Volumes of Normal Ovaries, Ovaries with Benign Lesions, and Ovaries with Cancer in Menopausal Women: Is There an Optimal Cut-off Value to Predict Malignancy?

Rami Aviram, MD,[1,3] Gilad Gassner, MD,[2] Ofer Markovitch, MD,[1,3] Ilan Cohen, MD,[2,3] Ami Fishman, MD,[2,3] Ronnie Tepper, MD[1,3]

[1]Ultrasound Unit, Meir Medical Center, 59 Tchernichovski Street, Kfar Saba, Israel 44281
[2]Department of Obstetrics and Gynecology, Meir Medical Center, 59 Tchernichovski Street, Kfar Saba, Israel 44281
[3]Sackler School of Medicine, Tel Aviv University, Ramat Aviv, Tel Aviv Israel 69978

Received 3 September 2006; accepted 29 June 2007

ABSTRACT: *Purpose:* To evaluate different ovarian volume cut-off values to distinguish between normal ovaries, benign lesions, and malignant lesions in menopausal women.

Methods: Transvaginal sonographic ovarian volume measurements were performed in 362 menopausal patients prior to gynecologic surgery. Based on the histopathologic results, a total of 466 ovaries were divided into 3 groups: normal ovary, benign lesion, and malignant tumor. Different ovarian volume cut-off values were analyzed via receiver operating characteristic curves to determine the optimal cut-off value.

Results: The mean ovarian volumes in the normal ovary, benign lesion, and malignant tumor groups were 3.4 $\pm$ 2.2 cm^3 (range, 0.6–9.6 cm^3), 102 $\pm$ 308 cm^3 (range, 0.3–3543 cm^3), and 368 $\pm$ 1176 cm^3 (range, 8.1–9908) cm^3, respectively. Cut-off values of 8 cm^3 and 10 cm^3 to distinguish between malignant and nonmalignant lesions had a sensitivity of 100% and 97% and a specificity of 39% and 45%, respectively.

Conclusion: In menopausal patients, any ovary with a volume >8 cm^3 can potentially harbor a cancer. © 2007 Wiley Periodicals, Inc. *J Clin Ultrasound* **36**:1–5, 2008; Published online in Wiley InterScience (www.interscience.wiley.com). DOI: 10.1002/jcu.20416

Keywords: ovary; normal volume menopause; benign ovarian lesions; cancer

The high mortality rates of ovarian cancer are attributed to diagnosis at an advanced stage. One of the factors contributing to this situation is the lack of an effective screening test that can enable early-stage diagnosis of ovarian cancer.

Transvaginal sonography is a reliable method for examining ovarian structure and determining its volume; however, its value as a screening tool has been questioned even in women with an increased risk for ovarian cancer.[1–3] Enlarged ovaries are measured either by their largest diameter or by their volume.[4] In menopausal women, there are several reference ranges for normal ovarian volume.[4–8] The reliability of reference ovarian volume cut-off values is of particular importance with regard to clinical decisions. Ovarian volume >10 cm^3 in menopausal women, with or without changes in ovarian texture, is generally considered to be an abnormal finding.[4,5] Abnormal sonographic findings in ovaries <10 cm^3 also require further evaluation. The purpose of this study was to evaluate several ovarian volume cut-off values, regardless of sonographic texture, to distinguish between normal ovaries, benign lesions, and ovarian cancer in a group of menopausal patients prior to gynecologic surgery by searching for an optimal cut-off value for the prediction of ovarian cancer.

