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GRADING SCALE OF VISCERAL ADIPOSE TISSUE THICKNESS AND THEIR RELATION TO THE NONALCOHOLIC FATTY LIVER DISEASE

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ABSTRACT - ***Context*** - The mesenteric fat is drained by the portal system, being related to the metabolic syndrome which is an important risk factor for non-alcoholic fatty liver disease (NAFLD). ***Objective*** - Graduate of visceral fat thickness and correlate with the NAFLD degree through ultrasonography method. ***Methods*** - We studied 352 subjects for age, gender, measures of subcutaneous fat thickness and visceral fat thickness as well as the presence and degree of liver fatty. Was analyzed the independent relationship between visceral fat thickness and NAFLD, and linear regression analysis was used in order to predict the visceral fat thickness from subcutaneous fat thickness. ***Results*** - The mean age of 225 women (63.9%) and 127 men (36.1%) was 47.5 ± 14.0 (18-77) years, 255 subjects had normal examinations, 97 had NAFLD thus distributed, 37 grade 1, 32 grade 2, and 28 grade 3. The subcutaneous fat thickness ranged from 0.26 to 3.50 cm with a mean of 1.3 ± 0.6 cm and visceral fat thickness ranged from 0.83 to 8.86 cm with a mean of 3.6 ± 1.7 cm. Linear regression showed that for every increase of 1 cm in subcutaneous fat thickness the visceral fat thickness will increase 0.9 cm. ***Conclusion*** - The visceral fat thickness measured by ultrasonography is a useful and seems to be able to help estimate the risk of NAFLD.

HEADINGS - Fatty liver. Intra-abdominal fat. Abdominal subcutaneous fat. Ultrasonography.

INTRODUCTION

The mesenteric fat is drained by the portal system, being related to the metabolic syndrome which is an important risk factor for non-alcoholic fatty liver disease (NAFLD) and has been known to associate with atherosclerosis, inflammation, and insulin resistance[7]. The NAFLD represents a spectrum of clinic pathologic conditions ranging from steatosis alone to nonalcoholic steatohepatitis.

The abdominal fat is composed of abdominal subcutaneous fat and intra-abdominal fat[12]. The computed tomography (CT) is recognized as the standard method for evaluation of visceral fat thickness (VFT) and subcutaneous fat thickness (SFT)[16], but exposure to ionizing radiation, high cost, and low availability difficult the wide use of CT in clinical studies. As alternative method the ultrasonography (US) is a reliable and convenient way of quantifying the VFT and SFT, and the several studies demonstrated a highly significant correlation between the intra-abdominal adipose tissue determined by CT and by US[2, 3 18].

NAFLD affects 16%-23% of general population, and clinical manifestations of NAFLD may range from simple steatosis and/or non-alcoholic steatohepatitis (NASH) to cirrhosis without history of alcohol abuse[1]. It has recently been demonstrated that the risk of hepatic steatosis increases exponentially by the addition of each component of metabolic syndrome: type 2 diabetes mellitus, hyperlipidemia, visceral obesity and hypertension[8]. The US is currently the most common method for screening of asymptomatic patients with elevated liver enzymes and suspected NAFLD, whose findings include hepatomegaly, diffuse increases in the echogenicity of the liver parenchyma, and vascular blunting. It is easily performed and has a low cost, but it also has some limitations how to be operator dependent and subject to significant intraobserver and interobserver variability[14, 17].

In this study evaluated and categorized the VFT and the liver steatosis degree, all measured by US, evaluating the correlation between VFT with NAFLD degree, to determine if these parameter could be an additional index to be used together with NAFLD degrees.

Declared conflict of interest of all authors: none

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METHODS

Subjects

Three hundred 22 individuals referred for abdominal US were enrolled into this prospective study. All the exams were done by the same sonographer. Individuals with body mass index (BMI) less than 20 kg/m^2, history of liver disease, endocrine disease, cardiopathies, kidney disease, and use of medications to alter lipid metabolism were not included in this study.

