ORIGINAL ARTICLE

The impact of high-density lipoprotein on oxidant–antioxidant balance in healthy elderly people

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KEY WORDS

aging, HDL cholesterol, oxidant–antioxidant balance

ABSTRACT

INTRODUCTION There is an inverse relationship between high-density lipoprotein cholesterol (HDL-C) levels and the risk of atherosclerosis.

OBJECTIVES The aim of the present study was to assess the oxidant–antioxidant balance in elderly people with different concentrations of HDL-C.

PATIENTS AND METHODS A total of 541 people aged 60 years or older were examined, of whom 90 individuals with no acute or severe chronic disorders had their waist circumference, body mass index, percentage of body fat, and blood pressure measured. Fasting and 120-minute glycemia was determined in an oral glucose tolerance test, following which 15 patients with type 2 diabetes were excluded. Fasting plasma levels of lipids, total antioxidant status, and thiobarbituric acid-reacting substances (TBARS), as well ast the activity of erythrocyte superoxide dismutase 1 (SOD-1) were assessed. Based on HDL-C levels, participants were divided into the high HDL-C group (≥40.0 mg/dl and ≥50.0 mg/dl for men and women, respectively; n = 50) and the low HDL-C group (<40.0 mg/dl and <50.0 mg/dl for men and women, respectively; n = 25).

RESULTS The groups did not differ in terms of age, blood pressure, body mass index, percentage of body fat, and glucose concentration. The high HDL-C group had lower waist circumference (P <0.02) and lower triglyceride concentrations (P <0.00001). Increased TBARS levels (P <0.0005) was observed in the low HDL-C group. There were no differences in SOD-1 activity and total antioxidant status between the groups.

CONCLUSIONS HDL-C levels, which are known to reflect the antiatherogenic activity of HDL, including antioxidant properties, may indicate increasing oxidative stress in healthy elderly individuals.

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Received: July 19, 2016.
Revision accepted: September 20, 2016.
Published online: September 20, 2016.
Conflict of interest: none declared.
Pol Arch Med Wewn. 2016; 126 (10): 731-738
doi:10.20452/pamw.3559

INTRODUCTION Atherosclerosis is the leading cause of death worldwide.[1] Importantly, metabolic disturbances such as dyslipidemia, hyperglycemia, and oxidative stress contribute to the development of atherosclerosis. The increasing prevalence of atherosclerosis is also associated with aging. It has been proved that older patients are at particularly high risk of coronary heart disease, stroke, or vascular dementia.[2-4] To decrease the burden of these diseases among elderly, simple noninvasive tools using various biomarkers are urgently needed to evaluate the risk of atherosclerosis in this population.

To assess cardiovascular risk, international guidelines recommend the measurement of total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol (HDL-C) levels.[5,6] However, these guidelines concern mainly young adults, while little is known on the relationship between blood lipids

and the risk of cardiovascular disease in the elderly population. Therefore, meeting targets in older adults is still challenging. Moreover, there is insufficient evidence to confirm that therapeutic interventions aimed at elevating HDL-C levels are beneficial, and also the molecular complexity of atherosclerosis should be considered.[7]

During the development of atherosclerosis, high TC and LDL-C levels are an unfavorable finding, while low TC levels might be a typical characteristic of late-onset dementia. Low HDL-C levels are always an unfavorable finding, and they may be a marker of either a chronic or a recent disease.[8]

The possibility of using HDL-C levels as a marker of atherosclerosis is currently investigated by basic, clinical, and public health sciences. Low HDL-C levels are associated with an increased overall cardiovascular risk both in younger and older individuals, with a stronger relationship between atherosclerosis and dyslipidemia observed in the elderly.[9,10] Clinical studies have also reported that low HDL-C levels are associated with increased incidence of either cardiovascular disease or dementia in this population.[11,12] Therefore, it is necessary to investigate different mechanisms underlying the atheroprotective activity of high-density lipoprotein, beyond the promotion of reverse cholesterol transport. These mechanisms employ the antioxidant, antithrombotic, anti-inflammatory, and antiapoptotic properties of the HDL molecule.[13]

Investigators agree that due to the involvement of numerous factors in the development of atherosclerotic plaque, increased oxidative stress (defined as an imbalance between the production and degradation of reactive oxygen species) appears to play an important role in chronic inflammatory response to dyslipidemia and related disorders.[14-16] It is known that LDL is involved in atherosclerosis through the plasma lipid peroxidation product-dependent pathway,[17] but the mechanism by which oxidative stress occurs at high and low levels of HDL-C is still unclear. Oxidative stress is characterized by oxidant and antioxidant imbalance that involves numerous enzymatic and nonenzymatic factors.

