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Fatty liver and the metabolic syndrome among Shanghai adults

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Abstract

Background and Aim: To explore the relationship between fatty liver and the metabolic syndrome in the adults of Shanghai and evaluate the value of fatty liver as a marker for risk factor clustering.

Methods: Questionnaires, physical examinations, laboratory tests (blood lipid and glucose) and real-time liver ultrasonographies were performed in Shanghai adults and analyzed using randomized, multistage, stratified cluster sampling. Prevalence of the metabolic syndrome was defined by the National Cholesterol Education Program–Adult Treatment Panel III (NCEP-ATPIII) criteria with the exception of abdominal obesity (waist circumference >90 cm in men and >80 cm in women); fatty liver was diagnosed in accordance with the presence of an ultrasonographic pattern consistent with 'bright' liver (brightness and posterior attenuation of liver).

Results: The study population consisted of 3175 subjects (1218 men) with a mean (± SD) age of 52.4 ± 15.1 years. Metabolic syndrome and fatty liver were found in 726 (22.87%) and 661 (20.82%) of sampled cases, respectively. After adjustment by age and sex, the prevalence of the metabolic syndrome and fatty liver in the general population of Shanghai were 15.30 and 17.29%, respectively. The risk for fatty liver in subjects with abdominal obesity, diabetes, dyslipidemia and hypertension increased 32.78-fold (95% confidence interval (CI) 14.85–72.35), 31.58-fold (95% CI 14.18–70.35), 22.64-fold (95% CI 10.26–49.99) and 23.25-fold (95% CI 10.54–51.30), respectively, compared with controls, whereas the risk for fatty liver in subjects with metabolic syndrome was increased by 39.33-fold (95% CI 17.77–87.05). After the 661 patients with fatty liver had been stratified by body mass index (BMI), the prevalence of abdominal obesity, hypertension and the metabolic syndrome were increased from 25.0, 47.2 and 36.1%, respectively, in people with normal BMI to 81.0, 73.8 and 55.4%, respectively, in obese persons. However, the prevalence of hypertriglyceridemia, high fasting glucose and low high-density lipoprotein–cholesterol showed no significant changes with increased BMI. Moreover, among fatty liver patients with normal BMI, the detection rate for one or more features of metabolic disorders was as high as 83.3% and that for five features was 2.8%. Compared with obesity (BMI ≥ 25 kg/m^2) and abdominal obesity, fatty liver had the highest clustering rate, specificity, positive predictive value and attributable risk percentage in detecting risk factor clustering in both sexes.

Conclusions: There is a high prevalence of metabolic syndrome and fatty liver among Shanghai adults. Metabolic disorders are closely related to fatty liver; moreover, fatty liver appears to be a good predictor for the clustering of risk factors for metabolic syndrome.

Key words: epidemiology, fatty liver, metabolic syndrome.

INTRODUCTION

Fatty liver is a disease with genetic, environmental, metabolic and stress-related components. In western Europe, Japan, Australia and the USA, ultrasound surveys of the general population have indicated that almost one-quarter of the adult population has hepatic steatosis, which is mainly associated with insulin

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resistance.[1,2] Because metabolic syndrome is a group of disorders centrally linked by insulin resistance, fatty liver is generally regarded as part of the metabolic syndrome.[3–7] However, few, if any, previous epidemiological surveys have investigated the associations between fatty liver and metabolic syndrome in a general population in China or the diagnostic value of fatty liver in detecting metabolic syndrome.[8] Therefore, we conducted a cross-sectional survey and used stratified multistage probability cluster sampling to determine the relationship between fatty liver and the syndrome, as well as assessing the value of using fatty liver in predicting the clustering of metabolic abnormalities in Shanghai, China.

METHODS

Survey design and study sample

We assigned a number to each of the 16 urban districts of Shanghai and selected two districts at random (Yangpu District and Pudong New District). Of 11 residential districts within Yangpu and Pudong, we randomly selected the Pingliang and Shanggang residential districts, which contained 30 and 26 neighborhood communities, respectively. From these, we selected eight neighborhood communities in total. Resident groups were randomly selected from each sample neighborhood community. From October 2002 to April 2003, investigations were conducted in every adult over 16 years of age in the selected resident groups at home, with 500 participants initially enrolled in each group. This program was approved by the Research Ethics Committee of the Shanghai Health Bureau and all participants provided written informed consent prior to their inclusion in the study. General physical examinations, laboratory assessments and ultrasound liver scans were performed on each study subject and took place at a mobile examination center following an overnight fast of at least 12 h.

