DISSERTATION ON

DOPPLER ULTRASOUND EVALUATION OF HEPATIC VENOUS WAVEFORM IN PORTAL HYPERTENSION BEFORE AND AFTER PROPRANOLOL

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BONAFIDE CERTIFICATE

This is to certify that the study entitled **"DOPPLER ULTRASOUND EVALUATION OF HEPATIC VENOUS WAVEFORM IN PORTAL HYPERTENSION BEFORE AND AFTER PROPRANOLOL"** is the bonafide work done by Dr.G.SUREKHA, M.D., P.G. at the Barnard Institute of Radiology, Madras Medical College, Chennai.

This dissertation submitted to Dr.MGR Medical University is in partial fulfillment of the University regulations for the award of M.D. Degree in Radiodiagnosis.

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CONTENTS

INTRODUCTION

Doppler ultrasonography (US) has enabled the noninvasive investigation of hepatic and portal hemodynamics. Thus, many investigators have attempted to assess portal hypertension with Doppler US in patients with cirrhosis. In particular, any Doppler technique that could be a suitable substitute for the invasive assessment of portal hypertension, such as measurement of the hepatic venous pressure gradient (HVPG), would be highly desirable.

However, at present, both the clinical usefulness and the value of Doppler US in the assessment of portal hypertension remain unsettled. Doppler indices that have been commonly used for evaluation of portal hypertension include the measurement of portal and splenic venous blood flow velocity and resistive index of splenic, hepatic, and superior mesenteric arteries. However, these indices are plagued by a lack of reproducibility and accuracy due to intra- and interobserver variability and interequipment variability.

The Doppler waveform of the hepatic vein in healthy subjects is normally triphasic (two negative waves and one positive wave) because of central venous pressure variations due to the cardiac cycle . It has been established that the normal triphasic hepatic vein waveform is transformed into a biphasic or monophasic waveform in patients with cirrhosis. Moreover, a monophasic waveform has been shown to correlate with a high Child-Pugh score and a poor survival rate.

Thus, it would be reasonable to hypothesize that abnormalities in the hepatic vein waveform are related to the degree of portal hypertension. To our knowledge, one study has been performed to examine a possible correlation between abnormalities in the hepatic vein waveform and the severity of portal hypertension in patients with cirrhosis. Thus, the purpose of our study was to prospectively evaluate hepatic vein Doppler waveforms and the response to drug treatment in patients with cirrhosis.

AIM

1. To prospectively evaluate Doppler ultrasonography hepatic vein waveform patterns in patients with portal hypertension and variceal bleeding.

2. To monitor the response to drug treatment (propranolol) in those patients.

REVIEW OF LITERATURE

Analysis of hepatic vein waveform by Doppler ultrasonography in 100 patients with portal hypertension was done by **Ohta M et al.**[1] He classified the Doppler waveform seen in patients with portal hypertension and examined the associations of the waveform type with the diagnosis of Budd-Chiari syndrome and severity of the liver cirrhosis. The Doppler pattern of right and left hepatic veins in 100 consecutive Japanese patients with portal hypertension and esophagogastric varices was classified into six types. Their classification of hepatic vein waveform in Doppler ultrasonography is useful in diagnosing Budd-Chiari syndrome, in judging the efficiency of treatment for hepatic vein lesions, and in assessing severe liver function in cirrhotic patients.

Kemal Arda et al.[2] studied 30 patients who had been diagnosed with chronic liver disease (Child-Pugh class A) and 30 healthy subjects. The diagnosis was confirmed with histopathologic examinations of biopsy specimens in 17 patients. He concluded that there was a significant difference ($p < 0.05$) between the control group and the patient group with respect to the presence of abnormal (type I + type II)

Doppler waveform. The diagnostic accuracy in the patients who had biopsy was 76.47% and that in the patients who did not was 69.23%.

Nevzat Karabulut et al.[3] Observed that there was an inverse correlation between the sonographic grade of the hepatosteatosis and the phasicity of hepatic venous flow ($r=-0.67$, $P<0.001$). And concluded that the hepatic vein pulsatility is significantly dampened in obese patients correlating with the grade of hepatosteatosis. The body habitus itself does not have an independent effect on hepatic venous waveform. The alteration in hepatic vein Doppler flow pattern in an obese population may suggest reduced vascular compliance in the liver because of fatty infiltration.

