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Serum Thrombospondin-2 Levels Are Closely Associated with the Severity of Metabolic Syndrome and Metabolic Associated Fatty Liver Disease

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Introduction

- Metabolic associated fatty liver disease (MAFLD) is the hepatic manifestation of obesity-related metabolic syndrome (MetS).
- There is an urgent need to identify non-invasive serum biomarkers for the detection of metabolic associated steatohepatitis (MASH) and hepatic fibrosis among patients with metabolic risk factors.
- Thrombospondin-2 (TSP2) is a secreted glycoprotein functionally involved in mediating cell-to-cell and cell-to-extracellular matrix (ECM) interactions.
- The role of TSP2 in metabolic disorder remains largely unexplored.

Objectives

- To investigate the associations of serum TSP2 with MetS and MAFLD seveiry, and the potential diagnostic value of serum TSP2 for identifying those at-risk of MASH.

Methodology

- Blood samples, clinical data, and liver biopsies were collected from consecutively recruited 252 morbidly obese individuals reciving bariatric surgery.
- Histopathology of liver biopsies were examined in a blinded manner by three independent international pathologists.
- Serum TSP2 levels were measured by ELISA.

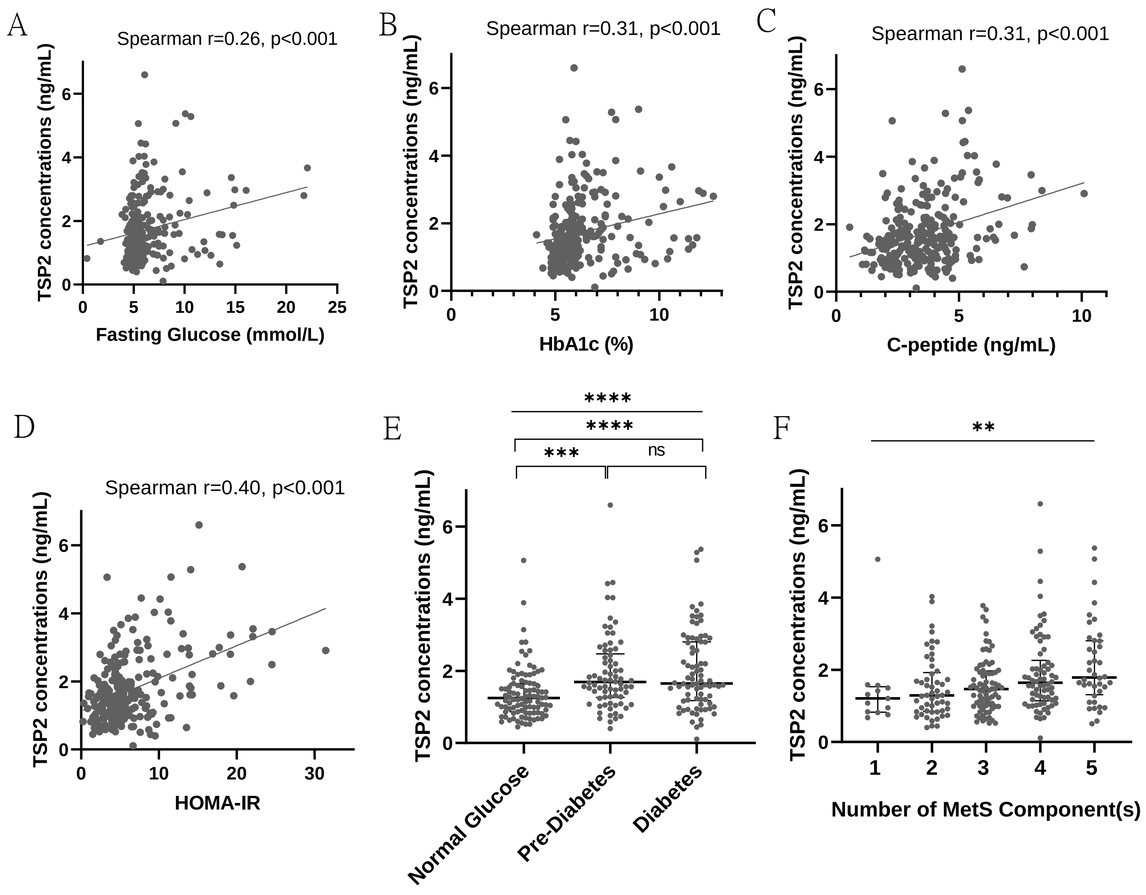
Results

➢ Clinical and biochemical characteristics of the 252 obese subjects included in this study

