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Coronary tortuosity is associated with an elevated high-sensitivity C-reactive protein concentration and increased risk of ischemic stroke in hypertensive patients

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Abstract

Objective: The clinical implication of coronary tortuosity is unclear. The present study was conducted to determine the relationships between coronary tortuosity and the high-sensitivity C-reactive protein (hs-CRP) concentration and between coronary tortuosity and cerebrovascular accident in hypertensive patients without coronary artery disease.

Methods: In total, 236 patients with normal coronary angiography findings were categorized into 3 different groups: control participants (n = 58), who had neither hypertension nor coronary tortuosity; patients with hypertension but no coronary tortuosity (H-NCT group, n = 93); and patients with both hypertension and coronary tortuosity (H-CT group, n = 85). The hs-CRP concentration was measured in every patient, and 168 hypertensive patients were followed up for at least 2 years to check for the development of cerebrovascular accident.

Results: The hs-CRP concentration was significantly higher in the H-CT group than in the control and H-NCT groups (4.33 ± 3.15 vs. 1.52 ± 1.31 and 2.31 ± 2.09 mg/L, respectively). The incidence of lacunar infarction was higher in the H-CT than H-NCT group during the follow-up.

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Conclusions: Hypertensive patients with coronary tortuosity have a higher serum hs-CRP level concentration and have a higher incidence of lacunar infarction than hypertensive patients without coronary tortuosity.

Keywords
Coronary tortuosity, high-sensitivity C-reactive protein, hypertension, cerebrovascular accident, lacunar infarction, coronary artery disease

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Introduction

Cardiovascular diseases such as coronary artery disease and stroke are the leading cause of mortality in both developed and developing countries, including China.[1] Inflammation has been established as an important contributor to the pathogenesis of atherosclerosis and its subsequent complications. Multiple studies have proven that the baseline level of C-reactive protein (CRP) can predict a higher risk of future coronary artery disease, cerebrovascular accident, and peripheral vascular disease even among healthy people. The CRP concentration is also frequently elevated in hypertensive patients, and previous studies have suggested a link between hypertension and low-grade inflammation.[2]

Coronary tortuosity is commonly observed by coronary angiography; however, its clinical implication remains unclear.[3] Previous studies have indicated a possible relationship between coronary tortuosity and hypertension, impaired left ventricular diastolic function, and irreversible myocardial perfusion.[4–6] However, whether a high CRP concentration plays a role in coronary tortuosity is unknown. Additionally, the relationship between cerebrovascular accidents and coronary tortuosity in hypertensive patients is unknown. Therefore, the present study was performed to determine the associations between the high-sensitivity CRP (hs-CRP) concentration and coronary tortuosity and between coronary tortuosity and cerebrovascular accidents in hypertensive patients without coronary artery disease.

Methods

Patients who had presented with a chief complaint of chest discomfort underwent coronary angiography. Those with normal coronary angiography findings were included in this study, which lasted from October 2009 to October 2011.

Normotensive patients without coronary tortuosity comprised the control group, hypertensive patients without coronary tortuosity comprised the H-NCT group, and hypertensive patients with coronary tortuosity comprised the H-CT group. The exclusion criteria were evidence of inflammatory, neoplastic, or infectious disease; abnormal liver or renal function; diabetes mellitus; obesity; and $\geq$50% stenosis of the three main coronary arteries. Patients with these conditions were excluded because these diseases may impact the hs-CRP concentration.

Hypertensive patients were diagnosed based on the World Health Organization essential diagnostic criteria. All patients with hypertension were being treated with

long-term standard antihypertensives. The definition of heart failure was based on the New York Heart Association heart function classification.

The study was performed on an inpatient basis. The study was started after obtaining permission from the ethics committee of Zhonda Hospital of Southeast University. The protocol was in compliance with the Declaration of Helsinki. Written consent was obtained from every participant.

Biochemical analyses

Blood samples were collected by venous puncture from all patients after a $\geq$8-hour fast. The hs-CRP concentration was measured using high-sensitivity latex-enhanced immunonephelometric method on a Siemens BN II (Siemens Healthineers, Erlangen, Germany).