Data collection

Interview

Selected individuals were interviewed in their homes using a questionnaire that gathered information on demographic characteristics, medical history, medication use and health-related habits, including questions on smoking habits, alcohol intake and physical activity.[9–11]

Physical examination

Bodyweight was measured in light clothing and without shoes to the nearest half kilogram. Height was measured to the nearest half centimeter. Body mass index (BMI) was calculated as weight (kg) divided by height squared (m^2). Waist circumference (to the nearest half centimeter) was measured at the mid-point between the lower border of the rib cage and the iliac crest, whereas hip circumference was similarly obtained at the widest point between the hip and buttock, enabling calculation of the waist-to-hip ratio. Three blood pressure readings were obtained at 1 min intervals and the second and the third systolic and diastolic pressure readings were averaged and used in the analyses.

Laboratory assessments

Venous blood samples were collected at 0 and 120 min following a 75 g oral glucose challenge for non-diabetics or 100 g steamed bread for diabetics. Samples were centrifuged at 2000 *g* for 10 min at 25°C immediately and specimens were then frozen and shipped to a central laboratory of the Shanghai Center for Disease Control and Prevention, where they were stored initially at –20°C and then –70°C. Subsequently, serum glucose was determined using a modified hexokinase method. Fasting serum total cholesterol and triglyceride concentrations were measured enzymatically with color absorptiometry based on a peroxidase-catalysed reaction. High-density lipoprotein–cholesterol (HDL-C) was measured after precipitation of other lipoproteins with a polyanion/divalent cation mixture. Low-density lipoprotein–cholesterol (LDL-C) was calculated from measured values of total cholesterol, triglycerides and HDL-C using the following formula:

$$\text{LDL} = (\text{Total cholesterol}) - (\text{HDL}) - (\text{Triglycerides}/5)$$

Low-density lipoprotein was not calculated if the triglyceride level was >4.52 mmol/L (400 mg/dL). All these serum biochemistries were performed using a Bayer model 1650 automated bio-analyzer (Bayer Diagnostic, Basingstoke, UK).

Ultrasonographic examination

Ultrasonographic examinations of the respondents' livers and gall-bladders were performed by an experienced ultrasonographist, using the Simens Sonoline-SI450 unit with a 3.5 MHz probe (Simens Medical Solutions, Erlangen, Germany).

Quality control

Field researchers were recruited from the following institutions: Shanghai First People's Hospital, Shanghai Center for Disease Control and Prevention, and Shanghai Second Medical University. Before the investigation, the researchers were given systematic training to ensure standardization of the investigation procedure. For further quality control, 5% of questionnaires, blood samples and ultrasonographic results were sampled for re-examination; kappa analysis of these samples showed good consistency in the diagnostic tests (data not shown).

Definitions

Obesity and abdominal obesity were categorized according to the new BMI criteria for Asians by the regional office for Western Pacific Region of the World Health Organization (WHO).[12] Hypertension was defined as given in the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC7).[13] Diagnoses of impaired fasting glucose, impaired glucose tolerance and diabetes mellitus (DM) were based on WHO criteria published in 1999 (WHO/NCD/NCS/99.2).[14] Dyslipidemia (including hypertriglyceridemia and low HDL-C) and metabolic syndrome were diagnosed on the basis of the Third Report of the National Cholesterol Education Program Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (NCEP-ATPIII)[15] and adapted Adult Treatment Panel III (ATPIII) criteria for metabolic syndrome, with the exception of abdominal obesity (waist circumference >90 cm in men and >80 cm in women).

Diagnosis of fatty liver was based on the presence of an ultrasonographic pattern consistent with 'bright' liver (brightness and posterior attenuation) with stronger echoes in the hepatic parenchyma than in the renal parenchyma, vessel blurring and narrowing of the lumen of the hepatic veins in the absence of findings suggestive of other chronic liver disease.[16,17] Gallstones were diagnosed on the basis of distinct ultrasonographic features, such as echo density, acoustic shadowing and gravitational dependence.[18]

We regarded participants who reported currently using antihypertensive or antidiabetic medications or fibrates as participants with high blood pressure or diabetes or hypertriglyceridemia, respectively.

