Archives of Gerontology and Geriatrics 52 (2011) 217–222

Contents lists available at ScienceDirect

Archives of Gerontology and Geriatrics

journal homepage: www.elsevier.com/locate/archger

Importance of high-density lipoprotein-cholesterol (HDL-C) levels to the incidence of cardiovascular disease (CVD) in the elderly

Elizabete Viana de Freitas *, Andréa Araújo Brandão, Roberto Pozzan, Maria Eliane Magalhães, Flávia Fonseca, Oswaldo Pizzi, Érika Campana, Ayrton Pires Brandão

Pedro Ernesto University-affiliated Hospital, Rio de Janeiro State University, Rua Almirante Benjamim Sodré 40/702, Laranjeiras, Rio de Janeiro, RJ, CEP 22240-080, Brazil

ARTICLE INFO

Article history:
Received 18 December 2009
Received in revised form 26 March 2010
Accepted 29 March 2010
Available online 24 April 2010

Keywords:
HDL-cholesterol
LDL-cholesterol
Health of the elderly
Cardiovascular disease

ABSTRACT

Studies about the impact of HDL-C levels on the incidence of cardiovascular disease (CVD) in the elderly are scarce. We decided to evaluate the relation of clinical and laboratory variables to the incidence of CVD events in the elderly stratified according to HDL-C behavior in an 8-year follow-up. We assessed 126 elderly (mean age: 70.01 ± 7.24 years; 33.3% were men) on two occasions (assessment 1 = A1, and assessment 2 = A2), with a minimum of 5-year interval. They underwent clinical and laboratory evaluation and were divided into three groups as follows: (1) GN ($n = 52$), normal HDL-C levels on A1 and A2; (2) GL ($n = 36$), low HDL-C levels on A1 and A2; (3) GV ($n = 38$), HDL-C levels varying from A1 to A2. The following CVD events were observed: coronary artery disease (angina pectoris = AP, myocardial infarction = MI, percutaneous/surgical coronary intervention); stroke; transient ischemic attack = TIA; carotid disease; and heart failure = HF. The groups did not differ in age or gender at A1 and A2. Triglyceride = TG mean levels were lower in GN at A1 ($p = 0.007$) and A2 ($p < 0.001$) than in GL. There were 14 CVD events in GN (26.9%), 23 (63.9%) in GL, and 13 (34.2%) in GV ($\chi^2 = 12.825$; $p = 0.002$). In logistic regression analysis, we observed that the higher the systolic blood pressure (SBP) (odds ratio [OR] = 1.0231; $p = 0.0338$) and the lower the HDL-C (OR = 0.9363; $p = 0.0035$), the higher the incidence of CVD events. Persistently low HDL-C levels over 8 years of follow-up were a risk factor (RF) for the development of CVD events in the elderly.

1. Introduction

Throughout the world, the number of people aged 60 years or older has rapidly increased (WHO, 2002). In Brazil, 10.5% of the total population is of 60 years or older, according to data currently available in the Brazilian Institute of Geography and Statistics website, and the mean life expectancy at birth is 72.05 years (IDB Brasil, 2006). In addition, the life expectancy for those who reach 60 years has increased significantly, modifying the epidemiological profile. It is worth noting that the prevalence of CVD in that population is high (Chaimowicz, 2006).

Epidemiological data have shown that the mortality due to CVD increases with age, reflecting the importance of the atherosclerotic process in the elderly, and emphasizing, therefore, the need for its prevention and detection. However, initial studies on geriatrics are controversial in regard to the predictive value of the RF for CVD in the elderly, especially those over the age of 75 years.

