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Original Article

Sonographic Measurement of Visceral Fat and Prediction of Metabolic Syndrome in the Elderly

Chien-Yuan Hung [a, b, c], Chen-Wang Chang [a, b, c], Chih-Jen Chen [a, b, c], Ching-Wei Chang [a, b, c], Hui-Yun Cheng [a, b, c], Ming-Jen Chen [a, b, c *]

[a] *Division of Gastroenterology, Department of Internal Medicine, Mackay Memorial Hospital, Taipei, Taiwan,* [b] *MacKay Junior College of Medicine, Nursing and Management, Taipei, Taiwan,* [c] *MacKay Medical College, New Taipei, Taiwan*

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SUMMARY

Background: Visceral fat is considered important in the pathogenesis of metabolic syndrome (MS). Here, we developed a novel method for determining visceral fat by measuring liver–kidney space (LKS) on abdominal sonography and expanded its utilization in the elderly to predict MS.
Methods: To assess the correlation between the LKS and MS, 317 consecutive outpatients scheduled for health evaluation were retrospective analyzed. Anthropometric measurements, blood pressure, fasting blood glucose levels, and lipid profiles were obtained following standard protocols. On sonography, the thickness of visceral fat between the liver and right kidney was measured. We also compared its accuracy to predict MS with sonographic fatty liver changes. A total of 72 elderly patients older than 65 years were evaluated (mean age: 66.02 [65–83]).
Results: In the current study, LKS = 4 mm enabled a better prediction of MS. The area under the receiver operating characteristic curve was 0.626. The sensitivity and specificity for the presence of visceral fat to predict MS in the elderly were 0.58 and 0.73, respectively. The accuracy to predict MS was 68.1% for the measurement of visceral fat compared with 59.6% for sonographic fatty liver change in the elderly.
Conclusion: Measuring LKS by sonography may be a practical method for evaluating visceral fat in the elderly and for predicting MS better than sonographic fatty liver changes. LKS was more associated with abdominal girth and BMI in the elderly from the study supporting the observation that LKS are well correlated with general adiposity.

1. Introduction

Obesity, an increasing global health problem, is strongly associated with cardiovascular disease (CVD).[1,2] The association between obesity and CVD was proposed to be related to visceral adiposity, through the predisposition of developing metabolic syndrome (MS). The proportion of people whose age exceeds 65 years is growing rapidly throughout the world, and the prevalence of MS is increasing accordingly. They carry high morbidity and mortality, including the clustering of metabolic risk factors.[3] MS comprises diabetes, hypertension, and hyperlipidemia, which lead to the development of atherosclerotic CVD.[4] An excess of visceral fat in the abdomen is known as central obesity, which causes the abdomen to protrude. The measurement of obesity through waist circumference (WC) has been established as a simple and practical method for the diagnosis of central obesity. For this reason, WC was proposed as a key element in MS diagnosis; it is routinely applied as part of the routine general physical examination in clinical practice.[5]

WC is composed of both subcutaneous and visceral fat, visceral fat being much more closely related to MS than the former. Visceral fat is located in the abdominal cavity and packed in between organs including perirenal depots. Visceral fat can be measured and evaluated using several techniques, including WC measurements,[6] abdominal sonography,[7–11] computed tomography (CT),[12–16] and magnetic resonance imaging (MRI),[17,18] or bioelectrical impedance analysis.[19] CT or MRI is an optimal technique for the accurate assessment of intraabdominal fat. However, they are difficult to obtain in all patients considering the issues of availability, radiation exposure, and/or cost.

* Corresponding author. Division of Gastroenterology, Department of Internal Medicine, MacKay Memorial Hospital, No. 92, Sec. 2, Chung-Shan North Road, Taipei, Taiwan.
E-mail address: mingjen.4099@mmh.org.tw (M.-J. Chen).

