Triglyceride/High-Density Lipoprotein Cholesterol Ratio: A Surrogate to Predict Insulin Resistance and Low-Density Lipoprotein Cholesterol Particle Size in Nondiabetic Patients With Schizophrenia

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Objective: Insulin resistance, changes in lipid parameters, and cardiometabolic adverse events have been reported in some patients during clinical trials of antipsychotic agents. The present study examined whether the triglyceride/high-density lipoprotein (HDL) ratio can be used as a better surrogate than other conventional lipid measures (low-density lipoprotein [LDL], HDL, triglyceride) in predicting insulin resistance and LDL particle size in nondiabetic patients with schizophrenia.

Method: Outpatients 18 to 75 years old diagnosed with schizophrenia or schizoaffective disorder (*DSM-IV* criteria) and receiving olanzapine, risperidone, or typical antipsychotics participated in a multicenter, cross-sectional study. Fasting blood samples were obtained to determine the levels of glucose, insulin, lipids, and lipid particle size. The study was conducted from July 2001 to March 2002.

Results: In the sample of 206 patients, significant correlations were found between various lipid measures (LDL, HDL, triglyceride, and triglyceride/HDL ratio) and the homeostasis model of assessment of insulin resistance ($P < .05$). However, stepwise multiple regression analysis suggested that the triglyceride/HDL ratio is a stronger predictor of insulin resistance and of LDL particle size than other conventional lipoprotein measures after other potential confounding variables, including age, gender, race, family history of diabetes, body mass index, and antipsychotic agent, were taken into consideration ($P < .001$). Further, logistic regression analysis indicated that the triglyceride/HDL ratio and male gender predict the existence of a small LDL particle size pattern (pattern B LDL phenotype), with a sensitivity of 75.9% and a specificity of 85.4%.

Conclusions: The triglyceride/HDL ratio, a simple, readily available and inexpensive measure, can be a useful surrogate to identify those with insulin resistance as well as those with more atherogenic small LDL particles in nondiabetic patients with schizophrenia.

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Mortality of schizophrenia patients is approximately twice that of the general population.[1,2] Cardiovascular disease is responsible for as much as 50% of the excess mortality associated with schizophrenia.[2] Elevated cardiovascular risk in the schizophrenia population may be attributable to numerous factors, but one source of elevated cardiovascular risk is a cluster of clinical features defining the metabolic syndrome: abdominal adiposity, atherogenic dyslipidemia, hypertension, and impaired fasting glucose or overt diabetes.[3] Recent data from the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) suggested that the metabolic syndrome is highly prevalent in US schizophrenia patients: 40.9% using the National Cholesterol Education Program (NCEP) criteria and 42.7% using the updated American Heart Association criteria that include a lower fasting glucose threshold of 100 mg/dL.[4] In contrast, the age-adjusted prevalence of the metabolic syndrome from the third National Health and Nutrition Examination Survey (NHANES III) was 23.7% using the NCEP criteria.[5]

There is strong evidence of an association between insulin resistance and diabetes.[6–10] Insulin resistance refers to the diminished ability of insulin to lower blood glucose, a consequent result to either decreased cellular glucose uptake or increased hepatic glucose output. When insulin resistance occurs, the body attempts to overcome the resistance by secreting more insulin, resulting in hyperinsulinemia. Insulin resistance has been reported in some patients during clinical trials of antipsychotic agents.[11,12] Beyond its role in the development of type 2 diabetes, insulin resistance has been associated with cardiovascular disease.[13–15]

Hyperlipidemia has been reported during treatment with atypical antipsychotics. A 5-year naturalistic study of patients treated with clozapine found a nonsignificant increase in fasting total cholesterol but a significant increase in fasting triglyceride level.[16] In a randomized, double-blind trial, patients treated with olanzapine and clozapine had significant increases in fasting total cholesterol level.[17] In a randomized 8-week study of 112 patients with first-episode schizophrenia, fasting total cholesterol and triglyceride levels were significantly increased in those treated with clozapine or olanzapine.[18] In a large-scale, matched case-control analysis with pharmacy and claims data, an increased incidence of hyperlipidemia was reported in patients with schizophrenia and mood disorders treated with clozapine, olanzapine, risperidone, quetiapine, ziprasidone, and first-generation antipsychotic agents, but not aripiprazole, compared to patients not treated with an antipsychotic agent.[19] The CATIE

study found a difference in association with lipid changes among the 5 antipsychotics studied. The study showed an association with greater mean increases in levels of triglycerides and total cholesterol in olanzapine-treated patients followed by quetiapine-treated patients. Patients treated with risperidone and ziprasidone experienced a mean decrease in these measures, and patients treated with perphenazine experienced a modest mean increase in levels of triglycerides and total cholesterol.[20]

