ORIGINAL RESEARCH

Relationship between obesity, metabolic syndrome, and nonalcoholic fatty liver disease in the elderly agricultural and fishing population of Taiwan

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Background: The purpose of this study was to explore the relationship between obesity, the metabolic syndrome, and nonalcoholic fatty liver disease (NAFLD) in the elderly agricultural and fishing population of Taipei, Taiwan.

Methods: The study participants comprised 6,511 (3,971 male and 2,540 female) healthy elderly subjects voluntarily attending a teaching hospital for a physical check-up in 2010. Blood samples and real-time ultrasound-proven fatty liver sonography results were collected.

Results: The prevalence of NAFLD in this elderly population was 27.2%, including mild NAFLD (16.0%), moderate NAFLD (10.3%), and severe NAFLD (0.9%). The prevalence of moderate or severe NAFLD for metabolic syndrome proved to be substantially greater ($P<0.0001$, χ^2 test) for one or two metabolic factors. Using multinomial logistic regression analysis, age, sex, metabolic syndrome, and higher body mass index had a statistically significant association with mild NAFLD. Age, sex, metabolic syndrome, higher body mass index, and higher alanine aminotransferase were significantly related to moderate NAFLD. In addition, higher body mass index, higher uric acid, and higher alanine aminotransferase levels were significantly related to severe NAFLD. The sensitivity and specificity of body mass index and waist circumference as markers of NAFLD were estimated to be 81% and 84%, respectively, and 77% and 69%, respectively.

Conclusion: The prevalence of mild or moderate NAFLD was related to obesity and metabolic syndrome. Higher body mass index was also related to severe NAFLD but not to metabolic syndrome. Targeting this population for control of obesity and improved metabolic function is important.

Keywords: agriculture, fishing, elderly, metabolic syndrome, nonalcoholic fatty liver disease

Introduction

Nonalcoholic fatty liver disease (NAFLD) consists of the accumulation of fat vacuoles in the cytoplasm of hepatocytes and is characterized by development of hepatic lesions similar to those caused by alcohol in subjects without significant alcohol consumption.[1] The prevalence of NAFLD is reported to be 3%–24% in the general population in various countries, and is increasing in parallel with the rising prevalence of obesity.[2] However, there is little information on the clinical relevance of this disorder as a health problem in the general population, given that the studies published generally include a limited number of subjects and the diagnosis is established on the basis of clear biochemical changes and liver biopsy.[3]

Because most individuals with NAFLD are asymptomatic, early detection by routine screening followed by appropriate clinical intervention would offer a practical means of preventing the hepatocellular damage associated with this condition. From an evidence-based medicine viewpoint, this disorder matches the Wilson criteria for screening, as it is a significant health problem.[4] The Wilson criteria includes: an adequately understood natural history of the disease; a recognizable latent or early symptomatic stage; a test that is easy to perform and interpret which should be devised and should be acceptable, accurate, reliable, sensitive, and specific; accepted treatment for the disease should be recognized; said treatment should be more effective the earlier it is applied; there should be a policy on who is treated; diagnosis and treatment are both cost effective; and case-finding should be a continuous process.

The pathogenesis of fatty liver is multifactorial, and it has been suggested that the presence of insulin resistance is an essential requirement for accumulation of hepatocellular fat.[5,6] Insulin resistance has been demonstrated to unify NAFLD in the metabolic syndrome, ie, NAFLD may be considered as an additional feature of the metabolic syndrome, with specific hepatic insulin resistance.[7] However, to the best of our knowledge, few evidence-based clinical studies have attempted to determine the possible etiological relationship between the metabolic syndrome and NAFLD in the elderly agricultural and fishing population of Taiwan, which is also faced with the burden of health-related disease. The purpose of this study was to determine the prevalence of obesity, NAFLD, and the metabolic syndrome in the elderly Taiwanese agricultural and fishing population, using a volunteer screening program in Taipei, Taiwan.

Materials and methods
Study design and data collection

This hospital-based, cross-sectional study was conducted in 6,542 healthy elders (2,553 males and 3,989 females) with an occupational background of agriculture or fishing and voluntarily attending a teaching hospital in northern Taiwan for an annual physical check-up between January 2010 and December 2010. Blood samples and ultrasonography results were collected. After exclusion of subjects without sonography information, the remaining 6,511 (2,540 males and 3,971 females) were enrolled for analysis.

