ORIGINAL RESEARCH

Relationship Between Non-Alcoholic Fatty Liver Disease and Abdominal and Pericardial Adipose Tissue in Middle-Aged and Elderly Subjects

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Objective: The present study aimed to explore the relationship between non-alcoholic fatty liver disease (NAFLD) and abdominal and pericardial adipose tissue in middle-aged and elderly subjects.

Methods: Between July 2019 and July 2020, 471 subjects attending the Health Care Medical Department of Peking Union Medical College Hospital for a medical examination were enrolled in the study. The volume and distribution of abdominal adipose tissue together with the volume of pericardial adipose tissue were calculated according to the results of the abdominal computed tomography. The differences between subjects with NAFLD and the normal population were analyzed.

Results: The volume of pericardial adipose tissue, abdominal visceral and subcutaneous adipose tissue, the total volume of abdominal adipose tissue, and volume of pelvic visceral adipose tissue were all significantly increased in subjects with NAFLD. For every 100 cm^3 increase in the volume of abdominal visceral adipose tissue, the incidence of developing NAFLD increased by 9.4%. According to the results of the receiver operating curve, the cutoff point of abdominal visceral adipose tissue for the diagnosis of NAFLD was 2691.1 cm^3.

Conclusion: Overall, the risk of NAFLD increases significantly with the increase in the volume of adipose tissue.

Keywords: fatty liver, abdominal adipose tissue, abdominal visceral adipose tissue, abdominal subcutaneous adipose tissue

Introduction

Non-alcoholic fatty liver disease (NAFLD) is the most common liver disease worldwide.[1] The diagnostic criteria for NAFLD are the presence of fatty infiltration in >5% of hepatocytes with the exclusion of a history of alcoholism and other diseases that cause hepatic steatosis.[2,3] The clinical manifestation is diverse, ranging from asymptomatic to hepatic steatosis and non-alcoholic steatohepatitis (NASH).[4] Approximately 10–25% of asymptomatic patients will also develop NASH, and 5–8% will develop cirrhosis within 5 years.[2,5] In addition, 12.8% of patients with cirrhosis will develop hepatocellular carcinoma within 3 years.

Obesity is a chronic disease, defined as a body mass index (BMI) > 30 kg/m^2, and is considered to be correlated with cardiovascular disease, hypertension, stroke, and other diseases.[6,7] It is also correlated with a range of cancers (colon cancer, breast cancer, endometrial cancer, kidney cancer, esophageal cancer, stomach cancer, pancreatic cancer, and gallbladder cancer) and, along with insulin

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resistance (IR), is a risk factor in the development of hepatic carcinoma.[8] NAFLD is closely correlated with obesity. It has been reported that the incidence of NAFLD is as high as 80% in patients with obesity, while in those with normal BMI and without metabolic risk factors, the incidence of NAFLD is only 16%.[9,10] Relatively few studies have reported on the correlation between NAFLD and visceral adipose tissue, although previous studies have reported on the correlation between NAFLD and waist circumference (WC). In the present study, computed tomography (CT) was used to determine the nature of the tissue and, when combined with computer software, the distribution of visceral adipose tissue and the area of muscle could be accurately calculated with less error.

Subjects and Methods
Study Subjects
Between July 2019 and July 2020, subjects aged from 50–100 years (69 ± 11) attending the Health Care Medical Department of Peking Union Medical College Hospital for a medical examination were enrolled in the study. Those with the COVID-19 infection were excluded from attending the hospital for a medical examination after July 2020. Subjects with an acute infection, a recent surgical history, and those with alcohol abuse (20 g/week for female and 30 g/week for male subjects) were excluded from the present study.

Methods
The present study was a retrospective cross-sectional study, and the population examined was fully reimbursed for medical expenses. General information was collected on the subjects, including gender, age, height, body weight, WC, and blood pressure. BMI was calculated according to the equation BMI = body weight (Kg)/height^2 (m^2). WC was measured as the plane perimeter from the anterior superior iliac crest to the midpoint of the inferior rib cage at the end of expiration. A chest, abdominal, and pelvic CT and abdominal ultrasonography were performed for all subjects. Abdominal and pericardial adipose tissue were measured in all subjects.

