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The association between triglyceride to high-density-lipoprotein cholesterol ratio and insulin resistance in a multiethnic primary prevention cohort

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ABSTRACT

The objective was to explore the clinical utility of triglyceride (TG) to high-density lipoprotein cholesterol (HDL-C) ratio in predicting insulin resistance (IR) in 4 ethnic groups and the relationship between IR and TG/HDL-C in comparison to that with other lipid measures. Apparently healthy Aboriginals, Chinese, Europeans, and South Asians (N = 784) were assessed for sociodemographics, lifestyle, anthropometry, lipids, glucose, and insulin. The homeostasis model assessment of IR was used as a measure of IR. Compared with other lipid parameters, TG/HDL-C was the highest correlate of the homeostasis model assessment of IR (age and sex adjusted) in Aboriginals (r = 0.499, P < .001), Chinese (r = 0.432, P < .001), Europeans (r = 0.597, P < .001), and South Asians (0.372, P < .001). For a 1-unit increase in TG/HDL-C, the odds of being insulin resistant increased about 4 times (odds ratio [OR], 3.95; 95% confidence interval [CI], 1.86-8.42; P < .001) in Aboriginals, 3.4 times in Chinese (OR, 3.44; 95% CI, 1.79-6.62; P < .001), 1.9 times in Europeans (OR, 1.94; 95% CI, 1.00-3.75; P = .049), and 1.8 times in South Asians (OR, 1.77; 95% CI, 0.91-3.45; P = .094) (age, sex, smoking, physical activity, body mass index, and waist circumference adjusted). Receiver operating characteristic curve analyses revealed areas under the curve (95% CI) of 0.777 (0.707-0.847) in Aboriginals, 0.723 (0.647-0.798) in Chinese, 0.752 (0.675-0.828) in Europeans, and 0.676 (0.590-0.762) in South Asians. Optimal cutoffs (sensitivity, specificity) of TG/HDL-C for identifying individuals with IR were 0.9 (93.0%, 51.9%), 1.1 (71.7%, 61.5%), 1.1 (73.5%, 70.9%), and 1.8 (52.0%, 77.9%) in Aboriginal, Chinese, European, and South Asian individuals, respectively. The TG/HDL-C ratio may be a good marker to identify insulin-resistant individuals of Aboriginal, Chinese, and European, but not South Asian, origin.

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1. Introduction

Insulin resistance (IR) is considered one of the major risk factors for the development of type 2 diabetes mellitus [1]. Thus, early identification of insulin-resistant individuals, preferably by using simple and inexpensive diagnostic tools, is essential for preventing the occurrence of type 2 diabetes mellitus. One such simple tool, the "hypertriglyceridemic waist" (the combination of an increased waist circumference and hypertriglyceridemia,) has already been established in the literature as an inexpensive tool to identify individuals at elevated risk of type 2 diabetes mellitus [2]. Another marker, triglyceride (TG) to high-density lipoprotein cholesterol (HDL-C) ratio, has recently been proposed as a simple marker of IR [3-7]. The potential clinical utility of TG/HDL-C to identify individuals with IR was first reported by McLaughlin et al [3] among 258 overweight and obese adults predominantly of white ancestry. Their results have been replicated in other studies involving predominantly white population [4,6], as well as in studies featuring other racial/ethnic groups such as Korean [7], African [8], non-Hispanic Black, and Mexican American [5]. However, the utility of TG/HDL-C in predicting IR has not been explored among North American Aboriginal, South Asian, or Chinese populations.

Chinese and South Asian populations represent more than two fifths of the world's population and are experiencing rapidly increasing rates of obesity. With greater amounts of visceral adipose tissue, these 2 groups are also at greater risk for IR when compared with European populations [9]. In addition, South Asians appear to develop IR during early stages of overweight, which leads to premature occurrence of type 2 diabetes mellitus in this ethnic group [10]. Similarly, Aboriginal people are very vulnerable to type 2 diabetes mellitus [11]. Consequently, early identification and treatment of IR in these high-risk groups are essential in the prevention of type 2 diabetes mellitus.

