

Supplementary Table S1 Baseline characteristics of all study participants (N=1053)

Variable	CAP < 248	CAP ≥ 248	p-value
N	233	820	--
<i>Clinical variables</i>			
Men, %	58.4	51.2	0.054
Age, years	61.8±8.26	59.5±10.4	<b>0.002</b>
Ever smoker, %	32.6	25.2	<b>0.025</b>
Duration of diabetes, years	17.3±9.05	16.7±9.29	0.394
BMI, kg/m <sup>2</sup>	23.6±2.90	28.3±4.50	<b>&lt;0.001</b>
WC, cm	84.1±8.65	96.9±11.8	<b>&lt;0.001</b>
Central obesity, %	44.2	87.3	<b>&lt;0.001</b>
Systolic BP, mmHg	136.0±19.2	136.0±16.4	0.972
Diastolic BP, mmHg	75.4±9.62	78.0±9.62	<b>&lt;0.001</b>
<i>Medical history</i>			
Hypertension, %	74.7	81.0	<b>0.035</b>
Dyslipidemia, %	80.3	95.0	<b>&lt;0.001</b>
Coronary heart disease, %	7.7	18.0	<b>&lt;0.001</b>
Stroke, %	6.9	4.4	0.124
<i>Use of NAFLD-related medications</i>			
GLP1rA, %	0.0	1.2	0.090
Pioglitazone, %	10.7	14.5	0.138
SGLT2i, %	18.5	18.7	0.944
<i>Biochemical variables</i>			
HbA1c, %	7.47±1.36	7.65±1.20	0.050
HbA1c, mmol/mol	58.1±14.8	60.1±13.1	0.050

Variable	CAP < 248	CAP ≥ 248	p-value
HDL-C, mg/dL	53.4±14.9	45.0±11.4	<b>&lt;0.001</b>
LDL-C, mg/dL	80.0±24.4	81.1±27.9	0.580
TG*, mg/dL	87.7 (68.2-116)	129 (93.0-185)	<b>&lt;0.001</b>
ALT*, U/L	19.0 (14.5-25.0)	24.0 (17.0-35.0)	<b>&lt;0.001</b>
AST*, U/L	20.0 (18.0-24.0)	22.0 (18.0-28.0)	<b>&lt;0.001</b>
eGFR, ml/min/1.73m <sup>2</sup>	75.6±23.0	81.7±25.8	<b>0.001</b>
Albumin, g/L	45.0±3.13	44.8±3.21	0.363
Platelets, x 10 <sup>9</sup> /L	258±72.0	262±67.3	0.373
<i>Transient elastography</i>			
CAP, dB/m	208±26.0	308±43.6	<b>&lt;0.001</b>
Steatosis grade			
Minimal, %	100	0	<b>&lt;0.001</b>
Mild, %	0	21.1	
Moderate, %	0	10.5	
Severe, %	0	68.4	
Liver stiffness*, kPa	4.5 (3.9-5.3)	6.30 (4.80-8.58)	<b>&lt;0.001</b>
<i>Diabetes microvascular complications</i>			
Diabetic retinopathy, %	57.1	53.9	0.390
Albuminuria, %	36.9	49.5	<b>&lt;0.001</b>
<i>Biomarker</i>			
TSP2*, ng/ml	2.05 (1.54-2.88)	2.47 (1.80-3.57)	<b>&lt;0.001</b>

\*Log-transformed before analysis; Data were presented as mean±standard deviation or median (25th to 75th percentile); TSP2, thrombospondin 2; BMI, body mass index; WC waist circumference; BP, blood pressure; NAFLD, non-alcoholic fatty liver disease;

GLP1rA, glucagon-like peptide 1 receptor agonists; SGLT2i, sodium-glucose co-transporter 2 inhibitors; HbA1c, glycated hemoglobin; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TG, triglycerides; ALT, alanine aminotransferase; AST, aspartate transaminase; eGFR, estimated glomerular filtration rate; CAP, controlled attenuation parameter; STDR, sight threatening diabetic retinopathy; Conversion factors for HDL / LDL-C from mmol/l to mg/dL x38.9; TG from mmol/l to mg/dL x88.2.

