

Serum HGF ,PCIII and PLT are Noninvasive Markers for the diagnosis of nonalcoholic fatty liver disease

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Research article

Keywords: Nonalcoholic fatty liver disease (NAFLD), Hepatocyte growth factor(HGF),Serum type iii procollagen (PCIII),platelet(PLT),Noninvasive diagnostic

Posted Date: December 4th, 2019

DOI: <https://doi.org/10.21203/rs.2.18035/v1>

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Abstract

Background/Aims: It was suggested that serum HGF,PCIII and PLT play important roles in nonalcoholic fatty liver disease (NAFLD). Thus, we aimed to evaluate their clinical utility in the diagnosis of patients with suspected NAFLD.

Methods:300 Patients with NAFLD were compared to 102 matched controls.All were subjected to history taking, anthropometric measurements, and abdominal ultrasonography, as well as laboratory assessments of liver functions, fasting lipid profile, GLU, serum PLT, HGF and PCIII.

Results:The levels of HGF,PCIII and PLT were higher in NAFLD cases than controls ,and with progressive increases as the severity of fatty liver increased $P < 0.05$.HGF,PCIII and PLT were correlated with various clinical parameters and severity of NAFLD $P < 0.05$.The optimal cut-off values for HGF in diagnosis of mild, moderate and severe fatty liver were 14.1pg/ml(AUROC 0.753, $P = 0.004$), 15.4pg/ml(AUROC 0.836, $P < 0.001$), 17.7pg/ml(AUROC 0.903, $P < 0.001$). PCIII had no value in differentiate mild from moderate fatty liver ,but its ability to diagnose severe fatty liver was significant. A cut-off value for PCIII to diagnose severe fatty liver was 7.9ng/L(AUROC 0.773).The optimal cut-off values for PLT in the diagnosis of mild, moderate and severe fatty liver were $194 \times 10^9/L$ (AUROC 0.732), $195 \times 10^9/L$ (AUROC 0.765), $200 \times 10^9/L$ (AUROC 0.925), respectively with $P < 0.001$. When three indicators were tested together,the AUROC(95%CI)curve for diagnose NAFLD was 0.881(sensitivity0.760,specificity 0.873) ($P < 0.001$) .

Conclusion:.Combined detection of serum HGF, PCIII and PLT may be an effective non-invasive method for diagnosing NAFLD.

Introduction

Non-alcoholic fatty liver disease (NAFLD) is a hepatic manifestation of metabolic syndrome, which is characterized by excessive accumulation of fat content in hepatocytes. The spectrum of NAFLD disease includes nonalcoholic simple fatty liver (NAFL), nonalcoholic steatohepatitis (NASH), liver fibrosis, liver cirrhosis and liver cancer. Numerous risk factors are associated with the development and progression of NAFLD, including obesity, visceral obesity, insulin resistance and features of the metabolic syndrom[1].The worldwide prevalence of NAFLD is currently estimated to be in the range of 6% to 37%, with a reported pooled overall global prevalence of 25%[2],As the global epidemic of NAFLD, the clinical and economic burden of NAFLD will become enormous.Although Liver biopsy is the gold standard for the diagnosis, grading, and staging in patients with NAFLD, but it has its own limitations, such as the risk of sampling error, high rates of inter- and intraobserver differences, risk of complications, and the high cost and so on[3]. Thus, it is important to develop efficient noninvasive diagnostic methods for NAFLD and numerous noninvasive diagnostic method have been developed worldwide.

Hepatocyte growth factor (HGF) is a multifunctional pleiotropic cytokine,is not only an anti-apoptotic and anti-fibrotic factor in the liver, but also a adipokine[4].HGF is initially produced as a biologically inactive,

single-chain precursor form, After proteolytic cleavage, it converts to the active form to Participate in various physiological activities[5]. Tojima[6] et al. showed that HGF overexpression could alleviate the pathological changes of hepatitis and liver fibrosis in a murine model of NASH induced by methionine-choline deficiency (MCD) diet due to its antioxidant, antiapoptotic and plasminolytic effects. Kroy DC[7] et al. also demonstrated the protective role of HGF in the development of NAFLD by knocking out of HGF receptor cMet in mouse hepatocytes. In addition, previous studies found that HGF was significantly high in patients with NASH and it correlated with Various parameters of metabolic syndrome[4].

The development of hepatic fibrosis is an important event in the progression of liver disease. Serum type III procollagen peptide (PIIIP), a degradation product of the type III collagen precursor and has been shown to be a negative prognostic factor in chronic hepatitis[8]. Serum PIIINP levels increased significantly along with the increasing severity of liver inflammation[9]. Procollagen-III peptide also could identify adipose tissue(AT)-associated inflammation in type 2 diabetes with or without nonalcoholic liver disease, Higher PIIINP levels correlated with greater BMI and visceral AT area and were associated with systemic signatures of AT-associated inflammation[10].

The platelet is the primary cell for hemostasis and tissue repair. Many studies have shown that PLT plays a role in the inflammatory response after hepatic damage[11, 12]. Recent clinical and experimental evidences also support that platelets play several roles in the progression of malignancies and inversely, cancer can also influence platelet count and activity[13]. Sangbin Han et al. 's findings suggested that platelets play an important role in HCC cells metastasis and preoperative platelet count was independently correlated with post-transplant HCC recurrence[14].

Thus, the current study attempted to evaluate the clinical utility of serum HGF, PIIIP and PLT levels in the diagnosis of suspected NAFLD.

