Is bioelectrical impedance analysis beneficial to estimate subclinical atherosclerosis in menopause? Prospective case-control study

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Summary

Aim: To evaluate body composition and basal metabolic rate in premenopausal and postmenopausal women, using the bioelectrical impedance analysis method, and to investigate its relationship with carotid intima media thickness (CIMT). *Materials and Methods:* The study was conducted in 40 premenopausal and 40 postmenopausal women who had been followed up in an obstetrics and gynecology outpatient clinic between January 2009 and September 2009, and data were obtained using the hospital's database. Body composition parameters and basal metabolic rate were measured via bioelectrical impedance analysis. CIMT was measured using the Doppler ultrasound method. *Results:* The mean CIMT of the postmenopausal group was statistically significantly higher than that of the premenopausal group ($p < 0.001$). There was a statistically significant negative correlation between basal metabolic rate and both right ($p = 0.015$, $r = -0.381$) and left ($p = 0.025$, $r = -0.354$) CIMT in the postmenopausal group. *Conclusion:* Bioelectrical impedance analysis may be a useful adjunctive tool for early detection of subclinical atherosclerosis in postmenopausal women.

Key words: Basal metabolic rate; Bioelectrical impedance analysis; Carotid intima media thickness; Subclinical atherosclerosis.

Introduction

Cardiovascular disease (CVD) is the leading cause of mortality in women. In 2013, CVD was the cause of death in 398,086 females in the United States. Of these deaths, 161,698 were due to coronary heart disease [1]. Some studies have recently assessed different methods of reducing the mortality rate and have focused on hormone therapy.

Ovaries produce the dominant female sex hormones estrogen and progesterone. Estrogen in circulation is thought to protect against atherosclerotic CVDs. This view is supported by an increase in the risk of CVD after the menopausal period which is characterized by a natural reduction in ovarian hormone production [2]. The first three years of menopause, especially those associated with dynamic hormonal imbalances, can create a specific cardiovascular hazard. Hormonal changes become most evident during the first three years of postmenopausal period. In case of dynamic hormonal imbalances, cardiovascular risk factors and a rapid prothrombotic diathesis in the blood can be detected [3]. Despite the optimal treatment, high rates of mortality increases the significance of the risk classification in CVD. The current trend in risk assessment is to identify CVD in early forms before clinical symptoms occur [4].

The surrogate markers of CVD in early stages are carotid intima media thickness (CIMT), carotid-femoral pulse wave velocity (PWV), and adjusted augmentation index (AI). They can be assessed by non-invasive and easily accessible methods. These methods may provide information about the cardiovascular function and the structure of an asymptomatic individual and may predict future cardiovascular events. Intima-media thickness is a risk factor which can be applied in a reliable repeatability and can be used in monitoring the progression of subclinical disease during the follow-up [5]. According to current epidemiological data, CIMT has a significant correlation with future cardiovascular events. CIMT can be reliably determined in vivo by carotid ultrasound and is a reliable, convenient method for assessing subclinical atherosclerosis [6].

Body composition is an important factor in evaluating mortality risk in postmenopausal women (especially in the 50-59 age range) [7]. The decrease in estrogen levels after menopause causes an increase in total and central fat mass and a decrease in bone and muscle mass. These changes in body composition cause a reduction in the levels of the usual physical activity and basal metabolic rate (BMR). As a consequence, the quality of life and the cardiovascular

condition relapses in this stage of climacteric period [8]. The gold standard of body composition analysis is cadaver analysis, so none of the in vivo techniques meet the measurement criteria with the highest accuracy [9]. Numerous techniques for body composition analysis are available: anthropometry, four-skinfold method, hydrostatic weighing, in vivo neutron activation analysis, anthropogammametry from total body K, nuclear magnetic resonance, dual-energy X-ray absorptiometry (DEXA), and bioelectrical impedance analysis (BIA). When we evaluate the complexity, invasiveness, and cost, only DEXA, CT, and BIA are the preferred methods for assessing body composition in clinical practice [10]. Among the all available techniques, BIA seems to be the most favourable in clinical practice because it is simple, cheap, non-invasive, and highly reproducible [10]. In addition, a study in the literature confirms the validity and predictive value of BIA in menopausal women [11].

