International Journal of Cardiovascular Sciences. 2018;31(1)4-11

ORIGINAL ARTICLE

Cardiovascular Risk Factors in Climacteric Women with Coronary Artery Disease

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Abstract

Background: The increased incidence of cardiovascular disease in women occurs during the climacteric period, especially after menopause.

Objective: The aim of this study was to identify risk factors among climacteric women with and without coronary artery disease (CAD).

Method: This cross-sectional study was performed in the Catheterization Laboratory at the Federal University Hospital of Maranhão, in the Northeast region of Brazil, between March 2012 and July 2013. We included 31 climacteric women who went to the care center for cardiac catheterization. They were divided into groups after catheterization results: Group I (with DAC) and Group II (without CAD). Statistical analysis: Categorical variables were described by means of frequencies and percentages, numerical variables by mean ± standard deviation or median (Quartile.3 - Quartile.1); the Shapiro-Wilk test was used to verify the normality of quantitative data. Fisher's exact test was used for categorical data comparisons. For continuous data, we used Student's test or the Mann-Whitney for unpaired samples; statistical significance was set at $p < 0.05$.

Results: We evaluated groups with CAD (n = 13) and without CAD (n = 18). The results showed a mean age between the groups of 57.92 ± 5.15 and 51.72 ± 4.63 years, respectively. Among the cardiovascular risk factors, the most prevalent among women with CAD were menopause (84.62%), systemic arterial hypertension (SAH) (69.23%) and sedentary life style (69.23%).

Conclusion: We concluded that, in addition to menopause itself, SAH and sedentary lifestyle were the most prevalent cardiovascular risk factors among women with CAD. (Int J Cardiovasc Sci. 2018;31(1)4-11)

Keywords: Cardiovascular Diseases; Coronary Artery Disease; Risk Factors; Women; Climacteric; Hypertension; Sedentary Lifestyle.

Introduction

The increase of Coronary Artery Disease (CAD) incidence in females, especially in the climacteric period, is related to hormonal, circulatory, and blood alterations that occur in women. These alterations are notoriously implicated in the genesis and progression of cardiovascular disease, which, in turn, constitutes the main cause of mortality among the middle-age population.[1] In the female aging process, alterations occur in the metabolic profile which modify adipose tissue composition and distribution, thus favoring weight gain and the progression of possible atherosclerotic processes.[2]

Among the main risk factors for cardiovascular diseases are: age, obesity, smoking, systemic arterial hypertension (SAH), dyslipidemia, diabetes mellitus (DM), family history, stress, and a sedentary lifestyle.[3] The body's exposure to these cardiovascular risk factors favors the development of the endothelial dysfunction process.[4]

Early detection of cardiovascular risk factors in climacteric women helps reduce morbidity and mortality

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DOI: 10.5935/2359-4802.20170056

Manuscript received on December 15, 2016; revised on January 31, 2017; accepted on April 17, 2017.

in this group. Thus, the objective of the present study was to identify cardiovascular risk factors among climacteric women with or without CAD.

Methods

This was a cross-sectional analytical study carried out in the Catheterization Laboratory of the University Hospital Presidente Dutra (HUPD), from the Federal University *Universidade Federal do Maranhão*, in Brazil. It is an intervention and imaging diagnosis unit that is linked to the Cardiovascular Surgical Service of HUPD. Data were collected between March 2012 and July 2013, starting from the moment the patients checked in for cardiac catheterization. These exams had been previously booked by the patients who had a referral, as is required by the Catheterization Lab.

The selection took place consecutively, from the moment the patients checked in for their elective cardiac catheterization.

We included all climacteric patients, between 40 and 65 years of age (period of menopausal manifestation),[3] who underwent cardiac catheterization at the catheterization lab. All patients received information about the research and signed a free consent form approved by the Research Ethics Committee of the University Hospital of The Federal University of Maranhão (HUUFMA). Exclusion criteria included: patients on statins; those who underwent coronary angioplasty or myocardial revascularization; and previous history of acute myocardial infarction. We also excluded patients who refused to participate in the research, and those who, for different reasons, withdrew from the research protocol.

Once the sample was defined, the patients were divided into groups according to cardiac catheterization results: Group I – with CAD; and Group II – without CAD. CAD was defined as the presence of obstruction in the coronary arteries demonstrated by cardiac catheterization. Patients were considered menopausal when their last period had occurred 12 months or longer before the procedure.[5] None of the patients included in this study were on hormone therapy. Socio-demographic variables were: age; self-declared skin color; level of education; and household income.

