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The association between estimated glucose disposal rate and metabolic dysfunction-associated steatotic liver disease and liver fibrosis in US adults

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Abstract

Background Metabolic dysfunction-associated steatotic liver disease (MASLD) is the most common chronic liver disease, also considered a metabolic syndrome, and is associated with poor prognosis. eGDR (estimated glucose disposal rate) is a new biomarker to assessment insulin resistance (IR). The association between eGDR and MASLD and liver fibrosis is currently unclear.

Objective The aim of this cross-sectional study is to appraise the association between eGDR and MASLD and liver fibrosis.

Methods This study have enrolled 3,100 participants from the 2017–2018 National Health and Nutrition Examination Surveys (NHANES). Binary logistic regression analysis was used to assess the association between eGDR and MASLD and liver fibrosis. Receiver operating characteristic (ROC) was applied to estimate the ability of eGDR to identify MASLD.

Results The mean age of the subjects was 54.59 (17.29) years, and 49.26% were female. The prevalence of MASLD and liver fibrosis was 62.19% and 11.15%, respectively. In the fully adjusted models, there were negative associations of eGDR with the controlled attenuation parameter (CAP) and liver stiffness measurement (LSM), with βs of -15.18 and −0.74 (all $p < 0.01$), respectively. There were negative associations of eGDR with MASLD and liver fibrosis, with odds ratios (ORs) and 95% confidence intervals of 0.53 (95% CI: 0.48–0.74) and 0.40 (95% CI: 0.28–0.57) (all $p < 0.01$). The area under the curve (AUC) of the eGDR for identifying MASLD and liver fibrosis is 0.74 and 0.75, respectively.

Conclusion The study findings suggest a significant association between eGDR and MASLD as well as liver fibrosis. eGDR may serve as a biomarker for identifying MASLD.

Keywords Insulin resistance, Estimated glucose disposal rate, Nonalcoholic fatty liver disease, Liver fibrosis

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Introduction

Non-alcoholic fatty liver disease (MASLD) is featured by hepatic steatosis in without other liver disease etiologies, alcohol consumption, or viral hepatitis [1]. This heterogeneous disorder includes simple steatosis, non-alcoholic steatohepatitis, liver fibrosis, cirrhosis, and hepatocellular carcinoma [2]. With a global prevalence of approximately 30% in adults, and it has become the most prevalent cause of chronic liver disease [3]. MASLD has been recognized as a metabolic disease [4] and has a significant association with type 2 diabetes, obesity, hypertension, dyslipidemia, and cardiovascular disease [5]. MASLD can increase all-cause mortality, with the main cause being non-hepatic comorbidities and their complications [6]. Additionally, cardiovascular events are the most common attributable cause of death in MASLD [7]. Given its significant impact on public health, a comprehensive understanding of MASLD is essential.

The gold standard for diagnosis and staging of MASLD is liver biopsy, which is restricted due to its shortcomings such as its invasive nature, sampling error, and expense [8]. At present, ultrasound is routinely applied for detecting MASLD in clinical practice. Nonetheless, ultrasound has poor sensitivity for mild steatosis [9]. Therefore, there is an eager need for the development of a method to diagnose MASLD.

There is evidence that insulin resistance (IR) plays a crucial role in the development of MASLD and is linked with the progression of liver fibrosis [10]. IR is the most important factor for hepatic inflammation leading to fibrosis [11]. IR markers could be used to screen MASLD in the population. The gold standard for assessing of IR is the hyper-insulinemic euglycemic clamp, which is limited due to its disadvantages including cost, invasiveness, and unavailability [12]. Some studies have suggested several noninvasive methods to assess IR including homeostasis model assessment-insulin resistance (HOMA-IR), triglyceride glucose index (TyG index), and estimated glucose disposal rate (eGDR) [13]. eGDR was developed as a validated score in patients with type 1 and type 2 diabetes, using clinical factors such as waist circumference (WC) or body mass index (BMI), hypertension, and glycosylated hemoglobin A1c (HbA1c) [14]. This score has shown high precision in comparison to the euglycaemic hyperinsulinaemic clamp method [15]. Previous studies have shown that HOMA-IR and TyG index are effective predictors for MASLD [5, 16]. However, the relationship between eGDR and MASLD has not been explored in existing research. Therefore, the study aims to investigate the association between eGDR and MASLD as well as liver fibrosis in adults.

Materials and methods

Study population

The study is a cross-sectional study with data from 1 cycle (2017–2018) of the National Health and Nutrition Examination Survey (NHANES), which is designed to provide a representative sample of the non-institutionalized U.S. resident population by a stratified, multistage probability cluster design. The Research Ethics Review Board of the National Centre for Health Statistics (NCHS) approved the protocols of the NHANES study. All the NHANES participants provided informed consent [17].

The inclusion criteria of this study are as follows: (1) receive the elastography measurements; (2) age of 20 years or above. The exclusion criteria of this study as following: (1) missing the information of controlled attenuation parameter (CAP) ($N=3306$); (2) age less than 20 years ($N=1079$); (3) positive viral hepatitis B surface antigen or positive for viral hepatitis C antibodies or viral hepatitis C RNA ($N=76$); (4) excessive alcohol consumption (man drinks an average of more than 2 cup/day, female drinks an average of more than 1 cup/day) ($N=1496$); (5) missing information on BMI, HbA1c ($N=160$); and (6) the outlier of eGDR (the absolute value of z-score more than 2.4) ($N=37$). Finally, only 3100 participants were included in this study (Fig. 1).

Data collection

Demographic data [18] were collected by interviewers at mobile examination centers to gather information on general demographic characteristics, including age, gender, race, education status, marital status as well as Ratio of family income to poverty (PIR), physical activity (PA), smoking, and alcohol consumption.

BMI was accounted by weight in kilograms divided by height in meters squared [19]. After a resting period of more than five minutes, trained personnel obtained systolic blood pressure (SBP) and diastolic blood pressure (DBP) using the Omron IntelliSense Blood Pressure Monitor (HEM-907XL). The average of three readings was recorded in millimeters of mercury (mmHg) [20]. The smoking status of individuals was determined by examining their responses to surveys that inquired about their current cigarette smoking habits. Physical activity (PA) was evaluated by analyzing the intensity levels at which the subjects participated in leisure activities [21].

