Ultrasound in Med. & Biol., Vol. 00, No. 00, pp. 1–8, 2018

0301-5629/$ - see front matter

https://doi.org/10.1016/j.ultrasmedbio.2018.07.006

● *Original Contribution*

PERFORMANCE OF HEPATIC ARTERY VELOCITY IN EVALUATION OF CAUSES OF MARKEDLY ELEVATED LIVER TESTS

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(*Received* 3 *May* 2018; *revised* 14 *June* 2018; *in final from* 5 *July* 2018)

Abstract——The purpose of this study was to assess the utility of peak systolic proper hepatic artery velocity (HAV) in differentiating causes of severely elevated liver function tests. HAV, hepatic artery resistive index and portal vein velocity of 41 patients with severely elevated liver function tests were evaluated. In 19 patients (46%), the causes were structural (*e.g.,* cholecystitis, cholangitis), whereas in 22 patients (54%) the causes were non-structural (*e.g.,* rhabdomyolysis, drug-induced liver injury). The average HAV for structural causes was 138 ± 68 cm/s, and for non-structural causes, 65 ± 29 cm/s ($p < 0.0001$). An HAV >100 cm/s was correlated with structural causes ($p = 0.0001$). With respect to diagnostic performance, this threshold was 79% sensitive and 86% specific, with a high positive likelihood ratio (5.8) and low negative likelihood ratio (0.24). The resistive index and portal vein velocity were not statistically different. In patients with severely elevated liver function tests, an HAV >100 cm/s can help distinguish structural from non-structural causes, which may guide management while awaiting definitive laboratory tests. (E-mail: kamaya@stanford.edu) **© 2018 World Federation for Ultrasound in Medicine & Biology. All rights reserved.**

Key Words: **Hepatic artery velocity, Hepatobiliary dysfunction, Transaminitis, Hepatitis, Liver function tests.**

INTRODUCTION

Abnormal liver function tests (LFTs) are common among hospital patients and affect up to 13% of the general population (Lee et al. 2008). However, abnormal LFTs are associated with increased mortality, with one study reporting an 8–9.5 times relative risk for liver-related death (Kim et al. 2004). Recent guidelines from the American College of Gastroenterology (ACG) recommend abdominal ultrasound as the first-line imaging test for patients with abnormal LFTs, in addition to laboratory testing including assessment for viral, metabolic, inherited, toxic, and extrahepatic causes depending on the clinical presentation and pattern of injury (Kwo et al. 2017). The American College of Radiology also recommends abdominal ultrasound as the first-line imaging test for scenarios classically associated with abnormal LFTs, such as jaundice accompanied by abdominal pain or right upper quadrant pain (Lalani et al. 2013; Yarmish et al. 2014).

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The most recent guidelines from the ACG have defined the degree of abnormal alanine aminotransferase (ALT) and aspartate aminotransferase (AST) elevations by multiples of the upper limits of normal, which differ by gender and was derived from population studies assessing liver-related mortality. Clinical assessment is based on the degree of abnormality, with normal ALT levels being 29–33 and 19–25 U/l for males and females. Borderline, mild, moderate and severe elevations are defined as <2 ×, 2–5 ×, 5–15 × and >15 × the upper limits of normal laboratory values, respectively (Kwo et al. 2017). A fifth category, massive elevation, is defined as >10,000 U/L. These categories are meant to risk-stratify patients who require immediate assessment and to guide evaluation of patients presenting with elevated aminotransferase levels. True normal values vary among local laboratories and published data, making it more difficult to categorize patients in clinical practice; nevertheless, ultrasound is recommended for further workup of any elevation of ALT and AST, regardless of severity (Kwo et al. 2017).