Methods

Patients and methods

A total of 300 patients diagnosed with NAFLD and 102 sex- and age-matched healthy volunteers without NAFLD were included in this study from November 2016 to November 2018. All patients were diagnosed with NAFLD based on ultrasound imaging made under fasting conditions. The grade of fatty liver was categorized as follows: (1) mild steatosis: increased echogenicity of the liver as compared with the renal cortex or spleen; (2) moderate steatosis: obscured hepatic and portal vein walls, and (3) severe steatosis: impaired visibility of the diaphragm[15]. Subjects with a history of excessive alcohol consumption (weekly consumption of ≥ 140 g for men or ≥ 70 g for women), other liver diseases such as chronic hepatitis, or use of drugs known to be associated with the development of fatty liver, body weight reduction or thyroid disorders were excluded[16].

Physical examination of each patient included body weight, height, calculation of body mass index (BMI). Blood samples were collected after 12 hours of fasting, the serum was obtained after

centrifugation at 3000 RPM for 15min and Stored in a - 80°C low temperature refrigerator. Analyses included liver function tests (AST, ALT, CHE, TBIL, DBIL, IBIL, TBA, TP, ALB and ALP), lipid profile (TC, TG, HDL, LDL), GLU, HGF, PCIII and PLT. The HGF, PIIIIP were assayed using ELISA kit purchased from WuHan Elliot biotechnology co. LTD. Other biochemical indicators were detected by automatic biochemical instrument purchased from Beijing anxin haichuang technology co, LTD.

Statistical analysis

A statistical analysis was performed using Medcalc 19.0. The measurement data conforming to the normal distribution were expressed by mean \pm standard deviation (SD). T-test was used for comparison between two groups. Univariate anova was used for multigroup comparison and Lsd-t test was used for further pairwise comparison.

The measurement data of non-normal distribution were expressed by [M (p25-p75)], mann-whitney test was used for comparison between two groups, and kruskal-wallis H test was used for comparison between multiple groups. X^2 test was used to compare counting data between groups. The area under the ROC curve (AUC) was calculated, and its diagnostic validity was tested by Z test, and the optimal cut-off value ($YI = Se + sp - 1$) was determined by Jordan index. $P < 0.001$ was considered statistically significant. Spearman rank correlation analysis was used to analyze the correlation between HGF, PCIII, PLT and clinical parameters and severity of NAFLD ($P < 0.05$).

Results

Table 1 showed the laboratory and clinical characteristics of NAFLD patients and the control group. Levels of BMI, GLU, ALT, AST, TG, ALP, GGT, GPRI (GGT/PLT),

DBIL, IBIL, TBA, TP, HGF, PCIII and PLT were significantly higher in the NAFLD patients compared with the control group, ALB was significantly lower in the NAFLD patients compared with the control group, (all $P < 0.05$). In terms of sex, age HDL and APRI (AST/PLT), no significant differences were found between the two groups.

Table 2 showed the laboratory and clinical characteristics of varying degrees of NAFLD patients and the control group. Levels of BMI, GLU, ALT, AST, TG, ALP, APRI,

CHE, TG, TC, LDL, TBIL, DBIL, IBIL, TBA, HGF, PCIII and PLT were correlated With

the severity of NAFLD (all $P < 0.05$). In terms of sex, age, no significant differences were found in all groups. Moreover, the levels of HGF were significantly higher in all NAFLD group compared with Control group, But, It showed no significant difference in Mild NAFLD group and Moderate NAFLD group. In addition, PIIIIP can distinguish severe NAFLD group from mild NAFLD group, moderate NAFLD group and normal group, but It showed no significant difference in mild NAFLD group and moderate NAFLD

group. Even more, PLT can distinguish normal group from all NAFLD group, but it showed no significant difference in mild NAFLD group and moderate NAFLD group, so as moderate NAFLD group and severe group.

Table 3 showed the Correlation analysis of HGF, PCIII and PLT with various clinical parameters. When correlating HGF, PCIII and PLT with clinical parameters, PLT and HGF were correlated positively with BMI, GLU, ALT, AST, ALP, APRI, GPRI,

ALB, DBIL, TBA, TG and HDL, respectively (all $P < 0.05$). PCIII was correlated positively with BMI, GLU, AST, GPRI and LDL (all $P < 0.05$), while it was not significantly correlated, ALT, ALP, APRI, TBA, TG and HDL.

Table 4 (As shown in supplementary material S1) showed HGF, PCIII and PLT were correlated positively with Severity of NAFLD, with statistical significance. (all $P < 0.05$).

