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Research Article

Use of the plasma triglyceride/high-density lipoprotein cholesterol ratio to identify cardiovascular disease in hypertensive subjects

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Abstract

This analysis evaluated the hypothesis that the plasma triglyceride (TG)/high–density lipoprotein cholesterol (HDL-C) concentration ratio can help identify patients with essential hypertension who are insulin–resistant, with the cardiovascular disease (CVD) risk profile associated with that defect. Data from a community–based study developed between 2003 and 2012 were used to compare CVD risk factors and outcome. Plasma TG/HDL-C cut–points of 2.5 (women) and 3.5 (men) subdivided normotensive (n = 574) and hypertensive (n = 373) subjects into ''high'' and ''low'' risk groups. Metabolic syndrome criteria (MetS) were also used to identify ''high'' and ''low'' risk groups. The baseline cardio–metabolic profile was significantly more adverse in 2003 in ''high'' risk subgroups, irrespective of BP classification or definition of risk (TG/HDL-C ratio vs. MetS criteria). Crude incidence of combined CVD events increased across risk groups, ranging from 1.9 in normotensive–low TG/HDL-C subjects to 19.9 in hypertensive–high TG/HDL-C ratio individuals (*P* for trends <.001). Adjusted hazard ratios for CVD events also increased with both hypertension and TG/HDL-C. Comparable findings were seen when CVD outcome was predicted by MetS criteria. The TG/HDL-C concentration ratio and the MetS criteria identify to a comparable degree hypertensive subjects who are at greatest cardio–metabolic risk and develop significantly more CVD. J Am Soc Hypertens 2014;8(10):724–731.

Keywords: Cardiovascular outcome; hypertension; metabolic syndrome; TG/HDL-C ratio.

It has been estimated that approximately 50% of patients with essential hypertension are resistant to insulin–mediated glucose disposal, and the cardio–metabolic risk factors associated with insulin resistance and cardiovascular disease (CVD) are significantly accentuated in these individuals.[1] In addition, electrocardiographic evidence of ischemic heart disease in asymptomatic patients with essential hypertension occurs to a significantly greater degree in those who are also insulin resistant.[2] Although these observations suggest that it is the insulin–resistant/hyperinsulinemic subset of patients with essential hypertension who are at greatest risk to develop CVD, we are unaware of any prospective studies that have shown this. Furthermore, even if this were the case, there is no clinically simple way to identify the subset of patients with essential hypertension who are insulin–resistant before manifest CVD appears. Direct measures of insulin resistance are not practical at a clinical level, and measurements of plasma insulin concentration,

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perhaps the best surrogate estimate of insulin resistance, suffer from the lack of a standardized assay.[3] Thus, it is not possible to identify a cut–point value of insulin concentration to identify individuals at ''high'' cardio–metabolic risk that is independent of the laboratory in which the measurements were being made. A diagnosis of the metabolic syndrome (MetS) provides another approach to identify individuals who are insulin resistant, with the metabolic abnormalities associated with this defect in insulin action.[4,5] We have recently evaluated the simpler approach of using the plasma concentration ratio of triglyceride (TG)/high–density lipoprotein cholesterol (HDL-C) to accomplish the same task, and results of these efforts suggested that the TG/HDL-C ratio identified individuals at increased CVD risk and incident disease comparably with that achieved with a diagnosis of the MetS.[6,7] This analysis was initiated to extend these observations, with the goal of comparing both CVD risk factor profile and outcome in normotensive and hypertensive subjects, further subdivided into ''high–'' risk and ''low–'' risk subgroups based up either their TG/HDL-C ratio or the MetS diagnostic criteria.