According to the standardized procedures to obtain the blood and urine specimens. The NHANES website has provided the detection protocols [22]. The blood samples collected at the mobile exam facility were stored at a temperature of 20 °C before being sent to the central labs. Standard methods were used in the labs to measure various components such as total cholesterol (TC), high-density lipoprotein cholesterol (HDL), Glycosylated hemoglobin A1c (HbA1c), uric acid (UA), creatinine

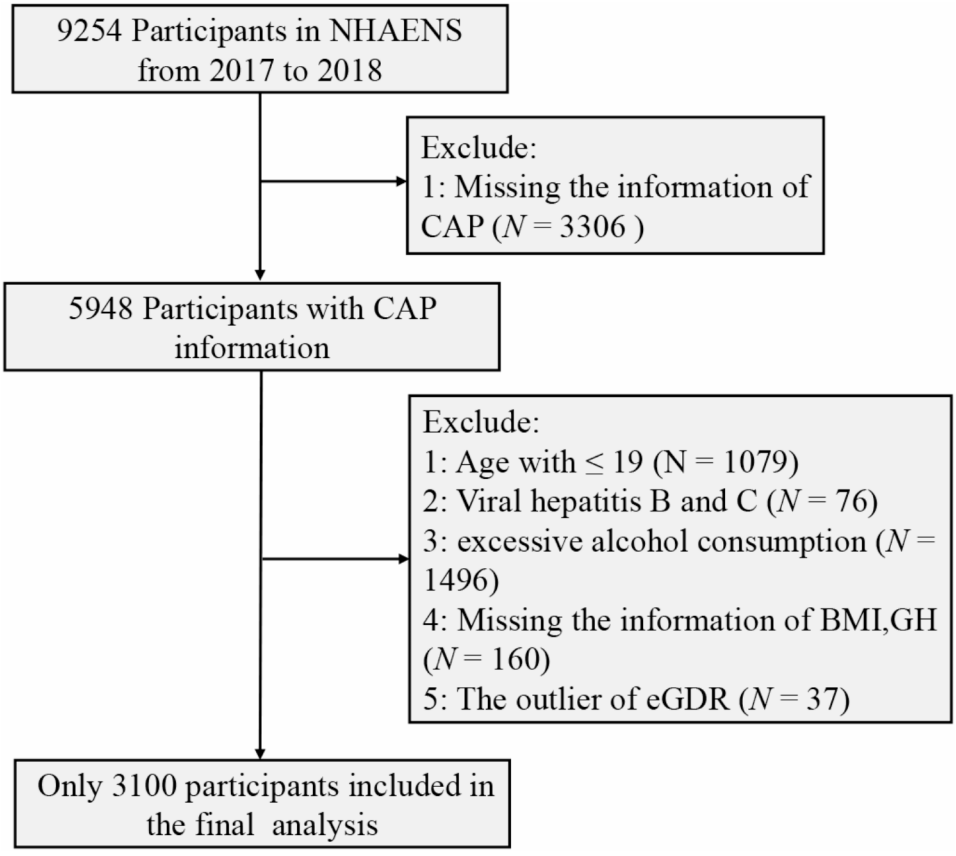

Fig. 1 Flow chart of study selection for this study
Abbreviations: NHANES: National Health and Nutrition Examination Survey; CAP: Controlled attenuation parameter; BMI: Body mass index; GH: Glycosylated hemoglobin A1c; eGDR: Estimated glucose disposal rate

(CR), alanine aminotransferase (ALT), and aspartate aminotransferase (AST). For the evaluation of fasting triglycerides, low-density lipoprotein cholesterol (LDL-C), and glucose, blood samples were taken after an 8–12 h fasting period [23], but this was only done for a specific group of individuals in the survey.

Hypertension was defined as SBP ≥ 140 mm Hg and/or DBP ≥ 90 mm Hg, taking antihypertensive medications, or having a previous diagnosis of hypertension [24]. Diabetes mellitus was defined as fasting glucose levels ≥ 7.0 mmol/L [25], taking hypoglycemic medications, or having a previous diagnosis of diabetes. Dyslipidemia was defined as TC levels ≥ 240 mg/dL (6.2 mmol/L) [26], taking lipid-lowering drugs, or having a previous diagnosis of dyslipidemia. The algorithm developed by the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) was employed to calculate the estimated glomerular filtration rate (eGFR) [27].

Definition of nonalcoholic fatty liver disease and liver fibrosis

The vibration-controlled transient elastography (VCTE) of participants was evaluated by experienced NHANES staff using the FibroScan 502 Touch device [28]. The CAP was applied to evaluate hepatic steatosis, while liver stiffness measurement (LSM) was used to assess hepatic fibrosis in the VCTE report. A cut-off value of 248 dB/m for CAP was utilized for the diagnosis of MASLD [29], and the cut-off value of 7.9 kPa for LSM was used for the diagnosis of Liver fibrosis [30].

Study variables

In this study, the formula eGDR = 19.02 – (0.22 * BMI) – (3.26 * hypertension) – (0.61 * HbA1c) was used to calculate eGDR (mg/kg/min) as previously described [31].

BMI represents body mass index (kg/m2), hypertension is indicated as 1 for yes and 0 for no, and HbA1c represents HbA1c (DCCT %).

Covariate

The covariates of this study include age, gender, race (Mexican American, other Hispanic, Non-Hispanic White, Non-Hispanic Black, other Race), marital status (married, never married, other), education status (primary school graduate or below, middle/high/special school, and college graduate or above), PIR (low,

moderate, high), fasting glucose, ALT, AST, eGFR, HLD-C, UA, diabetes mellitus, dyslipidemia, moderate PA, and smoking status (never smoke, former smoke, current smoking).

Statistical analyses

In this study, continuous and categorical variables were presented as quantitative variables, and qualitative variables were presented as median ± standard deviation (SD) and frequency percentages. The categorical variable of eGDR was categorized into quartiles: Q1 (≤ 4.87), Q2 (4.87–6.49), Q3 (6.49–9.31), and Q4 (≥ 9.31). And the participants were divided into four groups based on eGDR quartiles. The Kruskal–Wallis H test was used to assess differences among the four groups for continuous variables, while the chi-squared test was employed for categorical variables.

The Pearson correlation coefficient was used to assess the correlation between eGDR and CAP and LSM. Binary logistic regression analysis was employed to examine the association between eGDR and MASLD and liver fibrosis, with odds ratios (ORs) and 95% confidence intervals (CIs) used to present the results. Three models were defined based on the adjustment of factors. The Crude Model was unadjusted for any factors. Model I was adjusted for age, gender, race, marital status, education, PIR, fasting glucose, ALT, AST, eGFR, HDL-C, and UA. Model II was adjusted for the variables in Model I as well as diabetes mellitus, dyslipidemia, moderate PA, and smoking status. Additionally, the non-linear relationship between eGDR and MASLD and liver fibrosis was assessed using restricted cubic spline curves.