Ultrasonographic parameters

The US was carried out by using Toshiba Xario® (Ultrasound Imaging System, Japan), with linear-array probe (10.0 MHz) to measure the SFT, convex-array probe (3.5 MHz) for measuring VFT, and assessing the liver, and after a fasting period of 12 hours. Sonographic measurements were performed in all subjects by the samephysician specialized in diagnostic imaging, who was unaware of the patients' medical histories and laboratory findings.

- **SFT -** For measure the transducer was positioned between the xiphoid process and umbilicus on the xipho-umbilical line, and the images were taken during expiration, on a transverse plane with a probe depth of 4 cm, perpendicular to the skin, and was defined as the distance between the cutaneous boundary and the linea alba. The image was captured when the transducer just had contact with the skin to avoid compressing the subcutaneous adipose area, and the maximum SFT was measured five times and the mean value was taken (Figure 1).

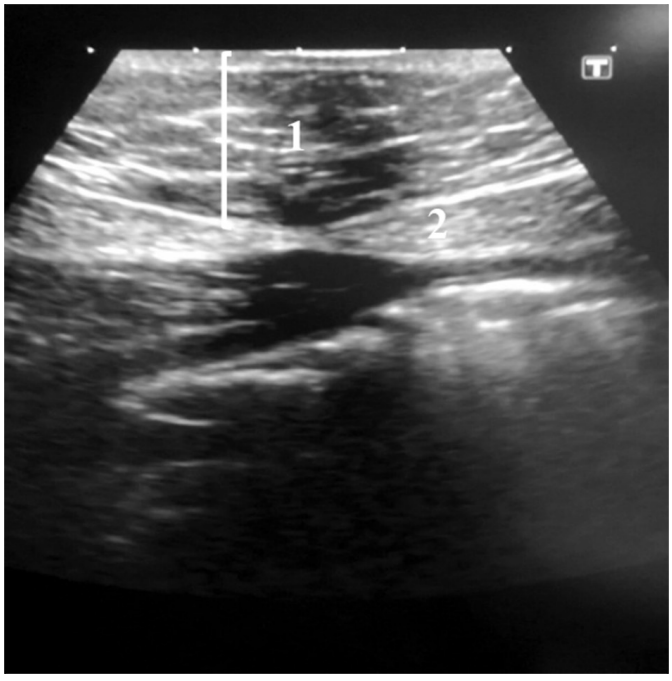

FIGURE 1. Sonographic scheme of measurements subcutaneousfat thickness (1): subcutaneous fat thickness, (2): rectusabdominis muscle

- **VFT -** For measure the transducer was positioned to 5 cm from the umbilicus on the xipho-umbilical line. The VFT was measured directly from frozen images on the screen using calipers positioned at the internal face of the rectus abdominis muscle and the posterior wall of the aorta. To avoid measurement errors, five measurements of VFT were performed for each subject and the mean value was utilized (Figure 2).

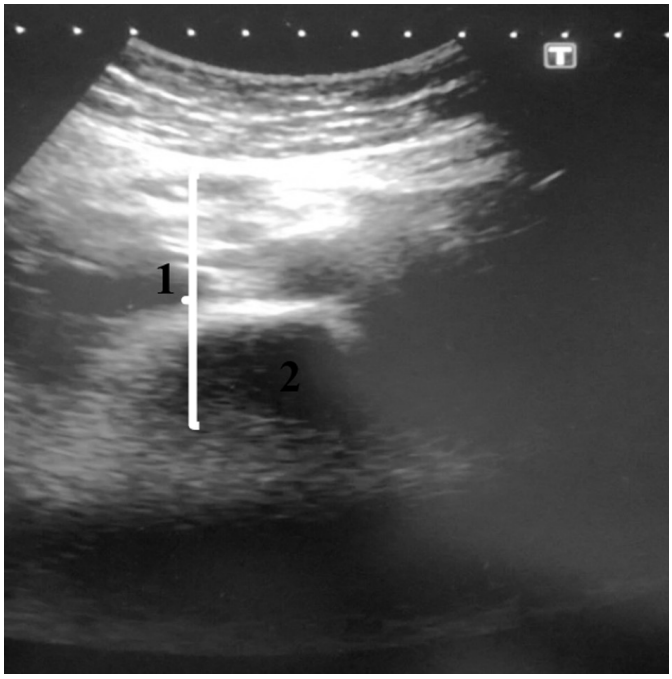

FIGURE 2. Sonographic scheme of measurements visceral fat thickness. (1): visceral fat thickness, (2): aorta