We analysed the following variables, which are considered cardiovascular risk factors according to the I Brazilian Guideline for the Prevention of Cardiovascular Diseases in Climacteric Women:[3] SAH, dyslipidemia, and DM (based on previous medical diagnosis); and blood pressure (BP), physical activity; smoking; alcoholism; weight, height; body mass index (BMI), and waist circumference (WC) (data from the Protocol-Chart).

For biochemical exams, we adopted the following reference values, considered within normality for the lipid profile: total cholesterol below 200 mg/dl; high-density lipoprotein (HDL-c) above 50 mg/dl; low-density lipoprotein (LDL-c) below 130 mg/dl; triglycerides below 150 mg/dl; and fasting blood sugar levels below 100 mg/dl.[6]

On the same day catheterization was performed, we measured the patients' BP, took anthropometric measurements, and collected blood at a 12-hour fasting period, all at the same time, in this sequence, between 7 a.m. and 9 a.m.

Processing of blood samples for serum extraction was performed with samples kept at room temperature for 20 minutes (between 18 and 24° C, mean of 22° C) and later centrifuged for 10 minutes at 3000 rpm. All exams were analysed at the laboratory at HUUFMA.

Statistical analysis

Categorical variables were described through frequencies and percentages, and numeric ones through mean ± standard deviation or median (Quartile.3 – Quartile.1), depending on normality. The Shapiro-Wilk test was chosen to verify the normality of quantitative data. To compare categorical data, we used Fisher's Exact test, and for continuous data, we used Student's t-test or the Mann-Whitney for unpaired samples, depending on normality.

Statistical significance was set at $p < 0.05$, and statistical analyses were performed with the software Data Analysis and Statistical Software (STATA®) version 12.0.

The present study represents a substudy of a more comprehensive research called "Endothelial Dysfunction and Cardiovascular Risk Assessment in Climacteric Women", which has the approval of the Research Ethics Committee from Hospital Universitário da Universidade Federal do Maranhão, under protocol number 182/11, in accordance with Resolution 196/96 and its complementary from The National Health Council of Brazil (CNS/MS).

Results

We evaluated 31 climacteric women divided into 2 groups: Group I - with CAD (n = 13), and Group II – without CAD (n = 18). Mean age was 57.92 ± 5.17 and 51.72 ± 4.63,

respectively, varying between 44 and 63 years of age, with statistical significance (p = 0.001). Socio-demographic data in the general group showed a higher frequency of brown women (70.97%); with > 8 years of education (51.61%); with a household income ≤ two monthly minimum wages (58.06%) (Table 1).

Table 1 – Sociodemographic characteristics of climacteric women with or without CAD – HUUFMA, São Luís, Brazil, 2013

Sociodemographic characteristics	General		CAD				p-value
			Present		Absent		
Age (Mean ± Standard deviation)	54.32 ± 5.7		57.92 ± 5.17		51.72±4.63		0.001*
Level of education (%)							
≤ 8 years	15	48.39	6	46.15	9	50.00	0.833†
> 8 years	16	51.61	7	53.85	9	50.00	
Self-declared skin color (%)							
White	6	19.35	3	23.08	3	16.67	
Black	3	9.68	0	-	3	16.66	0.443‡
Brown	22	70.97	10	76.92	12	66.67	
Household income (%)							
≤ 2 Monthly minimum wage	18	58.06	10	76.92	8	44.44	0.074‡
> 2 Monthly minimum wage	13	41.94	3	23.08	10	55.56	

** Student's t test; † Chi-square test; ‡ Fisher's exact test; CAD: coronary artery disease; HUUFMA: Hospital Universitário da Universidade Federal do Maranhão.*

Regarding the presence of cardiovascular risk factors with a medical diagnosis established before data collection for the study, results showed, in Group I, a higher prevalence of SAH (69.23%), followed by DM (23.08%), and high cholesterol (15.38%). We observed elevated percentages of women who claimed they did not consume alcohol or smoke in both groups. We also saw that 69.23% of women with CAD and 61.11% of women without CAD did not practice daily physical activities (Table 2).

Regarding the climacteric period in women with and without CAD, menopause was present among both groups, with 84.62% and 66.67%, respectively (Table 2).

Patients with CAD presented higher BMI and WC in comparison to those without CAD; in general, the women presented alterations of these measurements, with means of 27.57% ± 4.55 kg / m^2 and 91.00 ± 10.28 cm, respectively. Systolic blood pressure (SBP) was altered in both groups (Table 2).

With regards to values of lab variables, among women with and without CAD, the means of fasting blood sugar levels, total cholesterol and triglycerides were higher in Group I. However, HDL-c and LDL-c results were similar in both groups, with HDL-c below normality (Table 3).

Discussion

In the present study, the golden standard was the identification of climacteric women diagnosed with CAD during the data collection period of the study, after cardiac catheterization.

