RESEARCH LETTER

Evaluation of adipose tissue and liver radiodensity in overweight or obese patients with nonalcoholic fatty liver disease

Radosław Kempiński[1*], Katarzyna Neubauer[1*], Agnieszka Hałoń[2], Przemysław Podgórski[3], Robert Dudkowiak[1], Elżbieta Poniewierka[1]

1 Department of Gastroenterology and Hepatology, Wroclaw Medical University, Wrocław, Poland
2 Department of Pathomorphology and Oncological Cytology, Wroclaw Medical University, Wrocław, Poland
3 Department of General Radiology, Interventional Radiology and Neuroradiology, Wroclaw Medical University, Wrocław, Poland

Introduction Nonalcoholic fatty liver disease (NAFLD) is a common chronic liver disease that affects approximately 30% of the population.[1] Increasing incidence rates of NAFLD are related to the growing prevalence of obesity, which is associated with a wide range of complications, including metabolic syndrome. Moreover, 20% of patients with NAFLD will be diagnosed with nonalcoholic steatohepatitis (NASH), and 30% of patients with NASH will develop liver fibrosis, cirrhosis, and liver failure.[1]

Metabolic syndrome with insulin resistance has a well-established connection with abdominal obesity, most often described by waist circumference. Waist circumference correlates with subcutaneous adipose tissue (SAT) and visceral adipose tissue (VAT) as well as with the amount of fat in the liver.[2] The volumes of SAT and VAT might be objectively measured with imaging methods, including computed tomography (CT).

The aim of our study was to evaluate the correlation between CT indices (VAT, SAT, and liver radiodensity) and anthropometric and histologic parameters in overweight or obese patients with NAFLD.

Patients and methods The study group consisted of 44 consecutive overweight or obese patients with NAFLD. Liver steatosis was confirmed by a histologic examination.[3]

Complete clinical examination with anthropometric measurements (height, weight, body mass index [BMI], waist circumference, hip circumference, waist-to-hip ratio [WHR], and waist-to-height ratio) was performed. According to the percentage involvement of steatotic hepatocytes, patients were divided into 3 subgroups: mild steatosis (5%–33%), moderate steatosis (33%–66%), and severe steatosis (>66%).

The scoring system developed by the Nonalcoholic Steatohepatitis Clinical Research Network was used to assess the activity of NASH by calculating the nonalcoholic fatty liver disease activity score (NAS) (Supplementary material, *Table S1*).[4] The staging of fibrosis was assessed using the METAVIR score (F0-F4).

Liver radiodensity, given in Hounsfield units (HUs), was evaluated in 3 phases: native, arterial, and venous. Three regions of interest (2 cm in diameter) were analyzed, of which 2 were placed in the right lobe and 1 was placed in the left lobe of the liver. The mean value for the 3 regions was evaluated.

We evaluated VAT and SAT mass covering a 125-mm segment above the first sacral vertebral level (25 sections, 5 mm each). Fat was identified using an image display window of –195 to –45 HU and a window center of –120 HU. Manual tracing separating the visceral from the subcutaneous compartment was performed. The images were segmented semiatomatically using 3D Slicer software (https://www.slicer.org/). The fat volumes were calculated in ml and were then converted to mass, using a factor of 0.9196 kg/l as the density of adipose tissue. Adipose tissue distribution accessed on CT is shown in Supplementary material (*Figure S1*).

The *t* test was performed to compare the means in groups with normally distributed data. For nonnormal distribution, the Mann–Whitney test was used. Correlations between normally distributed data were calculated using the Pearson correlation coefficient. For nonparametric data series, the Spearman correlation coefficient was

Correspondence to:
Radosław Kempiński, MD, PhD, Department of Gastroenterology and Hepatology, Wroclaw Medical University, ul. Borowska 213, 50-556 Wrocław, Poland, phone: +48 71 733 21 20, email: radoslaw.kempinski@umed.wroc.pl
Received: February 10, 2019.
Revision accepted: February 21, 2019.
Published online: February 22, 2019.
Pol Arch Intern Med. 2019; 129 (5): 354-356
doi:10.20452/pamw.4457

* RK and KN contributed equally to this work.

TABLE 1 Correlation coefficient for liver radiodensity and the level of steatosis, nonalcoholic fatty liver disease activity score and stage of liver fibrosis

Parameter	Native phase, HU	Arterial phase, HU	Venous phase, HU
Steatotic hepatocytes, %[a]	−0.69; P <0.001	−0.58; P <0.001	−0.68; P <0.001
NAS, 0–8[b]	0.10; P = 0.53	0.01; P = 0.94	0.24; P = 0.13
Fibrosis, 0–4[b]	−0.42; P = 0.006	−0.26; P = 0.09	−0.23; P = 0.14

a Pearson correlation coefficient

b Spearman correlation coefficient

Abbreviations: HU, Hounsfield unit; NAS, nonalcoholic fatty liver disease activity score

used. A P value of less than 0.05 was considered statistically significant.