Supplementary Table S2 Pearson correlation and multivariable linear regression analyses showing the associations between circulating TSP2 level and baseline variables of cohort participants (N=1053)

	TSP2*, ng/ml			
	Univariate		Multivariable‡	
	Pearson correlation coefficient, r	p-value†	Standardized Beta	p-value
Age, years	0.06	<b>0.046</b>	-	-
Sex	--	<b>0.010</b>	-0.092	<b>&lt;0.001</b>
BMI, kg/m <sup>2</sup>	0.22	<b>&lt;0.001</b>	-	-
WC, cm	0.19	<b>&lt;0.001</b>	-	-
Ever smoker, %	--	0.348	-	-
Duration of diabetes, years	0.03	0.287	-	-
Systolic BP, mmHg	0.07	<b>0.027</b>	-	-
Diastolic BP, mmHg	-0.02	0.629	-	-
HbA1c, %	0.14	<b>&lt;0.001</b>	0.046	0.081
HbA1c, mmol/mol	0.14	<b>&lt;0.001</b>	0.046	0.081
HDL-C, mg/dL	-0.11	<b>0.001</b>	-	-
LDL-C, mg/dL	-0.05	0.100	-	-
TG*, mg/dL	0.15	<b>&lt;0.001</b>	-	-
ALT*, U/L	0.34	<b>&lt;0.001</b>	-	--
AST*, U/L	0.41	<b>&lt;0.001</b>	0.297	<b>&lt;0.001</b>
eGFR, ml/min/1.73m <sup>2</sup>	-0.12	<b>&lt;0.001</b>	-0.071	<b>0.011</b>
Albumin, g/L	-0.13	<b>&lt;0.001</b>	-0.115	<b>&lt;0.001</b>
Platelets, x10 <sup>9</sup> /L	-0.08	<b>0.009</b>	-	-
Albuminuria, %	--	<b>&lt;0.001</b>	0.085	<b>0.002</b>
CHD, %	--	0.125	--	--
Stroke, %	--	0.855	--	--
Diabetic retinopathy, %	--	0.186	-	-
CAP	0.29	<b>&lt;0.001</b>	0.102	<b>&lt;0.001</b>
LS	0.43	<b>&lt;0.001</b>	0.283	<b>&lt;0.001</b>
NFS	0.15	<b>&lt;0.001</b>	-	-

FIB-4*	0.20	<0.001	-	-
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\*Log-transformed before analysis; †Categorical data (Sex, albuminuria and presence of sight threatening diabetic retinopathy) was analysed with independent t-test; ‡Model selection was based on Akaike Information Criteria; BMI, body mass index; WC waist circumference; BP, blood pressure; HbA1c, glycated haemoglobin; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TG, triglycerides; ALT, alanine aminotransferase; AST, aspartate transaminase; eGFR, estimated glomerular filtration rate; CAP, controlled attenuation parameter; FIB-4, Fibrosis-4 index; NFS, NAFLD fibrosis score.

Supplementary Table S3 Associations of baseline variables with increasing quartiles of serum TSP2 levels in the study participants with NAFLD (N=820)

