



Association Between TG-to-HDL-C Ratio and In-Stent Stenosis Under Optical Coherence Tomography Guidance

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Abstract

We determined the relevance between the TG-to-HDL-C ratio and stent restenosis. Ninety-nine patients with in-stent stenosis (ISR) who were admitted to An Zhen Hospital in Beijing between April 2014 and June 2017 were selected. At the same time, 122 patients with coronary stenosis <50% were selected. All patients were tested for TG, HDL-C, and TG/HDL-C ratio. Optical coherence tomography (OCT) can assess microscopic status in all ISR patients. The proportion of male and Diabetic patients were significantly higher for ISR. There were differences in the prevalence of cigarette smokers among the different tissue types, among which the layered tissue type accounted for the highest proportion. In logistic regression analysis the study showed that male, diabetes mellitus, and the TG/HDL-C ratio are risk factors for ISR. The ISR ROC was 0.725 based on the TG/HDL-C ratio diagnosis. It is related to the degree of coronary stenosis and effective in diagnosing in-stent stenosis in ISR.

Keywords Optical coherence tomography · Coronary heart disease · In-stent restenosis · TG-to-HDL ratio

Introduction

Percutaneous coronary intervention has saved many patients' lives and improved the quality of life; however, with the passage of time, the initial stage of coronary intervention leads to ISR. ISR is a complex disease of coronary intervention. OCT is currently the endoluminal imaging technique with the highest resolution, with an axial resolution of 10 μ m. OCT can clearly display the vascular pathologic changes that cannot be visualized in the thin fibrous cap, vulnerable plaque, macrophages, and vascular microchannels. The high resolution of OCT has enhanced physicians' understanding of ISR from intimal morphology to guiding the treatment process [1].

At present, research on the mechanism underlying in-stent stenosis depends mainly on the pathologic results of OCT images and autopsy findings, and there are still many problems to be solved [2].

The TG-to-HDL-C ratio was known as the atherosclerosis index plasma (AIP) [3]. A large number of researches have confirmed that It can be used to assess the risk of coronary heart disease (CAD). TG/HDL-C is related to LDL-C, while AIP is negatively related to LDL-C particles. VLDL is more likely to be oxidized and cause atherosclerosis [4, 5]. Kasai verified that the TG-to-HDL-C ratio may predict the morbidity and prognosis of coronary heart disease in patients who suspected myocardial ischemia [6]. The purpose of this study was to estimate the predictive value of the TG-to-HDL-C ratio in patients with in-stent stenosis.

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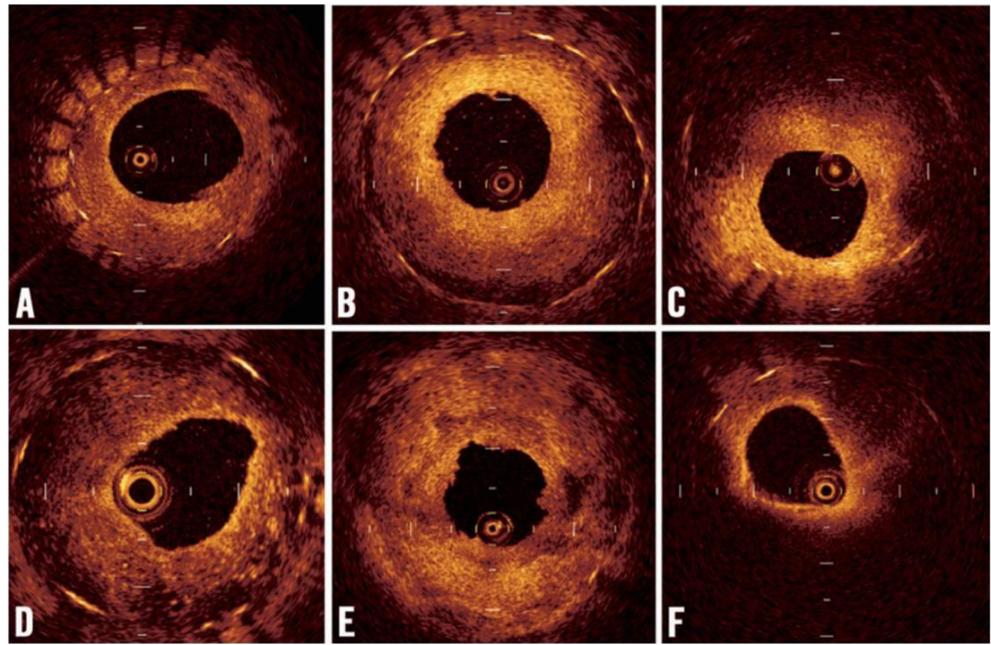
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Methodology

Objective

Ninety-nine of ISR patients who were admitted to Beijing An Zhen Hospital between April 2014 and June 2017 were selected for OCT examinations. At the same time, 122 patients with coronary stenosis <50% were selected. ISR is defined as the extent of stenosis within the stent and 5 mm at the ends of

Fig. 1 ISR typing under OCT



the stent >50% [7]. Exclusion criteria: acute and chronic heart failure; acute stroke; severe liver and kidney disease; thyroid dysfunction; coagulation dysfunction and malignant tumors.

