Bedside ultrasound in the diagnosis of nonalcoholic fatty liver disease

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Author contributions: Khov N and Sharma A performed the literature search and wrote the paper; Riley TR participated in drafting the outline and revised the paper.
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Received: November 18, 2013 Revised: January 25, 2014
Accepted: March 19, 2014
Published online: June 14, 2014

Abstract
Non-alcoholic fatty liver disease (NAFLD) is the most common liver disease in the United States. While the American Association for the Study of Liver Diseases guidelines define NAFLD as hepatic steatosis detected either on histology or imaging without a secondary cause of abnormal hepatic fat accumulation, no imaging modality is recommended as standard of care for screening or diagnosis. Bedside ultrasound has been evaluated as a non-invasive method of diagnosing NAFLD with the presence of characteristic sonographic findings. Prior studies suggest characteristic sonographic findings for NAFLD include bright hepatic echoes, increased hepatorenal echogenicity, vascular blurring of portal or hepatic vein and subcutaneous tissue thickness. These sonographic characteristics have not been shown to aid bedside clinicians easily identify potential cases of NAFLD. While sonographic findings such as attenuation of image, diffuse echogenicity, uniform heterogeneous liver, thick subcutaneous depth, and enlarged liver filling of the entire field could be identified by clinicians from bedside ultrasound. The accessibility, ease of use, and low-side effect profile of ultrasound make bedside ultrasound an appealing imaging modality in the detection of hepatic steatosis. When used with appropriate clinical risk factors and steatosis involves greater than 33% of the liver, ultrasound can reliably diagnose NAFLD. Despite the ability of ultrasound in detecting moderate hepatic steatosis, it cannot replace liver biopsy in staging the degree of fibrosis. The purpose of this review is to examine the diagnostic accuracy, utility, and limitations of ultrasound in the diagnosis of NAFLD and its potential use by clinicians in routine practices.

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Key words: Non-alcoholic fatty liver disease; Non-alcoholic steatohepatitis; Liver fibrosis; Liver biopsy; Liver disease; Liver cirrhosis; Steatosis; Bedside ultrasound

Core tip: Ultrasound is a non-invasive, widely available, and accurate tool in the detection of Non-alcoholic fatty liver disease (NAFLD). Ultrasound should be used as the first-line diagnostic test in patients with abnormal liver enzymes when other causes are excluded. Clinical risk factors, when used with ultrasound findings, have high accuracy in identifying NAFLD patients. We present an algorithm for chronic abnormal liver enzymes that illustrates the use of ultrasound in reducing the need for liver biopsy in the diagnosis of NAFLD. Clinicians should be aware of the known limitations of ultrasound, including the inability to grade or stage fibrosis in NAFLD patients.

Khov N, Sharma A, Riley TR. Bedside ultrasound in the diagnosis of nonalcoholic fatty liver disease. World J Gastroenterol 2014; 20(22): 6821-6825 Available from: URL: http://www.wjgnet.com/1007-9327/full/v20/i22/6821.htm DOI: http://dx.doi.org/10.3748/wjg.v20.i22.6821
INTRODUCTION

The potential role of ultrasound by the clinician is increasing. The estimated prevalence of non-alcoholic fatty liver disease (NAFLD) is approximately 34%. Strongly associated with metabolic syndrome, the incidence of NAFLD will continue to rise with the projected progression of the obesity epidemic[1,2]. NAFLD includes a wide spectrum of disease activity, from simple steatosis to non-alcoholic steatohepatitis (NASH)[3,4]. Simple steatosis has a benign and potentially reversible course, however, NASH can progress to advanced fibrosis, cirrhosis, and hepatocellular carcinoma[3,4]. The diagnosis of NAFLD remains under recognized as most patients are asymptomatic until late stages of disease[5]. Liver biopsy is the gold standard in diagnosing NAFLD and the most accurate tool for grading fibrosis, however, is invasive and carries the risk of complications[2,3]. Bedside ultrasound, as a non-invasive and readily available tool, has an important role in diagnosing NAFLD. In this paper we present a review of current knowledge and literature on the utility of bedside ultrasound in the diagnosis of NAFLD by the clinician.