Table 5 (As shown in supplementary material S2) showed the comparison of the diagnostic performance of HGF, PCIII and PLT in patients with varying degrees of fatty liver. NAFLD patients were diagnosed by ultrasound. When an ROC curve was made to set a cut off value for HGF levels to classify grades of fatty liver, the value to differentiate mild NAFLD cases was 14.1 pg/ml (AUROC 0.753, sensitivity 0.798, specificity 0.588), the value to differentiate moderate NAFLD cases was 15.4 pg/ml (AUROC 0.836, Sensitivity 0.833, specificity 0.696), the value to differentiate Severe NAFLD cases was 17.7 pg/ml (AUROC 0.903, sensitivity 0.920, specificity 0.764). PCIII had no value in differentiate mild from moderate fatty liver, but its ability to diagnose severe fatty liver was significant. A cutoff value of 7.9 ng/L for PCIII to diagnose severe fatty liver with a sensitivity of 96.0% and a specificity of 52.9%, and AUROC was 0.773. When an ROC curve was made to set a cut off value for PLT levels to classify grades of fatty liver, the value to differentiate mild NAFLD cases was 194×10^9 /L (AUROC 0.548, Sensitivity 0.782, specificity 0.441), the value to differentiate moderate NAFLD cases was 195×10^9 /L (AUROC 0.606, sensitivity 0.435, specificity 0.980), the value to differentiate Severe NAFLD cases was 200×10^9 /L (AUROC 0.790, sensitivity 0.800, specificity 0.990). When HGF, PCIII and PLT were detected together, the AUROC curve for diagnose NAFLD was 0.881 (sensitivity 0.760, specificity 0.873).

Fig. 1 showed ROC curve analysis about the diagnostic performance of HGF in patients with different degrees of fatty liver disease.

Fig. 2 showed ROC curve analysis about the diagnostic performance of PCIII in patients with different degrees of fatty liver disease.

Fig. 3 showed ROC curve analysis about the diagnostic performance of PLT in patients with different degrees of fatty liver disease.

Fig. 4 showed the ROC curve analysis about the diagnostic performance of combined detection of HGF, PCIII and PLT in patients with fatty liver disease.

Discussion

NAFLD has become an emerging public health concern, given its remarkable growth in the worldwide over the recent decades[17]. "Two hits" is the most accepted hypothesis in NAFLD. The "first hit" is closely related to insulin resistance, and the "second hit" is closely related to oxidative stress, lipid peroxidation, Immune disorders, inflammatory factors and so on[18]. NAFLD is considered to be the liver manifestation of metabolic syndrome and the prevalence of NAFLD is increasing in parallel with the global rise in obesity and type 2 diabetes mellitus (T2DM)[19]. Therefore, in addition to the changes of HGF, PCIII and PLT in NAFLD, our study also focused on their relationship with BMI, liver function, blood lipid, blood glucose and other indicators.

In the liver, the major producer of HGF in the liver is hepatic stellate cell and it plays a crucial role in liver regeneration after hepatectomy or massive liver damage, protection against hepatocyte apoptosis and necrosis, and suppression of liver fibrosis progression[5]. Our study also revealed significant differences between mild, moderate, and severe cases with respect to HGF, in that the more advanced the degree of fatty liver assessed by ultrasound, the higher the HGF level. That may be due to the fact that NAFLD is a chronic inflammatory state of the liver, at the initiation of the inflammatory response, IL-6 induces acute phase proteins, which are implicated in controlling the inflammation and in resetting homeostasis[20], these acute phase proteins include u-PA that promotes activation of pro-HGF to biologically active HGF[21]. HGF-MET signaling can also modulate adaptive immune response by facilitating the migration of Langerhans cells and dendritic cells to draining lymph nodes[22], thus modulate inflammation in the liver. PIIINP is a collagen that reflect extracellular matrix collagen turnover[23]. In animal studies, a high-fat diet induced NASH mouse model exhibited elevated PIIINP[24] and Hamza et al. also reported that mean serum levels of PIIINP in children with NAFLD (assessed by ultrasonography) were higher than those in control children[25]. Our results are consistent with previous studies and Elevated serum PIIINP has been previously been shown to be associated with elevated pro-inflammatory cytokines in liver disease[9]. PLTs have a role in thrombosis formation and evidence pointing to association between PLT count and liver injury[26]. In a study, it was reported that patients with moderate-to-severe NAFLD had higher PLT counts than milder form of NAFLD[27] and PLT count has been included in some scoring systems such as NAFLD fibrosis score[28]. In addition, platelets play a pivotal role in both hepatic regeneration and fibrosis pathophysiology and Platelets contain HGF [29], Our study also found that both PLT and HGF in NAFLD increased with the increase in severity of NAFLD, which may be the protective mechanism of the liver in the inflammatory state.

In addition, HGF, PCIII and PLT may represent links between obesity, inflammation, metabolism and cardiovascular risk factors[30–32]. Previous studies have also shown that recombinant HGF treatment reduced intracellular lipid content, likely by accelerating lipid secretion in hepatocytes through activation of microsomal triglyceride transfer protein and apolipoprotein B[33]. Besides, recombinant HGF treatment inhibited cholesterol overload-mediated hepatocyte lipotoxicity by suppressing production of reactive oxygen species [34]. HGF is also a potent suppressor of hepatic glucose production and output in a setting of insulin resistance and that it can potentially restore insulin responsiveness[35]. Quilliot D. et al.

[36] showed that circulating PIIINP correlated with markers of insulin resistance and signs of impaired ventricular dysfunction in non-diabetic obese subjects. Agarwal et al. [31] demonstrated that higher blood PIIINP levels were associated with greater carotid intima-media thickness and impaired brachial artery reactivity. Fay [WP](#) et al. showed PLT lifespan is known to be shorter in subjects with IR, and the interactions between inflammation and thrombosis provide a potential mechanism linking PLT count and MetS [37]. MPV is one of the PLT function indices which reflects the PLT production rate and stimulation and it has been reported that MPV was found significantly increased in adult patients who have diabetes, impaired fasting glucose, and hypertension [19, 38] [39]. The current study also highlights significant correlations between HGF, PCIII, PLT and other components of the metabolic syndrome, which makes it possible for them to jointly detect NAFLD. As shown in our results, when HGF, PCIII and PLT were detected together, the AUROC curve for diagnosing NAFLD was 0.881 (sensitivity 0.760, specificity 0.873).