Variable	TSP ng/ml				p for trend
	Q1: <1.77	Q2: 1.77-2.46	Q3: 2.47-3.56	Q4: >3.56	
N	205	205	205	205	
<i>Clinical variables</i>					
Men, %	54.6	52.7	50.2	47.3	0.118
Age, years	58.2±10.7	60.1±9.5	60.0±9.9	59.9±11.4	0.112
Ever-smoker, %	28.3	25.9	25.4	21.5	0.451
Duration of diabetes, years	16.2±9.9	16.8±9.2	17.6±9.4	16.4±8.6	0.640
BMI, kg/m <sup>2</sup>	27.6±3.8	27.7±4.2	28.1±4.9	29.7±4.9	<b>&lt;0.001</b>
WC, cm	95.7±9.9	95.1±10.8	97.0±13.9	99.9±11.7	<b>&lt;0.001</b>
Central obesity, %	88.3	82.9	82.9	95.1	<b>&lt;0.001</b>
Systolic BP, mmHg	134.0±17.5	134.0±16.6	138.0±16.1	137.0±15.1	<b>0.010</b>
Diastolic BP, mmHg	77.9±8.8	77.9±10.0	78.5±10.3	77.6±9.4	0.899
<i>Medical history</i>					
Hypertension, %	81.0	78.0	83.4	81.5	0.578
Dyslipidemia, %	94.6	94.6	95.6	95.1	0.720
Coronary heart disease, %	17.6	15.1	22.4	17.1	0.626
Stroke, %	2.4	2.4	2.0	2.0	0.670
<i>Biochemical variables</i>					
HbA1c, %	7.50±1.23	7.53±0.99	7.79±1.26	7.77±1.28	<b>0.005</b>
HbA1c, mmol/mol	58.5±13.5	58.8±10.8	61.7±13.8	61.4±14.0	<b>0.005</b>
HDL-C, mg/dL	46.0±11.6	45.4±10.6	45.4±11.2	43.2±12.2	<b>0.020</b>
LDL-C, mg/dL	81.8±29.0	82.4±26.1	83.5±28.6	76.8±27.7	0.117
TG*, mg/dL	128 (91-173)	121 (94-183)	120 (90-167)	146 (103-208)	<b>0.001</b>

Variable	TSP ng/ml				p for trend <b>&lt;0.001</b>
	Q1: <1.77	Q2: 1.77-2.46	Q3: 2.47-3.56	Q4: >3.56	
ALT*, U/L	19.0 (16.0-27.0)	22.0 (16.0-29.0)	23.0 (18.0-35.5)	33.0 (23.0-52.0)	
AST*, U/L	20.0 (17.0-23.0)	20.0 (17.0-24.0)	23.0 (19.0-29.0)	28.0 (22.0-39.0)	<b>&lt;0.001</b>
eGFR, ml/min/1.73m <sup>2</sup>	86.4±23.5	81.3±25.8	82.0±26.5	77.1±26.6	<b>0.001</b>
Albumin, g/L	45.4±2.71	44.6±3.07	44.8±3.12	44.2±3.74	<b>&lt;0.001</b>
Platelets, x 10 <sup>9</sup> /L	265.0±62.6	270.0±72.4	264.0±64.6	251.0±68.2	<b>0.023</b>
<i>Transient elastography</i>					
CAP, dB/m	298.0±37.8	299.0±42.9	312.0±43.4	324.0±45.5	<b>&lt;0.001</b>
Steatosis grade					
Mild, %	24.4	28.3	19.5	12.2	
Moderate, %	11.2	13.2	10.2	7.3	
Severe, %	64.4	58.5	70.2	80.5	
LS, kPa	5.75±2.10	6.37±4.56	6.95±2.94	10.60±7.12	<b>&lt;0.001</b>
<i>Diabetes microvascular complications</i>					
Diabetic retinopathy, %	53.2	49.3	58.0	55.1	0.348
Albuminuria, %	37.6	48.3	48.5	63.9	<b>&lt;0.001</b>
<i>Conventional fibrosis scores</i>					
NFS ≥ -1.455, %	58.0	62.0	62.9	72.7	<b>0.004</b>
FIB4 ≥1.3, %	21.5	26.8	35.1	45.4	<b>&lt;0.001</b>

\*Log-transformed before analysis. Data were presented as mean±standard deviation or median (25th to 75th percentile).

TSP2, thrombospondin 2; BMI, body mass index; WC waist circumference; BP, blood pressure; HbA1c, glycated hemoglobin; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TG, triglycerides; ALT, alanine aminotransferase; AST, aspartate transaminase; eGFR, estimated glomerular filtration rate; CAP, controlled attenuation parameter; LS, liver stiffness; NFS, non-alcoholic fatty liver disease fibrosis score; FIB4, fibrosis-4 index; Conversion factors for HDL / LDL-C from mmol/l to mg/dL x38.9; TG from mmol/l to mg/dL x88.2.

