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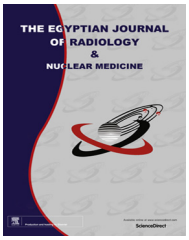

ORIGINAL ARTICLE

Investigation of computed tomography findings of portal hypertension at non-alcoholic fatty liver disease

Fatma Kulali [a,*], **Burcu Kaya-Tuna** [a], **Aslihan Semiz-Oysu** [a], **Zeynep Gamze Kilicoglu** [b], **Yasar Bukte** [a]

[a] *Umraniye Training and Research Hospital, Istanbul, Turkey*
[b] *Haydarpasa Numune Training and Research Hospital, Istanbul, Turkey*

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KEYWORDS

Hepatosteatosis;
Portal hypertension;
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Abstract *Background:* Non-alcoholic fatty liver disease (NAFLD) is very common and serious disease. It begins as a simple hepatosteatosis but can progress to cirrhosis. The early detection of portal hypertension (HT) can be helpful in the management of these patients.
Aims: To evaluate radiologic findings of portal hypertension at computed tomography (CT) of patients with non-alcoholic fatty liver disease for early diagnosis.
Methods and materials: Images of 225 cases who underwent non-enhanced abdominal CT were reviewed. The patients with the difference between hepatic and splenic attenuation (CT L-S) > 10 were enrolled in hepatosteatosis group. The remainings formed control group. The relationship between two groups about diameters of portal and splenic veins, craniocaudal (CC) span of liver, splenic index, caudate lobe/right lobe (C/RL) ratio was analyzed statistically by Mann–Whitney *U* Test and Student's *t*-test.
Results: Total 213 cases, as hepatosteatosis ($n = 149$) and control ($n = 64$) groups, were involved in this study. Liver CC span, splenic index and C/RL ratio between two groups were found to be statistically significant ($p < 0.01$).
Conclusions: The splenic index and C/RL ratio are important findings of portal HT and fibrosis. CT imaging can be beneficial for diagnosis and treatment of NAFLD patients.

1. Introduction

Hepatosteatosis is accumulation of fat more than 5% of liver weight in hepatocytes (1). Hepatosteatosis without history of alcohol consumption is called non-alcoholic fatty liver disease (NAFLD), which is a common cause of chronic liver disease

* Corresponding author at: Adem Yavuz Cad. No:1, Umraniye Egitim ve Arastirma Hastanesi, Radyoloji Klinigi, Umraniye, 34764 Istanbul, Turkey. Tel.: +90 (216) 632 1818/1462; fax: +90 (216) 6327124.
E-mail address: ftkulali@gmail.com (F. Kulali).
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(1,2). NAFLD, beginning only as simple steatosis, generally induces non-alcoholic steatohepatitis (NASH), and eventually may lead to cirrhosis and hepatocellular carcinoma (HCC) (3,4).

Early detection of NAFLD is necessary to prevent progression. Percutaneous liver biopsy is required for accurate diagnosis of NASH; however, imaging studies can be helpful in avoiding unnecessary biopsies (5–7). After exclusion of viral hepatitis and alcoholic liver disease with laboratory findings and history, diagnosis of NAFLD including NASH, can be done by imaging modalities (8–10). Ultrasound (US), computed tomography (CT) or magnetic resonance imaging (MRI) can detect the existence of steatosis (8–10). US is a non-invasive and cost-effective method for detection of hepatosteatosis; however, the visual grading of hepatosteatosis with US depends on the experience of the observer (3). Non-enhanced CT is a non-invasive procedure, which allows quantitative measurements for accurate diagnosis of hepatosteatosis (3,8,10). MRI can also be performed for the quantitative estimations of hepatosteatosis, but it is not cost-effective and scanning time is longer (5,11).

Despite many studies on evaluation of hepatosteatosis by US and CT in patients with NASH, a few studies analyzed the progression of NAFLD to portal hypertension (HT) on imaging (2,3). Our study was performed to investigate the role of CT on detection of development of portal HT in NAFLD patients. For this reason, we evaluated the CT images of NALFD patients for portal HT findings based on quantitative measurements.