Elevated low-density lipoprotein (LDL) cholesterol has long been considered as a major cause of cardiovascular disease.[21] Low-density lipoprotein cholesterol comprises a heterogeneous spectrum of lipoprotein particles. The size of LDL particles may play distinct roles in determining its atherogenicity. The predominance of small, dense LDL particles (pattern B LDL phenotype) has been reported to be particularly atherogenic.[22–24] Several mechanisms have been proposed to explain this association: small, dense LDLs have low affinity to the LDL receptor, low resistance to oxidative stress, prolonged plasma half-life, high binding affinity to surface components in the vessel wall, and efficient penetration into the intima. Despite the clinical importance of recognizing those individuals with a small LDL particle size pattern, LDL particle size determination is not universally available, is expensive, and has not been widely applied in clinical practice. Within the schizophrenia population, studies measuring LDL particle size are still rare.[25]

Low levels of high-density lipoprotein (HDL) cholesterol and elevated triglycerides are risk factors for insulin resistance; further, elevations of triglycerides are associated with the formation of small LDL particles.[21] The simple, readily calculated measure of triglyceride/HDL cholesterol ratio has been identified as a predictor of insulin resistance[26–28] and cardiovascular disease[29,30] in various populations. Studies have also suggested that the triglyceride/HDL ratio is a useful marker to predict the presence of small, dense LDL particles.[26,31–33]

This multicenter, cross-sectional study was designed to assess metabolic health in nondiabetic patients with schizophrenia or schizoaffective disorder. The findings comparing different antipsychotic agents (olanzapine, risperidone, or typical agents) with regard to various metabolic measures including lipids have been reported elsewhere.[25] The focus of the present analysis was to examine whether the triglyceride/HDL ratio can be used as a better surrogate than other conventional lipid measures (LDL, HDL, triglyceride) in predicting insulin resistance and LDL particle size in nondiabetic patients with schizophrenia.

METHOD

Subjects

Outpatients 18 to 75 years old diagnosed with schizophrenia or schizoaffective disorder (*DSM-IV* criteria; duration ≥ 5 years) were recruited from 28 study sites in the United States. Patients were psychiatrically stable, with no hospitalizations within the previous 3 months. Patients had been receiving olanzapine, risperidone, or typical antipsychotic agents continuously for at least 1 year and as monotherapy for the 3 months preceding the study. Exclusion criteria included unstable medical illnesses, substance dependence within the previous 3 months, known medical conditions that might affect changes in metabolic parameters, known history of diabetes or lipid disorder, and use of antidiabetic or lipid-lowering therapy or special diets to lower glucose or lipids levels. Patients on exercise programs aimed at lowering glucose or lipid levels were not excluded from the study. All procedures were approved by institutional review boards at all study sites and were conducted in compliance with the Declaration of Helsinki. The study was conducted from July 2001 to March 2002.

Procedures

After providing written informed consent, each patient underwent a physical examination and a psychiatric diagnostic evaluation, which included the Brief Psychiatric Rating Scale (BPRS) assessment. Eligible patients were admitted to an inpatient facility for an observed overnight fast. Patients received a low-fat meal and were not allowed to ingest alcoholic beverages. Patients were allowed to drink water during the fasting period. Vital signs and anthropometric measures were obtained in the beginning of the inpatient stay. Blood samples were obtained 11 hours (± 1 hour) after the completion of the meal the night before.