The TG/HDL-C ratio has been consistently shown to have higher correlations with IR compared with other lipid measures such as TG, total cholesterol (TC), HDL-C, TC/HDL-C ratio, or low-density lipoprotein cholesterol (LDL-C) [4,6,12]; and this relationship was consistent across studies using a variety of IR measures (including use of glucose clamp [13,14], modified insulin suppression test [4], or the homeostasis model assessment of IR [HOMA-IR] [6,13]). However, whether TG/HDL-C is a better correlate of IR compared with other lipid measures has not been explored among Aboriginal, Chinese, or South Asian populations. Thus, the purpose of our study was to explore the clinical utility of TG/HDL-C in predicting IR among individuals of Aboriginal, Chinese, European, and South Asian origin, as well as to explore the relationship between IR and TG/HDL-C in comparison to that of other lipid measures.

2. Methods

Apparently healthy individuals of Aboriginal, Chinese, European, and South Asian origin were recruited as part of the Multi-Cultural Health Assessment Trial (M-CHAT), a study designed to explore the relationship between ethnicity and body composition, and the way these relate to diabetes and cardiovascular disease (CVD) risk [15]. Details on recruitment of study participants have been published elsewhere [15]. Briefly, eligibility criteria included participants from Vancouver, Canada, who were between 30 and 65 years of age and did not experience a weight change of more than 2.5 kg in the 3 months before assessment date. Participants were recruited across body mass index (BMI) ranges (18.5-24.9, 25.0-29.9, and ≥30.0). Individuals diagnosed with CVD or on medications to treat CVD-related risk factors were not eligible to participate in the study. Ethnicity was self-reported. The study was approved by the Simon Fraser University Research Ethics Board.

After providing written informed consent, study participants were assessed for sociodemographics, health-related behaviors, anthropometry, and risk factors. Body mass index was calculated as weight in kilograms divided by height in meters squared. Leisure-time physical activity was assessed by the Modifiable Activity Questionnaire [16], presenting average minutes per week of activity over the previous year. Following the standard protocol for blood collection and shipment, blood samples were collected at the study site from fasting participants and then shipped to St Paul's Hospital, Vancouver, for analysis. Glucose levels were determined by a glucose hexokinase II method using an ADVIA 1650 analyzer (Bayer Health Care, Morristown, NJ). Insulin was measured by a solid-phase, enzyme-labeled chemiluminescent immunometric assay using Immulite 2500 analyzer (Diagnostic Products, Los Angeles, CA). Coefficients of variations for within- and interassay precision for serum insulin were less than 7.4%. The HOMA-IR, which has been shown to correlate well with the euglycemic-hyperinsulinemic clamp [17], was used as a surrogate of IR (insulin [microunits per milliliter] × glucose [millimoles per liter]/22.5). Total cholesterol, TG, and HDL-C were determined using standard protocols by the ADVIA 1650 analyzer (Bayer Health Care). Low-density lipoprotein cholesterol was calculated using Friedewald formula (TC – [HDL-C + TG/2.2]) [18]. Non–high-density lipoprotein cholesterol was calculated by subtracting HDL-C from TC.

Out of 822 participants initially recruited for the M-CHAT study, 38 participants were missing data for fasting insulin and consequently for HOMA-IR. These individuals were excluded from the study, leaving a final sample of 784 participants. Continuous variables are presented as means (95% confidence interval [CI]) or as geometric means (95% CI) if data are not normally distributed. Categorical variables are given in counts and percentages. Distributions of physical activity, glucose, insulin, HOMA-IR, TG, and TG/HDL-C deviated from normality; so the variables were log transformed using the natural logarithm (ln). The interethnic differences in risk factors expressed in continuous variables were determined using analysis of covariance while controlling for age and sex. Interethnic differences in categorical sociodemographic variables were explored using the χ^2 test. Partial correlation coefficients were calculated for each ethnic group to explore the relationship between various lipid parameters and HOMA-IR after holding the effects of age and sex constant.