CHARACTERISTIC SONOGRAPHIC FEATURES OF NAFLD

High diagnostic accuracy can be achieved by the ultrasound when sonographic features unique to NAFLD are standardized and used to aid in diagnosis. Bright hepatic echoes, increased hepatorenal echogenicity and vascular blurring of portal or hepatic vein have been classified as unique sonographic features of NAFLD. In a prospective study by Dasarathy et al[5], real time ultrasound was performed followed by a liver biopsy to evaluate the accuracy of ultrasound in hepatic steatosis. When steatosis was greater than 20% on biopsy, these sonographic features were able to predict the presence of NAFLD with greater than 90% sensitivity. Lower levels of fat content resulted in reduction of sensitivity[6]. A sonographic scoring system used by Hamaguchi et al[7] was developed based on similar pre-determined imaging findings. By using hepatorenal echo contrast, liver brightness, deep attenuation and vascular blurring, they were able to report similar sensitivities in detecting histologically proven NAFLD[7].

Subcutaneous tissue thickness, measured as the distance between the skin surface and the liver surface, has been shown to be another characteristic sonographic finding. When compared to other non-NAFLD liver diseases, NAFLD patients had thicker subcutaneous tissue, with a mean measurement of 25.6 ± 5.6 mm. In comparison, the non-NAFLD patients had a mean subcutaneous tissue thickness of 19.5 ± 5.2 mm. NAFLD was unlikely when the subcutaneous tissue thickness was less than 20 mm[8]. Along with subcutaneous tissue thickness, Riley et al[9] defined five characteristic sonographic findings for NAFLD that can be identified by the clinician:

(1) attenuation of image quickly within 4-5 cm of depth, making deeper structures difficult to decipher; (2) echogenic diffusely but particularly important to note brightness within the first 2-3 cm of depth; (3) liver uniformly heterogeneous; (4) thick subcutaneous depth (> 2 cm); and (5) liver fills entire field with no edges visible (viewed as helpful but not necessary for diagnosis), as shown in a prototypical bedside ultrasound image in Figure 1. Using these characteristic sonographic findings, bedside ultrasound yielded a sensitivity of 80% and specificity of 99%.

EASE OF CLINICAL USE AND INTERPRETATION

These typical sonographic features can be identified by the clinician with the use of bedside ultrasound. Ultrasound can result in an immediate diagnosis and development of a plan of care at the initial visit. Riley et al[9] demonstrated that clinical providers could be trained to identify ultrasound images consistent with NAFLD after a brief 20-min session. Healthcare providers were subsequently able to reliably identify NAFLD using the prototype image with substantial inter-observer agreement, κ = 0.76[9].

ULTRASOUND AS A DIAGNOSTIC TOOL

In patients with chronic hepatitis, an algorithm weighing the relative importance between characteristic ultrasound findings and clinical risk factors has been proposed for the diagnosis of NAFLD, as shown in Figure 2. To use the algorithm, viral hepatitis, autoimmune liver disease, alcoholic liver diseases, and genetic diseases must first be excluded. Clinical risks include any of the following: diabetes, body mass index (BMI) greater than 30, hepatomegaly, and hyperlipidemia[9]. Ultrasound features include any 4 of the following 5 sonographic features: (1) attenuation of image quickly within 4-5 cm of depth;
(2) echogenic diffusely but particularly important to note brightness within the first 2-3 cm of depth; (3) liver uniformly heterogeneous; (4) thick subcutaneous depth (>2 cm); and (5) liver fills entire field with no visible edges. Characteristic features for NAFLD on ultrasound were found to be the strongest independent predictor on multivariable analysis. Other clinical risk factors with significant correlation with the biopsy-proven diagnosis of NAFLD on multivariate analysis include the presence of diabetes, BMI >30, hepatomegaly, female gender, age >55, and triglyceride greater than 250. The severity of hepatic steatosis on ultrasound in the presence of metabolic syndrome is a better non-invasive tool for monitoring liver disease than liver enzymes. Normal alanine aminotransferase (ALT) level alone was not sufficient for exclusions of significant hepatic steatosis. Normal alanine aminotransferase (ALT) level alone was not sufficient for exclusions of significant hepatic steatosis. Aspartate aminotransferase (AST)/ALT ratio greater than 1, however, has been associated to findings of advanced fibrosis on liver biopsy. The recognition of appropriate clinical factors in conjunction with characteristic ultrasound findings can lead to an accurate diagnosis of NAFLD without the use of invasive testing, and also identify those individuals that should go onto have a liver biopsy.

