

Postmenopausal palpable ovary and ovarian cancer

M. Gojnić^{1,2}, M. Branković³, M. Maksimović^{1,2}, B. Parapid¹, V. Dugalić¹, K. Jeremić¹, B. Gutić²

¹School of Medicine, University of Belgrade, ²Clinical Center of Serbia, ³Clinical Centre Bezanijska Kosa, Belgrade (Serbia)

Summary

Introduction: Ultrasound (US) examination is a much more reliable method for evaluation of potential ovarian cancer risk than gynecologic palpation. The aim of our study was to analyze the US characteristics of patients with palpable ovaries in light of potential for malignancy. **Patients and Methods:** We analyzed 70 women ten years after menopause without increased CA 125 values. They underwent clinical and US exams (abdominal and transvaginal ultrasound), with special emphasis on US Doppler exam. **Results:** Bimanual gynecological examination showed palpable ovaries in 14 patients (palpable ovary group), and the remaining 56 patients were defined as the control group. US showed increased dimensions of palpable ovaries. Atypical follicular activity, deviation from verticalization, atypical ovaries and hyperechogenic punctations classified under germ cell cysts occurred statistically significantly more often in the palpable ovary group. Doppler flow showed pathological vascularization in five patients with palpable ovaries and the estrogen level was increased. After four to six months in these five patients we found a mild increase of estrogen levels and higher Doppler abnormality. Six months later, two patients had irregular bleeding and underwent surgical treatment. **Conclusion:** Every adnexal mass after menopause demands special attention. Bimanual gynecological exams should be used liberally. It is necessary to follow the dimensions of the ovary, describe the echostructure, as well as the edges of the ovary and other anatomical structures. Doppler flow measurement and estrogen levels are predictive and give more information. Controls should be in three to six month intervals in order to make a decision for surgical treatment.

Key words: Ovarian cysts; Postmenopause; Palpable ovary.

Introduction

Ovarian cancer is the fifth leading cause of death from cancer in women and the leading cause of death from gynecological cancer in the USA. Eighty percent of these patients are women older than 50 years, mostly postmenopausal [1].

The etiology of ovarian cancer is poorly understood. Possible factors are age at ovulation, total lifetime number of ovulatory cycles, gonadotropin and androgen stimulation of the ovary, pelvic contaminants and carcinogens, nulliparity and refractory infertility. Familial history of the disease is present in 5-10% cases, with mutations in the BRCA1 and BRCA2 tumor suppressor genes. Protective factors include multiparity, oral contraceptives, and tubal ligation or hysterectomy [2].

The nature of ovarian cancer is still unexplored. It is considered that there is no preinvasive phase. Early symptoms of ovarian cancer are often mild, making this disease difficult to detect. Some early symptoms may include an unusual feeling of fullness or discomfort in the pelvic region, unexplainable indigestion, and gas or bloating that is not relieved with over-the-counter remedies. Progression is very fast (50-150 days).

Stage at diagnosis, maximum residual disease following cytoreductive surgery, and performance status are the major prognostic factors [2].

Diagnosis of ovarian cancer starts with a physical examination, a tumor marker test, and transvaginal ultra-

sound (TVS). The diagnosis must be confirmed with surgery to inspect the abdominal cavity, biopsies, and search for cancer cells in the abdominal fluid [3].

Knowledge about menopausal changes is very important. Palpable ovaries in postmenopausal women should be the possible parameter for ovarian malignancy [4].

Since the ultrasound (US) examination is the main diagnostic method to describe adnexal changes, it is considered a much more reliable method for evaluation of the ovaries than gynecologic palpation [5]. Technological development, ability to perform Doppler flow, and finding the indefinite extraovarian cystic entities enable easy, non-invasive direct and indirect parameters of possible ovarian changes.

Normal postmenopausal ovaries are difficult to visualize sonographically [1]. Visualization of both ovaries should be > 90%. Sonographic characteristics of normal ovaries after menopause are: average volume 1.3-3.0 cm (at this point they are rarely palpable), no follicular activity, atypical ovaries, verticalization tendency, surface hyperechogenic punctations and calcified psammoma bodies in germinative occlusion cysts. However color-flow Doppler is most useful, indicating the presence or absence of blood flow [1].