Medical histories and measurements were obtained for the participants by well-trained nurses. Personal and family history of hypertension, type 2 diabetes, cardiovascular disease, and other chronic conditions were obtained by a structured health interview questionnaire. The study participants were asked to remove their shoes and any other belongings that could possibly add extra weight when they were weighed. Height and weight were evaluated according to body mass index (BMI). Waist circumference was measured to assess abdominal obesity. Blood pressure was measured twice for each subject in the sitting position, with an interval of 15 minutes between measurements, using a standard sphygmomanometer of appropriate width after a rest period for 30 minutes. Those taking antihypertensive therapy were considered to have known hypertension.[8] Fasting blood samples were drawn via venipuncture by clinical nurses. Overnight fasting serum and plasma samples (from whole blood preserved with ethylenediamine tetraacetic acid and sodium fluoride) were kept frozen at $-20°C$ until ready for analysis. All procedures were performed in accordance with the guidelines of the ethics committee at our institution and adhered to the tenets of the Declaration of Helsinki. Anonymity of participants and confidentiality of responses were ensured by using numerical codes for questionnaires and destroying the data at the end of study.

Dietary information was derived from a semiquantitative food frequency questionnaire.[9] Participants were asked to indicate their average frequency of consumption of typical servings of selected foods during the previous month.

Participants were asked to describe their alcohol intake using a multiple choice format. Beer, wine, and spirits were assessed separately. Current alcohol consumption was assessed by the question "How many cups, glasses, or drinks of these beverages do you usually drink a day or a month, and for how many years?" People who reported drinking alcohol were classified on the basis of the sum of their reported current consumption of all types of alcoholic beverages. Those who explicitly recorded zero for current consumption of any alcoholic beverage and zero or blank for previous alcohol consumption were deemed to be nondrinkers.[10,11]

Smoking habits were classified into three groups according to current smoking status, ie, those who had never smoked cigarettes, former smokers, and current smokers. Current smoking was defined as at least one cigarette per day during the preceding years.[11,12] Subjects were also divided into three categories according to areca nut use, ie, current chewers, nonchewers (never), and ex-chewers.[13] Current areca nut use was defined as use of at least one areca nut per day during the preceding years.

Physical activity was gauged as moderate (60 minutes or more of activities such as brisk walking, domestic chores, carrying or moving loads up to 20 kg daily) or vigorous (running,

cycling, swimming, carrying or moving loads over 20 kg). Anything short of moderate physical activity was considered to indicate a sedentary lifestyle.[9]

Metabolic components, diet, and usual lifestyle habits were recorded from individual records according to age group.

Diagnosis of metabolic syndrome

Metabolic syndrome was diagnosed using the Adult Treatment Panel III criteria, according to the presence of at least three of the following five risk factors: central obesity (waist circumference ≥90 cm in Asian men and ≥80 cm in Asian women); decreased high-density lipoprotein (HDL) cholesterol (fasting HDL cholesterol <40 mg/dL or on drug treatment to reduce HDL cholesterol); elevated blood pressure (systolic ≥130 mmHg and/or diastolic ≥85 mmHg, or antihypertensive drug treatment in a patient with a history of hypertension); hypertriglyceridemia (fasting plasma triglycerides ≥150 mg/dL or on drug treatment for elevated triglycerides); and hyperglycemia (fasting glucose level ≥100 mg/dL or on drug treatment for elevated glucose).[8,14,15]

Ultrasound examination and diagnosis

Hepatic ultrasonography was performed by two well-trained ultrasonographers using a Nemio SSA-550A probe (Toshiba, Tokyo, Japan). The ultrasonographic criteria used to diagnose fatty liver included liver and kidney echo discrepancy, increased liver echogenicity, echo penetration into the deeper portion of the liver, and clarity of the liver blood vessel structures.[16,17] All outpatients diagnosed by ultrasound as having NAFLD but without a history of Wilson's disease or intestinal bypass surgery, gluten enteropathy, ingestion of drugs known to cause hepatosteatosis (including methotrexate, tamoxifen, amiodarone, and nucleoside analogs), positive serology for hepatitis B or C virus, other known liver disease, or excessive alcohol consumption (≥30 g/day for males and ≥20 g/day for females) were enrolled in the study.[17,18] The degree of NAFLD on ultrasonography was classified as follows.

