Role of Portal Venous Pulsatility Index in Assessment of Hepatic Steatosis

Nadia Haleem Hamed, Manal Farouk Al Tohamy, Amr Osama Khalil, Mohammed Ibrahim Amin
Department of Radiodiagnosis, Faculty of Medicine, Zagazig University, Egypt.
Corresponding Author: Nadia Haleem Hamed
Email: nadiafadda1@gmail.com

Abstract

Background: Nonalcoholic fatty liver disease (NAFLD) is a clinico-pathological condition comprehending a liver disease spectrum that ranges from non-inflammatory isolated steatosis, defined by the presence of triglyceride (TG) accumulation in hepatocytes, to nonalcoholic steatohepatitis (NASH), which is a more aggressive form of the disease characterized by steatosis, inflammatory changes and hepatocyte cell ballooning associated with varying degrees of liver fibrosis. One of the ultrasound biomarkers used for liver fibrosis is the portal vein pulsatility, is an imaging biomarker measured by duplex Doppler assessment of the portal vein and quantified as the venous pulsatility index (VPI) which is calculated as (Vmax – Vmin) / Vmax, where Vmax is the maximum while Vmin is the minimum pulsed-wave Doppler ultrasound-estimated velocity of blood in the portal vein. Assessment of portal vein pulsatility is quantitative, noninvasive, rapid and can be performed with routine ultrasound scanners that are always available at any medical care center.

Background

Nonalcoholic Fatty Liver Disease

By definition, the abnormalities develop despite the absence of excessive alcohol consumption (typically defined as <20 g per day in women and <30 g per day in men). NAFLD usually develops in the context of the metabolic syndrome (MetS) and is strongly associated with obesity, insulin resistance (IR), type 2 diabetes mellitus (T2DM) and dyslipidemia. Patients with NAFLD exhibit an increased overall mortality compared to the general population. In line with the obesity epidemic and sedentary lifestyles, NAFLD has become increasingly common worldwide over the last decades (1).

Non-alcoholic fatty liver disease (NAFLD) is an important cause of morbidity and mortality worldwide both because of cardiovascular, hepatic and oncologic sequelae as well as because it is rapidly becoming the leading cause of end stage liver disease and liver transplant. While the metabolic syndrome is a common risk factor, there are differences among racial and ethnic groups, suggesting the complex interaction between hormonal, nutritional and genetic factors at play in disease pathogenesis. The clinical syndrome of NAFLD spans from bland steatosis to steatohepatitis which can progress to fibrosis and cirrhosis. The pathogenesis including roles of hormones, nutritional and intestinal dysbiosis, insulin resistance, lipotoxicity, and hepatic inflammation, and genes are examined. Non-invasive testing and liver biopsy indications are reviewed. Approved and investigational therapies for NAFLD and NASH are outlined in this review of a disease. (2).
Non-alcoholic fatty liver disease (NAFLD) is a clinical diagnosis that includes the presence of 5% or more hepatic steatosis as determined by liver imaging or biopsy in the absence of secondary causes of hepatic fat accumulation. Current estimates are that NAFLD affects 30% of the United States (US) population; 32% of the Middle East population; 30% of the South American population; 27% of Asian populations (highest in East Asians); 24% of the European population; and 13% of the African population.}

**Portal Venous Pulsatility Index**

**Introduction:**

Portal vein pulsatility, which is an imaging biomarker measured by duplex Doppler assessment of the portal vein and quantified as the venous pulsatility index (VPI). VPI is calculated as \((V_{\text{max}} - V_{\text{min}}) / V_{\text{max}}\), where \(V_{\text{max}}\) is the maximum and \(V_{\text{min}}\) is the minimum pulsed-wave Doppler ultrasound–estimated velocity of blood in the portal vein. Assessment of portal vein pulsatility is quantitative, noninvasive, and rapid and can be performed with routine ultrasound scanners that are available at the point of care. Although a few studies have investigated the distribution of VPI in patients with NAFLD, the accuracy of this method for identifying high-risk NAFLD is not known. Accordingly, we evaluated the value of VPI for diagnosing high-risk NAFLD in a sample of patients with biopsyproven NAFLD and assessed whether VPI adds diagnostic value to that of the existing NAFLD FS, FIB-4, BARD score, and APRI.

