Original article

High sensitive C-reactive protein, adiponectin, and urine albumin excretion rate in Chinese coronary artery disease patients with different glucose tolerance status

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Keywords: *C-reactive protein; adiponectin; urine albumin excretion rate; diabetes mellitus, type 2; coronary artery disease*

Background Serum high sensitive C-reactive protein (hs-CRP), adiponectin levels and urine albumin excretion rate (UAER) are probably associated with inflammation and atherosclerosis. The aim of this study was to determine the three markers in coronary artery disease (CAD) subjects with different glucose tolerance status in a Chinese population and further explore the levels of the three markers in these subjects and the possible association of these markers with CAD risk factors and the severity of CAD as well.

Methods A total of 242 subjects with angiographically documented CAD were recruited, and then assigned to three groups: the normal glucose tolerance (NGT) + CAD group, including 100 CAD patients with NGT; the impaired glucose tolerance (IGT) + CAD group, 40 CAD patients with IGT; the type 2 diabetes mellitus (T2DM) + CAD group, 102 CAD patients with T2DM. Serum hs-CRP, adiponectin levels as well as UAER were measured in all subjects.

Results Serum hs-CRP levels were increased in the T2DM + CAD group compared with the NGT + CAD group (4.71±2.59) vs (3.60±2.46) mg/L, P=0.037. Serum adiponectin levels were gradually decreased from the NGT + CAD to IGT + CAD to T2DM + CAD groups, (5.99±1.84), (5.82±1.72) and (4.65±1.71) mg/L, P=0.002 and 0.040 for NGT + CAD and IGT + CAD groups vs T2DM + CAD group, respectively. While the UAER was gradually increased from the NGT + CAD to IGT + CAD to T2DM + CAD groups, (6.42±2.51), (6.89±2.94) and (15.03±4.22) μg/min (P<0.001) for NGT + CAD and IGT + CAD groups vs T2DM + CAD group. Multiple linear stepwise regression analysis showed that waist-hip ratio (WHR) and low density lipoprotein cholesterol (LDL-C) were the significant determinants of serum hs-CRP levels; triglyceride (TG), high density lipoprotein cholesterol (HDL-C), age, WHR, T2DM, 2-hour serum insulin (2hINS), sex, and apolipoprotein B were the significant determinants of serum adiponectin levels; and systolic blood pressure (SBP), T2DM, and hemoglobin A1c (HbA1c) were the significant determinants of UAER in all subjects (R^2= 0.070, 0.352, and 0.214, respectively). However, no significant correlation was seen for hs-CRP, adiponectin and UAER with the severity of CAD. Hs-CRP levels were significantly correlated with UAER.

Conclusions There was a trend of increased serum hs-CRP levels from the NGT + CAD to IGT + CAD to T2DM + CAD groups, though it only showed significance in the T2DM + CAD group compared with the NGT + CAD group. Serum adiponectin levels were decreased and UAER was increased from the NGT + CAD to IGT + CAD to T2DM + CAD groups. Increased UAER and serum hs-CRP, and decreased adiponectin levels were associated with traditional CAD risk factors but failed to be correlated with the severity of CAD. Hs-CRP levels were significantly correlated with UAER.

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Coronary artery disease (CAD), as one of the major complications of type 2 diabetes mellitus (T2DM), is well known to be an atherosclerotic disease. The contribution of inflammation to the initiation and progression of atherosclerosis is receiving increasing attention. Many markers have been implicated in this process.

C-reactive protein (CRP), the classic acute-phase protein, is a sensitive marker of inflammation, and increased CRP was associated with not only CAD and DM but also their mortality.[1-4] Recently, CRP levels have been shown to be significantly associated with several cardiovascular risk factors, such as age, smoking status, lipoprotein(a), body mass index (BMI), hypertension and diabetes.[5,6]

