

The triglyceride glucose index can predict newly diagnosed biopsy-proven diabetic nephropathy in type 2 diabetes

A nested case control study

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Abstract

Insulin resistance is usually a key factor in the development of type 2 diabetes. The triglyceride glucose (TyG) index is a marker of insulin resistance which is also implicated in the risk of nephropathy among people with type 2 diabetes. This study aimed to examine associations and potential thresholds between TyG index and the risk of newly diagnosed biopsy-proven diabetic nephropathy in people with type 2 diabetes. A nested case–control study incorporating 950 incident biopsy-proven diabetic nephropathy cases and age, gender matched 4750 patients with treated type 2 diabetes as controls selected by risk-set sampling method was implemented. The dose–response association between TyG index with subsequent risk of newly diagnosed biopsy-proven diabetic nephropathy after adjustment for age, gender, blood pressure, and other major cardiovascular risk factors were examined by conditional logistic regression model. A non-linear relationship was identified between TyG index and the risk of newly diagnosed biopsy-proven diabetic nephropathy with a potential threshold of TyG at 9.05–9.09. Similar relationships with the same threshold were also found in the analyses by fasting glucose and triglyceride levels. TyG index might be a prognostic factor in predicting newly development of biopsy-proven diabetic nephropathy among patients with treated type 2 diabetes. In people with type 2 diabetes, TyG index above 9.05–9.09 could be a prognostic threshold to identify individuals at high risk of diabetic nephropathy. Further replication studies are warranted.

Abbreviations: DN = diabetic nephropathy, eGFR = estimated glomerular filtration rate, HOMA-IR = homeostasis model assessment of insulin resistance, IR = insulin resistance, TyG = triglyceride glucose index, UKPDS = UK Prospective Diabetes Study.

Keywords: diabetes, diabetic nephropathy, insulin resistance, prognosis, TyG index

1. Introduction

Diabetic nephropathy (DN) is the leading cause of chronic kidney disease in patients initialising renal replacement therapy, and is associated with increased cardiovascular mortality.^[1,2] In the UK Prospective Diabetes Study (UKPDS), the randomized controlled

trial of glycemic management of newly diagnosed type 2 diabetes, the annual incidence of clinically diagnosed DN was 2.0% with a 10-year prevalence of 25%.^[3] DN is more common in Asian populations.^[4] It has been estimated that in the 1990s, DN doubled as an indication for initializing renal replacement therapy.^[5]

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Insulin resistance (IR) has been reported to be associated with an increased risk of developing progressive DN among patients with diabetes, but only in cross-sectional studies.^[6,7] Some prospective studies have also reported that IR may precede and predict microalbuminuria in patients with diabetes.^[8] Furthermore, the frequency of factors associated with IR, like hypertension, central obesity, and dyslipidaemia also increase as DN progresses.^[6] However, prospective studies demonstrating that IR contributes to the development and progression of DN in type 2 diabetes are yet to be reported, probably due to the cost of insulin measurement and required study duration.

Several recent studies have shown that the triglyceride glucose (TyG) index is associated with IR,^[9,10] assessed by both hyperinsulinemic euglycemic clamp testing and homeostasis model assessment of insulin resistance (HOMA-IR). The clamp is considered as the gold standard method for measuring IR.^[12] But the clamp method is complex and not used in clinical practice, as it involves a primed-continuous infusion of insulin administered to raise the plasma insulin concentration to a predetermined physiological or pharmacological level. The plasma glucose concentration is then measured at 5-min intervals with a variable infusion of exogenous glucose administered to maintain the plasma glucose concentration constant at the fasting level. Since the plasma glucose concentration remains unchanged, the amount of exogenous glucose infused must equal the amount of glucose utilized in response to the hyperinsulinemia and, thus, provides a direct measure of whole-body sensitivity to insulin.^[11]

The other, more widely used HOMA-IR is calculated as (fasting plasma insulin level [in μ U/mL] × fasting plasma glucose level [in mmol/L])/22.5. A value of 1.00 is considered normal and higher values indicate progressively severe states of IR. This method is much more variable than the clamp due to the wide range of "normal" values for fasting plasma insulin. Also, it cannot be used in patients with diabetes, where the normal homeostatic relationship between plasma glucose and insulin levels no longer exists. It has theoretical limitations based on the fact that it attempts to measure insulin sensitivity in the fasting state when the majority of glucose uptake is independent of insulin. Thus, the TyG index has shown direct correlation with IR and been proposed as a reliable and simple surrogate marker of IR in clinical practice.^[13,14]

Consistent with these data, there is growing evidence to suggest that the TyG index is associated with cardiovascular disease.^[15–17] However, to the best of our knowledge, few studies have examined the relationship between the TyG index and the risk of development of DN among patients with type 2 diabetes. Therefore, in the present study, we have investigated the relationship between the TyG index and risk of newly diagnosed biopsy-proven DN among patients with type 2 diabetes.

2. Materials and methods

2.1. Data setting

We conducted this nested case-control study in Zhengzhou, Henan, China, which has 109 million residents. Both cases and controls were enrolled in the First Affiliated Hospital, Zhengzhou University, which is the largest hospital in China and provides both primary and secondary care to Henan residents. Health insurance coverage has been 90% since 2008, allowing most patients with DN to be diagnosed during a hospital admission. As the provincial renal center, most renal biopsies among patients with diabetes were processed in the hospital.

2.2. Case definition

A total of 950 patients with type 2 diabetes who were newly diagnosed with DN at the First Affiliated Hospital, Zhengzhou University between February 1, 2012 and February 28, 2018 were included in this study. The diagnosis of diabetes for cases and controls was based on the American Diabetes Association criteria.^[18] The diagnosis of DN was made based on histological characteristics, such as glomerular hypertrophy, thickened capillary basement membranes, diffuse mesangial expansion (sclerosis), nodular mesangial sclerosis, exudative lesions such as capsular drop or fibrin cap, mesangiolysis, mescapillary microaneurysm, or hyalinosis of afferent and efferent arterioles, using appropriate standard for renal biopsy including light microscopy, electron microscopy, and immunofluorescence examination.¹ Patients with other glomerular diseases concomitant with DN were excluded from this study. Renal biopsy was performed for precise diagnosis of renal lesions with the consent of each patient.

2.3. Matched controls

We used the inpatient administration system to select 5 controls for each case, matched for age and gender. Controls were patients with type 2 diabetes who attended outpatient departments or were admitted to the hospital between January 1, 2016 and December 31, 2017. Patients with estimated glomerular filtration rate (eGFR) <90 mL/min/1.73 m² and urine total protein >30 mg/24 h were excluded.^[9,19] Controls were selected using a risk set sampling method,^[10] by which the odds ratios estimated the incidence rates ratios. Controls were assigned an index date identical to that of corresponding cases.

2.4. Exposure definition

TyG index was calculated as the ln[fasting triglyceride (mg/dL) × fasting glucose (mg/dL)/2].^[20] In the dose–response analysis between TyG and risk of DN, TyG was treated as continuous variable. To understand the outcome distribution further, a histogram is shown of incidence rates ratios of outcome by TyG quartile group (Supplemental Figure S1, http://links.lww.com/MD/D371): Group 1 (TyG index <8.60), Group 2 (TyG index in 8.60–9.09); Group 3 (TyG index in 9.09–9.60), and Group 4 (TyG index \geq 9.60).

2.5. Ethics approval

Ethics approval was granted by the Clinical Research Ethics Committee of the First Affiliated Hospital of Zhengzhou University. Written informed consent was obtained from all participants before inclusion.

2.6. Co-variables and missing information

There was missing information on body mass index (56.2%), systolic blood pressure (37.4%), diastolic blood pressure (38.2%), fasting glucose (6.1%), HbA1c (6.7%), hematocrit (13.6%), mean corpuscular hemoglobin (13.6%), mean platelet volume (13.6%), monocyte (13.6%), red blood cell distribution width (13.6%), magnesium (22.1%), sodium (22.1%), chlorine (22.1%), activated partial thromboplastin time (32.8%), D-Dimer (32.8%), thrombin time (32.8%), fibrinogen (32.8%), and fibrinogen degradation products (32.8%). Multiple imputations were applied to replace missing values by using a chained

equation method based on all candidate predictors and primary outcome. Fifty-six imputed datasets were generated for missing predictors that were then combined across all datasets by using Rubin's rule to generate final model estimates.^[21]

2.7. Statistical analysis

In descriptive analyses, differences in participant characteristics by TyG index categories were assessed by logistic regression model for categorical variables, and generalized linear model for continuous variables.

Newly diagnosed biopsy-proven DN was defined as a binary outcome measure. A conditional logistic regression model was used to estimate the crude and adjusted incidence rates ratios of newly diagnosed biopsy-proven DN by TyG index categories. The dose-response relationships between TyG index and risks of newly diagnosed biopsy-proven DN were estimated using a linear model, a natural cubic spline model with three equally spaced knots determined from the levels of TyG index measures, and a quadratic spline model. The natural cubic spline model was chosen as the best fit model for the relationship curve by its minimum Akaike information criterion (AIC) compared with the linear model or quadratic spline model. The linear test was used in the natural cubic spline model to test the linearity of the relationship. The break-point test^[22] was carried out to target the potential thresholds (P5 to P95 of TyG index measures) by incorporating the piecewise term into the cubic spline model. The threshold with a significant break in the regression coefficients and achieving the minimum AIC was chosen as the final threshold.^[23] The 95% CI of the threshold was obtained from 1000 bootstrap samples. The associations between the TyG index and the risk of newly diagnosed biopsy-proven DN below and above the threshold were analysed such that the TyG index was treated as a continuous variable to observe the risk of DN with each 1 unit increase of the TyG index.

In the sensitivity analyses, the dose–response association between the TyG index and risk of DN was re-analyzed by the level of confounders (glucose and triglyceride) to examine whether the dose–response associations were consistent with those found in the main analyses. At each level of confounders, we also quantified the association between TyG index and risk of DN below and above threshold.

All analyses were performed using STATA (STATA/MP 15.0 StataCorp, College Station, TX). All *P* values were calculated using two-tailed tests and a *P* value < .05 was taken to indicate statistical significance. All methods were performed in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.

3. Results

Potential prognostic factors measured in cases and controls are shown in Table 1. Cases with newly diagnosed biopsy-proven DN had lower levels of hemoglobin, mean corpuscular hemoglobin, lymphocyte, monocyte, total bile acid, high density lipoprotein cholesterol, calcium, carbon dioxide combining power and eGFR, and higher levels of the remaining factors.

A non-linear ("J-shape") relationship was found between TyG index and risk of development of newly diagnosed biopsy-proven DN (*P*-values for linearity test < .0001). The dose–response relationship was derived from the natural cubic spline model with adjustment of covariables in Figure 1. In the sensitivity analysis

modeling the associations with fasting glucose and serum triglyceride (fasting glucose <8.0 mmol/L and fasting glucose \geq 8.0 mmol/L; triglyceride <1.5 mmol/L and triglyceride \geq 1.5 mmol/L), similar dose–response relationships were identified by fasting glucose level (Figure 1) and by serum triglyceride level (Figure 2). The individual-level incidence rates ratio distribution in four TyG categories based on the quartile of TyG (Group-1: TyG \leq 8.60; Group-2: TyG 8.60 < TyG \leq 9.09; Group-3: 9.09 < TyG \leq 9.60; and Group-4: TyG > 9.60) were presented in Supplemental Figure S1, http://links.lww.com/MD/D371, which indicated most patients' incidence rates ratio covering the estimated range of risk of DN shown in Figure 1.