1. Grade 1 (mild) steatosis: predominantly macrovesicular; involving up to 66% lobules; ballooning occasionally observed in zone 3; scattered mild acute lobular inflammation (polymorphonuclear cells) and occasional chronic inflammation (mononuclear cells); mild portal inflammation or no inflammation.
2. Grade 2 (moderate) steatosis: any degree, usually mixed with macrovesicular and microvesicular; ballooning obviously present in zone 3; mild or chronic lobular inflammation with polymorphonuclear cells possibly noted in association with ballooned hepatocytes, pericellular fibrosis; possible mild to moderate portal inflammation.
3. Grade 3 (severe) steatosis: typically involves >66% lobules (panacinar); commonly mixed steatosis; predominantly marked ballooning in zone 3; scattered acute and chronic lobular inflammation, possibly with polymorphonuclear cells concentrated in zone 3; areas of ballooning and perisinusoidal fibrosis; mild to moderate portal inflammation.[16–19]

Measurements of interobserver and intraobserver reliability

The Kappa statistic was used to assess agreement of interobserver and intraobserver reliability and ensure consistent diagnosis of NAFLD between specialists. A pilot study was performed using 50 randomly selected healthy subjects who were not the study subjects. For interobserver reliability, the Kappa value for diagnosis of NAFLD was 0.77 (95% confidence interval [CI] 0.69–0.88). The intraobserver reliability for diagnosis of NAFLD by one specialist was 0.81 (95% CI 0.76–0.87); for the other specialist, the Kappa value was 0.83 (95% CI 0.73–0.91).

Statistical analysis

The statistical analysis was performed using SAS for Windows version 9.1 (SAS Institute Inc., Cary, NC, USA). For univariate analysis, the χ^2 test was used to assess differences in categorical variables. Multinomial logistic regression is the extension of binary logistic regression when the categorical-dependent outcome has more than two levels.[20] This method was also used to provide a set of coefficients for each of the two comparisons of NAFLD and to investigate the independence of factors associated with the prevalence of NAFLD. Receiver operating characteristic curves were used to explore the characteristics of the diagnostic test by graphing the false positive rate (1-specificity) on the horizontal axis and the true positive rate (sensitivity) on the vertical axis for various cutoff values. A P-value of <0.05 was considered to represent a statistically significant difference between the test populations.

Results

The overall prevalence of NAFLD in the study population was 27.2% (1,769/6,511), which included mild NAFLD (16.0%), moderate NAFLD (10.3%), and severe NAFLD (0.9%). The prevalence of one or two metabolic risk factors
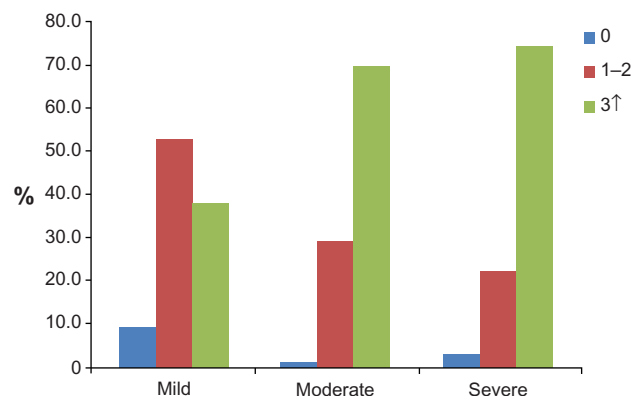
Figure 1 Prevalence of nonalcoholic fatty liver disease with metabolic syndrome factors among elderly screened subjects.

and metabolic syndrome was 51.8% and 33.4%, respectively. Figure 1 shows that the prevalence of moderate or severe NAFLD for metabolic syndrome was substantially greater ($P<0.0001$, χ^2 test) for one or two metabolic factors.

The age-specific prevalence in Chinese elderly subjects with individual metabolic components is shown in Table 1. The most common components in the different age subgroups were elevated blood pressure and central obesity, which was documented in about 60% and 50% of all subjects, respectively. There was a statistically significant difference in prevalence of elevated blood pressure, central obesity, hyperglycemia, and hypertriglyceridemia according to age ($P<0.001$, χ^2 test). Table 1 also shows that younger elderly subjects had a higher prevalence of smoking, areca nut use, and irregular breakfast habits than older elderly subjects.

