STUDY ON CEREBROVASCULAR ATHEROSCLEROSIS AND ITS ASSOCIATED FACTORS ON MENOPAUSAL WOMEN BASED ON RHEOENCEPHALOGRAPHY

Nguyen Hoang Tin[1,*], Phung Minh Thu[1], Vo Thi Trang[2], Banh Thi Ngoc Truc[1]

1. Can Tho University of Medicine and Pharmacy, Vietnam

2. Can Tho University of Medicine and Pharmacy Hospital, Vietnam

**Corresponding author: nhtin@ctump.edu.vn*

ABSTRACT

Background: *Population aging puts increasing pressure on the health care support for menopausal women. Menopausal women have a low level of circulating estrogens, leading to increased cardiovascular risks in general and cerebrovascular atherosclerosis in particular. The evaluation of brain circulation by rheoencephalography is one of the scientific community's interests because of its ease of implementation, low cost and non-invasiveness.* ***Objectives:*** *To evaluate cerebrovascular atherosclerotic status in menopausal women and investigate some associated factors through wave-form characteristics and parameters by rheoencephalography.* ***Materials and methods:*** *The descriptive cross-sectional study was conducted on 80 menopausal women. They were measured frontal-occipital lead of rheoencephalography by 5000 Vasoscreen machine - Medis branch (Germany).* ***Results:*** *Menopausal women had an increase in vascular tone of 67.5% (right) and 65.0% (left). Besides, the percentage decrease in blood flow's intensity accounted for 16.2% (right) and 13.8% (left). The rate of increase in vascular tone and decrease in blood flow intensity did not have a statistically significant relationship with lifestyle and body mass index. The rate of vascular hypertonia was highest in the group having a habit of eating red meat, the difference was statistically significant only in the left hemisphere ($p<0.05$). The rate of vascular hypertonia on menopausal women with central obesity was higher than that of the remaining group in both hemispheres ($p<0.05$).* ***Conclusions:*** *Menopausal women may face cerebrovascular atherosclerosis. Women who consume a lot of red meat had the highest rate of left vascular hypertonia. Central obesity may increase the risk of getting vascular hypertonia 3.75 times on the right hemisphere and 5.44 times on the left hemisphere of the brain.*

Keywords*: Rheoencephalography, Menopausal women, Cerebrovascular atherosclerosis.*

I. INTRODUCTION

In advanced countries, the woman is predicted to spend about one-third of her life on postmenopause. Life expectancy has also increased significantly for those ones [6]. Vietnamese women are expected to go through menopause by 1/4 to 1/3 of their life. During menopause, there is a marked increase in the percentage of android fat and a decrease in the

gynoid fat ratio. This is considered as a risk factor for coronary heart disease. Obese women with high BMI had higher estradiol and estrone levels than lean ones with low BMI. Levels of FSH and LH are negatively correlated with BMI. The risk of cardiovascular disease will increase if the woman has a family history, smoking, hypertension, diabetes, and stress. The American Heart Association estimates that physically inactive people are twice as likely to have cardiovascular disease as physically active people. There is a negative correlation between physical activity and estrone levels [14]. Currently, the assessment of cerebral vascular injury is mainly through Doppler ultrasound of cerebral blood vessels as it is non-invasive and allows a fairly accurate diagnosis of morphology and hemodynamics. Still, vascular Doppler ultrasound requires the experience of the sonographer, the cost is relatively expensive and only available in a few specialized medical facilities. Plus, the implementation process is quite time-consuming and not suitable for screening. Reoencephalography (REG) is a method that has great value in assessing the cerebrovascular status and cerebral circulation. This is also a non-invasive technique, which is easy to perform and can be used for continuous measurement in the diagnosis of cerebral atherosclerosis [2], [3]. Surveys for early detection and assessment of cerebral atherosclerotic lesions through assessment of cerebral circulation in our country are still of little interest, especially in the South of Vietnam in general and the Mekong Delta in particular [7], [12]. A REG study in patients with metabolic syndrome in Can Tho city - one of five large cities in Vietnam showed that female patients had a higher rate of vascular hypertonia than men [12]. Therefore, we aimed to evaluate cerebrovascular atherosclerotic status in menopausal women and investigate some associated factors through wave-form characteristics and parameters by rheoencephalography.