PATIENTS AND METHODS

Three hundred sixty-two menopausal patients underwent sonographic examination of the pelvis prior to scheduled gynecologic surgery. Most patients had undergone transvaginal sonographic

Correspondence to: R. Aviram

TABLE 1
Distribution of 77 Normal Ovaries, 316 Ovaries with Benign Lesions, and 73 Ovaries with Cancer by Volume with Different Ovarian Volume Cut-off Values

Ovarian Volume Cut-off Value (cm^3)	Normal Ovaries (n = 77)	Benign Lesions (n = 316)	Ovarian Cancers (n = 73)	Total
>8	4 (5%)	234 (74%)	73 (100%)	311
>10	0	222 (70%)	71 (97%)	293
>12	0	204 (65%)	69 (94%	273
>14	0	194 (61%)	66 (90%)	260

(TVUS) examination previously for measurement of ovarian volumes. In patients with large pelvic masses, transabdominal sonography was used to obtain the measurements. The indications for surgery were ovarian or uterine tumors. The examinations were performed with an Aloka SSD-680 (Aloka, Tokyo Japan), Acuson 128 XP (Siemens Ultrasound, Mountain View, CA), or HDI 5000 (Philips Ultrasound, Bothell, WA) scanner 1 to 5 days before surgery. The ovaries were measured in 3 planes, and ovarian volume was calculated using the ellipsoid formula V = D1 × D2 × D3 × 0.523, where D1, D2, and D3 are the 3 longest longitudinal, antero-posterior, and transverse diameters, respectively. Surgery was performed via laparoscopy or exploratory laparotomy. The ovarian surgical specimens were classified histologically as normal ovary, benign lesion, or malignant tumor. One comparison of the mean ovarian volumes of these groups and another comparison between the volumes of the purely solid malignant and benign tumors were made using the Mann-Whitney *U* test. Receiver operating characteristic (ROC) curves were measured to evaluate the sensitivity and specificity of different ovarian cut-off volumes (8, 10, 12, and 14 cm^3) in distinguishing between normal ovaries, benign lesions, and ovarian cancer.

RESULTS

From the 362 patients, a total of 466 ovaries were resected and examined histopathologically. Of these, 73 (16%) were involved with cancer, 316 (67%) had benign lesions, and 77 (17%) ovaries were normal. All the normal ovaries had solid appearance without a cystic component. In the group with benign lesions, 81 were described sonographically as cystic, 90 were solid, and 145 showed complex findings. In the ovarian cancer group, 17 lesions were described as being solid and 56 showed complex findings; 71 (97%) were >10 cm^3 and 2 (3%) were 8–10 cm^3 in volume. These latter 2 tumors represented 1 case of endometrioid carcinoma and 1 case of lipid cell tumor,

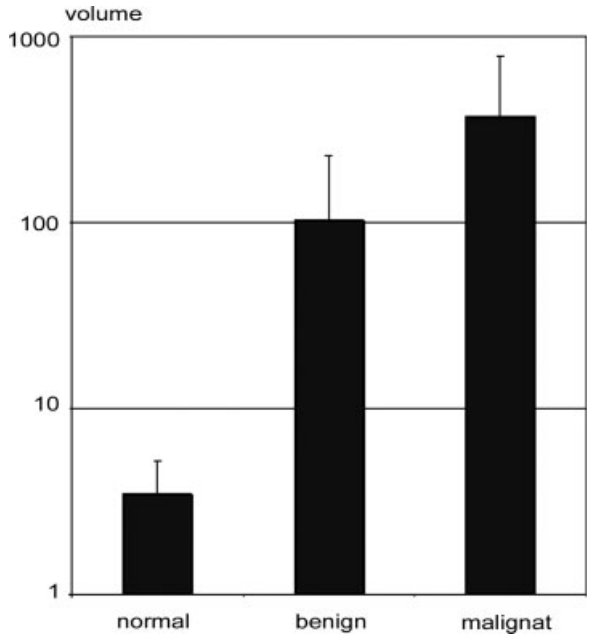

FIGURE 1. Mean ovarian volumes and standard deviations of normal ovaries, ovaries with benign lesions, and ovaries with cancer.