The CT machine adopted was a Siemens CT scanner with the scan conditions of 120 kV, a CARE Dose 4D scan, 0.5 mm layer thickness, and B30f reconstruction.

A Philips IU22 ultrasound machine was adopted for hepatic ultrasonography.

Pericardial adipose tissue was measured as the volume of adipose tissue within the pericardium in the CT image, with the lower edge being the lower edge of the heart and the upper edge being the aortic bifurcation, measured in cm^3.

Measurement of the abdominal adipose tissue: The upper edge of the abdominal border was the diaphragm border, and the lower edge was the upper edge of the iliac crest; all the adipose tissue within this range was recorded as the total volume of abdominal adipose tissue and was measured in cm^3. The volume of adipose tissue within the peritoneum was regarded as the volume of abdominal visceral adipose tissue and was measured in cm^3. And the volume of adipose tissue outside the peritoneum was considered as the volume of abdominal subcutaneous adipose tissue and was measured in cm^3.

The volume of pelvic visceral adipose tissue was related to the volume of all the intraperitoneal adipose tissue, with the upper edge being the superior edge of the iliac crest and the lower edge being the inferior margin of the pelvic floor, measured in cm^3.

Statistical Analysis
Visualization of adipose tissue was measured using Volume Soft (Syngo Via, Siemens). Excel 2010 was used to record all the data and SPSS 24.0 software was adopted to analyze it. The data included age, body weight, height, WC, BMI, volume of abdominal visceral adipose tissue, volume of abdominal subcutaneous adipose tissue, total volume of abdominal adipose tissue, percentage of abdominal visceral adipose tissue, and pericardial adipose tissue, which were expressed as x ± s. The rank-sum test and two-tailed t-test were used for comparison between groups. P<0.05 was considered statistically significant.

Results
An analysis of the normal distribution of age, volume of pericardial adipose tissue, volume of pelvic visceral adipose tissue, total volume of abdominal adipose tissue, volume of abdominal visceral adipose tissue, volume of abdominal subcutaneous adipose tissue, percentage of abdominal visceral adipose tissue, total volume of pelvic and abdominal visceral adipose tissue, BMI, and WC was conducted, and only two of these factors (volume of abdominal visceral adipose tissue, bilateral psoas major muscle area) satisfied the normal distribution.

The rank-sum test demonstrated that there was no difference in age between the subjects with NAFLD and

those without. However, the volume of pericardial adipose tissue, the volume of abdominal visceral adipose tissue, the volume of abdominal subcutaneous adipose tissue, the total volume of abdominal adipose tissue, and the volume of pelvic visceral adipose tissue were significantly increased in those with NAFLD (as illustrated in Table 1).

The data on the volume of abdominal visceral adipose tissue satisfied the normal distribution, and the *t*-test analysis suggested that subjects with more abdominal visceral adipose tissue were more likely to develop NAFLD (as shown in Table 2).

Binary logistic regression analysis was adopted for the volume of abdominal subcutaneous adipose tissue, the volume of abdominal visceral adipose tissue, and the volume of pericardial adipose tissue. It was found that each 100-cm^3 increase in the volume of abdominal visceral adipose tissue correlated with a 9.4% increase in the incidence of NAFLD, and each 100-cm^3 increase in the volume of abdominal subcutaneous adipose tissue correlated with a 2.6% increase in the incidence of NAFLD (as demonstrated in Table 3).

A receiver operating curve analysis was adopted to analyze the cut-off point of the volume of abdominal adipose tissue for the ultrasonographic diagnosis of NAFLD.

By calculating the cut-off point (the Yorden index), it was found that the cut-off point of the volume of abdominal adipose tissue for the detection of NAFLD was 5155.8 cm^3 and that of the volume of abdominal visceral adipose tissue for the detection of NAFLD was 2691.1 cm^3 (as shown in Table 4).