In the present study, we evaluated the activity of intracellular antioxidant enzyme, erythrocyte superoxide dismutase 1 (SOD-1), and the plasma levels of total antioxidant status (TAS) as well as thiobarbituric acid-reacting substances (TBARS) (to reflect plasma lipid peroxidation products) in elderly individuals with high or low HDL-C levels and no other abnormalities.

PATIENTS AND METHODS

Subjects and setting

The study included 541 elderly Caucasian volunteers from the Poznań metropolitan area in western Poland. Participants were aged 60 years or older (according to the United Nation's definition)[18] and reported no complaints. Assessment tools included a questionnaire developed by ourselves, which identified the recognized diseases or disabilities and unhealthy habits (ie, alcohol and drug use, smoking) as well as a particular diet or supplements. Nonsmoking elderly persons using no medication, no special diet, no supplements, and no alcohol, without acute or chronic disease, were included. The exclusion criteria were a history of dementia (including vascular dementia), stroke, coronary artery disease (accompanied by current steady-state electrocardiography), diabetes, neoplastic disease, or inflammatory disease. Additional biochemical exclusion criteria were albuminuria reflected by the albumin-to--creatinine ratio exceeding 30 mg of albumin/1 g of creatinine in a fresh morning urine sample and/or decreased estimated glomerular filtration rate (eGFR; <60 ml/min/1.73 m^2) based on the Modification of Diet in Renal Disease formula: eGFR (ml/min/1.73 m^2) = (186 × [creatinine]$^{-1.154}$ × [age]$^{-0.203}$ × 0.742 [for women] × 1.210 [for Afro-Americans]).

Next, 90 individuals were referred for a 75-gram oral glucose tolerance test (OGTT) according to the World Health Organization recommendations,[19] and, as a result, 15 elderly persons with newly diagnosed diabetes were excluded from the study.

Finally, the results of the measurement of plasma HDL-C levels allowed us to classify study participants into 2 groups: high HDL-C group (with HDL-C levels of 40.0 mg/dl or higher for men and 50.0 mg/dl or higher for women; n = 50) and low HLD-C group (with HDL-C levels of less than 40.0 mg/dl for men and less than 50.0 mg/dl for women; n = 25).

The study was performed in accordance with the 1975 Declaration of Helsinki for Human Research, and the study protocol was approved by the Bioethics Committee of the Poznan University of Medical Sciences, Poznań, Poland (statement numbers, 142/11 and 595/11). All participants gave their written informed consent.

Measurements

All patients underwent a complete physical examination including the measurement of systolic blood pressure (SBP) and diastolic blood pressure (DBP), percentage of body fat (FAT) using the bioimpedance method (BodyStat equipment, Bodystat Ltd, Ballakaap, Great Britain), and body mass index (BMI). SBP and DBP measurements were made on a validated OMRON model M10-IT sphygmomanometer (Omron Health Care, Kyoto, Japan), following the recommendations of the European Society of Hypertension. The mean of 3 measurements was used as a value of blood pressure.[20]

Blood sampling and biochemical analysis

Blood was collected from the ulnar vein twice: at 0 and 120 minutes of the 75-gram OGTT. Fasting blood samples were used to measure the concentration of glucose and lipids in plasma samples without symptoms of hemolysis. Oxidant–antioxidant balance indices were measured in fasting blood samples. Blood collected at 120 minutes of OGTT was used for the measurement of plasma glucose concentrations.

Glucose and lipid assays The OGTT was performed between 7:00 and 9:00 AM according to World Health Organization recommendations. Glucose concentrations were determined at 0 and 120 minutes of the OGTT, following a standard dose of 75-gram glucose load. Glucose and lipid parameters, including TC, HDL-C, and triglyceride (Tg) concentrations, were evaluated by enzymatic methods using a bioMérieux reagent kit (Marcy-l'Etoile, France) and the UV-160A Shimadzu spectrophotometer (Shimadzu Co., Kyoto, Japan). LDL-C levels were calculated using the Friedwald formula for lipid parameters expressed in mg/dl: LDL-C = TC – HDL-C – (Tg/5) if Tg <400 mg/dl.

Rreference sera RANDOX Assayed Human Multi-Sera Level 1 (as normal) and RANDOX Assayed Human Multi-Sera Level 2 (as pathological) (Randox, Crumlin, United Kingdom) were used for monitoring the accuracy of the measurements.

Oxidant–antioxidant balance indices Plasma TAS levels and activity of erythrocyte cytoplasmic superoxide dismutase Cu-,Zn-SOD (EC: 1.15.1.1) (SOD-1) were measured spectrophotometrically by a colorimetric assay based on the decrease in the optical density of the blank produced by each sample in analogy to its antioxidant property, using Randox reagent kits (Randox Laboratories Ltd., Crumlin, Co. Antrim, United Kingdom) and Stat Fax 1904 Plus spectrometer (Awareness Technology, Inc., Palm City, Florida, United States).