We conducted a subgroup analysis to assess the robustness of the results. The pre-specified potential effect modifiers were gender, age, eGFR, PIR, marital status, diabetes mellitus, dyslipidemia, moderate PA, and smoking status. These stratified factors led to the division of participants into different subgroups. We used the area under the receiver operating characteristic curve (AUROC) to test the predictive ability of eGDR for MASLD and liver fibrosis. We set the significance level at less than 0.05. We used the R software version 4.1.3 (www.R-project.org) and SPSS software (version 20; IBM Corp., Armonk, NY, USA) for data analysis.

Results

Characteristics of participants

After excluding participants with a missing CAP value, age less than 19, excessive alcohol consumption, viral hepatitis, a missed BMI, HbA1c, and an outlier of eGDR, the final analysis of this study included 3100 subjects (Fig. 1). Table 1 summarizes the clinic characteristics of the participants. The mean age of the subjects was 54.59 (17.29) years, and 49.26% were female. The prevalence of MASLD and liver fibrosis was 62.19% and 11.15%, respectively. The prevalence of MASLD and liver fibrosis, as well as CAP and LSM, increased with higher eGDR values ($p < 0.05$). We observed significant differences among the four groups in terms of age, gender, BMI, DBP, SBP, smoking status, race, marital status, education status, PIR, TC, TG, and HDL-C. Additionally, fasting glucose, Cr, eGFR, UA, HbA1c, AST, ALT, hypertension, diabetes, and dyslipidemia all showed significant differences ($p < 0.05$). However, LDL-C and PA did not exhibit significant differences across the eGDR quartiles ($p > 0.05$) (Table 1).

The eGDR association with CAP and LSM

As shown in Fig. 2, The eGDR and CAP showed a moderately negative linear correlation (r = -0.48, $P < 0.01$), and the eGDR and LSM showed a mildly negative linear correlation (r = -0.22, $P < 0.01$). We first assessed the association between eGDR and the CAP and LSM in a crude model. Higher eGDR was negatively correlated with CAP and LSM. The continuous variable analysis showed a negative association between eGDR, CAP, and LSM. After full adjustment, we found that an increase in each unit of eGDR was associated with a CAP decrease of 15.18 dB/m and an LSM decrease of 0.74 kPa. We regarded the eGDR as a categorical variable. Trend testing revealed a significant linear relationship between eGDR and CAP, and LSM in all three models (all p for trend < 0.05) (Table 2).

Association between the eGDR and MASLD

As depicted in Table 3, the crude model revealed a significant association between eGDR quartiles and MASLD. Participants in quartiles 2, 3, and 4 had ORs of 0.26 (95%CI: 0.19–0.33), 0.18 (95%CI: 0.14–0.24), and 0.07 (95%CI: 0.05–0.09) respectively, compared to quartile 1. In the fully adjustment model, participants in quartiles 2, 3, and 4 still showed a notable association with MASLD, with ORs of 0.54 (95%CI: 0.32–0.89), 0.51 (95%CI:0.30–0.86), and 0.25 (95%CI:0.14–0.45) respectively. Furthermore, the analysis of continuous variables (per 1 SD increase) indicated a significant association between eGDR and decreased risk of MASLD, with an OR of 0.53 (95%CI: 0.48–0.74) after full adjustments.

Association between the eGDR and liver fibrosis

The study findings presented in Table 3 demonstrate a strong association between eGDR quartiles and liver fibrosis. Participants in quartiles 2, 3, and 4 exhibited ORs of 0.26 (95%CI: 0.19–0.44), 0.25 (95%CI: 0.18–0.33), and 0.06 (95%CI: 0.03–0.10) respectively, when compared to quartile 1. In the fully adjustment model, participants in quartiles 2, 3, and 4 continued to display a significant association with MASLD, showing ORs of 0.41 (95%CI: 0.23–0.72), 0.28 (95%CI: 0.14–0.54), and 0.12 (95%CI:

Table 1 Baseline characteristics by the quartiles of estimated glucose disposal rate of adult Americans from the nation health and nutrition examination survey 2017–2018