A TyG index below 9.07 (95% confidence interval: 9.05–9.09) was estimated to be associated with the lowest risk of newly diagnosed biopsy-proven DN, as tested by linear threshold models. The thresholds were the same with fasting glucose levels and serum triglyceride levels. Table 2 shows that the risks of newly diagnosed biopsy-proven DN increase significantly with each 1 unit increase of TyG index above the TyG threshold (9.07) overall and by glucose and triglyceride levels (except triglyceride <1.5 mmol/L): adjusted incidence rates ratio (IRR) per TyG index unit for risk of newly diagnosed biopsy-proven DN 1.56 (95% CI: 1.27–1.91, P < .0001) overall; adjusted IRR for risk of newly diagnosed biopsy-proven DN 1.50 (1.09-2.06, P <.0001) in those with glucose <8.0 mmol/L and 2.06 (1.01-4.20, P <.0001) in those with glucose \geq 8.0 mmol/L; adjusted IRR for risk of newly diagnosed biopsy-proven DN 0.99 (0.41-2.40, P=.3562) in those with triglyceride <1.5 mmol/L and 1.92 (1.10–3.34, P < .0001) in those with triglyceride $\geq 1.5 \text{ mmol/L}$. The risks of newly diagnosed biopsy-proven DN did not increase significantly with 1 unit increase of TyG index above the TyG threshold overall and by glucose and triglyceride levels (Table 2).

4. Discussion

Our study was undertaken to relate TyG index, as a measure of insulin resistance, to the risks of newly diagnosed biopsy-proven DN in patients with type 2 diabetes. We focused our investigation on the dose–response relationships assessing the evidence for a nonlinear association, and for the existence of a threshold. In all our analyses, we found evidence that the associations are nonlinear. Threshold analysis provided evidence of a TyG index threshold: 9.07 (9.05–9.09). The significantly higher risks of newly diagnosed biopsy-proven DN were found above 9.07 of TyG index in people with type 2 diabetes.

Our investigation is the first study to explore the association between TyG index, as a surrogate for IR and the risk of newly diagnosed biopsy-proven DN in people with type 2 diabetes. In previous reports, a high TyG index had been found to be associated with the risk of type 2 diabetes in the general population,^[24] with subclinical atherosclerosis and arterial stiffness in postmenopausal women^[25] and with the risk of other diabetes related complications, such as coronary artery stenosis^[26] and Cardiac Autonomic Neuropathy.^[27] Consistent with these previous findings, we have found that a high TyG index (in particular TyG index \geq 9.07) is associated with a high risk of DN, which is the leading cause of end-stage renal disease in people with type 2 diabetes.

Non-linear dose–response relationships between TyG index and non-DN outcomes have previously been shown. For example, among patients with type 2 diabetes, a previous study was found that compared with patients with TyG index at 8.2,

Table 1

Clinical measurements among diabetic nephropathy cases and matched controls with type 2 diabetes.