The presence of atherosclerotic lesions is associated, among other RFs (Bilato and Crow, 1996; Wong and Ridker, 2000; Williams et al., 2002; Libby, 2006), with low-density lipoprotein-cholesterol (LDL-C) levels ≥ 100 mg/dl (2.6 mmol/l) and HDL-C levels < 40 mg/dl (1.04 mmol/l) (Aronow and Ahn, 1994; Aronow, 2002). On the other hand, elevated HDL-C levels have been known as antiatherogenic. Although not yet completely established, that effect of HDL-C has been attributed to its ability to mediate the reverse cholesterol transport. Other protective mechanisms of HDL-C have been proposed, such as the inhibition of LDL-C oxidation, the reduction in blood viscosity, the regulation of the synthesis of prostaglandins and thromboxane, the activation of fibrinolysis, the effect on endothelial function, and the anti-inflammatory action (Wilson et al., 1998; Mackness et al., 2000; Rader, 2003).

The EPESE study (Cornoni-Huntley et al., 1993) has suggested that, in the elderly, the HDL-C level is a more specific and powerful predictor of the death risk due to coronary artery disease (CAD) than total cholesterol (TC) level is. Corti et al. (1997), based on the EPESE data, concluded that abnormal cholesterol values were related to death due to CAD in the elderly, and, therefore, its exclusion from the studies assessing the relation of cholesterol to CVD is inappropriate. In the Northern Manhattan Study (Sacco et al., 2001), the authors concluded that a high HDL-C level is associated with a reduced risk of ischemic stroke in the elderly, being HDL-C, therefore, a significant and modifiable RF for stroke. Another study correlated low HDL-C levels with an increased

* Corresponding author. Tel.: +55 21 2553 7288; fax: +55 21 2553 6999.
E-mail address: elizabet.rlk@terra.com.br (E.V. de Freitas).

0167-4943/$ – see front matter. Published by Elsevier Ireland Ltd.
doi:10.1016/j.archger.2010.03.022

mortality risk for CAD and stroke in the elderly (Weverling-Rijnsburger et al., 2003). On the other hand, in the PROSPER study (Shepherd et al., 1999), the reduction in CVD events was not highly significant, and one should be cautious when analyzing those data until other studies confirm the benefits. However, the Heart Protection Study (Heart Protection Study Collaborative Group, 2002) found a reduction in major CVD events in patients with elevated HDL-C levels treated with simvastatin as compared with those receiving placebo.

This study aimed at assessing the relation of clinical and laboratory variables to the incidence of fatal and non-fatal CVD events, such as CAD (angina, acute myocardial infarction = AMI, and percutaneous or surgical myocardial revascula-rization), stroke, TIA, carotid disease, and HF, in the elderly stratified according to HDL-C behavior in an 8-year follow-up.

2. Patients and methods

We assessed 126 individuals, who were followed up for 7.92 ± 1.52 years at the outpatient clinic of the Pedro Ernesto University-affiliated Hospital. They were divided into three groups according to their HDL-C levels on an initial assessment (A1) and on a second assessment (A2), as follows: GN (normal group), comprising 52 individuals, 17 men (32.7%) and 35 women (67.3%) with normal HDL-C levels on both assessments; GL (low group), comprising 36 individuals, 11 men (30.6%) and 25 women (69.4%) with low HDL-C levels on both assessments; GV (variable group), comprising 38 individuals, 14 men (36.8%) and 24 women (63.2%) with variable HDL-C levels on both assessments.

The groups were formed based on the HDL-C levels recommended by the NCEP (2002), the normal values being $\geq$40 mg/dl for men and $\geq$50 mg/dl for women. Values below those cutoff points were considered low, and, therefore, abnormal.

The patients who agreed to participate in the study were interviewed and underwent clinical and laboratory examination at the A1. They were asked about any medication being taken, with an emphasis on the major classes of drugs that could influence CV morbidity and mortality, such as angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, statins, beta-blockers, calcium channel blockers, and diuretics. The procedure was repeated on the second assessment, with an emphasis on identifying fatal and non-fatal CV events, such as CAD (angina, AMI, and percutaneous or surgical myocardial revascularization), stroke and TIA, carotid disease and HF. In case of death, analysis of the existing medical records was used to identify the cause.