Coronary angiography

All three main coronary arteries (right coronary artery, left anterior descending artery, and left circumflex artery) were evaluated by standard angiography. The coronary artery was identified based on the standard criteria. Coronary artery tortuosity was defined as the presence of more than three 45-degree bends along the length of any of the three coronary arteries (Figure 1).

Clinical follow-up

All hypertensive patients were followed up for at least 2 years. Any incidence of cerebrovascular accident was documented solely based on clinical signs and symptoms. Ischemic stroke was defined as ischemia of the brain tissues as a result of thrombosis, embolism including transient ischemic attack (TIA), and lacunar stroke. Lacunar infarction was diagnosed by computed tomography or magnetic resonance imaging in patients with cerebrovascular sign and symptoms. TIA was defined by the 2009 American Heart Association/American Stroke Association criterion.[7]

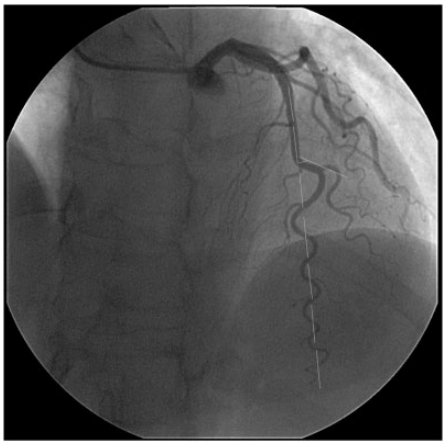

Figure 1. Diagnosis of coronary artery tortuosity

Statistical analysis

SPSS Version 15.0 for Windows (SPSS Inc., Chicago, IL, USA) was used to perform all statistical calculations. Continuous variables are expressed as the arithmetic mean $\pm$ standard deviation, and categorical variables are expressed as percentages. Continuous variables among groups were compared by one-way analysis of variance followed by Duncan's post hoc test. Categorical variables were compared by the chi-square test. Spearman's coefficients were employed for correlation analysis. A two-tailed p value of <0.05 indicated statistical significance.

Results

Baseline characteristics

In total, 236 patients were included in the present study. The control group comprised 58 patients, the H-NCT group comprised 93 patients, and the H-CT group comprised 85 patients. The important laboratory results and clinical and demographic

Table 1. Patients' baseline clinical characteristics

Variables	Control (n = 58)	H-NCT (n = 93)	H-CT (n = 85)
Men	26 (44.8)	48 (51.6)	42 (49.4)
Age, years	58 ± 7.9	62 ± 9.1	63 ± 8.6
Systolic blood pressure, mmHg	126 ± 10.1	142 ± 11.8	152 ± 13.0△
Diastolic blood pressure, mmHg	76 ± 10.2	81 ± 10.9	83 ± 12.8
Smoking	8 (13.7)	11 (11.8)	12 (14.1)
Aspirin treatment	6 (10.3)	15 (16.1)	19 (22.3)
LDL-cholesterol, mg/dL	127 ± 6.6	128 ± 6.7	130 ± 7.5
Hypertension duration, years	0.0 ± 0.0	7.6 ± 2.7	9.9 ± 3.9
White blood corpuscles, 10^9/L	5.2 ± 1.4	6.3 ± 2.8	6.1 ± 2.6
hs-CRP, mg/L	1.52 ± 1.31	2.31 ± 2.09	4.33 ± 3.15*
Structural heart disease	1 (1.7)	1 (1.0)	1 (1.1)
Heart failure	1 (1.7)	2 (2.1)	2 (2.3)
Atrial fibrillation	1 (1.7)	1 (1.0)	2 (2.3)

Data are presented as n (%) or mean ± standard deviation.
H-NCT, hypertension but no coronary tortuosity; H-CT, hypertension and coronary tortuosity; LDL-cholesterol, low-density lipoprotein cholesterol; hs-CRP, high-sensitivity C-reactive protein
△$p < 0.05$ compared with H-NCT group. *$p < 0.05$ compared with control group and H-NCT group.

information of all patients are shown in Table 1. As shown in the table, there were no significant differences between the H-NCT and H-CT group in most clinical characteristics such as age, sex, low-density lipoprotein cholesterol level, structural heart disease, and atrial fibrillation. However, systolic blood pressure was considerably higher in the H-CT than H-NCT group ($p < 0.05$). The hs-CRP concentration was similar between the control and H-NCT groups and significantly higher in the H-CT group than in the control and H-NCT groups ($p < 0.05$).

