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Role of triglycerides to high-density lipoprotein cholesterol ratio in non-alcoholic fatty liver disease progression

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Dear Editor,

We red with great interest the study by Catanzaro et al. investigating the association between triglycerides to high-density lipoprotein (TG/HDL-C) ratio and non-alcoholic fatty liver disease (NAFLD).[1] In a cohort of 231 patients, the authors observed no differences in HDL-C values between patients with NAFLD (n = 131) and those without (n = 100) (p = 0.490). Conversely, the former had higher TG and TG/HDL-C compared to the latter (both p < 0.001); the TG/HDL-C ratio showed a moderate diagnostic accuracy (area under the curve [AUC] = 0.675, 95% confidence interval [CI] 0.604–0.746) for the discrimination between patients with and without NAFLD.[1]

In agreement with these findings, we previously observed that TG/HDL-C ratio was significantly higher in non-diabetic patients with NAFLD compared to healthy controls (2.7 ± 1.7 vs. 1.3 ± 0.3; p = 0.011).[2] However, in a validation cohort of 145 non-diabetic patients with biopsy-proven NAFLD (median age 43 years, 81% males, 77% body mass index [BMI] > 25), we did not observed any association between TG/HDL-C and the diagnosis of non-alcoholic steatohepatitis (NASH) (odds ratio [OR] =1.10, 95% CI 0.93–1.31; p=0.337), and the presence of significant liver fibrosis (F ≥ 2) (OR = 1.16, 95% CI 0.98–1.38; p = 0.101).[2]

Here, in a larger heterogeneous cohort of NAFLD patients (n = 195), we explored the association between the TG/HDL-C ratio with type 2 diabetes mellitus (T2DM), as well as with the histological features of NASH, to assess its usefulness in clinical practice for the patient’s risk stratification. For this purpose, we performed correlations analysis between the TG/HDL-C ratio and both clinical and biochemical parameters, whereas the Mann-Whitney test for non-parametric variables was used to assess differences between diabetic and non-diabetic patients.

Clinical, biochemical and histological characteristics of the study cohort are reported in Table 1. The median age of the study population was 47 years (range 20 - 74) and most of the patients were male, 69.7%. T2DM was diagnosed in 64 out of 195 patients (32.8%).

Overall, the TG/HDL-C ratio did not correlate with anthropometrical or clinical variables. Concerning histology, no significant correlation was found between the TG/HDL-C ratio and hepatic steatosis or liver fibrosis confirming our previous data on non-diabetic NAFLD subjects.[2] When we stratified the study cohort according to the presence of T2DM, we did not find any differences in the TG/HDL-C ratio values (non-diabetic, median = 2.58, 95% CI 2.22–3.10; diabetic, median = 2.70, 95% CI 2.31–3.65; $p = 0.3668$, Figure 1A). Conversely, we found a significant association between the TG/HDL-C ratio and the homeostasis model of assessment of insulin resistance (HOMA-IR), the most used surrogate index of insulin resistance ($t = 6.82$, 95% CI 2.36–4.29, $p < 0.0001$; Figure 1B).

NAFLD patients are characterized by the presence of insulin resistance, high levels of triglycerides and low levels of HDL-cholesterol showing an atherosclerotic risk profile. The TG/HDL-C ratio has been widely investigated as surrogate marker of insulin resistance in both young and adult populations where it is able to identify apparently healthy subjects at increased cardiometabolic risk.[3]

In the setting of NAFLD, the TG/HDL-C index correlates with the direct measure of insulin resistance in non-diabetic subjects.[2] Here, we confirm the association between the TG/HDL-C index with insulin resistance by HOMA-IR, but more studies are necessary to better understand the potential use of this surrogate marker in clinical practice.[4,5]

In conclusion, in a low-risk population of NAFLD subjects, the use of the TG/HDL-C ratio is not useful for the patient's risk stratification in terms of liver disease, independently by the presence of T2DM. Notwithstanding this, its potential role as surrogate marker of insulin resistance or cardiovascular disease should be better explored both in cross-sectional and longitudinal studies.

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Tables

Table I - Clinical, biochemical and histological characteristics of the study cohort.

Variables	**Total (n = 195)**
Age (years)	47 (39 - 57)
Male gender, n (%)	136 (69.7%)
Body mass index (kg/m^2)	28.1 (25.1 - 31.2)
Waist circumference (cm)	99 (90 - 106)
ALT (UI)	53 (35 - 76)
AST (UI)	32 (26 - 44)
Albumin (g/dL)	4.5 (4.1 - 4.7)
Platelet (x10^9)	218 (189 - 259)
Glucose (mg/dL)	93 (85 - 110)
Insulin (MU/L)	13.2 (8.6 - 23.1)
Triglycerides (mg/dL)	124 (90 - 185)
Total Cholesterol (mg/dL)	190 (166 - 218)
HDL-cholesterol (mg/dL)	47 (40 - 55)
TG/HDL ratio	2.65 (1.80 - 4.11)
Histological features	
Steatosis grade, n (%)	
1	106 (54.4%)
2	63 (32.3%)
3	26 (13.3%)
Fibrosis stage, n (%)	
0-1	104 (53.3%)
2	35 (18%)
3-4	56 (28.7%)
NASH, n (%)	131 (67.2%)

Data are reported as median (interquartile range) and frequency and percentage.

Abbreviations. ALT, alanine aminotransferase; AST, aspartate aminotransferase; HDL, high density lipoprotein-cholesterol; NASH, non-alcoholic steatohepatitis; TG, triglycerides.

Figures

Figure 1 - TG/HDL-C ratio values according to the presence of type 2 diabetes (A) and its correlation with HOMA-IR index (B) in NAFLD patients.