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Original Article

Pentraxin 3 as a Noninvasive Biomarker of Fibrosis and Carotid Intima-media Thickness in Patients with Metabolic Associated Fatty Liver Disease

Alshymaa A. Hassnine[1*], Yasser Fouad[1], Zienab M. Saad[1], Alaa M. Mostafa[1], Hend M. Moness[2], Nehal I. Abbas[2], Nasr M. Osman[3] and Wafaa Abdelghany[1]

[1]*Department of Gastroenterology, Hepatology and Tropical Medicine, Faculty of Medicine, Minia University, Minia, Egypt;* [2]*Department of Clinical Pathology, Faculty of Medicine, Minia University, Minia, Egypt;* [3]*Department of Radiology, Faculty of Medicine, Minia University, Minia, Egypt*

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Abstract

Background and objectives: Metabolic-associated fatty liver disease (MAFLD) may increase the risk of cardiovascular events. In this study, we assessed the predictive value of pentraxin 3 (PTX3) for severe fibrosis and carotid intima-media thickness (CIMT) in patients with MAFLD.

Methods: 188 patients (114 with MAFLD, 74 with dual etiology MAFLD and chronic hepatitis C) were included. All participants underwent clinical history and examination, metabolic parameter assessment, serum level evaluation of PTX3, Fibrosis-4 index and nafld fibrosis score scores, abdominal ultrasound, and CIMT assessment.

Results: The serum PTX3 was significantly elevated in patients with advanced fibrosis compared to those with mild/moderate fibrosis (1.8 *vs* 1.4, $p = 0.006$). The PTX3 level was independently associated with advanced fibrosis (odds ratio = 1.26, 95% confidence interval 1.008–1.040). In MAFLD patients, the PTX3 levels in patients with low fibrosis compared to those with advanced fibrosis were 1.4 (1–2.1) *and* 1.9 (1.3–3.8), respectively ($p = 0.027$). A significantly greater CIMT was noted in patients with elevated PTX3 levels (3.85 (3.42–4) *vs* 4.05 (3.7–4.67), $p = 0.0001$) compared to those with low PTX3 levels.

Conclusions: Serum PTX3 levels can accurately predict advanced fibrosis and CIMT in MAFLD patients. Thus, it could be useful for management and risk stratification.

Introduction

Metabolic-associated fatty liver disease (MAFLD) affects about a quarter of the population, with the highest prevalence in the Middle East, and is becoming the primary cause of liver cirrhosis, hepatocellular carcinoma and liver transplantation.[1] In addition, MAFLD increases the risk of extra-hepatic events such as diabetes and cardiovascular diseases.[2,3]

Only a proportion of patients with MAFLD develop adverse outcomes, and there is robust evidence that the severity of liver fibrosis is the single major determinant of both hepatic and extra-hepatic complications.[4,5] Although liver biopsy is considered the standard reference for the diagnosis and staging of the disease,[6] there is still a low patient acceptance rate for liver biopsy, rendering it impractical for the majority of patients. Hence, there is an unmet clinical need for noninvasive biomarkers of hepatic fibrosis to identify those at risk.[7,8]

On the other hand, there is growing evidence to suggest a close relation between MAFLD and chronic hepatitis C (CHC), with both entities frequently coexisting, and this group of patients is likely to have different outcomes.[9–11]

Pentraxin 3 (PTX3), an acute-phase protein, is highly induced in injured tissues. Unlike C-reactive protein, which is principally synthesized in hepatocytes, PTX3 secretion is increased in hepatic stellate cells and immune cells, including neutrophils and monocytes, suggesting its potential role in the pathophysiology of liver

Keywords: MAFLD; CHC; Chronic hepatitis C; Pentraxin 3; Fibrosis; Non-invasive predictor; Carotid intimal thickness.