Supplementary Table S4 Subgroup analysis showing the associations of serum TSP2 level with  $\geq F3$  fibrosis in study participants with NAFLD stratified by the presence of obesity by Asian criteria (N=820)

Baseline variable	BMI < 27.5 kg/m <sup>2</sup>		BMI $\geq 27.5$ kg/m <sup>2</sup>	
	OR (95% CI)	p-value	OR (95% CI)	p-value
No. of events	34		104	
N	388		432	
BMI, kg/m <sup>2</sup>	1.10 (0.84-1.45)	0.479	1.16 (1.08-1.24)	<b>&lt;0.001</b>
AST*, U/L	17.7 (4.66-67.1)	<b>&lt;0.001</b>	5.93 (2.74-12.8)	<b>&lt;0.001</b>
CAP, dB/m	1.01 (1.00-1.02)	0.193	1.01 (1.001-1.02)	<b>0.025</b>
TSP2*, ng/ml	8.95 (3.34-24.0)	<b>&lt;0.001</b>	4.05 (2.31-7.08)	<b>&lt;0.001</b>

\*Log-transformed before analysis.

TSP2, thrombospondin-2; OR, odds ratio; 95%CI, 95% confidence interval; BMI, body mass index; AST, aspartate aminotransferase; CAP, controlled attenuation parameter.

Supplementary Table S5 Subgroup analysis showing the associations of serum TSP2 level with  $\geq$ F3 fibrosis in study participants with NAFLD stratified by their levels of conventional non-invasive fibrosis scores (N=820)

N	$\geq$ F3 fibrosis, %	Model	
		Adjusted OR of TSP2* (95% CI)	p-value
<b>FIB-4</b>			
< 1.3	556	13.7	3.02 (1.66-5.49) <b>&lt;0.001</b>
$\geq$ 1.3	264	23.5	14.0 (5.32-36.7) <b>&lt;0.001</b>
<b>NFS</b>			
< -1.455	297	14.1	2.98 (1.36-6.52) <b>0.006</b>
$\geq$ -1.455	523	18.4	7.09 (3.74-13.4) <b>&lt;0.001</b>

\*Log-transformed before analysis.

Model included BMI, AST and CAP.

TSP2, thrombospondin-2; OR, odds ratio; 95%CI, 95% confidence interval; FIB4, Fibrosis-4 index; NFS, non-alcoholic fatty liver disease fibrosis score; BMI, body mass index; AST, aspartate aminotransferase; CAP, controlled attenuation parameter.

Supplementary Table S6 Baseline characteristics of the cohort participants stratified by presence of  $\geq F3$  fibrosis (N=1053)

Variable	Without $\geq F3$ fibrosis	With $\geq F3$ fibrosis	p-value
N	911	142	
<i>Clinical variables</i>			
Men, %	52.8	52.8	0.997
Age, years	60.3 $\pm$ 9.78	58.2 $\pm$ 11.3	<b>0.018</b>
Ever smoker, %	26.5	29.6	0.435
Duration of diabetes, years	17.1 $\pm$ 9.42	15.1 $\pm$ 7.8	<b>0.017</b>
BMI, kg/m <sup>2</sup>	26.7 $\pm$ 4.21	31.2 $\pm$ 5.33	<b>&lt;0.001</b>
WC, cm	92.5 $\pm$ 11.0	105 $\pm$ 15.2	<b>&lt;0.001</b>
Central obesity, %	75.2	94.4	<b>&lt;0.001</b>
Systolic BP, mmHg	136 $\pm$ 17.3	137 $\pm$ 15.4	0.491
Diastolic BP, mmHg	77.2 $\pm$ 9.74	78.9 $\pm$ 9.15	0.056
<i>Medical history</i>			
Hypertension, %	79.3	81.7	0.503
Dyslipidemia, %	91.3	94.4	0.221
Coronary heart disease, %	15.5	17.6	0.517
Stroke, %	2.3	2.1	1.000
<i>Use of NAFLD-related medications</i>			
GLP1rA, %	9.7	2.8	<b>0.035</b>
Pioglitazone, %	13.2	16.9	0.229
SGLT2i, %	19.0	16.2	0.426
<i>Biochemical variables</i>			
HbA1c, %	7.59 $\pm$ 1.25	7.72 $\pm$ 1.20	0.256
HbA1c, mmol/mol	59.5 $\pm$ 13.6	60.8 $\pm$ 13.1	0.256
HDL-C, mg/dL	47.7 $\pm$ 12.8	41.6 $\pm$ 10.9	<b>&lt;0.001</b>