- **Fatty Liver Infiltration -** Liver fatty infiltration was assessed semiquantitative on the basis of abnormal intense, high-level echoes arising from the hepatic parenchyma, echo penetration into the deep portion of the liver, and clarification of blood vessel structure in the liver, and was defined as increased echogenicity of the liver parenchyma without obvious mass effect and slightly impaired or poor visualization of the intrahepatic vessels and of diaphragm. With the same kidney cortex and liver parenchyma echogenicity was evaluated as normal, no fatty liver. Fat infiltration in the liver is described in the ultrasonographic stages[14]. No steatosis, with the same kidney cortex and liver parenchyma echogenicity (Grade 0). Mild liver fatty infiltration (Grade 1) was defined as minimal diffuse increase in echogenicity of the liver parenchyma without mass effect and slightly impaired or poor visualization of the intrahepatic vessels and of diaphragm. Moderate liver fatty infiltration (Grade 2) was defined as medium grade diffuse increase of hepatic echogenicity with slightly impaired visualization of intrahepatic vessels

and diaphragm. Severe liver fatty infiltration (Grade 3) was defined as marked increase in the echogenicity with poor visualization of the posterior segment of the right lobe of the liver, intrahepatic vessel structure and diaphragm limits are vague or non-visualized.

Statistical analysis

Statistical analyses were performed using the IBM SPSS Statistics 20 statistical software (Armonk, NY, U.S.). Continuous variables were expressed as mean ± SD (Standard Deviation), and categorical variables by percentage. Student's *t*-test was performed to compare the means of continuous variables between independent samples. A linear regression analysis of the SFT was used as the independent variable. To assess the *cut-off* point of VFT for each NAFLD, a receiver-operating characteristics (ROC) curve was performed to determine the sensitivity and specificity using VFT as a additional parameter of the NAFLD degree. The area under the ROC curve (AUC) was calculated and the optimal cut-off point of VFT associated with the highest combination of sensitivity and specificity was determined. The level of statistical significance was set at 0.05. $P<0.05$ was considered statistically significant.

RESULTS

The total number of subjects studied was 352 (127 males and 225 females), the mean age was 47.5 ± 14,0 years (range 18–77 years), SFT range of 0.26 a 3.50 cm (mean 1.3 ± 0.6 cm) and VFT range of 0.83 a 8.86 cm (mean 3.6 ± 1.7 cm).

Two hundred fifty-five (72.4%) subjects had a normal US, and NAFLD was diagnosed in 97 (27.6%) subjects, with 10.2% degree 1, 9.4% degree 2, and 8.0% degree 3. Table 1 shows the comparison of the groups with and without NAFLD.

TABLE 1. Characteristics of patients with and without non-alcoholic fatty liver disease (NAFLD)

VARIABLES	NAFLD		*P*-value
	YES (n = 255)	NO (n = 97)	
Age (years)	46.6 ± 14.3	49.9 ± 12.4	0.048
Sex (M/F)	85/170	42/55	0.82
SFT (cm)	1.2 ± 0.6	1.7 ± 0.6	< 0.001
VFT (cm)	3.2 ± 1.4	4.9 ± 1.7	< 0.001

M: Male; F: Female; SFT: subcutaneous fat thickness; VFT: visceral fat thickness

Linear regression analysis showed that each increase of 1.0 cm in TSF increase 0.9cm in the VFT as evidenced in the equation forward (Table 2):y = 2,44 + 0,94x. According to the coefficient of determination ($r^2 = 0.12$), we conclude that 12% of VFT variation was due to variation of the SFT.