***Correspondence to:** Alshymaa A. Hassnine, Department of Gastroenterology, Hepatology and Tropical Medicine, Faculty of Medicine, Minia University, Minia 61111, Egypt. ORCID: https://orcid.org/0000-0003-1352-0948. Tel: +20-1092004294, E-mail: alshiamaa.ahmed@mu.edu.eg

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fibrosis.[12] However, data regarding the association between PTX3 and fibrosis as well as carotid intima-media thickness (CIMT), a subclinical measure of atherosclerosis, in MAFLD are limited and still controversial.[13–15] Furthermore, because the performance of biomarkers and noninvasive liver fibrosis scores varies widely according to disease etiology, whether PTX3 has a role as a biomarker in MAFLD and MAFLD/CHC dual etiology is unclear. Validation of the role of PTX3 in Egyptian patients, where the prevalence and phenotype of the disease are vastly different, is imperative before any further recommendations can be made. Such a tool, if sufficiently precise for predicting fibrosis across different etiologies, would have many advantages, including early identification of those at risk for progressive fibrosis and cirrhosis development.

In this study, we tested whether PTX3 can be a noninvasive marker for the prediction of liver fibrosis in patients with MAFLD with or without CHC. We also assessed the relationship between PTX3 and CIMT.

Methods

This cross-sectional study was conducted at Minia University Hospital and included 188 patients, of whom 114 were diagnosed with MAFLD and 74 were diagnosed with MAFLD and CHC. Individuals with alternative diagnoses were excluded, including those with excessive alcohol intake (>10 g per day for women and >20 g per day for men) and those with liver diseases other than CHC. MAFLD diagnosis was based on criteria recently proposed by the international panel of hepatology experts.[9,16,17]

This study complies with the standards of the Declaration of Helsinki and current ethical guidelines, and informed consent was obtained from the participants. Approval was granted by the Ethical Committee of the Faculty of Medicine, Minia University, Minia, Egypt (Approval number No:328-11/2019).

Case study details

All participants provided their clinical history via a standardized questionnaire that collected information on age, gender, smoking status, and alcohol intake. Weight (in kilograms) and height (in centimeters) were measured, and the body mass index (BMI) was calculated and expressed as kg/m^2. The waist circumference was measured in centimeters at the midpoint between the lowest rib and the top of the iliac crest. Hypertension was defined as a resting blood pressure of ≥130/80 mm Hg or the use of any antihypertensive medication. Type 2 diabetes mellitus was defined as a fasting plasma glucose value ≥126 mg/dL or the use of any antidiabetic medication. The homeostasis model assessment of insulin resistance (HOMA-IR) score was calculated as (fasting serum insulin (μU mL^{-1}) × fasting serum glucose (mmol/L, p value < 0.05)/22.5. Fasting blood samples were taken in the morning for all participants, and analyses for full blood count, liver biochemistry, lipid profile, fasting glucose and iron studies were performed. Fibrosis-4 index (FIB-4) and nonalcoholic fatty liver disease fibrosis (NFL) scores were calculated for every patient.

In the dual etiology cohort, hepatitis C virus (HCV) was diagnosed using HCV RNA levels via the COBAS AmpliPrep/COBAS TaqMan HCV Quantitative Test, version 2.0, with a lower limit of quantification of 20 IU/mL.

Enzyme-linked immunosorbent assay

Assessment of PTX3 by EIA (kits were supplied by BT BioMed, Bioassay Technology).

Abdominal ultrasonography

All patients received abdominal ultrasonography using the Acuson X300 (Siemens, USA) and CH5-2 probe. A single experienced examiner screened all patients in each center, and the diagnosis of fatty liver was based on ultrasound diagnostic criteria of fatty liver.[18]

Assessment of carotid intima-media thickness

High-resolution B mode ultrasonography (Acuson X300, Siemens, USA) was used to determine the intima medial thickness (IMT) with the use of an 18 MHz linear-array transducer. The IMT of the bilateral common carotid arteries (CCAs) was measured in the region of interest (ROI), which was 1 cm proximal to the CCA bifurcation. Semiautomated software (Syngo Arterial Health Package) was used for the analysis of longitudinal static images. The transducer was manually placed on a 1 cm segment of the ROI, and the IMT was automatically measured by calculating the distance between the lumen-intima and the media-adventitia interfaces in the far wall of the ROI. The left and right common carotid IMT were measured. The carotid intimal thickness value was calculated by average measurements of the left and right common carotid IMT.