Blood analyses were performed at the Covance Laboratories (Princeton, New Jersey). Fasting serum levels of glucose, total cholesterol, HDL, and triglycerides were analyzed using standard enzymatic methods and an automated analyzer (Roche Modular Analyzer, Roche Diagnostics, Indianapolis, Indiana). The triglyceride/HDL ratio was derived based on fasting serum levels of triglycerides and HDL.[26,27] Low-density lipoprotein levels were determined by the Direct LDL reagents (Roche Diagnostics, Indianapolis, Indiana). Coefficients of variations for inter- and intra-assay variability for glucose and lipids were < 5%. Fasting serum insulin levels were analyzed using IMMULITE 2000 (Diagnostic Products Corporation, Los Angeles, California). Coefficients of variations for inter- and intra-assay variability for serum insulin were < 9%. Fasting plasma glucose and serum insulin levels were averaged from samples drawn 15 minutes apart. The homeostasis model of assessment of insulin resistance (HOMA-IR) was calculated by the following formula: fasting plasma glucose (mg/dL) × fasting serum insulin (μU/mL)/405.[34]

Low-density lipoprotein mean particle size was determined using nuclear magnetic resonance spectroscopy (LipoScience, Raleigh, North Carolina).[35,36] Nuclear magnetic resonance spectroscopy capitalizes on the fact that each lipoprotein subclass particle of a given size emits its own characteristic signal, and the amplitude of the signal provides a direct measure of the lipoprotein particle concentration. Low-density lipoproteins are grouped by mean particle size as large (20.6–23.1 nm, pattern A LDL phenotype) and small (18.0–20.5 nm, pattern B LDL phenotype).

Statistical Analysis

The data were analyzed using SPSS (version 13.0; SPSS Inc, Chicago, Illinois). Descriptive statistics described demographics, clinical measures, and laboratory values. The homeostasis model of assessment of insulin resistance, triglyceride, triglyceride/HDL ratio, and LDL mean particle size were not distributed normally and were, therefore, log transformed before analysis. Pearson correlation coefficients were used to quantify relations between lipid measures and other variables. Stepwise multiple regression was used to examine whether triglyceride/HDL ratio is an independent predictor of HOMA-IR and LDL particle size when other potential confounding variables were also considered. The criteria of $P = .05$ for a variable to enter into the regression model and $P = .10$ for a variable to be removed were used in the multiple regression analysis. Further, logistic regression was used to examine predictors of pattern A versus pattern B LDL phenotypes. A receiver operating characteristic curve (ROC curve) and the area under the curve were also calculated to summarize the predictive power of the logistic model. For all statistical analyses, a P value of $< .05$ (2-tailed) was used to test for statistical significance.

RESULTS

Two hundred fifty-two patients enrolled in the study. Thirty-seven patients were missing fasting plasma glucose levels. Nine patients had fasting plasma glucose ≥ 126 mg/dL, suggesting undiagnosed diabetes,[37] and were excluded from the analyses per a priori decision. Among 206 total patients included in the analysis, 74 patients were treated with olanzapine (daily dose range, 7.5–20 mg, with mean 14.6 mg); 78 patients with risperidone (daily dose range, 2–10 mg, with mean 4.5 mg); and 54 patients with typical antipsychotic agents, with haloperidol and fluphenazine most commonly used. Demographic, clinical measures and laboratory values of the study subjects are summarized in Table 1.

Table 1. Demographic and Clinical Characteristics of the Study Sample (n = 206)