Variable	Without $\geq F3$ fibrosis	With $\geq F3$ fibrosis	p-value
N	911	142	
LDL-C, mg/dL	81.1 $\pm$ 27.3	79.4 $\pm$ 26.7	0.491
TG*, mg/dL	113 (83.2-162)	151 (109-209)	<b>&lt;0.001</b>
ALT*, U/L	21 (16-29)	38 (28-55)	<b>&lt;0.001</b>
AST*, U/L	21 (18-25)	32 (25-42)	<b>&lt;0.001</b>
eGFR, ml/min/1.73m <sup>2</sup>	80.5 $\pm$ 25.1	79.7 $\pm$ 26.8	0.742
Albumin, g/L	44.8 $\pm$ 3.19	45.0 $\pm$ 3.20	0.401
Platelets, x 10 <sup>9</sup> /L	264 $\pm$ 68.1	245 $\pm$ 68.2	<b>0.003</b>
<i>Transient elastography</i>			
CAP, dB/m	279.2 $\pm$ 55.4	335.4 $\pm$ 45.7	<b>&lt;0.001</b>
Steatosis grade, %			<b>&lt;0.001</b>
Minimal	25.4	2.8	
Mild	18.0	6.3	
Moderate	8.7	4.9	
Severe	48.2	85.9	
<i>Diabetes microvascular complications</i>			
Diabetic retinopathy, %	54.6	54.9	0.934
Albuminuria, %	44.5	61.3	<b>&lt;0.001</b>
<i>Biomarker</i>			
TSP2*, ng/ml	2.26 (1.62-3.07)	4.50 (3.01-6.59)	<b>&lt;0.001</b>

\*Log-transformed before analysis; Data were presented as mean $\pm$ standard deviation or median (25th to 75th percentile); TSP2, thrombospondin 2; BMI, body mass index; WC waist circumference; BP, blood pressure; NAFLD, non-alcoholic fatty liver disease; GLP1rA, glucagon-like peptide 1 receptor agonists; SGLT2i, sodium-glucose co-transporter 2 inhibitors; HbA1c, glycated hemoglobin; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TG, triglycerides; ALT, alanine aminotransferase; AST, aspartate transaminase; eGFR, estimated

glomerular filtration rate; CAP, controlled attenuation parameter; NFS, Non-alcoholic fatty liver disease fibrosis score; FIB4, Fibrosis-4 index; Conversion factors for HDL / LDL-C from mmol/l to mg/dL x38.9; TG from mmol/l to mg/dL x88.2.

Supplementary Table S7 Multivariable logistic regression analysis showing the association of serum TSP2 level with presence of  $\geq F3$  fibrosis at baseline (N=1053)

Baseline variable	Model	
	OR (95% CI)	p-value
BMI, kg/m <sup>2</sup>	1.14 (1.08-1.20)	<b>&lt;0.001</b>
AST*, U/L	7.70 (3.99-14.9)	<b>&lt;0.001</b>
Platelet, $\times 10^9/L$	0.996 (0.993-1.00)	0.060
CAP, dB/m	1.01 (1.004-1.02)	<b>&lt;0.001</b>
TSP2*, ng/ml	5.57 (3.45-8.97)	<b>&lt;0.001</b>

\*Log-transformed before analysis.

Variables included in the analysis consisted of age, BMI, duration of diabetes, albuminuria, HDL-C, TG, ALT, AST, platelet count, use of GLP1rA, CAP and TSP2 levels. Model selection was based on Akaike Information Criteria

TSP2, thrombospondin 2; BMI, body mass index; HDL-C, high-density lipoprotein cholesterol; TG, triglyceride; ALT, alanine aminotransferase; AST, aspartate aminotransferase; GLP1rA, glucagon-like peptide 1 receptor agonists; CAP, controlled attenuation parameter; OR, odds ratio; 95%CI, 95% confidence interval.