The sensitivity of bimanual gynecological examination is 30% [5]. About 65-75% ovarian cancers are first recognized in Stage III and IV. There is also a problem of false-positive results, so 5-10% of women undergo surgery for an adnexal mass [1].

The aim of the study was to analyze the US characteristics of patients with palpable ovaries in light of potential for malignancy.

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Patients and Methods

We analyzed 70 postmenopausal women who went through menopause between the age of 41 and 45 years. There was no case of increased CA 125 levels (under 35 U/ml).

The age of the examined patients ranged from 55 to 60 years (average 57.03 ± 1.54 years).

Body mass index (BMI) was normal since the patients with BMI more than 25 and less than 19.5 were excluded. Smokers were also excluded, as well as patients undergoing other therapy, except for 32 cases of antiarrhythmic therapy. Patients with the anamnesis of gynecological interventions or pathology were also excluded. None of the examined patients had used hormone replacement therapy in the menopausal period. They had had an average of 0-3 deliveries and 0-7 miscarriages in their reproductive period.

Patients were examined clinically and by US (abdominal and TVS); they underwent colposcopic examination, US breast examination, mamography and the special accent was on US Doppler examination.

Data were statistically analyzed by descriptive statistics (χ^2 test, *t*-test for 2 independent samples, Fisher's test).

Results

Out of 70 women, bimanual gynecological examination showed palpable ovaries in 14 (20%) and the remaining 56 (80%) formed the control group (Figure 1).

The average age of the patients with palpable ovaries was 57.14 ± 1.66 years, and 57.00 ± 1.52 years in the control group; the difference was not statistically significant ($t = 0.308$, $p = 0.759$, $p > 0.05$).

US findings showed the following results:

- All the patients with palpable ovaries had increased US dimensions of the ovary in the interval from 3.0 to 5.3 cm, on average 4.23 ± 0.72 cm, and in the control group it was 2.29 ± 0.62 cm. The difference was statistically significant ($t = 10.195$, $p < 0.0001$) (Figure 2).

- Atypical follicular activity was found ten years after menopause in 12 patients with palpable ovaries and in seven patients from the control group (Figure 3). The difference was statistically significant ($\chi^2 = 30.36$, $p < 0.01$).

- Atypical US shape – deviation from verticalization and atypical ovaries were found in nine patients with palpable ovaries and in ten control patients (Figure 3). The difference was statistically significant ($\chi^2 = 12.21$, $p < 0.01$).

- Hyperechogenic punctations classified as germinal inclusion cysts, were sporadically irregular in shape in ten patients with palpable ovaries and in 15 control patients (Figure 3). The difference was statistically significant ($\chi^2 = 9.72$, $p < 0.01$).

Doppler flow and its dynamics were normal in nine patients with palpable ovaries, but the remaining five patients had pathological vascularization. In the control group no patient had pathological vascularization. Fisher's test showed a statistically significant difference ($p = 0.011$, Figure 4).

In all the patients with pathological Doppler flow we found increased estrogen levels, unlike the patients with normal Doppler flow.

All the patients were advised to undergo control screening in four to six months. In the group with palpable ovaries and increased estrogen levels, we found a mild increase of estrogen levels again. Four of five cases with pathological Doppler flow had higher abnormality. The US picture had not changed except for the progress in follicular activity.

The next control was six months later. In two patients we found atypical bleeding, so fractionated curettage was performed. US of the abdomen did not show any significant changes, and MRI findings showed incompetent ovaries. These patients underwent surgical treatment. Histological examination showed adenocarcinoma Stage I in both patients.

Discussion

Nearly 2% of adnexal masses are ovarian carcinomas or borderline tumors [6]. Adnexal masses are described as simple adnexal cysts, as unilocular, anechogenic, with thin walls, without solid parts/papillae. Simple cysts occur in 10-15% women, and do not indicate operative treatment, but should be followed [7] since 0.3% of them have malignant potential [8]. However in light of US prediction of ovarian cancer, there is higher malignant potential in cases of unilocular-solid cysts (2%), multilocular cysts (8%), multilocular solid tumors (36%), and solid tumors (39%), without complete septa, with solid parts or papillae [8].