Levent Oguzkurt et al.[4] studied 40 patients with diffuse FIL and 50 normal healthy adults who served as control group underwent hepatic vein (HV) Doppler ultrasonography. And concluded that Patients with fatty liver has a high rate of an abnormal hepatic vein Doppler waveform pattern which can be biphasic or monophasic. They could not find a relation between the etiological factors for FIL and the occurrence of an abnormal HV Doppler waveform.

S. Jequier et al.[5] In his study concluded that not all healthy children have a triphasic flow pattern in all hepatic veins. Before suspecting hepatic abnormality with abnormal parenchymal compliance (cirrhosis, graft rejection) by virtue of lack of triphasic hepatic vein flow, a normal variant of the flow should be considered. Only the change of a previously documented triphasic flow to monophasic flow in a given vein should be assessed as a sign of possible abnormality.

Hashizume M. et al.[6] prospectively evaluated the prognostic value of the flat hepatic vein waveform, measured by Doppler ultrasound, in cirrhotic patients with portal hypertension. And concluded the prognostic accuracy in cases of cirrhosis with portal hypertension is significantly improved with acquistion of information obtained from hepatic vein waveform by Doppler ultrasound.

W Gorka et al.[7] in his study he concluded that Simple recognition of patterns seen in hepatic vein waveform morphology in patients with liver cirrhosis caused by hepatitis C is superior to portal Doppler flowmetry for predicting the size of esophageal varices.

H. Sugimoto et al.[8] in his study to recognize “normal” hepatic hemodynamics after live donor liver transplantation (LDLT), he

analyzed Doppler parameters on recipients with a right liver graft and donors after extended left hepatectomy. Theoretically these values should be the same. From April 2000 to October 2004, 20 LDLTs were performed using a right liver graft. The 10 recipients without postoperative complications and their donors were included in this study. Portal venous velocity (PVV; cm/s), hepatic arterial peak systolic velocity (cm/s), and hepatic venous peak velocity (HVPV; cm/s) were measured during the first 2 weeks. In donors PVV and HVPV after LDLT were significantly higher after than before left hepatectomy. And he concluded that "abnormal" hepatic hemodynamics in even those recipients without complications during the early postoperative period after LDLT.

Soon Koo Baik et al.[9] prospectively evaluated both the correlation between abnormal Doppler ultrasonography (US) hepatic vein waveforms and the hepatic venous pressure gradient (HVPG) and the response to drug treatment in patients with cirrhosis. And he concluded that Doppler US hepatic vein waveform assessment is useful in the noninvasive evaluation of the severity of portal hypertension and the response to vasoactive drugs in patients with portal hypertension and variceal bleeding.

Moon Young Kim et al.[10] prospectively evaluated the correlation between the extent of abnormal Doppler HV waveforms expressed as damping index (DI) and the hepatic venous pressure gradient (HVPG) and response to propranolol in patients with cirrhosis. And he concluded that Damping index of the HV waveform by Doppler ultrasonography might be a non-invasive supplementary tool in evaluating the severity of portal hypertension and in responding to propranolol in patients with liver cirrhosis.

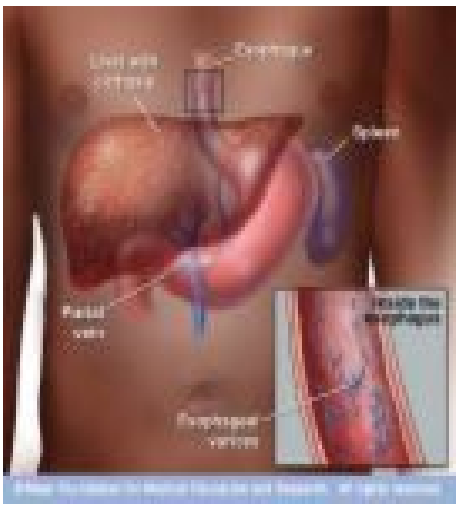
J F Pedersen et al.[11] examined the frequency of absent retrograde flow in a consecutive series of 139 patients referred for abdominal ultrasound. He used state-of-theart ultrasound scanners, and placed the Doppler gate so that in non-forced end-expiration it would sample the right hepatic vein 4–6 cm from the vena cava. There was no association between the hepatic vein flow pattern and age, sex or body mass index. 43 of 139 studied patients showed absent retrograde flow. Review of the case records revealed liver disease in 26 patients and no sign of liver disease in 17 patients. He Concluded that absent retrograde flow in the hepatic veins may be seen not only in patients with overt liver disease but also in apparently liver-healthy patients.

