



Evaluation value of coronary CTA for coronary plaque features and its correlation with platelet function and serum biochemical indexes

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ABSTRACT

Objective: To analyze the evaluation value of coronary CT angiography for coronary plaque features and its correlation with platelet function and serum biochemical indexes. **Methods:** A total of 450 patients with coronary heart disease were divided into calcified plaque group (CT value ≥ 130 HU) ($n=117$), soft plaque group (CT value ≤ 60 HU) ($n=150$) and mixed plaque group (CT value 60-130HU) ($n=183$) by coronary CT angiography (CTA), and 100 healthy subjects who received physical examination in our hospital during the same period were selected as control group. Differences in platelet function and serum biochemical indexes were compared among four groups of patients, and the judgment value of atheromatous plaque CT value from CTA for the severity of coronary heart disease was analyzed. **Results:** Platelet function parameters MPV, TEG-MA, P-selectin, PDGF-BB and vWF levels in peripheral blood of soft plaque group were higher than those of the other three groups; inflammatory factors CRP, IL-6, IL-12, IL-18 and IL-23 content in serum were higher than those of the other three groups; chemokines MCP-1, CXCL16, Fractalkine and RANTES content in serum were higher than those of the other three groups; adipocytokines Leptin and RBP4 content in serum were higher than those of the other three groups while SFRP5 content was lower than those of the other three groups. Atheromatous plaque CT value in patients with coronary heart disease was directly correlated with platelet function and the content of serum biochemical indexes. **Conclusions:** Coronary CTA can accurately assess coronary atheromatous plaque features, and can also be a reliable noninvasive method to judge coronary heart disease severity, treatment prognosis and so on.

1. Introduction


Coronary CT angiography (CTA) is the important tool for diagnosis of coronary heart disease, and many current studies have shown that the CTA can not only judge the degree of coronary stenosis, but can also make quantitative evaluation on plaque features[1]. Coronary heart disease patients with different plaque features are with different treatment outcome, and studies have found that acute coronary syndrome (ACS) is mainly secondary to

unstable soft plaque rupture while acute cardiovascular events less occur in the calcified plaque. So early clarifying the plaque features is of important significance in the establishment of treatment and the judgment of treatment outcome[2,3]. In the study, CTA was applied in the judgment of plaque features in patients with coronary heart disease in our hospital, and the correlation between different plaque CT value and specific disease severity was further analyzed.

2. Materials and methods

2.1. General information

A total of 450 patients with coronary heart disease treated in

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our hospital between June 2013 and May 2016 were selected as observation group, they were all diagnosed by coronary angiography and echocardiography, and patients with congenital heart disease and malignant tumor were excluded. 100 healthy subjects who received physical examination in our hospital during the same period were selected as control group. Observation group included 250 male cases and 200 female cases that were 45-72 years old; control group included 54 male cases and 46 female cases that were 43-71 years old. The two groups of research subjects showed no statistically significant difference in the distribution of gender and age.

2.2. Coronary angiography and results interpretation

Patients' heart rate before examination was controlled to be < 65 times/min, and those with rapid heart rate could orally take metoprolol. 64-slice spiral CT was used for examination, contrast agent (80 mL) was intravenously injected at 4 mL/s for scanning, imaging scanning was started 45 s after intravenous injection, and the image data were sent to a computer workstation for the multiplanar reformation that was carried out by two radiologists with intermediate professional title above. Finally, the obtained plaque CT value was referred to secondarily divide the included patients into calcified plaque group ($n=117$): CT value ≥ 130 HU and (189.63 ± 24.78) HU in average; soft plaque group ($n=150$): CT value acuties ≤ 60 HU and (31.83 ± 4.05) HU in average; mixed plaque group ($n=183$): CT value 60-130 HU and (94.36 ± 10.52) HU in average.