Characteristics	Total *N* = 3100	eGDR mg/kg/min				*P*
		< 4.87 *N* = 773	4.87–6.49 *N* = 777	6.49–9.31 *N* = 775	≥ 9.31 *N* = 775	
Age, year	54.59 (17.29)	59.48 (13.95)	60.59 (14.96)	54.42 (17.98)	43.87 (16.73)	< 0.01
Female, % (n)	1527 (49.26)	408 (52.78)	352 (45.30)	372 (48.00)	395 (50.97)	0.02
BMI, kg/m^2	29.35 (6.65)	36.51 (5.99)	28.61 (3.99)	28.15 (5.94)	24.13 (3.12)	< 0.01
DBP, mm Hg	71.85 (12.30)	73.93 (13.30)	74.49 (13.24)	71.40 (11.76)	67.18 (8.78)	< 0.01
SBP, mm Hg	127.35 (19.26)	135.22 (17.34)	135.49 (18.53)	126.37 (18.84)	110.95 (9.19)	< 0.01
Smoke status, n (%)						< 0.01
Never smoke	1938 (62.52)	442 (57.18)	470 (60.49)	486 (62.71)	540 (69.68)	
Former smoke	389 (12.55)	78 (10.09)	94 (12.10)	108 (13.94)	109 (14.06)	
Current smoking	773 (24.94)	253 (32.73)	213 (27.41)	181 (23.35)	126 (16.26)	
Race, n (%)						< 0.001
Mexican American	363 (11.71)	94 (12.16)	95 (12.23)	90 (11.61)	84 (10.84)	
Other Hispanic	280 (9.03)	66 (8.54)	65 (8.37)	67 (8.65)	82 (10.58)	
Non-Hispanic White	1054 (34.00)	278 (35.96)	258 (33.20)	277 (35.74)	241 (31.10)	
Non-Hispanic Black	714 (23.03)	238 (30.79)	170 (21.88)	162 (20.90)	144 (18.58)	
Other Race	689 (22.23)	97 (12.55)	189 (24.32)	179 (23.10)	224 (28.90)	
Marital status, n (%)						0.001
Never married	475 (15.35)	77 (9.97)	89 (11.45)	116 (15.03)	193 (24.94)	
Married	1717 (55.48)	435 (56.35)	457 (58.82)	408 (52.85)	417 (53.88)	
Other	903 (29.18)	260 (33.68)	231 (29.73)	248 (32.12)	164 (21.19)	
Education status, n (%)						0.012
Primary school graduate or below	291 (9.41)	83 (10.75)	77 (9.96)	70 (9.06)	61 (7.88)	
Middle/high/special school	1053 (34.06)	268 (34.72)	252 (32.60)	295 (38.16)	238 (30.75)	
College graduate or above	1748 (56.53)	421 (54.53)	444 (57.44)	408 (52.78)	475 (61.37)	
PIR, n (%)						0.001
Low	722 (26.83)	179 (26.72)	165 (24.05)	186 (28.57)	192 (28.07)	
Moderate	1113 (41.36)	305 (45.52)	296 (43.15)	272 (41.78)	240 (35.09)	
High	856 (31.81)	186 (27.76)	225 (32.80)	193 (29.65)	252 (36.84)	
Physical activity						
Moderate, n (%)	1243 (40.10)	332 (42.95)	295 (37.97)	307 (39.61)	309 (39.87)	0.095
Vigorous, n (%)	676 (21.81)	185 (23.93)	147 (18.92)	181 (23.35)	163 (21.03)	0.346
Laboratory results						
TC, mmol/L	4.86 (1.06)	4.74 (1.07)	4.98 (1.10)	4.94 (1.06)	4.80 (1.01)	< 0.001
TG, mmol/L	1.30 (1.28)	1.60 (1.49)	1.37 (0.95)	1.29 (1.73)	0.98 (0.64)	< 0.001
HDL-C, mmol/L	1.36 (0.38)	1.23 (0.32)	1.36 (0.37)	1.38 (0.41)	1.45 (0.37)	< 0.001
LDL-C, mmol/L	2.88 (0.95)	2.78 (1.00)	2.95 (0.99)	2.94 (0.90)	2.85 (0.88)	0.054
Fasting glucose, mmol/L	6.38 (2.05)	7.68 (3.13)	6.40 (1.74)	5.97 (1.07)	5.57 (0.87)	< 0.001
Cr, umol/L	82.31 (47.28)	87.96 (70.81)	86.73 (48.05)	80.01 (34.07)	74.47 (18.40)	< 0.001
eGFR, ml/min/1.73m2	105.59 (44.48)	122.14 (52.06)	93.12 (40.82)	105.23 (47.49)	101.92 (28.95)	< 0.001
eGDR, mg/kg/min	6.83 (2.73)	3.39 (1.16)	5.71 (0.46)	7.80 (0.88)	10.41 (0.72)	< 0.001
UA, umol/L	327.32 (87.52)	355.37 (91.16)	338.36 (88.32)	319.54 (82.17)	295.72 (76.37)	< 0.001
HbA1c, %	5.94 (1.12)	6.73 (1.60)	5.93 (0.91)	5.70 (0.72)	5.40 (0.42)	< 0.001
AST, U/L	21.29 (10.35)	21.78 (12.69)	21.64 (10.19)	21.35 (9.73)	20.38 (8.27)	0.038
ALT, U/L	21.38 (14.43)	23.50 (16.88)	21.73 (12.88)	21.60 (15.60)	18.66 (11.29)	< 0.001
CAP, dB/m	267.25 (62.34)	310.79 (55.01)	270.58 (55.12)	260.25 (58.97)	227.47 (49.81)	< 0.001
LSM, kPa	5.91 (4.90)	7.62 (6.56)	5.68 (3.98)	5.53 (4.12)	4.84 (4.02)	< 0.001
Disease						
Hypertension, n (%)	1806 (58.26)	746 (96.51)	729 (93.82)	331 (42.71)	0 (0.00)	< 0.001
Diabetes, n (%)	606 (19.55)	336 (43.47)	157 (20.21)	87 (11.23)	26 (3.35)	< 0.001
Dyslipidemia, n (%)	1505 (48.55)	481 (62.23)	465 (59.85)	349 (45.03)	210 (27.10)	< 0.001

Table 1 (continued)

Characteristics	Total *N* = 3100	eGDR mg/kg/min				*P*
		< 4.87 *N* = 773	4.87–6.49 *N* = 777	6.49–9.31 *N* = 775	≥ 9.31 *N* = 775	
MASLD, n (%)	1928 (62.19)	686 (88.75)	519 (66.80)	458 (59.10)	265 (34.19)	< 0.001
Liver fibrosis, n (%)	361 (11.65)	210 (27.17)	68 (8.75)	66 (8.52)	17 (2.19)	< 0.001

Note: Data are expressed as mean (SD) and numbers (percentage) as appropriate. All estimates were weighted to be nationally representative

Abbreviations: SD: standard deviation, PIR: Ratio of family income to poverty; BMI: body mass index; DBP: diastolic blood pressure; SBP: systolic blood pressure; HbA1c: glycated hemoglobin; TG: triglycerides; TC: total cholesterol; LDL-C: lower-density lipoprotein cholesterol; HDL-C: high-density lipoprotein cholesterol; ALT: Alanine aminotransferase, AST: Aspartate aminotransferase; Cr: creatinine; UA: uric acid; eGFR: estimated glomerular filtration rate; MASLD: metabolic dysfunction-associated steatotic liver disease