2. Materials and methods

Between July 2011 and November 2012, 225 consecutive patients who underwent non-enhanced abdominal CT with nonspecific symptoms, were reviewed at a single institution from PACS (Picture Archiving and Communications *System*). The exclusion criteria for this study were as follows: (a) the patients with liver mass; (b) the positive laboratory findings for viral hepatitis; (c) the patients with history of alcohol consumption. The remaining 213 cases were included in our study. The patients who had hepatosteatosis, constituted the study group. The patients without hepatosteatosis were evaluated as the control group. The CT images were examined by a radiologist. All CTs were performed at a multi-slice helical scanner (Somatom Sensation 40, Siemens Medical Solutions, Erlangen, Germany). Scanning parameters for non-enhanced CT images were as follows: tube voltage, 120 kVp; tube current, 20 mAs, helical thickness, 2.5 mm, interval, 2.5 mm, pitch, 1.5 and reconstruction slice thickness 1.25 mm.

3. Theory/calculation

For detection of hepatosteatosis, the difference of hepatic and splenic attenuation (CT L-S) was used (10). The region of interest (ROI) measurements at five segments of liver (segments V, VI, VII, VIII from right lobe and segment IVb from left lobe) and at splenic zones (superior, middle, inferior) were performed (Figs. 1 and 2). The mean attenuation values were estimated. For each measurement, a 200 mm^2 circle ROI was used. ROIs were measured from parenchymal area without vascularity, calcifications, visible biliary system and artifacts.

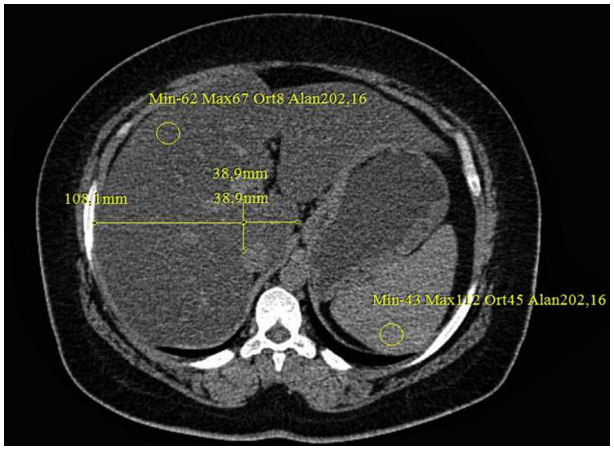

Fig. 1 The measurements of ROIs at liver and spleen and C/RL ratio were shown in 51 years-old male with NAFLD.

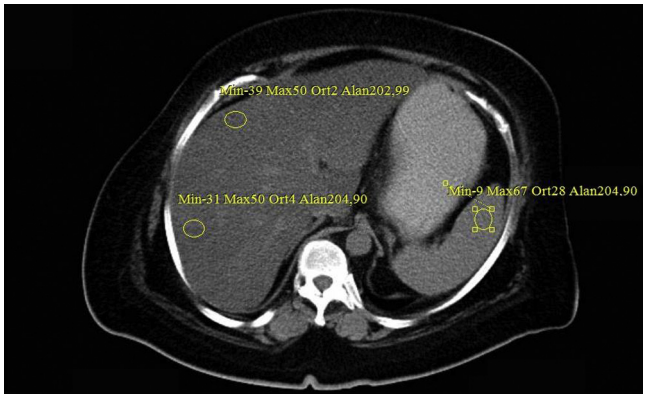

Fig. 2 Hepatosteatosis was demonstrated with the measurements of ROIs at liver and spleen in 64 years old female with NAFLD.

The patients with CT L-S > 10 were enrolled in our study group, and the remainings were reported as the control group.