Logistic regression, performed for each group separately, was used to explore the association between TG/HDL-C and IR. For each ethnic group, IR was defined by HOMA-IR as greater than the

Table 1 – Distribution of risk factors among individuals of Aboriginal, Chinese, European, and South Asian origin

	Aboriginal n = 174	Chinese n = 214	European n = 197	South Asian n = 199	Overall *P* value
Female	95 (54.6%)	116 (54.2%)	98 (49.7%)	100 (50.3%)	.677
Age	45.5 (44.2-46.7)	48.0 (46.8-49.1)	50.4 (49.2-51.6)	44.8 (43.6-46.0)	<.001 *,†,§,‖,¶
Current smoker	51 (29.3%)	7 (3.3%)	15 (7.6%)	6 (3.0%)	<.001
Physical activity (min/wk) [a,b]	260 (221-306)	170 (146-197)	272 (233-317)	143 (123-167)	<.001 *,‡,‖,¶
BMI (kg/m^2) [a]	29.0 (28.3-29.7)	25.8 (25.2-26.5)	27.8 (27.1-28.4)	27.8 (27.1-28.4)	<.001 *,§,‖
Fasting glucose (mmol/L) [a,b]	5.25 (5.16-5.34)	5.25 (5.17-5.33)	5.13 (5.05-5.22)	5.33 (5.25-5.42)	.015 ¶
Fasting insulin (μU/mL) [a,b]	72.53 (66.49-79.20)	60.34 (55.81-65.30)	59.26 (54.54-64.39)	77.01 (70.95-83.60)	<.001 *,†,‖,¶
HOMA-IR [a,b]	2.44 (2.21-2.68)	2.03 (1.86-2.21)	1.95 (1.78-2.13)	2.63 (2.40-2.88)	<.001 *,†,‖,¶
TC (mmol/L) [a]	5.09 (4.95-5.24)	5.32 (5.19-5.45)	5.20 (5.06-5.34)	5.34 (5.21-5.48)	.044
HDL-C (mmol/L) [a]	1.33 (1.28-1.38)	1.32 (1.28-1.36)	1.31 (1.27-1.36)	1.19 (1.14-1.23)	<.001 ‡,‖,¶
TC/HDL-C [a]	4.11 (3.91-4.31)	4.32 (4.14-4.50)	4.30 (4.11-4.50)	4.73 (4.55-4.92)	<.001 ‡,‖,¶
LDL-C (mmol/L) [a]	3.03 (2.90-3.16)	3.27 (3.16-3.39)	3.22 (3.10-3.35)	3.39 (3.27-3.51)	.001 *,‡
LDL-C/HDL-C [a]	2.45 (2.31-2.59)	2.64 (2.51-2.77)	2.68 (2.54-2.81)	3.01 (2.87-3.14)	<.001 ‡,‖,¶
Non–HDL-C (mmol/L) [a]	3.77 (3.62-3.91)	4.00 (3.87-4.14)	3.89 (3.75-4.03)	4.16 (4.02-4.30)	.001 ‡
TG (mmol/L) [a,b]	1.39 (1.28-1.51)	1.33 (1.23-1.43)	1.19 (1.10-1.29)	1.47 (1.36-1.59)	.003 ¶
TG/HDL-C [a,b]	1.08 (0.97-1.21)	1.05 (0.95-1.15)	0.95 (0.85-1.05)	1.27 (1.15-1.41)	.001 ‖,¶

Data are means (95% CI) or n (%).
[a] Means are adjusted for age and sex.
[b] Geometric means (95% CI).
* *P* < .05, Aboriginal vs Chinese.
† *P* < .05, Aboriginal vs European.
‡ *P* < .05, Aboriginal vs South Asian.
§ *P* < .05, Chinese vs European.
‖ *P* < .05, Chinese vs South Asian.
¶ *P* < .05, European vs South Asian.

75th percentile [19]. We constructed 2 models: model 1 contained age, sex, smoking, physical activity, BMI, and waist circumference; and model 2 was composed of variables from model 1 and TG/HDL-C. The improvement of the predictive power of model 2 compared with model 1 was explored using a step statistic as well as a receiver operating characteristic (ROC) curve analysis where the area under the ROC curve (AUC) corresponded to the *c* statistic from logistic regression models. Furthermore, ROC curve analysis was used to explore how accurately TG/HDL-C can identify individuals with IR in each ethnic group. As a measure of discrimination, AUC of 0.5, 0.7 ≤ AUC < 0.8, 0.8 ≤ AUC < 0.9, and ≥0.9 represent no, acceptable, excellent, and outstanding discrimination, respectively [20]. A maximum value of the Youden index was calculated as sensitivity + specificity − 1 and used as the optimal TG/HDL-C cutoff point to identify individuals with IR [21]. All analyses were performed using Statistical Package for Social Sciences version 19 (SPSS, Chicago, IL). *P* values ≤ .05 were considered statistically significant.