Statistical analysis

For descriptive statistics, values are expressed as the mean ± standard deviation, or median and interquartile range, as appropriate. The Mann–Whitney nonparametric test was used to determine significance. For categorical variables, data were presented as frequencies (percentages) with p values. Comparisons of distributions between groups were assessed using Fisher's exact test. Multivariate regression modeling with backward elimination was conducted to test the independent associations between PTX3 and significant fibrosis p value < 0.05), the sensitivity, specificity, NPV (negative predictive value), and PPV (positive predictive value) of PTX3 were evaluated.

Results

The characteristics of the total MAFLD cohort and its stratification based on the co-existence of CHC are depicted in Table 1. Besides those with MAFLD/CHC who were more likely to be male compared to those without CHC (p = 0.01), there were no statistically significant differences in patients' clinical or laboratory characteristics, noninvasive markers of fibrosis or assessments of carotid IMT between the two groups.

Pentraxin 3 is highly associated with the severity of fibrosis

Within the overall cohort, the serum PTX3 concentration was significantly higher in patients with advanced fibrosis than in patients with mild/moderate fibrosis (1.8 *vs* 1.4, p = 0.006) (Fig. 1). Other classic risk variables associated with the severity of fibrosis included older age (mean age was 55 *vs* 40, p = 0.0001), higher aspartate aminotransferase levels and lower platelet count (p = 0.0001, for both comparisons) (Table 2).

We then performed logistic regression to determine the effect of various clinical variables on the association between PTX3 and the presence of advanced fibrosis measured by noninvasive measures (FIB-4) in the overall cohort. In this analysis, PTX3, adjusted for gender, the presence of diabetes, the presence of hypertension, smoking status and BMI, was independently associated with ad-

Table 1. Baseline characteristics of MAFLD patients

	Overall cohort (n = 188)	MAFLD (n = 114)	MAFLD and HCV (n = 74)	*p* value
Clinical parameters				
Age (years)	46 (37–55)	45 (36–55)	48 (38–60)	0.1
Male (%)	60 (31.9)	28 (24.6)	32 (43.2)	0.01
Diabetes mellitus (%)	55 (29.3)	36 (31.6)	19 (25.7)	0.4
Hypertension (%)	42 (22.3)	26 (22.8)	16 (21.6)	1.00
Smoking (%)	19 (10.1)	9 (7.9)	10 (13.5)	0.2
BMI (kg/m^2)	29.3 (25.9–33)	29.5 (25.9–33.2)	29.3 (25.8–32.8)	0.6
Waist circumference (cm)	102 (97–110)	102 (97–110)	101.5 (95–108)	0.6
Laboratory parameters				
Hemoglobin (g/dL)	13 (11.9–14)	13 (11.6–13.8)	13.05 (12–14.4)	0.44
Total leucocytic count (/mm^3)	6.4 (5.2–8)	6.6 (5.5–8.2)	6 (5–7.9)	0.1
Platelet count (10^9/L)	256 (214–299)	256 (224–300)	256 (211–290)	0.4
Albumin (mg/dL)	4.8 (4.2–5)	4.8 (4–5.1)	4.8 (4.3–5.1)	0.5
ALT (U/L)	29 (19–41)	28 (19–42)	30 (20–41)	0.8
AST (U/L)	32 (20–43)	32.5 (18–44)	31 (20–41)	0.9
Bilirubin (total) mg/dL	0.8 (0.6–0.9)	0.8 (0.6–0.9)	0.8 (0.6–0.9)	0.7
Creatinine (mg/dL)	0.9 (0.7–1)	0.9 (0.7–1)	0.9 (0.7–1)	0.3
Fasting blood sugar (mg/dL)	100 (90–140)	100 (90–130)	100 (87–150)	0.9
Hemoglobin A1c (%)	7 (6.4–7.7)	7 (6.5–7.6)	7.2 (6.3–9)	0.5
HOMA-IR score	15.5 (4.9–24.4)	15.6 (4.5–22.5)	15.5 (7.3–25.2)	0.6
Total cholesterol (mg/dL)	225 (170–268)	225 (170–268)	223 (170–253)	0.3
Triglycerides (mg/L)	145 (111–184)	144 (109–188)	145 (113–177)	0.9
HDL-cholesterol (mg/L)	45 (35–55)	48 (35–55)	42.5 (34.7–55)	0.3
LDL-cholesterol (mg/dL)	140 (96–180)	140 (95–186)	122 (96–172)	0.3
Pentraxin 3 (mg/dL)	1.5 (1.1–2.95)	1.5 (1.1–2.95)	1.5 (1.1–2.7)	0.6
Noninvasive scores for fibrosis				
NFS	−1.9 (−3.5–(−0.72))	−2.04 (−2.94–(−1.05)	−1.76 (−3.26–(−0.68)	0.8
FIB-4	1.08 (0.64–1.66)	1.06 (0.61–1.63)	1.23 (0.67–1.76)	0.3
Carotid intima-media thickness				
Diameter	4 (3.5–4.5)	4 (3.6–4.3)	4 (3.5–4.5)	0.8
EDV	20.9 (15–27)	20 (15–26)	22 (15–27)	0.8
PSV	72 (58–95)	75 (59–95)	71 (58–96)	0.8