Discussion

Fatty liver is the accumulation of adipose tissue in the hepatic parenchyma. NAFLD is the infiltration of adipose tissue in the liver in the absence of excessive alcohol consumption and other causes of hepatic disease and is the most common cause of fatty liver disease. NAFLD is widely distributed worldwide and is now estimated to affect about a quarter of the global population. It is the most common chronic hepatic disease in adults and often coexists with obesity, metabolic syndrome (MS), hypertension, diabetes mellitus (DM), and

Table 1 The Relationship Between He Volume of Fat Liver and Incidence of Nonalcoholic Fatty Liver Disease

	Fatty Liver Condition	Cases	Average value ± Standard Deviation	Rank Mean	Sum of Rank	Z value	P value
Age	Normal Fatty liver	168 303	69.7±11.8 68.4±10.7	243.85 231.65	40,966.50 70,189.50	−0.932	0.351
Volume of pericardial adipose tissue	Normal Fatty liver	168 300	79.7±55.7 102.2±62.3	199.55 254.07	33,524.50 76,221.50	−4.183	<0.001
Volume of pelvic visceral adipose tissue	Normal Fatty liver	168 301	2007.7±1418.7 3033.2±1922.1	181.71 264.74	30,527.50 79,687.50	−6.361	<0.001
Total volume of abdominal adipose tissue	Normal Fatty liver	168 303	4380.3±1848.1 6535.3±2449.3	154.03 281.45	25,876.50 85,279.50	−9.733	<0.001
Volume of abdominal visceral adipose tissue	Normal Fatty liver	168 303	2102.5±1158.7 3279.8±1110.4	153.00 282.02	25,704.50 85,451.50	−9.854	<0.001
Volume of abdominal subcutaneous adipose tissue	Normal Fatty liver	168 303	2277.8±1028.2 3255.4862±1778.5	183.20 265.28	30,777.50 80,378.50	−6.269	<0.001
Percentage of abdominal visceral adipose tissue	Normal Fatty liver	168 303	46.6±13.5 51.8±11.1	201.16 255.32	33,794.50 77,361.50	−4.137	<0.001
Total volume of pelvic and abdominal visceral adipose tissue	Normal Fatty liver	168 301	4110.2±2235.1 6315.1±2539.8	156.57 278.77	26,304.50 83,910.50	−9.362	<0.001
Body mass index (BMI)	Normal Fatty liver	161 297	24.0±2.7 26.4±2.8	162.70 265.71	26,195.50 78,915.50	−7.953	<0.001
WC	Normal Fatty liver	166 302	86.7±7.9 94.2±7.8	157.54 276.80	26,152.00 83,594.00	−9.135	<0.001

Table 2 The Relationship Between the Volume of Visceral Fat and the Incidence of Nonalcoholic Fatty Liver

		Cases	Mean ± SD	F	P	T	P
Volume of abdominal visceral adipose tissue	Normal	168	2102.5±1158.7(cm^3)	1.904	0.168	−10.720	<0.001
	Fatty liver	303	3279.8±1110.4(cm^3)				

Table 3 The Relationship Between the Increased Volume of Abdominal Subcutaneous Adipose Tissue and Abdominal Visceral Adipose Tissue and the Incidence of Nonalcoholic Fatty Liver Disease

	Wald	ExpB(OR)	P	95% Confidence Interval of EXP(B)
Volume of abdominal visceral adipose tissue(100cm^3)	56.13	1.094	<0.001	1.069–1.120
Volume of abdominal subcutaneous adipose tissue(100cm^3)	6.85	1.026	0.009	1.007–1.046

Table 4 The Area Under the Curve(AUC) of the ROC Between the Fat Volume of Each Site and Nonalcoholic Fatty Liver Disease

	Region	Standard Deviationa	P	95% Confidence Interval
Volume of pericardial adipose tissue	0.613	0.028	<0.001	0.558–0.668
Volume of pelvic visceral adipose tissue	0.670	0.026	<0.001	0.618–0.721
Total volume of abdominal adipose tissue	0.773	0.023	<0.001	0.728–0.818
Volume of abdominal visceral adipose tissue	0.782	0.024	<0.001	0.735–0.829
Volume of abdominal subcutaneous adipose tissue	0.668	0.026	<0.001	0.617–0.719
Percentage of abdominal visceral adipose tissue	0.631	0.028	<0.001	0.576–0.685
Total volume of pelvic and abdominal visceral adipose tissue	0.760	0.024	<0.001	0.713–0.808
WC	0.756	0.024	<0.001	0.709–0.803
BMI	0.727	0.025	<0.001	0.678–0.776

hyperlipidemia.[11–14] Even for subjects with normal weight, approximately 7% have NAFLD.[15] The prevalence of NAFLD is influenced by age, gender, race, sleep apnea, and endocrine dysfunctions (hypothyroidism, hypoglycemia, hypogonadism, and polycystic ovary syndrome).[16,17]