**ULTRASOUND AS A SCREENING TOOL**

The prevalence of NAFLD and NASH may be higher than previously predicted creating the need for an accurate, non-invasive, and easily available modality for the diagnosis of NAFLD in the asymptomatic patient. When Williams et al. used ultrasound to screen asymptomatic individuals in the general population without known liver disease or significant alcohol use, they found non-alcoholic fatty liver disease to be more prevalent than previously reported. All individuals who had ultrasound findings suggestive of fatty liver had a liver biopsy to confirm their diagnosis. Using ultrasound as a screening tool, they found NASH and NAFLD to be present at 12.2% and 46% of the population, respectively.

Detection of NAFLD in potential living donor liver transplantation is an important part of the routine pre-transplant work-up. During the evaluation of living donors, invasive procedures for healthy donors should be minimized. It is well-recognized that the diagnostic accuracy of ultrasound diminishes with less than 20% hepatic steatosis. Identification of living donor candidates with a higher degree of hepatic steatosis by ultrasound may allow them to forgo unnecessary liver biopsy needed for such assessment. A study by Lee et al. evaluated 589 living donor candidates with ultrasound, CT scan, and liver biopsy. They found a higher incidence than previously reported. In their study, 51.4% living donor candidates has greater than 5% steatosis and 10.4% had greater than 30% steatosis. Ultrasound had a sensitivity of 92.3% when screening this population for a pre-transplant work-up.

In comparison to other non-invasive imaging techniques, ultrasound has comparable sensitivities, greater ease of use, availability, and lower cost in screening for moderate to severe degrees of NAFLD. Although other modalities such as dual-gradient echo magnetic resonance imaging (DGE-MRI) is more accurate with sensitivity and specificity greater than 90% when hepatic steatosis was greater than 5%, the difference between DGE-MRI's sen-
sitivity and ultrasound were statistically insignificant when steatosis was greater than 30%[17].

**LIMITATIONS OF ULTRASOUND**

Ultrasound is limited in its utility in several settings, as shown in Table 1. As previously mentioned, multiple studies have shown that ultrasound underestimates the prevalence of hepatic steatosis when less than 20% of steatosis is present. The sensitivity for detecting mild degrees of steatosis is low, ranging from 55%-90%[1,3,6,13,16,17]. Guajardo-Salinas et al[19] reported a low sensitivity in detecting all degrees of NASH in obese individuals (mean BMI 46-49) by ultrasound. In his retrospective chart review of ultrasound reports, the right upper quadrant ultrasound was an unreliable tool for screening fatty liver, with a sensitivity of 40%. In another study evaluating the diagnosis of NAFLD by ultrasound in obese patients undergoing bariatric surgery, de Moura Almeida et al[19] also found a low sensitivity of 64.9%. In this study, patients had an average BMI of 43.8. Low sensitivities in both these studies may be a result of the lack of clearly defined characteristic sonographic findings for the diagnosis of NAFLD. Nonetheless, severe obesity may also limit the ability to reliably detect liver echogenicity due to thick layers of subcutaneous fat[19,20].

When used in the setting of other chronic liver diseases, such as chronic hepatitis C, ultrasound had acceptably low sensitivity and specificity in identifying hepatic steatosis[22,21]. Perez et al[23] revealed in their chronic hepatitis C patients that ultrasound had only a sensitivity of 32% for detecting fat on biopsy in these patients. These low sensitivities suggest that ultrasound should not be the only modality used in detecting co-existing NAFLD in patients with chronic hepatitis C.

Perhaps the most important limitation of using ultrasound alone is its inability to correlate with the degree of fibrosis[22,20]. Ultrasound scoring systems fall short of distinguishing between progressive NASH and benign steatosis. Studies have shown poor correlation between sonographic findings and the histological stage of fibrosis on biopsy[22,23]. Ballestri et al[22] developed the ultrasound fatty liver indicator (US-FLI), a scoring system based on ultrasound findings that could predict the presence of steatosis. Although this score showed significant correlation with metabolic derangements, the US-FLI had poor performance in predicting the presence of NASH. Similarly, when Charatcharoenwitthaya and Lindor[23] evaluated various radiologic modalities in NASH, they found that neither ultrasound, CT scan, nor MRI were able to distinguish between NASH and other degrees of NAFLD. Other studies have also shown that ultrasound cannot be used to grade degrees of fibrosis and cannot replace needle biopsy in distinguishing simple steatosis from steatohepatitis[24,25].