BMI, body mass index; ALT, alanine aminotransferase; AST, aspartate aminotransferase; haemoglobin A1C, glycated haemoglobin; HOMA-IR score, homeostatic model assessment of insulin resistance; HDL, high density lipoproteins; LDL, low density lipoproteins; NFS, non-alcoholic fatty liver disease fibrosis score; FIB-4, fibrosis-4 index; MAFLD, Metabolic-associated fatty liver disease; HCV, hepatitis C virus; EDV, end diastolic velocity; PSV, peak systolic velocity.

vanced fibrosis (odds ratio = 1.26, 95% confidence interval 1.008–1.040) (Table 3).

To confirm the generalizability of the association between PTX3 and the presence of advanced fibrosis, the cohort was stratified according to the presence or absence of CHC. In this analysis, PTX3 remained associated with the presence of advanced fibrosis across both subpopulations. In MAFLD patients, the PTX3 levels in patients with low fibrosis compared to those with advanced fibrosis were 1.4 (1–2.1) *and* 1.9 (1.3–3.8), respectively ($p = 0.027$). However, in the MAFLD/CHC group, the values were 1.4 (0.9–1.85) *and* 1.8 (1.3–4.9), respectively ($p = 0.021$).

Clinical parameters associated with the level of pentraxin 3

Given that the level of PTX3 was a strong predictor of advanced fibrosis according to both univariate and multivariate analyses, we next examined clinical parameters associated with the level of PTX3. To this end, we categorized all patients in the cohort into two groups according to the median serum level of PTX3.

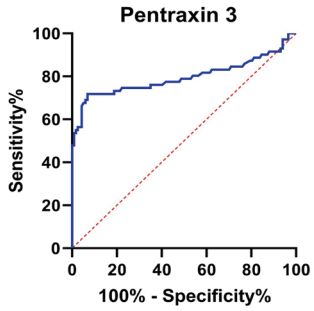

Fig. 1. The serum level of PTX3 in patients with no or mild fibrosis versus patients with severe fibrosis. Moderate fibrosis (*), severe fibrosis (**). FIB-4, fibrosis-4 index; NFS, nonalcoholic fatty liver disease fibrosis score; PTX3, pentraxin 3; US-FLI, ultrasound fatty liver index.

Table 3. Multiple logistic regression analysis for independent variables associated with significant fibrosis measured by noninvasive measures (FIB-4)

Clinical parameters	Odds ratio	95% confidence interval	*p* value
Pentraxin 3 (mg/dl)	1.067	1.01–1.12	0.02
Male (%)	1.15	0.57–2.33	0.6
Diabetes mellitus (%)	1.05	0.44–2.009	0.8
Hypertension (%)	1.59	0.68–3.76	0.2
Smoking (%)	2.32	0.79–6.77	0.1
BMI (kg/m^2)	0.998	0.929–0.1.07	0.9

BMI, body mass index; FIB-4, fibrosis-4 index.