Conclusion

NAFLD is a common clinical disease. Combined noninvasive monitoring of serum HGF, PCIII and PLT levels in patients with suspected NAFLD may be used as a reliable tool for early detection in order to offer proper therapy at the proper time if needed. Nevertheless, the significance of the combined detection warrants further research to be useful clinically.

Abbreviations

NAFLD, nonalcoholic fatty liver disease; ROC, receiver operating characteristic; SD, standard deviation; AUROC, area under the receiver operating characteristic; BMI, body mass index; AST, aspartate aminotransferase; ALT, alanine aminotransferase; ALP, alkaline phosphatase; CHE, Serum cholinesterase; TBIL, Serum total bilirubin; DBIL, Serum direct bilirubin; IBIL, Serum indirect bilirubin; TBA, Total bile acid; TP, total protein; ALB, albumin; ALP, alkaline phosphatase; γ -GTP, γ -glutamyl transpeptidase; LP, Lipid profile; TC, Cholesterol; TG, triglycerides; HDL, High density lipoprotein; LDL, Low density lipoprotein; GLU, fasting blood glucose; HGF, Hepatocyte growth factor; PCIII, type III procollagen; PLT, platelet.

Declarations

Acknowledgements We thank the Department of Otorhinolaryngology Head and Neck Tumor Key Laboratory of Shanxi Province, Taiyuan, Shanxi, China.

Author contributions

Xiuqin An, Xiaojuan Zheng, Zhangfeng Dou, Yue Li, Yuhong Suo, Yanan Ma, Meiqing Sun, Zhongyuan Tian and Lijun Xu were responsible for acquisition of data. Xiuqin An, Xiaojuan Zheng, Zhangfeng Dou and Yue Li were responsible for analysis and interpretation of data. Xiuqin An was responsible for drafting of the article. Xiuqin An and Jinchun Liu were responsible for study concept and design.

Funding

This work was supported by the science and technology department project of Shanxi provincial (No.201604D132042) and the project of shanxi provincial department of education("131" leading talents project for colleges and universities in Shanxi Province)

Availability of data and materials

Raw data were generated at First Hospital of Shanxi Medical University. Derived data supporting the findings of this study are available from the corresponding author [Jinchun Liu] on request.

Ethics approval and consent to participate

This study was approved by the Ethics committee of the First Hospital of Shanxi Medical University, which complies with the World Medical Association Declaration of Helsinki regarding ethical conduct of research involving human subjects and/or animals. All patients provided a written informed consent prior to inclusion in the study.

Consent for publication

Not Applicable

Competing interests

The authors declare that they have no conflict of interest.

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Tables

Table 1. Clinical ,laboratory, and anthropometric data of NAFLD patients compared to controls

	Control group	NAFLD group	Statistics	<i>P</i>
Male/female	52/50	156/144	=0.032	0.859
age	54.97±12.32	54.19±13.71	<i>t</i> =0.050	0.614
BMI(kg/m ²)	23.96±2.36	27.04±3.71	<i>t</i> =-7.864	0.000
GLU(mmol/L)	7.48±4.13	9.29±25.71	<i>Z</i> =-2.131	0.033
PLT(10 ⁹ /L)	169.72±60.82	201.78±66.36	<i>Z</i> =-4.286	0.000
ALT(IU/L)	22.69±13.05	36.02±43.16	<i>Z</i> =-3.753	0.000
AST(IU/L)	23.53±9.94	33.207±26.83	<i>Z</i> =-3.670	0.000
ALP(U/L)	89.95±78.75	107.55±100.25	<i>Z</i> =-2.254	0.024
APRI(AST/PLT)	0.16±0.105	0.17±0.14	<i>Z</i> =-0.370	0.711
GPRI(GGT/PLT)	0.206±0.23	0.27±0.49	<i>Z</i> =-0.043	0.010
GGT(U//L)	39.80±48.96	48.28±75.14	<i>Z</i> =-2.488	0.013
CHE(mmol/L)	7.41±1.65	8.36±4.27	<i>t</i> =-2.20	0.028
TP(g/L)	7.41±1.65	8.36±4.28	<i>Z</i> =-2.03	0.043
ABL(g/L)	47.039±6.07	42.29±6.16	<i>Z</i> =-5.463	0.000
TBIL(umol/L)	12.67±11.42	14.86±7.44	<i>Z</i> =-4.963	0.000
DBIL(umol/L)	2.17±1.19	2.94±2.69	<i>Z</i> =-3.604	0.000
IBIL(umol/L)	8.99±3.51	11.24±5.41	<i>Z</i> =-4.447	0.000
TBA(mmol/L)	5.322±4.46	7.83±9.44	<i>Z</i> =-2.639	0.008
TC(mmol/L)	4.422±1.19	4.87±1.39	<i>t</i> =-2.905	0.004
TG(mmol/L)	1.95±1.24	2.45±2.12	<i>Z</i> =-2.992	0.003
LDL(mmol/L)	2.49±0.81	2.72±0.86	<i>t</i> =-2.406	0.017
HDL(mmol/L)	1.03±0.34	1.11±0.56	<i>Z</i> =-0.771	0.441
HGFpg/ml	33.18±34.85	56.45±97.30	<i>Z</i> =-3.132	0.002
PCIIing/ml	7.82±7.69	15.11±13.31	<i>Z</i> =-4.476	0.000