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There were many modalities developed to evaluate the abdominal visceral fat by sonography with promising results. The modalities included measuring the circumference or thickness of peritoneal fat. Hirooka et al.[9] reported that the peritoneal circumference was better correlated with MS than subcutaneous fat which was measured by WC; the area under the receiver operating characteristic curve was 0.699 for peritoneal circumference and 0.684 for WC. Suzuki et al.[10] examined the ratio of the maximum thickness of preperitoneal fat to the minimum thickness of subcutaneous fat and found it was positively correlated with serum triglyceride levels and negatively correlated with high-density lipoprotein cholesterol ($r = -0.312$, $p < 0.05$). Kawasaki et al.[11] evaluated the visceral fat by sonography, the thickness of combined para- and perirenal fat was measured both sides between the kidney and the inner aspect of the abdominal musculature; the correlation between sonographic fat thickness and visceral fat area was 0.65.

Here, we developed a novel method for determining visceral fat by measuring by measuring liver–kidney space (LKS) on abdominal sonography and expanded its utilization in the elderly to predict MS.

2. Materials and methods

2.1. Subjects and measurements

To evaluate a novel method for determining visceral fat by measuring LKS on abdominal sonography to predict MS, a total of 317 outpatients (mean age: 45.3 years [20–83]) who underwent routine medical examination from December 2014 to December 2015 at MacKay Memorial Hospital (MMH) were enrolled in the validation group. The exclusion criteria were previous abdominal surgery, current acute illness, and current use of steroids.

A total of 72 adults older than 65 years (mean age: 66.0 years [65–83]) were consecutively enrolled as testing group from our outpatient clinic from January 2016 to July 2016. The exclusion criteria were abdominal surgery, current acute illness, and malignancy. The current use of drugs that modify lipid or glucose metabolism, including antidiabetic, antihypertensive, and hypolipidemic drugs, was allowed. This study protocol was approved by the Ethics Committee for Human Research at MMH (18MMHIS 008).

Demographic and anthropometric measurements included age, sex, weight, height, body mass index (BMI), and WC. All measurements were made while the patients were wearing minimal underwear and no shoes. The weight was measured to the nearest 0.1 kg with a calibrated scale, and the height was measured to the nearest 1 mm with a wall-mounted stadiometer. WC was measured with a plastic fiber tape measure placed directly on the skin while the patients stood on both feet, with the feet touching each other and both arms hanging freely. The measured point was midway between the iliac crest and lower rib. The measurement was recorded immediately at end expiration. Blood pressure was measured in the sitting position, using a standard sphygmomanometer after a rest period of 30 min. Blood samples were obtained after at least 8 h of fasting. All measurements were obtained by trained staff, and quality checks were conducted regularly. We used a self-reported diagnosis of diabetes and hypertension according to the previous medical history in the study.

2.2. Definition of MS

The patients were classified as having or not having MS according to the diagnostic criteria of MS proposed by the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III), which was considered to be more suitable for Asian patients.[20,21] According to the modified criteria, the presence of any three or more of the following factors is required for a diagnosis of MS: abdominal obesity, hypertriglyceridemia ($\geq$1.7 mmol/L or 150 mg/dL), low high-density lipoprotein (HDL) cholesterol level ($\leq$1.03 mmol/L or 40 mg/dL), elevated blood pressure (systolic blood pressure $\geq$ 130 mmHg and/or diastolic blood pressure $\geq$ 85 mmHg or current use of antihypertensive drugs), and impaired fasting glucose (fasting plasma glucose $\geq$ 6.1 mmol/L or 108 mg/dL) or patients receiving treatment for their condition. The modified NCEP ATP III criteria suggested the cut-off points of WC should be ethnicity-specific, where individuals of an Asian origin should use the cut-off point of 90 cm in men and 80 cm in women.