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Adiponectin, an adipocyte derived hormone, appears to be a modulator of systemic inflammation, and was found to be decreased in conditions such as T2DM and CAD.[7-11] Some authors have observed that sex, BMI and diabetes are the major determinants of serum adiponectin levels.[12] Urine albumin excretion rate (UAER) is a marker of endothelial dysfunction, and it has been demonstrated that increased UAER is associated with a higher risk of cardiovascular morbidity and mortality in patients with CAD, DM and even nondiabetic subjects.[13-17] The presence of microalbuminuria may represent an early sign of widespread derangement of endothelial function, inducing an atherogenic diathesis.[18]

In the present study, we examined serum hs-CRP, adiponectin levels and UAER in subjects with angiographically documented CAD in a Chinese population, and further explore the levels of the three markers in these subjects with different glucose tolerance status and the possible association of these markers with CAD risk factors and the severity of CAD as well.

METHODS

Participants

A total of 242 angiographically documented CAD patients recruited during June 2006 to May 2007 from the Department of Cardiology of Ruijin Hospital Affiliated to Shanghai Jiao Tong University School of Medicine participated in this study. During this period, 1680 patients were recommended to accept selective coronary angiography and 1100 were diagnosed with coronary artery disease. Among the 1100 CAD patients, 102 had T2DM, 40 had impaired glucose tolerance (IGT) and another 100 CAD subjects with normal glucose tolerance (NGT) were selected as controls. Of the 102 diabetic patients, 20 were newly diagnosed as T2DM through 75 g oral glucose tolerance test (OGTT) according to the 1999 World Health Organization criteria,[19] and of the 40 IGT patients, 28 were newly diagnosed. The three groups were further named as T2DM + CAD group, IGT + CAD group, and NGT + CAD group, respectively. The T2DM + CAD and NGT + CAD groups were matched for sex, age and BMI.

All subjects were Chinese living in Shanghai and its neighboring areas and all gave their informed consents. The Institutional Review Board of Ruijin Hospital approved the study protocol.

Oral glucose tolerance test

OGTT was performed in all subjects after an overnight fasting of 12 hours. Blood samples were collected before and at 2 hours after a standard oral glucose load of 75 g for the measurement of fasting plasma glucose (FPG), fasting serum insulin (FINS), hemoglobin A1c (HbA1c), triglyceride (TG), total cholesterol (TC), high density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C), apolipoprotein A (Apo A), apolipoprotein B (Apo B), lipoprotein(a) (Lp(a)), 2-hour plasma glucose (2hPG) and 2-hour serum insulin (2hINS). The blood samples were frozen at –80°C until assayed.

The homeostatic model of insulin resistance (HOMA-IR) and homeostatic model of insulin sensitivity (HOMA-IS)[20] were used to assess insulin resistance and insulin sensitivity respectively. They were calculated using the following formula: HOMA-IR = (FINS (μIU/ml) × FPG (mmol/L))/22.5; HOMA-IS = (20 × FINS (μIU/mL))/(FPG (mmol/L)–3.5).

Coronary angiography and diagnostic criteria for CAD

Selective coronary angiography was performed using the Judkins technique in all subjects. The severity of coronary atherosclerosis was estimated by calculating the coronary atherosclerosis score (CAS),[21] which is based on the number of stenotic coronary artery segments and the degree of their lumen stenosis. The extent and severity of CAD were assessed by assigning points to each lesion as follows: less than 50% stenosis of the luminal diameter, 1; 50%–74% stenosis, 2; 75%–99%, 3; and total obstruction, 4. The points for each lesion in the coronary arteries, including proximal, medial, and distal segments, were summed up to obtain a cumulative CAS. And the severity of CAD was also classified as one-, two- or three-vessel disease according to the number of stenotic coronary arteries in the three major vessels. Significant CAD was defined as more than 50% stenosis in at least one coronary artery segment.[22]

Clinical and biochemical measurements

All the subjects were questioned in detail about case histories. The anthropometric measurements, such as body height, body mass, waist circumference, hip circumference, and blood pressure, were determined by the same physicians. Of the 82 known diabetic subjects, 76 had ongoing antidiabetic therapy. Urine was collected for 24 hours for the measurement of the albumin excretion rate in all subjects.