KC Sudhamshu et al.[12] in his study Hepatic vein waveforms were classifi ed into three classical patterns. Flat waveform was uncommon. Mean hepatic vein velocity was significantly higher in cirrhotic patients (12.7 ± 6.4 vs 5.1 ± 2.1 and 6.2 ± 3.2 cm/s; $P < 0.0001$). The poorer the grade of cirrhosis, the higher was the mean velocity. Maximum forward velocity was never greater than 40 cm/s in controls. Degree of ascites was found to be highly correlated with mean velocity. "Very high" group (≥ 20 cm/s) presented clinically with moderate to massive ascites. Correlations between right portal flow and mean velocity was signifi cant ($P < 0.0001$, $r = 0.687$).. And he concluded that Doppler waveforms of hepatic vein, which is independent of liver dysfunction, should be obtained during normal respiration. Mean hepatic vein velocity reflects the change in hepatic circulation associated with progression of liver cirrhosis. It can be used as a new parameter in the assessment of liver cirrhosis.

PORTAL HYPERTENSION

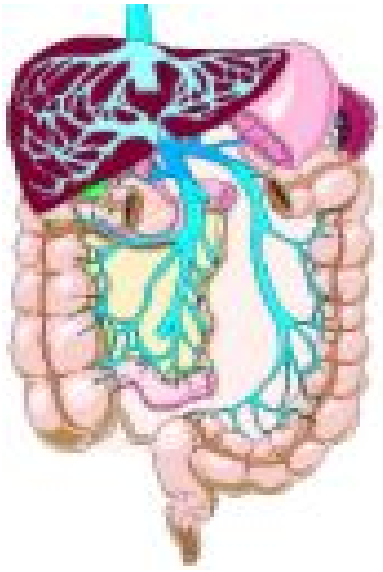
The portal system includes all the veins which drain the blood from the abdominal part of the digestive tube (with the exception of the lower part of the rectum) and from the spleen, pancreas, and gall-bladder. From these viscera the blood is conveyed to the liver by the portal vein. In the liver this vein ramifies like an artery and ends in capillary-like vessels termed sinusoids, from which the blood is conveyed to the inferior vena cava by the hepatic veins.

From this it will be seen that the blood of the portal system passes through two sets of minute vessels, viz., (a) the capillaries of the digestive tube, spleen, pancreas, and gall-bladder; and (b) the sinusoids of the liver. In the adult the portal vein and its tributaries are destitute of valves; in the fetus and for a short time after birth valves can be demonstrated in the tributaries of the portal vein; as a rule they soon atrophy and disappear, but in some subjects they persist in a degenerate form.



The portal vein (vena portæ) is about 8 cm. in length, and is formed at the level of the second lumbar vertebra by the junction of the superior mesenteric and lienal veins, the union of these veins taking place in front of the inferior vena cava and behind the neck of the pancreas. It passes upward behind the superior part of the duodenum and then ascends in the right border of the lesser omentum to the right extremity of the porta hepatis, where it divides into a right and a left branch, which accompany the corresponding branches of the hepatic artery into the substance of the liver.

In the lesser omentum it is placed behind and between the common bile duct and the hepatic artery, the former lying to the right of the latter. It is surrounded by the hepatic plexus of nerves, and is accompanied by numerous lymphatic vessels and some lymph glands.



The right branch of the portal vein enters the right lobe of the liver, but before doing so generally receives the cystic vein. The left branch, longer but of smaller caliber than the right, crosses the left sagittal fossa, gives branches to the caudate lobe, and then enters the left lobe of the liver. As it

crosses the left sagittal fossa it is joined in front by a fibrous cord, the ligamentum teres (obliterated umbilical vein), and is united to the inferior vena cava by a second fibrous cord, the ligamentum venosum.