2.3. Platelet function

Soon after admission, 2 mL of fasting cubital venous blood was collected from all subjects, and the platelet adhesion tester and platelet aggregation tester were used to detect platelet function indexes, including platelet count (PLT), mean platelet volume (MPV), maximal thrombus solidness (TEG-MA), P-selectin, platelet-derived growth factor BB (PDGF-BB) and von willebrand factor (vWF).

2.4. Serum biochemical indexes

Soon after admission, 2 mL of fasting cubital venous blood was collected from all subjects and centrifuged at 1 500 r/min for 10min to get supernatant, and the following indexes were detected: (1) inflammatory factors: ELISA was used to detect C-reactive protein (CRP), interleukin-6 (IL-6), interleukin-12 (IL-12), interleukin-18 (IL-18) and interleukin-23 (IL-23) content in serum; (2) chemokines: monocyte chemoattractant factor-1 (MCP-1), chemokine CXCL16, chemokine Fractalkine and T cell chemokine (RANTES); (3) adipocytokines: Leptin, secreted frizzled-related protein 5 (SFRP5) and retinol-binding protein 4 (RBP4).

2.5. Statistical methods

Data in the study was input in software SPSS23.0, measurement data was by t test, correlation analysis was performed by Pearson test and $P < 0.05$ indicated statistical significant differences.

3. Results

3.1. Platelet function parameters

MPV, TEG-MA, P-selectin, PDGF-BB and vWF levels in peripheral blood of soft plaque group, mixed plaque group and calcified plaque group were significantly higher than those of control group. MPV, TEG-MA, P-selectin, PDGF-BB and vWF levels in peripheral blood of mixed plaque group were significantly higher than those of calcified plaque group. MPV, TEG-MA, P-selectin, PDGF-BB and vWF levels in peripheral blood of soft plaque group were significantly higher than those of mixed plaque group and calcified plaque group. Differences in platelet function parameters MPV, TEG-MA, P-selectin, PDGF-BB and vWF levels were statistically significant ($P < 0.05$) while differences in PLT levels were not statistically significant among four groups ($P > 0.05$), shown in Table 1.

3.2. Inflammatory factors

CRP, IL-6, IL-12, IL-18 and IL-23 content in serum of soft plaque group, mixed plaque group and calcified plaque group were significantly higher than those of control group. CRP, IL-6, IL-12, IL-18 and IL-23 content in serum of mixed plaque group were significantly higher than those of calcified plaque group. CRP, IL-6, IL-12, IL-18 and IL-23 content in serum of soft plaque group were significantly higher than those of mixed plaque group and calcified plaque group ($P < 0.05$), shown in Table 2.

3.3. Chemokines

MCP-1, CXCL16, Fractalkine and RANTES content in serum of soft plaque group, mixed plaque group and calcified plaque group were significantly higher than those of control group. MCP-1, CXCL16, Fractalkine and RANTES content in serum of mixed plaque group were significantly higher than those of calcified plaque group. MCP-1, CXCL16, Fractalkine and RANTES content in serum of soft plaque group were significantly higher than those of mixed plaque group and calcified plaque group ($P < 0.05$), shown in Table 3.

3.4. Adipocytokines

Leptin and RBP4 content in serum of soft plaque group, mixed

Table 1

Comparison of platelet function parameters among four groups.

Groups	Case No.	PLT ($\times 10^9/L$)	MPV (fL)	TEG-MA (mm)	P-selectin ($\mu g/L$)	PDGF-BB (ng/L)	vWF ($\times 10^3$ mU/L)
Soft plaque group	150	191.52 \pm 23.48	8.45 \pm 0.91 ^{abc}	73.29 \pm 7.85 ^{abc}	254.95 \pm 30.17 ^{abc}	261.29 \pm 30.28 ^{abc}	489.55 \pm 56.78 ^{abc}
Mixed plaque group	183	189.77 \pm 20.75	8.12 \pm 0.89 ^{ab}	68.93 \pm 7.64 ^{ab}	174.38 \pm 20.15 ^{ab}	153.09 \pm 18.45 ^{ab}	327.58 \pm 40.18 ^{ab}
Calcified plaque group	117	185.46 \pm 21.38	7.79 \pm 0.85 ^a	62.17 \pm 7.21 ^a	69.73 \pm 7.21 ^a	83.62 \pm 9.15 ^a	243.19 \pm 25.76 ^a
Control group	100	176.48 \pm 20.43	7.48 \pm 0.81	57.34 \pm 6.05	32.74 \pm 4.09	39.48 \pm 4.52	153.82 \pm 20.12

