Supplementary data:

SCAP gene polymorphisms decrease the risk of nonalcoholic fatty liver disease in females with metabolic syndrome

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Materials and methods

Clinical and laboratory evaluation

Individual participants were interviewed personally by doctors using a standardized questionnaire about their demographic characteristics, lifestyle and medical history during the check-up interval. Alcohol consumption was evaluated by asking the subjects about the amount and type of alcoholic beverages consumed per day, and then estimating the mean ethanol intake per week according to the concentration of alcohol (50% alcohol for Chinese distilled spirit, 15% alcohol for rice wine, 12% alcohol for wine and 4% alcohol for beer).

The height and weight of the individual subjects were measured, their body mass index (BMI) was calculated as weight/height^2 (kg/m^2). Systolic and diastolic blood pressures were measured twice using a mercury sphygmomanometer and the averages were recorded.

Blood samples were collected after an overnight (>12 h) fasting. Fasting plasma glucose (FPG); serum lipid profiles, such as total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-c), low-density lipoprotein cholesterol (LDL-c) and very-low-density lipoprotein cholesterol (VLDL-c); serum liver functions, such as alanine transaminase (ALT) and aspartate transaminase (AST); and markers of hepatitis B and C virus were determined using a conventional autoanalyser. Ultrasonography was performed on all subjects by two experienced operators using a 3.5-MHz probe (Aloka SSD 5500, Japan).

Diagnostic criteria

MS was defined based on guidelines for metabolic syndrome proposed by Chinese Diabetes Society by at least three of the following items: (i) overweight or obesity defined as BMI > 25 kg/m^2; (ii) hyperglycemia: fasting plasma glucose > 6.1 mmol/L, or 2-h postprandial plasma glucose > 7.8 mmol/L, or treatment of previously diagnosed type 2 diabetes; (iii) hypertension: systolic BP > 140 mmHg or diastolic BP > 90 mmHg, or treatment of previously diagnosed hypertension; (iv) dyslipidemia : triglycerides >1.7 mmol/L, or HDL-C < 0.9 mmol/L (male), <1.0 mmol/L (female).

NAFLD was diagnosed according to the guidelines for diagnosis and treatment of NAFLDs issued by the Fatty Liver and Alcoholic Liver Disease Study Group of the Chinese Liver Disease Association (2008 and 2010). The following criteria of the clinical diagnosis were used. (i) There is no history of drinking alcohol, or ethanol intake per week is less than 140 g in men and 70 g in women. (ii) Specific diseases that can result in fatty liver, such as viral hepatitis, drug-induced liver disease, total parenteral nutrition and Wilson's disease can be ruled out. (iii) The result of the liver imaging study meets the imaging diagnostic criteria of diffuse fatty liver with unknown causes, and/or (iv) metabolic syndrome constituents, such as overweight, hyperglycemia, blood lipid disorder and hypertension occur, with an unexplained increase in serum levels of ALT and/or AST, γ-GT.

Fatty liver can be diagnosed by ultrasonography when the findings present the following: stronger liver echogenicity than kidney or spleen, deep attenuation of ultrasound signal and vascular blurring and narrowing of the hepatic vein lumen.

Table 1. Conditional logistic regression analysis assuming additive and dominant models between healthy control group and MS-NAFLD group.

SNP	Adjusted OR, 95% CI, *P*		χ^2, *P*	P_{HWE} control
	Dominant model	Additive model		
SREBF1				
4925115	1.431, 0.867–2.360, 0.161	1.555, 0.844–2.865, 0.157	2.146, 0.386	0.429
8066560	1.162, 0.679–1.989, 0.583	1.263, 0.685–2.328, 0.454	1.006, 0.608	0.965
2282180	0.954, 0.565–1.609, 0.860	0.98, 0.539–1.788, 0.952	0.428, 0.839	0.605
9902941	1.147, 0.680–1.934, 0.607	1.184, 0.648–2.165, 0.583	0.589, 0.751	0.692
SREBF2				
2228314	0.719, 0.431–1.199, 0.206	0.779, 0.427–1.423, 0.416	3.039, 0.222	0.497
5996080	0.824, 0.411–1.652, 0.585	0.804, 0.377–1.715, 0.573	1.293, 0.676	0.830
2267438	1.417, 0.886–2.266, 0.146	1.913, 0.937–3.906, 0.075	4.550, 0.109	0.399
9607852	1.569, 0.352–7.003, 0.555	1.569, 0.352–7.003, 0.555	0.405, 0.498	0.878
4822062	1.079, 0.509–2.289, 0.842	1.152, 0.523–2.536, 0.725	1.178, 0.705	0.721
17379759	1.057, 0.396–2.822, 0.912	1.057, 0.396–2.822, 0.912	0.002, 1.000	0.598
SCAP				
2101247	1.280, 0.824–1.986, 0.272	1.586, 0.729–3.452, 0.245	2.084, 0.351	0.548
2306628	0.860, 0.321–2.301, 0.763	0.860, 0.321–2.301, 0.763	0.095, 0.813	0.598
4858889	0.957, 0.512–1.788, 0.890	1.014, 0.509–2.020, 0.969	0.409, 0.949	0.973
17079634	1.141, 0.616–2.113, 0.674	1.259, 0.641–2.473, 0.504	0.706, 0.715	0.784