The tributaries of the portal vein are:

Lienal.Pyloric. Superior Mesenteric. Cystic. Coronary. Parumbilical. The Lienal Vein (v. lienalis; splenic vein) commences by five or six large branches which return the blood from the spleen. These unite to form a single vessel, which passes from left to right, grooving the upper and back part of the pancreas, below the lineal artery, and ends behind the neck of the pancreas by uniting at a right angle with the superior mesenteric to form the portal vein. The splenic vein is of large size, but is not tortuous like the artery.

The splenic vein receives the short gastric veins, the left gastroepiploic vein, the pancreatic veins, and the inferior mesenteric veins.

The short gastric veins (vv. gastricæ breves), four or five in number, drain the fundus and left part of the greater curvature of the

stomach, and pass between the two layers of the gastrolienal ligament to end in the splenic vein or in one of its large tributaries.

The left gastroepiploic vein (v. gastroepiploica sinistra) receives branches from the antero-superior and postero-inferior surfaces of the stomach and from the greater omentum; it runs from right to left along the greater curvature of the stomach and ends in the commencement of the splenic vein.

The pancreatic veins (vv. pancreaticæ) consist of several small vessels which drain the body and tail of the pancreas, and open into the trunk of the splenic vein.

The inferior mesenteric vein (v. mesenterica inferior) returns blood from the rectum and the sigmoid, and descending parts of the colon. It begins in the rectum as the superior hemorrhoidal vein, which has its origin in the hemorrhoidal plexus, and through this plexus communicates with the middle and inferior hemorrhoidal veins. The superior hemorrhoidal vein leaves the lesser pelvis and crosses the left common iliac vessels with the superior hemorrhoidal artery, and is continued upward as the inferior mesenteric vein. This vein lies to the left of its artery, and ascends behind the peritoneum and in front of the

left Psoas major; it then passes behind the body of the pancreas and opens into the splenic vein; sometimes it ends in the angle of union of the splenic and superior mesenteric veins.

The inferior mesenteric vein receives the sigmoid veins from the sigmoid colon and iliac colon, and the left colic vein from the descending colon and left colic flexure.

The Superior Mesenteric Vein (v. mesenterica superior) returns the blood from the small intestine, from the cecum, and from the ascending and transverse portions of the colon. It begins in the right iliac fossa by the union of the veins which drain the terminal part of the ileum, the cecum, and vermiform process, and ascends between the two layers of the mesentery on the right side of the superior mesenteric artery. In its upward course it passes in front of the right ureter, the inferior vena cava, the inferior part of the duodenum, and the lower portion of the head of the pancreas. Behind the neck of the pancreas it unites with the splenic vein to form the portal vein.

Besides the tributaries which correspond with the branches of the superior mesenteric artery, viz., the intestinal, ileocolic, right colic, and

middle colic veins, the superior mesenteric vein is joined by the right gastroepiploic and pancreaticoduodenal veins.

The right gastroepiploic vein (v. gastroepiploica dextra) receives branches from the greater omentum and from the lower parts of the antero-superior and posteroinferior surfaces of the stomach; it runs from left to right along the greater curvature of the stomach between the two layers of the greater omentum.

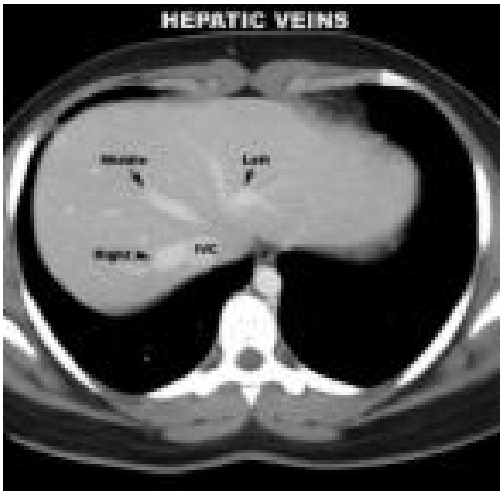
The pancreaticoduodenal veins (vv. pancreaticoduodenales) accompany their corresponding arteries; the lower of the two frequently joins the right gastroepiploic vein.

The Coronary Vein (v. coronaria ventriculi; gastric vein) derives tributaries from both surfaces of the stomach; it runs from right to left along the lesser curvature of the stomach, between the two layers of the lesser omentum, to the esophageal opening of the stomach, where it receives some esophageal veins. It then turns backward and passes from left to right behind the omental bursa and ends in the portal vein.