^a vs. control group, $P < 0.05$; ^b vs. calcified plaque group, $P < 0.05$; ^c vs. mixed plaque group, $P < 0.05$.**Table 2**

Comparison of inflammatory factor content in serum among four groups.

Groups	Case No.	CRP (mg/L)	IL-6 (ng/L)	IL-12 (ng/L)	IL-18 (ng/L)	IL-23 (ng/L)
Soft plaque group	150	3.89 \pm 0.45 ^{abc}	72.17 \pm 8.34 ^{abc}	95.94 \pm 10.12 ^{abc}	89.63 \pm 9.27 ^{abc}	93.21 \pm 10.18 ^{abc}
Mixed plaque group	183	2.18 \pm 0.25 ^{ab}	45.83 \pm 6.12 ^{ab}	75.48 \pm 8.11 ^{ab}	56.92 \pm 6.15 ^{ab}	59.74 \pm 7.12 ^{ab}
Calcified plaque group	117	1.21 \pm 0.18 ^a	31.29 \pm 3.85 ^a	34.95 \pm 4.12 ^a	20.45 \pm 2.78 ^a	29.53 \pm 3.41 ^a
Control group	100	0.78 \pm 0.09	20.38 \pm 2.79	11.18 \pm 1.79	7.39 \pm 0.82	13.84 \pm 1.76

^a vs. control group, $P < 0.05$; ^b vs. calcified plaque group, $P < 0.05$; ^c vs. mixed plaque group, $P < 0.05$.

plaque group and calcified plaque group were significantly higher than those of control group while SFRP5 content were significantly lower than that of control group. Leptin and RBP4 content in serum of mixed plaque group were significantly higher than those of calcified plaque group while SFRP5 content was significantly lower than that of calcified plaque group. Leptin and RBP4 content in serum of soft plaque group were significantly higher than those of mixed plaque group and calcified plaque group while SFRP5 content was significantly lower than those of mixed plaque group and calcified plaque group ($P < 0.05$), shown in Table 4.

3.5. Correlation between atheromatous plaque CT value and coronary heart disease

Pearson test showed that atheromatous plaque CT value was significantly negatively correlated with platelet function parameters MPV, TEG-MA, P-selectin, PDGF-BB and vWF levels, inflammatory factors CRP, IL-6, IL-12, IL-18 and IL-23 content, chemokines MCP-1, CXCL16, Fractalkine and RANTES content as well as condition judgment indexes Leptin and RBP4 content, and significantly positively correlated with condition judgment index

SFRP5 ($P < 0.05$).

4. Discussion

Coronary CTA can be used to determine the atheromatous plaque features in patients with coronary heart disease, different plaque components can show different CT values in the CT imaging, and the plaques that are rich in lipid core are generally with low CT value (< 60 HU), commonly known as soft plaque[4]. In the study, the plaque CT values of the included patients with coronary heart disease were detected at first through CTA, and then used for qualitative plaque grouping, and it was found that 450 patients with coronary heart disease included 117 cases with calcified plaque (CT value ≥ 130 HU), 150 cases with soft plaque (CT value ≤ 60 HU) and 183 cases with mixed plaque group (CT value 60-130 HU). Studies both at home and abroad have confirmed that soft coronary plaque group of patients are with the highest incidence of rupture and acute myocardial infarction, whereas patients with calcified plaque are with more stable condition. In order to define the value of atheromatous plaque grouping by CTA for judging the overall condition of patients

Table 3

Comparison of chemokine content in serum among four groups.