3. Results

There were significant ethnic differences across risk factors (Table 1). The highest prevalence of current smoking was among Aboriginals, and the lowest was among South Asians (*P* < .001). Body mass index was highest among Aboriginal and lowest among Chinese participants (*P* < .05). Fasting insulin and HOMA-IR levels were higher among individuals of Aboriginal and South Asian origin compared with their Chinese and European counterparts (*P* < .05). Levels of HDL-C were lowest, whereas those of TG, TG/HDL-C, LDL-C, LDL-C/HDL-C, non–HDL-C, and TC/HDL-C were highest, among South Asian participants (*P* < .05).

Age- and sex-adjusted correlation coefficients were calculated to explore the relationship between lipid parameters and HOMA-IR. As expected, all lipid parameters, except for HDL-C (which had a negative relationship), showed a positive relationship with HOMA-IR (Table 2). More importantly, compared with the rest of the lipid parameters, correlations with HOMA-IR were highest for TG/HDL-C in all 4 ethnic groups. A correlation coefficient expressing the linear relationship between TG/HDL-C and HOMA-IR was highest for European (*r* = 0.597, *P* < .001) followed by Aboriginal (*r* = 0.499, *P* < .001) and Chinese (*r* = 0.432, *P* < .001) participants and was lowest for South Asian individuals (*r* = 0.372, *P* < .001).

Table 2 – Results of age- and sex-adjusted correlation analyses between lnHOMA-IR and lipid measures in 4 ethnic groups

Lipid measure	Aboriginal (*r*)	Chinese (*r*)	European (*r*)	South Asian (*r*)
lnTG/HDL-C	0.499 ‡	0.432 ‡	0.597 ‡	0.372 ‡
lnTG	0.454 ‡	0.378 ‡	0.583 ‡	0.333 ‡
TC/HDL-C	0.362 ‡	0.377 ‡	0.517 ‡	0.340 ‡
HDL-C	−0.414 ‡	−0.396 ‡	−0.455 ‡	−0.278 ‡
LDL-C/HDL-C	0.249 †	0.305 ‡	0.409 ‡	0.273 ‡
Non–HDL-C	0.183 *	0.210 †	0.363 ‡	0.199 †
TC	0.057	0.074	0.232 †	0.112
LDL-C	0.001	0.076	0.151 *	0.081

* *P* < .05.
† *P* < .01.
‡ *P* < .001.

Table 3 – The association between TG/HDL-C and IR in 4 ethnic groups

	Model 1 discrimination overall C (95% CI) [b]	Model 2 discrimination overall C (95% CI) [b]	Step statistic [a]	Significance of the change from model 1 to model 2
Aboriginal	0.828 (0.758-0.898)	0.864 (0.806-0.922)	14.791	<.001
Chinese	0.816 (0.744-0.887)	0.854 (0.787-0.920)	16.729	<.001
European	0.836 (0.765-0.906)	0.857 (0.796-0.918)	4.013	.045
South Asian	0.834 (0.765-0.902)	0.841 (0.776-0.907)	2.863	.091

Model 1: age, sex, smoking, physical activity, BMI, and waist circumference. Model 2: model 1 + TG/HDL-C.
[a] The difference in the log-likelihood between model 1 and model 2, that is, the improvement in the predictive power model 2 with TG/HDL-C since model 1.
[b] Results of ROC curve analysis where the AUC corresponded to the *c* statistic from logistic regression models.

After adjusting for age, sex, smoking, physical activity, BMI, and waist circumference, TG/HDL-C was found to be significantly associated with IR in Aboriginals, Chinese, and Europeans, but not in South Asians. Namely, for a 1-unit increase in TG/HDL-C, the odds of being insulin resistant increased about 4 times (odds ratio [OR], 3.95; 95% CI, 1.86-8.42; P <.001) in Aboriginals, 3.4 times in Chinese (OR, 3.44; 95% CI, 1.79-6.62; P < .001), 1.9 times in Europeans (OR, 1.94; 95% CI, 1.00-3.75; P = .049), and 1.8 times in South Asians (OR, 1.77; 95% CI, 0.91-3.45; P = .094). In the Aboriginals, Chinese, and Europeans, the addition of TG/HDL-C to model 1 improved the power of model 2's predicted values to discriminate between people with and without IR (Table 3).