**Portal Venous Pulsatility Index in NAFLD**

Although various sonographic changes in the portal vein, such as reversal of flow or decrease in antegrade flow volume, have been previously described as possible indicators of liver disease, changes in portal vein pulsatility in these settings was first investigated in the 1990s. Westra et al. suggested that venous congestion of the hepatic parenchyma within the space confined by the liver capsule results in competition between inflow from the portal vein and hepatic artery during peak systole, which increases portal vein pulsatility. They suggested that pulsatile portal vein inflow may be affected by transmission of pulsations from the adjacent inferior vena cava, the location of the sample volume relative to the inferior vena cava, or other factors that have not yet been determined. It has been proved that VPI is significantly lowered in patients with NAFLD than in healthy subjects. They attributed this alteration to the decreased compliance of liver vasculature due to fatty infiltration. Balci et al. also reported similar results that VPI is significantly lowered in patients with NAFLS from the study of 105 patients with NAFLD and 35 healthy subjects.. Three years later, their findings were confirmed by Solhjoo et al. who compared the VPI of 31 patients with NAFLD with that of 31 healthy individuals.. In a more recent study, Balasubramanian et al. compared the VPI scores of 90 patients with NAFLD with those of 90 healthy control subjects and reached the same conclusion as prior investigators did. The normal portal vein waveform normally shows gentle undulations. In patients with cirrhosis, arterio-portal shunting is a major cause for pulsatility. Increased pulsatility may be measured by calculating the pulsatility index. Increased pulsatility, defined as an increase in the pulsatility index, occurs due to the transmission of pressure across the hepatic sinusoids during the end diastole.
Alternatively, an increased pulsatility index (>0.5) may occur with high right atrial pressure, which can be seen with right heart failure and tricuspid regurgitation. The basis of arterio-portal shunting is the structural distortion that may be seen in patients with cirrhosis in combination with a reversed portal venous flow and increased hepatic venular resistance. Further, hepatocellular carcinoma, which is commonly seen in cirrhotic patients, may cause peri-lesional shunting via draining veins. Arterio-portal shunting in cirrhosis cases can result in increased portal vein pulsatility. Therefore, increased portal vein pulsatility in cirrhotic patients, may prompt an evaluation for the presence of a vascular lesion. A secondary sign that may help in diagnosing arterio-portal shunts is pulsatility that is in sync with the adjacent hepatic artery waveforms (9).

Method of performance and images analysis
According to the standard protocol, pulsed-wave Doppler ultrasound assessment of the portal vein in all patients was performed after the patient had fasted for 4 hours. For imaging, the patient was in a supine or left lateral decubitus position and performed a breath-hold at the end of normal expiration. 3.5 MHz convex probe is used to examine the portal vein by spectral doppler ultrasonography. Ultrasound imaging data were retrieved through the PACS. Each ultrasound examination and the spectral waveform images are used to measure the maximum (Vmax) and minimum (Vmin) estimated portal venous velocity. These measurements were then used to calculate VPI, defined as (Vmax – Vmin) / Vmax (8)

Importance:
Paul, (8) found that VPI is lower in patients with higher liver fibrosis stage. Furthermore, prediction based on VPI performs at a level similar to that reported for shear-wave elastography and serum biomarkers in multiple studies. Moreover, the addition of VPI to all existing clinical prediction models resulted in statistically significant improvement in their diagnostic performance. This finding suggests that VPI measures a previously uncaptured sonographic sign of moderate or greater liver fibrosis in patients with NAFLD. (9)

Shin et al., (10) showed fibrosis progresses by one stage per 14.3 years in patients with NAFLD and by one stage per 7.1 years in patients with NASH. (10)
Although various sonographic changes in the portal vein, such as reversal of flow or decrease in antegrade flow volume, have been previously described as possible indicators of liver disease, changes in portal vein pulsatility in these settings was first investigated in the 1990s. Westra et al. suggested that venous congestion of the hepatic parenchyma within the space confined by the liver capsule results in competition between inflow from the portal vein and hepatic artery during peak systole, which increases portal vein pulsatility. It They suggested that pulsatile portal vein inflow may be affected by transmission of pulsations from the adjacent inferior vena cava, the location of the sample volume relative to the inferior vena cava, or other factors that have not yet been determined. (11)

It has been proved that VPI is significantly lower in patients with NAFLD than in healthy subjects. They attributed this alteration to the decreased compliance of liver vasculature due to fatty infiltration. (11)

Results of other studies suggested that VPI increases in patients with cirrhosis owing to reversed portal venous flow, increased hepatic venular resistance, and arterioportal shunting caused by hepatic structural
distortion. Further investigation is needed to better characterize the relations between VPI, steatosis, and liver fibrosis. (11)

Bley et al., (12) shows that VPI may be a predictor of high-risk NAFLD and may improve the prognostic performance of widely used clinical prediction aids used for this purpose. Because VPI is routinely available at no or minimal cost additional to conventional diagnostic ultrasound, further investigation of the utility of VPI for the diagnosis of high-risk NAFLD is required. With further validation, VPI may become an important component of low-cost noninvasive multiparametric high-risk NAFLD diagnosis. (12).