Groups	Case No.	MCP-1 (pg/L)	CXCL16 ($\mu g/L$)	Fractalkine (ng/L)	RANTES (ng/L)
Soft plaque group	150	22.57 \pm 3.18 ^{abc}	3.42 \pm 0.48 ^{abc}	78.95 \pm 8.11 ^{abc}	1 215.82 \pm 150.95 ^{abc}
Mixed plaque group	183	17.23 \pm 2.75 ^{ab}	2.84 \pm 0.35 ^{ab}	53.82 \pm 6.95 ^{ab}	689.73 \pm 75.82 ^{ab}
Calcified plaque group	117	15.43 \pm 1.84 ^a	2.31 \pm 0.29 ^a	39.74 \pm 4.11 ^a	342.95 \pm 40.28 ^a
Control group	100	13.27 \pm 1.94	1.87 \pm 0.23	30.27 \pm 3.89	214.83 \pm 25.96

^a vs. control group, $P < 0.05$; ^b vs. calcified plaque group, $P < 0.05$; ^c vs. mixed plaque group, $P < 0.05$.**Table 4**

Comparison of condition judgment index content in serum among four groups.

Groups	Case No.	Leptin (ng/L)	SFRP5 ($\mu g/L$)	RBP4 (g/L)
Soft plaque group	150	27.82 \pm 3.41 ^{abc}	16.02 \pm 1.88 ^{abc}	21.59 \pm 3.21 ^{abc}
Mixed plaque group	183	19.63 \pm 2.09 ^{ab}	21.55 \pm 2.74 ^{ab}	13.74 \pm 1.83 ^{ab}
Calcified plaque group	117	15.48 \pm 1.75 ^a	26.18 \pm 3.84 ^a	9.62 \pm 0.98 ^a
Control group	100	11.28 \pm 1.95	31.82 \pm 3.95	7.03 \pm 0.82

^a vs. control group, $P < 0.05$; ^b vs. calcified plaque group, $P < 0.05$; ^c vs. mixed plaque group, $P < 0.05$.

with coronary heart disease, the platelet function, serum biochemical indexes and other clinical common disease evaluation projects were further compared among various groups of research subjects in the study.

The basis of atheromatous plaque formation in patients with coronary heart disease is vascular intima damage, and as intima damage increases, the blood coagulation system is activated and induces hypercoagulable state. Platelet hyperfunction is an independent risk factor for acute cardiovascular events in patients with coronary heart disease, and therefore, the platelet function state was compared among groups at first in the study first so as to make clear the relation between different plaque features and platelet function. PLT, MPV, TEG-MA, PDGF-BB and vWF are the clinical common platelet function indexes[5,6]. P-selectin is the molecule released by α particle after platelet activation, and is the most specific platelet activation marker. PDGF-BB exists in platelets in the form of α -particle, and can reflect the platelet release function. In the case of endothelial damage, vWF is released into the blood, and can reflect the degree of endothelial cell damage. MPV is an index reflecting megakaryocyte growth and thrombopoiesis, and TEG-MA mainly reflects the platelet aggregation function[7,8]. It was found in the study that MPV, TEG-MA, P-selectin, PDGF-BB and vWF levels were higher in coronary heart disease patients with different plaques features, and as plaque CT value decreased, MPV, TEG-MA, P-selectin, PDGF-BB and vWF levels further increased, indicating that soft plaque group of patients are with the highest platelet activity and also the highest probability of long-term acute coronary embolic events.