TABLE 2. Linear regression analysis – dependent variable visceral fat thickness

Model	B	Std. Error	Beta (ST)	T	Sig
Constant	2.436	0.194		12.557	< 0.001
SFT	0.936	0.135	0.347	6.920	< 0.001

SFT: subcutaneous fat thickness; r = 0,347

The ROC curve was produced using as gold standard the US categorized as having NAFLD (yes or no) in order to find the best cut-off of VFT that indicate NAFLD.

The AUC curve between US and NAFLD was 0.833 (95% CI: 0.788–0.870). AUC curve between VFT and the individual with normal liver was 0.675 (95% CI: 0.601-0.709), cut-off of 3.53 cm. AUC between VFT and the individual with grade 1 NAFLD was 0.830 (95% CI: 0.776 to 0.860), cut-off of 4.29 cm. The AUC between VFT and the individual with grade 2 NAFLD was 0.630 (95% CI: 0.530 to 0.690), cut-off of 5.04 cm. The AUC between VFT and the individual with grade 3 NAFLD was 0.762 (95% IC: 0.711–0.806) with a cut-off 5.78 cm (Table 3). We found a positive correlation between VFT and NAFLD degree.

TABLE 3. Visceral fat thickness (VFT) cut-off x grade non-alcoholic fatty liver disease (NAFLD)

Grade NAFLD	VFT cut-off (cm)
Normal liver	3.53
Grade 1	4.29
Grade 2	5.04
Grade 3	5.78

With these results categorized in VFT degrees according to their thickness: Grade 0 <3.53 cm, Grade 1> 3.53cm to 4.29 cm, Grade 2> 4.29 cm to 5.04 cm, and Grade 3> 5.04 cm.

DISCUSSION

In this study, we showed the utility of the VFT in degrees according to their thickness where found a cut-off point for each NAFLD degree, can be indicated as an additional parameter in ultrasonographic grading of NAFLD. We evaluated the role of visceral fat accumulation and subcutaneous fat accumulation using US for measure of VFT and SFT for to determine the NAFLD degree, and evidenced that VFT measured by US can be used to forecast the NAFLD, given that the group with NAFLD presented significantly higher values of VFT and SFT, comparing with without NAFLD patients. Our results are in agreement with several studies that have shown an increased VFT measured indirectly by waist to hip ratio and directly by non-invasive imaging techniques in individuals with NAFLD is related to the severity of fatty liver[4, 6].

We categorized in degrees the VFT of according to their thickness in three degree: Grade 0<3.53 cm, Grade 1>3.53cm to 4.29 cm, Grade 2>4.29 cm to 5.04 cm, and Grade 3>5.04 cm. With this categorization we found that a VFT measure is a useful additional parameter in screening procedure in the diagnosis of NAFLD degree.

The link between visceral fat accumulation and NAFLD can be explained by resistance to the antilipolytic action of insulin inducing the rapid mobilization of fatty acids from visceral fat rather than from subcutaneous fat and their direct inflow to the liver, suggesting that VFT that might be a primary phenomenon, playing a crucial role in NAFLD[10].

NAFLD is characterized by histological findings of macrovesicular hepatic steatosis in individuals consuming little or no alcohol[11]. A limitation of the present study was the lack of histological data, which would better describe the grade of NAFLD, and the VFT could be less sensitive by ultrasound. However, US examination has been proposed as an alternative non-invasive, cheap and reliable technique to evaluate VFT and NAFLD, which was supported by high sensitivity, specificity and diagnostic agreement with computed tomography, however US proved to be useful in identifying intra-abdominal fat and NAFLD diagnosis[15].

US measurement of VFT showed significant correlation between VFT and visceral fat area measured by bioimpedance examinations and BMI, well with as the computed tomographically determined "gold standard" values of visceral fat quantity[19]. Using ultrasonography, was showed that VFT, rather than body weight or body fat, was the only independent risk factor for NAFLD[5]. Ours results showed that VFT is an independent risk factor for NAFLD, and in this study, the VFT increased in parallel with the NAFLD degree.