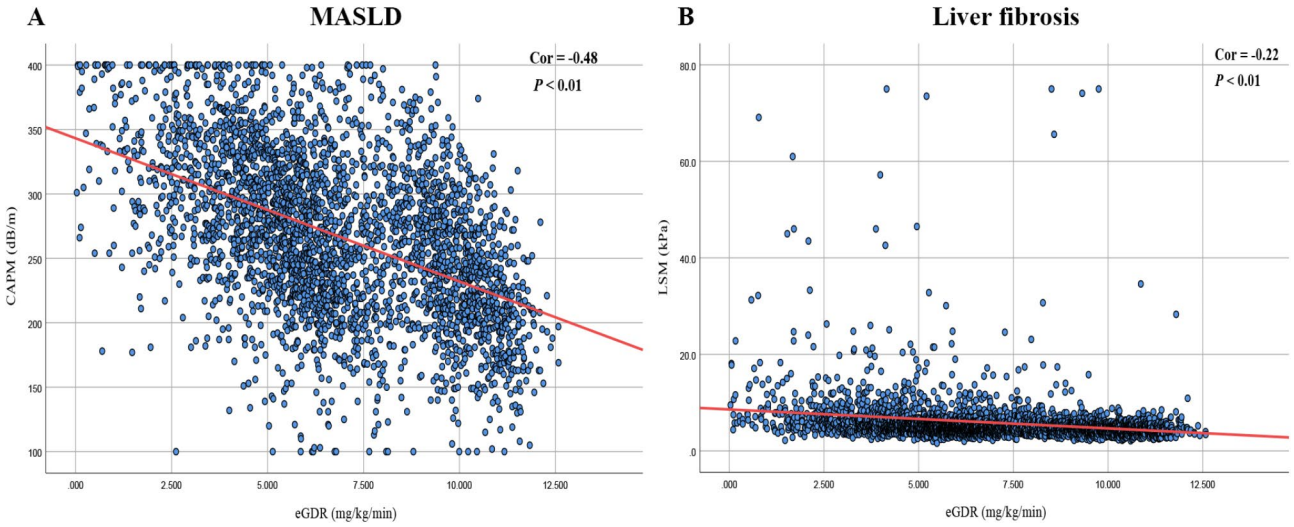

Fig. 2 The correlation between the eGDR and CAP (**A**) and LSM (**B**)
Abbreviations: eGDR: estimated glucose disposal rate; LSM: liver stiffness measurement

Table 2 Linear regression analysis between eGDR and CAP and LSM

Exposure	Crude Model β (95%CI)	*P*	Model I β (95%CI)	*P*	Model II β (95%CI)	*P*
CAP						
eGDR, Per 1 SD increase	-31.65 (-33.66, -29.64)	< 0.01	-15.90 (-19.88, -11.91)	< 0.01	-15.18 (-19.23, -11.12)	< 0.01
Quartiles						
eGDR < 4.87	Ref	1.0	Ref	1.0	Ref	1.0
eGDR 4.87–6.49	-40.21 (-45.67, -34.75)	< 0.01	-21.78 (-30.18, -13.38)	< 0.01	-21.00 (-29.56, -12.44)	< 0.01
eGDR 6.49–9.31	-50.55 (-56.01, -45.08)	< 0.01	-29.54 (-38.54, -20.54)	< 0.01	-28.17 (-37.35, -18.98)	< 0.01
eGDR ≥ 9.31	-83.32 (-88.78.-77.85)	< 0.01	-48.20 (-58.61, -37.79)	< 0.01	-46.47 (-57.06, -35,87)	< 0.01
P for trend	< 0.01		< 0.01		< 0.01	
LSM						
eGDR, Per 1 SD increase	-1.12 (-1.29, − 0.094)	< 0.01	-0.79 (-1.17, -0.42)	< 0.01	-0.74 (-1.12, -0.35)	< 0.01
Quartiles						
eGDR < 4.87	Ref	1.0	Ref	1.0	Ref	1.0
eGDR 4.87–6.49	-1.94 (-2.42, -1.46)	< 0.01	− 0.146 (-2.27, -0.64)	< 0.01	-1.30 (-2.13, -0.47)	< 0.01
eGDR 6.49–9.31	-2.09 (-2.57, -1.62)	< 0.01	-1.60 (-2.47, -0.72)	< 0.01	-1.41 (-2.30, 0.52)	< 0.01
eGDR ≥ 9.31	-2.79 (-3.26, -2.31)	< 0.01	-1.91 (-2.92, -0.90)	< 0.01	-1.72 (-2.75, -0.70)	< 0.01
P for trend	< 0.01		< 0.01		< 0.01	

Note: Crude Model: unadjusted any factor

Model I was adjusted for age, gender, race, marital, education, PIR, fasting glucose, ALT, AST, eGFR, HLD-C and UA. Model II was adjusted for Model I, diabetes mellitus, dyslipidemia, moderate PA, smoking status

Abbreviations: 95% CI: 95% confidence interval; OR: odds ratio; PIR: the ratio of family income to poverty; ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, eGFR: Estimated glomerular filtration rate, HLD-C: High-density lipoprotein cholesterol, UA: uric acid; PA: Physical activity

Table 3 The associations of eGDR with the risk of MASLD and liver fibrosis (NHANES 2017–2018)

eGDR, mg/kg/min	Case/totals	Crude Model OR (95%CI)	*P*	Model I OR (95%CI)	*P*	Model II OR (95%CI)	*P*
MASLD							
Per 1 SD increase	1928/3100	0. 37 (0.33–0.41)	< 0.01	0.47 (0.48–0.71)	< 0.01	0.53 (0.48–0.74)	< 0.01
Quartiles							
eGDR < 4.87	686/773	Ref.	1.0	Ref.	1.0	Ref.	1.0
eGDR 4.87–6.49	519/777	0.26 (0.19–0.33)	< 0.01	0.54 (0.32–0.87)	< 0.01	0.54 (0.32–0.89)	0.02
eGDR 6.49–9.31	458/775	0.18 (0.14–0.24)	< 0.01	0.48 (0.28–0.81)	< 0.01	0.51 (0.30–0.86)	0.01
eGDR ≥ 9.31	265/775	0.07 (0.05–0.09)	< 0.01	0.24 (0.13–0.42)	< 0.01	0.25 (0.14–0.45)	< 0.01
P for trend		< 0.01		< 0.01		< 0.01	
liver fibrosis							
Per 1 SD increase	265/3100	0. 35 (0.31–0.41)	< 0.01	0.37 (0.26–0.51)	< 0.01	0.40 (0.28–0.57)	< 0.01
Quartiles							
eGDR < 4.87	210/773	Ref.	1.0	Ref.	1.0	Ref.	1.0
eGDR 4.87–6.49	68/777	0.26 (0.19–0.44)	< 0.01	0.36 (0.20–0.61)	< 0.01	0.41 (0.23–0.72)	0.02
eGDR 6.49–9.31	66/775	0.25 (0.18–0.33)	< 0.01	0.24 (0.12–0.46)	< 0.01	0.28 (0.14–0.54)	0.01
eGDR ≥ 9.31	17/775	0.06 (0.03–0.10)	< 0.01	0.10 (0.03–0.27)	< 0.01	0.12 (0.04–0.32)	< 0.01
P for trend		< 0.01		< 0.01		< 0.01	

Note: Crude Model: unadjusted any factor

Model I was adjusted for age, gender, race, marital, education, PIR, fasting glucose, ALT, AST, eGFR, HLD-C and UA. Model II was adjusted for Model I, diabetes mellitus, dyslipidemia, moderate PA, smoking status

Abbreviations: 95% CI: 95% confidence interval; OR: odds ratio; PIR: the ratio of family income to poverty; ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, eGFR: Estimated glomerular filtration rate, HLD-C: High-density lipoprotein cholesterol, UA: uric acid; PA: Physical activity; MASLD: metabolic dysfunction-associated steatotic liver disease