2.3. Sonographic measurements of fatty liver and LKS

Abdominal ultrasonography was performed by single well-trained ultrasonographers with blindness the characteristics of subjects. Sonographic measurements were obtained with the patients in the supine position. All the patients were asked to hold their breath during the measurement as possible. The probe was kept perpendicular to the skin on the right lateral aspect of the middle abdomen. Longitudinal scanning was performed, and the probe was slowly moved laterally until the optimal position was found, at which the surface of the kidney was almost parallel to the edge of livers (Fig. 1). Special care was taken to keep the probe just touching the skin to prevent compression of the fat layers. Sonographic measurements of LKS (the distance between the lower liver margin and surface of the kidney) were taken three times directly from the screen using the electronic calipers and then mean values were calculated to the nearest 1 mm. To confirm the reliability of the measurements, three operators used this method on 20 targets and the interclass correlation was 0.827. Sonographic measurements of fatty liver change includes increased liver echogenicity and presence of liver and kidney echo discrepancy (Fig. 1).

2.4. Statistical analyses

Data are presented as mean $\pm$ standard error of mean, and $p < 0.05$ was considered significant. Pearson's correlation coefficient was used to investigate the correlations between sonographic LKS, fatty liver, and metabolic parameters indicating MS. The Spearman correlation test was used to assess the association of sonographic measurements and the rest of the studied variables. 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. All statistical analyses were performed using SPSS 15.0 for Windows (SPSS Inc., Chicago, IL, USA).

3. Results

3.1. Receiver operating characteristic curve results for visceral fat and cutoff value of LKS to predict MS

To evaluate the new method of determining visceral fat by measuring LKS on abdominal sonography to predict MS, a total of 317 outpatients were enrolled. In the current study, LKS = 4 mm enabled a better prediction of MS. The area under the receiver operating characteristic curve was 0.625 (Fig. 2). The Spearman correlation test was used to assess the association of sonographic measures of LKS and the rest of the studied variables. There was only an agreement with WC, and agreement Kappa value was 0.337 ($p < 0.05$).

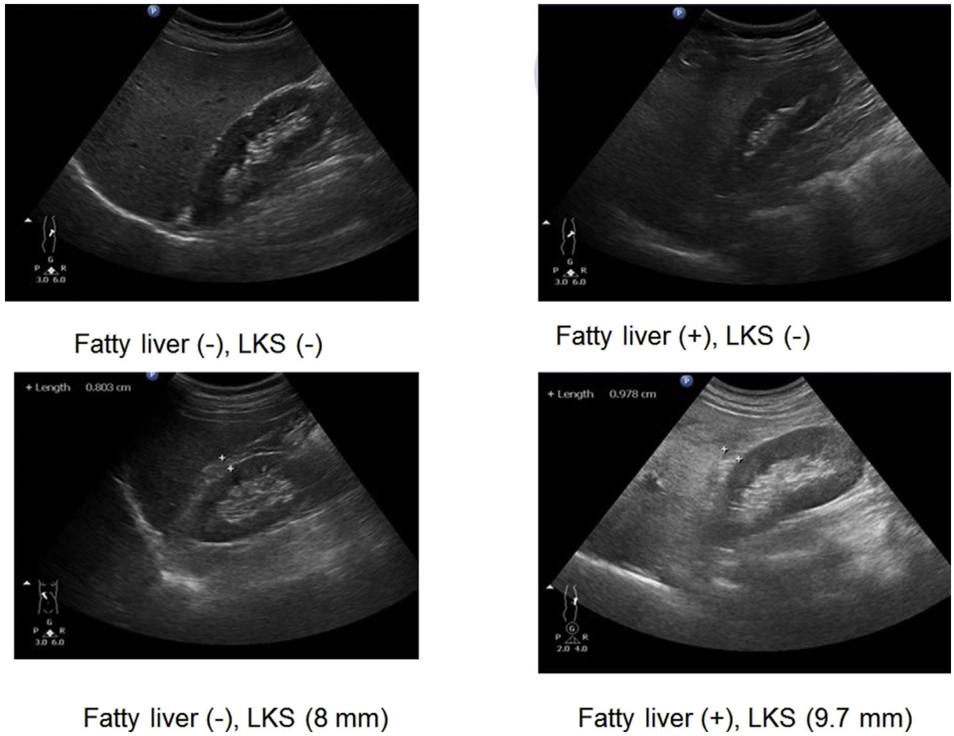

Fig. 1. Sonographic measurements of liver-kidney space, the distance between the lower liver margin and surface of the kidney. Sonographic measurements of fatty liver change, including increased liver echogenicity and presence of liver and kidney echo discrepancy.