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Anthypertexke testment, n (%) 335 (5.5.) 798 (16.6) 0001 Issuin fractament, n (%) 111 (1.9) 550 (10.7) .5383 Issuin fractament, n (%) 770 (6.69-0.06) 7.40 (6.27-8.62) 0000 Alnake transaminase (UA) 339.0 (2.27-157.71) 35.0 (2.30-04.60) 0000 Achied partial thrombogasin time (a) 31.15 (2.76.30-01.155.90) 7.85.0 (6.50-0.165.30) 0000 Achied partial thrombogasin time (a) 31.15 (2.76.30-0.155.90) 30.0 (2.7-6.90) 0.000 Bacophi (%) 0.04 (0.02-0.05) 0.03.80 (0.27-8.90) 0.000 Collect bilinching (morth) 12.6 (2.05-2.28) 2.2.4 (1.7-2.34) 0.000 Casion (morth) 12.16 (2.05-2.28) 2.2.4 (1.7-2.34) 0.000 Casion (morth (morth) 2.2.6 (1.7-6.30) 0.300 (1.2-6.35.90) 0.000 Creation corten (morth) 12.16 (2.95-2.28) 2.2.4 (1.7-2.34) 0.000 Creation corten (morth) 2.2.6 (1.7-0.30) 2.3.6 (1.7-4.22) 0.000 Creation corten (morth) 2.2.6 (1.7.0.6.2.2-5.6.3) 0.000 0.000 Creation corten (morth) 2.	Diastolic blood pressure (mm Hg)	79.0 (74.1–83.5)	76.3 (72.0-80.1)	.0001
Lowering (joid treatment, in (%) 113 (11.9) 508 (07.7) 5288 HbA1c (%) 77.6 (6.50-0.60) 7.4.0 (6.27-6.52) 0001 Alanie transminase (U) 33.90 (22.70-157.71) 35.00 (23.30-40.60) 0001 Alanie transminase (U) 34.90 (22.70-157.70) 35.00 (23.30-40.60) 0000 Alanie transminase (U) 4.60 (13.9-14.80) 36.00 (27.4-6.9) 0000 Order transminase (U) 4.60 (12.9-0.43.80) 6.60 (15.9-16.80) 0000 Choine (mond) 2.16 (2.9-2.29) 2.24 (2.12-2.34) 0000 Choine (mond) 1.02 (0.96.2-01.65.50) 10.18 (80.29-4.30) 0000 Choine (mond) 1.02 (0.96.2-16) 0.44 (0.09-2.20) 0001 Creatinine (unnul) 1.20 (6.69-2.16) 0.44 (2.09-2.20) 0001 Creatinine (unnul) 1.20 (6.69-2.16) 0.44 (0.29-0.50) 0001 Creatinine (unnul) 1.20 (6.69-2.16) 0.44 (0.29-0.57) 0001 Creatinine (unnul) 3.20 (1.74-4.22) 0001 0011 0.20 (2.14-4.22) 0001 Creatinine (unnul) 3.20 (1.59-4.61) 3.20	Antihypertensive treatment, n (%)	335 (35.3)	798 (16.8)	.0001
Insult expand, n (%) 797 (83.9) 3288 (86.8) 000 Alamic transminase (UL) 33.90 (22.7-157.71) 35.00 (23.9-04.60) 0001 Alamic transminase (UL) 33.90 (22.7-157.71) 35.00 (23.9-04.60) 0001 Alamic transminase (UL) 33.90 (22.7-0157.71) 35.00 (23.9-04.60) 0000 Anatotic parial transminase (UL) 46.27 (3.9-14.38) 38.00 (21.7-6.90) 0000 Bacaphi (%) 0.04 (0.2-0.05) 0.03 (0.2-0.05) 0.000 Calcium (mmoll) 2.16 (2.05-2.28) 2.2.4 (21.2-2.34) 0.000 Calcium (mmoll) 102.00 (69.8-016.50) 0.018 (8.83-8-60.50) 0.000 Creaction protein mgl) 2.28 (1.9-2.34) 0.000 Creaction protein mgl) 2.24 (1.9-2.34) 0.000 Creaction protein mgl) 2.28 (1.9-1.84) 2.16 (0.9-2.22) 0.000 Creaction protein mgl) 2.28 (1.9-1.23) 3.28 (1.7-4.42) 0.000 Creaction protein mgl) 3.50 (1.30-1.41.29) 3.26 (1.7-4.42) 0.000 Creaction protein mgl) 3.50 (1.3-1.46.00) 3.26 (1.7-4.42) 0.000	Lowering lipid treatment, n (%)	113 (11.9)	508 (10.7)	.5263
Hible (%) 7.76 (6.60-406) 7.740 (6.67-46.2) 0001 Akaine transmises (/L) 35.00 (92.70-157.71) 35.00 (92.30-40.60) 0001 Akaine transmises (/L) 78.87 (5.300) 30.10 (28.40-34.68) 0001 Direct billuotin (µm0/L) 46.62 (1.30-14.38) 3.60 (27-6.50) 0.001 Column (mm0/L) 46.80 (1.97-33.26) 5.60 (1.58-18.06) 0.000 Column (mm0/L) 16.00 (0.60.40, 0.22-0.65) 0.13 (8.83-105.00) 0.000 Column (mm0/L) 16.00 (0.60.40-35.60) 10.18 (8.483-105.00) 0.000 Column (mm0/L) 12.00 (88.30-105.50) 10.18 (8.483-105.00) 0.000 Creation (µm0/L) 2.28 (1.49-68.14) 21.66 (3.23-64.39) 0.000 Creation protein (mg/L) 2.27 (1.16-71.20) 3.28 (1.74-4.22) 0.000 Dimerge (ng/mL) 3.00 (1.5-4.66) 3.44 (2.74-4.22) 0.000 Creation protein column (nov/L) 2.96 (7.5-1.12.1) 1.44 (8.2-1.30) 0.001 Creation (µmo/L) 2.96 (7.5-1.21) 7.98 (5.5-1.02.0) 0.001 Creation (µmo/L) 2.96 (7.5-1.21) 1.46 (8.2-3.00) <td>Insulin treatment, n (%)</td> <td>797 (83.9)</td> <td>3268 (68.8)</td> <td>.0001</td>	Insulin treatment, n (%)	797 (83.9)	3268 (68.8)	.0001
Alamic transmisse (UL) 39.90 (22, 7-157, 71) 55.00 (65, 50-165, 30) 0001 Activate partal transmisse (UL) 78.57 (63, 00-115, 59) 78.50 (66, 50-165, 30) 0001 Activate partal transmisse (UL) 46.7 (1, 30-14, 30) 3.00 (2, 7-6, 60) 0001 Dict thirtubin (unwol) 46.6 (1, 30-14, 30) 3.00 (2, 7-6, 60) 0001 Bacaphil (%) 0.04 (0, 02-0, 65) 0.13 (0, 02-0, 65) 0.010 Calciam (mmol, 1) 12.16 (0, 65-22, 8) 2.24 (2, 12-2, 34) 0001 Calciam (mmol, 1) 12.60 (0, 90, 40-355, 60) 63.00 (1, 119-135, 50) 0001 Calciam probin (mpl, 1) 12.16 (1, 30-33, 41) 0.91 (0, 22, 54, 63) 0001 Cystem probins (mpl, 1) 5.72 (1, 16-12, 13) 3.26 (1, 74-4, 22) 0001 D_Dimer (ug/mL) 5.72 (1, 16-12, 13) 3.26 (1, 74-4, 22) 0001 Fibringen degadation products (mgL) 7.92 (6, 51-112, 2) 7.93 (6, 63-10, 9) 0001 Fibringen degadation products (mgL) 7.94 (6, 51-10, 9) 0.001 100 (0, 42-2, 13, 0) 0.001 Giobalin (f) 10.00 (13, 0-91+10, 1) 10.00 (13, 0-91+10, 1) <	HbA1c (%)	7.76 (6.60–9.06)	7.40 (6.27–8.62)	.0001
Akalare prophatase (IUL) 78 / (5.00 - 115.98) 78.50 (60.50 - 105.33) 0001 Direct binutin (µmwl/) 4.62 (1.30 - 14.38) 3.60 (127 - 6.90) 0.001 Direct binutin (µmwl/) 4.82 (1.30 - 14.38) 3.60 (127 - 6.90) 0.001 Choinestene (U/) 8.80 (1.97 - 33.6) 5.60 (1.68 - 16.08) 0.001 Choinestene (U/) 1.62 (0.55 - 22.8) 2.24 (2.12 - 23.4) 0.001 Choine (mmul/) 1.16 (0.55 - 28) 2.24 (2.12 - 23.4) 0.001 Creation (mmul/) 1.16 (0.55 - 28) 2.24 (2.12 - 23.4) 0.001 Creation (mmul/) 1.28 (1.49 - 56.14) 2.16 (1.32 - 34.4) 0.01 (1.9 - 16.4) 0.001 Creation probinase inhibitor 2.18 (1.49 - 56.14) 2.16 (3.23 - 42.4) 0.001 Cyber (ummul/) 1.57 (2.116 - 12.03) 3.26 (1.74 - 42.2) 0.001 Fibringen (up) 3.90 (3.15 - 4.66) 3.44 (2.74 - 42.2) 0.001 Gamma (utamaly transperificae (U/) 0.24 (2.74 - 23.03) 2.25 (2.22 - 36.0) 0.001 High density (uportain choisetrol (mmul/) 0.97 (7.4 - 12.1) 1.46 (0.82 - 34.6) 0.001	Alanine transaminase (U/L)	39.90 (22.70–157.71)	35.00 (29.30–40.60)	.0001
Advated partial thromopean in time (s) 31,16 (27,00-55,80) 90,10 (24,0-34,86) 0001 Basephil (%) 0.04 (0,20-0.65) 0.03 (0,20-0.65) 0.001 Choinestense (U) 8.80 (1,97-33,26) 5.50 (1,56-18.08) 0.001 Calcium (mmol/L) 1.216 (2,05-2.28) 2.24 (2,12-2.34) 0.001 Calcium (mmol/L) 1.216 (2,05-2.28) 2.24 (2,12-2.34) 0.001 Creation protein (mp/L) 2.281 (1,49-6.81,44) 2.106 (3,23-6.34) 0.001 Creation protein (mp/L) 2.211 (1,49-6.34,44) 2.106 (3,23-6.34) 0.001 Creation protein (mp/L) 5.77 (1,16-12.03) 3.26 (1,74-4.22) 0.001 D_Dimer (µg/mL) 3.50 (1,33-4.66) 3.44 (2,74-4.22) 0.001 Gamma (utamy transpectidase (ML) 3.50 (1,33-4.66) 3.44 (2,74-4.22) 0.001 Glacese (mm/L) 7.99 (6,51-11.22) 7.89 (5,83-0.90) 0.001 Glacese (mm/L) 1.90 (0,02-3.30) 1.15 (3,02-2.34) 0.001 Glacese (mm/L) 1.92 (2,74-8.20) 3.41 (2,02-3.30) 0.001 Glacese (mm/L) 1.94 (3,82-9.30) 3.41 (2,02-3.30)<	Alkaline phosphatase (IU/L)	78.87 (53.00–115.98)	78.50 (60.50–105.33)	.0001
Unext billions (µmolt) 4.62 (130–14.38) 368 (217–6.90) 0.001 Chainesterse (IL) 8.80 (197–53.26) 5.66 (1.55–18.08) 0.001 Calcium (mmolt) 1.16 (2.65–2.28) 2.24 (2.12–2.34) 0.001 Chaine (mmolt) 1.16 (2.05–2.28) 2.14 (1.31–3.5.59) 0.001 Creatinic (µmolt) 1.26 (0.65–2.16) 0.48 (0.83–1.05.00) 0.001 Creatinic (µmolt) 1.20 (0.65–2.16) 0.46 (0.09–2.22) 0.001 Creatinic (µmolt) 1.20 (0.65–2.16) 0.46 (0.09–2.22) 0.001 Statistic protein proteinase inhibitor 2.18 (1.34–6.33) 2.95 (1.74–4.22) 0.001 Calcium (mmolt) 3.90 (3.15–4.66) 3.44 (2.74–4.22) 0.001 Globulin (gh1) 2.84 (2.28–3.03) 2.58 (2.22–9.60) 0.001 Globulin (gh1) 2.84 (2.28–3.03) 2.58 (2.22–9.260) 0.001 Heindeglobi (gh2) 1.99 (0.74–1.21) 1.40 (0.82–1.30) 0.001 Heindeglobi (gh2) 1.97 (0.74–1.21) 1.40 (0.82–1.30) 0.001 Heindeglobi (gh2) 1.97 (0.74–1.21) 1.40 (0.82–1.30) 0.001 </td <td>Activated partial thromboplastin time (s)</td> <td>31.15 (27.60–35.80)</td> <td>30.10 (26.40–34.68)</td> <td>.0001</td>	Activated partial thromboplastin time (s)	31.15 (27.60–35.80)	30.10 (26.40–34.68)	.0001
bissprii (%) 0.04 (02-0.0) 0.03 (02-0.0) 0.001 Calcium (mmol/) 2.16 (2.6-2.28) 2.24 (2.12-2.34) 0.001 Calcium (mmol/) 12 (0.98.3-01.05.50) 101.88 (9.83-01.50.00) 0.001 Creation protein (mp/1) 128 (0.09.40-355.00) 63.00 (11.19-135.59) 0.001 Creation protein (mp/1) 2.18 (1.38-3.34) 0.91 (0.21-1.84) 0.001 D_Dimer (up/ml) 1.20 (0.89-2.16) 0.46 (0.09-2.22) 0.001 Fibringen degratation products (mg/1) 5.77 (1.16-1.23) 3.26 (1.74-4.22) 0.001 Biomer glutany transperipticase (U/1) 3.90 (0.15-4.66) 3.44 (2.74-4.22) 0.001 Glucose (mmol/1) 7.89 (5.6-1.030) 0.001 0.001 Glucose (mmol/2) 7.89 (5.6-1.030) 0.001 High destry lioportein cholesterol (mmol/1) 0.97 (7.4-1.21) 1.04 (0.82-1.30) 0.001 Hematocrit (K3) 11.01 (0.00 (84.99-117.00) 11.90 (0.22-3.46) 0.001 Hematocrit (K4) 5.24 (2.7-8.80) 3.40 (2.0-5.70) 0.001 Hematocrit (K3) 1.894 (3.80-23.00) 1.11 (3.80-23.46) <td< td=""><td>Direct bilirubin (µmol/L)</td><td>4.62 (1.30–14.38)</td><td>3.60 (2.17-6.90)</td><td>.0001</td></td<>	Direct bilirubin (µmol/L)	4.62 (1.30–14.38)	3.60 (2.17-6.90)	.0001
Linding strate 0.001 3.600 1.57-33.209 5.600 1.500 0.001 Chainer (mmol.) 1.162 0.692.226 2.242 2.12-2.34 0.001 Creatinine (mmol.) 1.2500 0.8500 0.500 0.11-35.59 0.001 Creatinine (mmol.) 2.2811 1.49-58.14) 2.160 0.061 0.001 D_Dimer (ug/mL) 1.200 0.69-2.16) 0.46 0.001 0.001 D_Dimer (ug/mL) 3.200 1.57-4.66) 3.44 0.74-4.22 0.001 Ehringgen eignation products (mg/L) 7.97 7.87 0.65 0.001 0.001 Globulin (g/L) 2.847 7.28 6.65 0.001 0.001 Ehringgen eignation products (mg/L) 7.99 6.51-11.22 7.89 6.63-10.90 0.001 Elidobin (g/L) 1.010.00 (64.98-117.00) 1.100 (02.92-134.00) 0.001 Elidobin (g/L) 1.010.00 (64.98-117.00) 1.100 (02.92-134.00) 0.001 Henaglobin (g/L) 1.521 (6.2-1-03) 3.40 (2.0-5.70) 0.0	Basophil (%)	0.04 (0.02–0.05)	0.03 (0.02–0.05)	.0001
Lacuar (mmol/) 2.16 (2.97-2.29) 2.24 (2.12-2.49) 0.001 Creation profiles (µmol/) 102.00 (98.50-105.50) 101.88 (98.3-105.50) 0.001 Creation profiles (µnl/) 2.28 (1.49-56.31.4) 21.06 (3.23-54.39) 0.001 Cysteine proteinase inhibitor 2.18 (1.49-53.4) 0.49 (0.21-16.4) 0.001 Dimer (µnl/) 1.20 (0.69-2.21) 0.46 (0.09-2.22) 0.001 Florinogen degradation products (mg/l) 5.72 (1.16-12.03) 3.26 (1.74-4.22) 0.001 Florinogen (µl/) 3.00 (3.15-4.66) 3.44 (2.74-4.22) 0.001 Glousen (µnd/l) 7.98 (5.51-12.2) 7.89 (5.53-10.90) 0.001 Glouse (µnd/l) 0.97 (0.74-12.1) 1.40 (0.82-13.0) 0.001 Hemoglobin (µl/l) 10.90 (4.84-17.00) 11.90 (0.22-13.400) 0.001 Inderest Bin/bin/bin 11.90 (1.22-13.40) 0.001 1.90 (0.22-13.40) 0.001 Inderest Bin/bin/bin (µnd/l) 5.24 (2.74-8.80) 3.40 (2.07-5.70) 0.001 Inderest Bin/bin/bin (µnd/l) 5.24 (2.74-8.80) 4.20 (3.74-4.22) 0.001 Inderest Bin/bin/bin (µnd/l) <td>Cholinesterase (U/L)</td> <td>8.80 (1.97–33.26)</td> <td>5.60 (1.58-18.08)</td> <td>1000.</td>	Cholinesterase (U/L)	8.80 (1.97–33.26)	5.60 (1.58-18.08)	1000.