The subcutaneous fat is superficial to the abdominal and back muscles. It has been suggested that subcutaneous abdominal fat has a strong association with visceral fat, and has independent significance after adjusting for visceral fat[9]. This study demonstrated that the variance in VFT can be explained by variations in TSF, because 12% of VFT variation was due to variation of the SFT, and to each increase of 1.0 cm in TSF increase 0.9 cm in the VFT. The opposite does not occur, because was showed that after severe weight loss, the SFT at the abdominal level is reduced in greater proportion than VFT, suggesting that visceral fat does not reflect nutritional status[13].

CONCLUSION

In the present study was showed that is possible classify the VFT in degrees according to their thickness and found a cut-off point for each NAFLD degree. Thus, the VFT could be an additional parameter that could be associated with NAFLD degree. These results could be applied in the routine of abdominal ultrasonography exams for help in graduating of liver steatosis, before of liver biopsy need (which is an invasive method firmly reluctant by most of patients), correlating with the VFT showing the utility and efficiency of this parameter.

Andrade LJO, Melo PRS, Paraná R, Datro C. Escala de classificação da espessura do tecido adiposo visceral e sua relação com a doença gordurosa hepática não alcoólica. Arq Gastroenterol. 2014,51(2):118-22.

RESUMO - ***Contexto*** - A gordura mesentérica é drenada pelo sistema venoso portal, estando relacionada à síndrome metabólica, que é um importante fator de risco para doença de infiltração gordurosa do fígado. ***Objetivo*** - Graduar a espessura do tecido adiposo visceral e correlacionar com o grau de doença de infiltração gordurosa do fígado através do exame ultrassonográfico. ***Métodos*** - Foram estudados 352 indivíduos, avaliando-se idade, gênero, medidas da espessura da gordura subcutânea e tecido adiposo visceral, a presença e o grau de doença de infiltração gordurosa do fígado. Foi analisada a relação independente entre tecido adiposo visceral e doença de infiltração gordurosa do fígado, e a regressão linear foi utilizada para prever a tecido adiposo visceral pela espessura da gordura subcutânea. ***Resultados*** - A idade média de 225 (63,9%) mulheres e 127 (36,1%) homens foi 47,5 ± 14,0 (18-77) anos, 255 indivíduos apresentaram exames normais, 97 apresentaram doença de infiltração gordurosa do fígado assim distribuídos: 37 grau 1, 32 grau 2 e 28 grau 3. A espessura da gordura subcutânea variou de 0,26 e 3,50 cm, com uma média de 1,3 ± 0,6 cm e a tecido adiposo visceral variou de 0,83 a 8,86 cm, com uma média de 3,6 ± 1,7 cm. A regressão linear demonstrou que para cada aumento de 1 cm da espessura da gordura subcutânea o tecido adiposo visceral aumentará 0,9 cm. ***Conclusão*** – O tecido adiposo visceral medido por ultrassonografia é um instrumento útil e parece ser capaz de estimar o risco de doença de infiltração gordurosa do fígado.

DESCRITORES - Fígado gorduroso. Gordura intra-abdominal. Gordura subcutânea abdominal. Ultrassonografia.

