Ultrasonographic Quantitative Analysis of Fatty Pancreas in Obese Children: Its Correlation with Metabolic Syndrome and Homeostasis Model Assessment of Insulin Resistance

Doo Ri Kim, MD[1], Mu Sook Lee, MD[1], Jeong Sub Lee, MD[1], Guk Myung Choi, MD[1], and Ki Soo Kang, MD[2]

Objectives To evaluate pancreatic echogenicity on transabdominal ultrasonography and the correlation of fatty pancreas with metabolic syndrome (MetS), as well as insulin resistance (homeostasis model assessment of insulin resistance [HOMA-IR]).

Study design This retrospective study included 135 obese children and adolescents who underwent transabdominal ultrasonography from January 2015 to December 2015. Fatty pancreas was quantitatively analyzed using the pancreato-perihepatic fat index (PPHFI). The correlation between the PPHFI and HOMA-IR was analyzed, and multivariate logistic regression analysis was used to determine factors that were independently correlated with MetS. Receiver operating characteristic curve analysis was performed to determine the best cut-off value of the PPHFI for diagnosing MetS.

Results The PPHFI and the HOMA-IR value were significantly higher in subjects with MetS than in those without MetS ($P < .0001$). The PPHFI also showed an association with the HOMA-IR value ($r = 0.70$; $P < .0001$). The PPHFI was an independent factor for diagnosing MetS (OR 4.36; $P = .032$). The best cut-off value for the PPHFI for a diagnosis of MetS was 2.34 with a sensitivity of 0.96 and specificity 0.70.

Conclusions These results suggest that an increased PPHFI is significantly correlated with MetS and insulin resistance, and that the PPHFI may be a useful indicator for diagnosing MetS in obese children and adolescents. The impact of the presence of fatty pancreas in obese children and adolescents must be evaluated *(J Pediatr 2017;■■:■■-■■).*

Insulin resistance is a major risk factor for type 2 diabetes, and it is associated with components of cardiometabolic syndrome, including hypertension, hyperlipidemia, and atherosclerosis.[1,2] Obesity has a direct cause-and-effect relationship with insulin resistance.[2]

In addition, obesity and metabolic syndrome (MetS) are among the most frequent causes of fatty pancreas.[3-5] According to recent animal studies,[6,7] obesity may result in a heavier pancreas and increased pancreatic triglycerides (TGs) and free fatty acids, and cause damage to the normal pancreatic structure and islets.

Various diagnostic modalities, such as transabdominal ultrasonography, endoscopic ultrasonography, computed tomography (CT), and magnetic resonance imaging (MRI), have been used to assess fatty pancreas; however, transabdominal ultrasonography remains the first-line screening tool in pediatrics. Although most reports on the evaluation of fatty pancreas using transabdominal ultrasonography have focused on qualitative analysis,[8,9] Jeong et al proposed pancreato-perihepatic fat indices (PPHFIs) that enable the analysis of pancreatic echogenicity quantitatively.[10] They also revealed that an increased PPHFI is significantly correlated with MetS. However, studies on transabdominal ultrasonography and quantitative analysis of fatty pancreas in obese children remain. Therefore, the present study performed the quantitative analysis of the fatty pancreas using transabdominal ultrasonography and evaluated the correlation of fatty pancreas with MetS, as well as insulin resistance. This study also examined the usefulness of the PPHFI as a screening tool for diagnosing MetS in obese children and adolescents.

ALP	Alkaline phosphatase	LDL	Low-density lipoprotein
ALT	Alanine aminotransferase	MetS	Metabolic syndrome
AST	Aspartate aminotransferase	MRI	Magnetic resonance imaging
BMI	Body mass index	PPHFI	Pancreato-perihepatic fat index
CT	Computed tomography	ROI	Region of interest
HbA1C	Glycated hemoglobin	TG	Triglyceride
HDL	High-density lipoprotein	WC	Waist circumference
HOMA-IR	Homeostasis model assessment of insulin resistance		

From the [1]Department of Radiology of Jeju National University Hospital; and [2]Department of Pediatrics of Jeju National University Hospital, Jeju National University School of Medicine, Jeju, Republic of Korea

The authors declare no conflicts of interest.

0022-3476/$ - see front matter.
https://doi.org10.1016/j.jpeds.2017.10.007

Methods

This retrospective study enrolled 135 children and adolescents who visited the Outpatient Department of the Obesity and Nutrition Clinic of Jeju National University Hospital on the island of Jejudo from January 2015 to December 2015. Children at or above the 95th percentile of body mass index (BMI) for their age and sex based on 2007 Korean National Growth Charts were defined as obese. Once the BMI reached 25 kg/m^2 or greater, they were categorized as obese regardless of the percentile score.[11] A total of 30 patients met the exclusion criteria; hepatitis A or B, Wilson disease, autoimmune hepatitis, or the use of drugs resulting in metabolic disturbances. This study was approved by the Institutional Review Board of Jeju National University Hospital, and the mandate for obtaining informed consent was waived.