The normal portal vein waveform normally shows gentle undulations. In patients with cirrhosis, arterio-portal shunting is a major cause for pulsatility. Increased pulsatility may be measured by calculating the pulsatility index, which is measured as a fraction of the difference between the peak systolic velocity and the end diastolic velocity divided by the average velocity. Increased pulsatility, defined as an increase in the pulsatility index, occurs due to the transmission of pressure across the hepatic sinusoids during the end diastole (7).

Alternatively, an increased pulsatility index (>0.5) may occur with high right atrial pressure, which can be seen with right heart failure and tricuspid regurgitation. The basis of arterio-portal shunting is the structural distortion that may be seen in patients with cirrhosis in combination with a reversed portal venous flow and increased hepatic venular resistance. Further, hepatocellular carcinoma, which is commonly seen in cirrhotic patients, may cause peri-lesional shunting via draining veins. Liver biopsies performed on cirrhotic patients may also result in arterio-portal fistula formation. Arterio-portal shunting in cirrhosis cases can result in increased portal vein pulsatility. Therefore, increased portal vein pulsatility in cirrhotic patients, depending on the clinical history, may prompt an evaluation for the presence of a vascular lesion or arterio-portal fistula. A secondary sign that may help in diagnosing arterio-portal shunts is pulsatility that is in sync with the adjacent hepatic artery waveforms (13).
Sluggish or Slow Portal Venous Flow

Normal main portal vein (MPV) peak systolic velocities range between 20 cm/sec and 40 cm/sec. A low flow velocity of <16 cm/sec in addition to a caliber increase in the MPV are diagnostic features of portal hypertension. Cirrhosis results in intrahepatic portal hypertension secondary to the increased resistance in hepatic venules caused by the intrahepatic fibrosis. Accurate velocity measurements within the MPV depend on many parameters, including the Doppler/beam-flow angle. False-positive velocities may be secondary to a Doppler angle that is closer to 90° with respect to the flow direction. The choice of Doppler frequency also affects velocity measurements, as higher frequencies produce more accurate velocities while lower frequencies allow for better penetration. Finally, the presence of a turbulent flow and sampling error may result in the under- or overestimation of the flow velocity (14).

Helical Flow Pattern

Helical blood flow is a type of secondary flow (defined as a minor flow superimposed on the primary flow pattern). A helical flow is caused by a disturbance in the laminar flow. A change in viscosity, vessel geometry, local asymmetries along the vessel wall, and changes in the flow direction and speed can cause accentuated helical patterns. Color Doppler imaging shows alternating red and blue bands in a spiral-like pattern. Helicity was first characterized within a region of caliber change at the level of the carotid bulb. Studies of the carotid artery indicate that a helical flow may be a marker of exposure to disturbed shear or turbulence. Further, some researchers have hypothesized that this pattern may play a significant role in preventing atherogenesis and fibrointimal hyperplasia (15).

Although it is usually transient, has been seen in both liver transplant and transjugular intrahepatic portosystemic shunt (TIPS) recipients. If there is prolonged persistence of the helical flow, it is associated with an increased portal venous velocity and portal vein stenosis. The helical flow in transplant patients is due to a change in the portal vein diameter between the donor vessel and the native vessel and is
accentuated when the discrepancy between the portal veins is greater than 50%. This is in keeping with other authors who have reported that an expansion of the cross-sectional area of a vessel caliber causes flow separation, inducing a circular pattern. Other studies have shown that shortly after liver transplantation, the helical flow within the portal vein resolves due to the decreased flow velocity and local turbulence. The helical flow has been seen in TIPS recipients as well. In a prospective analysis, the prevalence of the helical flow after TIPS placement was reported to be 28% with a variable timeline after placement. The TIPS procedure changes the hemodynamic parameters of the flow, including the portal vein velocity, flow direction, and flow pulsatility. The amount of turbulence created by these dynamic changes is variable among patients and presumably accounts for the unpredictability of whether a helical flow is present postoperatively (16).