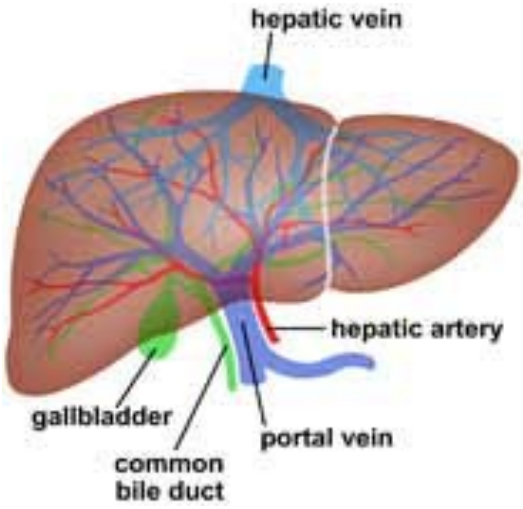
The Pyloric Vein is of small size, and runs from left to right along the pyloric portion of the lesser curvature of the stomach, between the two layers of the lesser omentum, to end in the portal vein.

The Cystic Vein (v. cystica) drains the blood from the gall-bladder, and, accompanying the cystic duct, usually ends in the right branch of the portal vein.

Parumbilical Veins (vv. parumbilicales).—In the course of the ligamentum teres of the liver and of the middle umbilical ligament, small veins (parumbilical) are found which establish an anastomosis between the veins of the anterior abdominal wall and the portal, hypogastric, and iliac veins. The best marked of these small veins is one which commences at the umbilicus and runs backward and upward in, or

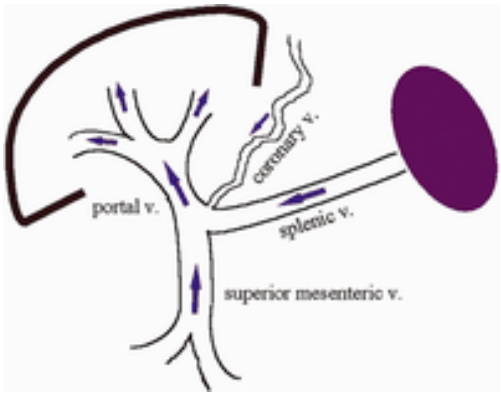


on the surface of, the ligamentum teres between the layers of the falciform ligament to end in the left portal vein.



Collateral venous circulation to relieve portal obstruction in the liver may be effected by communications between (a) the gastric veins and the esophageal veins which often project as a varicose bunch into the stomach, emptying themselves into the hemiazygos vein; (b) the veins of the colon and duodenum and the left renal vein; (c) the accessory portal system of Sappey, branches of which pass in the round and falciform ligaments (particularly the latter) to unite with the epigastric and internal mammary veins, and through the diaphragmatic veins with the azygos; a single large vein, shown to be a parumbilical vein, may pass from the hilus of the liver by the round ligament to the umbilicus, producing there a bunch of prominent varicose veins known as the caput medusæ; (d) the veins of Retzius, which connect the intestinal veins with the inferior vena cava and its retroperitoneal branches; (e) the inferior mesenteric veins, and the hemorrhoidal veins that open into the hypogastrics; (f) very rarely the ductus venosus remains patent, affording a direct connection between the portal vein and the inferior vena cava.

The Hepatic Veins (vv. hepaticæ) commence in the substance of the liver, in the terminations of the portal vein and hepatic artery, and are arranged in two groups, upper and lower. The upper group usually consists of three large veins, which converge toward the posterior surface of the liver, and open into the inferior vena cava, while that vessel is situated in the groove on the back part of the liver. The veins of the lower group vary in number, and are of small size; they come from the right and caudate lobes. The hepatic veins run singly, and are in direct contact with the hepatic tissue. They are destitute of valves.



The portal vein drains blood from the small and large intestines, stomach, spleen, pancreas, and gallbladder. The superior mesenteric vein and the splenic vein unite behind the neck of the pancreas to form the portal vein. The portal trunk divides into 2 lobar veins. The right branch drains the cystic vein, and the left branch receives the umbilical and paraumbilical veins that enlarge to form umbilical varices in portal hypertension. The coronary vein, which runs

along the lesser curvature of the stomach, receives distal esophageal veins, which also enlarge in portal hypertension.

