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Evaluation of the Relationship between Hot Flashes and Night Sweats and Severity of Coronary Artery Disease in Postmenopausal Women

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ABSTRACT

Introduction: Hot flashes (HF) and night sweats (NS) are due to vasomotor instability and could be recognized as cardiovascular risk markers. Therefore, this study aimed to evaluate the relationship between vasomotor instability and severity of coronary artery disease (CAD) in postmenopausal women.

Materials and Methods: This observational cross sectional study, was performed in Chamran Hospital, Isfahan University of medical sciences, Isfahan, Iran from 2011-2012. In this study, women within the age range of 45-60 years with angiography documented CAD were enrolled. Participants included 25 women with hot flashes, night sweats, or both and 17 women without these symptoms, respectively. In all participants, levels of follicular stimulating hormone/luteinizing hormone (FSH/LH) were measured. The severity of CAD was calculated using Gensini score. In order to evaluate the relationship between severity of CAD and other variables, Gensini scores lower than 50 and ≥50 were considered as low and high Gensini scores, respectively. Moreover, data analysis was performed using SPSS version 15.0.

Results: Our findings demonstrated that NS and HF were not associated with severity of CAD, determined by Gensini scores (P-values>0.05). However, a significant positive relationship was observed between FSH levels and severity of CAD in all participants (P=0.048). In cases in low Gensini score group, the relationship between LH and Gensini score was negative and non-significant, while Gensini score showed a positive and non-significant relationship (P-value> 0.05).

Conclusion: No significant association was observed between vasomotor symptoms of menopause and the severity of CAD. In addition, elevated FSH levels could be considered as a marker of severity of CAD.

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Introduction

It has been known that the majority of postmenopausal women experience common symptoms, including hot flashes (HF) and night sweats (NS), which are attributed to vasomotor instability(1). Estrogen alters vasomotor stability and menopausal symptoms are associated with tapered plasma estrogen levels. These symptoms might last from months to years, with HF

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occurring in about 80% of postmenopausal women and lasting for more than five years in one third of these females (2, 3). While the etiology of the mentioned symptoms remains not fully known, vascular changes were proposed as major causes (4-6).

Vasomotor menopausal symptoms (VMS) have adverse effects on cardiovascular risk factors (7) and are suggested as cardiovascular risk markers in postmenopausal women. Postmenopausal women, who experience VMS, often have higher blood pressure, body mass index, total cholesterol level, as well as low-density lipoprotein, triglyceride, waste-to-hip ratio, and blood glucose, compared to women without these symptoms (7, 8). VMS in Middle-aged women is associated with increased coronary artery and aorta calcification and decreased flow-mediated dilatation (7, 9). Most of these findings are derived from clinical trials, such as the study of women's health across the nation (SWAN).

The main clinical indication for hormone replacement therapy (HRT) is the treatment of these symptoms, which might lead to reduced quality of life in postmenopausal women (9). Among the women who undergo HRT, cardiovascular diseases are more prevalent in older females with HF, compared to those without these symptoms(10). This predisposition especially affects women at the first year of initiation of HRT (10).

Evidence suggests that women with symptoms of vasomotor instability have lower blood antioxidant levels, compared to those without these symptoms, parallel with the progression of atherosclerosis (11, 12). However, consumption of antioxidants could be accompanied with the improvement of HF and NS (13). Different plasma estrogen levels might be observed in post-menopausal women with chronic symptoms of vasomotor instability, alongside with protective effects on endothelial cells, compared to those without these symptoms (10). Estrogen metabolism and action (endogenous and exogenous) are also different in these cases (14, 15).

Severity of coronary artery disease (CAD) is an indicator of the involvement of total coronary artery vasculature, assessed by various methods including Gensini score. This scoring system is broadly and easily used, in which coronary artery is divided into eight segments with multiplication scores based on the location (proximal, middle, and distal). CAD is one of the leading causes of mortality in women (8). Due to the association between the presence of VMS and the involvement of coronary arteries, this study aimed to evaluate the relationship between VMS and the severity of CAD in postmenopausal women.

Materials and Methods

This observational cross-sectional study, was performed in Chamran Hospital, Isfahan University of medical sciences, Isfahan, Iran from 2011-2012. In this study, post-menopausal women within the age range of 45-60 years with angiography documented CAD were enrolled. CAD is defined as greater than 75% narrowing of coronary arteries. Meanwhile, menopause is the absence of menstrual periods for one year in women without a prior hysterectomy and bilateral oophorectomy. Participants included 25 women with hot flashes, night sweats, or both and 17 women without these symptoms, respectively. Exclusion criteria were uncontrolled diabetes, malignancy, neurologic diseases, infectious disea-ses, hyperthyroidism, and a history of hormone therapy. To collect data regarding the presence or absence of HF and NS, the following questions were asked: "Do you have difficulties with NS/HF?" and "Have you experienced HF and NS episodes in the past?" Afterwards, self-reports of VMS were gathered and plasma FSH and LH levels were measured by FSH and LH ELISA kits (Pishtaz Teb Diagnostic) in all the participants before angiography. Moreover, the severity of CAD was measured using Gensini scores based on the location and significance of the involved coronary artery (16). In order to evaluate the relationship between severity of CAD and other variables, Gensini scores lower than 50 and ≥50 were considered as low and high Gensini scores, respectively. Moreover, data analysis was performed using SPSS version 15.0.