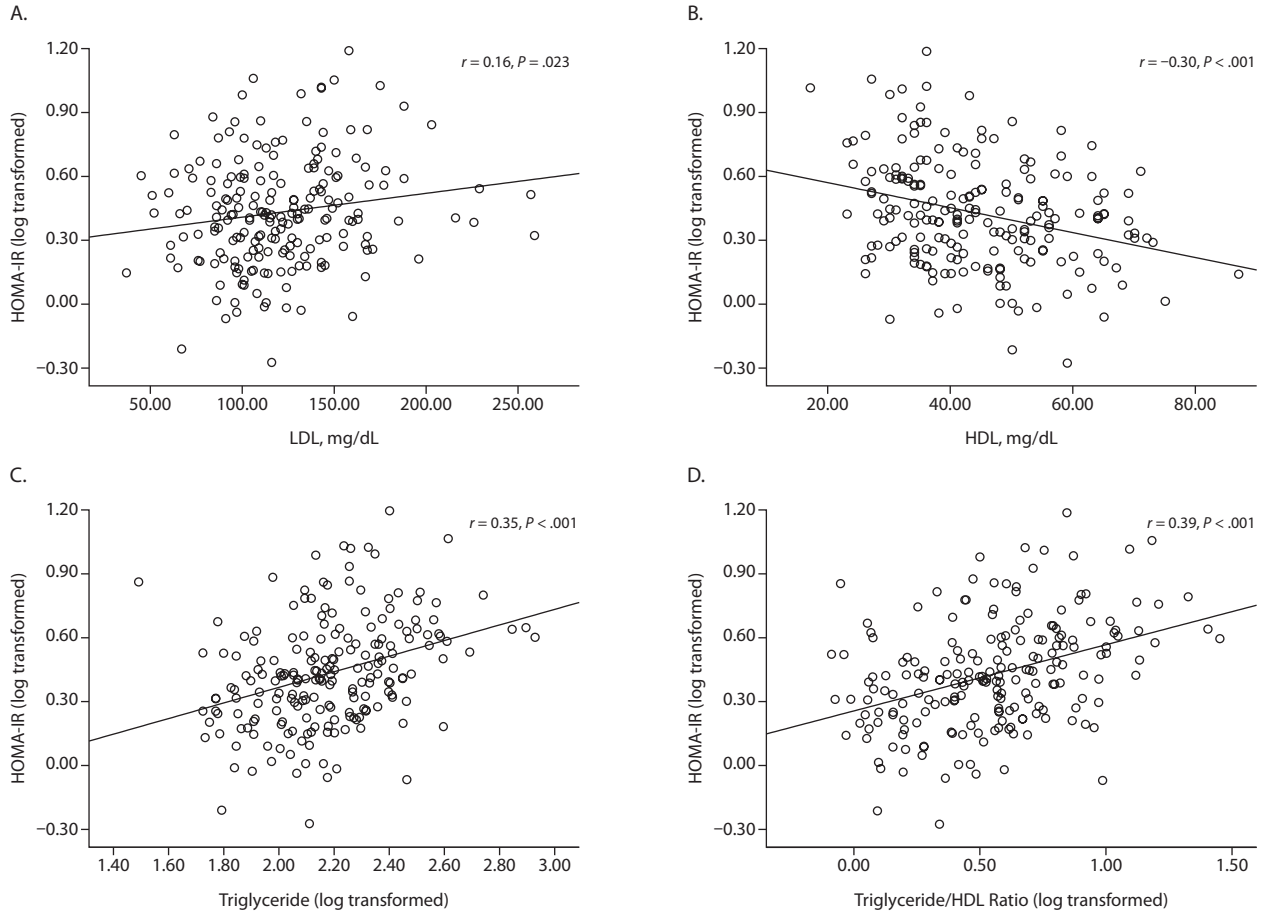
Characteristic	Mean ± SD	Range
Age, y	44 ± 11	19–73
Age at illness onset, y	25 ± 8	6–54
BPRS-total score	28 ± 4	21–35
Systolic blood pressure, mm Hg	122 ± 16	83–178
Diastolic blood pressure, mm Hg	78 ± 11	52–124
Weight, kg	82.9 ± 15.3	46.8–131.3
Body mass index (kg/m^2)	28.4 ± 4.0	20.5–35.4
Fasting plasma glucose, mg/dL	95 ± 10	70–124
Fasting serum insulin, μIU/mL	13.5 ± 8.4	2.6–59.5
HOMA-IR	3.2 ± 2.2	0.53–15.5
Hemoglobin A_{1c} (%)	5.6 ± 0.6	4.2–9.6
Total cholesterol, mg/dL	204 ± 42	85–364
HDL, mg/dL	44 ± 13	17–87
LDL, mg/dL	121 ± 36	37–259
Triglyceride, mg/dL	177 ± 115	31–849
Triglyceride/HDL ratio	4.7 ± 4.0	0.8–28.3
LDL particle size, nm	20.8 ± 0.76	19.0–22.0
	n	%
Gender		
Male	113	55
Female	93	45
Race		
Caucasian	123	59.7
African American	60	29.1
Hispanic	9	4.4
Asian	8	3.9
Other	6	2.9
Family history of diabetes[a]		
Yes	41	19.9
No	155	75.2
Antidepressant agents		
Yes	100	48.5
No	106	51.5
Mood stabilizer		
Yes	51	24.8
No	155	75.2
Benzodiazepine		
Yes	49	23.8
No	157	76.2

[a]Ten patients had missing information on family history of diabetes.
Abbreviations: BPRS = Brief Psychiatric Rating Scale, HDL = high-density lipoprotein, HOMA-IR = homeostasis model of assessment of insulin resistance, LDL = low-density lipoprotein.