Supplementary Table S8 Performance of serum TSP2 level in identifying the presence of fibrosis on vibration controlled transient elastography in patients with NAFLD (N=820)

Referent group	$\geq$ F1/F2 fibrosis (N=483)			$\geq$ F3 fibrosis (N=138)		
	F0 (N=337)			F0/F1/F2 (N=682)		
	AUROC (95% CI)	p-value	p-value	AUROC (95% CI)	p-value	p-value
TSP2	0.71 (0.67-0.74)	--		0.80 (0.76-0.84)	--	
BMI+AST	0.77 (0.74-0.80)		Referent	0.86 (0.82-0.89)		Referent
BMI+AST+TSP2	0.80 (0.77-0.83)	<b>0.001</b>	0.073	0.89 (0.86-0.92)	<b>0.011</b>	<b>0.014</b>
BMI+AST+ALT	0.78 (0.75-0.81)	<b>0.020</b>	Referent	0.86 (0.83-0.89)	0.453	Referent

TSP2, thrombospondin 2; BMI, body mass index; ALT, alanine aminotransferase; AST, aspartate transaminase

Supplementary Table S9 Reclassification table showing the category-free net reclassification index after the addition of serum TSP2 level into the model consisting of BMI and AST (N=820)

	N	Correctly reclassified	Incorrectly reclassified	Category-free NRI
With $\geq$ F3 fibrosis	138	86	52	24.6
Without $\geq$ F3 fibrosis	682	464	218	36.1
Overall (95%CI)				60.7 (53.1-78.3)

Original model: BMI + AST

New model: BMI + AST + TSP2

Supplementary Table S10 Baseline clinical characteristics of the study participants stratified by hepatic fibrosis progression (N=491)

Baseline variable	Without hepatic fibrosis progression	With hepatic fibrosis progression	p-value
N	448	43	
<i>Clinical variables</i>			
Men, %	51.3	60.5	0.253
Age, years	59.8±10.1	56.6±9.2	<b>0.045</b>
Ever smoker, %	25.2	16.3	0.192
Duration of diabetes, years	17.2±9.4	15.7±9.2	0.298
BMI, kg/m <sup>2</sup>	27.4±3.8	31.0±5.0	<0.001
WC, cm	94.6±10.1	104.4±10.6	<0.001
Systolic BP, mmHg	136.0±16.7	135.0±15.1	0.752
Diastolic BP, mmHg	77.8±9.8	78.6±9.8	0.621
<i>Medical history</i>			
Hypertension, %	80.4	81.4	0.873
Dyslipidemia, %	94.0	97.7	0.317
Coronary heart disease, %	19.2	16.3	0.641
Stroke, %	1.8	2.3	0.565
<i>Use of Medications</i>			
Insulin, %	54.5	60.5	0.450
Metformin, %	91.5	90.7	0.854
Sulfonylureas, %	35.7	25.6	0.183
DPP4i, %	46.4	46.5	0.992
GLP1rA, %	1.1	0.0	1.00
Pioglitazone, %	11.8	20.9	0.086
SGLT2i, %	19.9	14.0	0.348

ACEI/ARB, %	67.9	72.1	0.569
Beta-blockers, %	29.7	39.5	0.181
CCB, %	48.7	58.1	0.235
Diuretics, %	12.9	20.9	0.145
Statins, %	75.0	74.4	0.933

*Biochemical variables*

HbA1c, %	7.65±1.19	7.79±1.34	0.472
HbA1c, mmol/mol	60.1±13.1	61.6±14.6	0.472
HDL-C, mg/dL	45.9±11.5	41.3±8.3	<b>0.011</b>
LDL-C, mg/dL	81.5±27.6	87.9±26.0	0.144
TG*, mg/dL	122 (91-170)	137 (107-182)	0.177
ALT*, U/L	22 (17-31)	30 (21-42)	<b>0.001</b>
AST*, U/L	21 (18-25)	24 (20-31)	<b>0.002</b>
eGFR, ml/min/1.73m <sup>2</sup>	83.1±24.3	81.3±26.3	0.649
Albumin, g/L	44.7±3.1	44.1±4.2	0.175
Platelets, x 10 <sup>9</sup> /L	269.0±68.4	240.0±53.2	<b>0.008</b>