Total antioxidant status The measurement of TAS was done using $ABTS^{+}$ (2,2'-azino-bis(3--ethylbenzothiazoline-6-sulphonic acid) radical formation kinetics. The presence of antioxidants in plasma suppressed the bluish-green staining of the ABTS cation, which was proportional to the antioxidant concentration. Kinetics was measured at 600 nm. The intra- and interassay coefficients of variation (CVs) for TAS were 1.5% and 3.8%, respectively.

Red blood cell Cu-,Zn-superoxide dismutase EC: 1.15.1.1 The method employs xanthine and xanthine oxidase to generate superoxide radicals, which react with 2-(4-iodophenyl)-3-(4-nitrophenol)-5-phenyltetrazolium chloride (INT) to form a red formazan dye. SOD-1 activity was measured by the degree of inhibition of the reaction. Kinetics was measured at 505 nm. The intra- and interassay CVs for SOD-1 were 1.6% and 2.7%, respectively.

Thiobarbituric acid-reacting substances The plasma levels of TBARS, reflecting plasma lipid peroxidation products, were determined by the Okhawa method,[21] using Sigma reagents (Germany) and Specord M40 spectrometer (Germany). The intra- and interassay CVs for TBARS were 1.8% and 3.7%, respectively.

Statistical analysis Statistica 12.0 version for Windows (StatSoft, Kraków, Poland) was used for statistical analysis. The normality of value distribution was checked by the Shapiro–Wilk test. Then, the results with a Gaussian distribution were analyzed with the *t* test, and those with a non-Gaussian distribution were verified by the nonparametric Mann–Whitney test to assess the differences between high HDL-C and low HDL-C groups. The Spearman rank correlation test was used to evaluate the strength of association between 2 variables. A multiple regression analysis was performed to evaluate the relationship between independent variables and SOD-1, TAS, and TBARS. A *P* value of less than 0.05 was considered to reflect a significant difference and correlations. The results described by Gaussian distribution are presented as mean and SD, and those characterized by a non-Gaussian distribution—as median and interquartile range.

The correlations between the oxidative stress markers (TBARS, SOD-1, and TAS) and age, BMI, waist circumference (WC), blood pressure (SBP and DBP), FAT, plasma lipids, and glucose concentrations at 0 and 120 minutes of the OGTT were analyzed using a multiple regression analysis for the following 3 models: A) BMI, WC, and FAT (TABLE 4); B) SBP, DBP, FAT, and glucose concentrations at 0 and 120 minutes of the OGTT (TABLE 5); and C) TC, HDL-C, and Tg (LDL-C was not included as derivative of the analyzed variables) (TABLE 6).

The following groups and subgroups of patients were analyzed: 1) all subjects; 2) women/men; and 3) HDL-C = 1 (high HDL-C group)/HDL-C = 0 (low HDL-C group).

RESULTS The clinical and biochemical characteristics of all patients according to sex are presented in TABLE 1. Women had lower WC ($P < 0.01$) and higher FAT ($P < 0.0001$) as well as higher HDL-C concentrations ($P < 0.0001$) in comparison with men, which is a typically observed difference between sexes.

The oxidant–antioxidant status and the clinical and biochemical characteristics of high HDL-C and low HDL-C groups are presented in TABLE 2. The groups did not differ in terms of age, blood pressure, BMI, FAT, glucose concentrations (both fasting and after the OGTT); however, the high HDL-C group had lower WC ($P < 0.02$) and lower Tg levels ($P < 0.00001$).

The analysis of oxidative stress markers revealed increased TBARS levels in the low HDL-C group ($P < 0.0005$). There were no differences in antioxidant defense parameters (both intra- and extracellular) between the groups. The mean value of TAS in our population was 1.37 ±0.25 mmol/l, while the reference range for the European working population proposed by Randox Laboratories Ltd. was from 1.30 to 1.77 mmol/l.

The analyses of correlations between oxidative stress markers and other parameters in both groups were performed (TABLE 3). In the high