The study protocol was approved by a local ethics committee and complied with the Declaration of Helsinki.

Results In our study group, 18 patients (40.9%) were overweight (BMI, 25–30 kg/m^2) and 26 (59.1%) were obese (BMI >30 kg/m^2). Selected clinical data of patients are shown in Supplementary material (*Table S2*). The mean VAT, SAT, and the VAT/SAT ratio are shown in Supplementary material (*Table S3*). We found no significant difference in the volume of VAT between men and women with NAFLD. However, the volume of SAT was different between women and men (3724 ml vs 2808 ml; P = 0.01), as was the VAT/SAT ratio (0.65 vs 0.9; P = 0.03).

The correlations between the volume of VAT and SAT and selected anthropometric parameters are shown in Supplementary material (*Table S4*). The volume of SAT (as well as the total calculated adipose tissue, VAT + SAT) showed a strong positive correlation with weight, BMI, waist circumference, and hip circumference, but not with WHR. The volume of VAT correlated well with BMI, waist circumference, and WHR, but not with weight or hip circumference. The most precise parameter describing the amount of VAT was WHR; however, it showed no correlation with SAT and total adipose tissue (VAT + SAT) evaluated by CT.

The mean (SD) hepatocyte steatosis in our group was 36.3% (24.7): 21 patients (47.7%) had mild steatosis; 18 patients (40.9%), moderate; and 5 patients (11.4%), severe. In the case of liver steatosis, no correlations were found between either the volume of adipose tissue (VAT and SAT) or the distribution of fat (VAT/SAT ratio).

We observed NASH (NAS score, 5–8) in 11 patients (25%). The mean (SD) NAS was 2.94 (1.78). In patients with NAFLD, we did not find correlations between the severity of NASH and the volume or distribution of adipose tissue. Significant fibrosis (F2-F4) was diagnosed in 6 patients (13.5%). The severity of fibrosis did not correlate with VAT volume and fat distribution (VAT/SAT ratio), but was strongly positively correlated with SAT volume (P = 0.001) (Supplementary material, *Table S5*).

The mean (SD) radiodensity in the native phase was 40.3 (11.7) HU; in the arterial phase, 74.5 (22.9) HU; and in the venous phase, 79.2 (24.3) HU. The correlations between radiodensity and the level of steatosis, NAS, and stage of fibrosis are shown in TABLE 1. The percentage of steatotic hepatocytes correlated inversely with liver radiodensity in all phases (native phase, r = –0.69, P <0.001) (Supplementary material, *Figure S2*).

We chose the native phase to evaluate the sensitivity, specificity, and positive and negative predictive values of liver radiodensity as a marker of moderate to severe liver steatosis. For the cutoff value of 42 HU, the sensitivity of the test was 89.47%; specificity, 71.43%; positive predictive value, 73.91%; and negative predictive value, 88.24%. The negative predictive value was particularly high. Patients with liver radiodensity in the native phase above 42 HU were unlikely to have moderate or severe liver steatosis (Supplementary material, *Table S6*). The NAS did not correlate with liver radiodensity in any phase of CT.

Discussion Recently, NAFLD has been recognized as the most common chronic liver disease. Nonalcoholic steatohepatitis with advanced fibrosis was found in 60% of individuals older than 50 years with diabetes or obesity.[5] Therefore, there is an ongoing search for risk factors of NAFLD as well as objective, noninvasive, and easy-to-perform diagnostic markers of the disease and its complications. In our study, we attempted to answer the question whether radiodensity of the liver on CT is a good marker of steatosis, steatohepatitis, and the degree of fibrosis. Additionally, we attempted to evaluate the diagnostic value of simple anthropometric measurements when compared with CT indices.

Liver biopsy is currently the gold standard for staging of NAFLD. However, this method has also some limitations such as sampling error, inter- and intraobserver variability, and the risk of complications.[6] Alternative imaging methods are also not perfect.[7] It was shown that T1-weighted dual-echo magnetic resonance (MR) imaging and point-resolved 1H MR spectroscopy, in contrast to ultrasound and CT, strongly correlated with histopathologic assessment.[8] In another study, diagnostic accuracy in the estimation of liver-fat content was similar between CT and MR, but MR seemed to be better at lower degrees of steatosis.[9] In our study, we found a significant inverse correlation between liver radiodensity and the degree of steatosis. Therefore, the measurement of liver radiodensity can be a simple tool to evaluate the degree of steatosis, especially when clinically significant steatosis is suspected, because the CT has a high negative predictive value. Patients with liver radiodensity in the native phase above 42 HU are highly unlikely to have moderate or severe liver steatosis.

