RAPID COMMUNICATION

Fatty liver disease in severe obese patients: Diagnostic value of abdominal ultrasound

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Abstract

AIM: To evaluate the sensitivity and specificity of abdominal ultrasound (US) for the diagnosis of hepatic steatosis in severe obese subjects and its relation to histological grade of steatosis.

METHODS: A consecutive series of obese patients, who underwent bariatric surgery from October 2004 to May 2005, was selected. Ultrasonography was performed in all patients as part of routine preoperative time and an intraoperative wedge biopsy was obtained at the beginning of the bariatric surgery. The US and histological findings of steatosis were compared, considering histology as the gold standard.

RESULTS: The study included 105 patients. The mean age was 37.2 ± 10.6 years and 75.2% were female. The histological prevalence of steatosis was 89.5%. The sensitivity and specificity of US in the diagnosis of hepatic steatosis were, respectively, 64.9% (95% CI: 54.9-74.3) and 90.9% (95% CI: 57.1-99.5). The positive predictive value and negative predictive value were, respectively, 98.4% (95% CI: 90.2-99.9) and 23.3% (95% CI: 12.3-39.0). The presence of steatosis on US was associated to advanced grades of steatosis on histology ($P = 0.016$).

CONCLUSION: Preoperative abdominal US in our series has not shown to be an accurate method for the diagnosis of hepatic steatosis in severe obese patients. Until another non-invasive method demonstrates better sensitivity and specificity values, histological evaluation may be recommended to these patients undergoing bariatric surgery.

INTRODUCTION

Non-alcoholic fatty liver disease (NAFLD) has been recognized as an important and common clinical entity, affecting approximately 20% of the general population[1]. The prevalence of NAFLD in obese people has been estimated in 60%-95% and, currently, NAFLD has been suggested to be the liver component of the metabolic syndrome[2,3]. It has a large spectrum, ranging from simple hepatic steatosis to steatohepatitis (NASH) and cirrhosis.

Liver biopsy and histological evaluation have been considered the better methods for the diagnosis of steatosis and to establish the prognosis of NAFLD. However, there are controversies about the indication of biopsy in clinical practice, due the lack of an effective medical therapy for NAFLD and the risks associated with this procedure[4].

Nevertheless, various imaging modalities have been used to diagnose the presence of fat in the liver, as ultrasonography, computerized tomography scan and magnetic resonance imaging. Abdominal ultrasound (US), the

cheapest method, has been the most common modality used in clinical practice. Some parameters allow the diagnosis of fatty liver disease with a sensibility of 83% and a specificity of 100%: a diffuse hyperechoic echotexture; deep attenuation; increased liver echotexture compared with the kidney; and vascular blurring[5]. However, lower sensitivity values of US have been demonstrated among severe obese people[6]. The present study aimed to evaluate the reliability of abdominal US when it is compared to histology to diagnose hepatic steatosis in these patients and its relation to histological grades of steatosis.

MATERIALS AND METHODS

Study group selection

A consecutive series of obese patients who underwent bariatric surgery from October 2004 to May 2005 was selected. The eligible criteria for inclusion were: age above 18 years, preoperative abdominal US, and liver biopsy during the surgery and signer agreement to participate the study. All patients had body mass index above 40 kg/m^2, or 35 kg/m^2 associated to others conditions (hypertension, diabetes, dyslipidemia or sleep apnea)[7]. Patients with alcohol intake above 20 g/d or those who had other chronic liver diseases (HBV or HCV infection, hemochromatosis, autoimmune hepatitis, Wilson's disease, primary biliary cirrhosis, α-1 antitrypsin-deficiency) were excluded. The same surgeon team made all surgeries. Abdominal US was performed in all patients as part of routine preoperative time and different radiologists carried them out.

This study was performed in accordance with a protocol approved by Ethics Committee for Medical Research of Gonçalo Muniz Research Center. All included patients have consented to their participation in this study.

Clinical evaluation

The parameters studied included: age, gender, height, weight, waist circumference, history of hypertension, dyslipidemia, diabetes and drugs use. Laboratory evaluation included: hemoglobin, hematocrite, leucocytes, prothrombin time, ASL, ALT, total bilirubin, albumin, total cholesterol, HDL-cholesterol, triglycerides, fasting plasma glucose and insulin. Abdominal US exam was performed in all patients. Insulin resistance was calculated using Homeostasis Model Assessment Index (HOMA-IR). Patients were categorized as insulin resistant if the HOMA-IR value was equal or greater than 3.0, as previously described[8]. Ultrasonographic definition of steatosis was based on diagnosis criteria usually used in clinical practice, as mentioned above[5].

Liver biopsy and histological analysis

An intraoperative wedge biopsy was obtained at the beginning of the surgery and all samples were processed and examined by a single pathologist, using hematoxylin-eosin stain. Hepatic steatosis in the biopsy specimens, if present, was graded according the number of involved hepatocytes: Grade I (steatosis in 5%-25% of hepatocytes); Grade II (steatosis in 25%-50% of hepatocytes); Grade III (steatosis in 50%-75% of hepatocytes); Grade IV (steatosis in more than 75% of hepatocytes).