The effect of independent associated risk factors on each type of NAFLD was examined using the multino-

mial logistic regression model. As shown in Table 2, after adjustment for confounding factors, age (odds ratio [OR] 0.93, 95% CI 0.90–0.95), sex (male versus female, OR 0.68, 95% CI 0.55–0.81), central obesity (yes versus no, OR 1.78, 95% CI 1.32–2.19), hyperglycemia (yes versus no, OR 1.55, 95% CI 1.26–1.84), hypertriglyceridemia (yes versus no, OR 1.61, 95% CI 1.30–2.94), low HDL cholesterol (yes versus no, OR 1.65, 95% CI 1.23–2.08), and higher BMI (yes versus no, OR 1.77, 95% CI 1.49–2.06) appeared to be significantly related to mild NAFLD. Age (OR 0.97, 95% CI 0.94–0.98), sex (male versus female, OR 0.72, 95% CI 0.58–0.91), central obesity (yes versus no, OR 3.24, 95% CI 1.78–9.99), hyperglycemia (yes versus no, OR 4.55, 95% CI 2.65–10.27), hypertriglyceridemia (yes versus no, OR 3.98, 95% CI 1.90–8.61), low HDL cholesterol (yes versus no, OR 2.73, 95% CI 1.09–6.32), higher BMI (yes versus no, OR 2.91, 95% CI 2.00–4.05), and higher alanine aminotransferase (ALT, OR 1.05, 95% CI 1.02–1.09) appeared to be significantly related to moderate NAFLD. Central obesity (yes versus no, OR 7.77, 95% CI 3.41–26.90), higher BMI (yes versus no, OR 6.97, 95% CI 3.40–39.24), higher uric acid (OR 1.33, 95% CI 1.10–1.79), and higher ALT (OR 1.12, 95% CI 1.05–1.18) appeared to be significantly related to severe NAFLD.

In addition, Table 2 shows that age (OR 0.95, 95% CI 0.94–0.97), sex (male versus female, OR 0.62, 95% CI 0.50–0.77), metabolic syndrome (yes versus no, OR 1.53, 95% CI 1.08–2.17), and higher BMI (yes versus no, OR 1.74, 95% CI 1.43–2.12) appeared to be significantly related to mild NAFLD. Age (OR 0.97, 95% CI 0.95–0.99),

Table 1 Age-specific prevalence of metabolic components, diet, and usual life habits in the study participants

	60–64 years (n=2,140)	65–74 years (n=2,440)	75–84 years (n=1,607)	≥85 years (n=324)	Total (n=6,511)	P-value for χ² test
	Prevalence (%) (95% CI)	Prevalence (%) (95% CI)	Prevalence (%) (95% CI)	Prevalence (%) (95% CI)	Prevalence (%) (95% CI)	
Metabolic components						
Elevated blood pressure	53.5 (51.4–55.6)	61.7 (59.7–63.7)	65.9 (63.6–68.2)	67.0 (61.9–72.1)	60.3 (55.2–61.5)	<0.001
Central obesity	43.7 (41.5–45.9)	49.3 (47.3–51.3)	56.0 (53.8–58.4)	49.7 (44.2–55.2)	48.7 (47.5–49.9)	<0.001
Hyperglycemia	22.7 (20.9–24.5)	32.1 (30.3–33.9)	33.0 (30.6–35.4)	27.8 (22.9–32.7)	27.6 (26.4–28.8)	<0.001
Hypertriglyceridemia	31.8 (29.8–33.8)	30.4 (28.6–32.2)	25.8 (23.6–28.0)	24.1 (19.4–28.8)	29.4 (28.2–30.6)	<0.001
Low HDL cholesterol	27.0 (25.0–29.0)	28.1 (26.3–29.9)	29.0 (26.8–31.2)	30.2 (25.1–35.3)	28.1 (26.9–29.3)	0.44
Diet and usual lifestyle habits						
Smoking	11.5 (10.1–12.9)	11.6 (10.4–12.8)	9.1 (7.7–10.5)	6.8 (4.1–9.5)	10.7 (9.9–11.5)	0.01
Alcohol drinking	11.0 (9.6–12.4)	12.2 (10.8–13.6)	12.8 (11.2–14.4)	13.9 (10.2–17.6)	12.0 (11.2–12.8)	0.24
Areca nut use	5.7 (4.7–6.7)	3.2 (2.4–4.0)	0.8 (0.4–1.2)	1.2 (0.2–2.4)	3.3 (2.9–3.7)	<0.001
Irregular physical activity	31.4 (29.4–33.4)	27.9 (26.1–29.7)	29.5 (27.3–31.7)	28.1 (23.2–33.0)	29.5 (28.3–30.7)	0.07
Irregular breakfast	3.7 (2.8–4.4)	2.7 (2.1–3.3)	2.3 (1.5–3.1)	0.9 (0.0–1.9)	2.8 (2.4–3.2)	0.01
Irregular fruit	22.7 (20.9–24.5)	22.7 (21.1–24.3)	25.7 (23.5–27.9)	23.8 (19.1–28.5)	23.5 (22.5–24.5)	0.12
Irregular saturated fat	2.2 (1.6–2.8)	2.6 (2.0–3.2)	2.2 (1.4–3.0)	4.6 (2.2–7.0)	2.5 (2.1–2.9)	0.05