In cases of multilocular cysts, the eventual presence of at least one complete septum, solid parts and papillae should be analyzed. Papillary vegetation on the cyst wall is the most statistically significant predictor of a malignant ovarian mass [6, 8]. Thickness of the cyst wall and thickness of the septa inside the tumor do not seem to correlate with malignancy [8]. Correlations between size of tumor and malignancy are not clear yet, but there are indications that size of tumor could correlate with malignant potential [9].

Sensitivity of bimanual gynecological examination is about 30% [5]. Campbell *et al.* reported that normal US characteristics of the ovaries correlated with physiological findings at the time of laparotomy [10]. Rodriguez *et al.* demonstrated that TVS had a sensitivity of 90% and specificity of 100% when compared to surgical findings [11]. According to Granberg *et al.*, TVS characterized the tumor correctly as related to macroscopic examination (96%), sensitivity identifying benign and malignant tumors (82%), and specificity (92%) [4].

In order to recognize malignant entities, some authors developed scoring systems including US parameters. Sassone *et al.* published their results with a specificity of 83%, sensitivity of 100%, and positive and negative predictive values of 37% and 100%, respectively [12].

Kurjak *et al.* included Doppler flows and achieved a sensitivity of 97.3% and a specificity of 100%, compared with the simple morphological scoring system's sensitivity of 92.1% and specificity of 94.8% [13]. Pascual *et al.* showed that sensitivity and specificity of color Doppler

