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The 3-dimensional Ovarian Volume Assessment to Evaluate Whether Menopausal Related Symptoms and Hormone Levels Correlate with the Ovarian Volume

Menopozla ilişkili Semptomlar ve Hormon Düzeylerinin Over (Yumurtalık) Hacmi ile ilişkili Olup Olmadığını Değerlendirmek için 3-boyutlu Over Hacmi Değerlendirmesi

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ABSTRACT

Objective: To evaluate whether ovarian volume is correlated with hormonal status and frequent symptoms in menopausal period.

Methods: Sixty-two postmenopausal women who applied for routine yearly gynecological control included. After measurement of ovarian volumes by using Virtual Organ Computer-aided Analysis volume analysis, hormonal levels, and evaluation of symptoms with standardized menopause-specific quality of life questionnaire, comparisons and correlation analysis were performed.

Results: When the time of menopausal period increases the ovarian volume decreased ($p=0.026$), and earlier menopause age correlated with lower ovarian volume ($p=0.014$). Although the results did not reach statistically significance, a negative correlation between ovarian volumes and follicle stimulating hormone levels and a positive correlation between ovarian volumes and Estradiol levels were found ($p=0.46$, $p=0.26$). There was no correlation between ovarian volume analyses with hormonal status and menopausal symptoms.

Conclusion: Both the severity and type of menopausal symptoms and hormonal status do not relate with ovarian volume after the menopause. This finding may be useful to decide to perform oophorectomy or not at the time of hysterectomy in menopausal ages.

Keywords: 3D ovarian volume, menopausal symptoms, three-dimensional ultrasonography, menopause

Öz

Amaç: Menopoz döneminde over hacminin hormonal durum ve sık görülen semptomlarla ilişkili olup olmadığını değerlendirmek.

Yöntemler: Rutin yıllık jinekolojik kontrol için başvuran 62 postmenopozal kadın çalışmaya dahil edildi. Sanal organ bilgisayar destekli analiz (Virtual Organ Computer-aided Analysis yöntemi) hacim analizi kullanılarak over hacimleri ölçüldükten sonra, hormonal düzeyler belirlendi ve semptomlar standartlaştırılmış menopoz-spesifik yaşam kalitesi anketi ile değerlendirildi. Daha sonra karşılaştırmalar ve korelasyon analizleri yapıldı.

Bulgular: Menopoz süresi arttıkça over hacminin azaldığı görüldü ($p=0,026$) ve daha erken menopoz yaşı, daha düşük over hacmi ile ilişkili bulundu ($p=0,014$). İstatistiksel anlamlılığa ulaşmamış olsa da, over hacimleri ile folikül uyarıcı hormon düzeyleri arasında negatif korelasyon ve over hacimleri ile Estradiol düzeyleri arasında pozitif korelasyon saptandı ($p=0,46$, $p=0,26$). Over hacmi analizleri ile hormonal durum ve menopoz semptomları arasında herhangi bir ilişki bulunmadı.

Sonuç: Menopoz sonrası dönemde, menopoz semptomlarının şiddeti ve tipi ile hormonal durumun over hacmi ile ilişkisi yoktur. Bu bulgu, menopoz yaşlarındaki histerektomi sırasında ooferektomi yapıp yapılmayacağına karar vermede yararlı olabilir.

Anahtar Sözcükler: 3B over hacmi, menopoz semptomları, üç boyutlu ultrasonografi, menopoz

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INTRODUCTION

Menopause, the complete cessation of menstrual periods, related with many symptoms that reduce quality of life (QOL) of postmenopausal women. The World Health Organization defines QOL "as an individual's perception of their position in life in the context of culture and values system in which they live, in reference to their goals, standards, and concerns in life" (1). The range and severity of menopausal symptoms vary widely due to lifestyle, cultural and genetical (2).

The most menopausal symptoms consist not only about female genital tracts but also vasomotor, physical, somatic, cardiovascular and skeletal symptoms. (2) Eighty-five percent of postmenopausal women have experienced menopause-related symptoms in terms of the vasomotor symptoms, arthralgia, headache, rapid weight gain, fatigue, sexual dysfunction and urinary incontinence (3). These symptoms decrease QOL during post-menopausal period.

As it is known ovarian volume increases as from the pubertal beginning. During the premenopausal period the volume gradually decreases. In postmenopausal time atrophy is seen in ovaries but personal variations can be monitored (4). There are many studies in the literature that compared the ovarian volume with specifically fertility potentials, body mass index (BMI), hormonal status and bone mineral density (BMD) (5,6).