Testing methods

The TC, TG, HDL-C levels were determined, and the TG-to-HDL-C ratio was computed. All patients underwent coronary artery angiograms (CAG) and were divided into in-stent stenosis and control groups based on radiographic findings. OCT examinations were performed on the in-stent stenosis group. The types of stent stenosis included the following: type I (focal), length < 10 mm in the stent or on the edge of the stent; type II (diffuse), length > 10 mm and intra-stent; type III (diffuse), proliferative and length > 10 mm; type IV (diffuse), total occlusion.

Table 1 Baseline features

	ISR group <i>n</i> = 99	Control group <i>n</i> = 122	<i>P</i> value
Male (%)	76(76.77%)	53(43.44%)	0.001
Age (year)	58.80 ± 11.44	58.79 ± 10.22	0.740
Diabetes (%)	40(40.40%)	30(24.59%)	0.014
Hypertension (%)	69(69.70%)	69(56.56%)	0.051
Hyperlipidemia (%)	31(31.63%)	57(46.72%)	0.027
Smoking (%)	47(47.96%)	42(34.43%)	0.053
TG (mmol/l)	2.61 ± 1.47	1.82 ± 1.03	0.002
HDL-C (mmol/l)	1.00 ± 0.19	1.08 ± 0.23	0.051
TG-to-HDL-C ratio	2.68 ± 1.60	1.84 ± 1.34	0.011

OCT operation

Immediately after the CAG operation, FD-OCT (C7-XR Imaging Systems, St Paul, Minnesota, USA) was used. After injection of heparin, the PCI guide wire was positioned at the distal target vessel, then 200 µg of nitroglycerin was injected into the cavity. The OCT catheter was advanced along the guide wire to 10 mm above the target lesion and the contrast agent was injected into the target vessel. The OCT image quality was determined by an experienced technician at 20 mm/s. The OCT catheter was withdrawn and injected contrast medium during image acquisition. Image acquisition included the distance from the target lesion to the proximal and distal 5 mm regions. OCT target selection was as follows: single vessel lesion in single stents; single vessel lesion with the thickest neointima hyperplasia in single stents; and multiple stents to select the thickest stent lesion of the neointima. All data were collected and analyzed by OCT offline Review Software. All of the OCT images were fulfilled independently by two analysts, with inconsistencies re-analyzed and discussed by a third analyst.

Observation index

The following basic clinical features of ISR patients were recorded: age; gender; hypertension; diabetes mellitus; smoking history; and body mass index (BMI). The serum indices included the TC, TG, HDL-C, and TG-to-HDL-C ratio. The OCT indices were as follows: minimal scaffold area (MSA), the stent was implanted into the segments and the minimum area of the stent area was analysed; homogeneous intima, heterogeneous intima, and layered intima. ISR typing

under OCT:A homogeneous band of highly reflected signals;B The two layers are homogeneous and highly reflective, and the scaffold wires are visible;C Two layers of heterogeneity of the mixed signal band, but the scaffold wire is not visible;D Heterogeneity of the mixed signal bands, patchy distribution;E Heterogeneous mixed signal bands that incorporate low to high backscattering;F rich in lipids (Fig. 1). The Institutional Ethics Committee of Beijing An Zhen Hospital approved the research protocol. (No.2018022X).

Statistics

All data were analyzed by SPSS 23 software. The grouped data is expressed as a centage and was assessed by a chi-square test. The Variable data are expressed as the mean ± SD. AUC was counted to assess the value of the TG-to-HDL-C ratio in the diagnosis of stent stenosis. Logistic regression analysis was applied to analyze the risk factors for ISR and correction of TG-to-HDL-C ratio. *P* < 0.05 was statistically significant.

Results and discussion

Comparison of general data

The proportion of male and Diabetes patients were significantly higher for ISR (Table 1).