3.2. Differences among the presence and absence of LKS in patients with an abnormal WC

Although measurement of WC is convenient, visceral fat in women may not be accurately measured due to subcutaneous fat. We analyzed the differences among the presence and absence of LKS in patients with an abnormal WC (more than 90 cm in men and 80 cm in women). A total of 203 male patients had a WC of >90 cm and 46.3% of them had visceral fat; however, 114 female patients had a WC of >80 cm, and only 9.6% of them had visceral fat (Table 1). In the female group with an abnormal WC, presence of visceral fat could predict abnormalities in the BMI, body fat, abdominal girth (cm), TG, and HBA1c. However, the differences were not shown on TG and HbA1c in the male group. It indicates LKS was better than WC in predicting high TG and HbA1c levels in women.

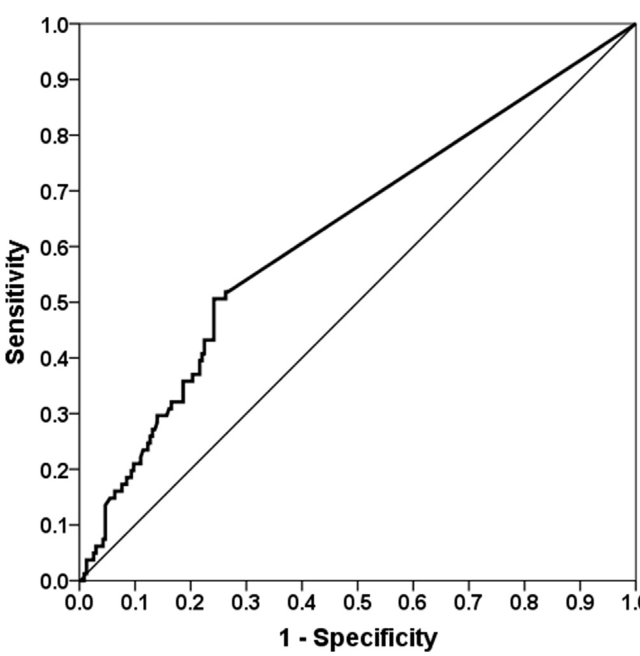

Fig. 2. Receiver operating characteristic curve results for liver-kidney space to predict metabolic syndrome.

3.3. Baseline clinical characteristics and prevalence of visceral fat in 72 elderly patients

Visceral fat was present in 37.5% of 72 elderly participants using the modified criteria of LKS of more than 4 mm (Table 2). The male (81.5%) was more prevalent of having visceral fat than woman (48.9%). Of the participants with visceral fat, 52.9% were diagnosed as MS; however, only 22.2% of participants without visceral fat were diagnosed as MS. The participants with visceral fat had higher BMI (6.59 (5.1–11.3) vs 6.04 (4.8–8.1); p = 0.0005) and HbA1c level (6.59 (5.1–11.3) vs 6.04 (4.8–8.1); $p = 0.039$). Table 2 summarizes the characteristics of the study cohort of 72 patients. The sensitivity and specificity for the presence of visceral fat to predict MS in the elderly were 0.58 and 0.73, respectively. For the comparison of accuracy between sonographic visceral fat and fatty liver and MS, the accuracy to predict MS were 68.1% for visceral fat and 59.6 for fatty change (Table 3). MS was diagnosed in 33.3% of 72 elderly participants using the modified NCEP ATP III criteria. The elderly MS participants with visceral fat had a higher BMI (27.92 [20.9–33.5] vs 25.3 [19.2–29.8]; p = 0.03) and WC (96.11 [73–116.5] vs 87.9 [73–100]; p = 0.02) than elderly MS participants without visceral fat.