There are insufficient published data on the evaluation and comparison of total body composition (TBC) and BMR using BIA in premenopausal and postmenopausal groups of women. In the present study, the authors aimed to evaluate body composition and BMR in premenopausal and postmenopausal women, using the BIA method, and to investigate its relationship with CIMT.

Materials and Methods

This prospective study was conducted in 40 postmenopausal and 40 premenopausal women (aged 38–58 years) from January 2009 to September 2009 in follow-up at the Obstetrics and Gynecology outpatient clinic, and relevant data were obtained from the women's files. Ethics committee approval was received for this study from the local ethics committee. Written informed consent was also obtained from all participants in the study.

The authors determined the sample size from the results obtained from the participants that they evaluated it preliminarily. From the differences, a domineering two-tailed α value of 0.05 and a β value of 0.20 (study power: 80%), they ruled out that at least 38 women in each group were mandatory for an analysis comparing two groups (G-Power 3 power analysis program). Therefore, assuming the probable dropouts, they agreed to include minimum 40 women in each group.

Exclusion criteria: Women aged under 35 years or over 65 years of age, with diabetes mellitus, with hypertension, with established cardiovascular disease, with cancer, who were taking lipid-lowering drugs, who were taking steroids, who were smoking and drinking alcohol, who were pregnant, who had a BMI > 35 kg/m², who were on hormone replacement therapy, who were in the surgical menopause, or with body metal implants (prostheses, pacemakers, etc.) were excluded, as were those showing the presence of immune suppression (human immune deficiency virus infection, drugs).

Inclusion criteria: A total of 40 healthy postmenopausal women whose last menstruation more than one year and FSH more than 25 mIU/ml were selected as study group. A total of 40 healthy premenopausal women with vasomotor symptoms, whose last menstruation had been in the last one year, and who had regular menstruation (cycle duration: 22-35 days and bleeding period: 3-10 days) were selected as the control group. All participants had healthy four limbs.

The BMI scale used was as follows: a BMI <18.5 kg/m²: underweight, a BMI 18.5–30 kg/m²: healthy-to-overweight, a BMI > 30 kg/m²: mildly obese, and a BMI > 35 kg/m²: moderate to morbid obese.

In each subject laboratory tests for lipid profile were performed with fasting blood. Triglycerides (TG), high-density lipoprotein (HDL), and low-density lipoprotein (LDL) levels measured. The conclusions were asserted as mg/dL.

In this study, the BIA method was used to calculate the body composition. This method is based on measuring the vectorial magnitude that called impedance following the application of alternating current (50 Hertz) to the body. Resistance is the defence of the body against the transmission of electric current and is applied by extracellular cells. On the other hand, reactance is the ability to store electrical charge for a certain period of time. High reactance values depend on the number of intact cell membranes and can be used as an indirect measurement of body cell mass [12]. Bioelectric impedance analysis was performed in all participants at 09:00-10:00 AM by same well-trained staff. The device calibration was made daily according to the manufacturers' manual. After eight hours of nighttime resting, BIAs were performed on the two groups, who had an empty stomach and an empty bladder, using a biodynamics BIA 450 (single frequency) bio- impedance analyzer. Each participant was instructed to drink eight glasses of water the day before, and not to drink tea, coffee, alcohol or smoke cigarettes. Any metal and decorative items on the women and, if any, large metal clothing items (such as a belt), and mobile phones, were removed. Each woman was asked to remain in the supine position on the examination table, but with their shoes and socks removed. In order to obtain the measurements, two electrodes were placed on the dorsal side of the right hand and right wrist, and two electrodes were placed on the dorsal side of the right foot and the right ankle, using four standard tetrapolar electrodes. After the placement of electrodes, the device was turned on and patient's height and weight data were entered. Then measurement was performed.

