ApoB/ApoA-I ratio in young patients with ischemic cerebral stroke or peripheral arterial disease

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Although smoking and hypertension are classic risk factors for atherothrombotic diseases, the relationship of dyslipidemia and vascular diseases, other than myocardial infarction, is less clearly established, especially in young subjects. In the current study, a detailed analysis of the lipid and apolipoprotein profiles was conducted in young patients of ischemic cerebral stroke (IS) and peripheral arterial disease (PAD). Plasma levels of C-reactive protein (hs-CRP), total cholesterol (TC), high-density lipoprotein cholesterol (HDLc), low-density lipoprotein cholesterol (LDLc), triglycerides (TG), and apolipoproteins A-I (ApoA-I) and apolipoproteins B (ApoB), which include the ApoB/ApoA-I ratio, were analyzed in a group of 81 patients who presented with IS (n = 46) or PAD (n = 35) as well as in 167 control subjects. Significant differences were observed for hs-CRP, TC, HDLc, LDLc, TG, ApoA-I, and ApoB levels, as well as for the ApoB/ApoA-I ratio, between the control and the IS or PAD groups. However, after adjustment for sex, age, smoking, hypertension, hs-CRP, and dyslipidemia (LDLc, TC, HDLc, TG, ApoA, ApoB, and ApoB/ApoA-I ratio), hs-CRP, ApoB, and the ApoB/ApoA-I ratio were independently associated with increased risks of IS or PAD. Increased ApoB/ApoA-I ratio and hs-CRP levels are independently associated with occurrence of IS and PAD in young patients and are significant markers of alterations on lipid and apolipoproteic profiles and inflammatory responses, respectively, in these patients. (Translational Research 2008;152:113–118)

Abbreviations: ApoA-I = apolipoprotein A-I; ApoB = apolipoprotein B; BMI = body mass index; CI = confidence interval; CRP = C-reactive protein; HDL = high-density lipoprotein; FVL = Factor V Leiden; IHD = ischemic heart disease; IS = ischemic stroke; LDL = low-density lipoprotein; MI = myocardial infarction; OR = odds ratio; PAD = peripheral artery disease; TC = total cholesterol; TG = triglyceride

Ischemic heart disease (IHD), peripheral artery disease (PAD), and ischemic stroke (IS) are multicausal diseases, resulting from the interaction of both acquired and genetic risk factors, although the underlying etiology of atherothrombotic events cannot be determined in over 40% of patients. The vast literature on this issue suggests that the role of both acquired and genetic factors on the clinical outcome of arterial thrombosis may differ significantly according to age and other demographic variants in different populations.[1–6]

Although smoking and hypertension are considered classic risk factors for atherothrombotic disease, the relationship of dyslipidemia and vascular diseases, other than myocardial infarction (MI), is less clearly established. It is widely accepted that low-density lipoprotein (LDL) cholesterol is linked to enhanced risk of IHD, but its relationship with IS or PAD is still controversial.[6] Recent evidence indicates that the lipid associated proteins, especially the apolipoproteins A-I and B, are more effective predictors of IHD than the

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Supported by CNPq, FAPEMIG, and CAPES.

Submitted for publication March 26, 2008; revision submitted June 4, 2008; accepted for publication June 25, 2008.

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1931-5244/$ – see front matter

doi:10.1016/j.trsl.2008.06.005

AT A GLANCE COMMENTARY

Background

Manifestations of atherosclerosis are rare conditions in young patients. Although well established for coronary arterial disease, much controversy still surrounds the role of markers of conventional lipid profile as risk factors for ischemic cerebral stroke (IS) or peripheral arterial disease (PAD) in young patients.