Serum hs-CRP levels were measured by enzyme linked immunosorbent assay (ELISA) (BioCheck Inc., USA). The mean intra- and interassay coefficients of variation (CVs) were 4.4% and 3.3%, respectively. Serum adiponectin levels were measured by radioimmunoassay (RIA) (LINCO Research Inc., USA). The mean intra- and interassay CVs were 3.9% and 8.5%, respectively. Urinary albumin was determined by rate nephelometry (Beckman Coulter Inc., USA). The mean intra- and interassay CVs were <6.0%. Plasma glucose concentrations were measured by a glucose oxidase method (Beckman Coulter Inc.). Serum insulin concentrations were determined by RIA (DSL Inc., USA). HbA1c was determined by high performance liquid chromatography (HPLC) (Tosho Inc., Japan). Serum TG and TC levels were measured by the enzymatic method; HDL-C levels were measured by a specific precipitation method; LDL-C levels were calculated according to the Friedewald formula (LDL-C = TC–HDL-C–TG/2.2);[23]

and Apo A, Apo B, and Lp(a) were determined by rate nephelometry (Beckman Coulter Inc.).

Statistical analysis

Statistical analysis was performed using the SPSS 11.5 statistical package. Data on hs-CRP, adiponectin, UAER, FINS, 2hINS, HOMA-IR, HOMA-IS and CAS were not distributed normally, so CAS was presented as median (minimum, maximum), and were compared by the nonparametric test, while the others were all analyzed by natural logarithmic transformation and reverted by reverse logarithm. Continuous variables were presented as mean ± standard deviation (SD), and were compared by the one-way analysis of variance (ANOVA) test. Discrete variables were presented as total number (percentage) and were compared by chi-square test. The relationships were explored using Spearman's correlation technique. To allow for covariates and confounders, we performed analysis of covariance and multiple linear regression. P values of <0.05 were considered statistically significant.

RESULTS

Characteristics of the subjects

The 242 angiographically documented CAD subjects included 183 men and 59 women (Table 1). Age (± SD) averaged (63.7±8.8) years. Among these subjects, 100 had NGT (NGT + CAD group), 40 had IGT (IGT + CAD group) and 102 had T2DM (T2DM + CAD group).

Univariate analysis

As shown in Table 1, the NGT + CAD group had significantly more current smokers and current drinkers than the other two groups. As expected, the FPG and 2hPG during OGTT were gradually increased from the NGT + CAD to the T2DM + CAD group. The FINS levels were similar among the three groups. The IGT + CAD group had significantly higher 2hINS concentrations than the T2DM + CAD and NGT + CAD groups, and no significant difference was found between the latter two. The HOMA-IS was similar between the NGT + CAD and IGT + CAD groups, and was significantly lower in the T2DM + CAD group, while the HOMA-IR was gradually increased from the NGT + CAD to IGT + CAD to T2DM + CAD groups. The levels of TG, LDL-C and Apo B were higher in the T2DM + CAD group than the NGT + CAD group.

The coronary atherosclerosis in the T2DM + CAD group was much more serious than the NGT + CAD group; as shown in Table 1. There was more frequent three-vessel disease and much higher CAS in the T2DM + CAD group