Body composition, as measured by BIA, body fat ratio (BFR), lean body mass (LBM –also referred to as fat-free mass), total body water (TBW), and BMR [calculated automatically by the formula: 31.2 * FFM (kg)] in women in the control group was matched with the postmenopausal group (in terms of age, weight, and BMI), and was compared between the groups.

CIMT of each participant was measured in the supine position via ultrasound. Ultrasonographic measurements were taken via superficial ultrasonography with 10-MHz linear probe from the right and left common carotid artery at 1 cm proximal, mid-line, and distal. The average of each proximal and distal CIMT measurement was recorded as average CIMT. Measurements of CIMT were performed by same trained and certified sonographer and calibrated daily. Usually the average of paired (right and left), carotid sites are analysed together. However there are studies showing that CIMT on the left side is greater than on the right side [13]. There are also studies in which only one side was evaluated [14]. For these reasons, CIMT was evaluated separately in the present study.

Statistical analyses were performed using Statistical Package for the Social Sciences software, version 23. Data were expressed as mean and range for continuous variables, and binary variables

Table 1. — *Comparison between demographic, anthropometric, biochemical, and clinical variables in premenopausal women and postmenopausal women. Data are reported as means and standard deviation.*

Variables	Premenopausal (mean ± SD)	Postmenopausal (mean ± SD)	*p* value
Age (years)	45.1 ± 4.1	51.2 ± 3.9	<0.001
BMI (kg / m²)	30.3 ± 4.9	29.2 ± 3.7	0.269
TG (mg/dL)	143 ± 38	194 ± 60	<0.001
HDL (mg/dL)	46.8 ± 10.3	38.1 ± 9.0	<0.001
LDL (mg/dL)	108 ± 28	134 ± 44	0.003
BMR (kcal/day)	1616 ± 192	1476 ± 175	0.001
Right CIMT(mm)	0.49 ± 0.09	0.60 ± 0.11	<0.001
Left CIMT (mm)	0.48 ± 0.09	0.61 ± 0.11	<0.001
BCM (%)	31.4 ± 10.5	29.9 ± 7.3	0.481
ECM (%)	34.6 ± 9.2	34.7 ± 9.1	0.942
Lean BM (%)	65.4 ± 8.99	64.7 ± 8.6	0.698
Fat mass (%)	34.6 ± 9.0	35.3 ± 8.6	0.703
ECM BCM	1.24 ± 0.57	1.27 ± 0.54	0.823
ICW (%)	52.4 ± 15.1	50.9 ± 12.3	0.643
ECW (%)	48.0 ± 13.7	49.0 ± 12.3	0.728
TBW (%)	100 ± 0	100 ± 0	1
TBW lean (%)	73.0 ± 3.5	73.2 ± 2.36	0.834
TBW TW (%)	47.8 ± 7.3	47.4 ± 6.9	0.799

TG: triglycerides, HDL: high density lipoprotein, LDL: low density lipoprotein BMR: basal metabolic rate; CIMT: carotis intima media thickness, BCM: body cell mass, ECM: extracellular mass, BM: body mass, ECM/BCM: extracellular mass / intracellular mass, ICW: intracellular water, ECW: extracellular water TBW: total body water TW: total weight, TBW/TW: total body water/total weight, BMI: body mass index (kg / m²).

were reported as counts and percentages. The significance of the differences between the groups was determined using an independent *t*-test for normal distributions, and by the Mann-Whitney U test for abnormal distributions. A *p* value of less than 0.05 was accepted as statistically significant.

Results

The study was conducted in 80 females, with an age range of 38–58 years, who were divided into two groups: "premenopausal" (n = 40) and "postmenopausal" (n = 40) women. The mean age of the premenopausal women was 45.1 ± 4.1 years, and the mean age of the postmenopausal women was statistically significantly higher at 51.2 ± 3.9 years (*p* < 0.001) (Table 1).

