Triglyceride-to-HDL Cholesterol Ratio in the Dyslipidemic Classification of Type 2 Diabetes

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Although LDL cholesterol is the main target in the treatment of diabetic dyslipidemia, it does not fully account for the cardiovascular risk associated with diabetes, neither alone nor in combination with triglycerides and HDL cholesterol. On the other hand, diabetic dyslipidemia also includes an overall increase in atherogenic particles identifiable by measuring apolipoprotein B (apoB), and a predominance of small, dense LDL particles (phenotype B). The latter, although associated with increased cardiovascular risk, is not routinely assessed because its measurement is not available to most clinical laboratories. Therefore, easily measurable predictors of LDL size, such as triglycerides or LDL cholesterol/apoB and triglyceride–to–HDL cholesterol ratios, have been proposed, with the latter being suggested as the best surrogate (1,2,3). However, no study has been conducted that compares all of these predictors.

The aim of the present study is to evaluate the triglyceride–to–HDL cholesterol ratio, non-HDL cholesterol, and apoB to predict LDL phenotype and to assess them in the risk classification of patients with type 2 diabetes.

RESEARCH DESIGN AND METHODS — A total of 107 type 2 diabetic patients (68% male, age 59 ± 10 years [means ± SD], time since diagnosis 8.5 years [range 0–37], HbA1c 7.35%) [3.7–16]) were consecutively included in the study. None of the patients were taking drugs or were in situations (not related to diabetes) known to affect lipoprotein metabolism.

Total cholesterol and triglycerides were measured by enzymatic methods and HDL cholesterol by a direct method (Roche Diagnostics, Basel, Switzerland). Hypertriglyceridemia was defined by triglycerides > 2.25 mmol/l (4). LDL cholesterol was obtained by Friedewald’s formula (if triglycerides < 3.39 mmol/l) or by ultracentrifugation. Non-HDL cholesterol was calculated by subtracting HDL cholesterol from total cholesterol. High non-HDL cholesterol was defined by the equivalent to an LDL cholesterol > 3.36 mmol/l, when pharmacological intervention is recommended, i.e., non-HDL cholesterol > 4.13 mmol/l (4). The triglyceride–to–HDL cholesterol ratio was expressed in mmol/l over mmol/l. Previously described cutoff points were used (1,2,6), as well as that calculated from the regression equation obtained from the samples included in the present study: triglyceride–to–HDL cholesterol ratio = 42.122 − 1.576 × LDL size (R = 0.625) for an LDL size of 25.5 nm. ApoB was measured by an immunoturbidimetric method (Tina-quant, Roche Diagnostics) calibrated against the World Health Organization/International Federation of Clinical Chemistry reference standard SP3–07. Its cutoff point (0.97 g/l) was defined as the equivalent to an LDL cholesterol of 3.36 mmol/l (7) in a previously described nondiabetic normolipidemic control group (8). LDL size was determined by polycrylamide gradient (2–16%) gel electrophoresis (3), and LDL phenotype B was defined by a predominant LDL diameter < 25.5 nm.

Patients were classified according to their triglyceride and apoB concentrations as well as according to their triglycerides, triglyceride–to–HDL cholesterol ratio, and their non-HDL cholesterol.

Statistical analysis was performed using the SPSS 10.0 statistical package for Windows (SPSS, Chicago, IL). Results are expressed as means ± SD (Gaussian distribution), median and ranges (non-Gaussian distribution), or as percentages. Nonparametric, bivariate correlations (Spearman) were performed between LDL size and other parameters. Concordance between the dyslipidemic phenotypic classifications was assessed using the kappa index (κ). Values between 0.21 and 0.40, 0.41 and 0.60, 0.61 and 0.80, and 0.81 and 1.0 showed fair, moderate, good, and very good concordance, respectively (9).

RESULTS — The patients showed the following lipoprotein concentrations (in mmol/l unless otherwise indicated): triglycerides 1.38 (0.56–9.25), LDL cholesterol 3.58 (0.94), HDL cholesterol 1.20 (0.29), non-HDL cholesterol 4.42 (1.18), apoB 1.16 (0.25) g/l, and LDL size 25.8 (24.4–27.0) nm. When comparing patients with phenotypes A and B, the former showed lower triglyceride–to–HDL cholesterol ratios (0.88 [0.30–3.17] vs. 2.33 [0.53], P < 0.0005). LDL size showed a direct correlation with HDL cholesterol (R = 0.439) and LDL cholesterol/apoB (R = 0.583) and an inverse correlation with triglycerides (R = −0.626) and the triglyceride–to–HDL cholesterol ratio (R = −0.643, P < 0.0005 for all). No correlation was found with non-HDL cholesterol or apoB. When patients were classified according to previ-
ously proposed cutoff points for triglycerides–to–HDL cholesterol, the concordance with their classification into LDL phenotypes A and B was fair (κ = 0.390 for a cutoff point of 0.9) to moderate (κ = 0.478 for a cutoff point of 1.33 and κ = 0.545 for a cutoff point of 1.64). When using the regression equation triglycerides/HDL cholesterol = 42.122 + 1.576 × LDL size (R = 0.625), for an LDL size of 25.5 nm, a triglyceride/HDL cholesterol cutoff point of 1.93 was obtained. When this cutoff point was used, the concordance of the patients' classification with LDL phenotype was also moderate, though slightly better than with the other cutoff points (κ = 0.554). It showed a sensitivity of 60% and a specificity of 92% to predict LDL phenotype B. We used 1.93 as the cutoff point to classify the patients (normal-high triglyceride–to–HDL cholesterol ratio) and compare their distribution with when the classification was performed using apoB and triglycerides (Fig. 1). Using these cutoff points, the concordance between hyperapoB and the hypertriglyceride–to–HDL cholesterol ratio was poor (κ = 0.175), whereas the concordance between hyperapoB and hyper–non-HDL cholesterol was moderate (κ = 0.522). Results were similar when cutoff points equivalent to LDL cholesterol of 2.59 mmol/l were used for non-HDL cholesterol and apoB, as well as when men and women were analyzed separately (data not shown).

**CONCLUSIONS** — The present study shows that the triglyceride–to–HDL cholesterol ratio is not superior to non-HDL cholesterol in classifying patients with type 2 diabetes into dyslipidemic phenotypes (14). This is also true for the triglyceride–to–HDL cholesterol ratio. In normotriglyceridemic subjects, however, non-HDL cholesterol identifies around half of the individuals with hyperapoB (14), whereas the triglyceride–to–HDL cholesterol ratio identifies <10% (Fig. 1). Therefore, based on current and previous results and the cost-effectiveness of the different components, a strategy consisting of the estimation of non-HDL cholesterol (as a surrogate of apoB) in all of the subjects and the measurement of apoB itself in the normotriglyceridemic subjects with normal non-HDL cholesterol is proposed for dyslipidemic risk classification of patients with type 2 diabetes. The triglyceride–to–HDL cholesterol ratio does not add useful information to the previously mentioned strategy.

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**References**

2. Hanak V, Muñoz J, Teague J, Stanley A, Bittner V: Accuracy of the triglyceride to high-density lipoprotein cholesterol ratio for prediction of the low-density lipoprotein phenotype B. *Am J Cardiol* 94:219–222, 2004