II. MATERIALS AND METHODS

2.1. Study population

All women reaching menopause, living in Can Tho city or some provinces of Mekong Delta, going to a general health check-up or being counseled by a clinic doctor to measure REG during the study period may have or may not have any symptoms of cerebral circulatory insufficiency.

2.1.1. Inclusion criteria

Women have gone through natural menopause when they were 40-55 years old, have had amenorrhea for 2 years and were willing to participate in the study.

2.1.2. Exclusion criteria

History of gynecological conditions such as hysterectomy, oophorectomy, severe trauma or taking any hormone medication. History of cerebrovascular diseases such as cerebral infarction, cerebral hemorrhage, non-atherosclerotic carotid stenosis (aneurysm, arteritis, arterial dissection, vasospasm, tissue damage after radiation therapy...) or taking any medications that can cause vasodilation or vasoconstriction. The ones who were being in the acute phase of a medical condition or had serious comorbidities. The patients had a mental illness. The patients did not cooperate well.

2.1.3. Study setting and time

The study was conducted in REG room of Department of Functional Diagnosis - Can Tho University of Medicine and Pharmacy Hospital. The research period was from January 2020 to December 2020, which was also the period of the worldwide outbreak of Covid-19 pandemic.

2.2. Methods

2.2.1. Study design: a descriptive cross-sectional study.

2.2.2. Study size: 80 patients.

2.2.3. Sampling method: subjects were invited to participate in the study by convenience sampling during the study period until the number of subjects was sufficient.

2.2.4. Study contents

According to Ronkin (1976), evaluation of cerebrovascular atherosclerotic status on menopausal women was based on criteria of increased vascular tone and decreased blood flow intensity on cerebral blood flow. Vascular hypertonia: wave-form criteria combined with 2/3 of the remaining hemodynamic parameters (non edge-sharp peak and blurred or disappear subwave, crest time >230ms, propagation time < 140ms, alpha/ T ratio >25%). Status of hypointensity: there are both criteria of alternating blood flow <22%/min and impedance ratio <0.7‰ [8].

Investigating some factors associated to the cerebrovascular atherosclerosis: life-style (sedentary, infrequently active, regularly active); protein eating habits (vegetarian, red meat, white meat); BMI: calculated according to the formula BMI=[weight(kg)]/ [height(m)]^2, unit: kg/m^2, WHO classification applicable to Asian adults (thin: <18.5kg/ m^2, normal: 18.5-22.9kg/m^2, overweight: 23-24.9kg/m^2, obese: ≥25kg/m^2); Central obesity: diagnosed according to the WHO classification for Asians with increased waist circumference (>80cm) or increased waist-hip ratio (WHR >0.85).

2.2.5. Study materials

VasoScreen 5000 impedance cerebral blood flow meter, Medis-Germany. The machine was the REG II model (2nd generation cerebral blood flow recorder). Dual channel meter (left, right) with one ECG channel. Measurement method: 6 electrodes including 2 emitters and 4 receivers. Transmitter current: using alternating current with a high frequency of 100kHz and a small strength of 1mA and aluminum round electrode, diameter 2cm (8 pieces). Convention: red electrode wire was right, yellow was left. Recording, printing, and storing the measured blood flow parameters to a computer via CardioVascular Lab software. Selecting pulse wave analysis by impedance plethysmography method.

2.2.6. Statistical analysis

All of the data obtained from the research were processed with SPSS 20.0 software according to medical statistics methods. Qualitative variables were presented as frequencies and percentages. To compare the proportional difference between 2 or more groups, we used the Chi-squared test (χ^2) with statistical significance determined when $p \leq 0.05$. Odds ratio (OR) and confidence interval (CI 95%) were used when testing the association between 2 qualitative variables, applied to the 2x2 table.

2.2.7. Ethics approval

All research subjects were explained specifically about the research purpose and methods so that the patients agreed to voluntarily participate and cooperate well in the research process. Patients had the right to refuse to participate in the study or to terminate the study at any stage of the study. All information of study subjects was kept confidential and only used for research purposes. All information was provided to the individual patient only and was accessible only to the researcher. In addition, this study did not have any intervention affecting the patient's health and psychotherapy.