**To-and-Fro Portal Venous Flow Pattern**

With increasing portal venous pressure, there is a progressive decrease in the portal venous flow velocities approaching the level of stagnation. As this occurs, the phenomenon of a to-and-fro flow can be encountered whereby the nearly stagnant blood column in the portal veins is seen to shift into and out of the liver with the respiratory cycle. The effect of transient flow reversal or cessation of the forward flow during inspiration can be simulated with the Valsalva maneuver, which also results in a transient hepatofugal flow. With worsening portal hypertension, stagnation of the blood column can lead to thrombosis or progress to a frank flow reversal (6).

**Flow Reversal**

A normal portal venous flow is hepatopetal. A flow reversal (or a hepatofugal flow) is seen in the case of portal hypertension. In particular, in patients with cirrhosis, obstruction of the hepatic venules and sinusoids by fibrosis, substantiated by arterio-portal and porto-systemic shunting, eventually leads to flow reversal. Flow reversal is detected using spectral and color Doppler. Sonographic pitfalls may occur due to the presence of variant portal vein anatomy, resulting in an apparent, false-positive flow reversal depending on the relative location of the ultrasound probe. Atypical intrahepatic arterial collaterals, which are mainly seen after liver transplantation rather than in patients with liver cirrhosis, show a flow from the hepatic capsule to the hilum and may be confused with a hepatofugal flow within the portal venous system. Further, aliasing due to a low pulse repetition frequency setting is a sonographic artifact that may be misinterpreted as a reversed portal venous flow (17).

Porto-systemic shunting or porto-systemic collateral formation is caused by the opening of normally collapsed porto-systemic anastomoses. Some common porto-systemic collateral vessels include coronary (left gastric) venous collaterals, gastric varices, esophageal and paraesophageal varices, abdominal wall varices, and recanalized paraumbilical veins, retroperitoneal-paravertebral varices, and pericholecystic, periportal, and perisplenic varices. Gastrorenal and splenorenal shunts are other examples of varices (18).

**Stagnant Portal Flow and Thrombosis**

Complete stagnation of portal venous flow is a function of advanced portal hypertension and is associated with severe liver fibrosis such that forward flow is virtually absent. Further, the portal vein thrombus is usually hypoechoic and can be difficult to discern on grayscale imaging alone. Therefore, evaluation of the MPV on both grayscale and color flow Doppler is necessary. An apparent absence of flow may also
be seen within areas of occlusion secondary to a bland or tumor thrombus. A helpful differentiating factor between a bland thrombus and either a tumor thrombus or recanalization of an occlusive bland thrombus is the identification of whether the blood flow is pulsatile, as in the case of tumor thrombi, or of a waveform similar to that of portal venous flow, as seen in the case of recanalized bland thrombi. The secondary signs of portal vein thrombosis observed by Doppler include the presence of perportal collaterals, representing cavernous transformation, with a flow in the hepatopetal direction (19).

**Portal Vein Aneurysm**
The normal MPV has a caliber of up to 13 mm, and a portal vein aneurysm is a focal saccular or fusiform dilatation of the portal venous system. A portal vein aneurysm can be congenital or acquired and occurs due to vein wall weakening with a caliber of at least 20 mm. The acquired causes include portal hypertension, pancreatitis, trauma, and post-surgical etiologies. Grayscale images typically show a focally enlarged MPV, while Doppler imaging shows a turbulent or yin-yang flow within the aneurysm, a stagnant flow, or a thrombus associated with the aneurysm (20).

**Hepatic Vein Flow Patterns in Cirrhosis Patients**
The normal waveform within the hepatic veins is triphasic with two hepatofugal phases related to the atrial and ventricular diastole. Fibrotic or inflammatory changes as well as fat deposition in the liver may create a monophasic flow pattern. In the case of end-stage cirrhosis, distorted architecture with changes in the underlying liver architecture can cause a striking reduction in the caliber or absence of the visualization of the hepatic veins. Early waveform changes in cirrhosis patients include spectral broadening and dampening of the normal, retrograde, pre-systolic wave of the hepatic vein waveform. Later, the normal triphasic waveform pattern may be diminished or replaced with a monophasic pattern. Therefore, the monophasic hepatic vein waveform indicates relatively high portal pressures (21).

**References**


www.turkjphysiotherrehabil.org