Methods

Study Population

A prospective epidemiologic study, focused on hypertension, renal disease, and other cardio–metabolic risk factors, was conducted between October 2003 and February 2012 in Rauch City (Rauch Project, phase 2).[8,9] This city lies in the center-southeast region of the province of Buenos Aires, 270 km from Buenos Aires (36°45′00″ south latitude and 59°04′00″ west longitude).The annual average temperature is 13.8°C. According to the National Census available at the time of the survey, there were 13,909 inhabitants in the urban area of Rauch City, 8246 of them older than 15 years of age, (4166 men and 4080 women). This region has had a strong influx of immigrants throughout the 19th and 20th centuries, so the vast majority of subjects were of European ancestry, primarily from Italy or Spain. Individuals of African and Asian ethnicity are a small minority of the population. There is undoubtedly some genetic admixture between subjects of European ancestry and Amerindian. Although there are no quantitative data concerning the genetic admixture in Rauch, we can nevertheless assume that it should be similar to that observed in the city of Buenos Aires. In a study performed in Buenos Aires in the year 2006, using eight erythrocyte genetic systems and GM/KM allotypes, the contributions to the genetic admixture were European 79.9%, Amerindian 15.8%, and African 4.3%.[10]

The program was approved by the relevant health authorities, and all the participants gave a written informed consent. In 2003, surveys were performed, and random samples were taken from subjects between 15 and 80 years old who lived in chosen blocks (n = 1308; 855 women 51 ± 17 years old and 453 men 52 ± 16 years old; *P* between gender = .628). The sample had a high prevalence of hypertension (43.20% in men and 28.50% in women) and obesity–overweight status (54.81% in men and 44.65% in women). Average alcohol intake was 163.02 ± 10.24 g per week and 25.32 ± 2.42 g per week for men and women, respectively. A subset of 1.2% of the population was illiterate, while the percentages with a level of education of incomplete primary, complete primary, incomplete secondary, complete secondary, tertiary or incomplete university, and complete university level were 16.5%, 37.4%, 17.5%, 9.4%, 5.2%, and 12.7%, respectively.[8] The methodology used to obtain measurements of clinical and biochemical variables have been previously published.[8,9] In brief, blood pressure (BP) was measured sitting, after a minimum resting period of 5 minutes, using a mercury sphygmomanometer. Phase I and V Korotkoff sounds were used to identify systolic BP (SBP) and diastolic BP (DBP) respectively; SBP and DBP values were an average of three different measurements separated by 2 minutes from one another. Weight was determined with individuals wearing light clothes and no shoes. Height was also measured without shoes, using a metallic metric tape; waist circumference (WC) was measured with a relaxed abdomen using a metallic metric tape on a horizontal plane above the iliac crest; body mass index (BMI) was calculated using the formula weight (kg)/height^2 (m^2).

Fasting plasma glucose, TG, HDL-C, and insulin (FPI) concentrations were determined after an overnight (12-hour) fast. Low-density lipoprotein cholesterol levels (LDL-C) were estimated by the Friedewald formula.[11] All of these measurements were performed in the Clinical Laboratory of Rauch Hospital. FPI concentrations were determined using an immunoradiometric assay, with two monoclonal antibodies against two different epitopes of the insulin molecule. The inter– and intra–assay coefficients of variation were 8.0% and 3.8%, respectively, being the lowest detectable level of 1.4 pmol/L. FPI concentrations provide a surrogate estimate of insulin resistance, highly correlated (r = 0.98) with the homeostasis model assessment of insulin resistance (HOMA-IR).[12]

Hypertension was defined as SBP ≥140 mm Hg, and/or DBP ≥90 mm Hg (mean of three readings in one occasion), and/or undergoing antihypertensive treatment. Previously published cut–points of plasma TG/HDL-C concentration ratios (expressed both in mg/dL) of 2.5 (women) and 3.5 (men) were used to classify both normotensive and hypertensive individuals as having either a ''high'' or ''low'' TG/HDL-C ratio.[6,7] Fifty-four subjects who had previously suffered CVD events were excluded. Measurements of SBP, DBP, TG, and HDL-C, and knowledge of anti-hypertensive drug use were available in 927 individuals, 623 women and 304 men, of similar age (mean age, 52 ± 16 years). These individuals were divided into four risk groups: (1) normotensive–low TG/HDL-C ratio; (2) normotensive–high TG/HDL-C ratio; (3) hypertensive–low TG/HDL-C ratio; and (4) hypertensive–high TG/HDL-C ratio.