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Original Article

Effect of coronary rotational atherectomy before stent implantation on serum inflammatory and plaque stabilization factors in patients with coronary artery disease

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Abstract: Objective: To explore the effect of interventional coronary rotational atherectomy on the correlation between serum inflammatory factors and plaque stability indexes in patients with coronary artery disease (CAD). Methods: Eighty-six patients with CAD and coronary calcification were randomized into an observation group and a control group. The former was treated with coronary rotational atherectomy and stent implantation, while the latter underwent stent implantation only. Changes in the levels of serum inflammatory factors and plaque stability indicators were determined in both groups before and after surgery. Results: The immediate success rate of operation in the observation group was higher than that in the control group (P<0.05). The levels of serum interleukin-6 (IL-6), serum interleukin-18 (IL-18), plaque stabilization factor pentraxin 3 (PTX3), and lipoprotein-associated phospholipase A2 (Lp-PLA2) were lower in both groups after surgery, but this decrease was greater in the observation group (P<0.05). In addition, the incidence of perioperative complications was lower in the observation group. There was no statistical difference in renal function between the groups. Conclusion: Coronary rotational atherectomy may reduce serum inflammatory factors and plaque stabilization factors to some extent. It is also useful for assistance in the interventional therapy of CAD, with good clinical application value.

Keywords: Coronary artery disease, coronary rotational atherectomy, inflammatory factors, plaque stabilization factors, safety

Introduction

From the beginning of the 21st century, human lifestyle has evolved greatly in both developing and developed countries. With this transition, ischemic heart diseases have prominently risen in prevalence and incidence, in relation to dietary patterns, insufficient physical activity, aging of the population, smoking, serious environmental pollution and lack of sufficient physical activity [1]. Recent epidemiological data show that coronary artery disease (CAD) has become a worldwide challenge for public health, and an important factor for mortality risk in China, gradually becoming more frequent in the younger population [2].

CAD is primarily caused by atherosclerotic pathological changes in blood vessels, resulting in calcification of the coronary arteries with vascular hemodynamic changes, leading to classic clinical manifestations [3]. The exact mechanisms underlying calcification remain unclear. It may be associated with inflammatory factors and lipid metabolism disorders. Thus, local atherosclerotic changes caused by cytokines and growth factors eventually result in vascular calcification [4].

At present, CAD treatments mainly include percutaneous coronary intervention (PCI) in internal medicine and coronary artery bypass grafting in surgical medicine. The former is often used as a common clinical treatment as it avoids surgical trauma and shows good outcomes. However, severe vascular calcification can hinder the smooth passage of the guide wire during operation, which can impede PCI.

Therefore, timely and effective measures to remove calcified plaques in coronary arteries may improve PCI results [5]. Coronary rotational atherectomy can ablate these plaques, enlarging the arterial lumen and softening remaining plaque tissue, which facilitates smooth operation during cardiovascular coronary surgery. On the other hand, research has shown that the severity of the coronary plaque and the level of inflammatory factors and plaque stabilization factors are positively correlated, with plaque promoting inflammation. Inflammation appears to peak and then begin to decline 72 hours after PCI, with plaque rotational ablation reducing compression of the stent to the plaque, thus reducing inflammation. Therefore, plaque reduction and vascular re-conduction could decrease serum levels of inflammatory markers [6, 7]. In this study, we aim to provide a theoretical basis for the clinical application of coronary rotational atherectomy in cardiovascular interventional surgery based on its clinical effects on serum inflammation factors and plaque stabilization indicators.

Materials and methods

Objectives of the study

Eighty-six cases of coronary artery calcification treated in the Department of Cardiovascular Medicine in our hospital from January 2016 to January 2017 were included. Patients were randomized into an observation group (n=43) and a control group (n=43), according to the patients' admission numbers. Inclusion criteria: 1). Patients diagnosed with coronary artery calcification by coronary angiography. 2). Patients diagnosed with coronary artery calcification by previous angiography with recent exacerbation. 3). Patients underwent PCI for the first time. 4). Patients with balloon dilatation insufficiency. 5). Patients aged 20 to 75.

Exclusion criteria: 1) Patients with valvular heart disease, congenital heart disease or macrovascular disease, who needed surgical treatment. 2) Patients with acute myocardial infarction or subacute myocardial infarction. 3) Patients with arrhythmia. 4) Patients allergic to contrast agents. 5) Patients with mental disorders unable to cooperate with the completion of the study. 6) Patients with major organ dysfunction (neurological, liver and kidney disease). 7) Patients with hematological diseases. 8) Patients with a history of pericardial disease.

