# High-density lipoprotein cholesterol in coronary artery disease patients: is it as low as expected?

Koroner arter hastalarında yüksek dansiteli lipoprotein kolesterol: Beklendiği kadar düşük mü?

Mehmet Uzunlulu, Aytekin Oğuz , \*Kürşat Tigen

Department of Internal Medicine, SSK Göztepe Training Hospital, İstanbul \* Department of Cardiology, Koşuyolu Heart and Research Hospital, İstanbul, Turkey

## Abstract

**Objective:** Epidemiological studies demonstrate that the high-density lipoprotein (HDL) cholesterol levels in Turkish people are lower compared to other populations. In the present study, the HDL cholesterol levels in subjects with or without angiographically documented coronary artery disease (CAD) were compared to assess whether HDL cholesterol levels were as low as expected.

**Methods:** A total of 420 consecutive patients with age of  $\geq$ 40 years (160 female, 260 male) undergoing coronary angiography were included in the study. Patients receiving fibric acid derivatives or niacin were excluded. Coronary artery disease group consisted of those patients with any atherosclerotic lesions in coronary angiography, and non-CAD group consisted of patients with no such lesions.

**Results:** Average HDL cholesterol levels were 45.0±10.5 mg/dl (44.4±10.9 mg/dl in men, 46.5±9.6 mg/dl in women) in CAD group, and 47.7±9.0 mg/dl (45.5±8.4 mg/dl in men, 48.9±9.2 mg/dl in women) in non-CAD group (p<0.05).

**Conclusion:** Compared to non-CAD patients, patients with CAD had lower HDL cholesterol levels, but in general HDL cholesterol levels were not as low as to be expected from epidemiological studies. (*Anadolu Kardiyol Derg 2005; 5: 268-70*)

Key words: Coronary artery disease, HDL cholesterol

## Özet

Amaç: Epidemiyolojik çalışmalar Türk halkında yüksek dansiteli lipoprotein (HDL) kolesterol düzeylerinin diğer toplumlardan daha düşük olduğunu göstermektedir. Bu çalışmada HDL kolesterol düzeylerinin beklendiği kadar düşük olup olmadığını saptamak amacıyla, anjiyografik olarak koroner arter hastalığı (KAH) bulunan ve bulunmayan hastalardaki HDL kolesterol düzeyleri karşılaştırıldı.

Yöntemler: Çalışmaya koroner anjiyografileri yapılmış olan 40 yaş ve üzeri toplam 420 hasta (160 kadın, 260 erkek) ardışık olarak alındı. Fibrik asit türevleri ve niyasin kullanan hastalar çalışmaya alınmadı. Koroner anjiyografide herhangi bir aterosklerotik lezyon saptanan hastalar KAH bulunan grubu, herhangi bir lezyon saptanmayan hastalar KAH bulunmayan grubu oluşturdu.

**Bulgular:** Çalışmamızda, HDL kolesterol ortalaması KAH bulunan grupta 45.0±10.5 mg/dl (erkeklerde 44.4±10.9 mg/dl, kadınlarda 46.5±9.6 mg/dl), KAH bulunmayan grupta 47.7±9.0 mg/dl (erkeklerde 45.5±8.4 mg/dl, kadınlarda 48.9±9.2 mg/dl) idi (p<0.05).

**Sonuç:** Koroner arter hastalığı bulunan hastalardaki HDL kolesterol düzeyleri, KAH bulunmayan hastalara göre daha düşük olmakla birlikte, genel olarak HDL kolesterol düzeyleri epidemiyolojik çalışmalarla karşılaştırıldığında beklendiği kadar düşük değildi. *(Anadolu Kardiyol* Derg 2005; 5: 268-70)

Anahtar kelimeler: Koroner arter hastalığı, HDL kolesterol

### Introduction

#### Methods

A low high-density lipoprotein cholesterol (HDL-C) is an independent risk factor for the development of coronary artery disease (CAD) (1,2). Epidemiological studies conducted in Turkey showed that the average HDL-C levels in Turkish people are lower compared to other countries (3,4). This study was undertaken to investigate the HDL-C levels of subjects with or without angiographically documented CAD, in order to determine whether HDL-C levels were as low as those reported in previous epidemiological studies. A total of 420 consecutive patients (160 female, 260 male) with age of  $\geq$ 40 years who underwent coronary angiography between June and October 2004 at the Department of Internal Medicine, SSK Göztepe Training Hospital, and Cardiology Unit, Koşuyolu Heart and Research Hospital were included in this study. Patients with a history of acute myocardial infarction within last two months, patients receiving fibric acid derivatives or niacin were excluded, as were the patients with a triglyceride