4. Discussion

There were different diagnostic criteria recommended by different panel groups. Experts from the International Diabetes Federation (IDF) and NCEP ATP III suggested that parameters must

Table 1
Differences among presence and absence of liver-kidney space in male and female patients with an abnormal waist circumference.

	Male			Female		
	LKS (+) N = 94	LKS (−) N = 109	p value	LKS (+) N = 11	LKS (−) N = 103	p value
Age	53.2 ± 9.3	50.9 ± 10.3	0.1	57.2 ± 12.4	52.3 ± 10.5	0.15
Body mass index	26.4 ± 3.5	23.5 ± 3.0	<0.001	26.9 ± 4.2	22.3 ± 3.5	0.0012
Body fat composition	25.9 ± 4.9	21.5 ± 4.8	<0.001	38.2 ± 11.7	28.9 ± 7.0	<0.001
Abdominal girth (cm)	91.9 ± 9.0	85.1 ± 7.1	<0.001	84.4 ± 8.4	75.1 ± 8.4	0.001
Triglyceride	159.4 ± 102.2	142.5 ± 76.9	0.18	85.2 ± 8.4	70.4 ± 16.9	0.05
HBA1c	5.76 ± 0.74	5.75 ± 1.0	0.93	6.22 ± 2.05	5.20 ± 0.73	0.002

Table 2
Baseline clinical characteristics and prevalence of visceral fat in 72 elderly patients.

	LKS (+) (n = 28)	LKS (−) (n = 44)	p value
Age	65.5 ± 5.1	66.0 ± 4.9	0.67
Sex (male, %)	23 (82.1%)	21 (47.7%)	0.003
Metabolic syndrome (+)	14 (50%)	10 (22.7%)	0.012
Body mass index	26.7 ± 3.5	23.9 ± 3.7	0.002
Body fat composition	27.3 ± 8.4	25.9 ± 7.7	0.46
Abdominal girth (cm)	92.4 ± 9.6	82.1 ± 9.4	<0.001
Fasting glucose	119.6 ± 50.9	104.4 ± 19.8	0.08
HbA1c	6.56 ± 1.38	6.04 ± 0.67	0.046
Triglyceride	137.3 ± 52.6	139.9 ± 87.4	0.44
Cholesterol	194.1 ± 26.7	205.2 ± 38.1	0.19
HDL	50.6 ± 22.3	56.4 ± 17.2	0.23
LDL	130.8 ± 24.2	132.5 ± 41.1	0.85

comprise central obesity, diabetes, hypertension, and hyperlipidemia. The measurement of obesity through WC has been established as a simple and useful method and is well associated with cardiovascular risk.[22] It has been proposed as a key element for the diagnosis of MS.

As is known, central obesity includes both subcutaneous and visceral fat. Moreover, the female sex hormone causes fat to be stored in the buttocks, thighs, and hips in women. In contrast, men are more likely to have fat stored in the abdomen due to sex hormone differences. Measurement of WC was thought to be an imprecise method in determining the degree and amount of visceral fat. Abdominal sonography in evaluating precise visceral fat to predict MS has been utilized.[8,9] Because visceral fat could accumulate between the kidney and liver as peri-renal fat in obese patients, we develop a novel method for measuring visceral fat using abdominal sonography. The purpose of this study was to evaluate a novel method of determining visceral fat by measuring LKS on abdominal sonography and analyze its utilization in the prediction of MS and its association with other risk factors in the elderly.