Statistical analysis

All data were analyzed using SPSS 11.0 software (SPSS, Chicago, IL, USA) at the Clinical Epidemiology Resource and Training Center, Zhongshan Hospital Affiliated to Fudan University. Unpaired *t*-test, χ^2 contingency test and Fisher's exact test were used whenever appropriate. Non-parametric methods were also used for non-normally distributed values. Logistic regression analysis (univariate and multivariate analysis) was used to calculate the risk for fatty liver and various parameters. Some analyses were adjusted for age and sex. Kappa analysis was performed for blood biochemical data and as a quality control for ultrasonography. All P values provided are for two-sided tests. $P < 0.05$ was considered statistically significant.

RESULTS

Sampling status

We used a stratified, multistage probability cluster sampling design to obtain a representative sample of the Shanghai civilian, non-institutionalized population. The neighborhoods investigated contained 4205 residents aged 16 years or more; people with a doctor's diagnosis of chronic viral hepatitis, cirrhosis or other severe diseases were excluded from the study. Physical examination and laboratory data were available for 3834 individuals aged 16 years and older. Of these, we used results from 3175 individuals (82.81%) who had complete data available for ultrasonographic examination and causes of fatty liver. Thus, 3175 individuals were included as subjects in the present study, corresponding to approximately 2.26/10 000 of the Shanghai population according to data collected in the Fifth China National Census in 2002 (http://www.china-un.ch/eng/ljzg/shjjtj/t85845.htm).

The study population included 1218 males and 1957 females (excluding pregnant women), giving a male to female ratio of 1 : 1.6; the age range of subjects was 16–88 years and no significant difference was noted between the ages of male and female subjects. In comparison with the sex and age composition obtained in the Fifth National Census of Shanghai (2002; http://www.sinoptic.ch/shanghaiflash/2003/200302.htm), the study population contained a higher percentage of elderly subjects and women (both $P < 0.001$). Therefore, some of the results were adjusted by age and sex in order to be more representative of the real situation in Shanghai.

General data

The prevalence of obesity, abdominal obesity, dyslipidemia, hypertension, impaired glucose tolerance, diabetes mellitus, cholelithiasis and fatty liver in the 3175 study subjects was 41.9, 36, 46.2, 47.59, 4.03, 16.1, 10.7 and 20.82%, respectively (Tables 1,2). The total prevalence of fatty liver increased with age in trend analysis ($P = 0.00000$) and peak prevalence (28.44%) was reached between the ages of 60 and 70 years (Table 3). After adjustment by age and sex, the overall prevalence of fatty liver among adults in Shanghai was found to be 17.29%, with the prevalence of fatty liver being significantly higher in males than in females (19.30 *vs* 15.08%, respectively; $P = 0.0019$). In addition, only 23 cases with fatty liver were in accordance with the criteria of alcoholic fatty liver.[19]

The prevalence of metabolic syndrome in the present study population, according to NCEP-ATPIII criteria, was 16.81% and the prevalence in males was significantly higher than in females (23.89 *vs* 12.57%, respectively; $P < 0.01$). After adjusting these results by sex and age, the present data indicate that the prevalence of metabolic syndrome in the general population of Shanghai is 9.17%. However, if the new criteria for Asian abdominal obesity proposed by the WHO is used instead of the NCEP-ATPIII criteria (i.e. adapted ATPIII criteria), a total of 726 individuals (22.87%) could be diagnosed as having metabolic syndrome and the prevalence in males remained significantly higher than that in females (27.83 *vs* 19.78%, respectively; $P < 0.001$). The prevalence of metabolic syndrome and its associated diseases increased with age (all P-values <0.001 in trend analysis; Table 3, some data not shown). After being adjusted for sex and age, the prevalence of metabolic syndrome in Shanghai adults was

Table 1 Anthropometric, clinical and laboratory data of the 3175 participants of the present study