One major goal of this analysis was to examine the relative predictive power of different conventionally available lipid parameters for the development of insulin resistance. Figure 1 shows that all 4 lipid parameters were significantly correlated with HOMA-IR ($P = .023$ for LDL, $P < .001$ for HDL, triglyceride, and the triglyceride/HDL ratio). A stepwise multiple regression model was developed to identify relevant lipid predictors of HOMA-IR when other important potential confounding variables, including age, gender, race, family history of diabetes, body mass index (BMI), and antipsychotic agent, were also taken into consideration. Only BMI and the triglyceride/HDL ratio entered into the regression model (Table 2). No other lipid variables, including LDL, HDL, or triglyceride, entered into the regression model. Body mass index, which entered into the model as the first predictor, explained 24% variability of HOMA-IR ($P < .001$). The triglyceride/DL ratio predicted an additional 6% variability of HOMA-IR ($P < .001$). The overall regression model indicated that higher BMI and a higher triglyceride/HDL ratio predict increased HOMA-IR ($P < .001$).

Another goal was to examine whether or not conventionally available lipid parameters can predict LDL particle size or the existence of pattern B LDL phenotype. Figure 2 shows that 3 lipid parameters (HDL, triglyceride, the triglyceride/HDL ratio) were significantly correlated with LDL particle size ($P < .001$). However, there was not a significant correlation between conventional LDL measure and LDL particle size ($P = .281$). A stepwise multiple regression model was developed to identify relevant lipid predictors of LDL particle size. With other important potential confounding variables, including age, gender, race, family history of diabetes, BMI, and antipsychotic agent, also considered as candidate predictors, only the triglyceride/HDL ratio and gender entered into the regression model (Table 3). No other lipid variables, including LDL, HDL, or triglyceride, entered into the regression model. The triglyceride/HDL ratio entered into the model as the first predictor, explaining 57% variability of LDL particle size ($P < .001$). Gender predicted an additional 3% variability of LDL particle size ($P = .001$). The overall regression model indicated that a higher triglyceride/HDL

Figure 1. Correlations Between Lipid Measures and HOMA-IR[a] (n = 206)



[a]The HOMA-IR was calculated by the following formula: fasting plasma glucose (mg/dL) × fasting serum insulin (μU/mL)/405.
Abbreviations: HDL = high-density lipoprotein, HOMA-IR = homeostasis model of assessment of insulin resistance, LDL = low-density lipoprotein.

Table 2. Stepwise Multiple Regression: Triglyceride/HDL Ratio Predicting HOMA-IR[a]

Predictor Variable[b]	R^2 Change	*df*	*F* Change	*P*
Step 1: BMI	0.24	1,188	59.0	< .001
Step 2: Triglyceride/HDL ratio[c]	0.06	1,187	17.3	< .001

[a]Final regression model equation with unstandardized coefficients: HOMA-IR (log transformed) = −0.42 + 0.03 × BMI + 0.22 × triglyceride/HDL ratio (log transformed). Standard errors corresponding to unstandardized coefficients are 0.11, 0.004, and 0.05 for constant, BMI, and triglyceride/HDL ratio, respectively. For the final regression model, adjusted $R^2 = 0.30$, $F_{1,187} = 40.7$, $P < .001$.
[b]Candidate predictor variables included age, gender, race, family history of diabetes, BMI, antipsychotic agent, triglyceride, LDL, HDL, and triglyceride/HDL ratio.
[c]Triglyceride, triglyceride/HDL ratio, and HOMA-IR were log transformed.
Abbreviations: BMI = body mass index, HDL = high-density lipoprotein, HOMA-IR = homeostasis model of assessment of insulin resistance, LDL = low-density lipoprotein.