The average BMI was 30.3 ± 4.9 kg/m² in premenopausal women, and 29.2 ± 3.7 kg/m² in postmenopausal women; the difference between the two groups was not statistically significant (*p* = 0.269) (Table 1).

The right CIMT of the postmenopausal group was significantly higher than that of the premenopausal group (*p* < 0.001). The left CIMT of the postmenopausal group was significantly higher than that of the premenopausal group (*p* < 0.001).

Although the BFR was higher in the postmenopausal women (35.3 ± 9.0) than in the premenopausal women, this difference was not statistically significant (*p* > 0.05). The anthropometric measurements made by BIA showed no statistically significant differences between premenopausal and postmenopausal women. However, BMR decreased in postmenopausal women (*p* < 0.01).

There was not a correlation between BMR and CIMT in the premenopausal group. In the postmenopausal group, a negative and statistically significant correlation was observed between BMR and left CIMT (*p* = 0.025, *r* = -0.354) (Figure 1), and between BMR and right CIMT (*p* = 0.015, *r* = -0.381) (Figure 2).

Discussion

Although menopause is a point in the climacterium between the last days of the female reproductive period and the beginning of old age, it is one of the most important turning points in women's lives. An increase in life expectancy and standards in recent years signifies that many postmenopausal women seek help for the elimination of menopausal symptoms. In particular, the increase in the risk of CVD that is emerging during the late period of climacterium, and which was the main subject of the present study, is a serious problem affecting mortality and morbidity.

The recently developed BIA method is based on the detection of a weak electrical current permeability in the human body. The resulting permeability findings, body fat amount, BFR, LBM, TBW amount, and ratio, can be determined using the relevant formulas [15, 16]. Previous studies have shown that data obtained via BIA are similar to those obtained with complex methods (e.g., densitometry and calculation of TBW) [15, 17, 18]. However, BIA is not a reference method for the evaluation of body composition. It is highly reliable and valid in a variety of populations, such as the elderly, athletes, children, and young people, but error sources affecting reactance and impedance values cannot be entirely determined during measure-
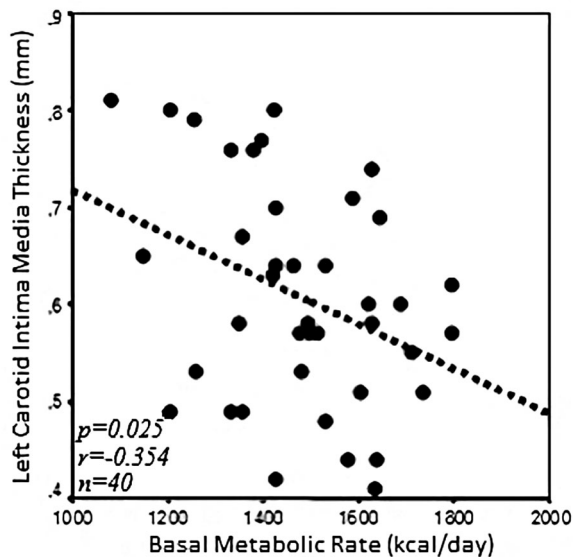
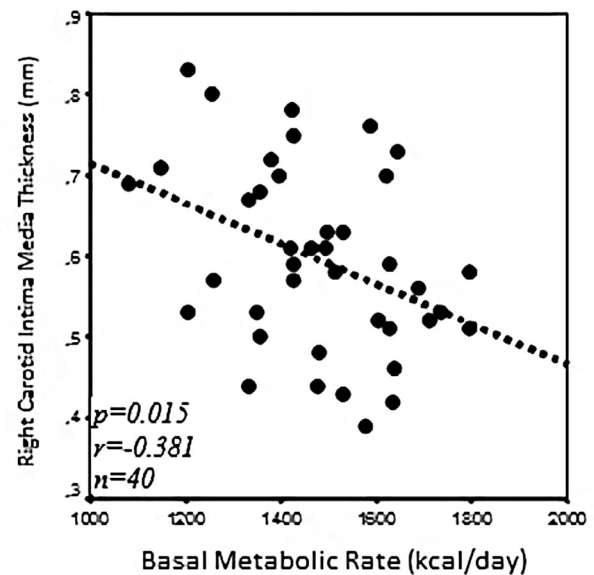Figure 1. — In postmenopausal group, BMR and left CIMT correlated figure.

