



METABOLIC PREDICTORS IN METABOLIC DYSFUNCTION- ASSOCIATED STEATOTIC LIVER DISEASE

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Relevance of the topic

Metabolic dysfunction-associated steatotic liver disease (MASLD) has emerged as the most prevalent chronic liver pathology globally, affecting approximately 30–38% of the adult population. The updated nomenclature adopted by international hepatology societies links hepatic steatosis directly to demonstrable cardiometabolic risk factors namely overweight/obesity, type 2 diabetes mellitus, dyslipidemia, and arterial hypertension.

The natural history of MASLD ranges from isolated steatosis to metabolic dysfunction-associated steatohepatitis (MASH), progressive architectural distortion, advanced bridging fibrosis, and decompensated cirrhosis. Hepatic fibrosis represents the single most important histological determinant of liver-related morbidity and overall mortality. Although percutaneous liver biopsy remains the historical gold standard for staging, its invasiveness, sampling error, and associated procedural complications limit its utility in broad epidemiological screening. Consequently, identifying circulating metabolic indices and surrogate biomarkers of fibrogenesis has become a clinical imperative. This investigation aims to evaluate the predictive utility of surrogate metabolic markers, specifically the triglyceride-glucose (TyG) index, HOMA-IR, and systemic inflammatory parameters, in determining the severity and progression of fibrosis in patients with MASLD.

Materials and Methods

A cross-sectional observational study was conducted at the clinical base between January 2024 and December 2026. A total of 134 patients meeting the



diagnostic consensus criteria for MASLD were prospectively enrolled. Inclusion criteria comprised:

1. Documented hepatic steatosis on abdominal ultrasonography (grades I–III);
2. Presence of at least one of the five recognized cardiometabolic criteria (elevated BMI/waist circumference, fasting hyperglycemia/T2DM, hypertriglyceridemia, low HDL-C, or hypertension).

Exclusion criteria included secondary etiologies of hepatic steatosis: significant alcohol consumption (> 20 g/day for females, > 30 g/day for males), chronic viral hepatitis (HBV, HCV, HDV), autoimmune hepatitis, drug-induced liver injury, and storage disorders. An age- and sex-matched cohort of 45 healthy individuals without steatosis or metabolic syndrome served as controls.

Venous blood samples were collected following a 12-hour overnight fast. Serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), gamma-glutamyl transferase (GGT), total cholesterol, triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), and fasting plasma glucose (FPG) were determined via standardized enzymatic methods on an automated clinical chemistry analyzer. Fasting serum insulin was measured by electrochemiluminescence immunoassay. Insulin resistance was calculated using the Homeostatic Model Assessment of Insulin Resistance.

Statistical Analysis

Continuous parameters are expressed as mean $\pm$ standard deviation (SD) for normally distributed variables, or median with interquartile range (IQR) for skewed data. Categorical variables are reported as frequencies and percentages (n, %). Group differences were tested using Student's independent t-test or Mann-Whitney U test, and the Chi-square test for categorical variables. Multivariate logistic regression analysis was conducted to establish independent predictors of advanced fibrosis (F3). Receiver operating characteristic (ROC)



curves were constructed to determine discriminatory performance (area under the curve, AUC). Statistical significance was defined as two-tailed $p < 0.05$.

Results

The clinical, biochemical, and demographic parameters of the study cohorts are summarized. Patients with MASLD demonstrated marked metabolic dysregulation, manifested by significant increments in lipid accumulation and systemic insulin resistance.

Among the 134 MASLD patients, transient elastography categorized fibrosis as: F0–F1 in 62 patients (46.3%), F2 in 36 patients (26.9%), and advanced fibrosis (F 3) in 36 patients (26.8%). A subgroup analysis comparing MASLD patients with mild-to-moderate fibrosis (F0–F2) versus advanced fibrosis (F3–F4) indicated that the latter group presented with substantially higher TyG index values (9.62 ± 0.54 vs. 8.95 ± 0.48 , $p < 0.001$) and higher median HOMA-IR (5.86 vs. 4.12, $p < 0.001$).

ROC curve analysis revealed that the TyG index exhibited an area under the curve (AUC) of 0.824 (95% CI: 0.748–0.900) for predicting advanced fibrosis, outperforming HOMA-IR alone (AUC: 0.762, 95% CI: 0.675–0.849). A TyG cutoff value of 9.30 achieved a sensitivity of 77.8% and a specificity of 76.5%.

Conclusion

Metabolic dysfunction is inextricably linked to the progression of hepatic architectural distortion in MASLD. The TyG index and HOMA-IR serve as robust, accessible, and non-invasive metabolic predictors of advanced liver fibrosis. Integrating routine computational indices like the TyG index into outpatient clinical algorithms improves risk stratification, facilitating timely therapeutic lifestyle and pharmacological interventions before irreversible fibrotic injury occurs.



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