To our knowledge although there are a number of studies on ovarian volume measurements in different periods of life, there is not any data about the relevance of ovarian volume and postmenopausal symptoms occurrence and severity. The purpose of our study was to evaluate the relationship between three- dimensional (3D) volume analyze and menopause-specific QOL (MSQOL) questionnaire and hormonal levels (7).

MATERIALS AND METHODS

After the approval of Ankara Numune Training and Research Hospital Ethics Committee of clinical trials (decision number E-15-517, date: 24.06.2015) was obtained, transvaginal 3D ultrasonography substructure support was provided by Gazi University local Projects of Scientific Investigation Committee. A power analysis was conducted to determine the required sample size, which was calculated to be 60 patients. This prospective study included 62 postmenopausal women that applied for annual routine gynecological controls to Gazi University Hospital outpatient clinics between November 2016 and November 2017. Written informed consent was obtained from all 62 women who participated in the study. Inclusion criteria were confirmed menopausal status and absence of previous hysterectomy, ovarian surgery, hormonal use currently or during the past 6 months and a personal history of gynecological malignancy. Given the broad age distribution of the patients, menopausal status was assessed based on the clinical criterion of amenorrhea lasting at least one year. If the patients that had ovarian and/or tubal masses during pelvic examination and chronic pelvic pain were excluded from the study.

Demographical characteristics of patients such as age, BMI, gravida, age of menopause and time that the patients spend in menopause were recorded. During routine pelvic examination, 3D ultrasonographic images were applied for ovarian volume analysis.

With 3D transvaginal ultrasonography probe, bilateral ovarian images were taken, and volume of ovaries were calculated by using Virtual Organ Computer-aided Analysis (VOCAL) volume analysis (GE Voluson E6 Ultrasound Systems). In order to enhance measurement reliability, all assessments were conducted by same physician. The VOCAL technique, a semi-automated 3D ultrasound method that enables accurate and reproducible volume measurements of irregularly shaped structures. Patients were questioned regarding the presence of stress urinary incontinence symptoms, and during the physical examination, the presence of incontinence was assessed by increasing intra-abdominal pressure and recorded accordingly. The blood serum levels of follicle stimulating hormone (FSH), estradiol (E2), free and total testosterone, dehydroepiandrosterone, androstenedione levels were assessed. In addition, mammography results and BMD measurements with dual-energy X-ray absorptiometry (DEXA) were also recorded.

In addition to these investigations, the postmenopausal symptoms that affect psychosocial, physical, and sexual functions of women were estimated upon to the serum hormone values and ovarian volumes. These estimations were done by using standard MSQOL questionnaire that was prepared by Sunnybrook Health Science Center (7).

Patients answered 29 different questions about vasomotor, physical, and sexual symptoms and were asked for grading their complaints with numbers 0 to 6.

Statistical Analysis

IBM Statistical package for the social sciences , version 22.0 (SPSS Inc., Chicago, IL, USA) was used for the statistical analysis. Mean levels of all patient's demographic data, 3D vocal volume analysis, serum hormone levels, MSQOL scoring results were calculated. The mean value differences between the groups with and without symptoms were tested using the Student's test or Mann Whitney U test whether the distribution of the data was normal or not, respectively. The correlation analysis was done with Pearson correlation (2-tailed) test. Differences were accepted as significant if the p values were less than 0.05.

RESULTS

Total number of 62 postmenopausal patients were included to the study. The demographic data of patients, serum levels of hormones, DEXA results and calculations of ovarian volume by 3D vaginal ultrasound were given in Table 1. The mean ovarian volume was calculated as 1.91 cm³. A negative correlation was found in the decrease of ovarian volume and the increase of menopausal period (p=0.026). In addition, a significantly positive correlation was seen between menopausal age and ovarian volume. The earlier menopause age significantly correlated with lower ovarian volume (p=0.014).

There was a non-significant negative correlation between FSH levels and positive correlation between E2 levels and ovarian volume were found (p=0.46 and p=0.26, respectively)

Patients' with and without postmenopausal symptoms were compared regarding ovarian volumes. No statistical difference was found between symptoms and 3D ovarian volume measurements (Table 2).

