Nutrition, Metabolism & Cardiovascular Diseases (2015) **25**, 434–435

Available online at www.sciencedirect.com

Nutrition, Metabolism & Cardiovascular Diseases

journal homepage: www.elsevier.com/locate/nmcd

LETTER TO THE EDITOR

Serum high sensitivity CRP concentrations predict the presence of carotid artery plaque in individuals without a history of cardiovascular events

We have previously reported that in a male Iranian population, high-sensitive C-reactive protein (hs-CRP) associates with several traditional cardiovascular disease (CVD) risk factors [1], and appears to be an independent predictor of coronary artery disease in symptomatic patients [2]. Carotid artery plaque (CAP) measurement by ultrasound is a way of estimating atheroma. The objective of this study was to investigate the association between serum hs-CRP and presence of CAP in individuals without a history of cardiovascular (CV) events, and the relationship between traditional CV risk factors and serum hs-CRP in this population.

A sample of 506 subjects [215 (42.5%) males], between 35 and 64 years old, were recruited from an urban population in Mashhad, Iran, using a stratified-cluster method as part of the Mashhad Stroke Heart Atherosclerosis Disorder (MASHAD) study cohort. The sample was selected randomly from a cohort of 9765 individuals for carotid duplex ultrasound. The mean age and gender characteristics of the sample shows this study population was a representative of the whole cohort. None of the subjects had a past history of a CV event. CAP was assessed by duplex-ultrasound of both common and internal carotid arteries. Comparisons were made between individuals in different tertiles for serum hs-CRP. The lowest tertile was used as the *reference* group for univariate and multivariate analysis.

Characteristics of subjects, including the CV risk profile of individuals within different tertiles of hs-CRP are shown in Table 1. Multivariate analysis showed that the presence of CAP ($p < 0.001$; OR, 0.44; CI, 0.24–0.80), or metabolic syndrome ($p < 0.001$; OR, 0.41; CI, 0.25–0.66) were significantly higher among the patients in the highest tertile of serum hs-CRP compared to the reference group. The area under the ROC curve for the presence of CAP was 0.61 (95%-CI 0.53–0.67). Using the cut-off point of 2.12 mg/L for serum hs-CRP, gave a sensitivity and specificity of 57% and 63% respectively for the presence of CAP. The area under the ROC curve for presence of metabolic

Table 1 Demographic and biochemical characteristics of individuals in different tertiles of hs-CRP.

	Lowest tertile (N = 169) [0.8 (0.6–0.9) mg/L]	Middle tertile (N = 168) [1.7 (1.3–2.2) mg/L]	Highest tertile (N = 169) [5.2 (3.5–10.2) mg/L]
Age (y)	48.5 ± 7.7	48.3 ± 7.9	48.5 ± 8.2
Male (%)	84 (39.1)	70 (32.6)	61 (28.4)*
Female (%)	85 (29.2)	98 (33.7)	108 (37.1)
SBP (mmHg)	118.1 ± 15.5	122.7 ± 19.2	125.7 ± 20.1***
DBP (mmHg)	77.5 ± 9.9	80.9 ± 12.5	82.4 ± 12.2***
FBG (mg/dL)	85.4 ± 27.7	94.2 ± 37.7	98.8 ± 37.8**
Total cholesterol (mg/dL)	181.9 ± 37.9	195.5 ± 42.0	198.9 ± 46.7**
LDL-C (mg/dL)	120.0 ± 33.6	127.4 ± 38.3	128.9 ± 40.9*
HDL-C (mg/dL)	43.7 ± 13.0	42.5 ± 9.1	41.2 ± 9.2
Triglyceride (mg/dL)	112 (84–157)	122 (79–158)	130 (82–189)**
BMI (kg/m^2)	26.4 ± 4.8	27.3 ± 5.1	28.7 ± 5.3***
WC (cm)	91.3 ± 10.6	94.6 ± 10.2	97.7 ± 13.9***
Diabetes mellitus (%)	14 (8.3)	18 (10.7)	39 (23.1)**
Hypertension (%)	21 (22.3)	29 (30.8)	44 (46.8)***
Current smoking (%)	52 (30.8)	49 (29.2)	48 (28.4)
Metabolic syndrome [6] (%)	51 (30.2)	68 (40.5)	89 (52.7)***
Presence of CAP (%)	21 (12.4)	17 (10.1)	40 (23.7)***

Values expressed as mean ± SD for data with normal distribution; for serum triglyceride and high sensitive CRP that had non-normal distributions, values are expressed as median and interquartile ranges.
BMI, body mass index; CAP, carotid artery plaque; CI, confidence interval; DBP, diastolic blood pressure; FBG, fasting blood sugar; HDL-C, high density lipoprotein cholesterol; hs-CRP, high sensitive C-reactive protein; LDL-C, low density lipoprotein cholesterol; OR, odds ratio; SBP, systolic blood pressure; WC, waist circumference.
*$p < 0.05$; **$p < 0.01$; ***$p < 0.001$.

http://dx.doi.org/10.1016/j.numecd.2014.12.009

syndrome was 0.60 (95%-CI 0.55–0.65). Using a cut-off value for serum hs-CRP of 1.74 mg/L gave a sensitivity and specificity of 60% and 60% respectively for the presence of metabolic syndrome.

The burden of conventional CV risk factors was higher amongst subjects in the highest tertile of serum hs-CRP compared to the subjects in the reference group. Moreover, we found an independent relationship between serum hs-CRP and the presence of either metabolic syndrome or CAP (subclinical atherosclerosis) in a group of non-symptomatic patients, who had no history of CV events. The association between serum hs-CRP and traditional CV risk factors including metabolic syndrome has been shown in previous studies [3]. Subclinical atherosclerosis, defined by the presence of coronary artery calcium, was reported to be independently associated with higher level of hs-CRP (>2 mg/L) in asymptomatic and non-hypertensive subjects [4].

The area under the ROC curve for hs-CRP as a determinant of metabolic syndrome was 0.56 and 0.62 for men and women respectively. Serum hs-CRP appears to have a better association with CVD in women compared to men in the Iranian population, although it appears to have a poorer association for our population in the Iranian compared to a Japanese population [5].

Acknowledgements

The Mashhad University of Medical Science Research Council supported this research project. grant number: 85134.

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3 December 2014