Table 2. the laboratory and clinical characteristics of varying degrees of NAFLD patients and the control group

	Control group [n=102]	Mild [n=119]	Moderate [n=156]	Severe [n=25]	Statistics	P
Male/female	52/50	58/61	81/75	17/8	=3.102	0.376
age	54.97±12.32	53.95±13.66	54.96±13.68	50.64±14.09	F=0.856	0.464
BMI(kg/m ²)	23.96±2.36	23.63±2.83	28.63±1.26 ^a	33.40±2.34 ^{ab}	F=247.176	0.000
3LU(mmol/L)	5.76	6.20	7.50	6.19	H=15.134	0.002
	[5.00-8.58]	(5.06-9.35) ^a	(5.85-9.62) ^{ab}	(5.07-7.78) ^a		
ALT(IU/L)	20.00	22.00	26.00 ^{ab}	21.00	H=14.977	0.002
	[14.75-28.25]	(15.00-50.00)	(16.00-44.75)	(15.00-38.00)		
AST(IU/L)	22.00	26.00 ^a	23.00	50.00 ^a	H=30.09	0.000
	(17.75-27.00)	(19.00-35.00)	(18.00-35.75)	(24.00-55.00)		
ALP(U/L)	83.00	87.00 ^a	82.00	102.00 ^{abc}	H=15.58	0.001
	(63.75-98.25)	(71.00-108.00)	(70.00-103.25)	(96.00-112.00)		
PRI(AST/PLT)	0.14	0.13	0.13	0.21 ^{abc}	H=11.15	0.011
	(0.10-0.20)	(0.09-0.21)	(0.096-0.19)	(0.14-0.24)		
PRI(GGT/PLT)	0.12	0.16 ^a	0.17 ^a	0.13	H=9.18	0.027
	(0.09-0.22)	(0.10-0.31)	(0.11-0.27)	(0.10-0.18)		
GGT(U//L)	23.00	28.00 ^a	29.00 ^a	27.00	H=8.21	0.042
	(16.00-39.25)	(20.00-59.00)	(19.00-52.75)	(17.50-38.00)		
3HE(mmol/L)	8.28±7.43	8.40±6.06 ^{ac}	8.00±3.14	8.11±1.15	F=3.481	0.016
TP(g/L)	67.20	68.40 ^a	67.90	67.80	H=8.50	0.020
	(62.95-72.23)	(64.10-73.5)	(63.96-73.08)	(65.75-73.05)		
ALB(g/L)	43.15	42.80 ^a	42.80 ^a	43.10	H=30.95	0.000
	(39.88-46.10)	(39.60-45.30)	(40.60-46.20)	(42.30-46.20)		
3BIL(umol/L)	12.20	11.10	12.80	13.70 ^b	H=36.269	0.000
	(9.10-16.75)	(9.70-16.30)	(10.50-15.82)	(11.15-19.85)		
3BIL(umol/L)	2.10	2.10	2.30 ^a	2.10	H=14.368	0.002
	(1.50-3.00)	(1.60-3.20)	(1.90-3.00)	(1.80-2.80)		
3BIL(umol/L)	9.45	8.80	10.45	11.20 ^b	H=26.493	0.000
	(7.08-13.98)	(7.70-13.10)	(8.10-12.30)	(9.50-16.55)		
3BA(mmol/L)	4.50	4.70	4.60	3.70 ^{abc}	H=10.747	0.013
	(2.40-7.35)	(2.60-9.20)	(2.80-8.17)	(2.95-5.45)		
TC(mmol/L)	4.42±1.19	4.31±1.38	4.56±1.38	4.88±1.00 ^b	F=3.578	0.014
TG(mmol/L)	1.60	1.60	1.86	1.95 ^{ab}	H=9.098	0.028
	(1.20-2.30)	(1.12-2.62)	(1.31-2.59)	(1.42-2.38)		
3DL(mmol/L)	2.49±0.81	2.72±0.88 ^a	2.71±0.87	2.79±0.78 ^a	F=3.412	0.026
3IDL(mmol/L)	0.97	1.02	0.97	1.23 ^{ac}	H=6.801	0.079
	(0.84-1.16)	(0.85-1.19)	(0.85-1.09)	(0.91-1.30)		

HGF(pg/ml)	18.22 (11.44-44.22)	23.85 (14.35-53.44) a	26.26 (15.69-99.84) a	35.29 (13.43-52.94) abc	<i>H</i> =11.364	0.010
PCIII(ng/ml)	5.74 (0.34-23.10)	6.62 (0.52-12.00)	8.19 ^a (1.84-24.61) ^a	16.13 ^{abc} (8.36-26.28)	<i>H</i> =33.347	0.000
PLT(10 ⁹ /L)	165.00 (103.75-211.00)	185.00 (152.00-224.25) ^a	200.00 (166.00-258.00) ^a	203.00 (166.00-240.00) ab	<i>H</i> =24.38	0.000

Note: a: there was a statistically significant difference from the normal control group, there was a statistical difference. b: there was a statistically significant difference from the mild fatty liver group; C: there was a statistically significant difference from the moderate fatty liver group.