Table 1. Clinical characteristics of the three groups

Characteristics	NGT + CAD	IGT + CAD	T2DM + CAD	P value
Case number (n)	100	40	102	
Sex (male/female, n)	79/21	28/12	76/26	0.503
Age (years)	63.3 ± 9.3	66.7 ± 8.4	63.0 ± 8.4	0.071
Body mass index (kg/m^2)	24.6 ± 3.6	25.3 ± 3.3	25.6 ± 3.0	0.078
Waist to hip ratio	0.95 ± 0.07	0.96 ± 0.06	0.96 ± 0.06	0.196
Systolic blood pressure (mmHg)	132 ± 18	138 ± 19	133 ± 17	0.237
Diastolic blood pressure (mmHg)	80 ± 8	80 ± 11	80 ± 10	0.951
Current smoking (n (%))	57 (57.0)	13 (32.5)**	40 (39.2)	0.012
Current drinking (n (%))	26 (26.0)	6 (15.0)	14 (13.7)*	0.027
Fasting plasma glucose (mmol/L)	4.8 ± 0.5	5.1 ± 0.8	7.4 ± 1.9$^{**\#\#}$	<0.001
2h plasma glucose (mmol/L)	6.1 ± 1.2	9.0 ± 1.1**	13.1 ± 3.9$^{**\#\#}$	<0.001
Fasting serum insulin (μIU/ml)$^{\Delta}$	9.2 ± 1.8	11.0 ± 2.0	10.0 ± 2.2	0.453
2h serum insulin (μIU/ml)$^{\wedge}$	60.3 ± 2.5	99.5 ± 2.2**	49.4 ± 2.7$^{\#\#}$	0.001
Hemoglobin A1c (%)	6.0 ± 0.4	6.2 ± 0.4	7.5 ± 1.5$^{**\#\#}$	<0.001
HOMA-IR$^{\Delta}$	2.0 ± 2.0	2.5 ± 2.2	3.0 ± 2.2**	0.001
HOMA-IS$^{\Delta}$	164.0 ± 1.8	164.0 ± 2.5	54.6 ± 2.5$^{**\#\#}$	<0.001
Triglyceride (mmol/L)	1.74 ± 0.87	1.98 ± 0.95	2.07 ± 1.18*	0.075
Total cholesterol (mmol/L)	4.42 ± 0.91	4.57 ± 1.36	4.70 ± 0.98	0.177
HDL cholesterol (mmol/L)	1.20 ± 0.34	1.25 ± 0.33	1.15 ± 0.29	0.183
LDL cholesterol (mmol/L)	2.57 ± 0.75	2.57 ± 0.94	2.81 ± 0.82*	0.078
Apo A (g/L)	1.16 ± 0.14	1.17 ± 0.16	1.23 ± 0.18$^{**\#}$	0.007
Apo B (g/L)	0.84 ± 0.19	0.90 ± 0.22	0.96 ± 0.24**	0.001
Apo B/Apo A	0.73 ± 0.18	0.77 ± 0.19	0.79 ± 0.21*	0.140
Lipoprotein(a) (g/L)	0.28 ± 0.23	0.25 ± 0.20	0.26 ± 0.20	0.613
1-vessel disease (n (%))	50 (50.0)	17 (42.5)	25 (24.5)**	0.001
2-vessel disease (n (%))	29 (29.0)	17 (42.5)	40 (39.2)	0.191
3-vessel disease (n (%))	21 (21.0)	6 (15.0)	37 (36.3)$^{*\#}$	0.015
Coronary atherosclerosis score	5 (2, 13)	5 (2, 12)	7 (2, 17)$^{**\#\#}$	0.002
hs-CRP (mg/L)$^{\wedge}$	3.60 ± 2.46	3.94 ± 1.95	4.71 ± 2.59*	0.110
Adiponectin (mg/L)$^{\Delta}$	5.99 ± 1.84	5.82 ± 1.72	4.65 ± 1.71**	0.005
UAER (μg/min)$^{\Delta}$	6.42 ± 2.51	6.89 ± 2.94	15.03 ± 4.22$^{**\#\#}$	<0.001

Data are shown as mean ± SD or as indicated. $^{*}P < 0.05$, $^{**}P < 0.01$ vs NGT + CAD group; $^{\#}P < 0.05$, $^{\#\#}P < 0.01$ vs IGT + CAD group. NGT: normal glucose tolerance; CAD: coronary artery disease; IGT: impaired glucose tolerance; T2DM: type 2 diabetes mellitus; HOMA-IR: homeostasis model assessment index for assessing insulin resistance; HOMA-IS: homeostasis model assessment index for assessing insulin sensitivity; HDL: high density lipoprotein; LDL: low density lipoprotein; Apo A: apolipoprotein A; Apo B: apolipoprotein B; hs-CRP: high sensitivity C-reactive protein; UAER: urine albumin excretion rate. $^{\Delta}$Natural logarithmic transformation was used in analysis, and geometric means ± approximate SD were reported.