Adjusted OR: adjusted for age, gender, smoking status, BMI.
Additive model: common homozygotes vs heterozygotes vs rare homozygotes.
Dominant model: common homozygotes vs combined heterozygous and rare homozygous.

Table 2. Conditional logistic regression analysis assuming additive and dominant models between healthy control group and MS+NAFLD group.

SNP	Adjusted OR, 95% CI, *P*		χ^2, *P*
	Dominant model	Additive model	
SREBF1			
4925115	1.528, 0.857–2.726, 0.151	1.319, 0.635–2.744, 0.458	4.131, 0.131
8066560	1.242, 0.682–2.262, 0.479	1.093, 0.522–2.289, 0.814	1.373, 0.539
2282180	0.853, 0.457–1.593, 0.618	0.787, 0.381–1.624, 0.517	0.860, 0.673
9902941	1.170, 0.646–2.122, 0.604	0.996, 0.476–2.081, 0.991	2.292, 0.322
SREBF2			
2228314	0.590, 0.309–1.123, 0.108	0.612, 0.295–1.270, 0.187	4.186, 0.123
5996080	0.629, 0.281–1.409, 0.260	0.677, 0.290–1.583, 0.369	2.387, 0.264
2267438	1.350, 0.790–2.308, 0.272	1.178, 0.537–2.583, 0.683	1.003, 0.607
9607852	2.212, 0.309–15.847, 0.429	2.212, 0.309–15.847, 0.429	0.053, 0.819
4822062	0.527, 0.184–1.510, 0.233	0.523, 0.179–1.528, 0.236	1.556, 0.471
17379759	0.272,0.055–1.352, 0.112	0.246, 0.042–1.421, 0.117	1.777, 0.454
SCAP			
2101247	0.721, 0.443–1.175, 0.190	0.508, 0.225–1.144, 0.102	4.280, 0.121
2306628	1.218, 0.400–3.704, 0.729	1.218, 0.400–3.704, 0.729	0.617, 1.000
4858889	1.224, 0.593–2.526, 0.585	1.338, 0.595–3.006, 0.481	0.208, 0.962
17079634	1.096, 0.527–1.096, 0.806	1.179, 0.519–2.680, 0.693	0.301, 0.914

Table 3. Clinical and biological characteristics of female subjects according to *SCAP* rs2101247 genotypes.

Character	*GG*	*GA*	*AA*	*P*
Age (years)	68.48 ± 7.828	68.36 ± 8.525	68.02 ± 10.850	0.998
Smokers (%)	5.0	1.4	4.1	0.525
BMI (kg/m^2)	26.66 ± 3.377	25.32 ± 3.175	26.25 ± 3.454	0.129
FPG (mmol/L)	7.85 ± 2.59	7.33 ± 2.05	7.29 ± 1.96	0.674
SBP (mm Hg)	137.45 ± 14.780	136.66 ± 15.970	141.35 ± 16.291	0.336
DBP (mm Hg)	78.95 ± 10.378	77.40 ± 8.182	80.37 ± 10.293	0.241
TG (mmol/L)	1.62 ± 0.83	1.72 ± 1.06	1.71 ± 1.17	0.984
TC (mmol/L)	5.18 ± 0.84	5.22 ± 0.98	5.38 ± 1.00	0.543
HDL-c (mmol/L)	1.32 ± 0.33	1.40 ± 0.44	1.31 ± 0.27	0.331
LDL-c (mmol/L)	3.12 ± 0.97	3.19 ± 0.89	2.99 ± 0.98	0.502
VLDL (mmol/L)	2.62 ± 0.46	2.65 ± 0.60	2.65 ± 0.63	0.863
ALT (U/L)	25.23 ± 13.60	23.40 ± 12.74	26.41 ± 13.53	0.277
AST (U/L)	21.03 ± 7.65	18.7 ± 4.55	20.35 ± 6.53	0.130