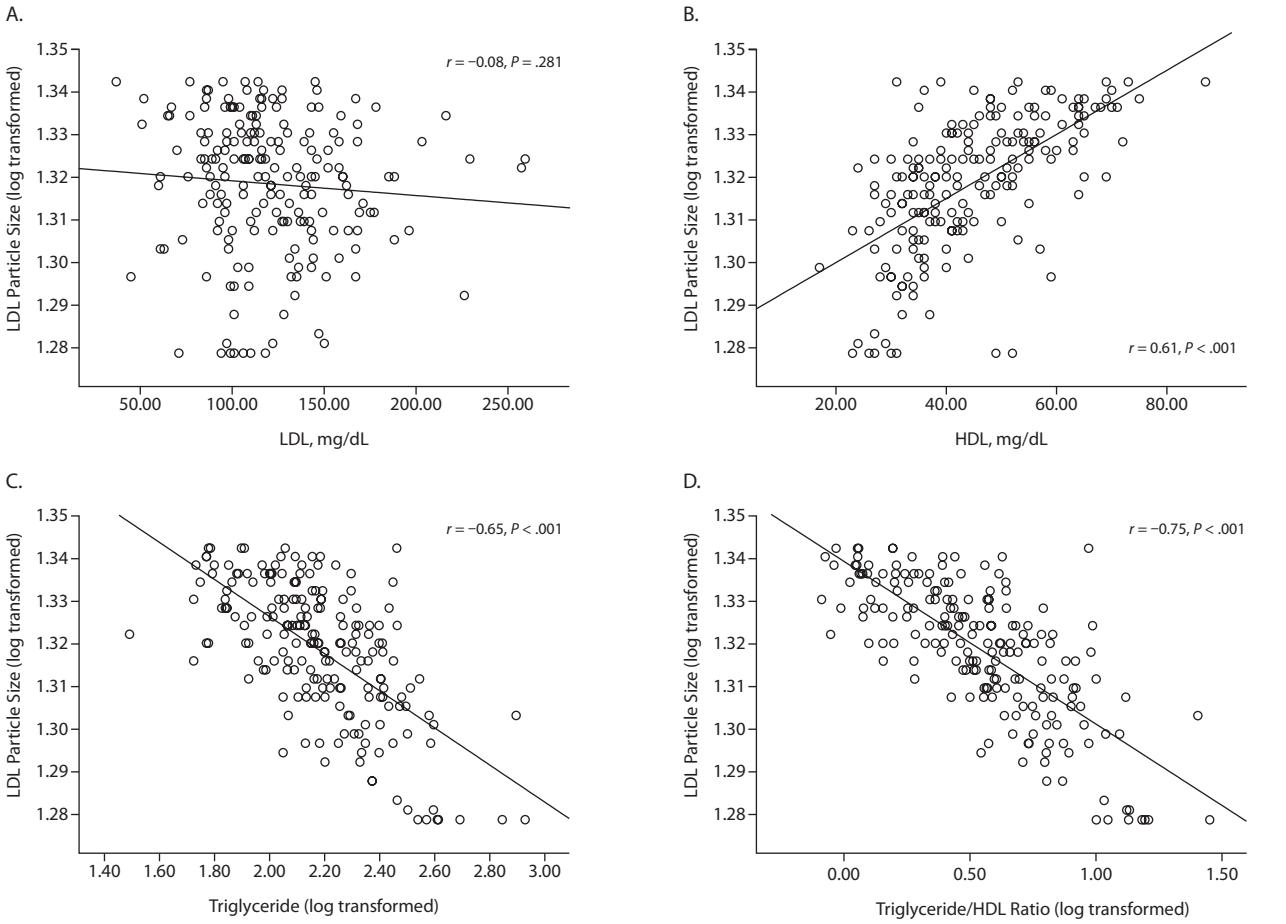
ratio and male gender predict a smaller LDL particle size ($P < .001$).

Among 195 patients with LDL particle size measures, 64 (32.8%) had pattern B LDL phenotype. A logistic regression model was developed, with the triglyceride/HDL ratio and gender predicting the existence of pattern B LDL phenotype (Table 4). With a probability cutoff point of 0.5 (corresponding to a triglyceride/HDL ratio cutoff point 5.5 for male, 6.6 for female), the logistic regression model correctly classified 161 of 195 patients (82.6%), with a sensitivity of 75.9% (probability of predicting pattern B when the subject actually had pattern B) and a specificity of 85.4% (probability of predicting pattern A when the patient actually had pattern A). The model appeared to appropriately fit the data (Hosmer-Lemeshow test $P = .98$), indicating no reason to reject the model. The ROC curve for a range of probability cutoff points is presented in Figure 3. The total area under the ROC curve was estimated to be 0.90 (95% CI, 0.85–0.94). The area under the curve may be interpreted as the probability that the predictions and outcomes are concordant. For example, a value of 0.50 means that the predictions were no better than guessing, whereas a value of 1.0 would indicate perfect prediction.

DISCUSSION

Insulin resistance has been associated with the development of changes in metabolic parameters and cardiovascular disease.[7,9] In past decades, various clinical characteristics, such as obesity, age, gender, race/ethnicity, a family history of diabetes, and lipid abnormalities, have been identified as predictors for insulin resistance.[38–40] Among conventional

Figure 2. Correlations Between Lipid Measures and LDL Mean Particle Size (n = 195)



Abbreviations: HDL=high-density lipoprotein, LDL=low-density lipoprotein.