TABLE 1 Characteristics of the study groups classified according to sex

Parameter	Total (n = 75)	Women (n = 43)	Men (n = 32)
age, y	68.0 (65.0–7.5)	69.0 (65.0–74.0)	67.5 (65.0–73.0)
BMI, kg/m^2	28.4 (26.0–31.4)	29.7 (26.5–31.5)	27.0 (25.2–29.7)
WC, cm	94.0 (87.0–102.0)	92.0 (82.0–101.0)	98.0 (91.0–106.0)[a]
FAT,%	43.0 (87.0–48.4)	46.0 (41.1–49.5)	29.5 (19.5–41.6)[a]
SBP, mmHg	135.0 (126.5–145.0)	140.0 (125.0–150.0)	135.0 (130.0–140.0)
DBP, mmHg	80.0 (75.0–90.0)	80.0 (75.0–90.0)	80.0 (80.0–85.0)
G0′, mg/dl	103.0 ±11.4	105.4 ±10.8	100.8 ±12.4
G120′, mg/dl	124.0 ±32.8	107.4 ±35.4	129.3 ±30.7
TC, mg/dl	201.0 ±32.8	209.5 ±35.5	191.5 ±42.3
Tg, mg/dl	109.0 (70.0–162.0)	97.8 (70.0–160.0)	115.0 (70.0–187.0)
HDL-C, mg/dl	56.6 (42.4–66.8)	64.2 (49.6–70.1)	45.0 (38.3–59.2)[a]
LDL-C, mg/dl	120.0 ±34.3	120.4 ±31.6	117.9 ±36.6
SOD-1, U/g Hb	1065.5 ±300.3	1129.0 ±324.9	1034.8 ±257.0
TAS, mmol/l	1.338 (1.204–1.510)	1.280 (1.170–1.470)	1.360 (1.260–1.521)
TBARS, μmol/l	2.350 (1.851–3.105)	2.167 (1.770–3.050)	2.408 (2.122–3.138)

Data are presented as mean ± SD for Gaussian distribution and median (interquartile range) for non-Gaussian distribution.

a significant differences compared with women

Abbreviations: BMI, body mass index; DBP, diastolic blood pressure; FAT; percentage of body fat; G0′ and G120′, glucose concentrations at 0 and 120 minutes of the oral glucose tolerance test; HDL-C, high-density lipoprotein cholesterol; Hb, hemoglobin; LDL-C, low-density lipoprotein cholesterol; SBP, systolic blood pressure; SOD-1, superoxide dismutase; TAS, total antioxidant status; TBARS, thiobarbituric acid-reacting substances; TC, total cholesterol; Tg, triglycerides; WC, waist circumference

TABLE 2 Characteristics of the study groups classified according to high-density lipoprotein cholesterol levels

Parameter	High HDL-C group (n = 50)	Low HDL-C group (n = 25)
age, y	69.5 (65.0–74.0)	67.0 (65.0–69.0)
BMI, kg/m^2	28.0 (25.2–30.8)	29.4 (26.5–32.9)
WC, cm	92.0 (84.5–101.0)	100.0 (93.0–102.0)[a]
FAT,%	42.6 (28.1–47.9)	43.0 (32.1–55.1)
SBP, mmHg	140.0 (125.0–150.0)	130.0 (130.0–140.0)
DBP, mmHg	80.0 (75.0–90.0)	80.0 (80.0–90.0)
G0′, mg/dl	102.3 ±10.7	105.0 ±12.9
G120′, mg/dl	122.3 ±35.0	125.0 ±29.4
TC, mg/dl	207.5 ±35.4	200.5 ±45.5
Tg, mg/dl	82.8 (70.0–125.0)	158.0 (121.9–213.0)[a]
HDL-C, mg/dl	65.2 (57.2–70.1)	39.0 (36.7–44.9)[a]
LDL-C, mg/dl	121.5 ±31.8	128.3 ±37.2
SOD-1, U/g Hb	1131.3 ±326.6	1103.4 ±238.5
TAS, mmol/l	1.344 (1.188–1.461)	1.380 (1.270–1.520)
TBARS, μmol/l	2.327 (1.737–2.593)	3.025 (2.350–3.560)[a]

Data are presented as mean ± SD for Gaussian distribution and median (interquartile range) for non-Gaussian distribution.

a significant differences compared with the high HDL-C group

Abbreviations: see TABLE 1

TABLE 3 Significant correlations between the oxidant–antioxidant status and clinical and biochemical parameters (P <0.05)

Correlation	r
high HDL-C group	
HDL-C vs WC	–0.386
HDL-C vs G120′	–0.359
SOD-1 vs TAS	0.548
TAS vs G0′	–0.347
TBARS vs age	–0.310
TBARS vs TAS	–0.380
TBARS vs G0′	0.281
TBARS vs G120′	0.442
TBARS vs LDL-C	0.300
low HDL-C group	
HDL-C vs WC	–0.432
HDL-C vs DBP	–0.472
TAS vs TG	0.474

Abbreviations: see TABLE 1

HDL-C group, a strong positive correlation between TAS and SOD-1 was observed, while no such correlation was found in the low HDL-C group. Moreover, the high HDL-C group showed a negative correlation between the TAS and glucose concentrations at minute 0 of the OGTT and between TAS and TBARS levels. In the low HDL-C group, TAS correlated positively with Tg levels, while no such correlation was observed in the high HDL-C group. In addition, we observed several negative correlations: between HDL-C levels and WC in both groups, between HDL-C levels and glucose concentrations at minute 120 of the OGTT in the high HDL-C group, and between HDL-C levels and DBP in the low HDL-C group.