NAFLD may increase the incidence of atherosclerosis, with some studies showing a 10.8% increase in the incidence of coronary atherosclerosis, a 37.3% increase in the incidence of cerebrovascular atherosclerosis, and a 24.5% increase in the incidence of peripheral vascular atherosclerosis in patients with NAFLD.[18] The most common cause of death in patients with NAFLD is cardiovascular disease, but with the development of fatty liver, some patients may also develop cirrhosis and hepatic carcinoma.[19,20] Liver biopsy is the gold standard for the diagnosis of fatty liver, but the operation is too complicated and not much used in clinical practice, while imaging examinations, such as ultrasonography, CT, or magnetic resonance imaging (MRI), are the common diagnostic methods in clinics.

Ultrasonography is widely used in clinical practice because it is inexpensive and well tolerated; it is now the imaging diagnosis of choice recommended by European guidelines for the management of NAFLD.[15] A typical feature in ultrasonography is a subjective classification of the degree of fatty liver as mild, moderate, or severe[22] based on a comparison of the echoes of the liver with the parenchyma of the right kidney.[21] The overall sensitivity, specificity, positive likelihood ratio, and negative likelihood ratio of ultrasonography for the detection of moderate-to-severe fatty liver compared with histology (the gold standard) were 84.8% (95% confidence interval [CI] of 79.5–88.9), 93.6% (95% CI of 87.2–97.0), 13.3 (95% CI of 6.4–27.6), and 0.16 (95% CI of 0.12–0.22), respectively. Therefore, ultrasonography is the best imaging tool to screen for fatty liver under current clinical conditions.[21]

NAFLD is considered to be a manifestation of MS in the liver and has a significant correlation with IR,[23] so the development of NAFLD also increases with the increase in BMI and obesity.[24] Like MS and DM, NAFLD occurs more frequently in patients with central obesity.[19,25] In a study in young East Asians, the umbilical plane measurement was used to assess abdominal adipose tissue, and it

was suggested that the increased area of this adipose tissue was significantly correlated with NAFLD and was an independent risk factor with an odds ratio (OR) of 1.17 for a 10 cm^2 increase in the area of the abdominal visceral adipose tissue.[26] In patients with NAFLD, increased abdominal visceral adipose tissue was also an independent risk factor for elevated alanine aminotransferase.[27] Therefore, the abdominal adipose tissue might also be an important risk factor for liver injury.

According to the results of the present study, there was no significant difference in age between the subjects with NAFLD and those without. Patients with NAFLD had more adipose tissue in all areas, both in the pericardium region and the abdominal and pelvic regions' given that you said, in all areas, with the relationship between the volume of abdominal visceral adipose tissue and the occurrence of NAFLD being particularly pronounced. The incidence of NAFLD increased by 9.4% for every 100 cm^3 increase in the volume of abdominal visceral adipose tissue, while the incidence of NAFLD increased by only 2.6% for a 100 cm^3 increase in the volume of abdominal subcutaneous adipose tissue. The visceral adipose tissue is generally considered to secrete more pro-inflammatory cytokines and free fatty acids, making it more likely to cause atherosclerosis.[28] Other studies have also found that visceral adipose tissue is more prone to result in various metabolic risk factors than subcutaneous adipose tissue.[29]

Studies on diet and exercise also suggest that a high-calorie diet, whether given in the form of glucose or fat, will increase the amount of adipose tissue in the liver, while a low-calorie diet will decrease the level of adipose tissue in the liver.[30] Physical activity and weight loss are still the most commonly used measures to reduce the incidence of fatty liver.[31] Although the development of fatty liver depends not only on the volume of adipose tissue but also on dietary habits and lifestyle,[25] the results of the present study showed that, generally speaking, an increase in the volume of adipose tissue leads to a significant increase in the incidence of NAFLD as well.

Ethics Approval and Consent to Participate

This study was conducted with approval from the Ethics Committee of Peking Union Medical College Hospital. This study was conducted in accordance with the declaration of Helsinki. Written informed consent was obtained from all participants.

Consent for Publication

All patient guardians signed a document of informed consent.

Disclosure

The authors declare that they have no competing interests.

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