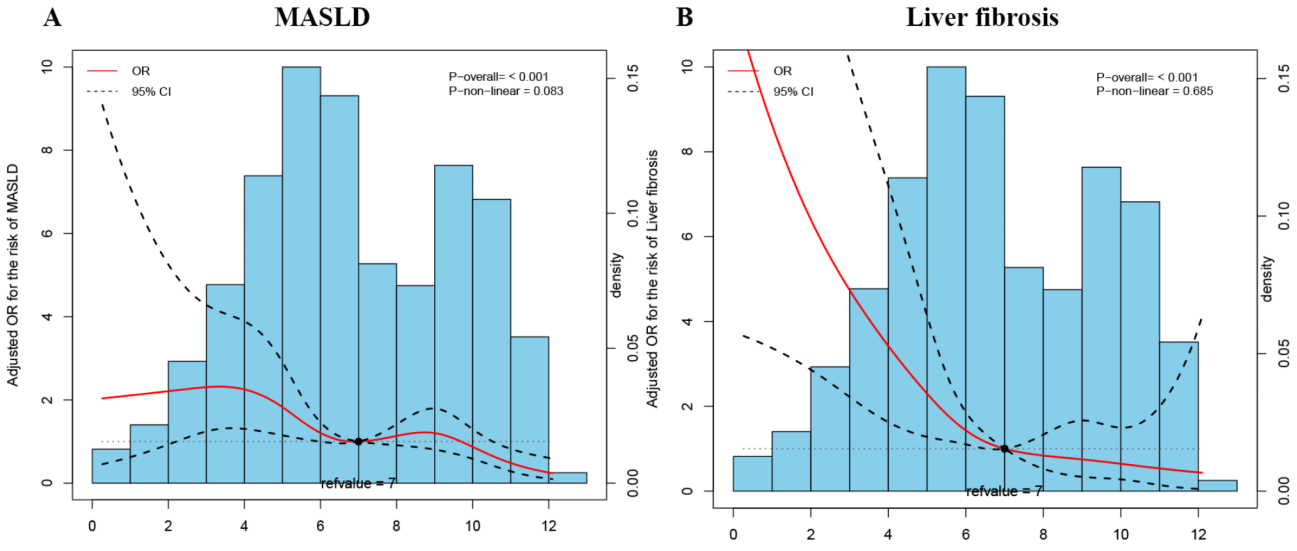

Fig. 3 The odds ratios and the histogram of the probability distribution for MASLD and liver fibrosis according to eGDR. The red curve with a light black dotted line indicates an adjusted odds ratio with 95% CI for MASLD and liver fibrosis according to eGDR 7.0 mg/kg/min. The number of knots for the cubic spline curves was three in the model. Adjustment factors included age, gender, race, marital status, education, PIR, fasting glucose, ALT, AST, eGFR, HDL-C, UA, diabetes mellitus, dyslipidemia, moderate PA, and smoking status

Abbreviations: 95% CI: 95% confidence interval; OR: odds ratio; MASLD: metabolic dysfunction-associated steatotic liver disease; eGDR: estimated glucose disposal rate; eGFR: estimated glomerular filtration rate; PIR: Ratio of family income to poverty; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; HDL-C: High-density lipoprotein cholesterol; UA: Uric acid; PA: Physical activity

0.04–0.32) respectively. Additionally, the analysis of continuous variables (per 1 SD increase) revealed a notable association between eGDR and a reduced risk of liver fibrosis, with an OR of 0.40 (95%CI: 0.28–0.57) after full adjustments.

Curve-fitting association of the eGDR with MASLD and liver fibrosis

The dose-response relationship between eGDR and MASLD and liver fibrosis is illustrated in Fig. 3. A statistically significant linear association was found between

eGDR and MASLD (p-nonlinear = 0.08). Conversely, the association between eGDR and MASLD showed nearly linear behavior (p-nonlinear = 0.69).

Subgroup analysis

We used subgroup analysis to validate the robustness of the results. Based on age, gender, eGFR, PIR, marital status, diabetes mellitus, dyslipidemia, smoking status, and moderate PA, we investigated the relationship between eGDR and MASLD and liver fibrosis in different populations. There was a significant interaction between eGDR and age for MASLD and liver fibrosis (P for interaction < 0.05); the other variables did not have any significant interactions with eGDR (Fig. 4).

Receiver operating characteristic curve for the prediction of MASLD and liver fibrosis

Figure 5 demonstrates the ROC curves for the eGDR in predicting the risk of MASLD and liver fibrosis. The receiver operating characteristic (ROC) curve was applied to calculate the optimal cut-off. The areas under the curve (AUCs) of the eGDR anticipating MASLD and liver fibrosis were 0.74 (95% CI: 0.73, 0.76), and 0.75 (95% CI: 0.72, 0.77), respectively. The sensitivity values were 78.10% and 74.50%, respectively. The specificity values were 57.70% and 64.50%. The eGDR's optimal cut-off values for predicting MASLD and liver fibrosis were 6.12 and 5.26 (Table 4).

Discussion

Major findings

This study found that eGDR negatively and significantly correlated with CAPM and LSM. The multivariable