a neoplasm composed entirely of cells resembling typical steroid hormone-secreting cells. In the group of histopathologically normal ovaries, all 77 ovaries were <10 cm^3, but 4 (5%) were 8–10 cm^3. In the group with benign lesions, 222 (70%) were >10 cm^3, 12 (4%) were 8–10 cm^3, and 82 (26%) were <8 cm^3 (Table 1).The mean ovarian volume of the normal ovary group was 3.4 ± 2.2 cm^3 (range 0.6–9.6 cm^3) and was significantly lower than that of the other 2 groups ($p < 0.01$). The mean ovarian volume of the ovarian cancer group was 368 ± 1176 cm^3 (range, 8.1–9908 cm^3) and was significantly different from that of the benign pathology group ($p < 0.01$) (Figure 1). Ninety of the 316 benign tumors (28%) and 17 of the 73 malignant tumors (23%) were purely solid. The mean ± SD ovarian volumes of the benign and malignant solid tumors were 80 ± 210 cm^3 and 227 ± 262 cm^3, respectively, and the difference was statistically significant ($p < 0.01$). The mean ± SD ovarian volume of the benign pathology group was 102 ± 308 cm^3 (range 0.3–3543 cm^3) and was significantly different from that of the normal ovary group ($p < 0.01$). The type of benign lesions, including those smaller than 8 cm^3, are listed in Table 2. The various types of ovarian cancer are listed in Table 3.

The areas under the ROC curves that distinguished normal ovaries from ovaries with cancer (Figure 2a), and normal ovaries from ovaries with benign lesions and ovaries with cancer (Figure 2b) were 0.999 and 0.914, respectively. An ovarian volume cut-off value of 8 cm^3 distin-

TABLE 2
Pathologic Diagnosis of 316 Benign Ovarian Lesions

Pathologic Diagnosis	Total Number	Benign Lesions <8 cm^3
Simple cysts	83	26
Serous cysts/serous/mucinous cystadenoma	91	23
Serous adenofibroma	6	—
Hyperplasia	25	16
Fibroma/thecoma/adenofibroma	65	7
Dermoid cyst	36	7
Struma ovarii	4	—
Endometrioma/endometriosis	2	2
Hemangioma	1	1
Other	—	—
Total	316	82

TABLE 3
Pathologic Diagnosis of 73 Malignant Ovarian Masses

Pathologic Diagnosis	Total Number
Papillary cystadenocarcinoma	40
Brenner tumor	7
Endometrioid carcinoma	6
Metastatic carcinoma	6
Granulosa cell tumor	5
Mucinous cystadenocarcinoma	2
Intestinal adenocarcinoma	1
Lipid cell tumor	1
Carcinosarcoma	1
Mesodermal mixed tumor	1
Sex cord stromal tumor	1
Other	2
Total	73

guished a normal ovary from an ovary with cancer, with a sensitivity of 100% and a specificity of 95%. Using the cut-off value of 10 cm^3 decreased the sensitivity to 97% and increased the specificity to 100%. A cut-off value of 8 cm^3 distinguished a normal ovary from the combined group of benign lesions and ovarian cancer with a sensitivity of 80% and a specificity of 95%, whereas the cut-off value of 10 cm^3 decreased the sensitivity to 74% and increased the specificity to 100%.

The area under the ROC curve which distinguished ovarian cancer from benign lesions was 0.75 (Figure 2c). Ovarian volume cut-offs of 8 cm^3 and 10 cm^3 distinguished cancer from benign lesions with a sensitivity of 100% and 97%, respectively, and a specificity of 25% and 31%, respectively. When ovarian volume cut-offs of 12 cm^3 and 14 cm^3 were used, the sensitivity decreased to 94% and 89% and the specificity increased to 35% and 39%, respectively.

The area under the ROC curve that distinguished ovaries with cancer from normal ovaries and ovaries with benign lesions was 0.799 (Figure 2d). Ovarian volume cut-offs of 8 cm^3 and 10 cm^3 distinguished cancer from benign lesions and normal ovaries with a sensitivity of 100% and 97% and a specificity of 39% and 45%, respectively.