Statistical analysis

Data were processed and analyzed using the Statistical Package for Social Science program, version 9.0 (SPSS Inc. Chicago, Illinois, USA). Descriptive statistics of the included variables has been carried out. The US and histological findings of steatosis were compared, considering histology as the gold standard. Subsequently, the sensibility, specificity, positive predictive value and negative predictive value for the US in the diagnosis of hepatic steatosis and theirs 95% confidence intervals were calculated using EPI INFO v6.0 (CDC, USA). A Chi-square test was used to compare categorical variables. All statistical methods were two-tailed and the statistical significance was obtained when $P < 0.05$.

RESULTS

Among the 123 severe obese patients with histological and abdominal US evaluation, 105 were finally included. Seventeen patients were excluded because they had a history of alcohol intake above 20 g/d, and one by hepatitis B infection (HBsAg positive).

Demographic and clinical profiles of these 105 individuals are shown in Table 1. The US examination was normal in 38 (36.2%) cases. Steatosis on US was described in 62 (59.0%) cases. Others imaging findings were: hepatomegaly in 8 (7.6%); colelithiasis in 14 (13.3%); and renal cyst in 3 (2.9%) cases.

The histological prevalence of steatosis was 89.5%. The sensitivity and specificity of abdominal US for the diagnosis of hepatic steatosis were, respectively, 64.9% (95% CI: 54.9-74.3) and 90.9% (95% CI: 57.1-99.5). The positive and negative predictive values were, respectively, 98.4% (95% CI: 90.2-99.9) and 23.3% (95% CI: 12.3-39.0). A false positive rate was found in 9.1% (95% CI: 0.5-37.3) and a false negative rate in 35.1% (95% CI: 26.0-45.2).

Table 2 shows the influence of body mass index on accuracy of abdominal US in the diagnosis of hepatic steatosis. The prevalence of steatosis in patients with body mass index between 35.0 kg/m^2 and 39.9 kg/m^2 and in patients with body mass index above 40 kg/m^2 was 83.3% and 91.3%, respectively.

All individuals were separated into two groups, according to the median of waist circumference (below and above the median value) and the sensibility, specificity, positive predictive value and negative value were analyzed in each group. These results are demonstrated in Table 3. The prevalence of steatosis in patients below and above the median value for waist circumference was 81.1% and 94.6%, respectively.

The presence of steatosis on US was associated with advanced grades of steatosis in the biopsy specimens ($P = 0.016$), as shown in Table 4.

DISCUSSION

Abdominal US has been largely used in clinical practice and in protocols of investigation of patients with NAFLD because it is a cheap and a safe method. As a screening test, its major requirement is a high degree of sensitivity and specificity. In non-obese patients the values of sensitivity

Table 1   Demographic and clinical characteristics of severe obese patients who underwent to bariatric surgery

Characteristics	Value
Female gender - *n* (%)	79 (75.2)
Age, in yr - mean ± SD	37.2 ± 10.6
BMI, in kg/m² - mean ± SD	43.8 ± 5.2
Elevated waist circumference - *n* (%)	105 (100)
Hypertension - *n* (%)	55 (52.4)
Diabetes - *n* (%)	10 (9.5)
Dyslipidemia - *n* (%)	75 (71.4)
Exposure to chemicals - *n* (%)	10 (9.5)
Elevated transaminases – *n* (%)	30 (28.6)
HDL cholesterol - mean ± SD	46.5 ± 5.2
Triglyceride - mean ± SD	157.3 ± 82.8
Fasting plasma glucose level - mean ± SD	102.6 ± 40.8
Insulin resistance - *n* (%)	52 (49.5)

BMI: Body mass index.

Table 2   Levels of sensibility, specificity, PPV and NPV for the ultrasound in the diagnosis of hepatic steatosis by body mass index (BMI) values

Variables	35.0 kg/m² ≤ BMI ≤ 40 kg/m²		BMI ≥ 40 kg/m²	
	Value (%)	95% CI	Value (%)	95% CI
Sensibility	65	40.9-83.7	64.4	52.2-75.0
Specificity	75	21.9-98.7	100	56.1-100
PPV	92.9	64.2-99.6	100	90.6-100
NPV	30	8.1-64.6	21.2	9.6-39.4

PPV: Positive predictive value; NPV: Negative predictive value; 95% CI: Confidence interval of 95%.

Table 3   Levels of sensibility, specificity, PPV and NPV for the ultrasound in the diagnosis of hepatic steatosis by waist circumference (WC) in severe obese patients

Variables	WC ≤ 116.9 kg/m²		WC ≥ 117.0 kg/m²	
	Value (%)	95% CI	Value (%)	95% CI
Sensibility	56.7	37.7-74.0	80	62.5-90.9
Specificity	85.7	42.0-99.2	100	19.8-100
PPV	94.4	70.6-99.7	100	85.0-100
NPV	31.6	13.6-56.5	22.2	3.9-59.8

PPV: Positive predictive value; NPV: Negative predictive value; 95% CI: Confidence interval of 95%.