The significant results (P <0.05) of the multiple regression analysis with respect to models A, B, and C, described in the Patients and methods section are included in TABLES 4, 5, and 6, respectively, to present a variable that correlated with the studied oxidative stress marker independently from other factors.

DISCUSSION A reduced HDL-C level is a well-established risk factor for coronary artery disease in young adults and should be measured to assess cardiovascular risk.[22] Aging itself increases the risk of cardiovascular events, and the identification of elderly individuals at high atherosclerotic risk is essential for the prediction, primary and secondary prevention, diagnosis, and prognosis of cardiovascular diseases.[23,24] Despite this, there have been no studies so far that would clearly demonstrate the benefits of raising HDL-C levels in elderly population.

In the present study, we evaluated oxidant–antioxidant balance indices in older individuals characterized by high and low concentrations of HDL-C. Lipid-lowering, antihypertensive,

TABLE 4 Significant results of multiple regression analysis between oxidative stress markers and clinical and biochemical parameters in model A (including age, BMI, WC, and body fat)

Correlation	B	β	*P*	*r*	R^2
TBARS vs age (all subjects)	–0.3570	–0.0407	0.0168	0.428	0.1832
TBARS vs age (HDL-C = 1)	–0.4009	–0.0338	0.0306	0.3917	0.1534
TBARS vs WC (women)	0.7292	0.0547	0.0251	0.5282	0.2790
TAS vs FAT (all subjects)	–0.3345	–0.0060	0.0441	0.3910	0.1528
TAS vs FAT (HDL-C = 1)	–0.4665	–0.0084	0.0202	0.4576	0.2094

Abbreviations: see **TABLE 1**

TABLE 5 Significant results of multiple regression analysis between oxidative stress markers and clinical and biochemical parameters in model B (including FAT, SBP, DBP, G0′, and G120′)

Correlation	B	β	*P*	*r*	R^2
TBARS vs G0′ (HDL-C = 1)	0.3382	0.0174	0.0482	0.5911	0.3494
TBARS vs G120′ (HDL-C = 1)	0.3289	0.0060	0.0354	0.5911	0.3494
TAS vs FAT (all subjects)	–0.3618	–0.0065	0.0125	0.4642	0.2155
TAS vs FAT (HDL-C = 1)	–0.4065	–0.0073	0.0086	0.5854	0.3427
TAS vs G0′ (women)	–0.4681	–0.0112	0.0446	0.5671	0.3216
SOD-1 vs G0′ (women)	–0.4597	–13.919	0.0492	0.5616	0.3154

Abbreviations: see **TABLE 1**

and antidiabetic drugs have been reported to reduce oxidative stress in humans.[25,26] Importantly, all subjects included in our study were drug-naive, and they were not using any medications that might have influenced the oxidant–antioxidant balance.

Enhanced oxidative stress measured by a concentration of malondialdehyde (MDA), reflecting lipid peroxidation products, was reported in patients with angiographically diagnosed coronary artery disease when compared with healthy controls.[27] Kumawat et al[28] compared elderly persons with younger individuals and found elevated MDA levels and decreased SOD-1 activity in the elderly group. In our study, we showed for the first time significantly higher TBARS levels (reflecting lipid peroxidation products) in individuals with low HDL-C levels in comparison with those with high HDL-C levels. However, our study showed no difference in SOD-1 activity and TAS between low and high HDL-C groups. Gupta et al[29] reported increased SOD-1 in the initial stages of coronary artery disease to protect and prevent lipid peroxidation, but it decreased thereafter with the severity of the disease. Thus, we suggest that in older individuals, dyslipidemia (low HDL-C and elevated Tg levels) promotes lipid peroxidation independently of antioxidant capacity or that inadequate antioxidant response might be observed in elderly individuals.

Our study also showed an inverse correlation between TAS and TBARS levels in the high HDL-C group only, which in our opinion is an additional benefit in this group. Our previous study showed a significant positive correlation between SOD-1 and TAS in normoglycemic patients, while no such correlation was observed in hyperglycemic ones.[30] In this study, we found a similar strong positive correlation between SOD-1 and TAS in the high HDL-C group, whereas in the low HDL-C group, a disintegration between intra- and extracellular antioxidant state was observed. In the low HDL-C group, a positive correlation between TAS and Tg levels might reflect the mobilizing effect of Tg on plasma antioxidant capacity associated with a decrease in HDL-C levels.