Analysis of the risk factors for ISR

Based on multiple factor logistic regression analysis, it was shown that males (OR = 3.564, 95% CI: 1.628–7.802), diabetes (OR = 2.021, 95% CI: 1.036–3.937), and the TG-to-HDL-C ratio (OR = 2.833, 95% CI: 1.410–5.714) were all risk factors for ISR (Table 2).

The value of TG-to-HDL-C ratio in the diagnosis of in-stent stenosis

The ISR ROC in diagnosing stent stenosis was 0.725 (Fig. 2).

Table 2 Logistic analysis for ISR risk factors

	P value	HR (95%CI)
Male (%)	0.001	3.564(1.628–7.802)
Diabetes (%)	0.039	2.021(1.036–3.937)
TG-to-HDL-C ratio	0.003	2.833(1.410–5.714)

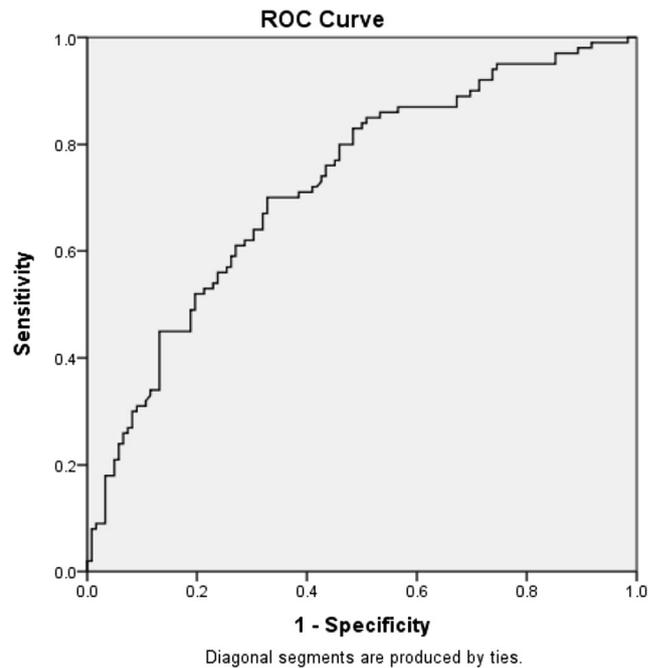


Fig. 2 The ISR ROC in diagnosing stent stenosis

Logistic regression analysis of the degree of coronary stenosis in ISR

The results of ordinal logistic regression in patients with ISR indicated that the TG-to-HDL-C ratio was related to coronary artery stenosis (Table 3).

Comparison of pattern appearance of restenotic tissue

The results showed that the prevalence of cigarette smokers was different among the different tissue types; layered had the highest proportion (Table 4).

Discussion

In recent years, the clinical application of antiplatelet agents, statins and other drugs have become more commonly used

Table 3 Logistic regression analysis of the degree of coronary stenosis for ISR

	P value	HR (95% CI)
Stent length (mm)	0.915	1.002(0.960–1.046)
MSA (mm ²)	0.600	1.066(0.839–1.355)
TG (mmol/l)	0.889	1.465(1.081–3.602)
HDL-C (mmol/l)	0.509	0.456(0.445–4.688)
TG-to-HDL-C ratio	0.036	1.398(1.023–1.910)

MSA Minimal scaffold area

Table 4 Comparison of pattern appearance of restenotic tissue

	Homogeneous intima <i>n</i> = 33	Heterogeneous intima <i>n</i> = 49	Layered intima <i>n</i> = 17	P value
Diabetes(%)	38.39%	36.73%	52.94%	0.503
Smoking(%)	46.88%	38.78%	76.47%	0.027
TG-to-HDL-C ratio	2.802 ± 1.829	2.775 ± 1.569	2.167 ± 1.134	0.404

with various new medical technologies constantly emerging. Restenosis after coronary artery stent implantation has still been a huge clinical challenge, however, seriously threatening the health of patients (Harun [8]; Katsuaki [9]). This study aimed to explore TG-to-HDL-C ratio in the process of in-stent restenosis, providing new, simple and reliable methods for the prevention and treatment of restenosis.