Table 2. Clinical, laboratory and carotid intima-media thickness according to fibrosis severity measured by noninvasive measures (FIB-4)

	No/mild fibrosis (n = 117)	Significant fibrosis (n = 71)	*p* value
Clinical parameters			
Age (years)	40 (35–51)	55 (45–62)	0.0001
Male (%)	36 (30.8)	24 (33.8)	0.7
Diabetes mellitus (%)	33 (28.2)	22 (31)	0.7
Hypertension (%)	22 (18.8)	20 (28.2)	0.1
Smoking (%)	9 (7.7)	10 (14.1)	0.2
BMI (kg/m^2)	29.3 (25.7–33.5)	29.4 (26.5–32.4)	0.6
Waist circumference (cm)	100 (96–109)	104 (99–112)	0.052
Laboratory parameters			
Hemoglobin (g/dL)	13 (12–14)	12.8 (11.5–14)	0.6
Total leucocytic count (/mm^3)	6.6 (5.05–8.35)	6.2 (5.2–8)	0.6
Platelet count (10^9/L)	274 (238–315)	215 (160–297)	0.0001
Albumin (mg/dL)	4.9 (4.1–5.15)	4.8 (4.2–5)	0.2
ALT (U/L)	28 (19–41)	33 (20–44)	0.1
AST (U/L)	23 (16–33)	43 (35–64)	0.0001
Bilirubin (total) mg/dL	0.8 (0.6–0.9)	0.8 (0.65–1)	0.4
Creatinine (mg/dL)	0.9 (0.7–1)	0.9 (0.8–1)	0.039
Fasting blood sugar (mg/dL)	100 (90–129)	90 (100–150)	0.2
Hemoglobin A1c (%)	7 (6.4–8.2)	7 (6.4–7.45)	0.6
HOMA-IR score	18.5 (5–26.8)	12.9 (4.4–22.3)	0.4
Total cholesterol (mg/dL)	225 (167–265)	225 (177–269)	0.4
Triglycerides (mg/L)	134 (103–183)	148 (119–188)	0.1
HDL-cholesterol (mg/L)	48 (35–55)	45 (35–55)	0.9
LDL-cholesterol (mg/dL)	125 (100–180)	145 (90–185)	0.7
Pentraxin 3 (mg/dL)	1.4 (1–1.92)	1.8 (1.3–4.85)	0.006
Carotid intima-media thickness			
Diameter	4 (3.5–4.3)	4 (3.5–4.6)	0.4
EDV	22 (15.6–27)	19 (13–26)	0.1
PSV	71 (58–96)	73 (57–103)	0.6

Patients were stratified as no/mild fibrosis or significant fibrosis based on FIB-4. BMI, body mass index; ALT, alanine aminotransferase; AST, aspartate aminotransferase; hemoglobin A1C, glycated hemoglobin; HOMA-IR score, homeostatic model assessment of insulin resistance; HDL, high-density lipoprotein; LDL, low-density lipoprotein; FIB-4, fibrosis-4 index; EDV, end diastolic velocity; PSV, peak systolic velocity.

Table 4. Clinical, laboratory and carotid intima-media thickness according to the pentraxin 3 level

	Low pentraxin 3 (n = 94)	High pentraxin 3 (n = 88)	*p* value
Clinical parameters			
Age (years)	42 (35–54)	50 (40–57)	0.01
Male (%)	34 (36.2)	25 (28.4)	0.2
Diabetes mellitus (%)	18 (19)	37 (42)	0.001
Hypertension (%)	12 (12.8)	37 (30.7)	0.004
Smoking (%)	12 (12.8)	6 (6.8)	0.2
BMI (kg/m^2)	28.7 (25.4–32.9)	29.73 (26.6–33)	0.4
Waist circumference (cm)	100 (96.7–110)	103 (98–110)	0.4
Laboratory parameters			
Hemoglobin (g/dL)	13 (11.7–14)	13 (12–14)	0.8
Total leucocytic count (/mm^3)	6.6 (5.2–8.05)	6 (5.2–7.9)	0.3
Platelet count (10^9/L)	260 (225–302)	245 (210–283)	0.06
Albumin (mg/dL)	4.9 (4.27–5.2)	4.8 (4.1–5)	0.1
ALT (U/L)	30 (21–42)	27 (18–41)	0.2
AST (U/L)	29.5 (18–41)	35 (20–45)	0.1
Bilirubin (total) mg/dL	0.8 (0.6–0.9)	0.8 (0.6–0.9)	0.5
Creatinine (mg/dL)	0.9 (0.7–1)	0.9 (0.7–1)	0.9
Fasting blood sugar (mg/dL)	100 (88.7–121)	103 (90–150)	0.1
Hemoglobin A1c (%)	7.2 (6.8–8.1)	6.95 (6.3–7.2)	0.3
HOMA-IR score	8.5 (4.1–21)	16.25 (6.9–26.7)	0.1
Total cholesterol (mg/dL)	220 (168–255)	227.5 (175–279)	0.3
Triglycerides (mg/L)	132.5 (103–177)	153 (116–189)	0.1
HDL-cholesterol (mg/L)	40 (33.7–52.7)	49 (35–55)	0.09
LDL-cholesterol (mg/dL)	125 (90–185)	150 (100–179)	0.6
Noninvasive scores for fibrosis			
NFS	−2.43 (−3.81–(−1.49))	−1.58 (−2.24–(−0.34))	0.0001
FIB-4	0.925 (0.53–1.39)	1.24 (0.81–2.12)	0.001
Carotid intima-media thickness			
Diameter	3.85 (3.42–4)	4.05 (3.7–4.67)	0.0001
EDV	22 (15.6–28)	19.5 (14.4–25.7)	0.08
PSV	75 (60–95)	70.4 (57–98.5)	0.5