III. RESULTS

Table 1. The cerebrovascular atherosclerosis on menopausal women

Position	Abnormal REG	Number (n=80)	Percentage (%)
Right	Increased vascular tone	54	67.5
	Low-intensity of blood flow	13	16.2
Left	Increased vascular tone	52	65.0
	Low-intensity of blood flow	11	13.8

The proportion of increased vascular tone was up to 67.5% on the right and 65.0% on the left hemisphere of the brain.

Table 2. The association of lifestyle and cerebrovascular atherosclerosis

Lifestyle	Right hemisphere of the brain		Left hemisphere of the brain	
	Increased vascular tone n (%)	Low-intensity of blood flow n (%)	Increased vascular tone n (%)	Low-intensity of blood flow n (%)
Sedentary (n=17)	11 (64.7)	4 (23.5)	10 (58.8)	4 (23.5)
Infrequently active (n=34)	21 (61.8)	5 (14.7)	21 (61.8)	6 (17.6)
Regularly active (n=29)	22 (75.9)	4 (13.8)	21 (72.4)	1 (3.4)
p	0.474	0.654	0.565	0.111

The rates of increase in vascular tone and decrease in blood flow's intensity did not have a statistically significant relationship with lifestyle of menopausal women.

Table 3. The association of protein eating habits and cerebrovascular atherosclerosis

Protein eating habits	Right hemisphere of the brain		Left hemisphere of the brain	
	Increased vascular tone n (%)	Low-intensity of blood flow n (%)	Increased vascular tone n (%)	Low-intensity of blood flow n (%)
Red meat (n=22)	18 (81.8)	7 (31.8)	19 (86.4)	6 (27.3)
White meat (n=54)	33 (61.1)	6 (11.1)	31 (57.4)	5 (9.3)
Vegetarian (n=4)	3 (75.0)	0 (0.0)	2 (50.0)	0 (0.0)
p	0.206	0.057	**0.046**	0.084

Table 4. The association of body mass index and cerebrovascular atherosclerosis

Body mass index	Right hemisphere of the brain		Left hemisphere of the brain	
	Increased vascular tone n (%)	Low-intensity of blood flow n (%)	Increased vascular tone n (%)	Increased vascular tone n (%)
Obese (n=38)	25 (65.8)	5 (13.2)	Obese (n=38)	25 (65.8)
Overweight (n=20)	16 (80.0)	6 (30.0)	Overweight (n=20)	16 (80.0)
Thin or normal (n=22)	13 (59.1)	2 (9.1)	Thin or normal (n=22)	13 (59.1)
p	0.335	0.144	p	0.335

Menopausal women with the habit of eating red meat had the highest rates of increased vascular tone and decreased blood flow, a statistically significant difference was only found when assessing the rate of increased vascular tone on left pons.

Table 5. The association of central obesity and cerebrovascular atherosclerosis

Central obesity	Right hemisphere of the brain		Left hemisphere of the brain	
	Increased vascular tone n (%)	Low-intensity of blood flow n (%)	Increased vascular tone n (%)	Low-intensity of blood flow n (%)
Yes (n=70)	50 (71.4)	12 (17.1)	49 (70.0)	10 (14.3)
No (n=10)	4 (40.0)	1 (10.0)	3 (30.0)	1 (10.0)
p	**0.047***	0.567	**0.013****	0.713

**: OR=3.75, CI95%=0.96-14.72; **: OR=5.44, CI95%=1.28-23.12*

The risks of getting vascular hypertonia in group of women with central obesity on the right and left hemisphere of the brain were 3.75 times and 5.44 times higher than that of the remaining group, respectively.

