

The association between serum apolipoprotein A-I and apolipoprotein B and the severity of angiographical coronary artery disease

Khadem-Ansari M H, Rasmi Y, Rahimi-Pour A, Jafarzadeh M

ABSTRACT

Introduction: The aim of this study was to investigate the relationship between serum apolipoprotein A-I (apoA-I) and apolipoprotein B (apoB) and the severity of coronary artery stenosis.

Methods: This case-control study was carried out on 106 patients who underwent angiography and 100 healthy controls. ApoA-I and apoB as well as the serum total cholesterol, high-density lipoprotein cholesterol (HDL-C), triglyceride and low-density lipoprotein cholesterol (LDL-C) levels were measured. Very low-density lipoprotein cholesterol levels and the LDL-C/HDL-C ratio were calculated.

Results: In an Iranian population with coronary artery disease (79 men and 27 women, aged 53 +/- 8.5 years), the increased levels of apoA-I and apoB were correlated with the number of involved vessels and the severity of coronary lesions. However, no significant correlation was found between the serum values of lipids as well as other lipoproteins and the number of vessels involved and the severity of coronary lesions.

Conclusion: ApoA-I and apoB are indicated as risk factors for cardiovascular and, possibly, cerebrovascular diseases. From this study, it may be concluded that apoA-I and apoB serum concentration levels are independent risk factors for coronary atherosclerosis in the Iranian population. It also demonstrates a direct relationship between the severity of coronary atherosclerosis and the number of lesions in the involved vessels. It can be regarded as an index for the relationship of apoA-I and apoB to the early, still clinically asymptomatic, steps of the pathogenesis of coronary disease.

Keywords: apolipoprotein, cardiovascular disease, coronary artery disease, coronary artery stenosis

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INTRODUCTION

Although studies of lipids and the degree of coronary atherosclerosis began in the late 1960s, uncertainty remains on which lipid measurement best discriminates the degree of coronary artery disease (CAD). Discussions on which is the "most influential" lipid parameter have been particularly unrewarding.⁽¹⁾ Epidemiological and clinical studies have consistently demonstrated that an elevated concentration of low-density lipoprotein cholesterol (LDL-C) in plasma is associated with an increased risk of CAD.^(2,3) Increased LDL-C concentration levels are a well-established risk factor for CAD and are currently recommended as the primary target for lipid-lowering therapy for the prevention and treatment of cardiovascular disease, although its unique superiority over other circulating predictors of CAD is unclear.⁽⁴⁾ However, there is considerable interest in the potential value of measuring circulating concentrations of apolipoproteins to assist in the assessment of the risk of CAD, as well as in their potential aetiological relevance to the disease.⁽⁵⁾ Apolipoproteins are important components of lipoprotein particles, and there is accumulating evidence that the measurement of various forms of apolipoproteins may improve the prediction of the risk of cardiovascular disease.⁽⁶⁻⁹⁾

Clinical trials using softer end-points, like coronary angiography, angina pectoris and nonfatal myocardial infarction, have been published and reviewed,⁽¹⁰⁾ with most pointing to the importance of apolipoprotein B (apoB) and apolipoprotein A-I (apoA-I) as risk indicators. ApoB is present as a single molecule in low-, intermediate- and very low-density lipoproteins (LDL, IDL and VLDL, respectively), while apoA-I is the major apolipoprotein associated with high-density lipoprotein (HDL).^(11,12) Also, the prevalence of dyslipidaemia, especially low levels of HDL cholesterol (HDL-C), is very high in Iranian

Department of Biochemistry, Faculty of Medicine, Urmia University of Medical Sciences, Urmia, Iran

Khadem-Ansari MH, PhD
Associate Professor

Rasmi Y, PhD
Assistant Professor

Department of Clinical Biochemistry, Faculty of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran

Rahimi-Pour A, PhD
Professor

Department of Pharmacy

Jafarzadeh M, MD
Pharmacologist

Correspondence to:
Dr Yousef Rasmi
Tel: (98) 441 277 0698
Fax: (98) 441 277 0698
Email: rasmiy@umsu.ac.ir

adults.⁽¹³⁾ There is abundant evidence that the risk of coronary atherosclerotic cardiovascular disease is directly related to plasma lipid and apolipoprotein levels, but the relationships between the serum apoA-I and apoB levels and the extent of CAD have not been consistently shown. To investigate the possible relationship of the serum levels of apoB and apoA-I, lipids and other lipoproteins with the severity of coronary lesions and number of vessels diseased, these parameters were examined in 106 angiographically-defined CAD patients and in a group of control subjects with no angiographical or clinical evidence of CAD.