Table 4   Ultrasound evaluation and grades of steatosis among severe obese patients with steatosis on biopsy (%)

Imaging profile	Grade of steatosis on histological evaluation	
	Grade Ⅰ / Ⅱ	Grade Ⅲ/Ⅳ
Ultrasound without steatosis	97.00	3.00
Ultrasound with steatosis	77.00	23.00

P = 0.016.

and specificity of US range from 83% to 94%, and 84% to 100% respectively[5,9].

The present study with severely obese patients evaluated the sensitivity and specificity of abdominal US for the diagnosis of hepatic steatosis and its relation to histology. The results showed a low performance of US to diagnosis steatosis, however similar results have been demonstrated in patients with body mass index ranging from 35.0 kg/m² to 82.2 kg/m², where the frequency of steatosis was 91.4%[6]. In this case, sensitivity and specificity of US in the diagnosis of steatosis was 49.1% and 75%, respectively[6]. These values are also demonstrated (sensitivity: 43%; specificity: 79%) for the diagnosis hepatic steatosis in patients infected with hepatitis C virus[10].

Several hypotheses may explain this low performance of US in severe obese people. The diagnosis made by different radiologists may introduce variability in interpretation of images. This could be related to the experience of each radiologist and to the lack of clear standards for the diagnosis of hepatic steatosis[11]. The second hypothesis is related to the adipose tissue thickness that may cause technical difficulties for the performance of this exam. The thick layers of subcutaneous fat in obese people may mislead the examiner's judgment of liver echogenicity, as cited in visualizing of the abdominal aorta[12] and renal carcinoma[13]. The image quality rate also has been discussed and different results have as been found. The analysis of 140 patients, who underwent

abdominal US, showed that obesity was also associated with a poor sonographic image[14]. However, another study did not find the same results[15]. Finally, the majority of screening values described in literature were calculated in patients with suspected liver disease. It is more appropriate to use groups of patients resembling those that have been investigated in clinical practice.

This investigation found a higher accuracy of US for the diagnosis of hepatic steatosis in patients with central obesity or more elevated waist circumference. This could be explained by the association between steatosis on ultrasonographic evaluation and histological evidence of steatosis in those patients, as previously showed[9,16]. In a multivariate model involving patients with hepatitis C, Hepburn found that the only statistically significant factor associated with steatosis on US was histological grade, with an odds-ratio of 3.6[10]. In addition, a better performance of ultrasound associated to a more elevated prevalence of NAFLD was also described in obese people undergoing bariatric surgery[6], obtaining results as high as those found in non-obese people[5,9].

The prevalence of steatosis among the patients in this study was elevated (89.5%) and the central obesity was frequent, as previously described studies[6,17,18]. Moreover, the prevalence of NAFLD also has been correlated to body mass index. These results are relevant when we considered that obesity is associated to increased visceral adiposity, free fatty acids and hyperinsulinemia, which are involved in the pathogenesis of NAFLD[19,20].

In conclusion, the results suggest that abdominal US may not be considered an accurate method for the diagnosis of hepatic steatosis in severe obese patients. The liver biopsy and histological evaluation should be recommended to these patients undergoing bariatric surgery, until other non-invasive method demonstrates better sensitivity and specificity values.

COMMENTS

Background

Non-alcoholic fatty liver disease (NAFLD) is a common entity among severe obese patients. Although liver biopsy was the best method for its diagnosis, various imaging modalities have been used to diagnose the presence of fat in the liver, and abdominal ultrasound (US) is the most used in clinical practice. Thus, it is important to elucidate if the abdominal US is a good method to diagnose hepatic steatosis in these patients.

Research frontiers

This study reported the findings of 105 patients with a histological prevalence of steatosis of 89.5%. Low sensitivity and negative predictive rates of US in the diagnosis of hepatic steatosis were described and a better performance of US was associated to advanced grades of steatosis on histology. More accurate methods may change this data.

Innovations and breakthroughs

Although the reliability of abdominal US for diagnose hepatic steatosis was previously reported, the current study showed different values of specificity and sensibility on severe obese patients by body mass index and waist circumference status and the relationship between grade of steatosis on histology and its presence on US evaluation.

Applications

Abdominal US results should be carefully analysed in obese patients. Because of the high prevalence of non-alcoholic fatty liver disease, a more accurate method for its diagnosis, as liver biopsy, is recommended in patients undergoing bariatric surgery.

Terminology

NAFLD means non-alcoholic fatty liver disease; NASH is named as non-alcoholic steatohepatits; HOMA-IR is homeostasis model assessment index - insulin resistance.

Peer review

The authors evaluate the use of US in severely obese patients in order to diagnose hepatic steatosis. They compare histological findings, which they consider to be the golden standard, with US data of the same patients. They observe 123 cases and conclude that US may not be considered an accurate method for the diagnosis of steatosis in these patients. The goals of the study, the materials and methods, results and other parts of the manuscript are well formulated and explain the study in well chosen terms. As a histologist, it is nice to hear that histology is the method of choice for this diagnosis, in spite of the fact that US based diagnosis would have been a very direct, non-invasive and cheap method to use.

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