Clinical follow-up

All 168 hypertensive patients were prospectively followed up for a mean of 3.1 ± 0.3 years. The incidence of overall cerebrovascular accident was higher in the H-CT than H-NCT group (7.1% vs. 2.2%, respectively); in particular, the incidence of lacunar stroke was significantly higher (7.1% vs. 1.1%, respectively; $p = 0.04$) (Table 2).

Table 2. Cardiovascular events during follow-up

Events	H-NCT (n = 93)	H-CT (n = 85)	p value
Stroke	2 (2.2)	6 (7.1)	0.114
Ischemic stroke	2 (2.2)	6 (7.1)	0.114
Lacunar infarction	1 (1.1)	6 (7.1)	0.04
Hemorrhagic stroke	0 (0.0)	0 (0.0)	

Data are presented as n (%). H-NCT, hypertension but no coronary tortuosity; H-CT, hypertension and coronary tortuosity.

Discussion

In the present study, the hs-CRP concentration was increased in hypertensive patients with concurrent coronary tortuosity. Additionally, hypertensive patients with coronary tortuosity were more susceptible to a higher incidence of lacunar stroke than hypertensive patients without coronary tortuosity. We believe that this is the first study to demonstrate the relationship between a high hs-CRP concentration, stroke, and coronary tortuosity in hypertensive patients without coronary artery disease. Earlier studies have indicated that

a high CRP concentration plays an important role in the pathogenesis of atherosclerosis and increases the incidence of adverse cardiovascular events.[8,9] We demonstrated that coronary tortuosity was associated with an increased hs-CRP concentration in hypertensive patients, indicating that coronary tortuosity may be directly or indirectly related to adverse cardiovascular events via a higher CRP level. In fact, our results showed that coronary tortuosity was associated with increased inflammation and a risk of lacunar stroke in hypertensive patients without evidence of coronary artery disease.

Our previous study of coronary tortuosity demonstrated that coronary tortuosity is positively correlated with hypertension while negatively correlated with coronary atherosclerosis.[5] Zegers et al.[3] hypothesized that coronary ischemia may be caused by coronary tortuosity through reduced coronary perfusion pressure distal to the tortuous segment of the coronary artery. Gaibazzi et al.[10] and Gaibazzi[11] found that patients with reversible perfusion defects had a higher prevalence of coronary artery tortuosity and coronary artery bridging than patients without reversible perfusion defects. Our study also proved that coronary tortuosity is associated with reversible cardiac blood flow defects in patients without coronary artery disease.[4] However, other studies have shown that the influence of coronary tortuosity on coronary blood flow may be small.[12–14] Wang et al.[15] showed that tortuosity of the internal carotid artery leads to a decrease in the perfusion pressure distal to the kink in the artery and that kinking of the internal carotid artery is an important element leading to cerebral tissue ischemia. Another study revealed an association between internal carotid artery tortuosity and TIA.[16] Future studies are warranted to determine whether hypertensive patients with versus without coronary tortuosity might obtain different benefits from intensive hypertensive therapy or other treatments.

The main limitation of the present study is the small number of patients. Multivariate logistic regression analyses should be performed in future studies involving larger numbers of patients to clarify the relationship between coronary tortuosity and stroke.

Conclusions

In conclusion, hypertension without coronary artery disease but with coronary tortuosity is associated with an elevated hs-CRP concentration and an increased prevalence of lacunar infarction during follow-up. Further studies with larger numbers of patients and longer follow-up times are required to clarify the relationship between coronary tortuosity and stroke. Future studies are needed to determine whether these patients might benefit more from intensive antihypertensive or other treatments.

Declaration of conflicting interests

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