

Cystic ovarian structures in the peri- and postmenopause: simple ultrasound prognostic factors

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Aim: To determine the efficacy of ultrasound (US) examinations and the added value of CA-125 measurement in the diagnosis of peri- and postmenopausal ovarian cysts.

Materials and Methods: Imaging properties of peri- (PEM) and postmenopausal (POM) ovarian cysts were examined preoperatively. According to US findings two groups were made: (1) simple cysts: unilocular, anechoic cysts without papillarization, (2) complex cysts: cystic structures with different parameters. Imaging characteristics, size were matched with histology and CA125 levels.

Results: 379 cystic structures (PEM: N=195, average age: 45.6yrs; range: 40-54yrs, POM: N=184, average age 61.2yrs; range: 41-88yrs) were analysed preoperatively. In the PEM group 75 simple ($\varnothing < 5\text{cm}$ N=32, $\varnothing \geq 5\text{cm}$ N=43) and 122 complex cysts ($\varnothing < 5\text{cm}$ N=29, $\varnothing \geq 5\text{cm}$, N=93), while in the POM group 49 simple ($\varnothing < 5\text{cm}$ N=9, $\varnothing \geq 5\text{cm}$ N=40) and 135 complex cysts ($\varnothing < 5\text{cm}$ N=15, $\varnothing \geq 5\text{cm}$ N=120) were found. In the PEM group malignancy was detected in complex cysts larger than 5cm (N=16, 17.58%). In the POM group we found malignancy in 40 cases, three of them smaller than 5cm. Majority of cysts were functional (54.36 %) in the PEM group. In the POM group serous cysts were the most frequent (38.04%), followed by malignant (21.74%) and mucinous cysts (13.04%). CA125 were elevated in 66 of 217 cases (30.41%), only 23 of these were malignant (NPV: 0.95, PPV: 0.35).

Discussion: Functional cysts are frequently found among perimenopausal ovarian cysts, and we detected malignancy only among complex cysts larger than 5cms. However, complex cyst of any size carry significant risk of malignancy in the postmenopause, thus surgery is recommended. Simple cysts can be followed by serial scan in both groups. CA-125 did not give added value to the detection of malignancy.

Introduction

It is well known fact that the number of ovarian cystic structures in the peri and postmenopausal age is increased. The detection of these cysts can be achieved by bimanual examination, serum tumour markers and transvaginal ultrasound examinations, as well. Functional and malignant cysts can be characterized by their symptoms at the same time. Moreover the detection of these structures the dignity is the second most important thing to determine. In case of ovarian malignancies CA-125 was recommended to increase the detection rate but it can be used effectively together with transvaginal US scans. The aim of this study was to determine the efficacy of grayscale ultrasound scans and the additive value of CA-125 in the detection of ovarian cystic structures in the peri- and postmenopause.

Materials

This study was performed in the Department of Obstetrics and Gynaecology at the University of Debrecen, Debrecen, Hungary. Imaging properties of peri- (PEM) and postmenopausal (POM) ovarian cysts were examined preoperatively. All patients underwent transvaginal ultrasound examinations preoperatively (ATL HDI-3000, Bothell, Washington equipped with 5,9MHz transvaginal probe). Patients at least at the age of 40 without climacteric symptoms were involved in the PEM group such as those who previously underwent hysterectomy under the age of 50 (range: 40-54yrs, average: 45.57yrs). The lack of regular menses for more than one year or hysterectomy in the anamnesis and the patient is at least 50 were put in the POM group (range: 41-88yrs, average: 61,24yrs). Overall 343 patients with 379 cystic structures were involved in the study. The US examinations were independent from the menstrual cycle and were repeated within three months in 168 cases (44,32%). When follow-up was performed only the preoperative US finding was chosen to participate. According to US findings two groups were made: (1) simple cysts: unilocular, anechoic cysts without papillarization, (2) complex cysts: cystic structures with different parameters. Imaging characteristics, size were matched with histology and CA125 levels. The cut-off level for CA-125 was 35 kIU/L. According to the size of the cysts two subgroups were made within each reproductive group and 5cm was chosen for this purpose. Risk factors affecting the formation of cystic structures in the ovary were also observed in this study such as parity, previous pelvic surgeries, family history of ovarian cancer.