All patients signed informed consent. This study was approved by the Medical Ethics Committee in Daqing Oilfield General Hospital.

Methods

Preparation before surgery: All elective surgical patients were given a dose of aspirin (300 mg) and clopidogrel (300 mg) or ticagrelor (180 mg) the night before the procedure. Remedial medication was taken prior to PCI, if not preprocessed. In addition, the activation of coagulation time was maintained >250 s with the use of heparin or bivalirudin (according to body weight) during the entire operation.

Treatment: Patients in the control group directly underwent PCI, while patients in the observation group underwent coronary rotational atherectomy before PCI. The HS-1 rotablator used in our center was manufactured by Boston Scientific (U.S). A small rotablator burr was employed, and pressure perfusion flushing fluid was used to reduce friction. The main components of this liquid included: 500 mL of 5% crystalline liquid, 2.5 mg of nitroglycerin, and 1 mL of verapamil and heparin. The rotation speed of the rotablator burr was set to $1.6*10^5$-$1.8*10^5$ rpm. Then, the rotablator burr was gradually increased, approximately 5 times for rotational ablation at each of the calcification sites, with a duration of 10-20 s. Patients' vital signs were intensely monitored throughout the operation. Rotational ablation was considered successful when resistance disappeared and the rotational sound became low frequency. Then, PCI was performed.

Outcome measures

Main outcome measures: Changes in serum interleukin-6 (IL-6) and interleukin-18 (IL-18) levels were observed. Peripheral venous blood (5-7 mL) was obtained from patients before surgery and on the third day after surgery, placed on an anticoagulant tube, and centrifuge at 3,000 rpm. Supernatants were separated and stored at -80°C. Enzyme-linked immunosorbent assay kits were used to measure serum contents of IL-6 and IL-18, according to manufacturers' instructions. The same method was used to determine levels of plaque stabilization

Table 1. Comparison of baseline data of patients between groups

Groups	Observation group	Control group	t/χ^2	*P* value
Gender			0.069	0.966
Male	25	26		
Female	18	17		
Age (year)	66.33±6.28	67.85±5.92	1.155	0.251
Hypertension	27	24	0.670	0.413
Diabetes	7	6	2.655	0.988
BMI	26.77±3.25	27.42±2.84	0.988	0.326
Creatinine values (μmol/L)	78.65±17.63	82.33±18.29	0.958	0.341
Dyslipidemia	33	35	0.070	0.791
Degree of stenosis (%)	74.01±10.39	75.21±9.55	0.558	0.579
Location of stenosis			0.768	0.681
Anterior descending branch	15	17		
Circumflex branch	13	15		
Right coronary artery	18	14		

Note: Abnormalities in triglycerides, cholesterol, and low-density lipoprotein are considered to be dyslipidemia.

factor pentraxin 3 (PTX 3) and lipoprotein-associated phospholipase A2 (Lp-PLA2) in both groups of patients.

Secondary outcome measures: The secondary outcomes included immediate operation success rate, incidence of perioperative complications (malignant arrhythmia, acute myocardial infarction, coronary artery dissection and perforation), and postoperative changes in renal function.

Statistical analysis

Continuous data were expressed as mean ± standard deviation (mean ± SD). The paired t-test was used for comparing pre-and post-treatment measurements. The Chi-square test was used for comparing the rates between groups, using α=0.05 as the test standard. SPSS V20.0 software was used for statistical analysis. Results were considered statistically significant when $P<0.05$.

Results

Comparison of baseline data of patients between groups

Results showed no statistically significant differences between the groups in terms of sex, age, pre-existent disease (hypertension and diabetes), degree of coronary stenosis and location of stenosis ($P>0.05$); see **Table 1**.

Changes in IL-6 and IL-18 levels between groups

No differences were found regarding these indicators before treatment in both groups. Serum IL-6 and IL-18 levels decreased in both groups after treatment ($P<0.05$). There was a significant difference between the observation group and the control group ($P<0.05$); see **Figures 1**, **2**.

Changes in serum plaque stabilization factors between groups

There were no significant differences in PTX3 and Lp-PLA2 levels between the two groups before treatment ($P>0.05$). After treatment, indicators in both groups were significantly lower ($P<0.05$). Both indicators were significantly lower in the observation group ($P<0.05$); see **Table 2**.

Comparisons of perioperative complications and immediate surgical success rates between groups

We found that the incidence of perioperative complications was lower in the observation group ($P<0.05$). In contrast, we observed a tendency for the immediate success rate in observation group to be higher than that in the control group, without statistical significance ($P>0.05$); see **Table 3**.