There are also many serum biochemical indexes directly related to coronary heart disease, and the levels of inflammatory cytokines and chemokines of all groups were further analyzed in the study. Chronic systemic inflammatory response has been confirmed to be throughout the whole course of coronary heart disease, and is also one of the main risk factors that add to the continuous increase of atheromatous plaque area and the occurrence of acute myocardial infarction[9,10]. Detection of the content of CRP, IL-6, IL-12, IL-18, IL-23 and other pro-inflammatory factors showed that CRP, IL-6, IL-12, IL-18 and IL-23 content in serum of patients with coronary heart disease were higher than those of healthy subjects, and as the plaque CT value decreased, the above factor levels further increased, indicating that soft plaque group of patients are with most serious systemic inflammatory state. High expression of chemokines is the basis for macrophages and lipid metabolites to accumulate in local coronary artery and form atheromatous plaque, and MCP-1 can mediate the activation of a variety of transcription factors and inflammatory mediators, leading to unstable plaque[11,12]. Chemokine CXCL16 can activate T lymphocytes and participate in the interaction between dendritic cells and T cells, and study has confirmed that it participates in the inflammatory reaction of atherosclerosis. Chemokine Fractalkine can be combined with receptor CX3CR1 and then prompt the directional migration of mononuclear cells and

NK cells, increase inflammatory response and prompt plaque to be unstable[13]. T cell chemokine (RANTES) can mediate mononuclear macrophages across the endothelium as well as promote cellular inflammatory factor expression and atherosclerosis. It was found in the study that soft plaque group of patients were with higher MCP-1, CXCL16, Fractalkine and RANTES content in serum, indicating that high expression of chemokine is the core factor of the coronary artery disease aggravation and plaque instability.

Leptin, SFRP5 and RBP4 are new molecules discovered in recent years that are directly related to coronary heart disease[14]. It has been found in the mouse models that Leptin can promote the development of atherosclerosis, and Leptin levels in patients with coronary heart disease are significantly higher than those in patients without coronary heart disease. SFRP5 can inhibit Wnt5a so as to stop the inflammatory mediators of macrophages and fat cells from being functional, and its level is negatively correlated with the severity of coronary heart disease[15,16]. RBP4 can interfere with the glucolipid metabolism so as to promote inflammation, and many studies have also found that RBP4 is directly related to the insulin resistance, obesity, atherosclerosis and so on[17]. In the study, serum levels of the above three factors were tested, and it was found that Leptin and RBP4 content in patients with coronary heart disease were higher while SFRP5 content was lower, which is consistent with the functions of three factors mentioned above. Leptin and RBP4 content of soft plaque group were higher than those of mixed plaque group and calcified plaque group while SFRP5 content was lower than those of mixed plaque group and calcified plaque group, showing that coronary heart disease develops as the plaque CT value decreases.

Finally, the correlation between atheromatous plaque CT value under CTA and the condition in patients with coronary heart disease was analyzed, and it was found that atheromatous plaque CT value in patients with coronary heart disease was negatively correlated with platelet function parameters MPV, TEG-MA, P-selectin, PDGF-BB and vWF levels, inflammatory factors CRP, IL-6, IL-12, IL-18 and IL-23 content, chemokines MCP-1, CXCL16, Fractalkine and RANTES content as well as condition judgment indexes Leptin and RBP4 content, and positively correlated with condition judgment index SFRP5. It is thus clear that at the same time of quantitative judgment of atheromatous plaque, coronary CTA can intuitively and accurately judge the overall disease severity, and is expected to become the reliable means for long-term treatment guide and prognosis judgment in patients with coronary heart disease.