Characteristics	All cases (n = 3175)	Men (n = 1218)	Women (n = 1957)	P
Age (years)	52.4 ± 15.1	52.3 ± 16.4	52.4 ± 14.3	0.865
BMI (kg/m^2)	24.52 ± 5.50	24.48 ± 3.52	24.60 ± 6.44	0.483
Waist circumference (cm)	80.28 ± 10.09	83.79 ± 9.70	78.06 ± 9.69	<0.001
Waist-to-hip ratio	0.836 ± 0.069	0.867 ± 0.064	0.817 ± 0.061	<0.001
Triglyceride (mmol/L)	1.34 ± 0.99	1.46 ± 1.10	1.26 ± 0.91	<0.001
Total cholesterol (mmol/L)	5.01 ± 0.97	4.84 ± 0.95	5.11 ± 0.97	<0.001
HDL-C (mmol/L)	1.53 ± 0.41	1.37 ± 0.37	1.62 ± 0.40	<0.001
LDL-C (mmol/L)	2.91 ± 0.84	2.84 ± 0.83	2.96 ± 0.84	<0.001
SBP (mmHg)	129.5 ± 19.5	131.7 ± 18.8	128.1 ± 19.8	<0.001
DBP (mmHg)	82.0 ± 12.3	84.0 ± 12.0	80.8 ± 12.2	<0.001
Fasting glucose (mmol/L)	5.76 ± 1.54	5.78 ± 1.56	5.74 ± 1.53	0.497
120 min glucose (mmol/L)	6.29 ± 3.31	6.27 ± 3.51	6.31 ± 3.19	0.754

BMI, body mass index; HDL-C, high-density lipoprotein–cholesterol; LDL-C, low-density lipoprotein–cholesterol; SBP, DBP, systolic and diastolic blood pressure, respectively.

Table 2 Prevalence of metabolic features among the 3175 participants in the present study

Characteristics	All cases (n = 3175)	Men (n = 1218)	Women (n = 1957)	P
Overweight	736 (23.2)	302 (24.8)	434 (22.2)	0.0892
Obesity	1331 (41.9)	545 (44.7)	786 (40.1)	0.0110
Abdominal obesity	1136 (36.0)	333 (27.3)	803 (41.0)	<0.001
Dyslipidemia	1466 (46.2)	526 (43.2)	940 (48.0)	0.007
Hypertension	1511 (47.59)	647 (53.12)	864 (44.15)	<0.001
Impaired fasting glucose	261 (8.22)	109 (8.95)	152 (7.77)	0.238
Impaired glucose tolerance	128 (4.03)	53 (4.35)	75 (3.83)	0.4698
Diabetes mellitus	512 (16.1)	220 (18.1)	292 (14.9)	0.0193
Cholelithiasis	339 (10.7)	110 (9.0)	229 (11.7)	0.0178
Fatty liver	661 (20.82)	258 (21.18)	403 (20.59)	0.6908

Data show the number of subjects in each group, with percentages given in parentheses.

P values are for comparisons between sexes, with the t-test used to test measurement data and χ^2 or Fisher's exact test used to evaluate differences in rates.

Table 3 Age-specific prevalence of fatty liver and metabolic syndrome among the 3175 participants in the present study

	Age (years)							
Characterictis	16–19 (n = 185)	20–29 (n = 123)	30–39 (n = 130)	40–49 (n = 750)	50–59 (n = 920)	60–69 (n = 655)	≥70 (n = 412)	P
Fatty liver	2 (1.08)	8 (6.50)	17 (13.08)	142 (18.93)	196 (21.13)	186 (28.40)	110 (26.70)	0.00000
Metabolic syndrome	1 (0.54)	4 (3.25)	14 (10.77)	109 (14.53)	220 (23.91)	226 (34.50)	152 (36.89)	0.00000

Data show the number of subjects in each group, with percentages given in parentheses.

P values are for trend analyses.

found to be 15.30% according to the adapted NCEP-ATPIII criteria.

Relationship between metabolic disorders and fatty liver

The 3175 individuals were divided into one of eight groups: (i) controls (BMI <23 kg/m^2, without central obesity, diabetes mellitus, dyslipidemia, hypertension, cholelithiasis or the metabolic syndrome as defined by adapted ATPIII criteria); (ii) the abdominal obesity group (waist circumference >90 cm in males and >80 cm in females); (iii) the obesity group (BMI ≥25 kg/m^2); (iv) the diabetes mellitus group; (v) the dyslipidemia group; (vi) the hypertension group; (vii) the cholelithiasis group; and (viii) the metabolic syndrome group. The relative risk (RR) for fatty liver and the corresponding 95% confidence intervals (CI) were calculated for each group (Table 4).