In addition to menopause, other cardiovascular risk factors were present among women with and without CAD, the most prevalent of which were sedentary life-styles and SAH. Studies that included women suggest an association between endothelial dysfunction and several cardiovascular risk factors.[7-9]

The prevalence of SAH progressively increases with age, and this process occurs in women, especially at the beginning of the post-menopausal stage.[3]

Table 2 – Climacteric women with and without CAD regarding cardiovascular risk factors – HUUFMA. São Luís, Brazil, 2013

Variables	General		CAD				p-value
			Present		Absent		
	n	%	n	%	n	%	
SAH							
Absent	10	32.26	4	30.77	6	33.33	0.880*
Present	21	67.74	9	69.23	12	66.67	
Diabetes Mellitus							
Absent	27	87.10	10	76.92	17	94.44	0.151*
Present	4	12.90	3	23.08	1	5.56	
High Cholesterol							
Absent	22	70.97	11	84.63	11	61.11	0.155*
Present	9	29.03	2	15.38	7	38.89	
Alcoholism							
Absent	27	87.10	12	92.31	15	83.33	0.621*
Present	4	12.90	1	7.69	3	16.67	
Current smoking							
Absent	30	96.77	12	92.31	18	100	0.232*
Present	1	3.23	1	7.69	0	0	
Physical activity							
Absent	20	64.52	9	69.23	11	61.11	0.641*
Present	11	35.48	4	30.77	7	38.89	
Menopause							
Absent	8	25.81	2	15.38	6	33.33	0.260*
Present	23	74.19	11	84.62	12	66.67	
BMI (Mean ± Standard Deviation)	27.57 ± 4.55		28.04 ± 4.31		27.24 ± 4.81		0.636†
WC (Median; Q3 - Q1)	88 (101 - 86)		88 (101 - 88)		88 (92 - 85)		0.348‡
SBP (Median; Q3 - Q1)	135 (170 - 120)		135 (180 - 125)		135 (160 - 120)		0.400‡
DBP (Mean ± Standard Deviation)	84.74 ± 11.27		84.23 ± 11.87		85.11 ± 11.15		0.834†

** Fisher's exact test; † Student's t test; ‡ Mann-Whitney; CAD: coronary artery disease; HUUFMA: Hospital Universitário da Universidade Federal do Maranhão; SAH: systemic arterial hypertension; BMI: body mass index; WC: waist circumference; SBP: systolic blood pressure; DBP: diastolic blood pressure.*

A sedentary life-style, reported by the patients themselves, was quite evident among the women of both groups. Studies suggest that regular daily physical activity has a positive effect on the endothelium and can attenuate vasodilatation, thus preserving nitric oxide (NO) bioavailability, which results in a healthier natural aging process for women.[10-12] Physical exercise can also attenuate the appearance of comorbidities such as diabetes and hypertension.[13,14] Diabetic women are 3 to 7 times more likely to develop CAD than those without diabetes.[3]

These factors increase oxidative stress, compromising endothelial cells – this initial compromise is only functional, caused by the local inflammatory process.

Table 3 – Climacteric women with and without CAD regarding laboratory variables – HUUFMA. São Luís, Brazil, 2013

Variables	General	CAD		p-value
		Present	Absent	
	Mean ± SD / Median (Q3-Q1)	Mean ± SD / Median (Q3-Q1)	Mean ± SD / Median (Q3-Q1)	
Fasting Blood Sugar	97 (120 - 90)	102 (155 - 95)	94 (103 - 89)	0.057*
Total Cholesterol	205.45 ± 43.56	205.38 ± 46.57	200.33 ± 42.50	0.756†
Triglycerides	133 (182 - 75)	149 (189 - 119)	116 (150 - 68)	0.466*
HDL-c	48.54 ± 11.77	48.07 ± 9.84	48.88 ± 13.27	0.853†
LDL-c	126.16 ± 3.34	127.30 ± 44.87	125.33 ± 32.21	0.887†

** Mann-Whitney; † Student's t test. All values expressed in mg /dl; CAD: coronary artery disease; HUUFMA: Hospital Universitário da Universidade Federal do Maranhão; HDL-c: high-density lipoprotein; LDL-c: low-density lipoprotein.*

As time goes by, structural alterations take place in the vessels, and those lesions will facilitate thromboembolic phenomena, clinically presented as myocardial infarction, stroke, and other ischemic events.[15]

Regarding the climacteric period, most women who participated in this study were already post-menopausal (Groups I and II), and had been for over five years (late menopause), which suggests that among these women, the menopausal state may indicate an independent cardiovascular risk. During the climacteric period, women go through a gradual transition process of physiological changes, probably due to a decrease in estrogen, which leads to more long-lasting changes in the post-menopausal period.[16] This hormonal change seems to present a direct effect on vasculature, considering estrogens protect the endothelium against atheromatous plaque.[17]