**DISCUSSION**

Ultrasound represents a non-invasive, widely available, and accurate tool in the detection of NAFLD. Although there is limited data available to support the use of ultrasound as a screening tool, ultrasound can be a powerful tool in the setting of known liver abnormality. Ultrasound should be used as the first-line diagnostic test in patients with abnormal liver enzymes. Standardized, characteristic sonographic findings are able to reliably identify patients with NAFLD. Clinical risk factors, when used with ultrasound findings, have high utility in identifying NAFLD patients and initiating an early plan of care. In a study by Riley et al[26], the risk of advanced fibrosis was increased in patients with a BMI greater than 30 for over 15 years. In this clinical setting, with abnormal liver enzymes and ultrasound findings suggestive of NAFLD, these patients would benefit from a liver biopsy to identify the degree of fibrosis.

Bedside ultrasound can be incorporated into the training of clinicians and used in hepatology practices at outpatient visits. There is also potential use of ultrasound when screening liver donor candidates. Ultrasound can be used to exclude candidates with existing hepatic steatosis without putting them through liver biopsy. An early ultrasound and diagnosis will allow a potential liver donor candidate with hepatic steatosis to initiate early intervention and re-evaluation at a later date.

In conclusion, the bedside ultrasound is a powerful and useful diagnostic tool in the detection of NAFLD. It is an accurate and reliable method that can reduce the need for liver biopsy in the appropriate clinical setting. Clinicians should be aware of the known limitations when interpreting ultrasound, most importantly the inability to grade or stage degree of fibrosis in NAFLD patients. While bedside ultrasound cannot replace liver biopsy in monitoring the progression from simple steatosis to NASH, its accessibility, ease of use, and low-side effect profile make it an appealing diagnostic tool when used in the appropriate clinical setting. As the incidence of NAFLD continues to rise, we expect an increase in the use of bedside ultrasound by clinicians as it becomes integrated into the routine practices of gastroenterologists and hepatologists.

Table 1 Strength and weakness of ultrasound to diagnosis non-alcoholic fatty liver disease

| Utility of ultrasound | Non-invasive | Easy of clinician use | Ease of clinician interpretation | Widely available | Low cost | Allows quick diagnosis | Limitations of ultrasound | Cannot grade degree of fibrosis | Limited use in pre-existing chronic liver disease | Limited use in obese patients | Low sensitivity when steatosis is less than 20%-30% |
|-----------------------|-------------|----------------------|---------------------------------|-----------------|---------|-----------------------|--------------------------|---------------------------|---------------------------------|---------------------|-------------------------------|

Notes:

1. Ultrasound scoring systems fall short of distinguishing between progressive NASH and benign steatosis.
2. Studies have shown poor correlation between sonographic findings and the histological stage of fibrosis on biopsy.
3. Ballestri et al developed the ultrasound fatty liver indicator (US-FLI), a scoring system based on ultrasound findings that could predict the presence of steatosis.
4. Although this score showed significant correlation with metabolic derangements, the US-FLI had poor performance in predicting the presence of NASH.
5. Similarly, when Charatcharoenwitthaya and Lindor evaluated various radiologic modalities in NASH, they found that neither ultrasound, CT scan, nor MRI were able to distinguish between NASH and other degrees of NAFLD.
6. Other studies have also shown that ultrasound cannot be used to grade degrees of fibrosis and cannot replace needle biopsy in distinguishing simple steatosis from steatohepatitis.
REFERENCES

1 Lee SS, Park SH, Kim HJ, Kim SY, Kim MY, Kim DY, Suh DJ, Kim KM, Bae MH, Lee JY, Lee SG, Yu ES. Non-invasive assessment of hepatic steatosis: prospective comparison of the accuracy of imaging examinations. J Hepatol 2010; 52: 579-585 [PMID: 20185194 DOI: 10.1016/j.jhep.2010.01.008]