By constructing ROC curves (Fig. 1), we identified the TG/HDL-C thresholds to discriminate between individuals with and without IR. Seventy-fifth percentile cutoffs for HOMA-IR were 3.81, 3.16, 2.88, and 3.61 in Aboriginal, Chinese, European, and South Asian individuals, respectively. According to the AUC, TG/HDL-C was shown to be a good marker for identifying individuals with IR for Aboriginals (AUC = 0.777; 95% CI, 0.707-0.847), Chinese (AUC = 0.723; 95% CI, 0.647-0.798), and Europeans (AUC = 0.752; 95% CI, 0.675-0.828), but not in South Asians (AUC = 0.676; 95% CI, 0.590-0.762). Maximum values of Youden indices (with respective sensitivities and specificities) that corresponded to optimal cutoffs of TG/HDL-C for identifying individuals with IR were 0.9 (93.0%, 51.9%), 1.1 (71.7%, 61.5%), 1.1 (73.5%, 70.9%), and 1.8 (52.0%, 77.9%) in Aboriginal, Chinese, European, and South Asian individuals, respectively.

4. Discussion

The results of our study indicate that TG/HDL-C is a better correlate of IR than other lipid measures tested across ethnic groups. In Aboriginals, Chinese, and Europeans, but not in South Asians, TG/HDL-C was significantly associated with HOMA-IR independent of age, sex, smoking, physical activity, BMI, and waist circumference. In addition, TG/HDL-C was shown to be a good clinical marker to identify individuals with IR in Aboriginals, Chinese, and Europeans, but not in South Asians.

Previous studies in other ethnic populations have reported significant correlations between TG/HDL-C and IR that were

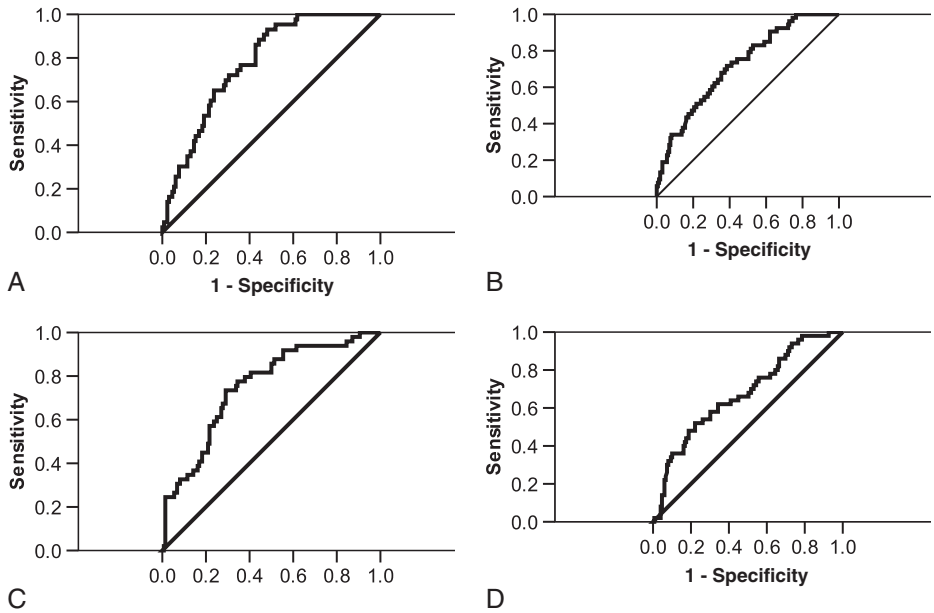

Fig. 1 – Receiver operating characteristic curves of the TG/HDL-C ratio for prediction of IR in Aboriginals (A), Chinese (B), Europeans (C), and South Asians (D).

higher than those of other lipid parameters [4,6,12-14]. McLaughlin and colleagues [4] showed that TG/HDL-C had the strongest correlation with IR when compared with TG, TC/HDL-C, HDL-C, non–HDL-C, and LDL-C. Likewise, TG/HDL-C was a better correlate of HOMA-IR compared with TG, HDL-C, TC, LDL-C, and TC/HDL-C among white people from the Framingham Offspring Cohort [12]. In addition, correlation coefficients for TG/HDL-C and IR were higher than those for IR with HDL-C, TG, and TC/HDL-C among overweight and obese nondiabetic postmenopausal women [13]. In our multiethnic sample consisting of individuals of Aboriginal, Chinese, European, and South Asian origin, TG/HDL-C was shown to be a better correlate of HOMA-IR compared with TC, LDL/HDL-C, and all the other above-mentioned lipid parameters, regardless of age and sex.