Statistical analysis

In this study, statistical analysis was performed using SPSS version 15.0 (SPSS Inc., Chicago, IL, USA). A two-tailed P-value of less than 0.05 was considered statistically significant. Qualitative variables were expressed as percentage and were compared between the study groups using chi-square test or Fisher exact test where appropriate. On the other hand, quantitative variables were expressed as mean± standard deviation and were compared between the groups using Mann-Whitney U and independent t-test. In addition, Pearson's correlation coefficient was applied to evaluate the relationship between factors.

Results

In total, 42 women with CAD were enrolled in the study, 25 (59.5%) of which had VMS and 17 (4.05%) had no VMS. In addition, 23 (54.8%) and 22 (52.4%) of the subjects had a history of HF and NS, respectively. Mean Gensini scores, as well as mean levels of LH and FSH were 40.9±40.82, 16.32±8.19, and 27.03±13.02, respectively.

Mean LH levels in asymptomatic and symptomatic women were 15.4±7.5 versus 16.9±8.7, respectively, which was indicative of no

significant difference between the two groups (P=0.577). Meanwhile, mean FSH levels in asymptomatic and symptomatic groups were 23.9±12.5 and 32.1±12.6, respectively, which demonstrated significant difference between the study groups (P=0.048). (Table 1).

Table 1. Statistical analysis of clinical parameters

Parameter	Gensini score		P-value
	<50	>=50	
Hot flashes (yes)	15(57.7%)	8(50.0%)	0.627
Night sweets (yes)	14(53.8%)	8(50.0%)	0.808
LH	16.9±8.7	15.4±7.5	0.577
FSH	23.9±12.5	32.1±12.6	0.048

Based on Pearson's correlation coefficient values, Gensini scores and LH levels in Low Gensini and high Gensini groups were -0.046 and 0.362, respectively. However, none of the obtained values were significant. In cases in low Gensini score group, the relationship between LH and Gensini score was negative and non-significant, while Gensini score showed a positive and non-significant relationship. Further, Gensini scores and FSH levels in the Low Gensini and high Gensini groups were reported to be -0.076 and 0.26, respectively, based on Pearson's correlation coefficient; nevertheless, none of the mentioned values were significant or positive (Table 2).

Table 2. Evaluation of the relationship between Gensini score and levels of LH/FH in separate groups and in study population by Pearson correlation coefficient

Low Gensini score	LH	R	-0.046
		P-value	0.823
	FSH	R	-0.076
		P-value	0.713
High Gensini score	LH	R	0.362
		P-value	0.168
	FSH	R	0.260
		P-value	0.332
Total	LH	R	0.01
		P-value	0.959
	FSH	R	0.315
		P-value	0.042

In total, Pearson's correlation coefficient between Gepnsini score and LH was 0.01, which was considered non-significant (P=0.959). On the other hand, Pearson's correlation coefficient between Gensini score and FSH was 0.315, which was significant (P=0.048) (Table 2).

Discussion

According to the results of the present study, no significant relationship was observed between the severity of CAD and variables of NS and HF. While HF/NS could be considered as cardiovascular markers, they have no such influence on the severity of CAD.

In the current research, mean age of menopause was 50-51 years, and HF/NS lasted for 2-5 years in postmenopausal women. These variables are some of the major physical symptoms of menopause; however, their prevalence, severity, and duration might significantly vary. In addition, they are associated with endocrine profile, caused by low levels of estrogen and increased sympathetic outflow in symptomatic women (7). While a significant association has been reported between HF/NS and the progression of atherosclerosis, our findings were indicative of no relationship between the severity of CAD and HF/NS symptoms.

In terms of chemical markers of menopause, a positive and significant relationship was observed between FSH levels and the severity of atherosclerosis in all the participants. Nevertheless, this marker failed to show such association in the separate analysis of the groups. Conversely, LH levels had a significant reverse association with Gensini scores in all the samples. In addition, a negative relationship was observed between the severity of atherosclerosis in cases with CAD and those with normal coronary angiography after group separation.

Increased levels of FSH/LH during menopause could change response to divesting estrogen level through a hormonal seesaw mechanism. According to our findings, the levels of FSH and LH were higher in patients aged 60-89 years with CAD, compared to normal cases within the same age range. This hormonal imbalance is considered as a risk factor for CAD at the late stages of life (17). The positive relationship between FSH and severity of atherosclerosis in our data indirectly reflects the association between pronounced estrogen drop and severity of CAD. The results of the current study suggested that enhanced circulating concentration of FSH could be regarded as a marker of the severity of CAD. In other words, increased FSH levels might be known as a risk factor for the development and progression of atherosclerosis. Major drawbacks of this study were small sample and low effect sizes. Therefore, it is recommended that further studies be conducted to clearly demonstrate the relationship between VMS and the severity of CAD.

Conclusion

The results were indicative of no significant association between VMS, such as HF and NS, and the severity of CAD. However, elevated FSH levels could be considered as a marker of the severity of CAD.

Conflict of Interest

The authors declare no conflicts of interest.

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