Pentraxin 3 was divided into low and high groups based on the median level. BMI, body mass index; ALT, alanine aminotransferase; AST, aspartate aminotransferase; hemoglobin A1C, glycated hemoglobin; HOMA-IR score, homeostatic model assessment of insulin resistance; HDL, high-density lipoprotein; LDL, low-density lipoprotein; NFS, nonalcoholic fatty liver disease fibrosis score; FIB-4, fibrosis-4 index; EDV, end diastolic velocity; PSV, peak systolic velocity.

Patients with elevated PTX3 levels were significantly older (50 *vs* 42 years, $p = 0.01$), more likely to have diabetes (42% *vs* 19%, $p = 0.001$), more likely to have hypertension (31% *vs* 13%, $p = 0.004$) and more likely to have severe fibrosis ($p = 0.001$) compared to those with low levels of PTX3 (Table 4). In addition, a significantly higher CIMT was noted in patients with elevated PTX3 levels (3.85 [3.42–4] *vs* 4.05 [3.7–4.67], $p = 0.0001$) compared to those with low levels of PTX3 (Table 4).

The AUC, sensitivity, specificity, NPV (negative predictive value), and PPV (positive predictive value) of PTX3 were evaluated (Table 5 and Fig. 2).

Discussion

In chronic liver disease, activated hepatic stellate cells are the main cell type that produces PTX3, which may increase the inflammatory response after liver injury and exert protective and immune modulatory effects. It was proposed that serum plasma levels of PTX3 may distinguish patients with nonalcoholic steatohepatitis from different patients, and higher plasma PTX3 levels indicated

Table 5. Sensitivity, specificity, PPV, NPV, and AUC of pentraxin 3 for detecting advanced fibrosis

	Pentraxin 3	NFS	FIB-4
Optimal cutoff point		>3.085	>1.18
AUC	0.796	0.569	0.879
95% confidence interval	0.732–0.851	12.7–47.2	66.4–93.4
p value	<0.001*	0.371	<0.001*
Sensitivity	71.83	27.5	82.8
Specificity	93.16	100	84
PPV	86.4	100	78.4
NPV	84.5	60.4	87.5
Accuracy	85.1	–	–

AUC, area under the curve; FIB-4, fibrosis-4 index; NFS, nonalcoholic fatty liver disease fibrosis score; NPV, Negative predictive value; PPV, Postive predictive value.

the extreme phases of hepatic fibrosis.

In this study, we measured the level of PTX3 in MAFLD patients with and without CHC, and the results were similar to those observed in daily clinical practice. Our principal finding is that PTX3 progressively increases with fibrosis severity and CIMT in MAFLD patients, and the association remains highly significant even after adjustment for multiple biochemical and clinical parameters. These data suggest that PTX3 has utility for both hepatic and cardiovascular risk stratification and the clinical management of patients with MAFLD.

Noninvasive biomarkers that predict hepatic fibrosis are urgently needed. The associations between PTX3 and fibrosis and between PTX3 and CIMT in patients with MAFLD are controversial due to the limited studies.[13–15] Here, we demonstrated that PTX3, an acute-phase protein whose expression is highly induced in injured tissues, is a precise marker for advanced liver fibrosis, consistent with recent findings in CHC patients Although these findings need to be validated in biopsy-proven cohorts, our data, in combination with other findings, suggest that PTX3 could be considered as a biomarker not only for predicting fibrosis progression but also for predicting cardiovascular complications.