Cloure (minute) 102.00 (92.30–102.30) 10.68 (95.36–105.00) 0.001 C reaction protein (mg1) 22.81 (1.49–58.14) 21.06 (3.23–61.39) 0.001 C reaction protein (mg1) 22.81 (1.49–58.14) 21.06 (3.23–61.39) 0.001 D_limer (µg/ml) 1.20 (0.69–2.16) 0.46 (0.09–2.22) 0.001 Ebrinogen (q2) 3.26 (1.74–4.22) 0.001 Ebrinogen (q2) 3.50 (15.4.66) 3.44 (2.74–4.22) 0.001 Globulin (g1) 26.47 (22.82–30.30) 25.55 (22.20–29.60) 0.001 Globulin (g1) 7.89 (5.51–11.22) 7.89 (5.63–10.90) 0.001 Hendpoin (p1) 0.97 (0.74–1.21) 1.04 (0.82–1.300) 0.001 Hendpoin (p1) 101.00 (64.88–117.00) 11.900 (102.20–134.00) 0.001 Hendpoin (p1) 11.01 (0.64 (3.60–29.00) 11.15 (3.80–2.346) 0.001 Hendpoin (p1) 12.44 (3.98–4.80) 4.24 (0.37–4.62) 0.001 Hendpoin (p1) 13.49 (2.09–5.70) 0.001 1.00 1.02.94 (3.99–4.80) 4.20 (3.77–4.62) 0.001 Hendpoin (p1) 2.42 (2.7–8.30) 3.2	Calcium (mmol/L)	2.10 (2.05-2.28)	2.24 (2.12-2.34)	.0001
Creation protein (mgL) 129:00 (1094-07-33:00) 63:00 (11.19-13:339) 0001 Cystein proteinase inhibitor 2.18 (1.48-3:3.4) 2.10 (6:22-84:38) 0001 D_Inner (µ/mL) 120 (0.69-22) 0001 Ehrinogen degradation products (mgL) 5.72 (11.6-12.03) 3.26 (1.74-4.22) 0001 Earna glutamy transpeptidase (/L) 3.50 (3:15-4.66) 3.44 (2.74-4.22) 0001 Glocose (mmO/L) 2.86 (7:22-0-29.60) 0.001 0.0001 Glocose (mmO/L) 7.89 (5:63-10.90) 0.001 High densyl ipoprotein cholesterol (mmO/L) 0.97 (0.74-1.21) 1.04 (0.82-1.30) 0.001 Hemoglobin (g/L) 101 (0 (84.98117.20) 1.90 (10.28-130) 0.001 Hemoglobin (g/L) 1.01 (0 (84.98117.20) 1.90 (10.28-130) 0.001 Hemoglobin (g/L) 1.84 (3.8029.00) 1.11 (5 (3.8023.46) 0.001 Hordsstim (mon/L) 2.50 (1.75-3.33) 2.47 (1.72-3.26) 0.001 Hordsstim (mon/L) 2.56 (1.75-3.33.00) 2.94 (23.00-337.00) 0.001 Mean corpuscular volume (L) 9.056 (5.51-05) 0.40 (6.83.0-42.23)	Chiofille (Infilo/L)	102.00 (96.50-105.50)	101.86 (98.36-105.00)	.0001
Orestamin protein (ng/L) 22.01 (14-9-C1-9) 21.00 (12-9-4-35) 0.001 Optimize infinitor 21.8 (13-8-3-34) 0.91 (0.21-1-64) 0.001 D_climer (µg/ml) 12.0 (0.69-21.6) 0.46 (0.09-2.22) 0.001 Ehringen (µg/atalation products (ng/L) 35.00 (13.00-91.80) 29.50 (17.00-61.00) 0.001 Gamma gutanny transpetidase (UL) 26.47 (22.82-30.30) 25.85 (22.20-29.60) 0.001 Glocose (mmol/L) 0.97 (0.74-1.21) 1.04 (0.82-1.30) 0.001 High density lipoprotein cholesterol (mmol/L) 0.97 (0.74-1.21) 1.04 (0.82-1.30) 0.001 Hematocti (%) 11.00 (84.96-117.00) 111.00 (83.90-23.46) 0.001 Indreet Blinubin (µmol/L) 52.4 (2.74-8.80) 3.40 (2.00-57.0) 0.001 Indreet Blinubin (µmol/L) 2.50 (1.75-3.33) 2.47 (1.72-3.6) 0.001 Indreet Blinubin (µmol/L) 2.50 (1.75-3.33) 2.47 (1.72-3.6) 0.001 Ive density lipoprotein cholesterol (mmol/L) 2.50 (1.75-3.33) 2.47 (1.72-3.6) 0.001 Ive density lipoprotein cholesterol (mmol/L) 2.50 (1.75-3.33) 2.47 (1.72-3.6) 0.001 <td>Creation protoin (mg/L)</td> <td>159.00 (109.40–355.00) 22.81 (1.40.58.14)</td> <td>03.00 (11.19-133.39)</td> <td>.0001</td>	Creation protoin (mg/L)	159.00 (109.40–355.00) 22.81 (1.40.58.14)	03.00 (11.19-133.39)	.0001
Optime (public) 2.10 (1.30-1.30) 0.31 (02.1-1.03) 0.01 (02.9-2.16) 0.40 (02-9.22) 0001 Fibringen degradation products (mg/L) 5.72 (1.16-12.03) 3.26 (1.74-422) 0001 Gamma gularnyl transpeptidase (UL) 350 (0.15-4.66) 3.44 (2.74-422) 0001 Gamma gularnyl transpeptidase (UL) 350 (0.15-4.66) 3.44 (2.74-4.22) 0.001 Gamma gularnyl transpeptidase (UL) 7.89 (5.5-11.22) 7.89 (5.63-10.30) 0.001 Glacose (mmol.) 7.98 (5.6-11.22) 7.89 (5.63-10.30) 0.001 Hendpoloni (QL) 101.00 (8.49-817.00) 119.00 (10.2.92-134.00) 0.001 Idenced Binubin (umol.) 5.24 (2.74-8.80) 3.40 (2.00-5.70) 0.001 Indract Binubin (umol.) 5.24 (2.74-8.80) 3.40 (2.00-5.70) 0.001 Indract Binubin (umol.) 2.50 (1.75-3.33) 2.47 (1.72-3.26) 0.001 Low density lipoprotein cholesterol (mmol.) 2.86 (75 (22.085-333.00) 329.44 (23.00-37.00) 0.001 Mean corpuscular hemoglobin concentration (gL) 326 (75 (22.085-333.00) 329.44 (23.00-37.00) 0.001 Mean corpuscular hemoglobin concentration (gL) <td>Creaction proteinace inhibitor</td> <td>22.01 (1.49-30.14)</td> <td>21.00 (3.23-34.39)</td> <td>.0001</td>	Creaction proteinace inhibitor	22.01 (1.49-30.14)	21.00 (3.23-34.39)	.0001
Description 1.20 (0.59-2.10) 0.40 (0.59-2.22) .0001 Fibringen degradation products (mg/L) 5.72 (1.16-12.03) 3.344 (2.74-4.22) .0001 Garma glutamyl transpeptidase (J/L) 35.00 (1.56-4.66) 3.44 (2.74-4.22) .0001 Globulin (g/L) 26.47 (22.82-30.30) 25.85 (22.20-29.60) .0001 Globulin (g/L) 0.74 (1.21) 1.04 (0.82-1.30) .0001 High density lipoprotein cholesterol (mmol/L) 0.74 (1.21) 1.04 (0.82-1.30) .0001 Hematopti (Ys) 18.18 (4.80-29.00) 11.15 (3.80-2.346) .0001 Indirect Bilirubin (µmol/L) 5.24 (2.74-8.80) 3.40 (2.00-5.70) .0001 Low density lipoprotein cholesterol (mmol/L) 2.50 (1.75-3.33) 2.47 (1.72-3.26) .0001 Low density lipoprotein cholesterol (mmol/L) 2.56 (1.57-3.33.00) 329.44 (323.00-337.00) .0001 Mean corpuscular volume (fL) 90.60 (85.99-95.10) 90.40 (86.30-94.23) .0001 Mean corpuscular volume (fL) 92.57 (320.85-333.00) 329.44 (323.00-337.00) .0001 Mean corpuscular volume (fL) 90.60 (85.99-95.10) 90.40 (86.30-94.23) <		2.10 (1.30-3.34)	0.46 (0.00, 2.22)	.0001
Introducts (ingl.) 3.12 (interl.2.0) 3.23 (interl.2.0) 3.24 (interl.2.0) 3.25 (interl.2.0) Gamma gutamyl transpetidase (U/L) 3.90 (interl.2.0) 2.55 (interl.2.2) 0.001 Gobulin (U/L) 2.64 (interl.2.0) 2.55 (interl.2.2) 0.001 Glubase (mm/L) 7.89 (is.51-11.22) 7.89 (is.51-01.90) 0.0001 Hemoglobin (igl.) 10.10 (08 (4.89-117.0) 11.9.00 (102.22-134.00) 0.0001 Hemoglobin (igl.) 10.10 (08 (4.89-117.0) 11.9.00 (102.22-134.00) 0.001 Hemoglobin (igl.) 11.15 (is.30-2.346) 0.001 Hemoglobin (igl.) 5.24 (i.72-4.8.0) 3.40 (2.00-5.70) 0.001 Indirect Bilmikin (unm/L) 2.50 (i.75-3.33) 2.47 (i.72-3.26) 0.001 Low density lipoprotein cholesterol (mmo/L) 2.50 (i.75-3.33) 2.47 (i.72-3.26) 0.001 Mean corpuscular hemoglobin concentration (g/L) 326 (i.68-9-65.10) 9.04 (8.30-9.70) 0.001 Mean corpuscular hemoglobin concentration (g/L) 326 (i.68-9-66) 0.91 (081-1.01) 0.001 Mean corpuscular hemoglobin concentration (g/L) 0.95 (0.85-1.05) 0.95 (0.17-1.07)	Eibringgen degradation products (mg/L)	5 72 (1 16-12 03)	3.26(1.74-4.22)	.0001
Tankagori (gL) 3.50 (0.13 - 0-91.80) 29.50 (17.0 - 41.21) 1.0001 Globalim (gL) 26.47 (22.82-30.30) 25.85 (22.20-29.60) .0001 Globalim (gL) 7.89 (5.65 - 11.22) 7.89 (5.63 - 10.90) .0001 High density lipoprotein cholesterol (mmol/L) 0.97 (0.74 - 1.21) 1.04 (0.82 - 13.00) .0001 Hematocti (%) 101.00 (84.96 - 117.00) 119.00 (102.92 - 134.00) .0001 Indirect Bilinubin (Lmol/L) 5.24 (2.74 - 8.80) 3.40 (2.00 - 5.70) .0001 Indirect Bilinubin (Lmol/L) 2.50 (1.75 - 3.33) 2.47 (1.72 - 3.26) .0001 Low density lipoprotein cholesterol (mmol/L) 2.60 (1.75 - 3.33) 2.47 (1.72 - 3.26) .0001 Mean corpuscular hemoglobin concentration (gL) 28.67 (32.08 - 53.33.00) 2.92.44 (23.20 - 337.00) .0001 Mean corpuscular hemoglobin concentration (gL) 36.06 (3.60 - 9.61.0) 90.40 (86.30 - 9.42.3) .0001 Mean plateiter volume (fL) 90.60 (85.99 - 96.10) 90.40 (86.30 - 94.2.3) .0001 Mean plateiter volume (fL) 8.90 (8.01 - 96.80) 5.56 (3.15 - 8.31) .0001 Mean plateiter volume (fL) 8.90 (Fibringen (g/L)	3.90 (3.15-4.66)	3.44 (2.74-4.22)	.0001
Contrast graduity in datappindes (a):Codes (17.83 0-10.5)Codes (17.8	Gamma dutamvl transpentidase (11/1)	35.00 (13.00–91.80)	29 50 (17 00-61 00)	0001
Location (gr/L) 7.98 (5.63-10.39) 1.0001 High density lipoprotein cholesterol (mmol/L) 0.97 (0.74-1.21) 1.04 (0.82-1.30) .0001 High density lipoprotein cholesterol (mmol/L) 0.97 (0.74-1.21) 1.04 (0.82-1.30) .0001 Hematocrit (%) 18.94 (3.80-29.00) 11.15 (3.80-2.346) .0001 Indirect Blinubin (µmol/L) 5.24 (2.74-8.80) 3.40 (2.00-5.70) .0001 Detassium (mmol/L) 4.33 (3.95-4.80) 4.20 (3.77-4.62) .0001 Low density lipoprotein cholesterol (mmol/L) 2.55 (1.75-3.33) 2.47 (1.72-3.26) .0001 Mean corpuscular hemoglobin concentration (g/L) 326.75 (320.85-333.00) 329.44 (32.00-337.00) .0001 Mean corpuscular volume (fL) 90.60 (85.99-95.10) 90.40 (86.30-94.23) .0001 Magnesium (mmol/L) 0.95 (0.25-1.05) 0.56 (0.17-1.07) .0001 Magnesium (mmol/L) 1.14 (15.83.35-144.37) 1.40.60 (37.60-143.23) .0001 Monocytes (%) 0.59 (0.25-1.05) 0.56 (0.17-1.07) .0001 Monocytes (%) 0.59 (0.25-1.61) 0.56 (0.17-1.07) .0001 Neutrophil (%	Globulin (a/l.)	26 47 (22 82-30 30)	25.85 (22.20–29.60)	0001
High density ipportetin cholesterol (mmol/L)1.070.74-1.211.040.082-1.30.0001Hematocti (%)101.00(84.98-117.00)119.00(10.2.92-134.00).0001Indirect Bilrubin (µmol/L)5.24(2.74-8.80)3.40(2.00-5.70).0001Indirect Bilrubin (µmol/L)5.24(2.74-8.80)3.40(2.00-5.70).0001Low density lipoprotein cholesterol (mmol/L)2.50(1.75-3.33)2.47(1.72-3.26).0001Lymphocyte (%)1.56(1.04-2.10)1.30(0.83-1.85).0001Mean corpuscular hemoglobin concentration (y/L)326.75(320.88-333.00)329.44(33.00-337.00).0001Mean corpuscular volume (fL)90.60(65.99-95.10)90.40(63.0-94.23).0001Mean corpuscular volume (fL)0.95(0.86-1.06).911(0.81-1.01).0001Mean corpuscular volume (fL)0.95(0.25-1.05)0.56(0.17-1.07).0001Monocytes (%).050.951.0001.0001Mean corpuscular femoglobin concentration (y/L)141.45(13.83-144.37)140.60(13.76-143.23).0001Mean corpuscular volume (fL)0.950.95.050.56(0.17-1.07).0001Monocytes (%).050.951.17.0001.0001Mean corpuscular volume (fL)1.190.10-1.4271.11(0.90-1.31).0001Mean corpuscular volume (fL).06.06.06.06.06.06.06.06	Glucose (mmol/L)	7 98 (5 51–11 22)	7 89 (5 63–10 90)	0001
Hemoglobiling(µ) 101.00 (84.98–117.00) 119.00 (102.92–134.00) .0001 Hemoglobiling(µ) 18.94 (3.80–29.00) 11.15 (3.80–2.346) .0001 Indirect Billrubin (µmol/L) 5.24 (2.74–8.80) 3.40 (2.00–5.70) .0001 Potassium (mmol/L) 4.34 (3.95–4.80) 4.20 (3.77–4.62) .0001 Low density lipoprotein cohesterol (mmol/L) 2.56 (1.75–3.33) 2.47 (1.72–3.26) .0001 Mean corpuscular hemoglobin concentration (µL) 326.75 (320.85–333.00) 329.44 (323.00–337.00) .0001 Mean corpuscular volume (IL) 90.60 (85.99–95.10) 90.40 (86.30–94.23) .0001 Mean corpuscular volume (IL) 8.90 (8.10–8.80) 8.83 (8.00–9.70) .0001 Mean patieter volume (IL) 8.90 (8.10–8.80) 8.83 (8.00–9.70) .0001 Monocytes (%) 0.59 (0.25–1.05) 0.56 (0.17–1.07) .0001 Monocytes (%) 6.70 (4.26–6.68) 5.56 (3.15–8.31) .0001 Prosphorus (mmol/L) 1.14 (1.55–1.47) 1.11 (0.30–1.31) .0001 Procalcitonin (g/ml) 1.42 (1.05–1.47) 1.11 (0.27–1.86) .0001 India blact of	High density lipoprotein cholesterol (mmol/L)	0.97 (0.74–1.21)	1.04 (0.82–1.30)	.0001
Hematocrit (%) 18.94 (3.80–29.00) 11.15 (3.80–2.346) .0001 Indirect Bilirubin (µm0/L) 5.24 (2.74–8.80) 3.40 (2.00–5.70) .0001 Detassium (mmo/L) 4.24 (3.95–4.80) 4.20 (3.77–4.62) .0001 Low density liporotein cholesterol (mmo/L) 2.50 (1.75–3.33) 2.47 (1.72–3.26) .0001 Mean corpuscular hemoglobin concentration (g/L) 326.75 (320.85–33.00) 329.44 (32.30–337.00) .0001 Mean corpuscular volume (fL) 90.60 (85.99–95.10) 90.40 (86.30–94.23) .0001 Mean potatele volume (fL) 8.90 (8.10–8.80) 8.83 (8.00–9.70) .0001 Mean platelet volume (fL) 8.90 (8.10–8.60) 8.83 (8.00–9.70) .0001 Mean platelet volume (fL) 8.90 (8.10–8.60) 8.83 (8.00–9.70) .0001 Moncytes (%) 0.59 (0.25–1.05) 0.56 (0.17–1.07) .0001 Sodium (mmo/L) 141.45 (138.35–144.37) 140.60 (137.60–143.23) .0001 Posphorus (mmo/L) 1.24 (1.05–14.7) 1.11 (0.90–1.31) .0001 Procelationin (mg/L) 1.24 (1.05–14.7) 1.11 (0.90–1.537) .0001 Posphorus (mmo	Hemoalobin (a/L)	101.00 (84.98–117.00)	119.00 (102.92–134.00)	.0001