Address for Correspondence: Mehmet Uzunlulu, MD, Merdivenkoy SSK Poliklinikleri Karsısı, Ressam Salih Ermez Caddesi, No: 14/6 Goztepe 34732 Istanbul / Turkey Tel: + 90 216 5676713, Fax: +90 216 566 88 68, e-mail: mehmetuzunlulu@yahoo.com level greater than 400 mg/dl. The study protocol was approved by the local ethics committee (date and number of approval: 06 June 2004/15) and the procedures were followed in accordance with Helsinki Declaration (as revised in 1983). Before the study procedures were commenced, written informed consent was obtained from all patients meeting inclusion criteria. Participants were divided into two groups, referred to as the CAD and non-CAD groups, on the basis of the presence or absence of angiographically detected atherosclerotic lesions, and the two groups were compared with respect to the average HDL-C, blood pressure, fasting blood glucose and other lipid values.

Venous blood samples were obtained after 12 hours of fasting. Enzymatic methods were used for the measurement of glucose, total cholesterol and triglyceride levels. High-density lipoprotein cholesterol was measured using Direct HDL-Cholesterol reagent (Randox) and the following performance characteristics were obtained: within-run [ Mean (mg/dl): 37.07-57.93, SD: 0.45-0.88, CV(%): 1.20-1.53, n: 30] and between-run [Mean] (mg/dl): 37.7-58.1, SD: 0.35-0.51, CV(%): 0.93-0.88, n: 20] variations. Low-density lipoprotein cholesterol (LDL-C) levels were calculated by Friedwald's formula (5). Two blood pressure (BP) measurements 3 minutes apart were performed from both arms. Measurements were done by the same investigator with a mercury sphygmomanometer after at least 5 minutes of rest, and Phase I and Phase IV sounds were used for determining systolic and diastolic blood pressure values. The BP values were approximated to the nearest 2 mmHg.

Statistical analyses were performed by GraphPad Prisma V.3 software package. For data analyses, descriptive methods (mean, standard deviation), independent t test (for quantitative data comparisons), and Chi-square test (for qualitative data) were used. The statistical significance was set at a p level of <0.05.

## **Results**

A total of 420 patients (260 male, 160 female) were included in the study. The CAD group (n=299) consisted of those patients with atherosclerotic lesions documented by coronary angiography, and non-CAD group (n=121) consisted of patients with no such lesions.

Table 1. Comparison of age,	, blood pressure	, fasting plasma	glucose
and lipid levels in the two gro	oups		

	CAD (-) (n=121) (Mean±SD)	CAD (+) (n=299) (Mean±SD)	Р
Age (years)	57.5±10.4	58.4±10.8	ns
Systolic blood pressure (mmHg)	134.2±26.5	133.6±22.7	ns
Diastolic blood pressure (mmHg)	83.2±12.3	81.3±12.5	ns
Fasting plasma glucose (mg/dl)	110.5±39.8	122.1±50.2	<0.05
Total cholesterol (mg/dl)	197.3±46.0	207.0±44.4	<0.05
Triglycerides (mg/dl)	126.3±59.1	168.2±90.1	<0.0001
LDL cholesterol (mg/dl)	124.4±37.6	127.7±39.6	ns
HDL cholesterol (mg/dl)	47.7±9.0	45.0±10.5	<0.05
Men	45.5±8.4	44.4±10.9	ns
Women	48.9±9.2	46.5±9.6	ns

LDL – low-density lipoprotein; NS- nonsignificant; SD-standard deviation

Results are outlined in Tables 1 and 2. There was no statistical difference with respect to age between the two groups (p > 0.05). Proportion of males (72.6% vs. 35.5%, p<0.001), smokers (35.1% vs. 13.2%, p<0.0001), diabetics (19.4% vs. 10.8%, p < 0.05) and hypertensives (53.5% vs. 44.6%, p < 0.0001) were higher in CAD group compared to non-CAD group.