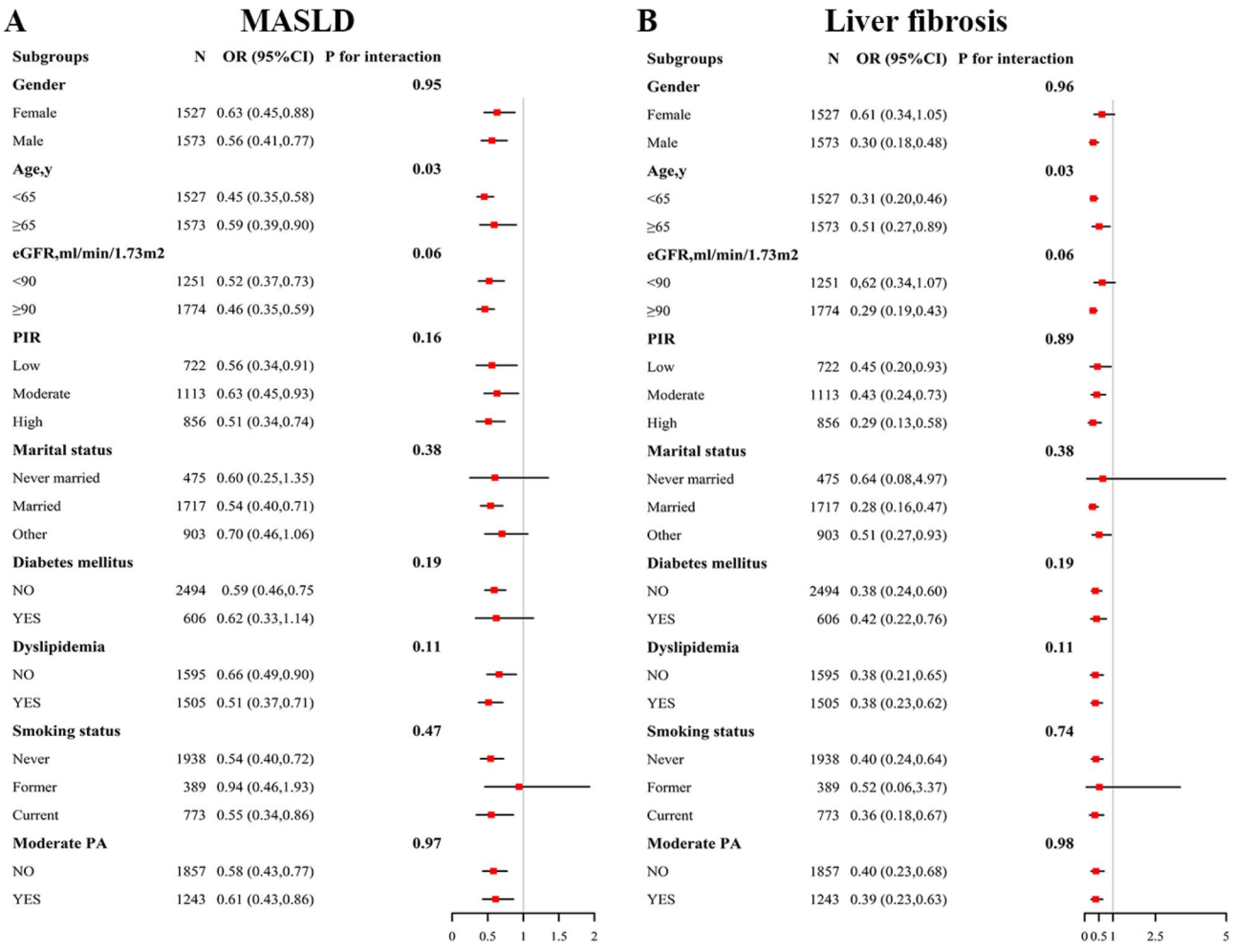

Fig. 4 The association between eGDR and MASLD (**A**) and liver fibrosis (**B**) in various subgroups. The results are adjusted for age, gender, eGFR, PIR, marital status, diabetes mellitus, dyslipidemia, smoking status, and moderate PA, if the above variables are not adjusted

Abbreviations: 95% CI: 95% confidence interval; OR: odds ratio; MASLD: metabolic dysfunction-associated steatotic liver disease; eGDR: estimated glucose disposal rate; PIR: Ratio of family income to poverty; eGFR: estimated glomerular filtration rate; PA: Physical activity

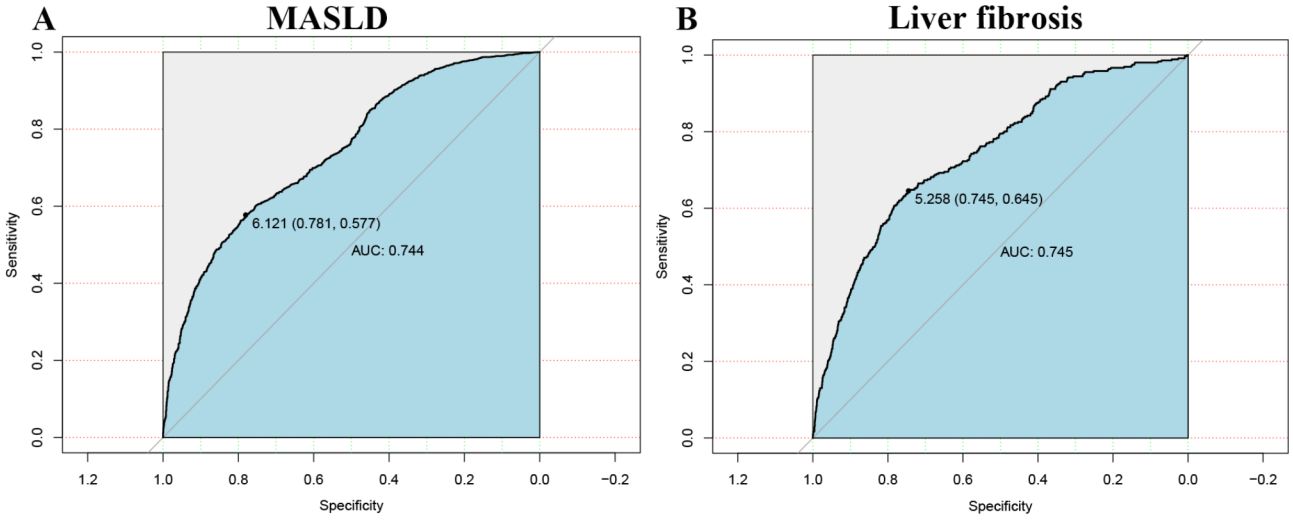

Fig. 5 Receiver operative characteristic (ROC) curves and corresponding areas under the curve (AUC)
Abbreviations: eGDR: estimated glucose disposal rate; MASLD: metabolic dysfunction-associated steatotic liver disease

Table 4 Areas under the ROC curves for each parameter of the eGDR for predicting MASLD and liver fibrosis

Parameters	Cut-off	Sensitivity	Specificity	AUC	95%CI	*P*-value
MASLD						
eGDR	6.12	78.10	57.70	0.74	0.73,0.76	< 0.01
LF						
LAD	5.26	74.50	64.50	0.75	0.72,0.77	< 0.01

Abbreviations: 95% CI: 95% confidence interval; eGDR: estimated glucose disposal rate; BMI: body mass index; HbA1c: glycated hemoglobin; LAD: left atrial diameter; MASLD: metabolic dysfunction-associated steatotic liver disease

logistic model also showed that lower levels of eGDR were linked to a much higher risk of MASLD and liver fibrosis, even after the possible covariant was considered. In addition, eGDR has a nonlinear relationship with MASLD and a linear relationship with liver fibrosis. The subgroup analysis confirmed the results' robustness. Meanwhile, the eDGR has a high predictive efficiency for MASLD and liver fibrosis; the AUC for MASLD and liver fibrosis prediction was 0.74 and 0.75, respectively.