Indirect Billingin (µmol/L) 5.24 (2.74–8.80) 3.40 (2.00–5.70).0001Potassium (nmol/L) 4.34 (3.95–4.80) 4.20 (3.77–4.62).0001Low density lipoprotein cholesterol (nmol/L) 2.50 (1.75–3.33) 2.47 (1.72–3.26).0001Lymphocyte (%)1.56 (1.04–2.10)1.30 (0.83–1.85).0001Mean corpuscular hemoglobin concentration (g/L) 326.75 (320.85–333.00) 329.44 (323.00–337.00).0001Mean corpuscular hemoglobin concentration (g/L) 90.60 (85.99–95.10) 90.40 (86.30–94.23).0001Magnesium (mmol/L) 0.95 (0.86–1.06) 0.91 (0.81–1.01).0001Magnesium (mmol/L) 0.59 (0.25–1.05) 0.56 (0.17–1.07).0001Monocytes (%) 0.59 (0.25–1.05) 0.56 (0.17–1.07).0001Monocytes (%) 6.70 (4.26–9.68) 5.56 (3.15–8.31).0001Prosphorus (mmol/L) 1.24 (1.05–1.47) 1.11 (0.90–1.31).0001Neutrophil (%) 6.70 (4.26–9.68) 5.56 (3.15–8.31).0001Procalcitonin (ng/mL) 1.46 (0.13.60–15.90) 13.94 (13.00–15.37).0001Red blood cell (10 ¹⁷² L) 3.89 (1.00–10.99) 3.67 (2.67–10.05).0001Total cholesterol (mmol/L) 1.42 (3.2–1.767) 4.10 (1.04–13.82).0001Total cholesterol (mmol/L) 1.02 (3.3–6.50).0001Total cholesterol (mmol/L) 1.02 (3.8–6.80) 2.55 (0.8–5.31).0001Total cholesterol (mmol/L) 1.02 (3.8–6.70).0001Total cholesterol (mmol/L) 1.02 (3.8–6.70).0001 </td <td>Hematocrit (%)</td> <td>18.94 (3.80–29.00)</td> <td>11.15 (3.80–2.346)</td> <td>.0001</td>	Hematocrit (%)	18.94 (3.80–29.00)	11.15 (3.80–2.346)	.0001
Potassium (mmol/L) 4.34 (3.95-4.80) 4.20 (3.77-4.62) .0001 Low density lipoprotein cholesterol (mmol/L) 2.60 (1.75-3.33) 2.47 (1.72-3.26) .0001 Lymphocyte (%) 1.56 (1.04-2.10) 1.30 (0.83-1.85) .0001 Mean corpuscular hemoglobin concentration (g/L) 326.75 (320.85-333.00) 329.44 (323.00-337.00) .0001 Mean corpuscular volume (fL) 90.60 (85.99-95.10) 90.40 (86.30-94.23) .0001 Mean potately volume (fL) 8.90 (8.10-9.80) 8.83 (8.00-9.70) .0001 Mean plately volume (fL) 8.90 (8.10-9.80) 8.83 (8.00-9.70) .0001 Monocytes (%) 0.59 (0.25-1.05) 0.56 (0.17-1.07) .0001 Sodium (mmol/L) 141.45 (138.35-144.37) 140.60 (13.60-143.23) .0001 Neutrophil (%) 6.70 (4.26-9.68) 5.56 (3.15-8.31) .0001 Prosptorus (mmol/L) 1.24 (1.05-1.47) 1.11 (0.90-1.31) .0001 Red bood cell distrbution width (%) 14.60 (13.60-15.90) 13.94 (13.00-15.37) .0001 Total bilibuiton (mmol/L) 1.14 (2.32-15.13) 4.05 (3.16-5.01) .0001 T	Indirect Bilirubin (µmol/L)	5.24 (2.74-8.80)	3.40 (2.00-5.70)	.0001
Low density lipoprotein cholesterol (mmol/L) $2.50 (1.75-3.33)$ $2.47 (1.72-3.26)$.0001Lymphocyte (%)1.56 (1.04-2.10)1.30 (0.83-1.85).0001Mean corpuscular hemoglobin concentration (g/L)326.75 (320.85-333.00)329.44 (323.00-337.00).0001Mean corpuscular volume (t)0.96 (0.85.99-95.10)90.40 (86.30-94.23).0001Magnesium (mmol/L)0.95 (0.86-1.06)0.91 (0.81-1.01).0001Mean platelet volume (t)8.90 (8.10-9.80)8.83 (8.00-9.70).0001Monocytes (%)0.59 (0.25-1.05)0.56 (0.17-1.07).0001Sodium (mmol/L)141.45 (138.35-144.37)140.60 (137.60-143.23).0001Neurophil (%)6.70 (4.26-9.68)5.56 (3.15-8.31).0001Prosphorus (mmol/L)1.19 (0.10-1.42)1.17 (0.27-1.86).0001Red blood cell (10 ¹⁷ L)1.99 (1.0-1.99)3.67 (2.67-10.05).0001Total cholesterol (mmol/L)1.46 (0.16.0-15.30)1.394 (13.00-15.37).0001Total cholesterol (mmol/L)1.01 (4.31-22.45).7.55 (4.50-13.10).0001Total cholesterol (mmol/L)1.01 (4.31-22.45).7.55 (4.50-13.10).0001Total cholesterol (mmol/L)1.10 (7.85-18.30)2.25 (0.08-5.31).0001Thyoid-stimulating hormone (µLU/mL)2.62 (0.38-5.60)2.25 (0.08-5.31).0001Total cholesterol (mmol/L)1.10 (7.85-18.30)5.10 (2.45-8.07).0001Total cholesterol (mmol/L)1.10 (7.85-18.30)5.10 (2.45-8.07).0001Total cholesterol (mmol/L)1.10 (7.85-18.30) </td <td>Potassium (mmol/L)</td> <td>4.34 (3.95–4.80)</td> <td>4.20 (3.77–4.62)</td> <td>.0001</td>	Potassium (mmol/L)	4.34 (3.95–4.80)	4.20 (3.77–4.62)	.0001
Lymphocyte (%) 1.56 (1.04–2.10) 1.30 (0.83–1.85) .0001 Mean corpuscular hemoglobin concentration (g/L) 326.75 (320.85–333.00) 329.44 (323.00–337.00) .0001 Magnesium (mmo/L) 90.60 (85.99–95.10) 90.40 (86.30–94.23) .0001 Magnesium (mmo/L) 0.95 (0.86–1.06) 0.91 (0.81–1.01) .0001 Magnesium (mmo/L) 8.90 (8.10–8.00) 8.83 (8.00–9.70) .0001 Monocytes (%) 0.59 (0.25–1.05) 0.56 (0.17–1.07) .0001 Sodium (mmo/L) 141.45 (138.35–144.37) 140.60 (137.60–143.23) .0001 Neutrophil (%) 6.70 (4.26–9.68) 5.56 (3.15–8.31) .0001 Procacitonin (ng/nL) 1.19 (0.10–1.42) 1.17 (0.27–1.86) .0001 Red blood cell (10 ¹² /L) 3.89 (1.00–10.99) 3.67 (2.67–10.05) .0001 Red blood cell distribution width (%) 14.60 (13.60–15.90) 13.94 (13.00–15.37) .0001 Total bilinubi (µmo/L) 10.14 (4.31–22.45) 7.55 (4.50–13.10) .0001 Total bilinubi (µmo/L) 10.14 (4.31–22.45) 7.55 (4.50–13.10) .0001 Total bilinubi (µmo/L)	Low density lipoprotein cholesterol (mmol/L)	2.50 (1.75–3.33)	2.47 (1.72–3.26)	.0001
Mean corpuscular hemoglobin concentration (g/L) 326.75 (320.85–333.00) 329.44 (323.00–337.00) .0001 Mean corpuscular volume (tl) 90.60 (85.99–95.10) 90.40 (86.30–94.23) .0001 Magnesium (mmo/L) 0.95 (0.86–1.06) 0.91 (0.81–1.01) .0001 Mean platelet volume (tL) 8.90 (8.10–9.80) 8.83 (8.00–9.70) .0001 Monocytes (%) 0.59 (0.25–1.05) 0.56 (0.17–1.07) .0001 Sodium (mmo/L) 141.45 (138.35–144.37) 140.60 (137.60–143.23) .0001 Neutrophil (%) 6.70 (4.26–9.68) 5.56 (3.15–8.31) .0001 Phosphorus (mmo/L) 1.24 (1.05–1.47) 1.11 (0.90–1.31) .0001 Procalcitonin (ng/mL) 1.9 (0.10–1.42) 1.17 (0.27–1.86) .0001 Red blood cell (10 ¹² /L) 3.89 (1.00–10.99) 3.67 (2.67–10.05) .0001 Total cholesterol (mmo/L) 4.12 (3.21–5.13) 4.05 (3.16–5.01) .0001 Total cholesterol (mmo/L) 1.71 (1.06–2.67) 1.63 (0.89–2.62) .0001 Total cholesterol (mmo/L) 1.71 (1.06–2.67) 1.63 (0.89–2.62) .0001 Total cholesterol (mmo/L)	Lymphocyte (%)	1.56 (1.04-2.10)	1.30 (0.83–1.85)	.0001
Mean corpuscular volume (fL) 90.60 (85.99–95.10) 90.40 (86.30–94.23) .0001 Magnesium (mmol/L) 0.95 (0.86–1.06) 0.91 (0.81–1.01) .0001 Monocytes (%) 0.59 (0.25–1.05) 0.56 (0.17–1.07) .0001 Sodium (mmol/L) 141.45 (138.35–144.37) 140.60 (137.60–143.23) .0001 Neutrophil (%) 6.70 (4.26–0.68) 5.56 (3.15–8.31) .0001 Procalcionin (ng/nL) 1.19 (0.10–1.42) 1.17 (0.27–1.86) .0001 Red blood cell (10 ¹² /L) 3.89 (1.00–10.99) 3.67 (2.67–10.05) .0001 Total cholesterol (mmol/L) 4.12 (3.21–5.13) 4.05 (3.15–8.31) .0001 Total cholesterol (mmol/L) 1.19 (0.10–1.42) 1.17 (0.27–1.86) .0001 Red blood cell (10 ¹² /L) 3.89 (1.00–10.99) 3.67 (2.67–10.05) .0001 Total cholesterol (mmol/L) 1.12 (3.21–5.13) 4.05 (3.16–3.01) .0001 Total bilirubin (µmol/L) 5.69 (2.37–17.67) 4.10 (1.04–13.82) .0001 Total bilirubin (µmol/L) 10.14 (4.31–22.45) 7.55 (4.50–13.10) .0001 Total bilirubin (µmol/L) 10.14	Mean corpuscular hemoglobin concentration (g/L)	326.75 (320.85-333.00)	329.44 (323.00-337.00)	.0001
Magnesium (mmol/L)0.95 (0.86-1.06)0.91 (0.81-1.01).0001Mean platlet volume (fL)8.90 (8.10-9.80)8.83 (8.00-9.70).0001Monocytes (%)0.59 (0.25-1.05)0.56 (0.17-1.07).0001Sodium (mmol/L)141.45 (138.35-144.37)140.60 (137.60-143.23).0001Neutrophil (%)6.70 (4.26-9.68)5.56 (3.15-8.31).0001Prosphorus (mmol/L)1.24 (1.05-1.47)1.11 (0.90-1.31).0001Proclationin (ng/mL)1.99 (1.00-10.99)3.67 (2.67-10.05).0001Red blood cell (10 ¹² /L)3.89 (1.00-10.99)3.67 (2.67-10.05).0001Total cholesterol (mmol/L)4.12 (3.21-5.13)4.05 (3.16-5.01).0001Total cholesterol (mmol/L)5.69 (2.37-17.67)4.10 (1.04-13.82).0001Total bilirubin (umol/L)10.14 (4.31-22.45)7.55 (4.50-13.10).0001Total bile acid (µmol/L)1.71 (1.06-2.67)1.63 (0.89-2.62).0001Thryoid-stimulating hormone (µLl/mL)2.62 (0.38-5.60)2.25 (0.08-5.31).0001Urine acid (µmol/L)11.70 (7.85-18.30)5.10 (2.45-8.07).0001White blood cell count (10 ⁹ /L)7.99 (5.00-16.14)6.40 (1.98-21.00).0001Vinte total protein (mg/24 h)597.50 (6.60-255.70)4.68 (1.28-7.98).0001Urine total protein (mg/24 h)597.50 (6.60-255.70)4.68 (1.28-7.98).0001Arbitroplobulin (mg/L)63.12 (31.00-80.23)25.88 (5.62-46.74).0001Settimated glomerular filtration rate (mL/min/1.73 m ²)53.70 (6.60-255.70)4.68 (1	Mean corpuscular volume (fL)	90.60 (85.99-95.10)	90.40 (86.30-94.23)	.0001
Mean platelet volume (fL)8.90 (8.10–9.80)8.83 (8.00–9.70)0.001Monocytes (%)0.59 (0.25–1.05)0.56 (0.17–1.07)0.001Sodium (mmol/L)141.45 (138.35–144.37)140.60 (137.60–143.23)0.001Neutrophil (%)6.70 (4.26–9.68)5.56 (3.15–8.31)0.001Phosphorus (mmol/L)1.24 (1.05–1.47)1.11 (0.90–1.31)0.001Procalcitonin (ng/mL)1.19 (0.10–1.42)1.77 (0.27–1.86)0.001Red blood cell (distribution width (%)14.60 (13.60–15.90)3.67 (2.67–10.05)0.001Total cholesterol (mmol/L)4.12 (3.21–5.13)4.05 (3.16–5.01)0.001Total bile acid (µmol/L)5.69 (2.37–17.67)4.10 (1.04–13.82)0.001Total bile acid (µmol/L)1.71 (1.06–2.67)1.63 (0.89–2.62)0.001Thyroid-stimulating hormone (µLU/mL)2.62 (0.38–5.60)2.25 (0.08–5.31)0.001Thromohin time (s)15.30 (17.85–17.30)5.10 (2.45–8.07)0.001Urine acid (µmol/L)7.99 (5.00–16.14)6.40 (12.32–17.32)0.001White blood cell court (10 ⁹ /L)7.99 (5.00–16.14)6.40 (12.82–17.33)0.001Urine total protein (mmol/L)7.99 (5.00–25.57.0)4.68 (1.28–7.98)0.001Carbon dioxide combining power (mmol/L)53.12 (31.00–80.23)25.88 (5.62–46.74)0.001g2-Microglobulin (mg/L)53.12 (31.00–80.23)25.88 (5.62–46.74)0.001g2-Microglobulin (mg/L)6.78 (3.75–9.77)1.74 (0.27–4.00)0.001	Magnesium (mmol/L)	0.95 (0.86-1.06)	0.91 (0.81-1.01)	.0001
Monocytes (%) 0.59 (0.25–1.05) 0.56 (0.17–1.07) 0.001 Sodium (mmol/L)141.45 (138.35–144.37)140.60 (137.60–143.23) 0.001 Neutrophil (%) 6.70 (4.26–9.68) 5.56 (3.15–8.31) 0.001 Phosphorus (mmol/L)1.24 (1.05–1.47) 1.11 (0.90–1.31) 0.001 Red blood cell (10 ¹² /L) 3.89 (1.00–10.99) 3.67 (2.67–10.05) 0.001 Red blood cell distribution width (%) 14.60 (13.80–15.90) 3.94 (13.00–15.37) 0.001 Total cholesterol (mmol/L) 5.69 (2.37–17.67) 4.10 (1.4–13.82) 0.001 Total bilicutin (µmol/L) 10.14 (4.31–22.45) 7.55 (4.50–13.10) 0.001 Total bilicutin (µmol/L) 1.71 (1.06–2.67) 1.63 (0.89–2.62) 0.001 Thyroid-stimulating hormone (µLl/mL) 2.62 (0.38–5.60) 2.25 (0.08–5.31) 0.001 Thrombin time (s) 15.30 (13.58–17.70) 14.60 (12.32–17.32) 0.001 Urine acid (µmol/L) 1.70 ($7.85–18.30$) 5.10 ($2.45–8.07$) 0.001 Thrombin time (s) 7.99 (5.00–16.14) 6.40 ($1.98–21.00$) 0.001 Urine total policutin (10^9 /L) 7.99 (5.00–16.14) 6.40 ($1.98–21.00$) 0.001 Urine total policutin (mg/24 h) 597.50 ($66.90–2255.70$) 4.68 ($1.28-7.98$) 0.001 Sp2-Microglobulin (mg/L) 53.12 ($31.0–80.23$) 25.88 ($56.2–46.74$) 0.001 B2-Microglobulin (mg/L) 6.78 ($3.75–9.97$) 1.74 ($0.27-4.00$) 0.001	Mean platelet volume (fL)	8.90 (8.10-9.80)	8.83 (8.00-9.70)	.0001
Sodium (mmol/L)141.45 (138.35–144.37)140.60 (137.60–143.23).0001Neutrophil (%) 6.70 (4.26–9.68) 5.56 (3.15–8.31).0001Phosphorus (mmol/L) 1.24 (1.05–1.47) 1.11 (0.90–1.31).0001Procalcitonin (ng/mL) 1.19 (0.10–1.42) 1.17 (0.27–1.86).0001Red blood cell (10 ¹² /L) 3.89 (1.00–10.99) 3.67 (2.67–10.05).0001Total cholesterol (mmol/L) 4.12 (3.21–5.13) 4.05 (3.16–5.01).0001Total bile acid (µmol/L) 5.69 (2.37–17.67) 4.10 (1.04–13.82).0001Total bilinubin (µmol/L) 1.71 (1.06–2.67) 1.63 (0.89–2.62).0001Total bilinubin (µmol/L) 2.62 (0.38–5.60) 2.25 (0.86–5.31).0001Triglyceride (mmol/L) 35.10 (278.40–435.28)250.99 (179.79–328.00).0001Thrombin time (s) 15.30 (13.58–17.70) 14.60 (1.38–21.00).0001Urine acid (µmol/L) 7.99 (5.00–16.14) 6.40 (1.98–21.00).0001White blood cell count (10 ⁹ /L) 7.99 (5.00–16.14) 6.40 (1.98–21.00).0001Carbon dioxide combining power (mmol/L) 23.00 (20.40–256.55) 24.81 (22.20–27.33).0001Urine total protein (mg/24) 597.50 (66.90–2255.70) 4.68 (1.28–7.98).0001Qarbon dioxide combining power (mmol/L) 53.12 (31.00–80.23) 28.88 (5.62–46.74).0001B2-Microglobulin (mg/L) 6.78 (3.75–9.97) 1.74 (0.27–4.00).0001	Monocytes (%)	0.59 (0.25–1.05)	0.56 (0.17–1.07)	.0001