Translational Significance

This manuscript reports on the significant alterations of the ApoB/ApoA-I ratio as well as of the conventional lipid profile in Brazilian young subjects, which developed IS or PAD. ApoB/ApoA-I ratio was independently associated with risk of IS and PAD. Thus, we believe that this manuscript constitutes a relevant contribution to the field.

concentrations of LDL cholesterol and other lipid fractions.[7–9] A direct relationship has been demonstrated among increased values of the apolipoprotein B (ApoB)/apolipoprotein A-I (ApoA-I) ratio, which indicates the balance between atherogenic and antiatherosclerotic particles and increased risk for IHD.[7–9] It is worth noting that the laboratorial determination of apolipoproteins has many advantages and may become a more feasible marker to estimate the risk of vascular disease.[9–12] Recent studies suggested that this association may be extended to other arterial disease and that the ApoB/ApoA-I ratio is a specific marker of all arterial ischemic events.[10,11] However, the assessment of distinctions in these markers and predictors of atherosclerosis by age has not received the necessary attention in the literature, especially with regard to young subjects. Thus, in the current study, a detailed analysis of the lipid and apolipoprotein profile were conducted in a group of young Brazilian survival patients of IS and PAD, in an attempt to identify additional insights into the underlying atherothrombotic disease process in these patients.

MATERIAL AND METHODS

Patients and control subjects. The Institutional Ethics Committee of the Federal University of Minas Gerais, Brazil, approved this study (ETIC 070/04), and a written informed consent was obtained from all participants. Patients (n = 81) who presented IS or PAD as a first thrombotic event and who did not present cardiopathic alterations in eco-transtoracic evaluations, as detected by duplex scan, were selected by physicians at the outpatient Hematology Unit of the University Hospital (Federal University of Minas Gerais, Belo Horizonte, MG, Brazil) to participate in this study. All selected participants underwent magnetic resonance, computer tomography, and arteriography to confirm the diagnosis of arterial thrombosis. Patients with a history of venous thrombosis or pulmonary embolism, as first thrombotic events, were not included, as well as those with coronary arterial disease, as defined by the history of a previous event or by the presence of stenosis in coronary angiography analysis. The presence of stenosis was confirmed by coronary angiography according to defined standard stenosis, that is, until 30%, slight atheromatosis; 30% to 69%, mild atheromatosis; and above 70%, serious atheromatosis. In addition, subjects under 8 years or older than 60 years, with nocturne paroxistic hemoglobinury, cancer, or hepatic, infectious, autoimmune, and mieloproliferative diseases, as well as those with coagulation disorders other than IS and PAD, who had been exposed to prolonged immobilization or who were recently submitted to surgery, were also excluded.

Baseline information on smoking habits, medication use, and personal history of diseases were gathered by trained medical staff during a standardized interview. In addition, all participants underwent an extensive standardized medical examination. Body mass index (BMI) was calculated as weight in kilograms divided by height in square meters. Systolic and diastolic blood pressure was measured on the right arm in a sitting position. Participants who were aware of having hypertension, who take antihypertensive medication, and/or who registered a blood pressure of 160/90 mm Hg at the baseline were defined as currently having hypertension. Individuals were classified as having diabetes mellitus if plasma glucose was equal or superior to 126 mg/dL in the fasting state, or if individuals were receiving oral antidiabetics or insulin. A regular smoker was defined as a subject who currently smokes at least 1 cigarette per day. All participants presented triglyceride (TG) levels below 400 mg/dL. None of them were using statins, but among patients, 23 (11 men and 12 women) were taking aspirin regularly, whereas 6 patients (3 men and 3 women) were undergoing Marevan therapy. The presence of the factor V Leiden and the G20210A and C677T mutations in the prothrombin and methylenetetrahydrofolate reductase genes, respectively, were also obtained from patients' medical records and were determined as previously described by Sabino et al.[13]

Patients were later distributed into 2 groups according to the anatomical site of the atherothrombotic event, which composed the IS (n = 46, 19 men and 27 women) and the PAD (n = 35, 14 men and 21 women) groups. The control group was composed of 167 (40 men and 127 women) nonrelated subjects who were paired by age, from the same geographical region of patients, and had no history of arterial or venous thrombosis.

Sample collection. Venous blood samples were obtained from each participant after a fasting period of 12–14 h. Participants were advised not to practice vigorous physical activity and to avoid ethanol ingestion during 24 and 72 h, respectively, preceding blood collection. All blood samples were collected after 3 months of the onset of IS and PAD. The sample collection was carried out using Vacuette tubes (Gei-