Systolic and diastolic BP means were not significantly different among groups (p > 0.05). Fasting plasma glucose (122.1±50.2 ma/dl vs. 110.5±39.8 ma/dl, p<0.05), total cholesterol (207.0±44.4 mg/dl vs. 197.3±46.0 mg/dl, p<0.05), and triglyceride (168.2±90.1 mg/dl vs. 126.3±59.1 mg/dl, p<0.0001) concentrations were higher in patients in the CAD group compared to non-CAD patients. However, LD-C levels did not differ significantly (124.4±37.6 ma/dl vs. 127.7±39.6 ma/dl. p>0.05) between aroups.

The HDL-C levels were lower in CAD patients compared to non-CAD patients (45.0±10.5 mg/dl vs. 47.7±9.0 mg/dl, p<0.05). The average HDL concentrations in CAD group were 44.4±10.9 mg/dl and 46.5±9.6 mg/dl for male and female patients, respectively. Corresponding values for non-CAD group were 45.5±8.4 mg/dl and 48.9±9.2 mg/dl, respectively for male and female patients. The percentage of statin or alcohol users was 38.1% in the CAD group vs. 4.1% in non-CAD group and 9.3% in the CAD group vs. 5.7% in non-CAD group, respectively.

## Discussion

The results of this study suggest that the HDL levels in Turkish population, even in patients with angiographically established CAD lesions, are not as low as expected from epidemiological studies.

The study conducted by Mahley et al. (3) in six different geographical regions of Turkey included approximately 9000 participants and showed that the HDL concentration in Turkish people is lower compared to people living in other countries. In that study, the average HDL in men and women was 34-38 mg/dl and 37-45 mg/dl, respectively. Also, a trend toward increased triglyceride levels was observed both for Turkish men and women (120-150 mg/dl and 90-110 mg/dl, respectively). Onat et al. (4) found that the average HDL cholesterol concentrations in adult Turkish men and women were  $37 \pm 12 \text{ mg/dl}$  and  $45 \pm 13 \text{ mg/dl}$ , respectively. Average LDL levels were 113  $\pm$  30 mg/dl and 121  $\pm$ 34 mg/dl, for men and women respectively. Therefore, these two studies indicate that although total and LDL cholesterol levels in Turkish people were not substantially different from other com-

Table 2. Distribution (n, %) of gender and risk	factors in the studied
groups	

		CAD (-) (n=121)	CAD (+) (n=299)			
Gender	Male	43 (35.5%)	217 (72.6%)	X <sup>2</sup> :50.10		
	Female	78 (64.5%)	82 (27.4%)	p<0.0001		
Smoking	Smoking (-)	105 (86.8%)	194 (64.9%)	X <sup>2</sup> :20.13		
	Smoking (+)	16 (13.2%)	105 (35.1%)	p<0.0001		
Diabetes	Diabetes (-)	108 (89.2%)	241 (80.6%)	X <sup>2</sup> :3.99		
	Diabetes (+)	13 (10.8%)	58 (19.4%)	p<0.05		
HT	HT (-)	67 (55.4%)	139 (46.5%)	X <sup>2</sup> :15.44		
	HT (+)	54 (44.6%)	160 (53.5%)	p<0.0001		
CAD-coronary artery disease; HT-hypertension						

munities, the co-existence of low HDL-C and high triglyceride poses a major CAD risk for this population.

On the other hand, assessment of the HDL-C levels in individuals with or without angiographically detected CAD was aimed in the present study. The average HDL-C levels were higher in both groups compared to those in the above-mentioned studies. Rubins et al. (6) examined 8500 Americans with coronary artery disease and found that the HDL cholesterol was 45 mg/dl in blacks and 38 mg/dl in whites. Our patients had higher HDL cholesterol levels compared to white Americans with coronary artery disease and similar HDL cholesterol levels compared to black Americans with the same condition.

Fibric acid derivatives and niacin are known to influence HDL cholesterol and triglyceride levels (7-9), and therefore patients receiving these agents were excluded in the present study. Studies with statins show that a reduction in LDL-C is associated with a lower risk of vascular disease, regardless of baseline cholesterol levels (10). The principal effect of statins at effective dose range is principally a reduction in total and LDL cholesterol, and the increase in HDL-C achieved with these agents is only around 5 to 6% (11-13). In our study, 38.1% of patients with CAD were on statins (mostly on low dose), which may explain relatively small but significant difference in terms of LDL-C levels between CAD and non-CAD groups. However, this cannot explain the fact that the HDL-C levels were higher than expected in both groups. In addition, average fasting plasma glucose concentrations and percentage of patients with diabetes were higher in the CAD group, and diabetic dyslipidemia is known to be characterized by low HDL-C (14), which might have led to lower HDL cholesterol in these patients.