Neutrophil (%) 6.70 ($4.26-9.68$) 5.56 ($3.15-8.31$) 0.001 Phosphorus (mmol/L) 1.24 ($1.05-1.47$) 1.11 ($0.90-1.31$) 0.001 Procalcitonin (ng/mL) 1.19 ($0.10-1.42$) 1.17 ($0.27-1.86$) 0.001 Red blood cell (10^{12} /L) 3.89 ($1.00-10.99$) 3.67 ($2.67-10.05$) 0.001 Red blood cell distribution width (%) 14.60 ($13.60-15.90$) 13.94 ($13.00-15.37$) 0.001 Total cholesterol (mmol/L) 4.12 ($3.21-5.13$) 4.05 ($3.16-5.01$) 0.001 Total bile acid (μ mol/L) 5.69 ($2.37-17.67$) 4.10 ($1.04-13.82$) 0.001 Total bile acid (μ mol/L) 10.14 ($4.31-22.45$) 7.55 ($4.50-13.10$) 0.001 Triglyceride (mmol/L) 1.71 ($1.62-2.67$) 1.63 ($0.89-2.62$) 0.001 Thyroid-stimulating hormone (μ Ll/mL) 2.62 ($0.38-5.60$) 2.25 ($0.08-5.31$) 0.001 Urine acid (μ mol/L) 351.00 ($27.84.0-435.28$) 250.99 ($179.79-328.00$) 0.001 Thrombin time (s) 11.70 ($7.85-18.30$) 5.10 ($2.45-8.07$) 0.001 White blood cell count (10^9 /L) 7.99 ($5.00-16.14$) 6.40 ($1.98-21.00$) 0.001 Carbon dioxide combining power (mmol/L) 23.00 ($0.2.45-53.42$) 94.93 ($90.17-108.39$) 0.001 Carbon dioxide combining power (mmol/L) 23.00 ($20.40-25.65$) 24.81 ($22.0-27.33$) 0.001 Carbon dioxide combining power (mmol/L) 597.50 ($66.90-2255.70$) 4.68 ($1.28-7.98$) 0.001 Carbon dioxide combining power (mmol/L) 597.50 (66.90	Sodium (mmol/L)	141.45 (138.35–144.37)	140.60 (137.60–143.23)	.0001
Phosphorus (mmol/L) $1.24 (1.05-1.47)$ $1.11 (0.90-1.31)$.0001Procalcitonin (ng/mL) $1.19 (0.10-1.42)$ $1.17 (0.27-1.86)$.0001Red blood cell (10 ¹² L) $3.69 (1.00-10.99)$ $3.67 (2.67-10.05)$.0001Red blood cell distribution width (%) $14.60 (13.60-15.90)$ $13.94 (13.00-15.37)$.0001Total cholesterol (mmol/L) $4.12 (3.21-5.13)$ $4.05 (3.16-5.01)$.0001Total blia caid (µmol/L) $5.69 (2.37-17.67)$ $4.10 (1.04-13.82)$.0001Total blinubin (µmol/L) $10.14 (4.31-22.45)$ $7.55 (4.50-13.10)$.0001Triglyceride (mmol/L) $1.71 (1.06-2.67)$ $1.63 (0.89-2.62)$.0001Thyroid-stimulating hormone (µU/mL) $2.62 (0.38-5.60)$ $2.25 (0.08-5.31)$.0001Urine acid (µmol/L) $15.30 (13.58-17.70)$ $14.60 (12.32-17.32)$.0001Thrombin time (s) $15.30 (13.58-17.70)$ $14.60 (12.32-17.32)$.0001Urea (mmol/L) $7.99 (5.00-16.14)$ $6.40 (1.98-21.00)$.0001White blood cell count (10^9 /L) $7.99 (5.00-16.14)$ $6.40 (1.98-21.00)$.0001carbon dioxide combining power (mmol/L) $23.00 (20.40-25.65)$ $24.81 (22.20-27.33)$.0001Qarbon dioxide combining power (mmol/L) $53.12 (31.00-80.23)$ $25.88 (5.62-46.74)$.0001 $g2$ -Microglobulin (mg/L) $53.12 (31.00-80.23)$ $25.88 (5.62-46.74)$.0001 $g2$ -Microglobulin (mg/L) $6.78 (3.75-9.97)$ $1.74 (0.27-4.00)$.0001	Neutrophil (%)	6.70 (4.26–9.68)	5.56 (3.15–8.31)	.0001
Procalcitonin (ng/nL)1.19 (0.10–1.42)1.17 (0.27–1.86).0001Red blood cell (10 ¹² /L)3.89 (1.00–10.99)3.67 (2.67–10.05).0001Red blood cell distribution width (%)14.60 (13.60–15.90)13.94 (13.00–15.37).0001Total cholesterol (mmol/L)4.12 (3.21–5.13)4.05 (3.16–5.01).0001Total bile acid (µmol/L)5.69 (2.37–17.67)4.10 (1.04–13.82).0001Total bile acid (µmol/L)10.14 (4.31–22.45)7.55 (4.50–13.10).0001Total bilinubin (µmol/L)1.71 (1.06–2.67)1.63 (0.89–2.62).0001Thyroid-stimulating hormone (µLU/mL)2.62 (0.38–5.60)2.25 (0.08–5.31).0001Urine acid (µmol/L)351.00 (278.40–435.28)250.99 (179.79–328.00).0001Thrombin time (s)15.30 (13.58–17.70)14.60 (12.32–17.32).0001Urea (mmol/L)7.99 (5.00–16.14)6.40 (1.98–21.00).0001estimated glomerular filtration rate (mL/min/1.73 m ²)35.79 (14.35–53.42)94.93 (90.17–108.39).0001Carbon dioxide combining power (mmol/L)2.30 (2.40–25.65)24.81 (22.20–27.33).0001urine total protein (mg/24 h)597.50 (66.90–2255.70)4.68 (1.28–7.98).0001 α -Microglobulin (mg/L)6.78 (3.75–9.97)1.74 (0.27–4.00).0001 β -Microglobulin (mg/L)6.78 (3.75–9.97)1.74 (0.27–4.00).0001	Phosphorus (mmol/L)	1.24 (1.05–1.47)	1.11 (0.90–1.31)	.0001
Red blood cell (10 ¹² /L) 3.89 (1.00-10.99) 3.67 (2.67-10.05).0001Red blood cell distribution width (%)14.60 (13.60-15.90) 13.94 (13.00-15.37).0001Total cholesterol (mmol/L)4.12 (3.21-5.13)4.05 (3.16-5.01).0001Total bile acid (µmol/L)5.69 (2.37-17.67)4.10 (1.04-13.82).0001Total bile acid (µmol/L)10.14 (4.31-22.45)7.55 (4.50-13.10).0001Triglyceride (mmol/L)10.14 (4.31-22.45)7.55 (4.50-13.10).0001Thyroid-stimulating hormone (µU/mL)2.62 (0.38-5.60)2.25 (0.08-5.31).0001Urine acid (µmol/L)351.00 (278.40-435.28)250.99 (179.79-328.00).0001Thrombin time (s)15.30 (13.58-17.70)14.60 (12.32-17.32).0001Urea (mmol/L)7.99 (5.00-16.14)6.40 (1.98-21.00).0001White blood cell count (10 ⁹ /L)7.99 (5.00-16.14)6.40 (1.98-21.00).0001Carbon dioxide combining power (mmol/L)23.00 (20.40-25.65)24.81 (22.20-27.33).0001Urine total protein (mg/24 h)597.50 (66.90-2255.70)4.68 (1.28-7.98).0001 α -Microglobulin (mg/L)53.12 (31.00-80.23)25.88 (5.62-46.74).0001 β 2-Microglobulin (mg/L)6.78 (3.75-9.97)1.74 (0.27-4.00).0001	Procalcitonin (ng/mL)	1.19 (0.10–1.42)	1.17 (0.27–1.86)	.0001
Red blood cell distribution width (%)14.60 (13.60–15.90)13.94 (13.00–15.37).0001Total cholesterol (mmol/L)4.12 (3.21–5.13)4.05 (3.16–5.01).0001Total bile acid (µmol/L)5.69 (2.37–17.67)4.10 (1.04–13.82).0001Total bilirubin (µmol/L)10.14 (4.31–22.45)7.55 (4.50–13.10).0001Triglyceride (mmol/L)1.71 (1.06–2.67)1.63 (0.89–2.62).0001Thyroid-stimulating hormone (µlU/mL)2.62 (0.38–5.60)2.25 (0.8–5.31).0001Urine acid (µmol/L)351.00 (278.40–435.28)250.99 (179.79–328.00).0001Urine acid (µmol/L)15.30 (13.58–17.70)14.60 (1.23–17.32).0001Urea (mmol/L)11.70 (7.85–18.30)5.10 (2.45–8.07).0001Urea (mmol/L)7.99 (5.00–16.14)6.40 (1.98–21.00).0001estimated glomerular filtration rate (mL/min/1.73 m²)35.79 (14.35–53.42)94.93 (90.17–108.39).0001Urine total protein (mg/24 h)597.50 (66.90–2255.70)4.68 (1.28–7.98).0001 α -Microglobulin (mg/L)53.12 (31.00–80.23)25.88 (5.62–46.74).0001 β 2-Microglobulin (mg/L)6.78 (3.75–9.97)1.74 (0.27–4.00).0001	Red blood cell (10 ⁻² /L)	3.89 (1.00–10.99)	3.67 (2.67–10.05)	.0001
Total bile acid (µmol/L)4.12 (3.21–5.13)4.05 (3.16–5.01).0001Total bile acid (µmol/L)5.69 (2.37–17.67)4.10 (1.04–13.82).0001Total bile acid (µmol/L)10.14 (4.31–22.45)7.55 (4.50–13.10).0001Triglyceride (mmol/L)1.71 (1.06–2.67)1.63 (0.89–2.62).0001Thyroid-stimulating hormone (µU/mL)2.62 (0.38–5.60)2.25 (0.86–5.31).0001Urine acid (µmol/L)351.00 (278.40–435.28)250.99 (179.79–328.00).0001Urine acid (µmol/L)15.30 (13.58–17.70)14.60 (12.32–17.32).0001Urea (mmol/L)11.70 (7.85–18.30)5.10 (2.45–8.07).0001Urea (mmol/L)7.99 (5.00–16.14)6.40 (1.98–21.00).0001estimated glomerular filtration rate (mL/min/1.73 m²)35.79 (14.35–53.42)94.93 (90.17–108.39).0001Urine total protein (mg/24 h)597.50 (66.90–2255.70)4.68 (1.28–7.98).0001 α -Microglobulin (mg/L)53.12 (31.00–80.23)25.88 (5.62–46.74).0001 β 2-Microglobulin (mg/L)6.78 (3.75–9.97)1.74 (0.27–4.00).0001	Red blood cell distribution width (%)	14.60 (13.60–15.90)	13.94 (13.00–15.37)	.0001
Total bile add (µH0/L) $3.69 (2.37-17.67)$ $4.10 (1.04-13.82)$ $.0001$ Total bile add (µH0/L) $10.14 (4.31-22.45)$ $7.55 (4.50-13.10)$ $.0001$ Triglyceride (mmol/L) $1.71 (1.06-2.67)$ $1.63 (0.89-2.62)$ $.0001$ Thyroid-stimulating hormone (µLU/mL) $2.62 (0.38-5.60)$ $2.25 (0.08-5.31)$ $.0001$ Urine acid (µmol/L) $351.00 (278.40-435.28)$ $250.99 (179.79-328.00)$ $.0001$ Urine mol/L) $15.30 (13.58-17.70)$ $14.60 (12.32-17.32)$ $.0001$ Urea (mmol/L) $11.70 (7.85-18.30)$ $5.10 (2.45-8.07)$ $.0001$ White blood cell court $(10^9/L)$ $7.99 (5.00-16.14)$ $6.40 (1.98-21.00)$ $.0001$ carbon dioxide combining power (mmol/L) $23.00 (20.40-25.65)$ $24.81 (22.20-27.33)$ $.0001$ Urine total protein (mg/24 h) $597.50 (66.90-2255.70)$ $4.68 (1.28-7.98)$ $.0001$ α -Microglobulin (mg/L) $53.12 (31.00-80.23)$ $25.88 (5.62-46.74)$ $.0001$ β 2-Microglobulin (mg/L) $6.78 (3.75-9.97)$ $1.74 (0.27-4.00)$ $.0001$	Total cholesterol (mmol/L)	4.12 (3.21-3.13) 5.60 (3.27, 17.67)	4.05 (3.16-5.01)	.0001
Total bindulin (plinb/L)10.14 ($(4.31-22.43)$)7.55 ($(4.50-13.10)$.0001Triglyceride (mmol/L)1.71 ($1.06-2.67$)1.63 ($0.89-2.62$).0001Thyroid-stimulating hormone (µU/mL)2.62 ($0.38-5.60$)2.25 ($0.86-5.31$).0001Urine acid (µmol/L)351.00 ($278.40-435.28$)250.99 ($179.79-328.00$).0001Urea (mmol/L)15.30 ($13.58-17.70$)14.60 ($12.32-17.32$).0001Urea (mmol/L)11.70 ($7.85-18.30$)5.10 ($2.45-8.07$).0001White blood cell count ($10^9/L$)7.99 ($5.00-16.14$)6.40 ($1.98-21.00$).0001cstimated glomerular filtration rate (mL/min/1.73 m ²)35.79 ($14.35-53.42$)94.93 ($90.17-108.39$).0001Urine total protein (mg/24 h)597.50 ($66.90-2255.70$)4.68 ($1.28-7.98$).0001 α -Microglobulin (mg/L)53.12 ($31.00-80.23$)25.88 ($5.62-46.74$).0001 β 2-Microglobulin (mg/L)6.78 ($3.75-9.97$)1.74 ($0.27-4.00$).0001	Total bille aciu (µmol/L)	5.09(2.37 - 17.07)	4.10 (1.04–13.62) 7.65 (4.60, 12.10)	.0001
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$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	Instantiating normalie (pio/mic)	2.02 (0.30-3.00) 351 00 (278 40-435 28)	250 99 (179 79–328 00)	.0001
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Order (milds / L)The field (1.00 milds / L)The field (1.00 milds / L)The field (1.00 milds / L)White blood cell count (10 ⁹ /L)7.99 (5.00-16.14)6.40 (1.98-21.00).0001estimated glomerular filtration rate (mL/min/1.73 m²)35.79 (14.35-53.42)94.93 (90.17-108.39).0001Carbon dioxide combining power (mmol/L)23.00 (20.40-25.65)24.81 (22.20-27.33).0001Urine total protein (mg/24 h)597.50 (66.90-2255.70)4.68 (1.28-7.98).0001 α -Microglobulin (mg/L)53.12 (31.00-80.23)25.88 (5.62-46.74).0001 β 2-Microglobulin (mg/L)6.78 (3.75-9.97)1.74 (0.27-4.00).0001	Lirea (mmol/l)	11 70 (7 85–18 30)	5 10 (2 45–8 07)	0001
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Carbon dioxide combining power (mmol/L) 23.00 (20.40–25.65) 24.81 (22.20–27.33) .0001 Urine total protein (mg/24 h) 597.50 (66.90–2255.70) 4.68 (1.28–7.98) .0001 α-Microglobulin (mg/L) 53.12 (31.00–80.23) 25.88 (5.62–46.74) .0001 β2-Microglobulin (mg/L) 6.78 (3.75–9.97) 1.74 (0.27–4.00) .0001	estimated glomerular filtration rate (ml /min/1 7.3 m ²)	35.79 (14.35–53.42)	94.93 (90.17–108.39)	.0001
Urine total protein (mg/24 h)597.50 (66.90–2255.70)4.68 (1.28–7.98).0001 α -Microglobulin (mg/L)53.12 (31.00–80.23)25.88 (5.62–46.74).0001 β 2-Microglobulin (mg/L)6.78 (3.75–9.97)1.74 (0.27–4.00).0001	Carbon dioxide combining power (mmol/L)	23.00 (20.40–25.65)	24.81 (22.20–27.33)	.0001
α-Microglobulin (mg/L) 53.12 (31.00-80.23) 25.88 (5.62-46.74) .0001 β2-Microglobulin (mg/L) 6.78 (3.75-9.97) 1.74 (0.27-4.00) .0001	Urine total protein (mg/24 h)	597.50 (66.90–2255.70)	4.68 (1.28–7.98)	.0001
β2-Microglobulin (mg/L) 6.78 (3.75–9.97) 1.74 (0.27–4.00) .0001	α -Microglobulin (mg/L)	53.12 (31.00–80.23)	25.88 (5.62–46.74)	.0001
	β2-Microglobulin (mg/L)	6.78 (3.75–9.97)	1.74 (0.27–4.00)	.0001