MAFLD is a systemic disease that increases the risk of both hepatic and extra-hepatic complications, and cardiovascular disease is the main cause of death in these patients and is also associated with the severity of liver fibrosis.[4,19] The CIMT is a standard method for the early evaluation of atherosclerosis. An interesting finding of this work is that PTX3 is associated with the severity of CIMT, suggesting that it could be a diagnostic biomarker for the prediction of hepatic fibrosis and cardiovascular complications.[19]

Mechanistically, as an acute-phase protein, PTX3 is highly induced in injured tissues and is upregulated in hepatic stellate cells and immune cells, suggesting a pivotal potential effect on the pathophysiology of liver fibrosis

Our study has several limitations that must be acknowledged. While our participants were a "real-world" sample of MAFLD patients, they were enrolled at a single tertiary care center. Fibrosis in our cohort was determined based on noninvasive blood biomarkers. Although these scores have been proven to be valid estimates of liver fibrosis and are more commonly used in daily practice than liver biopsy to determine the severity of fibrosis, it should be noted that liver biopsy is an imperfect reference tool and has several limitations, including sampling bias. Another limitation of our study cohort was the lack of diversity, with all participants being Egyptian.

Conclusions

In this study, we demonstrated that PTX3 accurately predicts the presence of advanced fibrosis and CIMT in a population with MAFLD. Thus, it could be useful for risk stratification and management. Further independent studies will be required to confirm these findings in larger cohorts and in the general population,

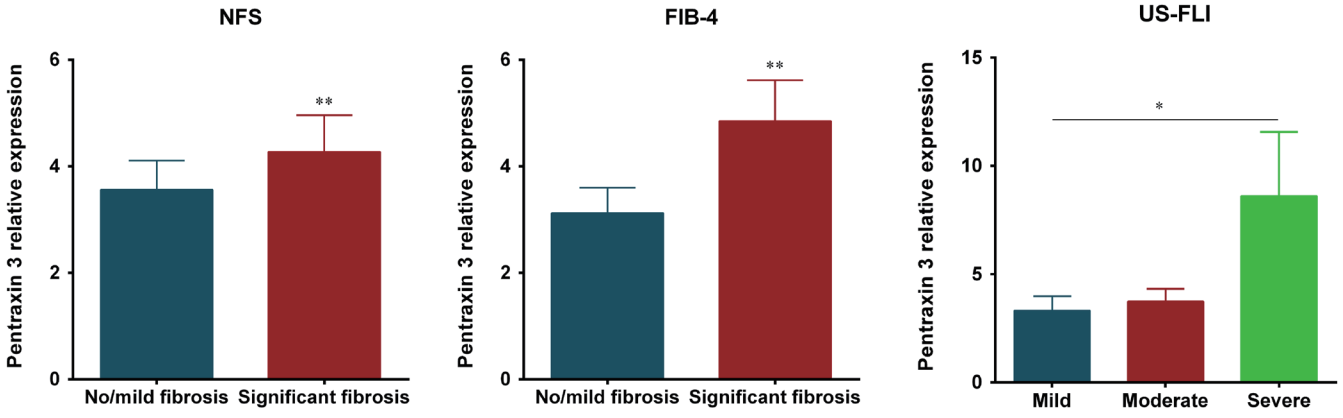

Fig. 2. Sensitivity, specificity, and AUC of pentraxin 3 in advanced fibrosis. AUC, area under the curve.

which has diverse representations of individuals of other races and ethnicities.

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Conflict of interest

None of the authors have financial relationships to disclose.

Author contributions

YF and ZS designed the study and wrote the manuscript. AH, WA, and AM contributed to the writing and conceptualization of the manuscript. The radiological examination was performed by NO, and the laboratory examination was performed by HM and NA. All authors contributed to revising the manuscript.

Data sharing statement

The original data are available upon reasonable request to the corresponding author.

Ethics statement

This study complies with the standards of the Declaration of Helsinki and current ethical guidelines, and informed consent was obtained from the participants. Approval was granted by the Ethical Committee of the Faculty of Medicine, Minia University, Minia, Egypt (Approval number No:328-11/2019).

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