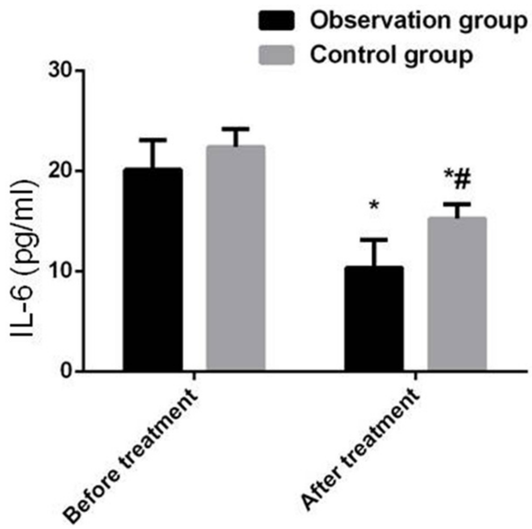

Figure 1. Comparison of serum IL-6 levels between groups. Note: *indicates that the serum IL-6 levels were significantly lower in both groups after treatment (P<0.001). #indicates that serum IL-6 levels were significantly lower in both groups after treatment (P<0.001).

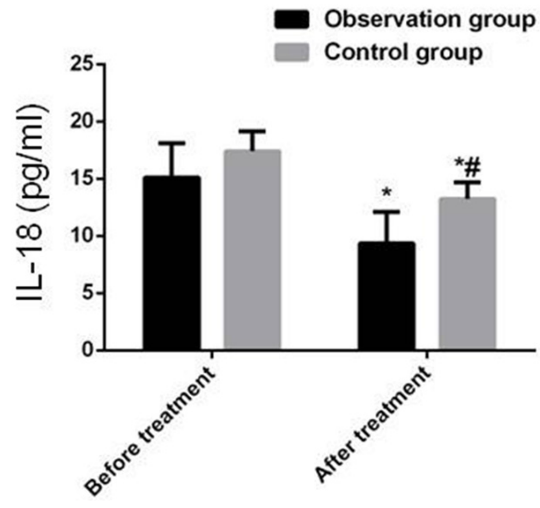

Figure 2. Comparison of serum IL-18 levels between groups. Note: *indicates that the serum IL-8 levels were significantly lower in both groups after treatment (P<0.001). #indicates that serum IL-8 levels were significantly lower in both groups after treatment (P<0.001).

Comparison of postoperative renal function changes between groups

No significant changes were observed in creatinine values between groups at various time points: 24 h after operation, 48 h after operation, 4 days after operation and one week after operation; see **Figure 3**.

Discussion

Advances in modern medicine have improved the diagnosis and treatment of CAD, involving rapid progress in interventional therapy in internal medicine through PCI [8]. However, coronary calcification increases the difficulty of the operation and decreases its clinical efficacy. Previous studies have demonstrated that approximately 20% of CAD patients have coronary sclerosis. In addition, coronary calcification increases with age. Thus, effective clinical treatment of coronary calcification would be significantly beneficial for patients [9, 10].

After originating in the past century, coronary rotational atherectomy was predominantly discarded as an independent treatment. Further studies on calcification and restenosis after PCI have reframed coronary rotational atherectomy as an auxiliary measure to assist in vascular recanalization, gradually becoming a first-line interventional treatment again [11].

Previous studies have confirmed the impact of inflammation on cardiovascular disease, with inflammatory factors and fibrosis playing an important role in the calcification of coronary arteries [12]. IL-6 and IL-18 appear to be particularly important. Inflammatory mediators promote IL-6 secretion, increasing blood viscosity and the production of procoagulant factors. This leads to coronary atherosclerotic changes that promote the progress of CAD [13]. On the other hand, IL-18 favors the proliferation of foam cells, leading to the formation of vascular fatty streak. In addition, it induces chemotaxis and adhesion of mononuclear cells, facilitating coronary thrombosis [14]. Therefore, both mediators can be used as indexes to assess the severity of CAD. Our results show that levels of serum IL-6 and IL-18 in the observation group were decreased significantly, suggesting that coronary rotational atherectomy can effectively reduce the size of calcified plaques on coronary arteries and alleviate inflammation, thus improving prognosis [15, 16].