Figure 1. The dose–response association between TyG and risk of biopsy-proven diabetic nephropathy overall and by fasting glucose level. Body mass index, systolic blood pressure, diastolic blood pressure, antihypertensive treatment, lowering lipid treatment, insulin treatment, HbA1c, alanine transaminase, alkaline phosphatase, activated partial thromboplastin time, direct bilirubin, Basophil, cholinesterase, calcium, chlorine, creatinine, C reaction protein, cysteine proteinase inhibitor, D_Dimer, fibrinogen Degradation Products, gamma glutamyl transpeptidase, globulin, glucose, high density lipoprotein cholesterol, hemoglobin, hematocrit, indirect Bilirubin, potassium, low density lipoprotein cholesterol, lymphocyte, mean corpuscular hemoglobin concentration, mean corpuscular volume, magnesium, mean platelet volume, monocytes, sodium, neutrophil, phosphorus, procalcitonin, red blood cell distribution width, total cholesterol, total bilirubin, triglyceride, thyroid-stimulating hormone, urine acid, thrombin time, shite blood cell count, estimated glomerular filtration rate, carbon dioxide combining power, urine total protein, α-microglobulin, β2-microglobulin were adjusted.



Figure 2. The dose-response association between TyG and risk of biopsy-proven diabetic nephropathy by triglyceride level. Body mass index, systolic blood pressure, diastolic blood pressure, antihypertensive treatment, lowering lipid treatment, insulin treatment, HbA1c, alanine transaminase, alkaline phosphatase, activated partial thromboplastin time, direct bilirubin, Basophil, cholinesterase, calcium, chlorine, creatinine, C reaction protein, cysteine proteinase inhibitor, D_Dimer, fibrinogen Degradation Products, gamma glutamyl transpeptidase, globulin, glucose, high density lipoprotein cholesterol, hemoglobin, hematocrit, indirect Bilirubin, potassium, low density lipoprotein cholesterol, lymphocyte, mean corpuscular hemoglobin concentration, mean corpuscular volume, magnesium, mean platelet volume, monocytes, sodium, neutrophil, phosphorus, procalcitonin, red blood cell, et distribution width, total cholesterol, total bile acid, total bilirubin, triglyceride, thyroid-stimulating hormone, urine acid, thrombin time, white blood cell count, estimated glomerular filtration rate, carbon dioxide combining power, urine total protein, α-microglobulin, β2-microglobulin were adjusted.