Table 4 Relationship between multiple metabolic disorders and fatty liver

Group	No. subjects	Fatty liver (%)	RR	95% CI	χ^2	*P*
Control	516	1.14	–	–	–	–
Obesity	522	39.22	28.49	12.9–62.9	144.76	<0.0001
Abdominal obesity	474	41.72	32.78	14.9–72.4	165.10	<0.0001
Diabetes mellitus	512	41.19	31.58	14.2–70.4	147.85	<0.0001
Dyslipidemia	1466	31.86	22.64	10.3–50.0	114.51	<0.0001
Hypertension	1535	30.23	23.25	10.5–51.3	118.07	<0.0001
Cholelithiasis	339	31.27	20.30	9.0–46.0	90.03	<0.0001
Metabolic syndrome	726	48.21	39.33	17.8–87.1	189.84	<0.0001

RR, relative risk; CI, confidence interval.

Table 5 Prevalence of metabolic alterations fitting the criteria of metabolic syndrome in patients with fatty liver according to classes of body mass index

BMI group	*n*	Abdominal obesity	Impaired fasting glucose	Low HDL-C	Hypertriglyceridemia	Hypertension
Normal	36	9 (25.0)	15 (41.7)	12 (33.3)	12 (33.3)	17 (47.2)
Overweight	103	42 (40.8)	42 (40.8)	37 (35.9)	52 (50.5)	62 (60.2)
Obesity	522	423 (81.0)	223 (42.7)	176 (33.7)	245 (46.9)	385 (73.8)
Total	661	474 (71.71)	280 (42.36)	225 (34.03)	312 (47.20)	464 (70.20)

Data show the number of subjects in each group, with percentages given in parentheses.
Normal (weight): body mass index (BMI) <23 kg/m^2; overweight: BMI 23–24.9 kg/m^2; obese: BMI ≥ 25 kg/m^2.

Table 6 Presence of positive criteria for metabolic syndrome in patients with fatty liver according to classes of body mass index

		No. positive criteria				
Group	*n*	≥1	≥2	≥3	≥4	5
Normal	36	30 (83.3)	22 (61.1)	13 (36.1)	5 (13.9)	1 (2.8)
Overweight	103	93 (90.3)	72 (70.0)	48 (46.6)	21 (20.4)	6 (5.8)
Obese	522	511 (97.9)	457 (87.5)	289 (55.4)	154 (29.5)	46 (8.8)
Total	661	634 (95.92)	551 (83.36)	350 (52.95)	180 (27.23)	53 (8.02)

Data show the number of subjects in each group, with percentages given in parentheses.
Normal (weight): body mass index (BMI) <23 kg/m^2; overweight: BMI 23–24.9 kg/m^2; obese: BMI ≥ 25 kg/m^2.
Note that the presence of three or more positive criteria defines the metabolic syndrome.

Relationship between fatty liver and metabolic disorders

The 661 individuals with fatty liver were stratified on the basis of BMI into a normal bodyweight group (BMI <23 kg/m^2), an overweight group (BMI 23–24.9 kg/m^2) and an obese group (BMI ≥25 kg/m^2). Analyses revealed that increased BMI in patients with fatty liver was associated with significant increases in the prevalence of abdominal obesity and hypertension; the prevalence of abdominal obesity increased from 25.0% among normal weight patients to 81.0% among obese patients (χ^2 value = 60.38; $P < 0.0001$) and the prevalence of hypertension increased from 47.2 to 73.8% (χ^2 value = 27.63; $P < 0.0001$). In contrast, there was little difference in the prevalence of low HLD-C, hypertriglyceridemia and high glucose among the groups (Table 5).