METHODS

We studied 106 patients (79 males and 27 females) with suspected CAD undergoing coronary angiography. Population-based controls (n = 100; 68 males and 32 females), who were symptomatically normal, were included in the study. Controls were matched by age and gender. Fasting blood samples were drawn from all the participants of the study after 12 hours of fasting. Serum was separated after 15 minutes at room temperature by bench centrifuge. Total cholesterol and triglycerides (TG) in serum were measured using enzymatic methods.^(14,15)

The HDL fraction was separated from the plasma by precipitation with polyethylene glycol and the cholesterol content was measured using a colorimetric method, as described by Warnick et al.⁽¹⁶⁾ LDL-C was measured by direct enzymatic assay using the LDL-C biosystem kit (Biosystem, Barcelona, Spain) and VLDL cholesterol was calculated using Friedewald's formula.⁽¹⁰⁾ The LDL-C/HDL-C ratio was calculated. Serum apoA-I and apoB measurements were performed following the instructions on the binding kit of the mini-nephelometer (Binding, Birmingham, UK). Informed consent was obtained from the patients on their history of diabetes mellitus or hypertension, hyperlipidaemia, current use of antihypertensive medications, smoking, and previous myocardial infarction or stroke. According to the results of the angiography, the subjects were classified into four subgroups depending on the number of diseased vessels: the patients with minimal stenosis, single-vessel diseased (1VD) group, the two-vessel diseased (2VD) group, and the three-vessel diseased (3VD) group.

RESULTS

The group of 106 patients comprised 79 (74.5%) men and 27 (25.5%) women at a mean age of 53 years. 64% of the patients (age range: 46–106 years) were aged between 50 and 59 years. Table I shows the main characteristics of the study population. A total of 14.1% of individuals

Table I. Characteristics of patients with coronary artery disease and controls.

Characteristics	CAD patients	Controls
Total no.	106	100
Mean age \pm standard deviation (years)	53 \pm 8.5	51 \pm 10
Males (%)	74.5	68
History of hypertension (%)	35.5	0
History of hyperlipidaemia (%)	33	0
History of familial CHD (%)	27.3	0
History of diabetes mellitus (%)	18.8	0
History of familial hyperlipidaemia (%)	8.5	0
Smoking (%)	45.2	0
History of cerebrovascular disease (%)	2.8	0
History of myocardial infarction (%)	40.5	0
History of renal disease (%)	14.1	0

CAD: coronary artery disease

(15 patients) had renal disease, 2.8% (3 patients) had cerebrovascular disease, and 18.8% (20 patients) had diabetes mellitus. The underlying heart disease included hypertension in 38 (35.8%) patients, hyperlipidaemia in 35 (33%) patients, a history of familial coronary heart disease in 29 (27.3%) patients, a history of familial hyperlipidaemia in nine (8.5%) patients, and myocardial infarction in 43 (40.5%) patients.

As shown in Table II, the mean levels of serum apoA-I and apoB in patients and controls were 110.1 \pm 12.4 mg/dL and 130.6 \pm 14.9 mg/dL vs. 164.8 \pm 8.2 mg/dL and 92.1 \pm 7.2 mg/dL, respectively (p < 0.05). The results were not gender-dependent in both the patient and control groups, and were almost similar in both genders (p > 0.05). There was a marked increase in serum concentration levels of apoB, with the number of coronary vessels involved (p < 0.05). The highest levels were found in patients with three involved coronary vessels (143.4 \pm 8.7 mg/dL); the serum concentration levels in patients with two vessels involved, a single vessel and minimal stenosis were 132.0 \pm 6.2 mg/dL, 120.0 \pm 6.2 mg/dL and 104.2 \pm 6.8 mg/dL, respectively. We also found a decrease in serum concentration levels of apoA-I in relation to the severity of stenosis (p < 0.05). Serum concentration levels in patients with a single vessel, two vessels and three vessels stenosis were 118.0 \pm 8.8 mg/dL, 107.0 \pm 6.5 mg/dL and 101.9 \pm 9.5 mg/dL, respectively. The highest values were obtained in patients with a minimal extension of coronary atherosclerotic lesion (130.0 \pm 7.2 mg/dL). No significant differences were observed between the serum levels of lipids or routinely-measured lipoproteins (VLDL-C, LDL-C, and HDL-C) and the number of involved coronary artery vessels or the severity of coronary lesions (Table II).

Table II. Comparison of the mean serum levels of apoA-I, apoB, triglyceride, cholesterol, LDL-C, HDL-C, VLDL-C and LDL-C/HDL-C ratio with the number of coronary artery vessels involved.