The prevalence of MS varies in different countries but is highly age-dependent. The prevalence of MS in the general population may increase with age, from 3.1% in those aged 25−29 years to 41.0% in those older than 70 years from a Hong Kong population survey.[21] Huang et al.[23] demonstrated that MS defined by NCEP ATP III criteria to be as high as 21.5% in elderly Taiwanese men and 37.6% in women. MS was diagnosed in 33.3% of 72 elderly participants older than 65 years using the same NCEP ATP III criteria in our study, which is comparable to the Hong Kong survey. Individuals with MS have approximately five- and twofold increased risk for type 2 diabetes and CVD, respectively.[24] The more the components of the MS are evident, the higher is the cardiovascular mortality rate.[25] In our study, we can further regroup the elderly patients with MS according to the presence of excessive visceral fat. The elderly MS participants with excessive visceral fat had a higher BMI (27.92 vs 25.3; $p = 0.03$) and WC (96.11) vs 87.90; ($p = 0.02$) than elderly MS participants without excessive visceral fat. It needs further evaluation to clarify the role of LKS in the outcomes of cardiovascular mortality. Further study on pathogenesis is needed because visceral fat in the omentum, perirenal fat, and pericardiac fat may have different properties.[25] Moreover, this variation may exist among different racial and ethnic groups.

There were many modalities developed to evaluate the abdominal visceral fat by sonography with promising results including measuring the circumference or thickness of peritoneal fat. In the earlier period, Armellini et al. measured the length from the inner side of the abdominal musculature to the posterior wall of the aorta to estimate the area of intra-abdominal fat and reported that it correlated well (r = 0.669) with the amount of visceral fat.[25] Hirooka et al.[9] reported the peritoneal circumference is better correlated with MS than subcutaneous fat which was measured by WC; but the method need a complex equation. Suzuki et al.[10] examined the ratio of the maximum thickness of preperitoneal fat to the minimum thickness of subcutaneous fat and found it was positively correlated with serum triglyceride levels. But the method was not used to diagnose MS. Kawasaki et al.[11] evaluated the visceral fat by sonography, the measured the thickness of combined para- and peri-renal fat was measured both sides between the kidney and the inner aspect of the abdominal musculature; however, the ratio did not correlate with elevated blood pressure or hyperlipidemia. In our study, measurement of LKS by sonography is a simple and reliable method for determining MS in the elderly. The area under the receiver operating characteristic curve was 0.63 which is comparable to previous studies. The accuracy rate in

Table 3
The sensitivity, specificity, positive predict value (PPV), negative predict value (NPV), and accuracy using liver-kidney space or sonographic fatty liver change to predict MS in the elderly patients.

	Metabolic syndrome (+)	Metabolic syndrome (−)	
Visceral fat (LKS) (+)	14	13	PPV = 0.52
Visceral fat (LKS) (−)	10	35	NPV = 0.78
	Sensitivity = 0.58	Specificity = 0.73	Accuracy = 0.68
	Metabolic syndrome (+)	Metabolic syndrome (−)	
Fatty liver (+)	14	10	PPV = 0.58
Fatty liver (−)	14	34	NPV = 0.71
	Sensitivity = 0.5	Specificity = 0.77	Accuracy = 0.67

predicting MS was 68.1% by determining excessive visceral fat and 59.6% by determining sonographic fatty change. The LKS was more associated with abdominal girth and BMI in the elderly from the study supporting the observation that LKS are well correlated with general adiposity, in agreement with previous results.

This study has several limitations. The major limitation of the measurement of LKS is that it cannot provide any information about fat distribution and fat volume. We do not provide the correlation between LKS and total abdominal fat volume which were measured by CT or MRI in these general populations. It is difficult to be obtained in all patients considering the issues of radiation exposure. Second, our measurements were recorded from a cross-sectional study, and follow-up studies are needed to examine the significance and impact on the reduction of risks if there is LKS regression after weight loss. However, our method has an important strength if we proposed sonography as a part of the routine general physical examination in clinical practice. Sonography is a simple and reliable method to predict MS. Individuals with MS could be identified early through a sonographic check-up from other purposes such as cancer or hepatitis surveillance so that their cardiovascular risk factors can be identified.

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