We found that, in women with CAD, alterations in the levels of fasting blood sugar, total cholesterol, triglycerides, and HDL-c were more evident; however, mean levels of LDL-c remained within normality. Menopause by itself seems to cause an increase in total cholesterol, LDL-c and triglyceride levels, which also happens throughout the aging process, especially in women.[18] These factors also highlight the importance of LDL-c as a cardiovascular risk factor.[19]

Studies consider that total cholesterol and LDL-c continue to increase in women until the age of 70.[20] Gonadal failure in the post-menopausal climacteric may be related to the elevation of total cholesterol and LDL-c levels, due to a decrease in the hepatic activity of 7-α-hydroxylase, with a reduction of biliary acid synthesis and, therefore, a decrease in cholesterol excretion.[21]

Galvão et al.[22] found an association between triglycerides and endothelial dysfunction, suggesting that triglycerides play an important role in endothelial dysfunction: they found that elevated levels of triglycerides cause an increase in lipolysis with a consequent increase of inflammatory markers, such as ultra-sensitive C-reactive protein (us-CRP) and interleukin 6, which leads to endothelial dysfunction.[23]

It is interesting to highlight that HDL-c levels, in general, were altered among climacteric women, with values below 50 mg/dl. Such results corroborate other studies that also found reduced values of HDL-c in women in the same age group as those in our study.[24,25] Studies suggest that the protective effect of HDL-c may be decreasing in women in menopausal transition. Thus, it is possible that increased levels of HDL-c have a cardioprotective effect, while increased levels of LDL-c are associated to cardiovascular diseases (CVD).[26]

In general, the women presented a slightly altered SBP. This finding is acceptable for the stage in which those patients are, considering an increased BP in climacteric women may be related to weight gain and/or hormonal alterations, especially after menopausal transtions.[27] It is noteworthy that BP measurements were taken on the day of cardiac catheterization, which may also have contributed to this finding, considering their emotional state at that time.

Post-menopausal women, in addition to a weight gaining tendency, are also susceptible to lipid metabolism alterations, which may be related to the reduction of estrogen and consequent elevation of total cholesterol, lipoprotein, and triglyceride levels, which results in a lipid profile that is highly favorable to atherogenesis, especially when associated to DM and hypertension.[28]

In both groups of climacteric women, alterations were found in the WC and BMI. Both measurements represent the distribution of body fat deposition, especially abdominal fat. The increase of fat among women is expected, and it is more present in post-menopausal individuals.[29] That increases the risk for cardiovascular events, especially in women with central obesity. Metabolic effects on menopausal women can also contribute to the development of atherosclerosis favored by endothelial dysfunction.[30]

This accumulation of fat, also known as central, visceral, or android obesity, has been recognized as a cardiovascular risk factor and it is more important than total body fat – that may be justified by the higher production of cytokines by visceral fat, when compared to its production by peripheral fat.[31]

Suwaid et al.[32] have demonstrated that obesity may be independently associated to endothelial dysfunction in patients with normal coronary angiography or in those with mild CAD.

The limitations of our study include the identification of several women already medically diagnosed with CAD and on statins before the beginning of data collection for this study. We propose further studies in this area, especially multicenter studies with larger samples.

Conclusion

We have concluded that, in addition to menopause itself, SAH and a sedentary life-style were the most prevalent cardiovascular risk factors among women with CAD.

Author contributions

Conception and design of the research: Melo JB, Figueiredo Neto JA. Acquisition of data: Melo JB, Campos RCA, Carvalho PC, Andrade MVG, Rocha TPO, Farias WKS, Moraes MJD, Santos JC, Meireles MF. Analysis and interpretation of the data: Melo JB, Figueiredo Neto JA. Statistical analysis: Melo JB. Obtaining financing: Campos RCA. Writing of the manuscript: Melo JB, Carvalho PC, Meireles MF. Critical revision of the manuscript for intellectual content: Melo JB, Campos RCA, Carvalho PC, Figueiredo Neto JA.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

Sources of Funding

There were no external funding sources for this study.

Study Association

This article is part of the thesis of master submitted by Jorgileia Braga de Melo, from Universidade Federal do Maranhão.

Ethics approval and consent to participate

This study was approved by the Ethics Committee of the Hospital Universitário da Universidade Federal do Maranhão under the protocol number 005900/2011-00. All the procedures in this study were in accordance with the 1975 Helsinki Declaration, updated in 2013. Informed consent was obtained from all participants included in the study.

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