As given in Table 6, even in fatty liver patients of normal weight, the detection rate of one or more metabolic syndrome features (central obesity, high fasting glucose, hypertriglyceridemia, low HDL-C and/or hypertension) was as high as 83.3% and in obese fatty liver patients the rate was 97.9%. Three or more features (i.e. metabolic syndrome) were detected in 36.1, 46.6 and 55.4% of individuals in the normal weight, overweight and obese groups, respectively. Five features of the metabolic syndrome were detected in 2.8, 5.8 and 8.8% of the patients in these three groups, respectively. In contrast, 27 of 661 fatty liver patients (4.08%), corresponding to 16.7, 9.7 and 2.1% of the normal weight, overweight and obese groups, respectively, showed no evidence of these metabolic features. Interestingly, 16 of 23 patients diagnosed as alcoholic fatty liver were among these patients lacking measurable metabolic disorders (Table 6).

DISCUSSION

People with the metabolic syndrome are at an increased risk of developing diabetes mellitus and cardiovascular disease, as well as increased mortality from cardiovascular disease and all causes, including fatty liver disease.[6,20,21] There are no well-accepted criteria for the diagnosis of metabolic syndrome. Previous estimates of the prevalence of metabolic syndrome in the US and Europe have differed because of differences in the definitions used and the populations studied.[6,20,21] The recently released Executive Summary of the Third Report of the National Cholesterol Education Program Expert Panel on Detection, Evaluation and Treatment of the High Blood Cholesterol in Adults draws attention to the importance of metabolic syndrome and provides a working definition of this syndrome for the first time.[22] The criteria used to define metabolic syndrome can easily be measured in clinical practice and are suitable for epidemiologic purposes.[6,20,21] Using the new definition of metabolic syndrome according to ATPIII, the prevalence of metabolic syndrome among US adults is approximately 22%.[6] Current epidemiological data suggest that the prevalence of metabolic syndrome in Asians is comparable to, or slightly lower than, that in Western populations.[23,24] In the present cross-sectional study, the age- and sex-adjusted prevalence of metabolic syndrome in the general population of Shanghai was 9.17%. Studies on BMI and body fat have shown that Asians have a higher percentage of body fat at a lower BMI compared with Caucasians.[23–25] According to these results, rates of obesity and metabolic syndrome would be underestimated in Asians if the NCEP obesity criteria were used. Therefore, instead of using the original NCEP definitions for obesity, studies in Asian populations have applied Asian–Pacific criteria for abdominal obesity, as waist circumference ≥90 cm in men and ≥80 cm in women, and for obesity s BMI ≥25 kg/m^2 in both sexes.[26] So, we followed the NCEP ATPIII criteria, with the exception of waist circumference, and the age- and sex-adjusted prevalence of metabolic syndrome in the present survey population increased significantly (to 15.30%); this gives a better reflection of the prevalence of metabolic syndrome in the region.

Fatty liver (especially non-alcoholic fatty liver) is mainly associated with obesity, diabetes, hyperdyslipiemia and insulin resistance, which are the main features of metabolic syndrome.[1,2] The present results indicate that approximately 20.82% of Shanghai adults (17.29% after adjustment for age and sex) have fatty liver and most of these (92.43%) are cases of non-alcoholic fatty liver.[19] Marceau *et al.*[4] analyzed liver biopsies obtained from 551 heavily obese patients and found that 86% of them suffered from fatty liver. Furthermore, in the presence of one more features, such as abdominal obesity, impaired glucose tolerance, diabetes mellitus, hypertension or dyslipidemia, the risk for fatty liver increased by up to 99-fold.[4] Recently, Marchesini *et al.*[5] assessed the prevalence of metabolic syndrome as defined by NCEP ATPIII in 304 consecutive, non-alcoholic fatty liver disease patients without overt diabetes and found that the prevalence of metabolic syndrome increased with increasing BMI from 18% in normal weight subjects to 67% in obese subjects. Liver biopsy was available in 163 cases (54%). Patients who underwent liver biopsy were fairly representative of the whole population. However, there were no differences in average glucose and lipid levels or in arterial pressure between subjects who did or did not undergo liver biopsy.[5]

