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Increased serum soluble corin in dyslipidemia: A cross-sectional study

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ABSTRACT

Background
Natriuretic peptides have been associated with dyslipidemia. As a physiological activator of natriuretic peptides, corin might also be associated with dyslipidemia. However, this association has not yet been studied in Chinese populations.
Methods
Serum soluble corin and blood lipid profiles were determined for 2496 participants aged above 30 y. A logistic regression model was applied to evaluate the association between serum soluble corin and dyslipidemia.
Results
Serum soluble corin was significantly increased in participants with dyslipidemia in both men ($P < 0.001$) and women ($P < 0.001$). After controlling for the confounding factors, OR of dyslipidemia positively increased with increasing levels of serum soluble corin in men (P for trend = 0.011) and women (P for trend = 0.043). Participants with a high corin level were more likely to have dyslipidemia than those with a low corin level in men (OR, 95% CI: 1.45, 1.07–1.97) and women (OR, 95% CI: 1.33, 1.04–1.70).
Conclusion
Serum soluble corin was significantly and positively associated with dyslipidemia. Our findings suggested that serum soluble corin may be a marker or risk factor for dyslipidemia.

1. Introduction

Dyslipidemia plays a vital role in the development of cardiovascular disease, which is the first leading cause of death worldwide [1,2]. It affects more than half of middle-aged and elderly individuals and is increasingly prevalent in China [3,4]. Fundamentally, lipid metabolism is complicated and can be disturbed in a variety of ways leading to changes in plasma lipoprotein function or levels [5]. However, the mechanism of dyslipidemia is still not very clear.

Recently, human corin, a type II transmembrane serine protease highly expressed in the heart [6], was found to play a physiological role in activation of natriuretic peptides [7,8]. More recently, decreased natriuretic peptides were reported to be associated with increased lipid accumulation by an animal experiment study [9]. In addition, large scale population-based studies [10,11] have found a decreased level of natriuretic peptides in dyslipidemia. These findings indicate an association of dyslipidemia with decreased natriuretic peptides. As a physiological activator of natriuretic peptides, decreased corin might be associated with dyslipidemia. If so, circulating soluble corin may be regarded as an indicator or potential risk factor for dyslipidemia despite the unknown molecular forms and biological function of circulating soluble corin. To verify this assumption, researches into the relationship between circulating soluble corin and dyslipidemia should be done in populations. To date, some small sampled case–control studies have examined circulating soluble corin in some disease states, such as chronic kidney disease [12], pregnant hypertension [13], and heart failure [14]. However, soluble corin has not been studied in relation to dyslipidemia in populations.

2. Material and methods

2.1. Participants and baseline data

A cross-sectional study was conducted in Suzhou from January to May 2010. More detailed information on subject recruitment and baseline data collection have been published elsewhere [15]. Briefly, from 3061 eligible residents aged over 30 y with a Han ethnicity in the

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study fields, 2706 (participating rate: 88%) persons participated in this study. Among them, 2498 participants received serum soluble corin measurement. After excluding 2 participants for lacking blood lipid profiles, 2496 participants were finally included in the current analysis. Study participants underwent a clinical examination including a personal interview and physical examination. Information on demographic factors, medical history, medication use, and lifestyle factors was collected by personal interview using standard questionnaires. A physical examination was conducted, and fasting blood samples were collected for laboratory tests, including total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and fasting plasma glucose. For this analysis, dyslipidemia was defined as TC ≥ 6.22 mmol/l or LDL-C ≥ 4.14 mmol/l or TG ≥ 2.26 mmol/l or HDL-C < 1.04 mmol/l based on the recommendations of the Working Group on Dyslipidemia in China [16]. This study was approved by the Soochow University Ethics Committee. Written informed consent was obtained from all study participants.

2.2. Serum soluble corin measurement

Blood samples were obtained by venipuncture in the morning after a requested overnight fast (at least 8 h). All plasma and serum samples were frozen at −80 °C until laboratory testing. Soluble corin was reported to be stable in blood samples frozen at −80 °C after several cycles of freezing and thawing [17]. We used a quantikine human corin immunoassay (R&D Systems, Inc.) to measure soluble corin concentration in serum. All the samples were processed in a duplicate assay. A standard curve was constructed from which corin concentrations of unknown samples were determined. Intra- and inter-assay coefficients of variation were >2.7% and 6.3%, respectively.