Abbreviations: CI, confidence interval; HDL, high-density lipoprotein.

Table 2 Multinomial logistic regression of associated factors for nonalcoholic fatty liver disease (all univariate significant factors were included among elderly screened subjects)

Factors	Mild NAFLD versus no NAFLD			Moderate NAFLD versus no NAFLD			Severe NAFLD versus no NAFLD		
	OR	95% CI	*P*-value	OR	95% CI	*P*-value	OR	95% CI	*P*-value
Model I									
Age (years)	0.93	0.90–0.95	0.001	0.97	0.94–0.98	0.001	1.04	0.98–1.19	0.32
Sex (male versus female)	0.68	0.55–0.81	<0.001	0.72	0.58–0.91	0.01	1.01	0.46–1.43	0.99
Elevated blood pressure	1.06	0.88–1.25	0.11	1.12	0.66–4.91	0.31	1.02	0.84–11.23	0.56
Central obesity	1.78	1.32–2.19	0.01	3.24	1.78–9.99	<0.001	7.77	3.41–26.90	<0.001
Hyperglycemia	1.55	1.26–1.84	0.01	4.55	2.65–10.27	0.005	1.44	0.61–14.33	0.32
Hypertriglyceridemia	1.61	1.30–2.94	0.02	3.98	1.90–8.61	0.002	1.32	0.58–26.20	0.35
Low HDL cholesterol	1.65	1.23–2.08	0.01	2.73	1.09–6.32	0.01	1.57	0.59–15.22	0.31
BMI (≥25 versus <25 kg/m^2)	1.77	1.49–2.06	<0.001	2.91	2.00–4.05	<0.001	6.97	3.40–39.24	<0.001
Uric acid (mg/dL)	1.02	0.92–1.11	0.33	1.08	0.96–1.18	0.22	1.33	1.10–1.79	0.01
ALT (U/L)	1.03	0.91–1.16	0.42	1.05	1.02–1.09	0.04	1.12	1.05–1.18	0.03
Model II									
Age (years)	0.95	0.94–0.97	<0.001	0.97	0.95–0.99	0.001	1.04	0.99–1.09	0.12
Sex (male versus female)	0.62	0.50–0.77	<0.001	0.67	0.51–0.87	0.003	1.01	0.42–2.43	0.99
Metabolic factors									
1–2 versus none	1.34	0.98–1.84	0.07	4.36	1.75–10.84	0.002	0.69	0.08–5.91	0.73
≥3 versus none	1.53	1.08–2.17	0.02	14.84	5.96–36.93	<0.001	2.46	0.30–20.11	0.40
BMI (kg/m^2)									
≥25 versus <25	1.74	1.43–2.12	<0.001	3.03	2.30–4.00	<0.001	11.67	2.60–52.38	0.001
Uric acid (mg/dL)	1.04	0.97–1.11	0.28	1.06	0.98–1.15	0.17	1.37	1.07–1.76	0.01
ALT (U/L)	1.02	0.97–1.06	0.68	1.04	1.01–1.10	0.03	1.08	1.03–1.15	0.04

Abbreviations: ALT, alanine aminotransferase; BMI, body mass index; CI, confidence interval; OR, odds ratio; HDL, high-density lipoprotein; NAFLD, nonalcoholic fatty liver disease.

