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Lipid accumulation product index in HIV-infected patients: a marker of cardiovascular risk

Q1 *Milena Maria Moreira Guimarães, Dirceu Bartolomeu Greco, Allyson Nogueira Moreira, Nathalia Sernizon Guimarães*, Cláudia Maria Vilas Freire, Bruna Guimarães Rolfs, Lucas José de Campos Machado*

Universidade Federal de Minas Gerais, Belo Horizonte, MG, Brazil

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ABSTRACT

The lipid accumulation product (LAP) index is an emerging cardiovascular risk marker. We aimed to assess the accuracy of this index as a marker of cardiovascular risk in HIV-infected patients. A cross-sectional study of 133 HIV-infected patients on antiretroviral drugs and 20 non-infected controls was conducted at the outpatient clinic of a referral center of infectious and parasitic diseases. Evaluations included LAP index, homeostasis model assessment (HOMA) index, anthropometric measurements, blood pressure, glucose tolerance test, and cholesterol and triglyceride levels. Body mass index (BMI) was similar in both groups; however, waist circumference was greater in the HIV-infected patients. Triglyceride levels were significantly higher ($p < 0.001$) and HDL cholesterol levels were lower in HIV-infected patients ($p < 0.001$). Plasma glucose ($p = 0.01$) and insulin ($p = 0.005$) levels two hours after a glucose load, HOMA-IR index ($p < 0.001$) and LAP index ($p < 0.001$) were higher in the HIV-infected patients. A positive and significant correlation was found between HOMA-IR index and LAP ($r = 0.615$; $p < 0.01$), BMI ($r = 0.334$; $p < 0.01$) and waist circumference ($r = 0.452$; $p < 0.01$) in the HIV-infected patients. In male HIV-infected patients and controls, ROC curve analyses revealed that the best cut-off value of LAP to define the presence of insulin resistance was 64.8 (sensitivity 86%, specificity 77% and area under the curve 0.824). These results confirm that insulin resistance is more common in HIV-patients on antiretroviral drugs than in HIV-negative controls. A positive and significant correlation was found between the LAP index and the HOMA index, with LAP $\geq$ 64.8 constituting an additional risk factor for cardiovascular disease in male HIV patients.

* *Corresponding author.*
E-mail address: nasernizon@hotmail.com (N.S. Guimarães).

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Introduction

The introduction of highly-active antiretroviral therapy (HAART) has significantly improved the clinical outcome of individuals with the human immunodeficiency virus (HIV), resulting in increased survival rates[1–3]; however, the success of antiretroviral therapy is tempered by long-term side effects that include dyslipidemia, insulin resistance, overt type 2 *diabetes mellitus*, and changes in fat distribution (peripheral lipoatrophy and visceral adiposity).[4–6]

The pattern of these metabolic abnormalities in patients receiving antiretroviral therapy resembles that of the metabolic syndrome, which is known to increase the risk of cardiovascular disease. However, whether and how soon these antiretroviral therapy-induced abnormalities may result in a clinically detectable increased risk of cardiovascular disease remains unknown, as does the impact of the underlying HIV infection *per se*. Indeed, while results from long-term observational studies on the risk of cardiovascular disease in HIV-infected patients remain unavailable in the literature, calculating the predicted risk of cardiovascular disease may prove useful for the clinical management of these patients.

Insulin resistance is an independent risk factor for cardiovascular disease and the early recognition of insulin resistance in these patients is important for the prevention of cardiovascular involvement.

Euglycemic-hyperinsulinemic clamping is currently the gold standard for measuring insulin resistance. However, it is unsuitable for clinical practice, since it is complex, expensive and unfeasible for large populations.[7] Taking into consideration the technical limitations of clamping and alternative methods (those that rely on the measurement of insulin itself) for identifying insulin resistance, some investigators have speculated that insulin resistance and, therefore, cardiovascular risk could be determined based on variables associated with the effects of insulin instead of measuring insulin directly.[8,9]

The lipid accumulation product (LAP) index, which is based on a combination of waist circumference and fasting triglyceride levels, could be useful in this situation. LAP is determined by the following equation for women: (circumference of waist [cm] – 58) × (triglycerides [mmol/L]); for men: [waist (cm) – 65] multiplied by triglyceride level (mmol/L). Results are expressed in cm mmol/L.[10] Kahn[10] was the first to describe LAP, reporting in the National Health and Nutrition Examination Survey (NHANES III) that LAP was a better indicator of cardiovascular risk in adults than body mass index (BMI).

Therefore, the aim of this study was to determine the accuracy of the LAP index as a marker of cardiovascular risk in HIV-infected patients and non-infected controls.

Patients and methods

Design and patients

This cross-sectional study was conducted at the outpatient clinic of a referral and training Center in Infectious and Parasitic Diseases in Brazil. The sample was selected for convenience. Sample size calculation of the case group assumed: (a) number of patients infected by HIV in 2013, age group 19–40 years, Belo Horizonte ($n = 157$)[11]; (b) prevalence of lipodystrophy (84%)[12]; (c) variation of 5%; (d) confidence level equal to 95%. The minimum sample size was 90 individuals.

The case group comprised 133 HIV-infected patients aged between 18 and 55 years, who had been receiving antiretroviral (ARV) drugs for a minimum of three months prior to admission, regardless of the time of infection diagnosis. The control group consisted of 20 HIV-negative controls.

Exclusion criteria consisted of metabolic disorders such as hyperlipidemia, diabetes mellitus and lipodystrophy prior to the diagnosis of HIV-infection; use of glucocorticoids or any other steroids, growth hormones, beta-blockers, thiazides or any drugs associated with metabolic abnormalities and body fat redistribution. Other criteria included any relevant clinical event at the time of enrollment to the study; refusal to participate; pregnancy or breastfeeding; and alcohol abuse.

The study was approved by the COEP and conducted according to the norms of the code of ethics for human research, National Health Council, Resolution n° 466/2012 and all participants gave their written informed consent.

Study protocol

Anthropometric data were measured according to the procedures standardized by the World Health Organization.[13] To measure height, the stadiometer of the anthropometric scale of the brand "Filizzola®" was used. Body weight was determined on an anthropometric scale of the Tanita brand with a capacity of 150 kg. Waist circumference was defined as the smallest measurement at the midpoint between the lateral iliac crest and the lowest rib.[14] BMI (weight in kg divided by height in meters squared) was calculated.

The skin folds were measured with the aid of a plicometer (Lange® caliper, Santa Cruz, CA, USA) with an accuracy of 0.1 mm. Bicipital (DCB) and triceps skinfolds were measured in the anterior and posterior region. The subscapular skinfold (DCSE) was measured obliquely in relation to the longitudinal axis, following the orientation of the costal arcs, being located two centimeters below the angle. The supra-iliac cutaneous fold was obtained obliquely in relation to the longitudinal axis, in the mid point between the last costal arch and the iliac crest, on the median axillary line.[15]

Blood pressure was measured in the right arm, at the level of the heart, using a Welch Allyn Tycos® sphygmomanometer, model 705014 (New York, NY, USA). Values above 140 × 90 mmHg were considered high.

The subjects were asked about the practice, type, duration and frequency of physical activity (FA) being classified as very active (FA >5 days/week and ≥30 min/session), active (FA 3 or 4 days/week and ≥20 min/session), not very active (those individuals who perform physical activity, but insufficient to be classified as active because it does not comply with the recommendations regarding frequency or duration), and sedentary (those who do not perform any physical activity).[16]

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