References

- [1] Khazai B, Luo Y, Rosenberg S, et al. Coronary atherosclerotic plaque detected by computed tomographic angiography in subjects with diabetes compared to those without diabetes. *PLoS One* 2015; **10**(11): e0143187.
- [2] Guan SF, Qu XK, Han WZ, et al. Clinical features of plaques with

- different characteristics detected by CT coronary angiography for patients with coronary heart diseases. *J Shanghai Jiaotong Univ (Med Sci)* 2014; **34**(8): 1176-1179.
- [3] Gan L, Feng C, Liu C, et al. Association between serum N-terminal pro-B-type natriuretic peptide levels and characteristics of coronary atherosclerotic plaque detected by coronary computed tomography angiography. *Exp Ther Med* 2016; **12**(2): 667-675.
- [4] Rodriguez-Granillo GA, Carrascosa P, Bruining N, et al. Defining the non-vulnerable and vulnerable patients with computed tomography coronaryangiography: evaluation of atherosclerotic plaque burden and composition. *Eur Heart J Cardiovasc Imag* 2016; **17**(5): 481-491.
- [5] Liang H, Huang HJ, Zhou XL, et al. Changes of platelet function after antiplatelet therapy and single nucleotide polymorphism of COX-1 and COX-2 in elderly patients. *Chin General Pract* 2014; **17**(20): 2345-2348.
- [6] Jamasbi J, Megens RT, Bianchini M, et al. Differential inhibition of human atherosclerotic plaque-induced platelet activation by dimeric GPVI-Fc and anti-GPVI antibodies: Functional and imaging studies. *J Am Coll Cardiol* 2015; **65**(22): 2404-2415.
- [7] Wang JQ, Liu JG, Wang CL. Correlation analysis between visualization of hemorrhheologic changes and platelet function in patients with acute coronary syndrome after percutaneous coronary intervention. *Chin J Pathophysiol* 2014; **30**(2): 214-219.
- [8] Jacobin-Valat MJ, Laroche-Traineau J, Larivière M, et al. Nanoparticles functionalised with an anti-platelet human antibody for *in vivo* detection of atherosclerotic plaque by magnetic resonance imaging. *Nanomedicine* 2015; **11**(4): 927-937.
- [9] Sun LQ. Effect of Erigeron breviscapus on serum C-reactive protein as well as interleukin-6, -12, -18 and -23 in elderly patients with acute coronary syndrome. *Chinese J Gerontol* 2014; **34**(1): 249-252.
- [10] Matusiak A, Chałubiński M, Broncel M, et al. Putative consequences of exposure to *Helicobacter pylori* infection in patients with coronary heart disease in terms of humoral immune response and inflammation. *Arch Med Sci* 2016; **12**(1): 45-54.
- [11] Zhu SS, Wang QC, Hu J. Clinical significance of serum chemokine CXCL16 detection before and after coronary heart disease and unstable angina treatment. *Chin J Clin Rat Drug Use* 2015; **8**(3): 88-91.
- [12] Zhang CY, Cao Z, Yang Y, et al. The serum level change of Fractalkine, monocyte chemoattractant protein-1 and interleukin-8 in patients with coronary heart disease and its significance. *J Bengbu Med Coll* 2016; **41**(4): 485-488.
- [13] Tian J, Hu S, Wang F, et al. PPARG, AGTR1, CXCL16 and LGALS2 polymorphisms are correlated with the risk for coronary heart disease. *Int J Clin Exp Pathol* 2015; **8**(3): 3138-3143.
- [14] Chen Y, Feng YM. Correlation between serum leptin level with coronary heart disease risk stratification and lesion degree of coronary artery. *J Hainan Med Univ* 2015; **21**(1): 32-35.
- [15] Zeng R, Xu CH, Xu YN, et al. Association of leptin levels with pathogenetic risk of coronary heart disease and stroke: a meta-analysis. *Arq Bras Endocrinol Metabol* 2014; **58**(8): 817-823.
- [16] Li YY, Dong WP, Lu H, et al. Correlation of serum Leptin, SFRP5 and RBP4 with coronary heart disease. *Acta Univ Med Anhui* 2016; **51**(8): 1160-1163.
- [17] Dong H, Li X, Tang Y. Serum retinol-binding protein-4 level is a high risk factor for coronary heart disease in Chinese. *Clin Lab* 2015; **61**(11): 1675-1678.