Gomez-Marcos et al[31] found a negative correlation between SOD-1 activity and HDL-C levels and a positive correlation between SOD-1 and Tg levels in hypertensive and diabetic patients, while Grygiel et al[32] found a negative correlation between Tg levels and SOD-1 activity and a positive correlation between HDL-C levels and SOD-1 activity in postmenopausal obese women. In the present study, the results of the multiple regression analysis concerning SOD-1 activity in the whole study population, as well as separately in men and women, suggest that SOD-1 activity may be negatively affected by Tg levels, and, on the other hand, that SOD-1 activity may increase compensatory to a decrease in HDL-C levels. In particular, increasing Tg levels might be responsible for 42% of dysregulation of SOD-1 activity in elderly individuals with low HDL-C levels and no other abnormalities.

We also found that linear changes of plasma HDL-C levels may be inversely correlated with 43% of variability in plasma TBARS levels either in men or in women, suggesting a significant protective role of HDL in plasma lipid peroxidation in elderly people. Interestingly, in individuals with high HDL-C levels, increasing glucose concentrations at 0 and 120 minutes of the OGTT might explain an increase of 35% in plasma TBARS levels, which is another reason for increasing oxidative stress independently of antioxidant activity. Additionally, an increase in FAT may be associated with a decrease of 34% in TAS levels in the high HDL-C group.

No differences in SOD-1 activity and TAS levels between the groups might be caused by metabolic factors affecting the oxidant–antioxidant balance, which were discussed above, as well as by the lack of comorbidities in the study population.

Concerning the oxidant–antioxidant system in our study group, higher prooxidant activity was observed in individuals with low HDL-C levels. Dyslipidemia was shown to be involved in the development of oxidative stress in elderly subjects, and low HDL-C concentrations are an unfavorable

TABLE 6 Significant results of multiple regression analysis between oxidative stress markers and clinical and biochemical parameters in the model C (including TC, HDL-C, Tg, and LDL-C not included as a derivative of the analyzed variables)

Correlation	B	β	*P*	*r*	R^2
TBARS vs HDL-C (all subjects)	–0.4708	–0.0261	0.0005	0.5131	0.2633
TBARS vs HDL-C (women)	–0.3694	–0.0210	0.0184	0.6570	0.4317
TBARS vs HDL-C (men)	–0.5603	–0.0378	0.0120	0.6576	0.4325
TBARS vs TC (men)	0.3989	0.0083	0.0403	0.6576	0.4325
SOD-1 vs Tg (all subjects)	–0.3846	–1.852	0.0092	0.3718	0.1382
SOD-1 vs HDL-C (all subjects)	–0.3161	–6.035	0.0271	0.3718	0.1382
SOD-1 vs Tg (men)	–0.6319	0.2386	0.0138	0.5165	0.2668
SOD-1 vs Tg (women)	–0.3908	–1.857	0.0286	0.5829	0.3398
SOD-1 vs HDL-C (women)	–0.3706	–8.010	0.03052	0.5829	0.3398
SOD-1 vs HDL-C (men)	–0.6032	–11.604	0.0161	0.5165	0.2668
SOD-1 vs Tg (HDL-C = 0)	–0.5420	–1.695	0.0253	0.6489	0.4210

Abbreviations: see **TABLE 1**

finding in this population. In healthy elderly individuals, low HDL-C levels may result in reduced antioxidant defense. Low HDL-C levels, which are known to describe the antiatherogenic function of HDL, including its antioxidant properties, might reflect elevated oxidative stress in otherwise healthy elderly individuals.

Contribution statement SD-G contributed to all parts of the study: conceived and designed the experiments, examined participants, participated in sample collection, took part in analytical procedures, performed statistical analysis, interpreted data, and wrote the manuscript. LB contributed to sample collection and analytical procedures, interpreted the laboratory data, and took part in statistical analysis. MZ-D participated in sample collection, analytical procedures, and data interpretation. KH examined participants of the study and participated in the discussion of the data. MC contributed to examination of participants, as well as interpretation and discussion of the data. MM-W participated in the interpretation and discussion of the data. EW contributed to sample collection and analytical procedures, as well as data interpretation. WB participated in interpretation of the data and critically revised the paper. All authors reviewed the results and approved the final version of the manuscript.

REFERENCES

1 Mendis S, Puska P, Norrving B. Global atlas on cardiovascular disease prevention and control. Policies, strategies and interventions. WHO, World Heart Federation, World Stroke Organization. 2011; 1-164.

2 Fleg JL, Forman DF, Berra K, et al. Secondary prevention of atherosclerotic cardiovascular disease in older adults: a scientific statement from the American Heart Association. Circulation. 2013; 128: 2422-2446.

3 Abbott AL, Paraskevas KI, Kakkos SK, et al. Systematic review of guidelines for the management of asymptomatic and symptomatic carotid stenosis. Stroke. 2015; 46: 3288-3301.