Although liver biopsy is the gold standard for the diagnosis of fatty liver, ultrasonography is the modern diagnostic test of choice for fatty liver epidemiological surveys because it is non-invasive, safe, widely available, portable and sensitive (up to 89%) and specific (up to 93%) for the detection of steatosis.[16,17] Our diagnoses of fatty liver were based on real-time ultrasonographic examinations, in which false-negative and false-positive errors are inevitable compared with liver biopsy examinations. Therefore, strict quality controls were used in the present study and tests of consistency showed that the ultrasonographic examinations used in the present epidemiological field investigation had good reliability. The present survey demonstrated that obesity, abdominal obesity, diabetes mellitus, dyslipidemia, hypertension and cholelithiasis increased the risk for fatty liver by 28.49-, 38.15-, 36.72-, 26.35-, 27.02- and 23.49-fold, respectively, indicating that abdominal obesity is more closely related with fatty liver than are the other factors. However, patients with metabolic syndrome had the highest the risk for fatty liver (RR = 39.33) and as many as 48.21% of patients suffering from metabolic syndrome also had fatty liver. Conversely, the prevalence of abdominal obesity, impaired fasting glucose, low HDL-C, hypertriglyceridemia and hypertension in subjects with fatty liver were 71.71, 42.36, 34.03, 47.2 and 70.2%, respectively. Metabolic syndrome was present in 52.95% of fatty liver patients. In addition, the prevalence of abdominal obesity, hypertriglyceridemia and hypertension increased as BMI increased in fatty liver patients, but the prevalence of low HDL-C and impaired fasting glucose did not differ significantly in groups with different BMI. Even among fatty liver patients with normal BMI, the detection rates for one or more, three or more and five features were as high as 83.3, 36.1 and 2.8%, respectively. These results suggest that fatty liver is closely related with multiple metabolic disorders and that perhaps fatty liver (independent of obesity) should be regarded as one of the components of metabolic syndrome and that fatty liver patients with metabolic disorders may be at increased risk of cardiovascular events.[20,21]

More than 80 years have passed since the introduction of the concept of the clustering of metabolic and physiological abnormalities in 1923 by Kylin.[27] There are still many cloud-clusters over metabolic syndrome that need to be further unraveled. The role of obesity and its central distribution in metabolic syndrome has continued to be a subject of some debate.[6,20,21] The question as to whether we could have a uniform, worldwide definition for metabolic syndrome awaits an answer. Analysis of risk factor clustering in the present survey showed that the rate of risk factor clustering and its attributable risk percentage (ARP) in individuals with fatty liver was higher than in subjects with obesity and abdominal obesity. Although Youden's index (sensitivity (%) + specificity (%) – 1) of the determination for risk factor clustering by fatty liver fell between the BMI and waist circumference in both sexes, fatty liver had the highest specificity and positive predictive value in determining risk factor clustering. The present study suggest that fatty liver has good consistency as a marker of risk factor clustering compared with classic markers (such as obesity and abdominal obesity); moreover, fatty liver may not be influenced by sex. Because ultrasound scans of the liver are used widely across China, because there is no current consensus on the criteria for diagnosing obesity worldwide and because fatty liver is a more specific means of providing important prognostic information than obesity, we propose that fatty liver, and not BMI or waist circumsference, should be regarded as an important component used to diagnose metabolic syndrome. Further investigations are required to provide new evidence to support this recommendation.

A previous study by Bellentani and Tiribelli demonstrated that 16.4% of patients with fatty liver diagnosed by ultrasonographic examination did not have obesity, diabetes mellitus or hyperlipidemia.[3] Of the 661 fatty liver patients examined in that survey, 27 individuals (4.08%) showed no evidence of abdominal obesity, impaired glucose tolerance, dyslipidemia or hypertension, and even 2.1% of fatty liver patients with obesity showed no evidence of metabolic disorders. These observations suggest that even though fatty liver is regarded as a liver disease induced by metabolic disorders and stress, the condition may also appear in people with normal BMI, blood lipids and plasma glucose. However, in the present study population, this circumstance was mainly associated with excessive drinking (data not shown).

In summary, metabolic syndrome and fatty liver are highly prevalent in the general population of Shanghai and a strong association exists between fatty liver and the risk factors characteristic of metabolic syndrome. Moreover, fatty liver appears to be a good predictor for the clustering of risk factors for metabolic syndrome. Thus, studies of the direct medical costs associated with fatty liver are urgently needed. Because fatty liver is highly associated with the clustering of metabolic and physiological abnormalities, our work further underscores the urgent need to develop comprehensive efforts directed at controlling the epidemic of metabolic syndrome in China.

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