The percentage of smokers, and average total cholesterol and triglyceride concentrations were significantly higher in the CAD group. The LDL cholesterol levels were also higher in the CAD group, but the difference was not significant. Intensive blood pressure lowering therapy might be responsible for the slightly lower systolic and diastolic BP values in patients with CAD.

We conclude that our patients with CAD had lower HDL cholesterol levels compared to non-CAD patients, but neither group of patients had such low levels that would be expected from epidemiological studies.

## References

 Assmann G, Schulte H, von Eckardstein A, Huang Y. High-density lipoprotein cholesterol as a predictor of coronary heart disease risk. The PROCAM experience and pathophysiological implications for reverse cholesterol transport. Atherosclerosis 1996;124 (Suppl): S11-20.

- Sacks FM. Expert Group on HDL Cholesterol. The role of high-density lipoprotein (HDL) cholesterol in the prevention and treatment of coronary heart disease: expert group recommendations. Am J Cardiol 2002; 90:139-43.
- 3. Mahley RW, Palaoglu KE, Atak Z, et al. Turkish Heart Study: lipids, lipoproteins, and apolipoproteins. J Lipid Res 1995; 36: 839-59.
- Onat A, Yıldırım B, Uslu N, et al. Plasma lipoprotein and apolipoproteins in Turkish adults: overall levels, association with risk factors, and HDL as a predictor of coronary risk in women. Arch Turk Soc Cardiol 1999; 27:72-9.
- 5. Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein in plasma, without use of the preparative ultracentrifuge. Clin Chem 1972; 18: 499-502.
- Rubins HB, Robins SJ, Collins D, et al. Distribution of lipids in 8,500 men with coronary artery disease. Department of Veterans Affairs HDL Intervention Trial Study Group. Am J Cardiol 1995; 75: 1196-201.
- McLaughlin PR, Gladstone P. Diabetes Atherosclerosis Intervention Study (DAIS): quantitative coronary angiographic analysis of coronary artery atherosclerosis. Cathet Cardiovasc Diagn 1998; 44: 249-56.
- Rubins HB, Robins SJ, Collins D, et al. Gemfibrozil for the secondary prevention of coronary heart disease in men with low levels of high-density lipoprotein cholesterol. Veterans Affairs High-Density Lipoprotein Cholesterol Intervention Trial Study Group. N Engl J Med 1999; 34: 410-8.
- Elam MB, Hunninghake DB, Davis KB, et al. Effect of niacin on lipid and lipoprotein levels and glycemic control in patients with diabetes and peripheral arterial disease: the ADMIT study: A randomized trial. Arterial Disease Multiple Intervention Trial. JAMA 2000; 284: 1263-70.
- 10. MRC/BHF Heart Protection Study Collaborative Group. MRC/BHF Heart Protection Study of cholesterol-lowering therapy and of antioxidant vitamin supplementation in a wide range of patients at increased risk of coronary heart disease death: early safety and efficacy experience. Eur Heart J 1999; 20: 725-41.
- Downs JR, Clearfield M, Weis S, et al. Primary prevention of acute coronary events with lovastatin in men and women with average cholesterol levels. Results of AFCAPS/TexCAPS. JAMA 1998; 279: 1615-22.
- The Long-term Intervention with Pravastatin in Ischaemic Disease (LIPID) Study Group. Prevention of cardiovascular events and death with pravastatin in patients with coronary heart disease and a broad range of initial cholesterol levels. N Engl J Med 1998; 339: 1349-57.
- Scandinavian Simvastatin Survival Study Group. Randomised trial of cholesterol lowering in 4444 patients with coronary heart disease: the Scandinavian Simvastatin Survival Study (4S). Lancet 1994; 344: 1383-9.
- 14. Steiner G. Treating lipid abnormalities in patients with type 2 diabetes mellitus. Am J Cardiol 2001; 88(Suppl): 37N-40N.