Table 3. Correlation analysis of HGF, PCIII and homa-ir with various clinical parameters

	HGF		PCIII		PLT	
	r	P	r	P	r	P
age	0.056	0.612	0.165	0.137	0.066	0.554
BMI	0.432	<0.001	0.311	0.004	0.373	0.001
GLU	0.305	0.005	0.152	0.170	0.261	0.017
ALT	0.403	<0.001	0.109	0.328	0.391	<0.001
AST	0.465	<0.001	0.227	0.039	0.472	<0.001
ALP	0.305	0.005	0.152	0.170	0.261	0.017
APRI	0.415	<0.001	0.109	0.328	0.398	<0.001
GPRI	0.488	<0.001	0.226	0.040	0.443	<0.001
GGT	0.285	0.009	0.112	0.315	0.242	0.027
CHE	0.125	0.262	0.135	0.235	0.138	0.215
TP	0.163	0.142	0.007	0.948	0.084	0.449
ABL	0.378	<0.001	0.180	0.104	0.251	0.022
TBIL	0.163	0.142	0.007	0.948	0.084	0.449
DBIL	0.378	<0.001	0.180	0.104	0.251	0.022
IBIL	0.262	0.017	0.222	0.043	0.222	0.044
TBA	0.322	0.003	0.164	0.139	0.954	<0.001
TC	0.162	0.148	0.007	0.948	0.084	0.449
TG	0.398	<0.001	0.180	0.104	0.251	0.022
LDL	0.269	0.017	0.228	0.041	0.221	0.047
HDL	0.329	0.003	0.169	0.146	0.901	<0.001

Table 4 The relationship between HGF, PCIII and PLT and the degree of NAFLD

	<i>r</i>	<i>P</i>
HGF	0.501	<0.001
PCIII	0.397	<0.001
PLT	0.470	<0.001

Table 5 The comparison of the diagnostic performance of HGF, PCIII and PLT in patients with varying degrees of fatty liver

	group	AUC[95%CI]	cut-off	SE	SP	<i>P</i>
HGF [pg/ml]	Mild	0.753[0.691-0.809]	14.1	0.798	0.588	0.004
	Moderate	0.836[0.785-0.879]	15.4	0.833	0.696	<0.001
	Severe	0.903[0.837-0.948]	17.7	0.920	0.764	<0.001
PC[[ng/ml]	Mild	0.597[0.529-0.662]	7.9	0.697	0.568	0.114
	Moderate	0.628[0.566-0.687]	7.8	0.698	0.558	0.086
	Severe	0.773[0.690-0.842]	7.9	0.960	0.529	<0.001
PLT (10 ⁹ /L)	Mild	0.732 (0.669-0.789)	194	0.782	0.441	<0.001
	Moderate	0.765[0.709-0.816]	195	0.435	0.980	<0.001
	Severe	0.925[0.865-0.965]	200	0.800	0.990	<0.001