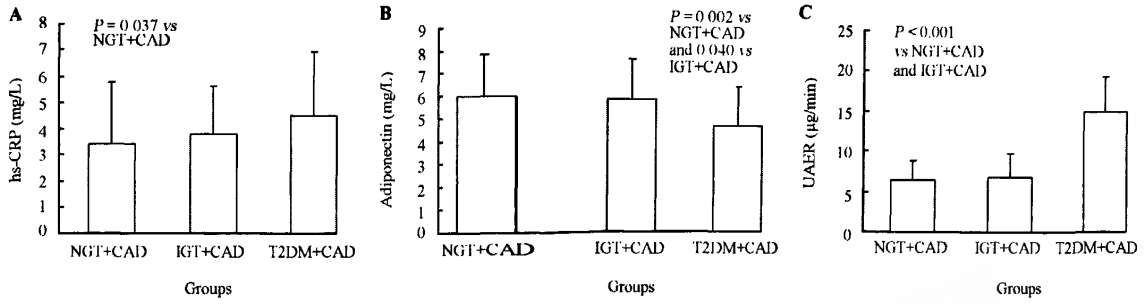

Figure 1. Serum levels of hs-CRP (A), adiponectin (B), and UAER (C) in all the subjects. Natural logarithmic transformation was used analysis, and geometric means ± approximate SD were reported (vertical lines). NGT: normal glucose tolerance; CAD: coronary art disease; IGT: impaired glucose tolerance; T2DM: type 2 diabetes mellitus; hs-CRP: high sensitivity C-reactive protein; UAER: ur albumin excretion rate.

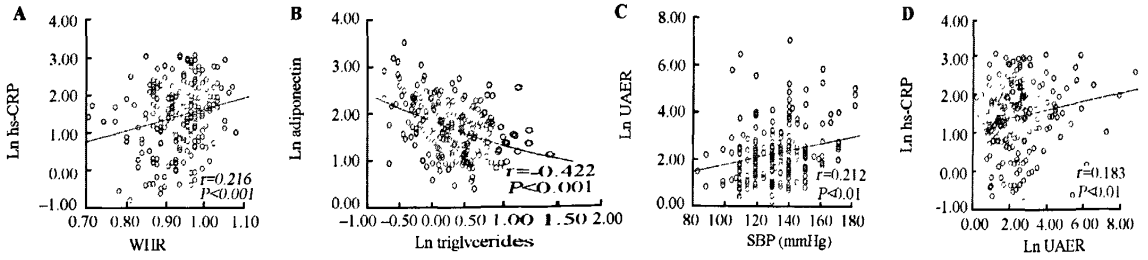

Figure 2. Correlations of hs-CRP with WHR (A), adiponectin with triglycerides (B), UAER with SBP (C), and hs-CRP with UAER (D) 242 subjects studied. Hs-CRP, adiponectin, triglycerides, and UAER were natural logarithmic transformed in analysis. Hs-CRP: hi sensitivity C-reactive protein: WHR, waist to hip ratio; UAER: urine albumin excretion rate; SBP: systolic blood pressure.

compared with the other two groups.

There was a trend of increase in serum hs-CRP concentrations according to the degree of impaired glucose tolerance. Though, it only reached a significant difference between the T2DM + CAD and NGT + CAD groups; (4.71±2.59) vs (3.60±2.46) mg/L, P=0.037 (Table 1, Figure 1A). Serum adiponectin levels were decreased from the NGT + CAD to IGT + CAD group and further decreased in the T2DM + CAD group; (5.99±1.84), (5.82±1.72) and (4.65±1.71) mg/L with P=0.002 for the NGT + CAD and P=0.040 for the IGT + CAD groups vs T2DM + CAD group (Table 1, Figure 1B). UAER was increased from a low value in the NGT + CAD group to a higher value in the IGT + CAD group and a highest value in the T2DM + CAD group; (6.42±2.51), (6.89±2.94) and (15.03±4.22) μg/min with a P <0.001 for both the NGT + CAD and IGT + CAD groups vs the T2DM + CAD group (Table 1, Figure 1C).