IV. DISCUSSION

4.1. Cerebrovascular atherosclerotic status on menopausal women

Throughout the study, we found out that menopausal women had an increased rates of the bilateral hemispheric vascular tone of 67.5% (right) and 65.0% (left), the rates of a decreased intensity of blood flow were 16.2% (right) and 13.8% (left). A study in patients with metabolic syndrome also showed a higher rate of increase in vascular tone and decrease in intensity of blood flow in both hemispheres were higher than the control group in all 3 leads of REG [12]. The study in hypertensive patients also gave similar results, the rates of increased vascular tone in 3 leads (forehead - mastoid, mastoid - occipital, frontal - occipital) were 54%, 58% and 58%, respectively. The rates of low-intensity of blood flow were 50%, 48% and 38%, respectively [5]. As for patients with type 2 diabetes, the study showed that vascular tone in the group of patients was higher than the general population ($p<0.01$), clearly expressed in parameters of propagation time and alpha/T ratio. The blood flow's intensity in the group of patients was lower than that of normal people ($p<0.01$), clearly expressed in alternating blood flow parameters [7]. The study in patients with cerebral artery stenosis showed that the rate of increase in vascular tone was 76.5%, the rate of decrease in blood flow's intensity was 70.6%, the rate suggestive of atherosclerosis on REG was 36.4% [9]. Thus, it can be seen that the great role of REG in the diagnosis of atherosclerosis in different subjects is shown by the increase in vascular tone and decrease in blood flow's intensity on both hemispheres of the brain. The results of each study on different disease groups had differences. Perez and Guijarro suggested that cerebral blood flow was also influenced by the thick-ness of the scalp and by extracranial circulation [10].

4.2. Some factors associated with the cerebrovascular atherosclerosis

Our study showed that the rate of increase in vascular tone and the rate of de-crease in blood flow's intensity on menopausal women did not have a statistically significant relationship with lifestyle. Although the highest rate of increase in vascular tone occurred on menopausal women with a habit of eating red meat, the difference was statistically significant only in the left hemisphere ($p<0.05$). A study on patients with metabolic syndrome has not yet found an association between physical activity and an increase in

vascular tone on cerebral blood flow, but it showed that physical activity somewhat improved atherosclerosis in this group of patients [12]. Thus, the studies had not found a relationship between lifestyle and cerebral blood flow, possibly because the exploitation of information about habits was not able to comprehensively assess the treatment intensity and effectiveness. Physical activity improved general well-being and also had a positive effect on disorders of metabolic syndrome, reducing obesity and increasing insulin sensitivity [1].

Besides, we did not find a relationship between the BMI of menopausal women with changes in cerebral blood flow in both sides of the hemisphere. Research on hypertensive patients also did not record the association between overweight-obesity with decreased cerebral vascularity and increased cerebral vascular hypertonicity in all three leads [5]. In patients with type 2 diabetes, the rate of cerebral atherosclerosis in the obese group accounted for 78.9%, which was 1.2 times higher than that of the non-obese group. However, the research also did not find a statistically significant difference between the two groups [7]. Thus, studies in different patient populations showed that obesity was not associated with disorders on cerebral blood flow. The study of the average thickness of the carotid intima-media layers also did not find a difference between the overweight-obese BMI group and the normal BMI group [11]. However, the link between obesity and vascular complications has been proven. Research showed that obesity not only caused insulin resistance and diabetes but also participated in lipid metabolism disorders, leading to atherosclerosis, promote inflammation and enhance atherogenesis independent of the effects of insulin resistance [15].

Notably, we also found that the rate of vascular tone increase in the group of women with central obesity was higher than that in the group without central obesity meanwhile we evaluated in both hemispheres of the brain ($p<0.05$). Central obesity was associated with a 3.75 times increase in the risk of right cerebral vascular tone and 5.44 times increase in the risk of left one. In another study, the rate of increased vascular tone on cerebral blood flow in central obese patients with metabolic syndrome was higher than the group without central obesity at fronto - masoidal leads, comparable in the mastoid - occipital leads, and lower in the fronto - occipital leads ($p>0.05$) [12]. This difference may happen because patients with metabolic syndrome had a very high rate of central obesity, as central obesity was also one of the diagnostic criteria for metabolic syn-drome according to the National Cholesterol Education Program Adult Treatment Panel - III report of 2001 (updated in 2004) with a cut-off waist point for Asians [4]. With a small sample size, the difference between groups with and without central obesity may not be clear. The study about the average thickness of the common carotid intima-media layer in patients with metabolic syndrome showed no correlation with BMI but a positive correlation with waist circumference and the waist-hip ratio [13]. This result was similar to our study, the cerebrovascular atherosclerosis status in menopausal women, in spite of not being related to BMI, was positively associated with central obesity, diagnosed based on waist circumference and WHR.

V. CONCLUSIONS

Menopausal women may face with cerebrovascular atherosclerosis in both hemispheres. The group of menopausal patients who consume a lot of red meat has the highest rate of left vascular hypertonia. Central obesity may increase the risk of getting vascular hypertonia 3.75 times on the right hemisphere and 5.44 times on the left hemisphere of the brain.

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