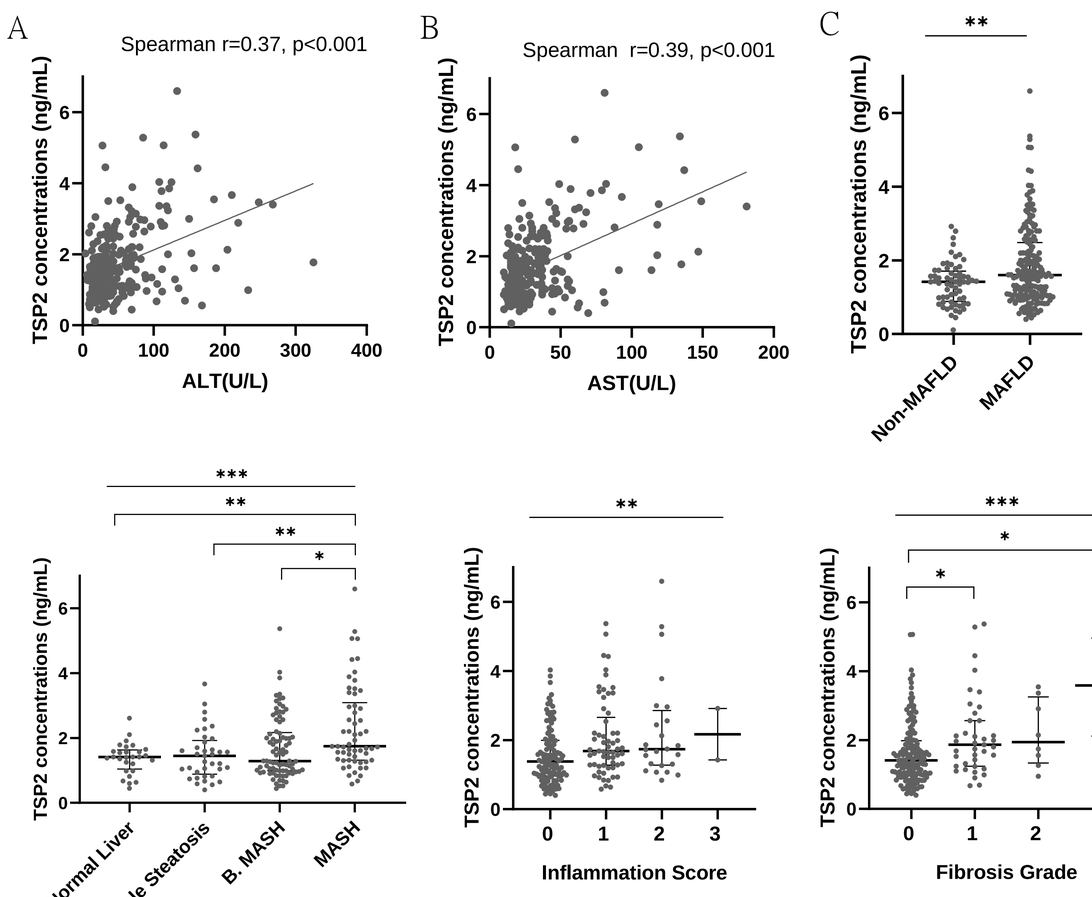
Parameters	Overall (n=252)	Non-MAFLD (n=64)	MAFLD (n=188)	P value (Non-MAFLD vs MAFLD)
Age (years)	30.00 (25.00-37.00)	29.50 (25.00-39.75)	30.00 (24.00-36.00)	0.403
Sex, men (n, %)	106 (42.1%)	15 (23.4%)	91(48.4%)	<0.001
BMI(kg/m2)	38.24 (33.38-44.47)	33.62 (29.99-39.41)	39.82 (35.33-45.31)	<0.001
Waist circumference (cm)	120.00 (109.00-133.88)	105.50 (99.00-120.00)	123.95 (112.25-135.88)	<0.001
Waist-to-hip ratio	0.97 ± 0.07	0.94 ± 0.06	0.99 ± 0.07	<0.001
Systolic BP (mmHg)	127.00 (120.00-136.75)	124.00 (115.00-131.00)	129.00 (121.25-138.00)	0.003
Diastolic BP (mmHg)	80.00 (74.00-89.00)	77.50 (71.25-87.00)	82.00 (74.25-90.00)	0.015
Glucose(mmol/L)	5.49 (4.92-6.66)	5.05 (4.77-5.74)	5.63 (4.98-7.00)	<0.001
HbA1c(%)	5.80 (5.30-6.70)	5.50 (5.10-6.00)	5.90 (5.43-6.90)	0.001
Fasting insulin(mIU/L)	19.64 (13.53-27.41)	13.88 (9.96-19.45)	21.12 (15.66-28.96)	<0.001
C-Peptide (ng/mL)	3.51 (2.55-4.42)	2.53 (2.03-3.42)	3.74 (2.97-4.49)	<0.001
HOMA-IR	4.84 (3.28-7.44)	3.26 (2.17-5.07)	5.43 (4.01-8.66)	<0.001
TC (mmol/L)	4.94 (4.38-5.62)	4.80 (4.23-5.34)	5.03 (4.40-5.74)	0.026
TG (mmol/L)	1.66 (1.24-2.44)	1.33 (1.07-1.88)	1.81 (1.31-2.69)	<0.001
HDL-C (mmol/L)	1.01 (0.88-1.19)	1.09 (0.95-1.31)	0.99 (0.86-1.16)	0.001
LDL-C (mmol/L)	3.06 ± 0.73	2.86 ± 0.62	3.13 ± 0.76	0.011
ALT (U/L)	37.50 (22.00-68.00)	20.00 (15.00-28.00)	46.65 (29.70-75.00)	<0.001
AST (U/L)	24.00 (18.00-39.00)	18.00 (14.25-22.00)	30.00 (20.00-47.00)	<0.001
AST/ALT ratio	0.71 (0.56-0.88)	0.89 (0.72-1.08)	0.65 (0.54-0.80)	<0.001

Data shown as n(%), mean (standard deviation) or median (interquartile range).

➢ Serum TSP2 levels were closely associated with obesity-related glucose dysregulation, insulin resistance and metabolic syndrome



➢ Serum TSP2 was closely associated with the severity of MAFLD and could differentiate MASH from benign steatosis and borderline MASH



➢ Serum TSP2 as a non-invasive biomarker for identification of at-risk MASH patients

At-risk MASH:
NAFLD activity score (NAS) ≥ 4 and fibrosis grade ≥2 among patients with metabolic risk factors

TSP2	
Cut-off value	2.88ng/mL
Sensitivity	75.0%
Specificity	89.3%

Summary

- ➢ Tsp2 is an important mediator linking MAFLD with metabolic dysfunction
- ➢ TSP2 is a promising noninvasive biomarker for differentiating MASH from benign steatosis and identifying at-risk MASH patients

➢ **Acknowledgement**
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