With regard to clinical applicability, we found TG/HDL-C to be a good marker for identifying individuals with IR among apparently healthy individuals of Aboriginal, Chinese, and European origin. This is consistent with other studies that have found TG/HDL-C to also be an independent predictor of future diabetes mellitus [22] and of retinopathy and chronic kidney disease incidence in people with type 2 diabetes mellitus without prior CVD [23]. The hypertriglyceridemic waist has also been identified as a potential clinical marker of the diabetogenic profile. [2] However, the hypertriglyceridemic waist is limited by the fact that the waist circumference is not routinely measured in clinical practice; this therefore limits the wider utilization of this otherwise good marker for identification of at-risk individuals. It has also been shown that another method, the total integrated insulin response, has a stronger correlation with IR than TG/HDL-C [24]. However, the authors themselves concluded that this method is limited by the lack of a standard assay for insulin measurement and the complexity of assessing insulin action directly and further suggested that lipid-based indices such as TG/HDL-C can help to more consistently identify insulin-resistant individuals at increased risk for CVD and diabetes [24]. Therefore, given that TG and HDL-C are routinely measured in clinical practice as part of a lipid panel, TG/HDL-C can be readily calculated (or even provided by the laboratory) and used to identify individuals with IR at risk for type 2 diabetes mellitus.

Unlike with the other 3 ethnic groups, TG/HDL-C was not a good indicator of IR in South Asians (AUC = 0.665). This was unexpected given that South Asians have a high propensity to develop type 2 diabetes mellitus at a younger age and at a lower BMI and waist circumference than other ethnicities [25]. Our knowledge to date suggests that South Asians have a unique body composition phenotype (increased abdominal adiposity with greater levels of visceral and deep subcutaneous adipose tissues while at lower levels of BMI). As a result, it has been postulated that the way excess energy is stored within adipose tissue depots plays a significant role [26]. Indeed, studies have shown that, compared with Europeans, South Asians have greater amounts of visceral adipose tissue for the same total body fat [9]. They also possess a greater amount of deep subcutaneous adipose tissue [27,28], which has been reported to have a stronger relationship with IR than superficial subcutaneous adipose tissue [29,30]. It has been suggested that the higher lipolytic activity of deep subcutaneous adipose tissue may account for its stronger association with IR [31], but findings with regard to differences in the tissues' lipolytic activity are somewhat contrasting in the literature [32]. Although the exact mechanism for the observed ethnic differences is still unclear, the unique body phenotype of South Asians may be a factor that drives IR [26]. Longitudinal studies are needed to make causative conclusions on the relationship between TG/HDL-C and IR in South Asians.

Certain limitations to our study should be acknowledged. Firstly, as our study participants were purposely recruited across a range of BMI values, our sample may not be representative of the general population. Nonetheless, we believe this recruitment method served as an advantage to be able to investigate these relationships across a range of body sizes; and we indeed found that TG/HDL-C was significantly associated with IR in all ethnic groups regardless of BMI. A second limitation is that HOMA-IR was used as a surrogate of IR; but this was based on the findings that HOMA-IR correlates well with measurements obtained by euglycemic-hyperinsulinemic clamp, a criterion standard for evaluating insulin sensitivity [17]. Especially given the invasiveness and the complexity of the clamp method, the HOMA-IR method is considered a more feasible option in large population health studies [33]. An additional limitation is that although we did adjust our analyses for age, sex, and physical activity—all factors affecting plasma TG levels—we did not adjust for diet. Finally, given the cross-sectional design of this study, prospective studies are needed to explore whether the independent association between TG/HDL-C and IR persists or changes over time.

Despite its limitations, this is among the first studies to explore the clinical utility of TG/HDL-C in identifying insulin-resistant individuals among Aboriginals, Chinese, and South Asians. Furthermore, given that our study population was composed of people without CVD and who were not on CVD-related medications, our results suggest that TG/HDL-C would be a very useful marker in primary care to identify insulin-resistant individuals with increased risk for CVD and diabetes. As part of this study, we also identified ethnic-specific optimal cutoffs of TG/HDL-C for identifying individuals with IR. Namely, when examining Chinese and Europeans, a finding of TG/HDL-C of 1.1 should alert a physician that individuals could be insulin resistant. In Aboriginals, an even lower TG/HDL-C of 0.9 is suggestive of individuals being at increased risk for CVD and diabetes. This simple measure may allow physicians to get at-risk individuals started early in lifestyle intervention programs.