4 Justin B Ng, Turek M, Hakim AM. Heart disease as a risk factor for dementia. Clin Epidemiol. 2013; 5: 135-145.

5 Jellinger PS, Smith DA, Mehta AE, et al. AACE Task Force for the Management of Dyslipidemia and Prevention of Atherosclerosis. Endocr Pract. 2012; 18: S1-S78.

6 Reiner Z, Catapano AL, De Backer G, et al. ESC/EAS guidelines for the management of dyslipidaemias. The Task Force for the management of dyslipidaemias of the European Society of Cardiology (ESC) and the European Atherosclerosis Society (EAS) developed with the special contribution of: European Association for Cardiovascular Prevention & Rehabilitation. Eur Heart J. 2011; 32: 1769-1818.

7 Hoefer IE, Steffens S, Ala-Korpela M, et al.; ESC Working Group Atherosclerosis and Vascular Biology. Novel methodologies for biomarker discovery in atherosclerosis. Eur Heart J. 2015; 36: 2635-2642.

8 Zuliani G, Cavalieri M, Galvani M, et al. Relationship between low levels of high-density lipoprotein cholesterol and dementia in the elderly. The InChianti Study. J Gerontol A Biol Sci Med Sci. 2010; 65: 559-564.

9 Doonan RJ, Hafiane A, Lai C, et al. Cholesterol efflux capacity, carotid atherosclerosis, and cerebrovascular symptomatology. Arterioscler Thromb Vasc Biol. 2014; 34: 921-926.

10 Neves AL, L Couto. Cardiovascular risk in overweight/obese and lean hypertensive patients. Rev Port Cardiol. 2014; 3: 223-228.

11 Lin GM, Li YH, Lin CL, et al. Low high-density lipoprotein cholesterol and low/normal body mass index are associated with increased mortality in coronary artery disease patients in Taiwan. Circ J. 2013; 77: 2079-2087.

12 Dias IH, Polidori MC, Li L, et al. Plasma levels of HDL and carotenoids are lower in dementia patients with vascular comorbidities. J Alzheimers Dis. 2014; 40: 399-408.

13 Meurs I, Van Eck M, Van Berkel TJ. High-density lipoprotein: key molecule in cholesterol efflux and the prevention of atherosclerosis. Curr Pharm Des. 2010; 16: 1445-1467.

14 Singh U, Jialal I. Oxidative stress and atherosclerosis. Pathophysiology. 2006; 13: 129-142.

15 Rodrigo R, Libuy M, Feliu F, Hasson D. Oxidative stress-related biomarkers in essential hypertension and ischemia-reperfusion myocardial damage. Dis Markers. 2013; 35: 773-790.

16 Konior A, Schramm A, Czesnikiewicz-Guzik M, Guzik TJ. NADPH oxidases in vascular pathology. Antioxid Redox Signal. 2014; 20: 2794-2814.

17 Tzu-Ching Y, Yi-Jie C, Shwu-Fen C, et al. Malondialdehyde mediates oxidized LDL-induced coronary toxicity through the Akt-FGF2 pathway via DNA methylation. J Biomed Sci. 2014; 3: 11.

18 Huber B. Implementing the Madrid Plan of Action on Ageing. Generational Issues and Integration Section Division for Social Policy and Development United Nations Department of Economic and Social Affairs. Mexico City, Mexico; 2005 (ESA/P/WP.201).

19 World Health Organization, Prevention of diabetes mellitus. Tech. Rep. 844. World Health Organization, Geneva, Switzerland, 1994.

20 O'Brien E, Asmar R, Beilin L, et al. Practice guidelines of the European Society of Hypertension for clinic, ambulatory and self blood pressure measurement. J Hypertens. 2005; 23: 697-701.

21 Ohkawa H, Ohishi N, Yagi K. Assay for lipid peroxides in animal tissues by thiobarbituric acid reaction. Anal Biochem. 1979; 95: 351-358.

22 Kapur NK, Ashen D, Blumenthal RS. High density lipoprotein cholesterol: an evolving target of therapy in the management of cardiovascular disease. Vasc Health Risk Manag. 2008; 4: 39-57.

23 Mostowik M, Palka I, Gajos G, et al. Mitral and aortic annular calcifications and cerebrovascular ischemic episodes in patients with coronary artery disease. Pol Arch Med Wewn. 2014; 124: 373-379.

24 Gajos G, Zalewski J, Mostowik M, et al. Polyunsaturated omega-3 fatty acids reduce lipoprotein-associated phospholipase A(2) in patients with stable angina. Nutr Metab Cardiovasc Dis. 2014; 24: 434-439.

25 Adameova A, Xu YJ, Duhamel TA, et al. Anti-atherosclerotic molecules targeting oxidative stress and inflammation. Curr Pharm Des. 2009; 15: 3094-3107.