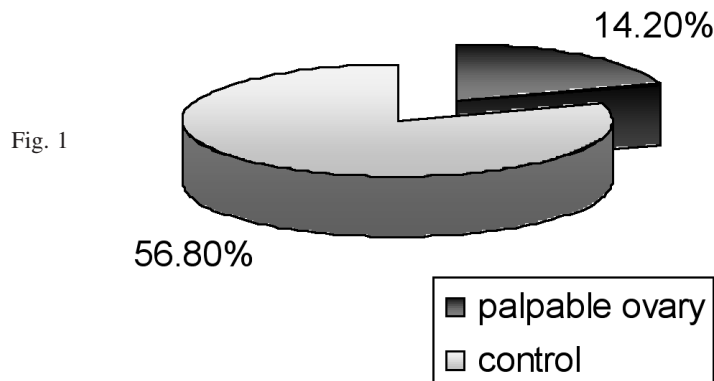


Fig. 1

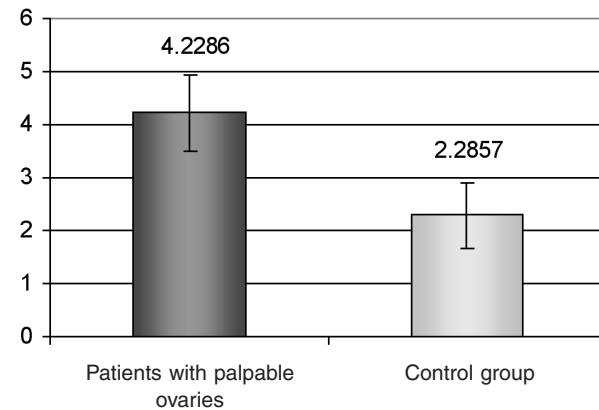


Fig. 2

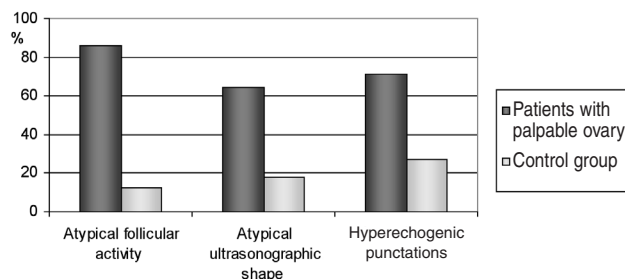


Fig. 3

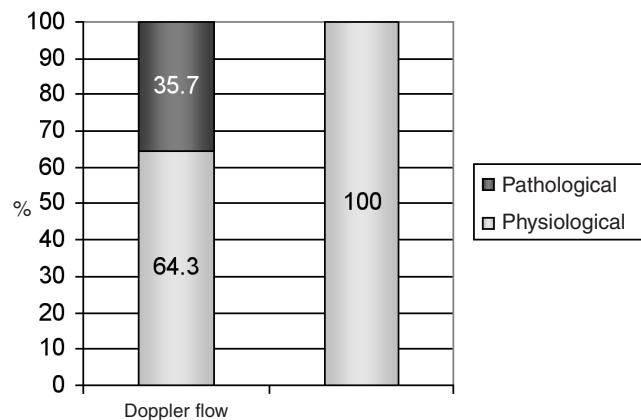


Fig. 4

Figure 1. — Incidence of palpable ovaries in examined postmenopausal women.

Figure 2. — Ultrasonographic dimensions (volume) of postmenopausal ovaries.

Figure 3. — Atypical ultrasound findings in postmenopausal women.

Figure 4. — Doppler flow in patients with palpable ovaries and the control group.

TVS were 84.6 and 99.2%, respectively [14], and Marret *et al.* showed a sensitivity 90% [6].

Combined US and a diagnostic algorithm perform significantly better than morphologic assessment, color Doppler or CA125 measurement alone [6].

In cases of US signs for benign and maybe functional cysts, spontaneous resolution may be controlled by sonographic exam at three and six months [6, 15], as we also performed. Prognosis of regression is age-dependent. In patients younger than 60 years spontaneous regression has been found in 30-53% cases [16], but above 60 years regression has been found in 8-24% of cases [17]. Age of patients, anamnesis of menstrual bleeding, BMI, other diseases, usage of medication, hormone therapy and smoking should be considered. In cases of an suspicious ovarian mass, there is necessity for an expert examination [6].

Most data show that estrogen therapy may increase the risk of epithelial ovarian cancer [18], but the results are inconsistent [19]. Estrogen therapy is not contraindicated in ovarian cancer survivors, but in some cases, estrogens alone could stimulate ovarian cancer growth. There is a

possible increase in ovarian epithelial tumors with > 10 years use of estrogen therapy [19]. According to our results, increased estrogen level was found in all the patients with pathologic Doppler flow and the risk for ovarian cancer. In our study group, none had used hormone therapy, but the estrogen level increased naturally. These patients were operatively treated, and the histological examination showed adenocarcinoma Stage I. This stage is recommended for screening [20], but for more detailed results, it is necessary to increase the number of patients in future studies.

In the literature the sensitivity of aspirate cytology was analyzed and varied from less than 50% to almost 100% [21]. The consequences of malignant cyst aspiration, spontaneous resolution and post-aspiration recurrence have been described [21]. Although there is a possibility of puncture in some cases, our opinion is not to perform this intervention because of potential dissemination of a malignant process, and we advise usage of more precise diagnostic procedures.

We recommend following patients in four to six month intervals. Operative procedures are recommended in

cases of changes in size and morphology of pelvic organs, increasing morphologic complexity, rising CA-125, and vascular characteristics - color and pulse Doppler [6, 14, 15]. Our advice is to perform operative treatment (laparoscopy or open-surgery) in cases of postmenopausal cysts larger than 5 cm, that do not show regression within six to eight weeks, or active cysts larger than 10 cm, solid, or complex adnexal tumors, papillary excrescence, multilocular cysts, or possibility of torsion or rupture.

Conclusion

According to our results, we conclude that every adnexal mass after menopause (postmenopausal palpable ovarian syndrome) demands special attention.

Bimanual gynecological exams should be used liberally. It is necessary to follow the dimensions of the ovary, describe the echostructure, as well as the edges of the ovaries and other anatomical structures. Doppler flow measurement and estrogen levels are predictive and important for accurate information. All the findings should be followed and compared in three to six month intervals, in order to make a decision about eventual surgical treatment.

It is also important to consult with the patient, to give her all the information in order to achieve compliance to adequate controls.

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Address reprint requests to:
M. GOJNIC, M.D.
Medical Faculty of Belgrade
Institute of Gynecology and Obstetrics
38 Milesevska Street
11000 Belgrade (Serbia)
e-mail: miroslavagojnicdugalic@yahoo.com