

C-Reactive Protein and Metabolic Syndrome in Elderly Women

A 12-year follow-up study

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Aging is associated with increased inflammatory activity (1,2). Serum C-reactive protein (CRP) is a sensitive marker of systemic low-grade inflammation and is an important predictor of type 2 diabetes (3,4) and cardiovascular disease (CVD) (5). Cross-sectional studies have found associations of CRP with metabolic syndrome (6–9) and its components, including obesity (10), insulin resistance (6,7,10), dyslipidemia (10), elevated blood pressure (11), and endothelial dysfunction (10). Prospective studies (3,4) in middle-aged individuals have observed that increased serum CRP levels predict the development of metabolic syndrome. No such data are available in the elderly. We tested the hypothesis that changes in serum CRP levels predict the development of metabolic syndrome in a population-based sample of elderly women followed-up for 12 years.

RESEARCH DESIGN AND METHODS

The subjects were examined as a part of the large population-based risk factor survey in 1982 (12). The women, aged 60–70 years, were invited for the baseline examinations of the present study in 1991–1992. None of them had diabetes. In 2003, all eligible women were invited for the 12-year follow-up study, and 113 of them participated. After excluding women with CRP >10 mg/l or missing data, the final study population included 103 women. The study protocol was approved by the ethics

committee of the University of Kuopio. All participants gave written informed consent.

Venous blood samples were taken after a 12-h fast. Serum assays for high-sensitivity CRP (13), triglycerides, and HDL cholesterol (14) have been described earlier. Waist circumference and blood pressure were measured according to the MONICA protocol (15). Diseases, medications, smoking, and alcohol consumption were assessed by a self-administered questionnaire. Metabolic syndrome was defined by the National Cholesterol Education Program criteria (16).

Statistical analyses were performed using SPSS for Windows, Release 11.5. If required, CRP was log transformed to obtain a normal distribution. Comparisons between groups were analyzed using independent-samples *t* test and χ^2 test. To test changes during 12 years, paired-samples *t* test and McNemar tests were used. Logistic regression analysis was used to calculate odds ratios for the development of metabolic syndrome in women with CRP increases as compared with those with a CRP decrease. A 0.05 significance level was used for all statistical tests.

RESULTS — At baseline and after 12 years of follow-up, 11 and 46% of the women, respectively, had metabolic syndrome ($P < 0.001$ for difference). At baseline, the mean CRP was twice as high

in women with metabolic syndrome as compared with those without it (3.1 vs. 1.5 mg/l).

While CRP increased in 37 women who developed metabolic syndrome during 12 years (from 1.7 to 3.2 mg/l, $P = 0.001$), it did not change in 55 women who remained free of it or in 11 women with metabolic syndrome already at baseline. An increment of 1 mg/l in CRP during 12 years was associated with a 37% ($P = 0.007$) increase in the risk of developing metabolic syndrome after adjustment for baseline age, smoking, the use of drugs for hypercholesterolemia, hormone replacement therapy, and prevalent CVD. The 1 mg/l increment in CRP was associated with a 26% ($P = 0.047$) increase in the risk after further adjustment for waist circumference and with a 31% ($P = 0.018$) increase after additional adjustment for triglycerides. Adjustment for changes in other components of metabolic syndrome had no effect on the association.

Of women for whom CRP decreased, increased by 0–1 mg/l, or increased by >1 mg/l, metabolic syndrome developed in 22, 50, and 60%, respectively, during 12 years ($P = 0.005$ for difference). Compared with women for whom CRP decreased, those with a CRP increment of 0–1 mg/l had a 4.5-fold higher ($P = 0.011$) and those with a CRP increase of >1 mg/l had a 6.2-fold higher ($P = 0.002$) risk of developing metabolic syndrome after adjustment for baseline age, smoking, the use of drugs for hypercholesterolemia, hormone replacement therapy, and prevalent CVD (Table 1, model 1). The association of CRP change with the risk of developing metabolic syndrome was weakened after further adjustment for waist circumference or triglycerides, while changes in other components of metabolic syndrome did not affect the association (Table 1, models 2–6).

CONCLUSIONS — The new finding of the present 12-year follow-up study is that even a slight increment in serum CRP level was associated with an increased risk

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Abbreviations: CRP, C-reactive protein; CVD, cardiovascular disease.

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Table 1—Odds ratio (95% CI) for developing metabolic syndrome in women without it at baseline according to changes in CRP levels

CRP change	n	Model 1	Model 2	Model 3	Model 4	Model 5	Model 6
<0 mg/l	41	1	1	1	1	1	1
0–1 mg/l	26	4.5 (1.4–14.3)	2.7 (0.8–9.3)	3.7 (1.1–12.3)	3.9 (1.2–12.9)	6.1 (1.6–23.8)	5.2 (1.6–17.4)
>1 mg/l	25	6.2 (1.9–19.9)	4.4 (1.3–15.0)	4.7 (1.4–15.6)	5.8 (1.8–19.0)	8.2 (2.2–31.5)	7.5 (2.2–25.6)
P for trend		0.002	0.018	0.010	0.003	0.002	0.001

Model 1: adjusted for age, smoking, the use of drugs for hypercholesterolemia, hormone replacement therapy, and cardiovascular diseases at baseline. Model 2: adjusted for variables in model 1 and change in waist circumference during follow-up. Model 3: adjusted for variables in model 1 and change in triglycerides during follow-up. Model 4: adjusted for variables in model 1 and change in HDL cholesterol during follow-up. Model 5: adjusted for variables in model 1 and change in blood glucose during follow-up. Model 6: adjusted for variables in model 1 and change in systolic blood pressure during follow-up.

of developing metabolic syndrome in elderly women. Women with any increase in CRP level had a 5–6 times higher risk of metabolic syndrome than those whose CRP levels decreased. The relationship was independent of changes in abdominal obesity and other components of metabolic syndrome. These data emphasize CRP measurement to identify individuals at an increased risk of metabolic syndrome.

The present results agree with the findings from cross-sectional studies (6–9) and few prospective studies (3,4) of the association between elevated CRP levels and metabolic syndrome. Because most of these studies have only included middle-aged individuals or have not specifically studied elderly individuals, we investigated the association in a population-based cohort of elderly women with a follow-up of 12 years. Randomized clinical trials that include lifestyle interventions are needed to find out whether suppressed inflammation reduces the risk of developing metabolic syndrome, type 2 diabetes, and CVD.

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