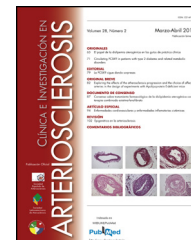




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ORIGINAL ARTICLE

Association between endothelial dysfunction, epicardial fat and sub-clinical atherosclerosis during menopause

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Received 26 June 2017; accepted 17 July 2017

KEYWORDS

Menopause;
Endothelial dysfunction;
Arterial stiffness;
Carotid intima-media thickness;
Epicardial fat

Abstract

Background: Menopausal transition is critical for the development of early, subclinical vascular damage. Multiple factors, such as atherosclerosis, increased epicardial fat, and endothelial dysfunction can play a role. Hence, the objective of this study was the comparison of epicardial adipose tissue and carotid intima media thickness in order to establish the best predictor of carotid stiffness in middle-aged women with endothelial dysfunction.

Methods: A total of 43 healthy women aged 40–59 years old with endothelial dysfunction previously demonstrated by flow mediated dilation were recruited to have anthropometric, biochemical, hormonal and ultrasound determinations of carotid intima media thickness and epicardial fat thickness.

Results: Carotid arterial stiffness parameters (local pulse wave velocity [4.7 ± 0.7 vs 4.8 ± 0.5 vs 5.6 ± 0.5 m/s, respectively, $p < 0.001$], pressure strain elastic modulus [55.2 ± 13.4 vs 59.2 ± 11.8 vs 81.9 ± 15.6 kPa, respectively, $p < 0.001$], arterial stiffness index β [4.4 ± 1.4 vs 5.0 ± 1.1 vs 6.4 ± 1.3 , respectively, $p < 0.001$]) and epicardial fat thickness (2.98 ± 1.4 vs 3.28 ± 1.9 vs 4.70 ± 1.0 mm, respectively, $p = 0.007$) showed a significant and proportional increase in the group of late post-menopausal women when compared to early post-menopausal and pre-menopausal groups, respectively. Among body fat markers, epicardial fat was the strongest predictor of local pulse wave velocity, independent of age.

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<http://dx.doi.org/10.1016/j.arteri.2017.07.006>

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Please cite this article in press as: Cabrera-Rego JO, et al. Association between endothelial dysfunction, epicardial fat and sub-clinical atherosclerosis during menopause. Clin Investig Arterioscler. 2017. <http://dx.doi.org/10.1016/j.arteri.2017.07.006>

PALABRAS CLAVE

Menopausia;
Disfunción endotelial;
Rigidez arterial;
Espesor íntima media
carotídeo;
Grasa epicárdica

Conclusions: In menopausal women with endothelial dysfunction, menopausal transition is associated with increased carotid arterial stiffness and epicardial fat thickness, independent of age. Ultrasound measured epicardial fat was a better independent predictor of arterial stiffness than carotid intima media thickness in these women.

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Interacción de la disfunción endotelial, la grasa epicárdica y la aterosclerosis subclínica durante la menopausia

Resumen

Introducción: La transición menopáusica es crítica para el desarrollo de daño vascular subclínico precoz. Múltiples factores como la aterosclerosis, el aumento del tejido adiposo epicárdico (TAE) y la disfunción endotelial pueden desempeñar un papel en este proceso. El objetivo de este estudio fue comparar la medición del TAE y el espesor íntima media carotídeo (IMC) para establecer el mejor predictor de rigidez carotídea en mujeres de mediana edad con disfunción endotelial.

Métodos: Se incluyeron 43 mujeres entre 40-50 años con disfunción endotelial demostrada por dilatación mediada por flujo. Se evaluaron variables antropométricas, bioquímicas, hormonales y se determinó por ultrasonografía el espesor de IMC y TAE.

Resultados: Los parámetros de rigidez arterial carotídea (velocidad de onda del pulso local [$4,7 \pm 0,7$ vs $4,8 \pm 0,5$ vs $5,6 \pm 0,5$ m/sec, $p < 0,001$], módulo de elasticidad de deformación de presión [$55,2 \pm 13,4$ vs $59,2 \pm 11,8$ vs $81,9 \pm 15,6$ Kpa, $p < 0,001$], índice β de rigidez arterial [$4,4 \pm 1,4$ vs $5,0 \pm 1,1$ vs $6,4 \pm 1,3$ $p < 0,001$]) y el espesor del TAE ($2,98 \pm 1,4$ vs $3,28 \pm 1,9$ vs $4,70 \pm 1,0$ mm, $p = 0,007$) mostraron un incremento significativo y proporcional en el grupo de mujeres en posmenopausia tardía comparado con los grupos de posmenopausia temprana y premenopausia respectivamente. Entre los marcadores de adiposidad el TAE fue el mejor predictor de la velocidad de onda del pulso independientemente de la edad.

Conclusiones: En mujeres menopáusicas con disfunción endotelial la transición menopáusica se asoció con un incremento en la rigidez arterial y espesor del TAE, independiente de la edad. El espesor del TAE fue mejor predictor independiente de rigidez arterial que el espesor IMC en estas mujeres.

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Introduction

Menopause is a physiological state in women and part of the natural aging process.¹ While women are better protected against atherosclerosis during the fertile period, this effect can change after menopause.² The sharp increase in coronary artery disease risk during the postmenopausal stage may reflect the cumulative impact of early, often asymptomatic, cardiovascular changes occurring during the menopausal transition, defined as the period between the end of the reproductive stage and the start of postmenopause.³ Recent observations pointed out the relation between the menopausal transition and the speed of progression of atherosclerosis.⁴

In addition to aging,⁵ endothelial dysfunction and excessive visceral fat accumulation have been suggested to contribute to subclinical cardiovascular diseases during a rapid menopausal transition. Previous studies showed that ovarian atresia in the early stages of menopause is

associated with endothelial dysfunction.⁶ Healthy middle-aged early postmenopausal women have more endothelial dysfunction than those in perimenopause or in the late postmenopausal stages.⁷ The need of measurable biomarkers to detect early, asymptomatic vascular damages is therefore compelling. Carotid intima-media thickness (CIMT) has been used to predict an early endothelial dysfunction in menopausal women, although results are quite controversial.^{8,9} The impact of excessive visceral adiposity on the cardiovascular risk profile in the post-menopause has been evaluated before, whereas its role in the menopausal transition is not well established, yet. Epicardial fat is an emerging marker of visceral organ-specific adiposity that can be easily measured with standard cardiac ultrasound.¹⁰ Echocardiographic epicardial fat thickness has been related to subclinical atherosclerosis and metabolic syndrome.^{11,12} Recently epicardial fat has been associated with higher cardiovascular risk in pre- or post-menopausal women.¹³⁻¹⁵ Nevertheless, whether epicardial fat may predict an early

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