplasms when using a cutoff of 0.40 for the resistance index for benign tumors. Conway’s study⁷ evaluated 116 simple cysts by TVS. There were no malignancies, and all of the cysts exhibited normal or undetectable blood flow. Other investigators have questioned the role of Doppler in differentiating between benign and malignant masses due to the significant overlap between Doppler values for benign vs malignant cysts. It is clear that Doppler analysis cannot be used as the sole measure of a growth’s malignant potential. The role of Doppler, especially in light of 3D power Doppler imaging

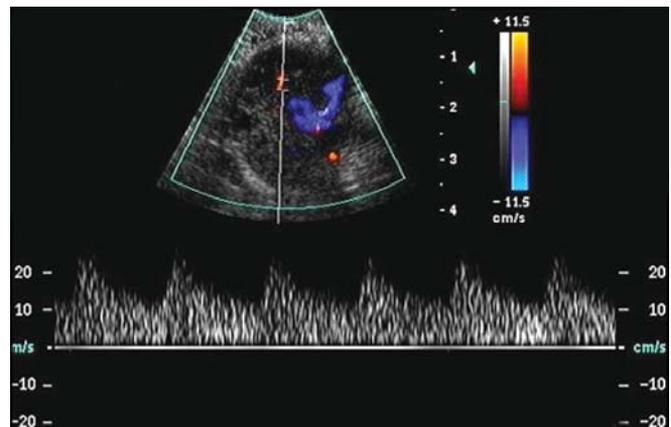


Fig. 3: Color and pulsed Doppler of ovarian blood flow

and tumor angiogenesis is intriguing and the future may hold more vascular parameters to analyze.

ROLE OF CA-125

Many investigators have incorporated the level of CA-125 in their ‘scoring’ of a woman’s risk of having an ovarian carcinoma when evaluating a postmenopausal woman with a simple ovarian cyst. CA-125 is a nonspecific tumor marker that has been shown to be elevated in 80 to 90% of women with epithelial serous ovarian tumors. It can be elevated in many gynecologic as well as nongynecologic medical conditions. When used in conjunction with an abnormal sonographic finding, this nonspecific test can raise the suspicion for an ovarian malignancy. Auslender et al²⁶ followed 34 postmenopausal women with CA-125 levels and vaginal ultrasound with simple ovarian cysts. The cysts measured less than 5 cm in diameter and there were no cases of malignancy found. The CA-125 levels were all normal in these cases. Other investigators have found the combination of transvaginal ultrasound and CA-125 useful in helping to distinguish between low- and high-risk adnexal masses.

MANAGEMENT

Now that it is understood and accepted that simple postmenopausal ovarian cysts, especially if they are less than 5 cm and have a normal CA-125 in an asymptomatic woman are nearly always benign, the next logical question deals with management. Again, the old adage of the palpable ovarian syndrome being a strong case for surgical removal and exploration begs updating. Conway et al⁷ showed that of the 1,769 postmenopausal patients that had persistent simple ovarian cysts (116 or 59.5%), 26% were surgically managed and 74% were expectantly managed; 67% of those managed surgically were done laparoscopically and 33% had total abdominal hysterectomies with bilateral salpingo-oophorectomies. Again, the most common pathology diagnosis was serous cystadenoma. There were no ovarian malignancies. Their conclusion was that with their findings and additional support from the literature, simple ovarian cysts, less than 5 cm in postmenopausal patients are very unlikely to be malignant and are capable of being followed conservatively. In their study, a large number of surgical candidates (by previous standards) had spontaneous resolution and thus no surgical intervention was needed. Furthermore, they concluded that for those opting for surgical intervention, the information presented illustrates a role for laparoscopic approach. Of those followed expectantly, the recommendation is for ultrasound every 3 to 6 months for up to 2 years with CA-125 measurements. Patient compliance and having a scan performed by an experienced sonographer are crucial. The indications for surgical (preferably laparoscopically) removal of the ovary are as follows: increasing size, development of solid components, abnormal Doppler flow, CA-125 elevation and noncompliance with follow-up.