Table 3. Stepwise Multiple Regression: Triglyceride/HDL Ratio Predicting LDL Particle Size[a]

Predictor Variable[b]	R^2 Change	*df*	*F* Change	*P*
Step 1: Triglyceride/HDL ratio[c]	0.57	1,181	237.2	<.001
Step 2: Gender (1 = female, 2 = male)	0.03	1,180	10.9	.001

[a]Final regression model equation with unstandardized coefficients: LDL mean particle size (log transformed) = 1.35 – 0.04 × triglyceride/HDL ratio (log transformed) – 0.01 × gender. Standard errors corresponding to unstandardized coefficients are 0.003, 0.002, and 0.002 for constant, triglyceride/HDL ratio, and gender, respectively. For the final regression model, adjusted $R^2 = 0.59$, $F_{2,180} = 130.6$, $P < .001$.
[b]Candidate predictor variables included age, gender, race, family history of diabetes, BMI, antipsychotic agent, triglyceride, LDL, HDL, and triglyceride/HDL ratio.
[c]Triglyceride, triglyceride/HDL ratio, and LDL particle size were log transformed.
Abbreviations: BMI = body mass index, HDL = high-density lipoprotein, LDL = low-density lipoprotein.

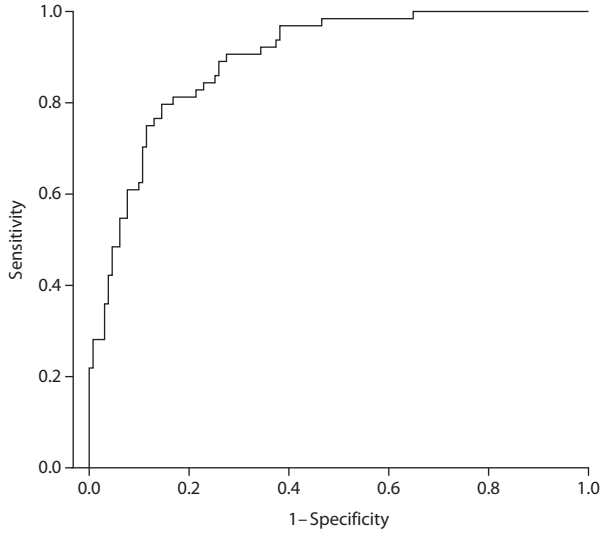
Table 4. Logistic Regression: Triglyceride/HDL Ratio Predicting Small LDL Particle Size (pattern B)[a]

Predictor Variable	β	SE	Wald	*df*	*P*	Odds Ratio	95% CI
Triglyceride/HDL ratio[b]	7.7	1.2	43.5	1	<.001	2,278.6	229.0–22,667.7
Gender (1 = female, 2 = male)	0.6	0.4	1.7	1	<.188	1.8	0.8–4.0
Constant	–6.4	1.1	34.4	1	<.001	0.002	

[a]Small LDL particle size (pattern B): 0 = no, 1 = yes.
[b]Triglyceride/HDL ratio was log transformed.
Abbreviations: HDL = high-density lipoprotein, LDL = low-density lipoprotein, SE = standard error.

lipid measures, plasma LDL, HDL, and triglyceride levels are associated with insulin resistance[41] and cardiovascular disease.[42,43] In recent years, the triglyceride/HDL ratio has emerged as a newer predictor of insulin resistance. A study of 258 nondiabetic, normotensive, overweight patients found that the triglyceride/HDL ratio was a useful surrogate to identify insulin resistance.[27] Another study of 1,135 patients in good general health reported that the triglyceride/HDL ratio was the more effective predictor of insulin resistance as measured by the insulin suppression test compared to other conventional lipid measures (LDL, HDL, and triglyceride) (McLaughlin et al[26]). A study of 125 nondiabetic African Americans reported that the triglyceride/HDL ratio was not a reliable marker of insulin resistance as measured by frequently sampled intravenous glucose tolerance test.[44] However, a study in 185 nondiabetic African Americans found a significant correlation between the triglyceride/HDL ratio and insulin sensitivity as measured by the clamp technique; the relationship was stronger in men than in women.[28]

Figure 3. Receiver Operating Characteristic Curve for Model of Small Size LDL (Pattern B) Versus Large Size LDL (Pattern A)[a]



[a]Model corresponds to Table 4.