2.3. Statistical analysis

Consistent with a previous study [14], a sex-difference in serum soluble corin level was also observed in our study participants. Therefore, all data analyses were performed in men and women individually. Baseline characteristics were presented in individuals with and without dyslipidemia. Data were compared between the two groups using a Student's t-test, Wilcoxon rank-sum test, or the chi-square test as appropriate. For lacking a normal distribution, the average level of serum soluble corin was compared between the two groups using a Wilcoxon rank-sum test. A Spearman correlation analysis was used to evaluate the correlation between serum soluble corin and blood lipid profiles as well as the related variables such as age, cigarette smoking, alcohol drinking, body mass index, waist circumference, blood pressures, and fasting plasma glucose. In addition, multivariate non-conditional logistic regression models were performed to assess the associations of serum soluble corin with dyslipidemia. All study participants were categorized into 4 groups according to the quartiles of serum soluble corin distributed in men and women individually. Odds ratios (ORs) and 95% confidence intervals (CI) of dyslipidemia were calculated for upper quartiles of serum soluble corin with the lowest quartile as a reference. Trends in the ORs of dyslipidemia across increasing corin categories were determined, modeling corin category as an ordinal variable. The potential covariates such as age, cigarette smoking, alcohol drinking, systolic blood pressure, body mass index and fasting plasma glucose were included in the multivariate models. Then, participants were categorized into 2 groups: the low corin group and the high corin group (divided by the median of serum soluble corin in men and women individually). The rationality is the similar prevalence of dyslipidemia distributed in the lower two quartiles and the upper two quartiles. The OR and 95% CI of dyslipidemia associated with the high corin group compared with the low corin group was also determined. A two-tailed P value less than 0.05 was considered statistically significant. Statistical analysis was conducted using SAS statistical software (ver 9.1).

2.4. Sensitivity analysis

We previously found increased serum soluble corin in hypertensive individuals [18] indicating a probable modifiable effect on the association between serum soluble corin and dyslipidemia. To examine whether hypertension affects the association, participants with hypertension were excluded.

3. Results

3.1. Baseline characteristics

A total of 2496 participants including 960 men and 1536 women with an average age of 52 ± 10 y were included in the current analysis. Among them, 658 (26%) participants had dyslipidemia. The baseline characteristics were presented in Table 1. No significant difference in proportions of cigarette smoking and alcohol drinking was observed between individuals with and without dyslipidemia in men and women (all $P > 0.05$). In contrast, participants with dyslipidemia were more likely to be hypertensive and have higher body mass index, waist circumference and fasting plasma glucose in both sexes (all $P < 0.05$). The median level of serum soluble corin was significantly higher in participants with dyslipidemia than those without dyslipidemia in both men and women (all $P < 0.001$).

3.2. Correlations of serum soluble corin with blood lipid profiles

We applied a Spearman correlation analysis to examine the correlations of serum soluble corin with blood lipid profiles and other related variables in men and women respectively. As shown in Table 2, serum soluble corin positively correlated to TC ($r = 0.125$), TG ($r = 0.261$), LDL-C ($r = 0.165$) and inversely correlated to HDL-C ($r = -0.236$) in men (all $P < 0.05$). Serum soluble corin also significantly correlated to other lipid-related variables such as age, cigarette smoking, alcohol drinking, blood pressures, body mass index, waist circumference, and fasting plasma glucose (all $P < 0.05$). The results of correlation analysis in women are similar. As shown in Table 3, serum soluble corin significantly correlated to TC ($r = 0.153$), TG ($r = 0.083$), and LDL-C ($r = 0.148$) (all $P < 0.05$), but not to HDL-C ($P > 0.05$). As expected, serum soluble corin also significantly correlated to age, blood pressures, body mass index, waist circumference, and fasting plasma glucose (all $P < 0.05$).

3.3. Associations of dyslipidemia with serum soluble corin

We first examined the association between serum soluble corin quartiles and each blood lipid profile. After adjustment for age, cigarette smoking, alcohol drinking, body mass index, systolic blood pressure, and fasting plasma glucose, we observed a significant association of serum soluble corin quartiles with elevated TG (P for trend = 0.001) and decreased HDL-C (P for trend = 0.002) in men (Supplementary Table 1), and with elevated TC (P for trend = 0.021) in women (Supplementary Table 2). Then we examined the association between serum soluble corin quartiles and dyslipidemia. As shown in Table 4, the univariate analysis showed a significant association of dyslipidemia with serum soluble corin quartiles, where the ORs of dyslipidemia significantly increased with the increasing quartiles in both men and women (all P for trend < 0.001). After controlling for the confounding factors, the trend that ORs of dyslipidemia increased with increasing quartiles of serum soluble corin persisted in both men (P for trend = 0.011) and women (P for trend = 0.043). However, the OR of dyslipidemia for each quartile became smaller whereas the OR of dyslipidemia for the highest quartile remained significant in men (OR = 1.66, P = 0.021) rather than in women (OR = 1.32, P = 0.117).

Notably, the prevalence of dyslipidemia distributed in quartiles of serum soluble corin was 23.85%, 24.48%, 31.54%, 38.08% in men and 20.26%, 20.42%, 27.53%, 29.43% in women (Table 4). Obviously,