sex (male versus female, OR 0.67, 95% CI 0.51–0.87), metabolic syndrome (1–2 metabolic factors versus none, OR 4.36, 95% CI 1.75–10.84; ≥3 metabolic factors versus none, OR 14.84, 95% CI 5.96–36.93), higher BMI (yes versus no, OR 3.03, 95% CI 2.30–4.00), and higher ALT (OR 1.04, 95% CI 1.01–1.10) were significantly related to moderate NAFLD. Higher BMI (yes versus no, OR 11.67, 95% CI 2.60–52.38), higher uric acid (OR 1.37, 95% CI 1.07–1.76), and higher ALT (OR 1.08, 95% CI 1.03–1.15) were significantly related to severe NAFLD.

The good sensitivity and specificity of BMI and waist circumference for the diagnosis of severe NAFLD is shown in Table 3. For BMI, the estimated area under the curve was 0.88 (95% CI 0.82–0.94) for diagnosis of severe NAFLD and the cut-off value estimated as 27.85 kg/m^2 with 81% sensitivity and 84% specificity. The area under the curve for waist circumference as an indicator of severe NAFLD was 0.82 (95% CI 0.74–0.89) and the cut-off value, sensitivity, and specificity were 90.75 cm, 77%, and 69%, respectively.

Discussion

Undoubtedly, good health and appropriate training are necessary for agricultural and fishing populations. Long

Table 3 Receiver operating characteristic results for BMI and waist circumference as markers of nonalcoholic fatty liver disease

Variable	Area under curve	95% CI	Cut-off value	Sensitivity	Specificity
Mild NAFLD					
BMI	0.61	0.59–0.63	24.75 (kg/m^2)	0.65	0.54
Waist circumference	0.57	0.53–0.58	86.25 (cm)	0.57	0.53
Moderate NAFLD					
BMI	0.76	0.73–0.78	25.35 (kg/m^2)	0.77	0.61
Waist circumference	0.69	0.66–0.71	89.25 (cm)	0.63	0.65
Severe NAFLD					
BMI	0.88	0.82–0.94	27.85 (kg/m^2)	0.81	0.84
Waist circumference	0.82	0.74–0.89	90.75 (cm)	0.77	0.69

Abbreviations: BMI, body mass index; CI, confidence interval; NAFLD, nonalcoholic fatty liver disease.

and/or irregular working hours may have adverse effects on health. In Taiwan, there are few published population-based studies addressing the prevalence and possible etiology of NAFLD in the elderly Chinese population which, as in other countries, also faces the burden of liver disease. Due to the increased frequency of NAFLD in elderly subjects, it is useful for identifying treatment needs and rehabilitation services, and for planning and implementing comprehensive NAFLD preventive care programs. Preventive health examinations are an important health promotion strategy,[21,22] and could help to identify disease at an early stage, delay development of subsequent adverse outcomes, and significantly save health care resources and lives.[21]

The well-established term "metabolic syndrome" remains the most useful and widely accepted description of the cluster of metabolically related cardiovascular risk factors which also predict a high risk for developing diabetes.[23] Previous studies have indicated that the metabolic syndrome can be viewed as a strong predictor of NAFLD.[23–25] Clinical manifestations of NAFLD are usually absent or subtle with abnormal aminotransferase or incidental radiographic findings of fatty liver.[26] The pathogenesis of NAFLD is thought to involve a multi-hit process including insulin resistance, oxidative stress, apoptotic pathways, and adipocytokines.[26,27] In this study, the metabolic syndrome was significantly related to mild or moderate NAFLD but not to severe NAFLD. More than 80 years have passed since the introduction of the concept of a clustering of metabolic and physiological abnormalities; however, there are still many uncertainties over metabolic syndrome that need to be further unraveled.[28] The documented prevalence of NAFLD in this study is clinically significant and a "wake-up call" for government health practitioners and policy makers to be on the alert and also formulate policy to help curtail the impact of NAFLD, especially by measures to reduce the components of metabolic syndrome in view of the association.

