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Correlation between lipoprotein(a) serum concentration and severity of coronary artery stenosis in an Iranian population according to Gensini score

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Abstract

Objectives: To investigate the correlation between serum lipoprotein(a) concentration and existence as well as severity of coronary atherosclerosis.

Design and methods: A cross-sectional study was conducted on 826 patients who underwent angiography through measuring blood sugar, serum lipids, lipoprotein(a) and evaluation of coronary stenosis by Gensini score.

Results: Gensini score=6 was considered as a cut-off point for coronary disease and 40 mg/dL was determined as lipoprotein(a) cut-off point. Its higher concentration was significantly more frequent in patients with Gensini score>6 (OR: 2.50, $p=0.001$), independent of gender, smoking, diabetes mellitus and hyperlipidemia. This finding was significant in patients <55 years old. There was a significant relationship between severity of coronary stenosis and higher concentration of serum lipoprotein(a).

Conclusion: LP(a) serum concentration is an independent risk factor for coronary atherosclerosis in the Iranian population especially at the ages below 55. Also it demonstrates a direct relationship between severity of coronary atherosclerosis (by Gensini score) and serum LP(a).
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Keywords: Lipoprotein(a); Coronary atherosclerosis; Coronary stenosis; Severity

Introduction

Atherosclerosis is the leading cause of death all around the world [1–3] and cholesterol content of low-density lipoproteins is a major independent risk factor for vascular atherosclerosis [4]. "Lipoprotein(a)" [LP(a)] is a genetically-determined low-density lipoprotein with a unique "Apo(a)" molecule that changes inconsistently and minimally in response to environmental, physical or life style modifications and it predisposes persons to thrombotic complications of atherosclerosis [4–8]. There is a controversy about correlation of LP(a) serum concentration with coronary atherosclerosis in different populations. While many studies proposed atherogenic mechanism(s) for LP (a) [5–8] and emphasize on the atherogenesity of LP(a) [6–16], several studies failed to demonstrate this association, including Ridker and colleagues [17] who found no evidence of association between LP(a) level and future myocardial infarction, and Gurewich and Mittelman [18] who disagreed with the existence of such relationship. Moreover there is no definite study about this issue in Iran with such great sample size and using ELISA as the analytical method; while a preceding study by Rahmani et al. recruited 251 participants and LP(a) concentration was measured by immunoturbidometric assay [19]. Considering the socioeconomic importance of the prevalence of atherosclerotic lesions and the above-mentioned controversy we tried to determine whether there is any correlation between LP (a) mean serum concentration and coronary artery atherosclerosis and its severity.

Methods and materials

Study patients

This cross-sectional study was conducted in "Tehran Heart Center", (a referral hospital affiliated to Tehran University of Medical Sciences) from July 2004 to July 2005. After obtaining

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informed consent, we included all patients who underwent angiography for any reason ($n=826$). Complete medical history was taken from all patients. For each patient, fasting blood samples were obtained and checked for fasting blood sugar, triglycerides (TG) (with enzymatic Gop-PAP method), total cholesterol (with enzymatic–calorimetric CHOD-PAP method), high-density lipoprotein cholesterol (HDL-C) (with direct enzymatic method), low-density lipoprotein cholesterol (LDL-C) (with Freidwald equation), and LP(a) serum concentration (with ELISA method) before undergoing angiography. All biochemical assays were assessed by Pars Azmoon kits accredited by Bioactiva Diagnostica [Germany], except for LP(a) which was assessed by Biopool US Inc. kit [US]. Since LDL-C measurement with Freidwald equation is falsified when TG is over 400 mg/dL, we excluded results of LDL-C in patients with TG > 400 mg/dL. Severity of coronary atherosclerosis was quantified by Gensini score. Two experienced cardiologists performed all angiography procedures by Philips Integris H5000. Catheters (Judkins, left and right) from Cordis Corporation [US] and guide wire (0.014 inch Hi Torque floppy) from Guidant Corp. [US].

Statistical analysis

We investigated the relationship between (1) LP(a) mean serum concentration and existence of coronary atherosclerosis, (2) LP(a) mean serum concentration and severity of coronary atherosclerosis measured by Gensini scoring, and (3) existence of coronary stenosis based on age stratification.