Auslender's study from the prior section²⁶ supports the conservative management of small, simple cysts in the postmenopausal woman with repeat ultrasounds and CA-125. Kroon et al¹⁵ in his 1995 study concluded that nonpalpable ovarian cysts commonly detected by ultrasound in asymptomatic women have a low-risk for malignancy. They recommended ultrasound follow-up of stationary lesions and that surgery can be confined to symptomatic cases of those with a family history of ovarian, breast or colon cancer.

CONCLUSION

Simple cysts of the ovary are quite common, with a prevalence of 5 to 17%. Advances in the technology of ultrasound and the increasing frequency of use of TVS has made it all the more important to have knowledge of the natural history of simple asymptomatic postmenopausal

cysts. This knowledge impacts not only upon the management protocols and cost-analyses; but also has psychosocial impact and health implications on the patient, especially if managed surgically. Previously, due to the paucity of data, postmenopausal women with asymptomatic simple cysts were managed much too aggressively. Current available data now suggest a more conservative approach with serial ultrasounds, Doppler evaluation and CA-125 levels. Further studies are needed in order to have definitive guidelines for the gynecologic practitioner.

REFERENCES

1. Barber HRK, Graber EA. The PMPO syndrome. *Obstet Gynecol* 1971; 38:921-23.
2. American Cancer Society Reference information 2004: <http://www.cancer.org/downloads/STT/CAFF2003PWSecured.pdf>
3. Young RC, Walton LA, Ellenberg SS, Homesley HD, Wilbanks GD, Decker DG. Adjuvant therapy in stage I and II epithelial ovarian cancer. Results of two prospective randomized trials. *N Engl J Med* 1990;322:1021-27.
4. Ujevic B, Funduk-Kurjak B, Kurjak A. Ultrasound in the postmenopause. In Kurjak A, Chervenak F (Eds): *Donald School Textbook of Ultrasound in Obstetrics and Gynecology*. New Delhi: Jaypee Brothers Medical Publishers (P) Ltd 2003; 726-46.
5. Oyelese Y, Kueck A, Barter J, Zalud I. Asymptomatic postmenopausal simple ovarian cyst. *Obstet Gynecol Surv* 2002;57(12):803-09.
6. Wolf SI, Gosink BB, Feldesman MR, Lin MC, Stuenkel CA, Braly PS, Pretorius DH. Prevalence of simple adnexal cysts in postmenopausal women. *Radiology* 1991;180:65-71.
7. Conway C, Zalud I, Dilena M, Maulik D, Schulman H, Haley J et al. Simple cyst in the postmenopausal patient: Detection and management. *J Ultrasound Med* 1998;17:369-72.
8. Andolf JM, Jorgensen C. Simple adnexal cysts diagnosed by ultrasound in postmenopausal women. *J Clin Ultrasound* 1988;16:301-03.
9. Aubert JM, Rombaut C, Argacha P, Romero F, Leira J, Gomez-Bolea F. Simple adnexal cysts in postmenopausal women: Conservative management. *Maturitas* 1998;30:51-54.
10. Bailey CL, Ueland FR, Land GL, DePriest PD, Gallion HH, Kryscio RJ, et al. The malignant potential of small cystic ovarian tumors in women over 50 years of age. *Gynecol Oncol* 1998;69:3-7.
11. Kazandi M, Sendag F, Akercan F, Terek MC, Ozsaran A, Dikmen Y. Ovarian cysts in postmenopausal tamoxifen-treated breast cancer patients with endometrial thickening detected by transvaginal sonography. *Eur J Gynaecol Oncol* 2002;23: 257-60.
12. Seoud M, El-saghir N, Salem Z, Shamseddine A, Awwad J, Medawar W, Khalil A. Tamoxifen and ovarian cysts: A prospective study. *Eur J Obstet Gynecol Reprod Biol* 2001;100:77-80.
13. Bar-Hava I, Orvieto R, Vardimon D, Manor Y, Weissman A, Nelinger R, et al. Ovarian cysts and cyclic hormone replacement therapy: Is there an association? *Acta Obstet Gynecol Scand* 1997;76:563-66.