Table 1. The demographic data, DEXA values, hormone levels, mammography results and 3D ovarian volume calculations of patients

Variables	Mean Values $\pm$ SD
Age	55.51 $\pm$ 5.05
Menopause age	48.82 $\pm$ 4.23
Menopausal period	6.30 $\pm$ 5.38
Gravida	3.25 $\pm$ 2.28
BMI	29.66 $\pm$ 5.05
BMD T score (L1-4)	0.41 $\pm$ 1.57
BMD T score (Femur)	-0.86 $\pm$ 1.10
FSH (mIU/mL)	73 $\pm$ 24
E2 (pg/mL)	21.4 $\pm$ 11.2
T. test (ng/dL)	0.27 $\pm$ 0.21
DHEA (ng/mL)	109.7 $\pm$ 54.70
F. test (pg/mL)	1.51 $\pm$ 0.64
Androstenedion (ng/mL)	0.78 $\pm$ 0.36
TSH (mIU/mL)	2.40 $\pm$ 3.30
Mammography (BIRADS)	1.87 $\pm$ 0.74
OV (cm ³)	1.9 $\pm$ 1.3
ROV (cm ³)	1.99 $\pm$ 1.59
LOV (cm ³)	1.7 $\pm$ 1.4

SD: Standard deviation, BMI: Body mass index, BMD: Bone mineral density, FSH: Follicle stimulating hormone, E2: Estradiol, T. test: Total testosterone, DHEA: Dehydroepiandrosterone, F. test: Free testosterone, TSH: Thyroid stimulating hormone, OV: Total ovarian volumes, ROV: Right ovarian volumes, LOV: Left ovarian volumes, DEXA: Dual-energy X-ray absorptiometry

Table 3 shows the data of grading of vasomotor, psychosocial, physical and sexual symptoms according to MSQOL questionnaire in detail. Ovarian volume calculation was not significantly correlated with each of these symptoms and rating of the answers of the MSQOL questions.

DISCUSSION

This study evaluated the ovarian volume after the menopause with demographic, anthropometric and hormonal parameters and also menopausal symptoms and QOL of patients. According to our results, ovarian volume changes the hormonal values. However menopausal symptoms seem much more multifactorial; these symptoms were not associated with ovarian volume.

There is an ongoing debate on the impact of ovarian function on common menopausal symptoms after the menopause. This discrepancy may also lead to another uncertainty for the decision of prophylactic oophorectomy at the time of hysterectomy regarding to cause any iatrogenic benefit or harm to our patients.

During menopausal symptoms ovarian androgen secretion gradually decreases and postmenopausal ovaries maintain to be an important resource for androgens (8). In our study we aimed to analyze the correlation between the ovarian stromal volume and androgen values and also menopausal symptoms. There was no statistically meaningful correlation between the androgen levels and ovarian stromal volume decrease. This result can be interpreted in two different point. The ovaries are not an important resource for androgens during menopause or the ovarian androgen synthesis during menopause is minimal or negligible.

Previous studies evaluated 3D and 2D ultrasonographic ovarian volumes in women who were in reproductive ages. Nardo et al. (13) reported 3D ovarian stromal volume did not correlate with

Table 2. Comparison of 3D ovarian volume between presence and absence of menopausal symptoms

Vasomotor symptoms, (n)	Ovarian volume (cm ³)	p-value
Exist (22)	1.89 $\pm$ 0.95	0.713
Not exist (40)	2.03 $\pm$ 1.75	
Stress incontinence	Ovarian volume (cm ³)	p-value
Exist (5)	3.05 $\pm$ 3.73	0.512
Not exist (57)	1.85 $\pm$ 0.95	
Urge incontinence	Ovarian volume (cm ³)	p-value
Exist (8)	1.72 $\pm$ 0.58	0.356
Not exist (54)	2.01 $\pm$ 1.55	
Dyspareunia	Ovarian volume (cm ³)	p-value
Exist (8)	2.18 $\pm$ 1.09	0.579
Not exist (54)	1.92 $\pm$ 1.5	
Loss of libido	Ovarian volume (cm ³)	p-value
Exist (21)	1.72 $\pm$ 1.03	0.579
Not exist (41)	2.14 $\pm$ 1.67	