Bivariate correlation analyses showed that hs-CRP levels were associated with glucose related variables such as 2hPG and HbA1c, serum lipids such as TC, LDL-C, Apo B, and Apo B/Apo A, and BMI, WHR (Figure 2A), SBP and UAER. After adjustment for sex, age and BMI, partial correlation analyses showed that hs-CRP levels were also positively associated with TC, LDL-C, Apo B, Apo B/Apo A, WHR, and UAER (r= 0.206, 0.218, 0.183, 0.148, 0.136, and 0.145, respectively, P <0.05 or 0.01). Bivariate correlation analyses showed that adiponectin concentrations were associated with glucose, insulin and insulin resistance related variables such as FPG, 2hP FINS, 2hINS and HOMA-IR, serum lipids such as T (Figure 2B), HDL-C, Apo B, and Apo B/Apo A, and se age, BMI, WHR, DBP and smoking. After adjustment f sex, age and BMI, adiponectin concentrations were al positively associated with HDL-C (r= 0.272, P <0.01 and negatively associated with 2hPG, 2hINS, TG, Apo I Apo B/Apo A, and WHR (r= –0.150, –0.139, –0.37 –0.243, –0.219 and –0.206, respectively, P <0.05 or 0.0 Similarly, bivariate correlation analyses showed th UAER was associated with glucose and insulin relate variables such as FPG, 2hPG, HbA1c, HOMA-IR ar HOMA-IS, serum lipids such as TG, LDL-C, and Apo I and BMI, SBP (Figure 2C), DBP, and hs-CRP (Figu 2D). After adjustment for sex, age and BMI, UAER wa positively associated with FPG, 2hPG, HbA1c, Apo I Apo B/Apo A, SBP, DBP, and hs-CRP (r=0.285, 0.28 0.342, 0.192, 0.158, 0.180, 0.151, 0.139 and 0.14 respectively, P <0.05 or 0.01), and negatively associate with HOMA-IS (r= –0.190, P <0.01). Bivariate an partial correlation analyses among the three marke showed that there was a significant relationship betwee hs-CRP and UAER, and no significant correlation wa found between any other two markers.

Adjusted analysis

In a multiple linear stepwise regression analysis with model including all the variables significantly associate with hs-CRP in bivariate correlation analyses a independent variables, the significant determinants c serum hs-CRP levels were WHR and LDL-C in a

subjects, LDL-C in the T2DM + CAD group, and 2hPG and BMI in the NGT + CAD group (R^2= 0.070, 0.064 and 0.165, respectively). No variables reached a significant difference in the IGT + CAD group (Table 2).

We also did a multiple linear stepwise regression analysis for determining the significant determinants of serum adiponectin concentrations. The results showed that the significant determinants of serum adiponectin levels in all subjects were TG, T2DM, 2hINS, HDL-C, Apo B, age, sex, and WHR while they were HDL-C, TG in T2DM + CAD group and were TG, DBP, and sex in the IGT + CAD group and HDL-C, Apo B, age and WHR in the NGT + CAD group (R^2= 0.352, 0.235, 0.376 and 0.345, respectively).

Similarly, the significant determinants of UAER were SBP, HbA1c, and T2DM in all subjects while HbA1c and LDL-C were significant in the T2DM + CAD group with FPG and SBP being significant in the IGT + CAD group and in NGT + CAD group SBP was significant (R^2= 0.214, 0.113, 0.408 and 0.103, respectively) (Table 2).

Table 2. Multiple linear stepwise regression analysis for hs-CRP, adiponectin, and UAER in all subjects

Dependent variable	Standardized regression coefficient		
	Model 1 ln hs-CRP	Model 2 ln adiponectin	Model 3 ln UAER
Age	–	0.184**	–
Sex	–	0.156*	–
Waist to hip ratio	0.214**	–0.128*	–
Systolic blood pressure	–	–	0.263**
Diabetes mellitus	–	–0.149*	0.242**
2-hour serum insulin	–	–0.125*	–
Hemoglobin A1c	–	–	0.193*
Triglyceride	–	–0.232**	–
HDL-cholesterol	–	0.179**	–
LDL-cholesterol	0.171*	–	–
Apo B	–	–0.135*	–
Adjusted R^2	0.070	0.352	0.214

*P < 0.05, **P < 0.01 for levels of significance of regression coefficient at two-tailed testing. hs-CRP: high sensitivity C-reactive protein; UAER: urine albumin excretion rate; HDL: high density lipoprotein; LDL: low density lipoprotein. Apo B: apolipoprotein B.