In summary, our study explored the association between TG/HDL-C and IR among individuals of Aboriginal, Chinese, South Asian, and European origin. The TG/HDL-C ratio outperformed other lipid parameters in their association with IR and was independently associated with IR over and above age, sex, smoking, physical activity, BMI, and waist circumference. The TG/HDL-C ratio has the advantage in that it is a simple, inexpensive biomarker and is easily calculated from the TG and HDL-C values that are routinely measured in clinical practice as part of a lipid panel. The TG/HDL-C ratio could potentially allow for an early discovery of insulin-resistant individuals, leading to early implementation of

lifestyle intervention programs that could significantly decrease incidence of type 2 diabetes mellitus. The results of our study suggest that TG/HDL-C may be a good marker for early identification of insulin-resistant individuals at increased risk for type 2 diabetes mellitus among apparently healthy Aboriginal, Chinese, and European, but not South Asian, populations.

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Conflict of Interest

The authors declare no conflicts of interest with this investigation.

REFERENCES

[1] Lilloja S, Mott DM, Spraul M, et al. Insulin resistance and insulin secretory disfunction as precursors of non–insulin-dependent diabetes mellitus. NEJM 1993;329:1988-92.
[2] Lemieux I, Almeras N, Mauriege P, et al. Prevalence of 'hypertriglyceridemic waist' in men who participated in the Quebec Health Survey: association with atherogenic and diabetogenic metabolic risk factors. Can J Cardiol 2002;18: 725-32.
[3] McLaughlin T, Abbasi F, Cheal K, et al. Use of metabolic markers to identify overweight individuals who are insulin resistant. Ann Intern Med 2003;139:802-9.
[4] McLaughlin T, Reaven G, Abbasi F, et al. Is there a simple way to identify insulin-resistant individuals at increased risk of cardiovascular disease? Am J Cardiol 2005;96:399-404.
[5] Li C, Ford ES, Meng Y-X, et al. Does the association of the triglyceride to high-density lipoprotein cholesterol ratio with fasting serum insulin differ by race/ethnicity? Cardiovasc Diabetol 2008;7:4.
[6] Fan X, Liu EY, Poole Hoffman V, et al. Triglyceride/high-density lipoprotein cholesterol ratio: a surrogate to predict insulin resistance and low-density lipoprotein cholesterol particle size in nondiabetic patients with schizophrenia. J Clin Psychiatry 2011;72:806-12.
[7] Kimm H, Lee SW, Lee HS, et al. Association between lipid measures and metabolic syndrome, insulin resistance and adiponectin: usefulness of lipid ratios in Korean men and women. Circ J 2010;74:931-7.
[8] Bovet P, Faeh D, Gabriel A, et al. The prediction of insulin resistance with serum triglyceride and high-density lipoprotein cholesterol levels in an East African population. Arch Intern Med 2006;166:1236-7.
[9] Lear SA, Humphries KH, Kohli S, et al. Visceral adipose tissue accumulation differs according to ethnic background: results of the Multicultural Community Health Assessment Trial (M-CHAT). Am J Clin Nutr 2007;86:353-9.
[10] Grundy SM, Brewer Jr HB, Cleeman JI, et al. Definition of metabolic syndrome: report of the National Heart, Lung, and Blood Institute/American Heart Association conference on scientific issues related to definition. Circulation 2004;109: 433-8.
[11] Young TK, Reading J, Elias B, et al. Type 2 diabetes mellitus in Canada's First Nations: status of an epidemic in progress. CMAJ 2000;163:561-6.
[12] Kannel WB, Vasan RS, Keyes MJ, et al. Usefulness of the triglyceride–high-density lipoprotein versus the cholesterol–high-density lipoprotein ratio for predicting insulin resistance and cardiometabolic risk (from the Framingham Offspring Cohort). Am J Cardiol 2008;101:497-501.