note[SE[sensitivity][SP[specificity

Figures

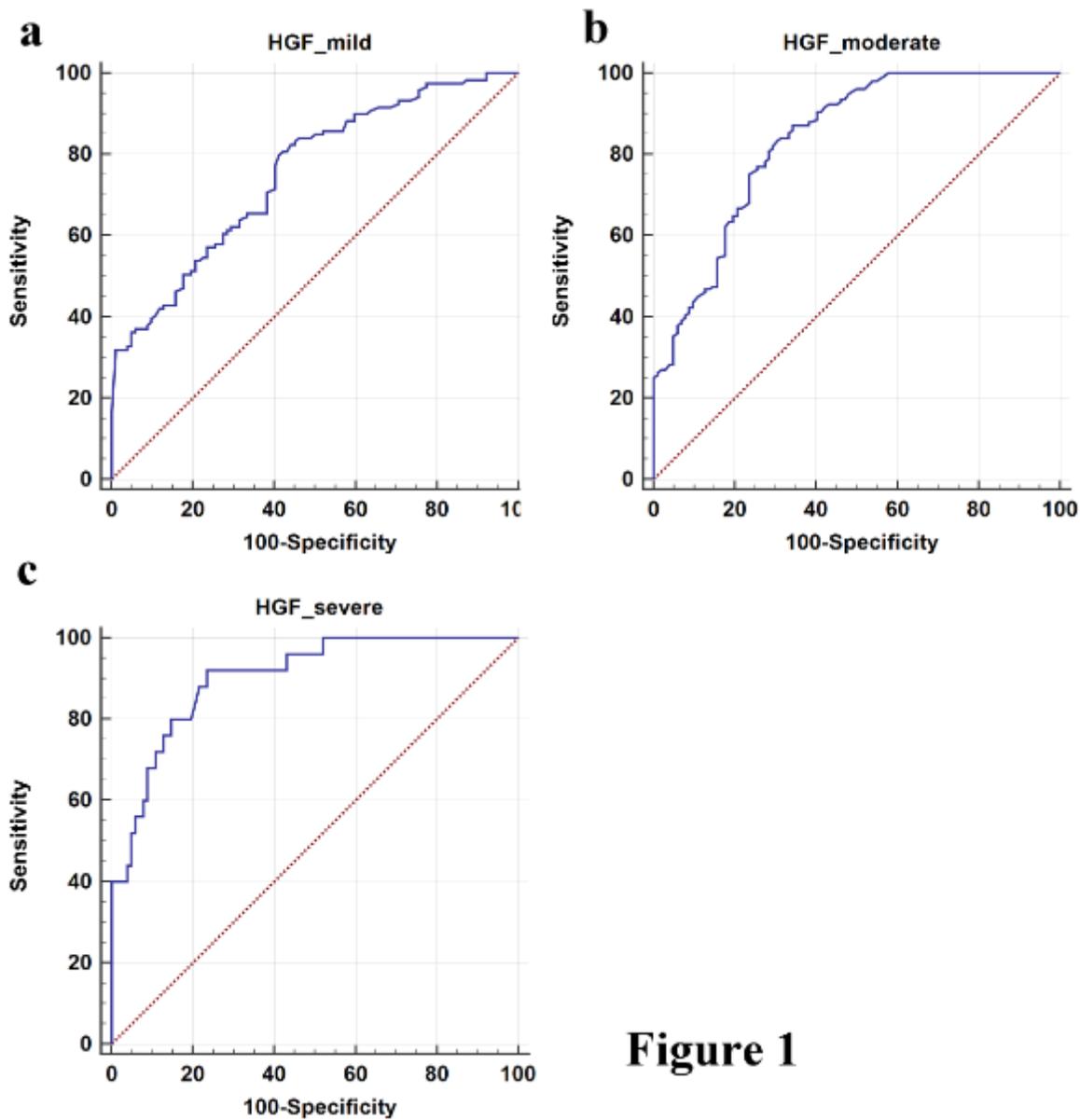


Figure 1

Figure 1

showed ROC curve analysis about the diagnostic performance of HGF in patients with different degrees of fatty liver disease.

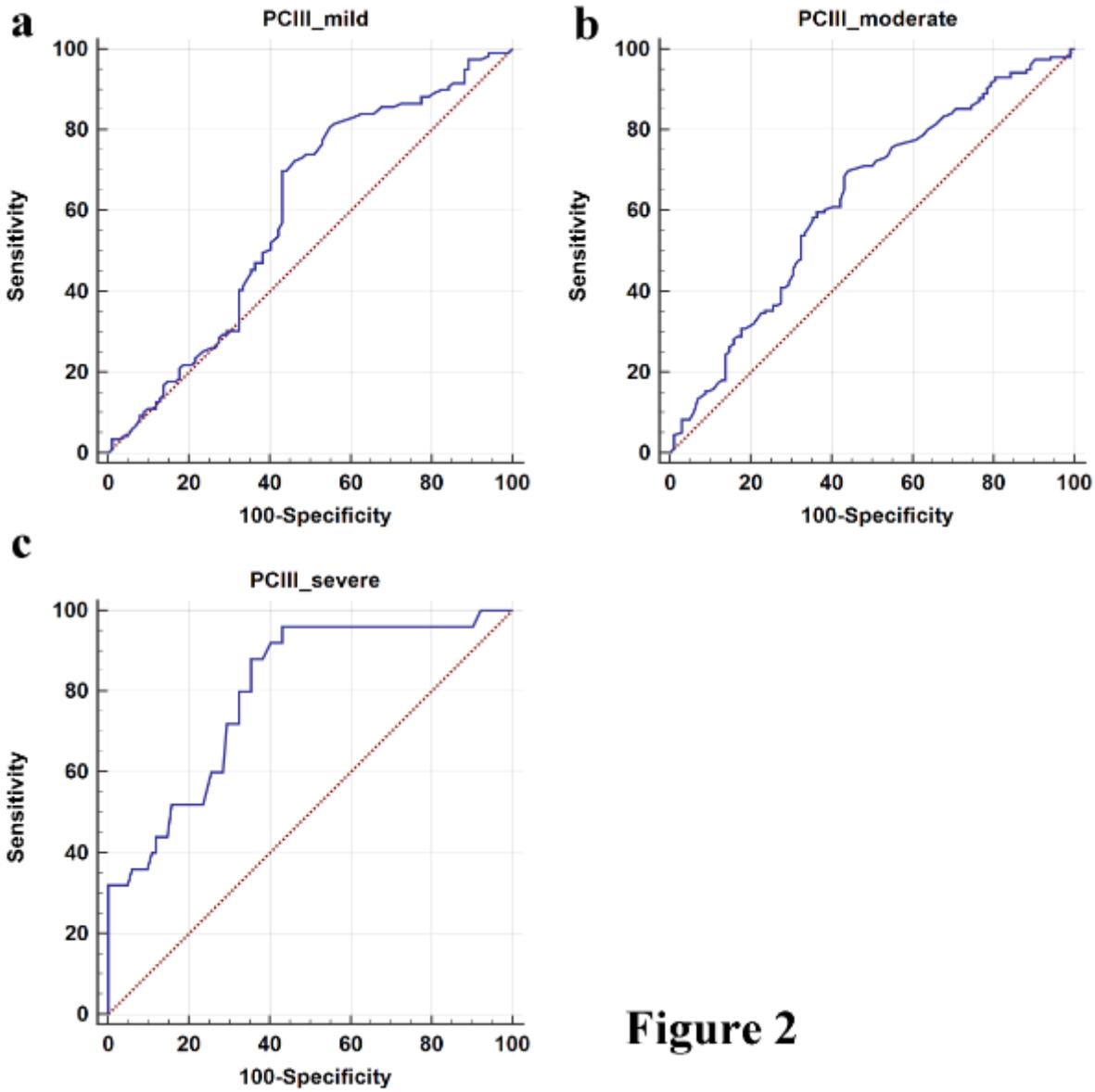


Figure 2

Figure 2

showed ROC curve analysis about the diagnostic performance of PCIII in patients with different degrees of fatty liver disease.