BMI and waist circumference are also good predictors of NAFLD.[23,29] In this study, higher BMI was associated with an increased risk for NAFLD even after adjusting for other confounding factors. Using the Western criteria for obesity, only 2%–3% of Asian subjects can be identified as obese.[29] Asians have a higher proportion of visceral fat and a lower proportion of lean body mass than Caucasians with the same BMI.[23] It is of note that we used the receiver operating characteristic curve to find the cut-off values for BMI and waist circumference as diagnostic tests for each type of NAFLD. The cut-off values for BMI and waist circumference were

estimated at 27.85 kg/m^2 and 90.75 cm, respectively, and imply that a BMI higher than 27.85 kg/m^2 or a waist circumference greater than 90.75 cm should be considered medium risk for severe NAFLD. In addition, consultation did not suggest a clear BMI cut-off point for overweight or obesity applying to all Asians.[30] In this study, public health action may be best targeted to a BMI of 27.85 kg/m^2 and stepwise health interventions proposed for the elderly population to prevent severe NAFLD. However, further studies are needed to identify the sensitivity and specificity of clinical markers more accurately in the context of, eg, health screening for the diagnosis of NAFLD.

It is interesting that being elderly and female were significant risk factors for NAFLD in this study. Such a finding would appear to be inconsistent with the results of studies done in the general population or occupational groups elsewhere.[16,23,31,32] A possible reason is that the proportion of obesity in males was higher than in females aged <50 years, but the prevalence of obesity for males proved to be substantially greater than for females aged ≥60 years.[33] In Asian countries, the peak age for diagnosis of NAFLD has been reported to be 40–49 years in men and ≥50 years in women.[34] The risk of NAFLD appears to increase with advancing age. Several academic studies using different diagnostic methods have reported similar results.[1,5,16,17,23]

In addition to obesity metabolic disorders, other risk factors including higher uric acid and higher ALT level for NAFLD were identified in this study. One clinical study showed that a fructose load might lead to a more substantial increase in serum uric acid levels in patients suffering chronic hepatitis than would be the case for normal subjects.[35] Determination of serum ALT is the most common test used for identification of patients suffering from liver disease, and also acts as a surrogate marker for disease severity and/or an index of hepatic activity.[23] The possible mechanism for such a finding may relate to the fact that increased serum ALT concentrations are related to hepatic insulin resistance and suggest that a raised ALT reflects fatty changes in the liver.[2] However, we were not able to determine the degree of increase in serum uric acid or ALT levels prior to development of liver disease because of the cross-sectional nature of our study. Further epidemiological and etiological investigations are needed to clarify the causal relationship between uric acid, ALT, and NAFLD.

The results of this study indicate a relatively high prevalence of NAFLD and metabolic syndrome in the elderly Chinese population. An increasing number of people are likely to have a sedentary lifestyle and an energy-dense diet

as the country becomes more modernized and urbanized.[36] Several studies have shown the benefits of dietary modification, weight loss, and exercise in reducing insulin resistance and in normalization of ALT in patients with NAFLD.[37–42] Research also indicates that even small degrees of weight loss of around 5%–10% of total body weight have a clear benefit and suggests that changes in the amount of dietary fat delivered to the liver and subsequent changes in lipid metabolism are as important as weight loss.[42]

Methodological considerations

This study has several limitations. First, NAFLD was diagnosed in our elderly study participants by ultrasonography, whereas liver biopsy is the gold standard. However, liver biopsy is an invasive procedure with unpredictable risks, so is ethically unacceptable for use in this type of research.[26] Previous reports indicate that ultrasonography has been widely used for detection of NAFLD with high sensitivity (up to 89%) and specificity (up to 93%).[43] However, different studies may elect to set slightly different definitions, such that our estimation of what constituted NAFLD could have suffered from some level of misclassification bias. Second, the potential impact on the prevalence and the observed NAFLD-related risk factors in the study were the result of the screening of elderly population from one single area, therefore some estimations were inevitable. However, the study still retained sufficient statistical power to evaluate the various risk factors for NAFLD given its reasonably large sample size. Finally, our measurements were taken at a single point in time, so may not reflect long-term exposure to important environmental or biochemical factors.[14]

Conclusion

The prevalence of mild or moderate NAFLD was related to obesity and severity of the metabolic syndrome. Higher BMI was related to severe NAFLD but not to the metabolic syndrome. It is important that we target this population for control of obesity and improved metabolic function.

Acknowledgments

Disclosure

We certify that all the affiliations with or financial involvement in, within the past 5 years and foreseeable future, any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript are completely disclosed (eg, employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, royalties). The authors have no proprietary interest in any aspect of this study. No additional financial support from public or private sources was received for this research.

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