[13] Karelis AD, Pasternyk SM, Messier L, et al. Relationship between insulin sensitivity and the triglyceride–HDL-C ratio in overweight and obese postmenopausal women: a MONET study. Appl Physiol Nutr Metab 2007;32:1089-96.
[14] Stein E, Kushner H, Gidding S, et al. Plasma lipid concentrations in African American adults: associations with insulin resistance and the metabolic syndrome. Metabolism 2007;56: 954-60.
[15] Lear SA, Birmingham CL, Chockalingam A, et al. Study design of the multicultural community health assessment trial (M-CHAT): a comparison of body fat distribution in four distinct populations. Ethn Dis 2006;16:96-100.
[16] Kriska AM, Bennett PH. An epidemiological perspective of the relationship between physical activity and NIDDM: from activity assessment to intervention. Diabetes Metab Rev 1992;8:355-72.
[17] Matthews DR, Hosker JP, Rudenski AS, et al. Homeostasis model assessment: insulin resistance and β-cell function from fasting plasma glucose and insulin concentrations in men. Diabetologia 1985;28:412-9.
[18] Friedwald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. Clin Chem 1972;18:499-502.
[19] Hivert MF, Sullivan LM, Fox CS, et al. Associations of adiponectin, resistin, and tumor necrosis factor–α with insulin resistance. J Clin Endocrinol Metab 2008;93: 3165-72.
[20] Hosmer DW, Lemeshow S. Applied logistic regression. 2nd ed. John Wiley & sons, Inc.; 2000. p. 156-64.
[21] Schisterman EF, Perkins NJ, Liu A, et al. Optimal cut-point and its corresponding Youden index to discriminate individuals using pooled blood samples. Epidemiology 2005;16:73-81.
[22] He S, Wang S, Chen X, et al. Higher ratio of triglyceride to high-density lipoprotein cholesterol may predispose to diabetes mellitus: 15-year prospective study in a general population. Metabolism 2011, doi:10.1016/j.metabol.2011.05.007.
[23] Zoppini G, Negri C, Stoico V, et al. Triglyceride–high-density lipoprotein cholesterol is associated with microvascular complications in type 2 diabetes mellitus. Metabolism 2011, doi:10.1016/j.metabol.2011.05.004.
[24] Abbasi F, Reaven GM. Comparison of two methods using plasma triglyceride concentration as a surrogate estimate of insulin action in nondiabetic subjects: triglycerides × glucose versus triglyceride/high-density lipoprotein cholesterol. Metabolism 2011:1-4, doi:10.1016/j.metabol.2011.04.006.
[25] Enas AE, Chacko V, Pazhoor SG, et al. Dyslipidemia in South Asian patients. Current Atherosclerosis Reports 2007;9: 367-74.
[26] Sniderman AD, Bhopal R, Prabhakaran D, et al. Why might South Asians be so susceptible to central obesity and its atherogenic consequences? The adipose tissue overflow hypothesis. Int J Epidemiol 2007;36:220-5.
[27] Kohli S, Snidermaan AD, Tchernof A, et al. Ethnic-specific differences in abdominal subcutaneous adipose tissue compartments. Obesity 2010;18:2177-83.
[28] Anand SS, Tarnopolsky MA, Rashid S, et al. Adipocyte hypertrophy, fatty liver and metabolic risk factors in South Asians: the Molecular Study of Health Risk in Ethnic Groups (mol-SHARE). PLoS one 2011;6:e22112.
[29] Misra A, Garg A, Abate N, et al. Relationship of anterior and posterior subcutaneous abdominal fat to insulin sensitivity in nondiabetic men. Obes Res 1997;5:93-9.

[30] Kelley DE, Thaete FL, Troost F, et al. Subdivisions of subcutaneous abdominal adipose tissue and insulin resistance. Am J Physiol Endocrinol Metab 2000;278:E941-8.
[31] Monzon JR, Basile R, Heneghan S, et al. Lipolysis in adipocytes isolated from deep superficial subcutaneous adipose tissue. Obesity Res 2002;10:266-9.
[32] Enevoldsen LH, Simonsen L, Stallknecht B, et al. In vivo human lipolytic activity in preperitoneal and subdivisions of subcutaneous abdominal adipose tissue. Am J Physiol Endocrinol Metab 2001;281:E1110-4.
[33] Ferrannini E, Mari A. How to measure insulin sensitivity. J Hypertens 1988;16:895-906.