Despite these recommendations, ultrasound of the liver may not elucidate the etiology of the patient's abnormal liver tests, with a reported overall diagnostic

yield of 26%−30% in patients with abnormal liver tests (Chadwick and Marks 2016; Rothschild et al. 2002). In patients with acute viral hepatitis, one study found that only 19 of 791 patients exhibited abnormal echogenicity associated with histologic hepatocellular degeneration. In this same study, the "starry sky" gray-scale sonographic pattern, which has traditionally been associated with acute hepatitis, was observed in only 32.2% of hepatitis patients, but was also observed in 30.9% of normal controls (Giorgio et al. 1986), suggesting that acute hepatitis is difficult to diagnose sonographically. Moreover, the sensitivity of ultrasound in identifying structural causes of abnormal liver tests has been reported to vary between 32% for choledocholithiasis and 61% for cholecystitis (Giljaca et al. 2015). Thus, the structural hepatobiliary cause of abnormal LFTs may be challenging to diagnose, and non-structural causes, such as rhabdomyolysis, may be sonographically occult. Although recommended laboratory tests such as hepatitis antibody tests, autoimmune markers and toxin screens can be obtained rapidly, other polymerase chain reaction-based tests and culture results may take days to produce a result (Chadwick and Marks 2016; Kwo et al. 2017).

Given recent advances in sonographic resolution and color Doppler sensitivity, it is now possible to better visualize and accurately measure the proper hepatic artery velocity (HAV). We have noticed that HAV increases in the setting of obstructive physiology and hypothesize that this may be caused by sinusoidal compression resulting in decreased portal venous inflow, which may in turn cause a compensatory increase in hepatic artery flow *via* the hepatic arterial buffer response (HABR) (Eipel et al. 2010). Other structural causes, such as liver abscesses and metastases, may increase arterial blood flow by localized inflammation or increased vascularity of the metastases, respectively. The purpose of our study was to determine if peak systolic HAV can help delineate the underlying etiology of moderate to severely elevated AST or ALT levels and improve the diagnostic performance of this sonographic metric.

METHODS

Patients

Our institutional review board (IRB) approved this retrospective study, and the study was compliant with the Health Insurance Portability and Accountability Act (HIPAA). The need for informed consent was waived by the IRB because of the retrospective nature of the study. After querying the electronic database at our hospital, we reviewed the medical records of non-transplanted patients from September 2015 to July 2017 who received an abdominal ultrasound within 2 d to evaluate severely elevated ALT (>500 U/L) or AST (>500 U/L) with an acute presentation (n = 120). After exclusion of patients with expected altered hemodynamics (specifically cirrhosis, pressor requirement, extracorporeal membrane oxygenation, cannulation, ventricular assist device and immediate post-operative state from a hepatectomy, n = 33); no HAV measurement (n = 23); incorrect HAV measurement (n = 1); no follow-up (n = 12); and delayed abdominal imaging (ultrasound performed > 48 h after peak LFTs; n = 10), 41 patients were included in the final analysis group (Fig. 1). Pertinent available records were reviewed, including age; sex; liver tests; clinical setting (inpatient vs. emergency department, none of the patients were in an outpatient setting); and background prevalence of known chronic liver disease, such as chronic viral hepatitis. The ultimate etiology of the patient's abnormal liver tests was determined by the primary provider's impression in the medical record. Etiologies were subdivided into structural causes, which can be broadly defined as macroscopic etiologies of liver compromise such as cholecystitis (obstruction of the cystic duct), choledocholithiasis (obstruction of the common bile duct), cholangitis, metastases/mass (space-occupying lesion) and hepatic abscess, or non-structural causes, which can be broadly defined as microscopic or non-hepatobiliary causes of liver compromise such as drug-induced liver injury, rhabdomyolysis and sepsis from a non-hepatobiliary source.

Ultrasound technique

A sonographer certified by the American Registry for Diagnostic Medical Sonography performed each ultrasound examination, which was then reviewed by a board-certified radiologist with abdominal imaging expertise. Gray-scale and color Doppler views of the liver, gallbladder, proper hepatic artery, portal vein and hepatic veins were obtained using 2.5- to 5.5-MHz curved array or vector transducers using either the GE Logiq E9 (GE Healthcare, Waukesha, WI, USA) or ACUSON S2000 (Siemens Medical Solutions, Mountain View, CA, USA) ultrasound machine. Spectral Doppler evaluation of the extrahepatic proper HAV was most commonly evaluated *via* the right lateral intercostal approach at the level of the porta hepatis. The HAV was measured in centimeters per second with angle correction, using a Doppler angle <60°. Both the HAV and HAV resistive index (RI) were calculated on the ultrasound machine.

Ultrasound imaging analysis

The following objective features were evaluated for each case: peak systolic HAV, RI, portal vein velocity (PVV), portal vein diameter and liver size. Additionally, a radiologist blinded to the original interpretation and