Results

In the PEM group 75 simple ($\emptyset < 5\text{cm}$ N=32, $\emptyset \geq 5\text{cm}$ N=43) and 122 complex cysts ($\emptyset < 5\text{cm}$ N=29, $\emptyset \geq 5\text{cm}$, N=93), while in the POM group 49 simple ($\emptyset < 5\text{cm}$ N=9, $\emptyset \geq 5\text{cm}$ N=40) and 135 complex cysts ($\emptyset < 5\text{cm}$ N=15, $\emptyset \geq 5\text{cm}$ N=120) were found. In the PEM group malignancy was detected in complex cysts larger than 5cm (N=16, 17.58%). In the POM group we found malignancy in 40 cases, three of them smaller than 5cm. Majority of cysts were functional (54.36 %) in the PEM group. In the POM group serous cysts were the most frequent (38.04%), followed by malignant

(21.74%) and mucinous cysts (13.04%). It should be noticed that in the POM group we can meet functional cysts in 5.43% of the cases (N=10). Details are shown in Table 1.

The factors affecting the formation of cystic structures in the ovary can be seen in Table 2. We found at least one delivery in 84.96% of the cases. 210 cysts caused some kind of complaint for the patient (55.41%) the most common was pelvic pain in 160 cases (42.22%). In 336 cases laparotomy was performed (88.65%). Previous interventions affecting the pelvis were found overall in 114 cases (30,08%), majority of these were hysterectomy (N=71, 18,73%). Family history for ovarian cancer was found in 4 cases (1.06%).

CA125 evaluation was performed in 217 cases, elevated in 66 cases (30.41%), only 23 (10.60%) of these were malignant (NPV: 0.95, PPV: 0.35). Results are shown in Table 3.

Discussion

Cystic structures of the ovaries can be found in 11-16% of the cases in postmenopause and more frequently in the perimenopause. The risk of malignant transformation of benign cysts is still an open question in the literature. It was proven in several studies that the risk of malignant transformation is directly proportional to the number of EGF receptors in the cystic fluid. In our study we did not observe this connection.

According to the fact that ovarian pathologies depend on the functional state of the ovaries the division of the population into peri-and postmenopausal groups are necessary. Koonings et al. found 13% risk for malignant transformation in the perimenopause, which increases to 45% in the postmenopausal group. This transformation is more likely to develop in larger cysts. Modesitt et al advised 10cms for cut off level while Osmer et al found 3cms of diameter for the border between low risk and high-risk groups. 5cms was recommended by Auslender et al. and Reimer et al. and so it was used in this study as well.

In this study it was shown that perimenopausal cystic structures carry malignancy in 4.22% of the cases which correlates with the results of Ekerhovd et al (0.7%) and Osmer et al. (0.8%). Echogenicity, wall structure, septation and presence of papillarization should be noticed when considering about complexity of a cyst because this is compulsory for a correct diagnostic decision. Timmermann et al and Ueland et al designed scoring systems based on the volume of cysts and wall structures to help these decisions. These systems were not used in this study.

In the postmenopausal group the risk of malignancy is not irrelevant which fact was supported by our result: 40 cysts found out to be malignant (10.55%) of the cases, 39 of them proved to have complex morphological findings. Our data correlates with the results of Osmer et al (9.6%) and Ekerhovd et al. (10%). According to these facts surgical removal of these structures is necessary. Simple postmenopausal cysts can carry malignancy in only 0.26% of the cases, their regular

follow-up is recommended with or without determination of CA-125. CA-125 alone has a very low screening sensitivity for stage I. ovarian cancer (60%) and a specificity of 99% (Bast et al.). In combination with TVS sensitivity increases up to 85% (Jacobs et al.). In this study the detection rate was only 30.41%. It can be elevated in benign diseases such as endometriosis, PID, fibroids and Meigs-syndrome. Several studies support that it has to be used together with ultrasound scans to improve its diagnostic benefit and should not be used alone for the decision of the dignity of ovarian cysts. A diagnostic algorithm based on ultrasonography can easily decrease the number of surgeries and high hospital costs.

References:

1. Sassone AM, Timor-Tritsch IE, Artner A, Westhoff C, Warren WB. Transvaginal sonographic characterization of ovarian disease: evaluation of a new scoring system to predict ovarian malignancy. *Obstet Gynecol* 1991; 78: 70–6.
2. Ueland FR, DePriest PD, Pavlik EJ, et al. Preoperative differentiation of malignant from benign ovarian tumors: the efficacy of morphology indexing and Doppler flow sonography. *Gynecol Oncol*. 2003;91:46–50.
3. Granberg S, Wikland M, Jansson I. Macroscopic characterization of ovarian tumors and the relation to the histological diagnosis: criteria to be used for ultrasound evaluation. *Gynecol Oncol*. 1989;35:139–144.
4. Tan PL, Willatt JM and Lindsell D The ability of ultrasound to detect gynaecological neoplasms and their ultrasound morphological features *Australasian Radiology* 2007; 51, 260–266.
5. Kurjak et al. Three-dimensional Ultrasonography and Power Doppler in Ovarian Cancer Screening of Asymptomatic Peri- and Postmenopausal Women *Croat Med J* 2005;46(5):757-764.
6. Modesitt SC, Pavlik EJ, Ueland FR, et al. Risk of malignancy in unilocular ovarian cystic tumors less than 10 centimeters in diameter. *Obstet Gynecol*. 2003;102:594–599.
7. Osmers RGW, Osmers M, von Maydell B, Wagner B, Kuhn W. Evaluation of ovarian tumors in postmenopausal women by transvaginal sonography. *Eur J Obstet Gynecol Reprod Biol* 1998;77:81–8.
8. 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* 1996;24:175–8.
9. Einhorn N, Sjovall K, Knapp RC, Hall P, Sculli RE, Bast RC Jr, et al. Prospective evaluation of serum CA125 levels for early detection of ovarian cancer. *Obstet Gynecol*. 1992; 80:14-8.
10. Jacobs IJ, Skates SJ, MacDonald N, Menon U, Rosenthal AN, Davies AP, et al. Screening for ovarian cancer: a pilot randomised controlled trial. *Lancet*. 1999; 353:1207-10.

11. Collins WP, Bourne TH, Campbell S. Screening strategies for ovarian cancer. *Curr Opin Obstet Gynecol* 1998;10:33-9
12. Padilla LA, Radosevich DM, Milad MP Accuracy of the pelvic examination in detecting adnexal masses. *Obstet Gynecol* 2000; 96:593-8
13. Hartge P, Hayes R, Reding D, Sherman ME, Prorok P, Schiffman M, Buys S. Complex ovarian cysts in postmenopausal women are not associated with ovarian cancer risk factors: preliminary data from the prostate, lung, colon, and ovarian cancer screening trial. *Am J Obstet Gynecol* 2000; 183: 1232-7.
14. Curtin JP. Management of the adnexal mass. *Gynecol Oncol* 1994;55:S42-6.
15. Reimer T, Gerber B, Müller H, Jeschke U, Krause A, Friese K Differential diagnosis of peri- and postmenopausal ovarian cysts *Maturitas* 31 (1999) 123-132.
16. Owens OJ, Stewart C, Leake RE, McNicol AM. A comparison of biochemical and immunohistochemical assessment of EGFR expression in ovarian cancer. *Anticancer Res* 1992;12:1455-8.
17. Scambia G, Benedetti-Panici P, Ferrandina G, et al. Epidermal growth factor, oestrogen and progesterone receptor expression in primary ovarian cancer: correlation with clinical outcome and response to chemotherapy. *Br J Cancer* 1995;72:361-6.
18. Koonings PP, Campbell K, Mishell DR Jr, et al. Relative frequency of primary ovarian neoplasms: a 10-year review. *Obstet Gynecol.* 1989;74:921-926.
19. 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;184:48-54.
20. Osmers RG, Osmers M, von Maydell B, Wagner B, Kuhn W. Preoperative evaluation of ovarian tumors in the premenopause by transvaginasonography. *Am J Obstet Gynecol* 1996;175:428-34.
21. Bailey CL, Ueland FR, Land GL, DePriest PD, Gallion HH, Kryscio RJ, van Nagell JR Jr. The malignant potential of small cystic ovarian tumors in women over 50 years of age. *Gynecol Oncol* 1998; 69:3-7.

22. Conway C, Zalud I, Dilella M, Maulik D, Schulman H, Haley J, Simonelli K. Simple cysts in the postmenopausal patient: detection and management. *J Ultrasound Med* 1998; 17:369-72
23. Bast RC Jr, Klug TL, St John E, Jenison E, Niloff JM, Lazarus H, et al. A radioimmunoassay using a monoclonal antibody to monitor the course of epithelial ovarian cancer. *N Engl J Med* 1983;309:883-8.
24. Jacobs I, Bast RC Jr. The CA 125 tumour-associated antigen: a review of the literature. *Hum Reprod* 1989;4:1-12.
25. Timmerman D, Moerman P, Vergote I. Meigs' syndrome with elevated serum CA 125 levels: two case reports and review of the literature. *Gynecol Oncol* 1995;59:405-8.
26. Jacobs I, Oram D, Fairbanks J, Turner J, Frost C, Grudzinskas JG. A risk of malignancy index incorporating CA 125, ultrasound and menopausal status for the accurate preoperative diagnosis of ovarian cancer. *Br J Obstet Gynaecol* 1990; 97:922-9.
27. Bast et al. *Cancer Treat Res* 2002