26 Shimabukuro M, Higa N, Takasu N. Comparison of the antioxidant and vascular effects of gliclazide and glibenclamide in type 2 diabetic patients: a randomized crossover study. J Diabetes Complications. 2006; 20: 179-183.

27 Kotur-Stevuljevic J, Memon L, Stefanovic A, et al. Correlation of oxidative stress parameters and inflammatory markers in coronary artery disease patients. Clin Biochem. 2007; 40: 181-187.

28 Kumawat M, Sarama TK, Singh I, et al. Decrease in antioxidant status of plasma and erytrocytes from geriatric population. Disease Markers. 2012; 33: 303-308.

29 Gupta S, Sodhi S, Mahajan V. Correlation of antioxidants with lipid peroxidation and lipid profile in patients suffering from coronary artery disease. Expert Opin Ther Targets. 2009; 13: 889-894.

30 Dzięgielewska-Gęsiak S, Wysocka E, Michalak S, et al. Role of lipid peroxidation products, plasma total antioxidant status, and Cu-, Zn--superoxide dismutase activity as biomarkers of oxidative stress in elderly prediabetics. Oxid Med Cell Longev. 2014: 987 303.

31 Gómez-Marcos MA, Blázquez-Medela AM, Gamella-Pozuelo L, et al. Serum superoxide dismutase is associated with vascular structure and function in hypertensive and diabetic patients. Oxid Med and Cell Longev. 2016; 2016: 9 124 676.

32 Grygiel-Górniak B, Marcinkowska J, Szczepanik A, Przysławski J. Nutritional habits and oxidative stress in postmenopausal age. Pol Arch Med Wewn. 2014; 124: 298-305.

ARTYKUŁ ORYGINALNY

Wpływ lipoprotein o wysokiej gęstości na równowagę oksydacyjno-antyoksydacyjną u zdrowych osób w podeszłym wieku

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SŁOWA KLUCZOWE

cholesterol HDL, równowaga oksydacyjno-antyoksydacyjna, starzenie się

STRESZCZENIE

WPROWADZENIE Obserwuje się odwrotną zależność między stężeniem cholesterolu frakcji lipoprotein o wysokiej gęstości (*high-density lipoprotein cholesterol* – HDL-C) a ryzykiem miażdżycy.

CELE Celem badania była ocena równowagi oksydacyjno-antyoksydacyjnej u osób w podeszłym wieku w zależności od stężenia HDL-C.

PACJENCI I METODY Przebadano 541 osób w wieku ≥60 lat, z czego u 90 osób bez ostrych i przewlekłych chorób zmierzono obwód pasa, wskaźnik masy ciała, procentową zawartość tkanki tłuszczowej oraz ciśnienie tętnicze. W 0. i 120. minucie doustnego testu tolerancji glukozy oznaczono glikemię, po czym wykluczono 15 osób z cukrzycą typu 2. Na czczo oceniono profil lipidowy, całkowity stan antyoksydacyjny i stężenie substancji reagujących z kwasem tiobarbiturowym (*thiobarbituric acid-reacting substances* – TBARS) w osoczu oraz aktywność dysmutazy ponadtlenkowej w erytrocytach (*superoxide dysmutase 1* – SOD-1). Ze względu na stężenie HDL-C badanych podzielono na grupy: o wysokim stężeniu HDL-C (≥40,0 mg/dl u mężczyzn i ≥50,0 mg/dl u kobiet; n = 50) i o niskim stężeniu HDL-C (<40,0 md/dl u mężczyzn i <50,0 mg/dl u kobiet; n = 25).

WYNIKI Grupy nie różniły się pod względem wieku, ciśnienia tętniczego, wskaźnika masy ciała, procentowej zawartości tkanki tłuszczowej i stężenia glukozy. Osoby w grupie o wysokim stężeniu HDL-C miały niższy obwód pasa (p <0,02) i stężenie triglicerydów (p <000001). Zwiększone stężenie TBARS (p <0,0005) obserwowano w grupie z niskim stężeniem HDL-C. Między grupami nie stwierdzono różnic pod względem całkowitego stanu antyoksydacyjnego i aktywności SOD-1.

WNIOSKI Stężenie HDL-C, uznawane za wykładnik przeciwmiażdżycowego potencjału HDL, w tym właściwości antyoksydacyjnych, może odzwierciedlać narastający stres oksydacyjny u zdrowych osób w podeszłym wieku.

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Praca wpłynęła: 19.07.2016.
Przyjęta do druku: 20.09.2016.
Publikacja *online*: 20.09.2016.
Nie zgłoszono sprzeczności interesów.
Pol Arch Med Wewn. 2016; 126 (10): 731-738
doi:10.20452/pamw.3559