The Gensini score is computed by assigning a severity score to each coronary stenosis according to the degree of luminal narrowing and its importance based on location. Reduction in the lumen diameter, and the angiographic appearance of concentric lesions and eccentric plaques were quantitatively evaluated. More specifically, reductions of 25%, 50%, 75%, 90%, 99% and complete occlusion were given Gensini scores of 1, 2, 4, 8, 16 and 32 respectively. Each principal vascular segment was assigned a multiplier in accordance with the functional significance of the myocardial area supplied by that segment, i.e. the left main coronary artery was assigned the significant multiplier × 5; the proximal segment of left anterior descending coronary artery (LAD) was given × 2.5; the proximal segment of the circumflex artery was weighted by a factor of × 2.5; the mid segment of the LAD was assigned a factor of × 1.5; the right coronary artery, the distal segment of the LAD, the posterolateral artery, and the obtuse marginal artery were all given × 1; and all other areas were assigned a factor of × 0.5 [20].

Chi square test was utilized to analyse categorial variables substituted by Fisher's exact test when necessary. For continuous variables, *t*-student test was used. Multiple comparison adjustment was used when suitable. Data were analysed by SPSS ver.13. Since two different cardiologists performed all angiography procedures, we selected a random sample quantity ($n=58$) of each cardiologist's patients, thereafter each cardiologist interpreted patients' angiogram of the other cardiologist again. The inter-observer reliability of the cardiologist's review reports was calculated by intraclass correlation (ICC). p value ≤ 0.05 was considered to be significant.

Table 1
Patient's characteristics

Condition		Frequency	Valid percentage
Sex	Male	507	63.1
	Female	269	36.9
Smoker		218	27.1
Diabetic		194	24.2
Hypertensive		310	38.5
LP(a) > 40		77	9.9
GS < 6		273	33.9

GS: Gensini score, LP: lipoprotein.

Table 2
Relationship of abnormal LP(a) serum concentration with GS groups according to age

Age groups	GS groups	LP(a) serum concentration		Total	Odds ratio (CI)
		≤ 40 mg/dL	>40 mg/dL		
55 years or younger	GS I	145 (94.8%)	8 (5.2%)	153 (100%)	2.78
	GS II	189 (86.7%)	29 (13.3%)	218 (100%)	(1.23–6.26)
	Total	334 (90.0%)	37 (10.0%)	371 (100%)	
56 years and older	GS I	114 (95.0%)	6 (5.0%)	120(100%)	2.32
	GS II	278 (89.1%)	34 (10.9%)	312 (100%)	(0.95–5.68)
	Total	322 (90.7%)	40 (9.3%)	432 (100%)	
Total	GS I	259 (94.9%)	14 (5.1%)	273 (100%)	2.50
	GS II	467 (88.1%)	77 (11.9%)	530 (100%)	(1.38–4.51)
	Total	729 (90.9%)	77 (9.9%)	803 (100%)	

Results

Patients' characteristics are shown at Table 1. Initially 826 patients enrolled in the study. GS, LP(a) serum level and age of patients were missed in 23 patients. Therefore final analysis was done on 803 patients. The difference in prevalence of high concentration of LP(a) between genders was not statistically significant.

Gensini score (GS) ranged from 0 to 214 in all participants. The Gensini score in 90% of patients who showed normal or minimal stenotic angiograms was equal or below 6. Therefore we regarded GS ≤ 6 as the 90 percentile for normal angiograms. We call the group with GS ≤ 6 as GS I and those with GS more than 6 as GS II. Considering 40 mg/dL as a cut-off point for LP (a) serum normal level, the frequency of abnormal LP(a) serum concentration was significantly higher in GS II group (odds ratio = 2.50, $p=0.001$). It remained significantly higher in GS II group after controlling for gender and smoking by stratified analysis (odds ratio = 2.82, $p=0.001$). Controlling the effect of hyperlipidemia and diabetes mellitus by stratification did not change the result.

We studied the relationship of LP(a) serum concentration with severity of coronary artery stenosis based on the Gensini score.

GS rises companion to LP(a) serum concentration rising. Mean GS in three different LP(a) serum levels including ≤ 30 mg/dL, 31–60 mg/dL and ≥ 61 mg/dL was 40, 49 and 56 respectively that shows a direct relationship between GS and serum LP(a) level.

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