For assessment of progression to portal HT, diameters of portal and splenic veins, craniocaudal (CC) span of liver, splenic index, and caudate lobe/right lobe (C/RL) ratio were estimated (Fig. 3). The portal and splenic venous measurements were done at the level of liver hilum and splenic hilum, respectively. Splenic index was calculated by the formula of longitudinal length × anterior posterior (AP) diameter × mediolateral diameter. The mediolateral diameter was measured at the level of splenic hilus. C/RL ratio was estimated by using technique previously described (12). C/RL < 0.65 is accepted as normal.

Statistical analyses were performed using Number Cruncher Statistical System (NCSS) 2007 and the Power Analysis and Sample Size (PASS) 2008 Statistical Software (Utah, USA). Mann–Whitney *U* Test or Student's *t*-test was used, where appropriate, and $p < 0.05$ was used to determine statistical significance.

4. Results

Total 213 cases, as study ($n = 149$) and control ($n = 64$) groups, were involved in this study. Of 213 patients, 48%

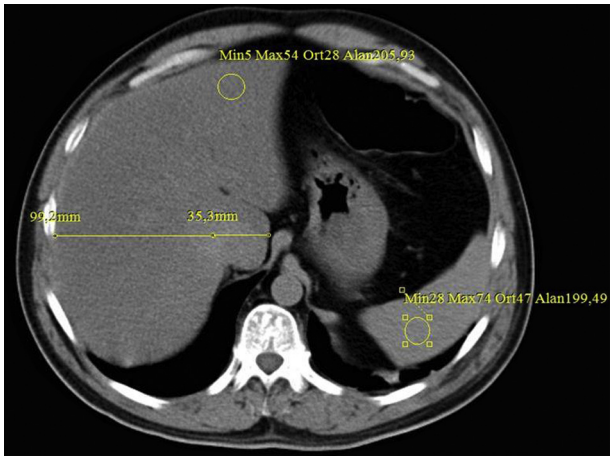

Fig. 3 The measurements of ROIs at liver and spleen and C/RL ratio were estimated in 45 years-old male with NAFLD.

Table 1 The mean values of measurements of the study and control groups were shown. There were statistically significant differences between two groups about liver span, C/RL ratio and splenic index.

Parameters	The study group (mean)	The control group (mean)	*p*
Liver span (mm)	186	173	*0.001*[a,**]
Splenic index	498	424	*0.024*[b,*]
Portal venous diameter (mm)	12	12	*0.310*[a]
Splenic venous diameter (mm)	7	8	*0.164*[a]
C/RL ratio	0.32	0.28	0.001[a,**]

[a] Student-*t* test.
[b] Mann–Whitney *U* Test.
* $p < 0.05$.
** $p < 0.01$.

($n = 102$) were women and 52% ($n = 111$) were men. In study and control groups, the mean age was 49 and 52 years, respectively. The mean age of control group was a little higher, but not statistically significant ($p > 0.05$).

The mean liver CC spans in the study and control groups, were 186.5 mm and 173.5 mm, respectively. Despite high mean liver spans in both groups, there was a statistically significant difference between two groups ($p < 0.01$). All C/RL ratios were within normal limits in both groups. The mean C/RL ratios were estimated 0.32 and 0.28 in the study and control groups, respectively. The mean C/RL ratio of study patients was significantly higher than that of the control group ($p < 0.01$). The mean splenic indexes in the study and control groups were 499 cc and 424 cc, respectively. The mean splenic index was statistically higher in the study group ($p < 0.05$). The splenic index that can be calculated accurately at CT, is an important indicator of portal HT. The mean diameters of portal and splenic veins were found to be 12 mm and 8 mm, respectively, in both study and control groups ($p > 0.05$), which showed no significant difference between two groups. The distribution of mean values and statistically relationships between groups are shown in Table 1.