*Transient elastography*

CAP, dB/m	301±41	339±36	<0.001
Severe steatosis, %	62.3	93.0	<0.001

*Diabetes microvascular complications*

Diabetic retinopathy, %	52.5	48.8	0.650
Albuminuria, %	46.4	51.2	0.552

*Conventional non-invasive fibrosis scores*

NFS $\geq$ -1.455, %	60.9	79.1	<b>0.019</b>
FIB4 $\geq$ 1.3, %	28.6	32.6	0.582
<i>Biomarker</i>			
TSP2*, ng/ml	2.29 (1.70-3.15)	3.21 (2.40-4.35)	<b>&lt;0.001</b>

\*Log-transformed before analysis; Data were presented as mean±standard deviation or median (25th to 75th percentile); TSP2, thrombospondin 2; BMI, body mass index; WC waist circumference; BP, blood pressure; NAFLD, non-alcoholic fatty liver disease; GLP1rA, glucagon-like peptide 1 receptor agonists; SGLT2i, sodium-glucose co-transporter 2 inhibitors; HbA1c, glycated hemoglobin; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TG, triglycerides; ALT, alanine aminotransferase; AST, aspartate transaminase; eGFR, estimated glomerular filtration rate; CAP, controlled attenuation parameter; NFS, non-alcoholic fatty liver disease fibrosis score; FIB4, Fibrosis-4 index; Conversion factors for HDL / LDL-C from mmol/l to mg/dL x38.9; TG from mmol/l to mg/dL x88.2.

Supplementary Table S11 Multivariable logistic regression analysis showing the association of baseline serum TSP2 level with the presence of  $\geq F3$  fibrosis in study participants without history of brain injury and rheumatoid arthritis (N=796)

Baseline variable	Model	
	OR (95% CI)	p-value
BMI, kg/m <sup>2</sup>	1.14 (1.08-1.20)	<b>&lt;0.001</b>
AST*, U/L	8.32 (4.23-16.30)	<b>&lt;0.001</b>
CAP, dB/m	1.008 (1.002-1.014)	<b>0.007</b>
TSP2*, ng/ml	5.11 (3.12-8.37)	<b>&lt;0.001</b>

\*Log-transformed before analysis.

Variables included in the analysis consisted of age, sex, duration of diabetes, albuminuria, HDL-C, TG, ALT, AST, platelet count, CAP and TSP2 levels; Model selection was based on Akaike Information Criteria.

TSP2, thrombospondin 2; BMI, body mass index; HDL-C, high-density lipoprotein cholesterol; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CAP, controlled attenuation parameter; OR, odds ratio; 95%CI, 95% confidence interval.

Supplementary Table S12 Multivariable logistic regression analysis showing the association of baseline serum TSP2 level with hepatic fibrosis progression in study participants without history of brain injury and rheumatoid arthritis (N=479)