people with TyG index at 8.9 had a higher risk of coronary artery stenosis and this risk significantly increased among those with a TyG index of 9.7.^[26] In another study, in the general population, compared with people whose TyG index was below 8.21, the risk of incident type 2 diabetes significantly increased with a TyG index of 8.21 to 5.56, plateaued and then increased at a TyG index > 8.97.^[24] However, in those studies, the TyG index was modeled as a categorical variable grouped by percentiles, a

method no longer recommended as it is found to be less informative.^[28] In our study, TyG was modeled as a continuous variable, applying a flexible cubic spline regression model to derive a more accurate dose–response relationship, "J-shape" and a convincible threshold, TyG at 9.05 to 9.09 for future replications and clinical practice.

The mechanism behind the association between TyG index and risk of newly diagnosed biopsy-proven DN could be the

Table 2

Adjusted incidence rates ratio for risk of newly diagnosed biopsyproven diabetes nephropathy by 1 unit increase in TyG overall and in groups classified by TyG threshold (9.07).

	TyG < 9.07	TyG \geq 9.07
Overall	0.87 (0.72-1.05)	1.56 (1.27-1.91)
Fasting glucose < 8.0 mmol/L	0.78 (0.233-2.64)	1.50 (1.09–2.06)
Fasting glucose \geq 8.0 mmol/L	1.00 (0.638-1.56)	2.06 (1.01-4.20)
Triglyceride < 1.5 mmol/L	0.53 (0.185-1.53)	0.99 (0.41-2.40)
Triglyceride \geq 1.5 mmol/L	0.91 (0.361-2.31)	1.92 (1.10–3.34)

Body mass index, systolic blood pressure, diastolic blood pressure, antihypertensive treatment, lowering lipid treatment, insulin treatment, HbA1c, alanine transaminase, alkaline phosphatase, activated partial thromboplastin time, direct bilirubin, Basophil, cholinesterase, calcium, chlorine, creatinine, C reaction protein, cysteine proteinase inhibitor, D_Dimer, fibrinogen Degradation Products, gamma glutamyl transpeptidase, globulin, glucose, high density lipoprotein cholesterol, hemoglobin, hematocrit, indirect Bilirubin, potassium, low density lipoprotein cholesterol, lymphocyte, mean corpuscular hemoglobin concentration, mean corpuscular volume, magnesium, mean platelet volume, monocytes, sodium, neutrophil, phosphorus, procalcitonin, red blood cell, red blood cell distribution width, total cholesterol, total bile acid, total bilirubin, triglyceride, thyroid-stimulating hormone, urine acid, thrombin time, white blood cell count, estimated glomerular filtration rate, carbon dioxide combining power, urine total protein, α-microglobulin, β2-microglobulin were adjusted.

progression of IR in people with type 2 diabetes.^[29] Previous findings suggest that the deteriorated IR in people with type 2 diabetes is associated with significantly changed levels of hormone, like parathyroid hormone,^[30] cortisol,^[31] peptide hormone^[32,33] that could lead to microalbuminuria and declined eGFR in people with type 2 diabetes.

Our findings have some potential implications for the clinical practice. First, this dose-response relationship and especially the threshold found in our study could be used as a prognostic index in clinical practice to identify potentially high-risk individuals that could warrant more intensive treatment to postpone the progress of DN. In practical terms, the need to reduce and then cease metformin, an insulin sensitizer, could accelerate progres-sion to end-stage renal disease.^[34] The careful use of a thiazolidinedione, while monitoring for and avoiding fluid overload, could be a strategy to reduce progression while maintaining euglycemia.^[35] Finally, while the clinical utilisation of HOMA is restricted by its cost and lack of utility in insulintreated diabetes, the TyG Index, a measurement of fasting glucose and triglycerides, could be used as a marker of IR.^[20,36] This index has the advantage of being clinically applicable as both triglyceride and glucose concentrations are inexpensive and routinely measured in those with diabetes.^[20]

Our study has some limitations. First, the control population were patients admitted to hospital, and therefore unlikely to be representative of the Chinese type 2 diabetes population. However, those with DN were also hospital patients, partly because there are no distinctive differences between primary and secondary care settings in China. The potential selection bias in our study would therefore be lower than in settings without this continuum. Future validation studies are warranted in other type 2 diabetes populations, including those from ambulatory care (primary and secondary). Secondly, the proportion of people with missing data was significant, particularly for some covariables. Although our analyses were carried out using imputed datasets, further validation studies with datasets with less missing data are also warranted.

In summary, we have identified a non-linear relationship between the TyG index, a proxy for IR, and risk of newly diagnosed biopsy-proven DN in people with type 2 diabetes. The TyG index threshold of 9.05 to 9.09 may be useful for identifying high-risk individuals for further intensive intervention. These findings may suggest a greater role for insulin sensitizers in the prevention of DN. Further replication studies are warranted.

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