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.


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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 1971 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. 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%. 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>
<thead>
<tr>
<th>Authors</th>
<th>Number of women</th>
<th>Number of cysts</th>
<th>Percentage of women with cysts</th>
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<tbody>
<tr>
<td>Wolf et al6</td>
<td>149</td>
<td>22</td>
<td>14.8</td>
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<tr>
<td>Conway et al7</td>
<td>1769</td>
<td>116</td>
<td>6.6</td>
</tr>
<tr>
<td>Andolf and Jorgensen8</td>
<td>534</td>
<td>30</td>
<td>5.6</td>
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<tr>
<td>Aubert et al9</td>
<td>622</td>
<td>36</td>
<td>5.7</td>
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<tr>
<td>Bailey et al10</td>
<td>7705</td>
<td>256</td>
<td>3.3</td>
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Table 1: Prevalence of simple ovarian cysts in asymptomatic postmenopausal women
finding in postmenopausal breast cancer patients on
tamoxifen with an incidence of 13.2% (5/38) and Seoud et
al\textsuperscript{12} found an incidence of ovarian cysts to be 25% (18/72).
In 1997, Bar-Hava et al\textsuperscript{13} 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 al\textsuperscript{14} 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 al\textsuperscript{10} 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 Andolf\textsuperscript{15}
followed 83 postmenopausal women with small completely
unilocular 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.
Levine\textsuperscript{16} 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.

Moses\textsuperscript{17} 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 al\textsuperscript{18} 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 al\textsuperscript{19} 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.\textsuperscript{10} Goldstein et al\textsuperscript{20} 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,
diabetic cyst and mucinous cyst. Rodriguez et al\textsuperscript{21}
reported 3 out of 7 serous inclusion cysts, 2 paraovarian
cysts, one mucinous inclusion cyst and one benign epithelial
cyst. Conway et al\textsuperscript{7} found 67% of cysts removed from 18
women were benign serous cystadenomas. Hall and
McCarthy\textsuperscript{22} 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 al\textsuperscript{23} 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.\textsuperscript{5}
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. 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 al\(^2\) 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 study\(^7\) 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 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 al\(^2\) 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.

<table>
<thead>
<tr>
<th>Table 2: Sonographic findings suggesting malignancy</th>
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<tr>
<td>• Diameter &gt;10 cm</td>
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<tr>
<td>• Multiple septations</td>
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<tr>
<td>• Thick septae</td>
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<tr>
<td>• Solid components</td>
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<tr>
<td>• Papillary projections</td>
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<tr>
<td>• Bilaterality</td>
</tr>
<tr>
<td>• Ascites/pelvic fluid</td>
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<tr>
<td>• Neovascularization</td>
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<td>• Doppler resistance index &lt;0.4</td>
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Fig. 1: A small simple cyst in postmenopausal ovary

Fig. 2: Highly vascular ovary visualized by color Doppler

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


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