So, diabetes related variables such as FPG, 2hPG, 2hINS, and HbA1c, serum lipids such as TG, HDL-C, LDL-C, and Apo B, blood pressure including SBP and DBP, obesity related variables including WHR and BMI, and sex, age, and T2DM were the significant determinants of hs-CRP, adiponectin and/or UAER in all subjects and/or each group.

The relationship between the three markers and the severity of CAD was also examined. However, none of these markers showed any significant correlation with the severity of CAD.

DISCUSSION

The present study demonstrated that in this Chinese population serum hs-CRP levels and UAER were increased, and serum adiponectin levels were decreased from the NGT + CAD to the IGT + CAD group and from that group to the T2DM + CAD group. Though, it did not reach a statistically significant difference between the NGT + CAD and IGT + CAD groups for these markers as well as the IGT + CAD and T2DM+CAD groups for hs-CRP levels. Increased UAER and serum hs-CRP and decreased adiponectin concentrations were associated with traditional CAD risk factors but failed to be correlated with the severity of CAD. We also found that hs-CRP concentrations were significantly correlated with UAER.

Evidence from laboratory, clinical, and epidemiological investigations regarding the contribution of inflammation to atherosclerosis are accumulating quickly. These findings suggest that atherosclerosis is a chronic inflammation condition that evolves as a result of a combination of biochemical, physical, and possibly infectious processes. Biochemical markers, such as hs-CRP and adiponectin have been used for detecting and assessing the severity of systemic inflammation. UAER, a marker of endothelial dysfunction, is attracting increasing interest because it probably represents an atherogenic diathesis. In the present study, we selected hs-CRP, adiponectin, and UAER as markers of systemic inflammation and/or endothelial dysfunction to further explore the levels of the three markers in CAD subjects with different glucose tolerance status, and the possible association of these markers with CAD risk factors and the severity of CAD as well.

Data from previous studies have shown that UAER[13-17] and serum hs-CRP levels[1-4] were increased and adiponectin levels[7-12] were decreased in patients with T2DM or CAD compared with respective controls. In the present study population, we found that serum hs-CRP levels were higher in diabetic CAD patients compared with nondiabetic controls, serum adiponectin levels were gradually decreased, and UAER was gradually increased from the NGT + CAD to IGT + CAD to T2DM + CAD groups. As we know, IGT is an intermediate hyperglycemia situation between normal glucose and diabetes. Considerable clinical and epidemical studies showed that the incidence of CAD was increased in IGT patients. Our results were consistent with the previous studies showing that it was more dangerous in IGT than normal glucose. Especially, we did find elevated hs-CRP and UAER, and decreased adiponectin in CAD subjects with IGT as compared with NGT, though it did not reach a statistically significant difference. It suggests that there might be more extensive systemic inflammation and endothelial dysfunction in the IGT + CAD group. So, it is necessary to carefully control elevated plasma glucose, not only in diabetes but also in IGT status. It is very important to control the traditional cardiovascular risks and prevent the deterioration of CAD.

In our study, hs-CRP was associated with several

cardiovascular risk factors which had been mostly reported earlier.[5,6,24,25] Significantly positive association of hs-CRP were found with glucose related variables including 2hPG and HbA1c, serum lipids including TC, LDL-C, Apo B and Apo B/Apo A, and BMI, WHR and SBP. The association of hs-CRP with HbA1c, LDL-C, and Apo B/Apo A was different from previous studies.[5,6,24,25] We also found that the significant determinants of serum hs-CRP levels were WHR and LDL-C in all subjects, and WHR had the strongest correlate. These were different from other studies,[24,25] which found that age, smoking status, Lp(a), and adiponectin were the significant determinants of CRP. Our results indicated that obesity, especially central obesity, was the main determinant for hs-CRP.