Evidence-based medicine has shown that abnormal lipid metabolism, especially elevated LDL, is the significant risk factor for CAD [10, 11]. However, after lipid-lowering treatment, coronary heart disease still occurs in 60%~70% of patients (Wan [12]; SW. [13]). Studies have found (Yu-Jin [14]) that the TG/HDL-C ratio can be used to assess the incidence risk of CAD. Sarwar [15] suggested that TG is one of the key factors underlying vascular sclerosis in patients of cardiovascular disease. Hadaegh [16] indicated that the TG-to-HDL-C ratio is more valuable as an independent predictor of mortality in cardiovascular disease patients. In the final analysis it reflects the proportion of atherosclerotic factors and anti-atherosclerotic factors. In some patients, TG is still in the normal range and the level of HDL-C is lower. Coronary heart disease is still possible and the risk of disease is higher [17]. Tanaka [18] confirmed that HDL and the TG/HDL-C ratio have more predictive value for acute myocardial infarction. In China, type IV hyperlipidemia reflects abnormal metabolism of blood lipids, which is mainly with extremely low-density lipoprotein, and is closely related to the diet structure of carbohydrates in China. Therefore, in view of the characteristics of lipid metabolism in China, the relationship between plasma three acylglycerol and coronary atherosclerotic heart disease appears to be clinically significant. The study indicated that the proportion of male and Diabetes patients was significantly higher for ISR.

According to the results of the PROCAM study [19], the occurrence of coronary heart disease lowered by 1/3–1 times with a single increase in TG. The incidence of CAD was 3–4 times high. The study showed that male (OR = 3.564, 95% CI: 1.628–7.802), diabetes mellitus (OR = 2.021, 95% CI: 1.036–3.937), and the TG-to-HDL-C ratio (OR = 2.833, 95% CI: 1.410–5.714) are risk factors for ISR. The TG-to-HDL-C ratio was corrected with the degree of coronary stenosis. The ISR ROC curve was 0.725.

OCT is currently the intraluminal imaging tool with the highest resolution and is able to clearly observe the substructure of stent intimal hyperplasia and quantitative analysis of

intimal thickness [20, 21]. According to the difference in optical backscatter and the attenuation coefficient caused by different neointimal tissue components, OCT can be divided into 3 morphologies (homogeneous, heterogeneous, and layered), which are associated with different clinical events [22]. Homogeneous intima is considered relatively stable and the probability of degeneration is higher than heterogeneous intima. The risk of new atherosclerosis and adverse cardiovascular events in homogeneous intima is lower than heterogeneous intima. Heterogeneous endometrium is considered a relatively immature endometrium, and the secondary clinical adverse events secondary to the occurrence of new atherosclerotic lesions are relatively large [23, 24]. Follow-up results from Kim [25] showed that the incidence of ISR 9 months after stent placement was 15% and increased to 28% at 24 months.

Up to date, the treatment for ISR is still in controversial. Currently, the most commonly used interventional therapy measures include Balloon Dilatation, Drug-eluting Stent (DES), Drug Coated Balloon (DCB), etc. [26]. Although the AHA guidelines in 2010 recommended DCB as an IIA for treating ISR, there are still some discrepant in data from various studies. A recent meta-analysis showed that DCB was superior to DES or PTCA in the treatment of ISR. Tada [27] showed that the treatment outcomes after 7 months of ISR was different due to the different pathological morphology of OCT. There was no difference between ISR and TLR in patients with heterogeneous diseases. Progress in understanding the pathophysiological mechanism of restenosis and reasonable evaluation of the imaging of restenosis can provide doctors an appropriate treatment method. However, in general, the treatment of restenosis after drug stenting is still a challenge in clinical practice.

The study showed that smoking varied in different tissue types, with layered having the highest proportion.

Conclusion

This paper presented an experimental study involving the association between the TG-to-HDL-C ratio and in-stent stenosis. This study indicated that the proportion of male and Diabetes patients were significantly higher for ISR. There were differences in the prevalence of cigarette smoking among different tissue types, with the layered tissue type accounting for the highest proportion. Male gender, patients

with diabetes mellitus, and the TG-to-HDL-C ratio was shown to be dangerous factors and associated with the degree of coronary stenosis for ISR. The ISR ROC was 0.725. The TG-to-HDL-C ratio was confirmed to be an independent hazard and effective in diagnosing in-stent stenosis for ISR.

In conclusion, on the basis of definite prediction of dangerous factors for ISR, clinical control of lipid metabolic disorders and prevention and treatment of dyslipidemia should be emphasized. HDL is not only involved in the reverse process of TC, but also has anti-inflammatory, anti-oxidative, and vascular endothelium protective functions. Therefore, the TG-to-HDL-C ratio is more accurate in assessing the risk of CAD. It can more sensitively reflect an individual's risk of atherosclerosis and is a valuable predictor of clinical value.

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Compliance with Ethical Standards

Conflict of Interest None declared.

Ethical Approval The Institutional Ethics Committee of Beijing An Zhen Hospital approved the research protocol (No.2018022X).

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