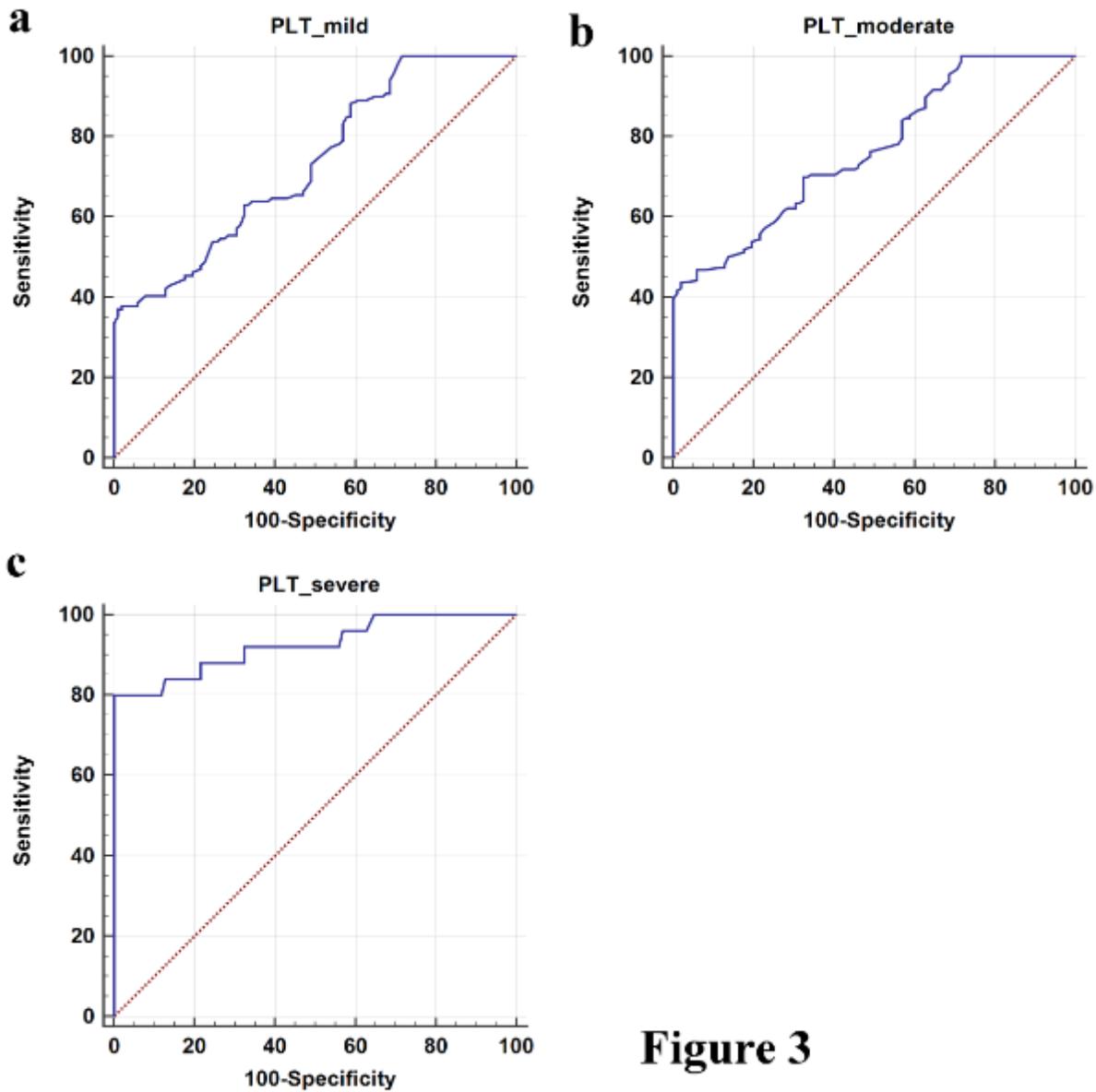


Figure 3

Figure 3

showed ROC curve analysis about the diagnostic performance of PLT in patients with different degrees of fatty liver disease.

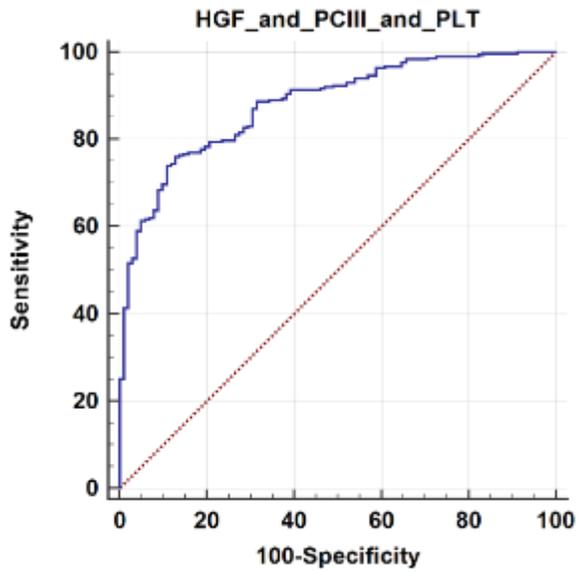


Figure 4

Figure 4

showed the ROC curve analysis about the diagnostic performance of combined detection of HGF, PCIII and PLT in patients with fatty liver disease.