2 Chen CH, Lin ST, Yang CC, Yeh YH, Kuo CL, Nien CK. The accuracy of sonography in predicting steatosis and fibrosis in chronic hepatitis C. Dig Dis Sci 2008; 53: 1699-1706 [PMID: 17939048 DOI: 10.1007/s10046-007-0048-2]

3 Barisić N, Lerotic I, Smrcič-Duvnjak I, Tomašić V, Duvnjak M. Overview and developments in noninvasive diagnosis of nonalcoholic fatty liver disease. World J Gastroenterol 2012; 18: 3945-3954 [PMID: 22912545 DOI: 10.3748/wjg.v18.i30.3945]

4 Ahmed MH, Barakat S, Almobarak AO. Nonalcoholic fatty liver disease and cardiovascular disease: has the time come for cardiologists to be hepatologists? J Obes 2012; 2012: 483135 [PMID: 23320150]

5 Hernaez R, Lazo M, Bonekamp S, Kamel I, Brancati FL, Guallar E, Clark JM. Diagnostic accuracy and reliability of ultrasonography for the detection of fatty liver: a meta-analysis. Hepatology 2011; 54: 1082-1090 [PMID: 21618575 DOI: 10.1002/hep.24452]

6 Dasarathy S, Dasarathy J, Khiyami A, Joseph R, Lopez R, McCullough AJ. Validity of real time ultrasound in the diagnosis of hepatic steatosis: a prospective study. J Hepatol 2009; 51: 1081-1087 [PMID: 19846224 DOI: 10.1016/j.jhep.2009.09.001]

7 Hamaguchi M, Kojima T, Itoh Y, Harano Y, Fuji K, Nakajima T, Kato T, Takeda N, Okuda J, Ida K, Kawaihito Y, Yoshikawa T, Okanoue T. The severity of ultrasonographic findings in nonalcoholic fatty liver disease reflects the metabolic syndrome and visceral fat accumulation. Am J Gastroenterol 2007; 102: 2708-2715 [PMID: 17984848 DOI: 10.1111/j.1572-0241.2007.01526.x]

8 Riley TR, Bruno MA. Sonographic measurement of the thickness of subcutaneous tissues in nonalcoholic fatty liver disease versus other chronic liver diseases. J Clin Ultrasound 2005; 33: 439-441 [PMID: 16281268 DOI: 10.1002/jcu.20164]

9 Riley TR, Mendoza A, Bruno MA. Bedside ultrasound can predict nonalcoholic fatty liver disease in the hands of clinicians using a prototype image. Dig Dis Sci 2006; 51: 982-985 [PMID: 16783524 DOI: 10.1007/s10620-006-0943-6]

10 Riley TR, Khan A. Risk factors and ultrasound can predict chronic hepatitis caused by nonalcoholic fatty liver disease. Dig Dis Sci 2006; 51: 41-44 [PMID: 16416209 DOI: 10.1007/s10620-006-3082-6]

11 Kim HC, Choi SH, Shin HW, Cheong JY, Lee KW, Lee HC, Huh KB, Kim DJ. Severity of ultrasonographic liver steatosis and metabolic syndrome in Korean men and women. World J Gastroenterol 2005; 11: 5314-5321 [PMID: 16149138]

12 Lee JY, Kim KM, Lee SG, Yu E, Lim YS, Lee HC, Chung YH, Lee YS, Sub DJ. Prevalence and risk factors of non-alcoholic fatty liver disease in potential living liver donors in Korea: a review of 589 consecutive liver biopsies in a single center. J Hepatol 2007; 47: 239-244 [PMID: 17400323]

13 Grandison GA, Angulo P. Can NASH be diagnosed, graded, and staged noninvasively? Clin Liver Dis 2012; 16: 567-585 [PMID: 22824881]

14 Williams CD, Stengel J, Asike MI, Torres DM, Shaw J, Conneras M, Landt CL, Harrison SA. Prevalence of nonalcoholic fatty liver disease and nonalcoholic steatohepatitis among a largely middle-aged population utilizing ultrasound and liver biopsy: a prospective study. Gastroenterology 2011; 140: 124-131 [PMID: 20858492 DOI: 10.1053/j.gastro.2010.09.038]