Our results in nondiabetic patients with schizophrenia are consistent with most previous findings, indicating that the triglyceride/HDL ratio is a stronger predictor of insulin resistance as measured by HOMA-IR compared to other conventional lipid measures (LDL, HDL, triglyceride); and further, the predictive value of triglyceride/HDL ratio for insulin resistance is independent of age, gender, race, family history of diabetes, BMI, or antipsychotic agent.

A predominance of small, dense LDL subclass particles (pattern B) is more prevalent among men than women.[45] The presence of smaller LDL particles is also associated with older age.[46] In a study of 658 outpatients followed at cardiology clinics, men had significantly smaller LDL particle size than women; LDL particle size correlated with the triglyceride/HDL ratio better than with either triglyceride or HDL alone; further, no clinical variables other than the triglyceride/HDL ratio were significant in the logistic regression model analysis for the prediction of pattern B LDL phenotype; and a triglyceride/HDL ratio of ≥ 3.8 had 79% sensitivity and 81% specificity.[32] In the McLaughlin et al study[26] mentioned earlier, the triglyceride/HDL ratio was also the more effective predictor for LDL particle size compared to other conventional lipid measures. In a recent study[33] of 146 relatively healthy Asian Indians, the triglyceride/HDL ratio correlated inversely with the LDL size; the triglyceride/HDL ratio was a better surrogate for LDL particle size than triglyceride or HDL levels; and a triglyceride/HDL ratio of ≥ 3.8 had 76% sensitivity and 93% specificity in predicting pattern B LDL phenotype. In another recent study of 150 patients without diabetes or cardiovascular disease, Tsimihodimos et al[47] found that the triglyceride/HDL ratio is the more effective predictor among various clinical parameters for the presence of pattern B LDL phenotype. Consistent with previous findings, our results suggest that the triglyceride/HDL ratio is a better predictor of LDL particle size than LDL, HDL, or triglyceride in nondiabetic patients with schizophrenia; and a higher triglyceride/HDL ratio and male gender are associated with a smaller LDL particle size. In our study sample, a triglyceride/HDL ratio of 5.5 in men and 6.6 in women had 75.9% sensitivity and 85.4% specificity in predicting pattern B LDL phenotype. The sensitivity and specificity are similar to those reported in other studies. However, the optimal triglyceride/HDL ratios in predicting pattern B LDL phenotype seem to be higher in our study sample than those reported in nonpsychiatric populations.

To our knowledge, this is the first study examining the usefulness of triglyceride/HDL ratio in predicting insulin resistance and LDL particle size in the schizophrenia population. The triglyceride/HDL ratio seems to not only provide an estimate of insulin resistance but also identify patients who have an atherogenic lipoprotein profile. The triglyceride/HDL ratio, a simple, readily available, and inexpensive calculated measure, could help clinicians identify patients who may be at higher risk of metabolic disturbances and cardiovascular diseases and allow for early interventions.

The strengths of the present study include the relatively large sample size and the reliable fasting condition for blood sample collection. A major limitation is that HOMA-IR itself is a surrogate measure for insulin resistance, largely a function of fasting insulin values. While HOMA is a valid method to measure insulin resistance in clinical and epidemiologic studies, it is not as definitive as more labor-intensive measures of insulin resistance, such as the clamp technique or frequently sampled intravenous glucose tolerance test.[48] The exclusion of patients with possibly undiagnosed diabetes and the lack of patients on other atypical antipsychotic agents (such as quetiapine, ziprasidone and aripiprazole) may limit the generalizability of the results to the entire schizophrenia population. Finally, any causal relationship cannot be drawn based on the cross-sectional study design. The clinical utility of our findings needs to be confirmed, and the optimal cutoff point of triglyceride/HDL ratio needs to be established in large prospective studies, especially in relation to individual antipsychotic agents.

Drug names: aripiprazole (Abilify), clozapine (Clozaril, FazaClo, and others), haloperidol (Haldol and others), olanzapine (Zyprexa), quetiapine (Seroquel), risperidone (Risperdal and others), ziprasidone (Geodon).

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Author contribution: Dr Fan was responsible for the analysis and interpretation of the data for this article. All authors were responsible for the writing of the article.

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