Anthropometric variables, such as height, weight, waist circumference (WC), BMI, and blood pressure, were measured. WC was evaluated at the midportion between the 12th rib margin and upper portion of the iliac crest during the end of normal respiratory expiration. BMI was calculated using the formula of body weight in kilograms divided by height in meters squared: BMI = weight (kg) x [height (m)^2].

Biochemical tests of whole blood, which were performed after overnight fasting, included measurements of fasting plasma glucose, insulin, glycated hemoglobin A1c, lipid profile (high-density lipoprotein [HDL] cholesterol, low-density lipoprotein [LDL] cholesterol, and TG), liver tests (aspartate aminotransferase [AST], alanine aminotransferase [ALT], and total bilirubin), amylase, and alkaline phosphatase (ALP). The homeostasis model assessment of insulin resistance (HOMA-IR) was used to quantify insulin resistance [fasting serum insulin (μU/mL) × fasting plasma glucose (mmol/L)/22.5].[12]

MetS was defined using the 2007 International Diabetes Federation consensus criteria. This included central obesity (WC ≥90th percentile; 2007 Korean National Growth Charts) and 2 or more of the following 4 factors: TG level >150 mg/dL, HDL cholesterol <40 mg/dL, systolic blood pressure >130 mm Hg or diastolic blood pressure >85 mm Hg, and fasting plasma glucose level >100 mg/dL.[11,13]

All subjects were asked to fast after midnight and underwent transabdominal ultrasonography. The examinations were performed using a 5-8 MHz curved linear transducer (Philips iU22; Bothell, Washington) by a single radiologist with 13 years of experience. Transverse and longitudinal sonograms, both showing the liver and diaphragm, were routinely obtained to evaluate hepatic steatosis. Also, transverse and longitudinal sonograms of the pancreas were obtained to include as much pancreatic tissue and perihepatic fat as possible, simultaneously. The quality of the ultrasonograms was assessed by 3 radiologists.[10]

Hepatic steatosis was graded according to echo patterns as follows: grade 0, normal liver echotexture; grade 1, slight and diffuse increase in parenchymal echotexture with normal visualization of the diaphragm and intrahepatic vessel borders; grade 2, moderate and diffuse increase in parenchymal echotexture with slightly impaired visualization of the diaphragm and intrahepatic vessel borders; and grade 3, significant increase in parenchyma echotexture with poor visualization of the diaphragm and intrahepatic vessel borders.[14,15]

For quantitative analysis of pancreas fat, the brightness of the pancreas and perihepatic fat were measured on transverse and longitudinal images using a region of interest (ROI) method (**Figure 1**), which was determined by the rectangular method. On both sonograms, ROIs for the pancreatic body were selected from the central portion of the pancreatic parenchyma, as much as possible, and away from the main pancreatic duct and retroperitoneal fat. The perihepatic fat was defined as the layer of fatty tissues between the anterior hepatic capsule and muscular abdominal layer. The ROI for the brightness of perihepatic fat on both sonograms was selected in the area of homogenous echogenicity. The mean brightness of the pancreatic body and perihepatic fat was calculated by using the average of the mean brightness values on both sonograms. Then, the PPHFI was calculated by using the ratio of mean brightness of the pancreatic body to that of the perihepatic fat.[10]

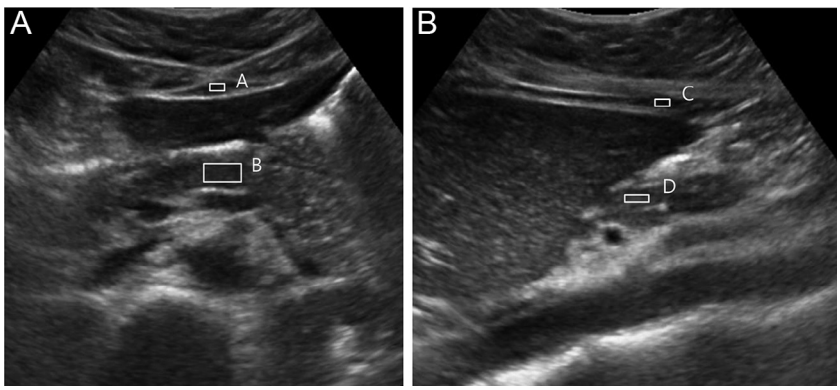

Figure 1. The PPHFI. On **A,** transverse and **B,** longitudinal sonograms; ROIs for pancreatic body were placed in the central portion of the pancreas body and ROIs for perihepatic fat brightness were placed in area with homogenous echogenicity. The PPHFI was calculated by (B + D)/(A + C).

FLA 5.5.0 DTD ■ YMPD9521_proof ■ November 29, 2017