14. Valentin L, Akrawi D. The natural history of adnexal cysts incidentally detected at transvaginal ultrasound examination in postmenopausal women. *Ultrasound Obstet Gynecol* 2002;20:174-80.
15. Kroon E, Andolf E. Diagnosis and follow-up of simple ovarian cysts detected by ultrasound in postmenopausal women. *Obstet Gynecol* 1996;85:211-14.
16. Levine D, Gosink BB, Wolf SI, Feldesman MR, Pretorius DH. Simple adnexal cysts: The natural history in postmenopausal women. *Radiology* 1992;184:653-59.
17. Modesitt SC, Pavlik EJ, Ueland FR, DePriest PD, Kryscio RJ, van Nagell JR Jr. Risk of malignancy in unilocular ovarian cystic tumors less than 10 centimeters in diameter. *Obstet Gynecol* 2003;102(3):594-99.
18. Shushan A, Peretz T, Uziely B, Lewin A, Mor-Yosef S. Ovarian cysts in premenopausal and postmenopausal tamoxifen-treated women with breast cancer. *Am J Obstet Gynecol* 1996;175:141-44.
19. Cohen I, Potlog-Nahari C, Shapira J, Yigael D, Tepper R. Simple ovarian cysts in postmenopausal patients with breast carcinoma treated with tamoxifen: Long-term follow-up. *Radiology* 2003;227(3):844-48.
20. Goldstein SR, Subramanyam B, Snyder JR, Beller U, Raghavendra BN, Beckman EM. The postmenopausal cystic adnexal mass: The potential role of ultrasound in conservative management. *Obstet Gynecol* 1989;73:8-10.
21. Rodriguez MH, Platt LD, Medearis AL, Lacarra M, Lobo RA. The use of transvaginal sonography for evaluation of postmenopausal ovarian size and morphology. *Am J Obstet Gynecol* 1988;159(5):810-14.
22. Hall DA, McCarthy KA. The significance of the postmenopausal simple adnexal cyst. *J Ultrasound Med* 1986;5(9):503-05.
23. Ekerhovd E, Wienerroith H, Staudach A, Granberg S. Preoperative assessment of unilocular adnexal cysts by transvaginal ultrasonography: A comparison between ultrasonographic morphologic imaging and histopathologic diagnosis. *Am J Obstet Gynecol* 2001;184(2): 48-54.
24. Folkman J. A novel antivascular therapy for cancer. *Cancer Biol Ther* 2004;3(3):338-39.
25. Kurjak A, Zalud I, Alfirevic Z. Evaluation of adnexal masses with transvaginal color ultrasound. *J Ultrasound Med* 1991;10:295-97.
26. Auslender R, Atlas I, Lissak A, Bornstein J, Atad J, Abramovici H. Follow-up of small, postmenopausal ovarian cysts using vaginal ultrasound and CA-125 antigen. *J Clin Ultrasound* 1997;24:175-78.

ABOUT THE AUTHORS

Ivica Zalud (Corresponding Author)

Professor and Acting Chair, Department of Obstetrics and Gynecology and Women's Health, John A Burns School of Medicine, University of Hawaii, USA, e-mail: ivica.zalud@gmail.com

Raydeen Busse

Assistant Professor, Department of Obstetrics and Gynecology and Women's Health, John A Burns School of Medicine, University of Hawaii, USA

Biserka Funduk Kurjak

Professor, Department of Obstetrics and Gynecology, Dubrovnik International University, Croatia