DISCUSSION

The early detection of ovarian cancer is often based on sonography, especially in obese patients. Sonographic detection of ovarian pathology, particularly in menopausal patients, is possible when there is a recognized ovarian volumetric or morphologic change. The morphologic changes include cystic and complex findings in an enlarged ovary. An enlarged ovary in menopause (ovarian volume >10 cm^3) is generally considered to be an abnormal finding, regardless of the ovarian morphology.[5]

Whereas cystic and complex sonographic findings in enlarged ovaries in menopausal patients are suspicious for neoplasms, size criteria are especially valuable in the differentiation between solid benign and solid malignant ovarian tumors.

An excellent correlation has been reported between ovarian volumes of normal and abnormal ovaries determined sonographically in postmenopausal patients, and those obtained via direct measurement during surgery.[9] Ovarian volumes are routinely calculated on 2-dimensional sonograms using the ellipsoid volume formula.[10] Several reference values for ovarian volumes in menopausal patients have been published in the last 25 years, including ovarian volumes with an upper limit of 8 cm^3 or 10 cm^3 or those in the 96th percentile.[3–8] Several authors have demonstrated a gradual reduction in ovarian volume with increasing age.[11–13] Tepper et al[12] noted a gradual decline in ovarian volume during the postmenopausal years from 8.6 $\pm$ 2.3 cm^3 in the first postmenopausal year to 2.2 $\pm$ 1.4 cm^3 15 years after menopause and recommended different cut-off points for abnormal ovarian volumes in correlation with the patient's age. Zalel et al[14] examined the deviation of abnormal postmenopausal ovarian volume from an ovarian volume nomogram. In their report, the calculated sonographic ovarian volumes of 85 ovarian tumors in patients who were scheduled for an exploratory laparotomy ranged from 98 cm^3 to 161 cm^3. In 21 of these patients with ovarian malignancy, the ovarian volumes ranged from 23.2 to 903.7 cm^3 compared with 2.2 to 8.6 cm^3 in healthy women. A deviation of more than 2 standard deviations from the average ovarian volume was found in 100% of the women diagnosed with malignant ovarian tumors and in 86% of the women with benign lesions.