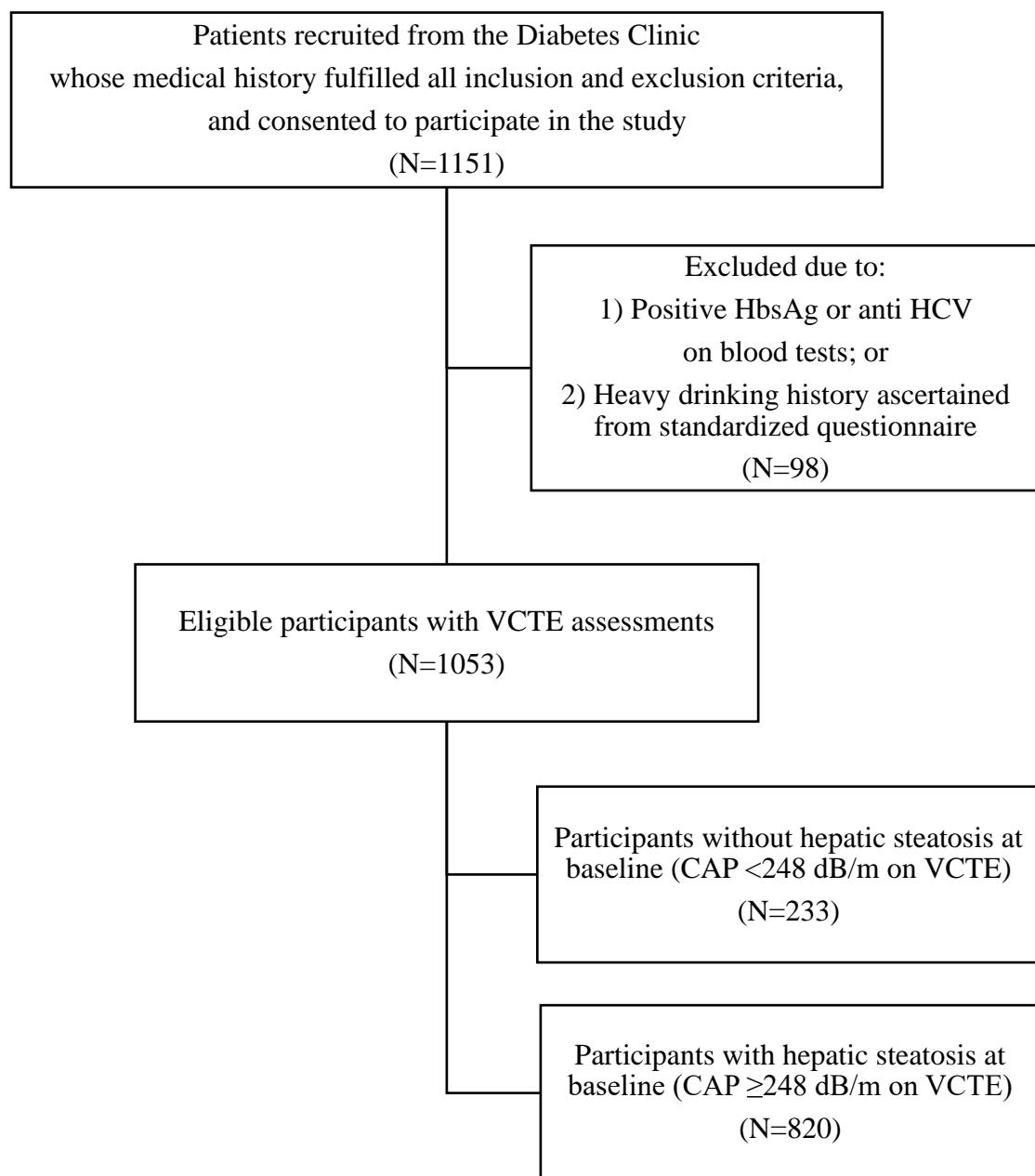
Baseline variable	Model	
	OR (95% CI)	p-value
BMI, kg/m <sup>2</sup>	1.09 (1.02-1.15)	<b>0.009</b>
Platelet, x10 <sup>9</sup> /L	0.992 (0.987-0.997)	<b>0.004</b>
CAP, dB/m	1.016 (1.010-1.020)	< <b>0.001</b>
TSP2*, ng/ml	1.96 (1.07-3.59)	<b>0.030</b>

\*Log-transformed before analysis.

Variables included in the analysis consisted of age, sex, BMI, HDL-C, ALT, AST, platelet count, CAP and TSP2 levels; Model selection was based on Akaike Information Criteria.

TSP2, thrombospondin 2; BMI, body mass index; HDL-C, high-density lipoprotein cholesterol; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CAP, controlled attenuation parameter; OR, odds ratio; 95%CI, 95% confidence interval.

Supplementary Figure 1 Study flow chart



HbsAg, hepatitis B surface antigen; anti-HCV, antibody against hepatitis C; VCTE, vibration controlled transient elastography; CAP, controlled attenuation parameter.