Relationships between adiponectin and several risk factors related to CAD have been investigated to further explore potential targets of the probably of the antiatherosclerotic properties of adiponectin.[12,26,27] Previous studies showed that adiponectin levels were associated with sex, BMI, WHR, CAD, DM, FINS, 2hPG, HbA1c, insulin resistance, TG, TC, and HDL-C.[28-30] In the present study, we found that the significant determinants of serum adiponectin levels in all subjects were T2DM, 2hINS, TG, HDL-C, Apo B, age, sex, and WHR, and TG was the strongest correlate. These combined findings clearly supported the recent point of view that adiponectin probably has antiatherosclerotic properties[12,26,27] and directly influences the concentrations of circulating HDL-C and TG.[26] Previous studies reported that there was a significant association between CRP and adiponectin levels.[25,27,31,32] Although we did not find an association between the two markers in our study subjects with definite T2DM and CAD, our findings did not necessarily contradict those of previous studies. The lack of correlation in the present study was in agreement with several other previous research reports, and suggested the possibilities that the role of systemic inflammation, as part of the relationship of adiponectin with atherosclerosis, might decrease during the course of the disease.[26,29]

Recently, CRP levels have been reported to be significantly associated with markers of endothelial damage in type 1 diabetic patients, obese nondiabetic women, and healthy subjects, thus supporting the notion that endothelial dysfunction might represent a critical intermediate phenotype in the relationship between inflammation and cardiovascular disease.[33-36] With regard to the association between hs-CRP and UAER, two previous studies found controversial results.[36,37] In the present study, we found that there was a significant bivariate relationship between hs-CRP and UAER even after adjustment for sex, age and BMI, but in multivariate regression analysis, hs-CRP failed to be associated with UAER. Previous studies have reported that HbA1c, diabetes mellitus, SBP, DBP and HDL-C were the independent determinants of UAER.[37-39] In addition to these variables, we found that FPG and LDL-C were al significantly correlated with UAER in our stu population, and SBP was the strongest correlate.

Regarding the severity of CAD, we found that there w more frequent three-vessel disease and much higher C/ in the T2DM + CAD group compared with the other tv groups, and we also observed that serum hs-CRP leve were higher in the T2DM + CAD group compared wi the NGT + CAD group, serum adiponectin levels we decreased, and UAER was increased in the T2DM CAD group compared with the other two groups. Giv the above results, it seemed that hs-CRP, adiponectin, a UAER might, to some extent, be correlated with t severity of CAD which was estimated by the number diseased vessels and the CAS.[21,22] Unexpectedly, none the three markers showed any significant correlaion wi the severity of CAD. Thus, the increase of hs-CRP a UAER, and decrease of adiponectin, might reflect t diffuse atherosclerotic process in the vascular syste rather than the degree of localized obstruction fro lesions, as proposed by one previous study.[40] It w further confirmed that CAD, an atherosclerotic diseas was a multifactorial disease. Not only markers systemic inflammation and/or endothelial dysfunctic such as hs-CRP, adiponectin, and UAER, but also t other risk factors such as blood glucose, WHR, bloc lipids, and blood pressure were integrated together a involved in the initiation and progression atherosclerosis.

In conclusion, in this cross-sectional study performed in Chinese population, serum hs-CRP levels were increase in the T2DM + CAD group compared with the NGT CAD group, and serum adiponectin levels were decrease and UAER was increased from the NGT + CAD to IGT CAD to T2DM + CAD group. Increased UAER an serum hs-CRP, and decreased adiponectin levels wer associated with traditional CAD risk factors but failed t be correlated with the severity of CAD. Hs-CRP level were significantly correlated with UAER. It suggeste that the increased CRP and UAER as well as th decreased adiponectin integrated with the traditional ris factors, aggravated the coronary artery disease.

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