REFERENCES

1. Angulo P. Non-alcoholic fatty liver disease. N Engl J Med. 2002 Apr 18; 346:1221-31.
2. Armellini F, Zamboni M, Rigo L, Bergamo-Andreis IA, Robbi R, De Marchi M, et al. Sonography detection of small intra-abdominal fat variations. Int J Obes. 1991;15:847-52.
3. Armellini F, Zamboni M, Robbi R, Todesco T, Rigo L, Bergamo-Andreis IA, et al. Total and intra-abdominal fat measurements by ultrasound and computerized tomography. Int J Obes Relat Metab Disord. 1993;17:209-14.
4. Dâmaso AR, do Prado WL, de Piano A, Tock L, Caranti DA, Lofrano MC, et al. Relationship between nonalcoholic fatty liver disease prevalence and visceral fat in obese adolescents. Dig Liver Dis. 2008;40:132-9.
5. Despre's JP. Visceral obesity and dyslipidemia: contribution of insulin resistance and genetic susceptibility. In: Angel A, Anderson H, Bouchard C, Lau D, Leiter L, Mendelson R (eds). Progress in Obesity Research: Proceedings of the Seventh International Congress on Obesity (Toronto, Canada, August 20–25, 1994). John Libbey & Company, London, vol 7; 1996. p.525–32.
6. Eguchi Y, Eguchi T, Mizuta T, Ide Y, Yasutake T, Iwakiri R, et al. Visceral fat accumulation and insulin resistance are important factors in nonalcoholic fatty liver disease. J Gastroenterol. 2006;41:462-9.
7. Fujioka S, Matsuzawa Y, Tokunaga K, Tauri S. Contribution of intra-abdominal fat accumulation to the impairment of glucose and lipid metabolism in human obesity. Metabolism. 1987;36:54-9.
8. García-Monzón C, Martín-Pérez E, Iacono OL, Fernández-Bermejo M, Majano PL, Apolinario A, et al. Characterization of pathogenic and prognostic factors of nonalcoholic steatohepatitis associated with obesity. J Hepatol. 2000;33:716-24.
9. Goodpaster BH, Thaete FL, Simoneau JA, Kelley DE. Subcutaneous abdominal fat and thigh muscle composition predict insulin sensitivity independently of visceral fat. Diabetes. 1997;46:1579-85.
10. Koda M, Kawakami M, Murawaki Y, Senda M. The impact of visceral fat in nonalcoholic fatty liver disease: cross-sectional and longitudinal studies. J Gastroenterol. 2007;42:897-903.
11. Ludwig J, Viggiano TR, McGill DB, Oh BJ. Nonalcoholic steatohepatitis: Mayo Clinic experiences with a hithertounnamed disease. Mayo Clin Proc. 1980; 55: 434-8.
12. Mårin P, Andersson B, Ottosson M, Olbe L, Chowdhury B, Kvist H, et al. The morphology and metabolism of intraabdominal adipose tissue in men. Metabolism. 1992;41:1242-8.
13. Mayo-Smith W, Hayes CW, Biller BM, Klibanski A, Rosenthal H, Rosenthal DI. Body fat distribution measured with CT: correlations in healthy subjects, patients with anorexia nervosa, and patients with Cushing syndrome. Radiology. 1989;170:515-8.
14. Osawa H, Mori Y. Sonographic diagnosis of fatty liver using a histogram technique that compares liver and renal cortical echo amplitudes. Journal of Clinical Ultrasound. 1996;24:25–29.
15. Ribeiro-Filho FF, Faria NA, Ajzen S, Zanella MT, Ferreira SR. Methods of estimation of visceral fat: advantages of ultrasonography. Obes Res. 2003;11:1488-94.
16. Rossner S, Bo WJ, Hiltbrandt E, Hinson W, Karstaedt N, Santago P, et al. Adipose tissue determinations in cadavers: a comparison between cross-sectional planimetry and computed tomography. Int J Obes. 1990;14:893-902.
17. Strauss S, Gavish E, Gottlieb P, Katsnelson L. Interobserver and intraobserver variability in the sonographic assessment of fatty liver. American Journal of Roentgenology. 2007;189:W320–3.
18. Suzuki R, Watanabe S, Hirai Y, Akiyama K, Nishide T, Matsushima Y, et al. Abdominal wall fat index, estimated by ultrasonography, for assessment of the ratio of visceral fat to subcutaneous fat in the abdomen. Am J Med. 1993;95:309-14.
19. Szebeni A, Halmy L.Significance of ultrasound-measured visceral fat thickness in obesity. Orv Hetil. 2010;151:1580-4.

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