Figure 2. — In postmenopausal group, BMR and right CIMT correlated figure.

ments [19, 20]. Measurements made at different times of the day, characteristics of electrode placement position, skin temperature, exercise, food, and postural changes are factors that affect BIA [21-23]. A proximal placement of the electrodes for the hand and foot that is incorrect by 1 cm can change resistance measuring by 2.1%, and incorrect placement in both extremities can double the change in impedance measurements (4.1%) [24]. Tanaka *et al.* [11] stated that the predictive accuracy of BIA in postmenopausal women is not inferior to that in premenopausal women. Practical methods that can generate accurate results and can be used in detecting and monitoring changes that occur in body composition are required. Following the evaluation of the literature, and the results of the present study, it is believed that BIA is useful in this group of women.

Most human energy is spent on basal metabolism; 12% of 24 hours' energy is used in physical activity, 73% in BMR, and 15% is used in thermal efficiency. BMR is calculated by the formula of lean body mass [25]. The present BIA device creates its own calculations after impedance has been determined, and the mean BMR measured by BIA in postmenopausal women was significantly lower than in premenopausal women in this study. The body structures of both groups were similar, thus this study has implications for the BMR evaluation stage.

Wakatsuki *et al.* [26] studied three groups consisting of premenopausal women, postmenopausal women, and women in surgical menopause. It was found that LDL levels were higher in the postmenopausal and surgical menopause groups; the authors did not observe a statistically significant difference in HDL levels between the three groups. We compared blood lipid profiles and found that LDL and triglyceride values were increased in postmenopausal women compared with the premenopausal group. We found a significant decrease in the values of HDL in the postmenopausal group.

In the present study, we detected significantly increased CIMT in both the right and left common carotid artery in postmenopausal women compared to the premenopausal group. The presence of subclinical atherosclerosis in the coronary arteries can be reliably predicted with CIMT measurements; the B-mode ultrasound method is relatively safe and inexpensive. The increase in intima-media ratio is an independent risk factor for future myocardial infarction and stroke [27]. Kim *et al.* [28] examined the relationship between subclinical atherosclerosis and risk factors such as BMI, smoking, hypertension, and triglycerides, in premenopausal and postmenopausal women, and reported that premenopausal risk factors are closely associated with subclinical atherosclerosis. Although the present study groups did not have these risk factors, the increase in CIMT in the women in the postmenopausal group appeared to increase the risk of the development of subclinical atherosclerosis.

In their study identifying atherosclerosis in the early stages, Anand *et al.* [29] observed that CIMT is an indication of subclinical coronary artery disease that would be possible to evaluate with ultrasonography of the carotid artery, while Ruby *et al.* [30] reported that the increase of CIMT is an independent indication of subclinical atherosclerosis. In the present study, the authors aimed to identify the single most influential factor for CIMT in the postmenopausal period, and they observed a negative correlation between BMR and both left and right CIMT.

Linear regression analysis showed that the most influential factor for CIMT is BMR, and the authors concluded that one of the most important causes of subclinical atherosclerosis in postmenopausal women may be a decrease in BMR.

The authors did not coincide any study that associates basal metabolic rate with subclinical atherosclerosis directly. Although it is difficult to generalise the findings of this study, due to its single-centre design, small sampling size and single evaluation with BIA, the fact that a reduction in BMR was associated with an increase in CIMT in postmenopausal women due to an independent relationship between them may be an important factor in the etiopathogenesis of subclinical atherosclerosis. Hence the authors concluded that BIA may be a useful adjunctive tool for early detection of subclinical atherosclerosis in postmenopausal women. However, there is a requirement for clinical studies in larger groups to elucidate the pathophysiological role of BMR in subclinical atherosclerosis.

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