Severity of stenosis	No. (male/female)	ApoA-I (mg/dL)	ApoB (mg/dL)	Triglyceride (mg/dL)	Cholesterol (mg/dL)	HDL-C (mg/dL)	LDL-C (mg/dL)	VLDL-C (mg/dL)	LDL-C: HDL-C
Minimal	11 (5/6)	130.0 ± 7.2*	104.2 ± 6.8*	170 ± 97	210 ± 58	42 ± 18	125 ± 64	34 ± 19	3.3 ± 1.5
1VD	25 (17/8)	118.0 ± 8.8*	120.0 ± 6.2*	250 ± 116	235 ± 112	43 ± 18	142 ± 107	50 ± 23	3.5 ± 2.1
2VD	30 (24/6)	107.0 ± 6.5*	132.0 ± 6.2*	245 ± 123	205 ± 43	36 ± 10	120 ± 38	49 ± 24	3.6 ± 1.5
3VD	40 (33/7)	101.9 ± 9.5*	143.4 ± 8.7*	213 ± 126	188 ± 42	39 ± 13	108 ± 38	42 ± 25	3.0 ± 1.2
Minimal + 1VD + 2VD + 3VD	106 (79/27)	110.1 ± 12.4*	130.6 ± 14.9*	226 ± 116	206 ± 64	39 ± 15	121 ± 62	45 ± 23	3.3 ± 1.6
Control	100 (68/32)	164.8 ± 8.2	92.1 ± 7.2	123 ± 28	184 ± 18	41 ± 8	117 ± 19	25 ± 5	2.9 ± 0.9

*significant vs. control and each other

DISCUSSION

The current risk prediction guidelines for CAD prevention emphasise the use of LDL-C for CAD risk assessment, but recent evidence suggests that apolipoproteins may be more strongly associated with CAD incidence than LDL-C.⁽¹⁵⁻¹⁷⁾ In addition, several observations have resurrected an older notion that specific apolipoproteins, apoB and apoA-I, may in fact be more powerful lipid-related predictors of risk for CAD.⁽¹¹⁾ Clinical and epidemiological studies have established the association between coronary risk and high serum levels of cholesterol and LDL-C, apoB, as well as of low concentrations of HDL-C and apoA-I.⁽¹⁸⁾ The results from our community indicate that the apoB/apoA-I ratio and apoB are independent risk factors for CAD and are superior to any of the cholesterol ratios.⁽¹⁹⁾ According to the above discussion, we evaluated whether apoA-I and apoB (the protein component of serum lipoproteins) could be used instead of traditional lipid and lipoprotein measures for detecting the severity of coronary atherosclerosis.

For this purpose, the relationships between the serum levels of apoA-I and apoB, LDL-C, VLDL-C, TG, total cholesterol, HDL-C and ratio of LDL-C/HDL-C with the severity of coronary artery lesions were studied. As shown in Table II, the patients were divided into four groups according to the severity of coronary artery lesions. Our data shows that there were no differences in the LDL-C, VLDL-C, TG, total cholesterol, HDL-C and ratio of LDL-C/HDL-C levels among subgroups of patients. We examined whether levels of LDL-C, HDL-C, VLDL-C, TG, total cholesterol and the ratio of LDL-C/HDL-C, which is considered as an index of atherogenicity, are related to CAD, but did not find an association with CAD except for TG. High levels of TG were observed in patients when compared to controls in the present study. Higher total cholesterol, LDL-C, apoB, TG, lower HDL-C and apoA-I levels were reported in patients with CAD.⁽²⁰⁾

The statistical analysis revealed strong relations between apoA-I and apoB levels and the presence of CAD

as defined by the observation of vessel stenosis, which to our knowledge has not been reported in this uniformity before. Hence, this study directly documents the role that the extent of CAD plays in the link between blood apoA-I and apoB concentration levels and clinical events. Moreover, apoA-I and apoB exhibited a highly significant relationship to the number of stenosed coronary vessels. In the absence of an association between traditional lipids and lipoproteins and CAD, especially among subgroups of patients, the presence of lower levels of apoA-I and higher levels of apoB in subgroups of patients, when compared to controls, indicates that conventional risk factors may not be significant in causing CAD in the Iranian population; and in addition to the conventional lipid profile, concentrations of apoA-I and apoB can prove to be a valuable tool in the risk assessment of a population and the severity of coronary stenosis. Less evidence exists on the relationship between apoA-I and apoB levels and the severity of CAD, although Garfagnini et al have shown that the apoA-I and apoA-I/apoB ratio are better than HDL-C in assessing the severity of coronary damage.⁽²¹⁾ Future studies should also examine the role of other apolipoproteins, such as apoB-48, apoC-III and apoA-V, as predictors of CAD in different populations.

In conclusion, the present study revealed that various well-known coronary risk factors of lipid metabolism are powerful discriminators of both the presence and the extent of CAD. This suggests that the measurement of apoB and apoA-I should be routinely added to the routine lipid profile in order to assess the atherogenic potential of lipid disorders.

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