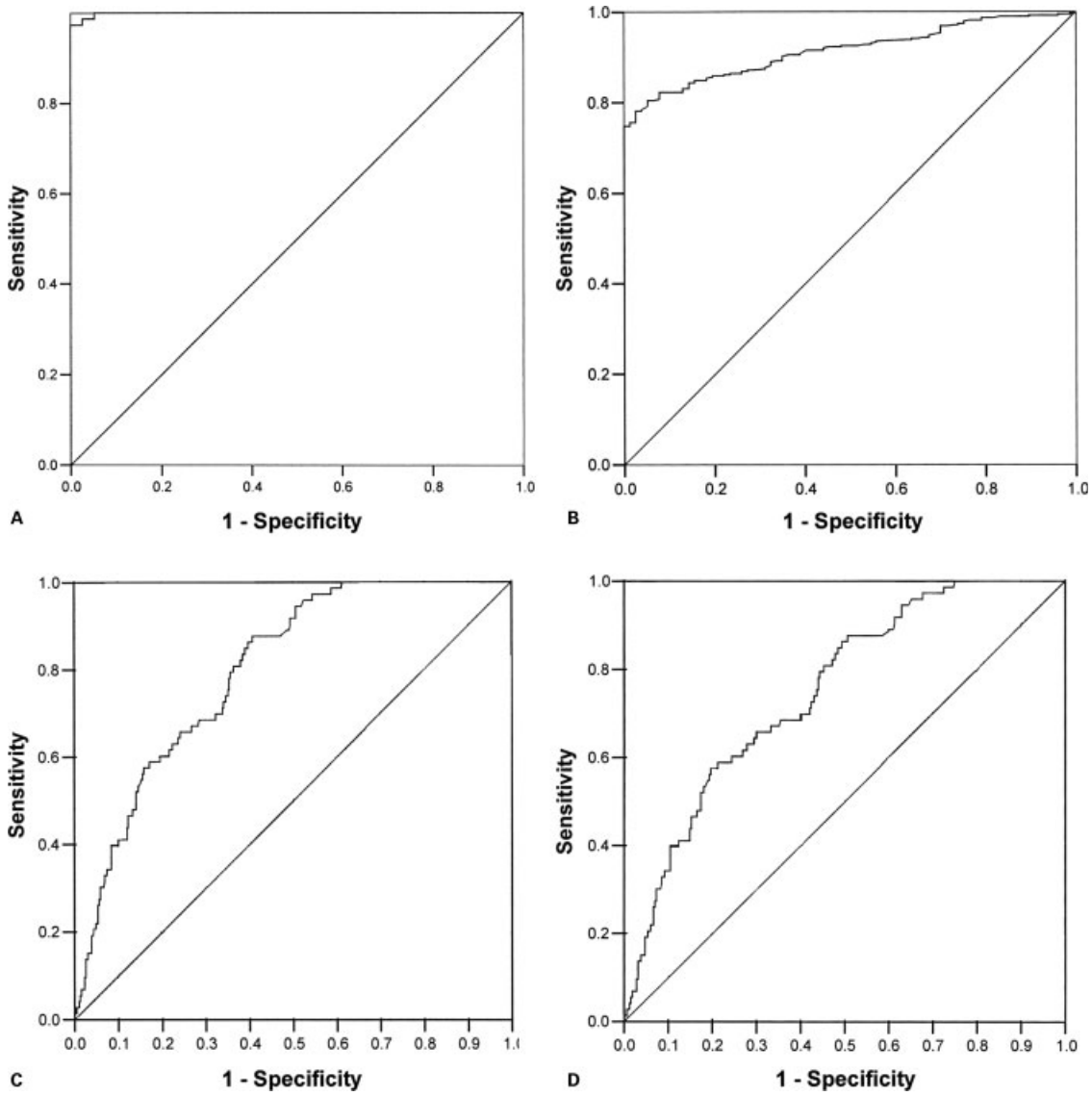

FIGURE 2. Diagnostic value of ovarian volume measurement in distinguishing between different groups of ovaries. ROC curves represent the relative trade-offs between the true positive (sensitivity) and false positive (1-specificity) results for every possible cut-off. When the area under the ROC curve is close to 1, as in Figure 2A, the test is considered excellent. The test is very good in Figure 2B and is good in Figures 2C and 2D. **(A)** Normal ovaries versus ovaries with cancer. **(B)** Normal ovaries versus ovaries with benign lesions and ovaries with cancer. **(C)** Ovaries with cancer versus ovaries with benign lesions. **(D)** Ovaries with cancer versus normal ovaries and ovaries with benign lesions.

In our study, several ovarian volume cut-off values were considered in a series of menopausal patients scheduled for gynecologic surgery. These cut-off values were 8, 10, 12, and 14 cm^3. Ovarian volume of <8 cm^3 has a 100% negative predictive value and allows the ruling out of ovarian cancer in postmenopausal women as demonstrated by the area under the ROC curves (Figure 2a and 2b). A volume of >10 cm^3 would not include any normal ovaries but would have excluded 2 rare ovarian small-size malignancies that could potentially have been missed. A decrease of the cut-off value to 8 cm^3 included all ovarian malignancies; however, it also included a few normal ovaries. The mean volumes in the groups of benign ovarian lesions and of ovarian cancer differed significantly. More importantly, a significant difference was found between the mean volumes of the purely solid benign ovarian lesions and the ovarian cancers. Nevertheless, a significant cut-off value that distinguishes between benign lesion and ovarian cancer could not be reached because of the wide overlap between these entities, resulting in low specificity.

We conclude that there is no optimal ovarian volume cut-off for the prediction of ovarian cancer and that any enlarged ovary (>8 cm^3) can potentially harbor a cancer.

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