15 Yamashiki N, Sugawara Y, Tamura S, Kaneko J, Matsu Y, Togashi J, Okhi T, Yoshida H, Omata M, Makuchii M, Kokudo N. Noninvasive estimation of hepatic steatosis in living liver donors: usefulness of visceral fat area measurement. Transplantation 2009; 88: 575-581 [PMID: 19966642 DOI: 10.1097/TP.0b013e3181b1c19]

16 Festi D, Schiurmerini R, Marzi L, Di Biase AR, Mandolesi D, Montrone L, Scialici E, Bonato G, Marcheisini-Degigan G, Colecchia A. Review article: the diagnosis of non-alcoholic fatty liver disease – a availability and accuracy of non-invasive methods. Aliment Pharmacol Ther 2013; 37: 392-400 [PMID: 23278163 DOI: 10.1111/apt.12186]

17 Mottin CC, Moretto M, Padoin AV, Swarowski AM, Toneto MG, Glock L, Repetto G. The role of ultrasound in the diagnosis of hepatic steatosis in morbidity obese patients. Obes Surg 2004; 14: 635-637 [PMID: 15186630 DOI: 10.1381/j.0966892304039480]

18 Guajardo-Salinas GE, Hilmy A. Prevalence of nonalcoholic fatty liver disease (NAFLD) and utility of FibroScan II to detect liver fibrosis in morbidity obese Hispanic-American patients undergoing gastric bypass. Obes Surg 2010; 20: 1647-1653 [PMID: 19957049 DOI: 10.1007/s11695-009-0027-0]

19 de Moura Almeida A, Cotrim HP, Barbosa DB, de Athayde LG, Santos AS, Bincourt AG, de Freitas LA, Rios A, Alves E. Fatty liver disease in severe obese patients: diagnostic value of abdominal ultrasound. World J Gastroenterol 2008; 14: 1415-1418 [PMID: 18332958 DOI: 10.3748/wjg.v14.i14.1415]

20 Mishra P, Younossi ZM. Abdominal ultrasound for diagnosis of nonalcoholic fatty liver disease (NAFLD), Am J Gastroenterol 2007; 102: 2716-2717 [PMID: 18042105 DOI: 10.1111/j.1572-0241.2007.01520.x]

21 Perez NE, Siddiqui FA, Mutchnick MG, Dhar R, Tobi M, Ullah N, Saksonau F, Wheeler DE, Ehrnpire MN. Ultrasound diagnosis of fatty liver in patients with chronic liver disease: a retrospective observational study. J Clin Gastroenterol 2007; 41: 624-629 [PMID: 17577120 DOI: 10.1097/01.jcg.0000225680.45088.01]

22 Ballestri S, Lonardo A, Romagnoli D, Carulli L, Losi L, Day CP, Loria P. Ultrasonographic fatty liver indicator, a novel score which rules out NASH and is correlated with metabolic parameters in NAFLD. Liver Int 2012; 32: 1242-1252 [PMID: 22520641 DOI: 10.1111/j.1478-3244.2012.02848.x]

23 Charatcharoenwitthaya P, Lindor KD. Role of radiologic modalities in the management of non-alcoholic steatohepatitis. Clin Liver Dis 2007; 11: 37-54, viii [PMID: 17544971 DOI: 10.1016/j.cld.2007.02.014]

24 Lupsor M, Badea R. Imaging diagnosis and quantification of hepatic steatosis: is it an accepted alternative to needle biopsy? Rom J Gastroenterol 2005; 14: 419-425 [PMID: 16400362]

25 Saadeh S, Younossi ZM, Remer EM, Gramlich T, Ong J, Hurley M, Mullen KD, Cooper JN, Sheridan MJ. The utility of radiological imaging in nonalcoholic fatty liver disease. Gastroenterology 2002; 123: 745-750 [PMID: 12198701 DOI: 10.1053/gast.2002.35534]

26 Riley TR, Taheri M, Schreiberman IR. Does weight history affect fibrosis in the setting of chronic liver disease? J Gastrointestin Liver Dis 2009; 18: 299-302 [PMID: 19795023]

P-Reviewers: Chen JL, Chen GY, Wang JG, Zhu F S-Editor: Qi Y L-Editor: A E-Editor: Ma S