5. Discussion

NAFLD is a common disease and defined as hepatosteatosis without history of alcohol consumption (9). NAFLD can be seen without symptoms or with elevated liver enzymes or more severe forms such as fibrosis, liver failure, cirrhosis or HCC (3,4). The accurate diagnosis is done by percutaneous liver biopsy. Because it is an invasive method, we hypothesized that CT can be used as a non-invasive method for early diagnosis of portal HT in NAFLD. The imaging findings such as coarse echogenity of liver, blunt liver edge, surface nodularity, caudate lobe hypertrophy, shrunken right lobe, increased diameters of portal and splenic veins, splenomegaly, ascites, varices are accepted as advanced fibrosis (4). CT is an effective method for detection of these findings with quantitative measurements.

In this study, we emphasized that the demonstration of the presence of portal HT at CT can be helpful for detection of whether biopsy is required or not. So, the unneeded biopsies can be avoided. The splenic index, portal and splenic venous diameters, which were not searched before in hepatosteatosis patients, were also investigated in this study. Liver spans, splenic indexes and C/RL ratios in NAFLD patients were significantly higher in study group. Therefore, it was shown that the non-enhanced CT can be used efficiently for demonstration of the presence of portal HT in NAFLD patients. Before decision of biopsy, non-enhanced CT can easily be applied. Biopsy candidates can be selected accurately.

In previous studies, Boyce et al. and Saadeh et al. reported that CT can be used as a screening tool for identifying hepatosteatosis (13,14). But, in contrast to our study, the evaluation of progression to steatohepatitis and cirrhosis was not investigated. The imaging features of portal HT were not assessed.

To date, few studies have involved in the effects of US and CT findings on determination of hepatosteatosis and fibrosis. The roles of US and CT were examined on detection of steatosis and fibrosis in 118 NASH patients who underwent biopsy (3). The sensitivities of both US and CT were decreased by increasing fibrosis. Despite these limitations, US and CT were found to be effective for detection of steatosis and fibrosis in patients with NAFLD (3). In another study, the relationship between US and CT findings and histopathological grade and stage were investigated in 22 biopsy proven NASH patients (15). They reported that the mean liver densities and liver/spleen density ratio were statistically lower in their study group when compared with the control group ($p < 0.05$). In contrast to previous study (3), US was demonstrated as an inadequate method to define histopathological severity in NASH patients (15). They found a correlation between CT attenuation of liver and histopathological grade ($p < 0.05$) but not stage (15). In light of these studies, CT was used for detection of portal HT in this study.

In the study by Oliva et al., CT findings of 68 patients with NASH were analyzed (2). Of 68, 12 patients underwent liver biopsy. As a result, NASH patients had statistically higher CC liver span ($p < 0.05$) and C/RL ratio ($p < 0.05$) than those of the controls ($n = 9$) (2). The similar results were achieved, but, additionally, the splenic indexes were also higher in NAFLD patients in our study. The number of patients was smaller compared to our study group.

Hitherto, to the best of our knowledge, none of the previous studies researched about the progression of portal HT with measuring splenic index, diameters of portal and splenic veins in NAFLD patients. In NAFLD patients, the splenic index is accepted as an essential feature of portal HT. Our study is the largest series that investigated the portal HT findings in NAFLD patients at CT. There were statistically significant difference between groups according to CC liver span, splenic index, C/RL ratio ($p < 0.05$). The higher CC liver span, splenic index and C/RL ratio were noted as the findings of portal HT in the study group. Therefore, the portal HT findings at CT imaging in NAFLD patients can lead to biopsy for diagnosis of NASH. Unnecessary procedures may be prevented. The limitation of this study was the lack of histopathological results of NAFLD patients. Further investigations proven by biopsy are needed.

6. Conclusions

NAFLD is a common and severe disease which may cause portal HT and fibrosis. The early diagnosis of portal HT is important. The splenic index and C/RL ratio that are crucial signs of portal HT can be easily measured on CT in NAFLD patients. So, as a non-invasive modality CT has an important role for diagnosis and treatment of these patients additional to clinical findings.

Conflict of interest

The authors have nothing to disclose.

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