Risk factors for MASLD include unhealthy lifestyle, obesity, type 2 diabetes (T2DM), and dyslipidemia [32]. MASLD patients often have an abnormal glucose metabolism. Therefore, they were associated with a higher risk of T2DM [33]. A meta-analysis included 24 studies with 35,599 T2DM patients, and the results indicated that the pooled prevalence of MASLD in T2DM patients was 59.67% (95% CI: 54.31–64.92%) [34]. A study included 3861 patients with T2DM with a BMI ≥ 24 kg/m2 and found that 1751 patients (45.4%) have MASLD, and metabolic disorders were significantly associated with MASLD [35]. Currently, the relationship between T2DM and MASLD remains unclear. However, insulin resistance (IR) is one of the key events in T2DM and MASLD [36]. T2DM and IR are important etiological factors in MASLD. Meanwhile, T2DM, MASLD, and IR have a two-way street of interplay [37]. eGDR is a new model for assessing IR in epidemiological studies. Compared to the euglycemic hyperinsulinemic clamp, eGDR has a good correlation with IR [38]. A cross-sectional study enrolled 207 patients and found that patients with lower levels of eGDR have a higher risk of IR compared to those with the highest levels of eGDR (OR:3.1, 95% CI: 1.2–8.1) [39].

Comparisons with previous studies

Currently, some studies have looked at the link between different IR biomarkers and MASLD. The findings show that IR greatly raises the risk of MASLD [40–42]. A cross-sectional study included 10,761 Chinese adults and used ultrasonography to identify MASLD. The results found that, compared to the lowest TyG index category, the highest TyG index category had a greater risk of MASLD, with an OR (95% CI) of 6.3 (5.3–7.5) [40]. The study investigation 8208 adults from the NHANES (1999–2018) who had steatotic liver disease caused by metabolic dysfunction. There were 4209 men and 3999 women in the study, with a median age of 49 years. The results showed that people in the highest quartiles of TyG-related indices were significantly more likely to die from any cause than people in the lowest quartiles of TyG-related indices. The HR (95% CI) for TyG index, TyG-WC, and TyG-WHtR were 1.25 (1.05–1.50), 1.28 (1.07–1.52), and 1.50 (1.25–1.80), respectively [41]. A

study conducted on 1,776 adults with a BMI of less than 30 kg/m2 from NHANES 2017–2018 found that TyG, TyG-BMI, and TyG-WC showed a positive association with MASLD. The OR with 95% CI was 3.387 (95% CI: 2.328, 4.928), 1.032 (95% CI:1.019, 1.045), and 1.010 (95% CI: 1.007, 1.013), respectively [42]. This study's findings are consistent with the above studies. Therefore, we use eGDR as a surrogate marker of IR, which can predict MASLD risk.

Underlying mechanism

The role of IR in the pathogenesis of MASLD remains unclear. However, it mainly involves glucose metabolism disorders, lipid metabolism disorders, oxidative stress, and inflammation [43]. IR reduces the sensitivity of the liver to insulin, which increases fatty acid synthesis in the liver [37]. IR promotes lipolysis from the adipose tissue, which increases the level of free fatty acids and leads to the deterioration of liver fat burden [44]. IR impaired the inhibitory effect of insulin on the glucose production from the liver, which increased the level of glucose [45]. Inflammation plays an important role in the pathogenesis of IR, and IR can induce inflammation [46], leading to macrophage aggregation and excessive secretion of pro-inflammatory cytokines [47]. IR causes oxidative stress and promotes apoptosis by impairing the functions of mitochondria and the endoplasmic reticulum [48].

Clinical practice

Early identification of MASLD is crucial for the patient's prognosis [49]. Currently, the gold standard for diagnosing MASLD is a liver biopsy; however, its invasive nature and operational complexity limit its widespread use [50]. Therefore, in clinical practice and epidemiological studies, there is a need for rapid, accessible, accurate, and inexpensive methods to determine MASLD. Routine tests can obtain eGDR, a biomarker, and regular blood tests can effectively monitor it. Therefore, eGDR may be a suitable tool for the non-invasive diagnosis of subjects with MASLD.

Strength and limitations

A strength of this study is its use of NHANES data to eliminate potential confounding effects. There are some limitations to this study. First, our study is cross-sectional, which is unable to establish a causal relationship. Second, we adjusted for common confounding factors. However, the differences between groups remain. Third, we only explored the baseline eGDR and did not investigate the impact of changes in eGDR on MASLD. Finally, our results are only applicable to the American population, and further research is needed to determine whether they are applicable to populations in other regions.

Conclusion

The study demonstrated that CAPM and LSM are negatively correlated with eGDR, and eGDR is associated with MASLD and liver fibrosis.

Abbreviations

ALT	Alanine aminotransferase
AST	Aspartate aminotransferase
AUROC	Area under the receiver operating characteristic curve
BMI	Body mass index
CAP	Controlled attenuation parameter
CIs	Confidence intervals
CKD-EPI	Chronic Kidney Disease Epidemiology Collaboration
CR	Creatinine
DBP	Diastolic blood pressure
eGDR	Estimated glucose disposal rate
eGFR	Estimated glomerular filtration rate
HbA1c	Glycosylated hemoglobin A1c
HDL-C	High-density lipoprotein cholesterol
HOMA-IR	Homeostasis model assessment-insulin resistance
IR	Insulin resistance
LDL-C	Low-density lipoprotein cholesterol
LSM	Liver stiffness measurement
MASLD	Metabolic dysfunction-associated steatotic liver disease
NCHS	National Centre for Health Statistics
NHANES	National Health and Nutrition Examination Survey
ORs	Odds ratios
PA	Physical activity
PIR	Ratio of family income to poverty
SBP	Systolic blood pressure
SD	Standard deviation
T2DM	Type 2 diabetes
TC	Total cholesterol
TyG index	Triglyceride glucose index
UA	Uric acid
WC	Waist circumference

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None.

Author contributions

W.Q-L and X.Z-L participated in the data analysis, and data interpretation, and wrote the manuscript. L-C wrote the manuscript. X-L participated in the study design and provided critical revision. All the authors read and approved the final version of the manuscript.

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Data availability

The corresponding author will provide the raw data supporting the conclusions of this article without any hesitation or reservation.

Declarations

Ethics approval and consent to participate

The studies involving human participants received ethical approval from The Second Affiliated Hospital of Nanchang University Medical Research Ethics Committee. Written informed consent for participation was not required for this study in accordance with national legislation and institutional requirements.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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