Laboratory assessment included the following measures: TC, TG, HDL-C and LDL-C. The normal values were as follows: TC < 200 mg/dl; LDL-C < 130 mg/dl; and TG < 150 mg/dl (NCEP, 2002).

CAD was characterized by percutaneous or surgical myocardial revascularization, positive myocardial scintigraphy (I Diretriz Brasileira sobre Cardiologia Nuclear, 2006), and echocardiography with well-defined alterations in coronary contractility (Diretriz para Indicações e Utilização da Ecocardiografia na Prática Clínica, 2004). Stroke was characterized by the existence of well-defined alterations of cerebral lesion on brain computed tomography or magnetic resonance imaging and/or motor deficit. Transient ischemic accident was characterized by loss of consciousness or transient motor deficit accurately documented in hospital records. Carotid disease was considered when the presence of atherosclerotic plaques was evidenced on echo-Doppler (Asrafian et al., 2007).

BP at rest was measured twice during the visit at a minimum 5-min interval, with the patient at the sitting position, and the mean value of those measures was adopted. BP measurement and its classification were performed according to the criteria of the JNC7 (2003).

Statistical analysis was carried out with the 8.0.0 version of the "SPSS for Windows" program. Logistic regression was used to assess the probability of the occurrence of an event.

3. Results

As regards the age, follow-up duration and gender, the comparison of the means of the three groups showed no statistically significant difference (Table 1).

The comparisons of the anthropometric, metabolic and blood pressure variables on assessments 1 and 2 are shown in Tables 2 and 3, respectively. At both assessments, a significant difference was observed only in the comparison of the HDL-C and TG means, in which GL showed lower HDL-C and higher TG means as compared with the other two groups (Table 2).

When comparing the SBP and DBP means on both assessments (Tables 2 and 3), no statistically significant difference was observed between the three groups, which showed no difference in regard to the prevalence of arterial hypertension.

On A1, no statistically significant difference was observed in the distribution of overweight and glucose intolerance in the three groups. On A2, however, both overweight and glucose intolerance were more prevalent in GL and less prevalent in GN, and the difference was statistically significant.

Regarding the distribution of medications that could impact CVD morbidity and mortality, the comparison of the three groups showed no statistically significant difference.

Table 4 shows the distribution of CVD events in the three groups according to HDL-C levels. The group with low HDL-C levels on both assessments had a significantly higher percentage of CV events as compared with those of the other two groups. The incidences of CVD events were as follows: 14 (26.9%) in GN; 23 (63.9%) in GL; and 13 (34.2%) in GV ($\chi^2 = 12.825$; $p = 0.002$).

Table 5 shows the distribution of the type of CVD events, evidencing a statistically significant difference between the groups ($p = 0.016$). In GN, 63.5% of the individuals had no events, while in GL, that percentage was only 27.8%. It is worth emphasizing that CAD occurred in 5 (9.6%) GN individuals and in 15 (41.7%) GL individuals.

In the logistic regression model, the occurrence of events was considered to be a dependent variable. The independent variables obtained on the first assessment were as follows: age, gender, smoking habit, BMI1, SBP1 and DBP1, respectively, LDL-C1, HDL-C1, TG and glucose levels. In that model, SBP and HDL-C maintained a significant correlation with the incidence of CDV

Table 1
Epidemiological variables: age on first assessment, gender and follow-up duration, mean $\pm$ SD, or *n* (%).

Variables	GN	GL	GV	Stat. test	*p*
Number	52	36	38		
Age on A1	70.87 ± 7.57	68.75 ± 7.79	70.03 ± 6.16	$F = 0.912$	0.405
Gender					
Males	17 (32.3)	11 (30.6)	14 (36.8)	$\chi^2 = 0.345$	0.841
Females	35 (67.37)	25 (69.4)	24 (63.2)		
Follow-up duration (years)	7.92 ± 1.52	8.11 ± 1.53	7.90 ± 1.30	$F = 0.710$	0.494