In our study, the distribution of adipose tissue was different in women and men. The VAT/SAT ratio was significantly higher in men than in

women, which is compatible with anthropometric data of the higher prevalence of abdominal obesity in men. The absolute amount of VAT proved to be similar both in men and women. The WHR correlated positively with the amount of VAT, but not SAT. On the contrary, the hip circumference correlated with SAT, but not VAT.

The amount of VAT impacts liver steatosis to a larger extent than BMI and SAT.[10] In a study on 2017 patients followed for a median of 4.43 years, Kim et al[11] found that larger areas of VAT were longitudinally associated with a higher risk of NAFLD. In our study, we attempted to assess the correlation between the amount and distribution of adipose tissue and histopathologic parameters obtained during liver biopsy. Surprisingly, we found no impact of either the amount or distribution of adipose tissue on liver steatosis. Similarly, there was no significant correlation between steatohepatitis (expressed as NAS) and VAT, SAT, or the VAT/SAT ratio. The degree of fibrosis correlated positively with the amount of SAT and total adipose tissue (VAT + SAT). This may reflect the BMI of patients that is included in NAFLD fibrosis score (NFS), which is a well-established noninvasive tool to identify liver fibrosis in patients with NAFLD.[12]

In summary, radiodensity assessed by CT might be an indicator of liver steatosis in overweight or obese patients with NAFLD. Moreover, CT may facilitate the evaluation of adipose tissue distribution, and WHR is a good marker of the volume of VAT.

SUPPLEMENTARY MATERIAL

Supplementary material is available with the article at www.mp.pl/paim.

ARTICLE INFORMATION

ACKNOWLEDGMENTS The research was supported by Polish National Science Center (grant No. NN519463239; to EP).

CONFLICT OF INTEREST None declared.

HOW TO CITE Kempiński R, Neubauer K, Hałoń A, et al. Evaluation of adipose tissue and liver radiodensity in overweight or obese patients with nonalcoholic fatty liver disease. Pol Arch Intern Med. 2019; 129: 354-356. doi:10.20452/pamw.4457

REFERENCES

1 Vernon G, Baranova A, Younossi ZM. Systematic review: the epidemiology and natural history of non-alcoholic fatty liver disease and non-alcoholic steatohepatitis in adults. Aliment Pharmacol Ther. 2011; 34: 274-285.

2 Fox CS, Massaro JM, Hoffmann U, et al. Abdominal visceral and subcutaneous adipose tissue compartments: association with metabolic risk factors in the Framingham Heart Study. Circulation. 2007; 116: 39-48.

3 Chalasani N, Younossi Z, Lavine JE, et al. The diagnosis and management of non-alcoholic fatty liver disease: practice Guideline by the American Association for the Study of Liver Diseases, American College of Gastroenterology, and the American Gastroenterological Association. Hepatology. 2012; 55: 2005-2013.

4 Kleiner DE, Brunt EM, Van Natta M, et al. Design and validation of a histological scoring system for nonalcoholic fatty liver disease. Hepatology. 2005; 41: 1313-1321.

5 Rinella ME. Nonalcoholic fatty liver disease: a systematic review. JAMA. 2015; 313: 2263-2273.

6 Sumida Y, Nakajima A, Yoshito I. Limitations of liver biopsy and non-invasive diagnostic tests for the diagnosis of nonalcoholic fatty liver disease/nonalcoholic steatohepatitis World J Gastroenterol. 2014; 20: 475-485.

7 Koplay M, Sivri M, Erdogan H, Nayman A. Importance of imaging and recent developments in diagnosis of non-alcoholic fatty liver disease. World J Hepatol. 2015; 7: 769-776.

8 van Werven JR, Marsman HA, Nederveen AJ, et al. Assessment of hepatic steatosis in patients undergoing liver resection: comparison of US, CT, T1-weighted dual-echo MR imaging, and point-resolved 1H MR spectroscopy. Radiology. 2010; 256: 159-168.

9 Maruzzelii L, Parr AJ, Miraglia R, et al. Quantification of hepatic steatosis: a comparison of computed tomography and magnetic resonance indices in candidates for living liver donation. Acad Radiol. 2014; 21: 507-513.

10 Milić S, Lulić D, Štimac D. Non-alcoholic fatty liver disease and obesity: biochemical, metabolic and clinical presentations. World J Gastroenterol. 2014; 20: 9330-9337.

11 Kim D, Chung GE, Kwak MS, et al. Body fat distribution and risk of incident and regressed non-alcoholic fatty liver disease. Clin Gastroenterol Hepatol. 2015; 14: 132-138.

12 Angulo P, Hui JM, Marchesini G, et al. The NAFLD fibrosis score: a noninvasive system that identifies liver fibrosis in patients with NAFLD. Hepatology. 2007; 45: 846-854.