Research has shown that the stability of coronary plaques affects the prognosis of patients with CAD, indicating that plaque assessment is important for monitoring disease progress. Animal models have shown that many factors (including PTX3 and Lp-PLA2) are involved in the regulation of plaque stability [17], suggest-

Table 2. Changes in serum plaque stabilization factors between groups

Groups	Control group	Observation group	t value	*P* value
PTX3 (ng/mL)				
Before treatment	3.28±0.13	3.31±0.11	0.770	0.443
After treatment	1.89±0.22	1.28±0.09	16.280	<0.001
t value	35.669	93.660		
P value	<0.001	<0.001		
Lp-PLA2 (ng/mL)				
Before treatment	7.79±0.84	7.81±0.33	0.145	0.885
After treatment	3.21±0.23	2.06±0.15	27.463	<0.001
t value	34.484	84.017		
P value	<0.001	<0.001		

Table 3. Comparison of postoperative situation of patients between groups

Groups	Perioperative complications				Immediate surgical success rates (n, %)
	Malignant arrhythmia	Acute myocardial infarction	Coronary artery dissection	Coronary artery perforation	
Observation group	2	1	0	1	41/43 (95.35)
Control group	4	2	2	2	35/43 (81.40)
χ^2 value	3.458				2.829
P value	0.0431				0.093

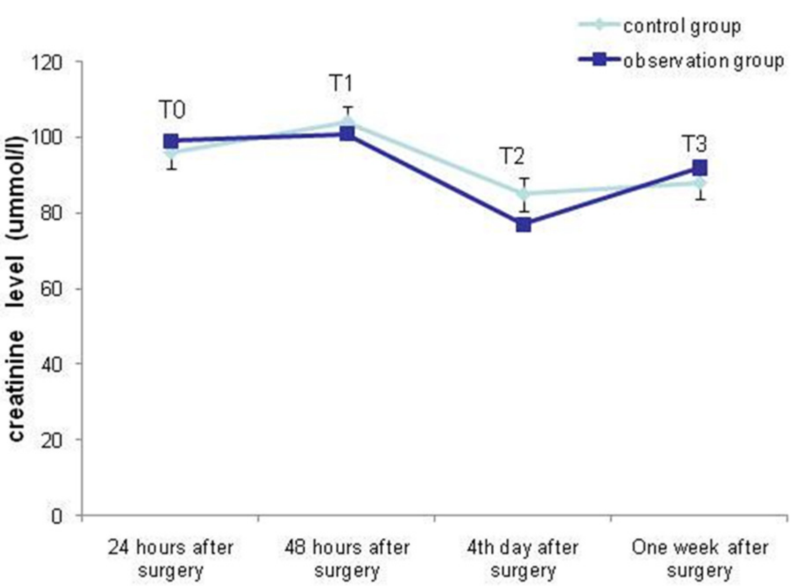

Figure 3. Comparison of postoperative renal function changes between groups. T0, t=0.645, P=0.520; T1, t=0.792, P=0.431; T2, t=1.873, P=0.065; T3, t=0.945, P=0.347.

ing that the dynamic observation of these indicators has significant clinical value. PTX3 is produced by vascular epithelial cells and smooth muscle cells. Studies have shown that PTX3 is highly expressed in unstable plaques, significantly deteriorating plaque stability [18]. Lp-PLA2 is released by foam cells when stimulated by inflammatory factors; with studies confirming that it is directly linked to acute cardiovascular events caused by plaque rupture. Our results show that these indicators decreased in both groups after PCI, indicating the effectiveness of this procedure. However, these changes were greater in the observation group, suggesting that the benefits of PCI can be increased to some extent by coronary rotational atherectomy [19-21].

Coronary rotational atherectomy mechanically eliminates inelastic plaques to a certain degree, increasing the smoothness of calcification lesions, increasing vascular lumen, and facilitating stent implantation [22]. Our results show a robust tendency towards increasing immediate operation success rates in the experimental group, indicating the potentiating clinical effect of coronary rotational atherectomy on PCI. In addition, due to the easier stent implantation and reduced vascular damage, this method minimizes the burden of the operation on the heart. Indeed, our results found a lower incidence of perioperative complications in the observation group, supporting the previous research [5].

Because PCI requires the use of intravenous contrast agents, it can impact kidney function, with contrast-medium nephropathy being a major complication of PCI [23]. We found no statistically significant difference in postoperative renal function between groups, suggesting that coronary rotational atherectomy does not increase the incidence of renal dysfunction after operation, which finding is in consistent with conclusions from the previous research [24].

In conclusion, we confirmed the clinical effectiveness of coronary rotational atherectomy in the treatment of CAD. Nevertheless, our results should be interpreted in the context of our small sample size. Side effects and related treatments should be explored in large multicenter samples in order to corroborate these clinical results. Furthermore, indications for coronary rotational atherectomy should be further studied and refined.

Disclosure of conflict of interest

None.

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