Data were given as mean $\pm$ standard deviation
3D: Three-dimensional

Table 3. MSQOL questionnaire results

Symptoms	Data
Vasomotor symptoms	8.69±6.25
Hot flushes/flushes	3.61±2.49
Night sweats	2.46±2.34
Sweating	2.63±2.2
Psychosocial symptoms	18.8±11.2
Being dissatisfied with my personal life	2.37±2
Feeling anxious or nervous	2.95±2.1
Experiencing poor memory	3.27±2.26
Accomplishing less than I used to	2.78±2.21
Feeling depressed/down/blue	2.69±1.98
Being impatient with other people	2.39±2.12
Feelings of wanting to be alone	2.39±1.94
Physical Symptoms	51.68±23.62
Flatulence(wind) or gas pains	2.8±2.37
Aching in muscles and joints	4.39±2.53
Feeling tired or worn out	3.75±2.28
Difficulty sleeping	3.24±2.79
Aches in back of neck or head	3.47±2.56
Decrease in physical strength	3.71±2.28
Decrease in stamina	2.93±2.24
Feeling a lack of energy	3.19±1.91
Drying skin	3.61±2.6
Weight gain	3.54±2.45
Increased facial hair	2.29±2.2
Changes in appearance, texture or tone of your skin	2.17±2
Feeling bloated	3.02±2.3
Low backache	3.78±2.75
Frequent urination	2.78±2.17
Involuntary urination when laughing or coughing	3.02±2.2
Sexual Symptoms	11.88±7.8
Change in your sexual desire	3.68±2.7
Vaginal dryness during intercourse	3.97±2.7
Avoiding intimacy	4.24±2.96

Data was given as mean ± standard deviation
MSQOL: Menopause-specific quality of life

biochemical indices of PCOS. Flaws et al. (14) found that hormone replacement therapy using did not change ovarian volume. However, till the negative correlation of FSH levels and positive correlation of E2 levels make think that menopausal period is also dynamic period of life.

Although many factors have impact on bone mineral density (BMD), in a study a positive correlation between ovarian volume and BMD at the femoral neck both in T scores and Z scores was reported (5).

Our results contrast with Armeni et al.'s (5) findings as there was not a significant difference in BMD T score of both femoral neck and lumbar spine according to ovarian volume values.

It is already come to be known that the prevalence of menopausal symptoms are related with many different factors like lifestyle, education of women, socioeconomic statute (15). There are different questionnaires that can evaluate the menopausal symptoms and QOL during this period. MSQOL is the most popular questionnaire for QOL evaluation during menopause period. As we already mentioned that menopausal symptoms are multifactorial and are affected by lifestyles; Korean and Chinese studies assessed the applicancy of this questionnaire in their countries. They found this questionnaire as a valid and reliable scale for assessment of menopausal symptoms and QOL (16,17). In our country, the studies that evaluated menopausal symptoms also used MENQOL questionnaire. According to the results of these studies this questionnaire seems as a valid assessment for our population (18,19). In our study the questionnaire results were compared with ovarian volume, a clear correlation cannot be found. The symptoms did not increase when the volume decreased.

Study Limitations

The main limitation of our study is the variability in patients' age ranges and duration of menopause. If the study is repeated with a larger sample size, patients can be stratified according to menopausal duration and age, allowing for group-based comparisons of symptoms and ovarian volumes. Such comparisons may enable a more objective and accurate evaluation of the relationship between ovarian volume, hormonal status, and clinical symptoms.

CONCLUSION

In our study, there was a correlation between hormone levels and ovarian volume; but this change did not reflect to symptoms. These results remarked that menopausal symptoms are multifactorial and affected by many other factors than hormonal status.

In conclusion ovarian volume was not correlated with menopausal symptoms and serum hormonal levels. This finding may be important and kept in mind for the decision of prophylactic oophorectomy at the time of hysterectomy after the menopause.

Ethics

Ethics Committee Approval: The approval is obtained Ankara Numune Training and Research Hospital Ethics Committee of clinical trials (decision number E-15-517, date: 24.06.2015).

Informed Consent: Written informed consent was obtained from all 62 women who participated in the study.

Footnotes

Authorship Contributions

Surgical and Medical Practices: G.I.S., İ.G., E.İ.B., S.C.İ., N.B., M.A.O., Concept: İ.G., N.B., M.A.O., Design: İ.G., N.B., M.A.O., Data Collection or Processing: İ.G., E.İ.B., Analysis or Interpretation: G.I.S., İ.G., E.İ.B., S.C.İ., Literature Search: G.I.S., Writing: G.I.S., E.İ.B.

Conflict of Interest: No conflict of interest was declared by the authors.

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