Portal hypertension may be defined as a portal pressure gradient of 12 mm Hg or greater and is often associated with varices and ascites. Many conditions are associated with portal hypertension, of which cirrhosis is the most common cause.

Causes:

Causes of increased resistance to flow are described as follows:

1. Prehepatic
    - Portal vein thrombosis
    - Splenic vein thrombosis
    - Congenital atresia or stenosis of portal vein
    - Extrinsic compression (tumors)
    - Splanchnic arteriovenous fistula

2. Intrahepatic,

a) Predominantly Presinusoidal

- Schistosomiasis (early stage)
- Primary biliary cirrhosis (early stage)
- Idiopathic portal hypertension (early stage)
- Nodular regenerative hyperplasia: Pathogenesis probably is obliterative venopathy. The presence of nodules that press on the portal system also has been postulated to play a role, although nodularity is present in most cases without clinical evidence of portal hypertension.
- Myeloproliferative diseases: These act by direct infiltration by malignant cells.
- Polycystic disease
- Hepatic metastasis
- Granulomatous diseases (sarcoidosis, tuberculosis): Clinical liver dysfunction is rare in sarcoidosis. Portal

hypertension is an unusual, although well-recognized manifestation of hepatic sarcoidosis. Sarcoid granulomas frequently localize in the portal areas, resulting in injury to the portal veins.

b) Predominantly Sinusoidal And/Or Postsinusoidal

- Hepatic cirrhosis
- Acute alcoholic hepatitis
- Schistosomiasis (advanced stage)
- Primary biliary cirrhosis (advanced stage)
- Idiopathic portal hypertension (advanced stage)
- Acute and fulminant hepatitis
- Congenital hepatic fibrosis

- Vitamin A toxicity: Noncirrhotic portal fibrosis is observed with various toxic injuries, and one of these includes vitamin A toxicity. This probably is due to vascular injury. Excessive doses of vitamin A taken for months or years can lead to chronic hepatic disease. Intake of doses ranging from as small as 3-fold the recommended daily dose continued for years to doses as high as 20-fold the

approved dose in a few months can lead to hepatic disease. The pericellular fibrosis characteristic of vitamin A toxicity may lead to portal hypertension.

- Peliosis hepatitis
- Venoocclusive disease
- Budd-Chiari syndrome

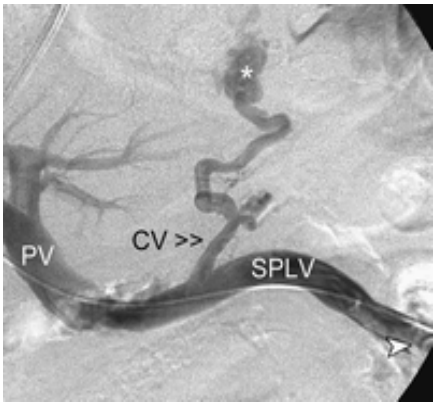
3. Posthepatic

- Inferior vena cava (IVC) obstruction
- Right heart failure
- Constrictive pericarditis
- Tricuspid regurgitation
- Budd-Chiari syndrome
- Arterial-portal venous fistula
- Increased portal blood flow
- Increased splenic flow

Hemodynamic Measurement Of Portal Pressure :

Direct portal measurements usually are not performed due to the invasive nature, the risk of complications, and the interference of anesthetic agents on portal hemodynamics. The most commonly used method is measurement of the hepatic venous pressure gradient (HVPG), which is an indirect measurement that closely approximates portal venous pressure.

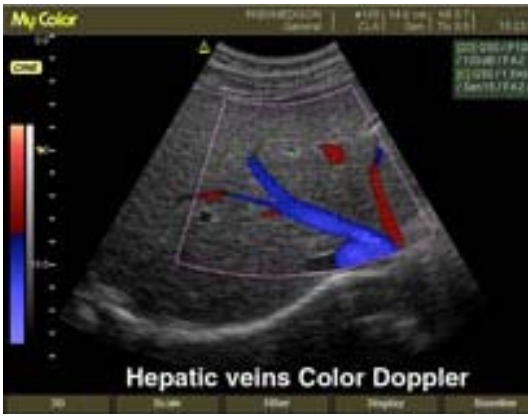
A fluid-filled balloon catheter is introduced into the femoral or internal jugular vein and advanced under fluoroscopy into a branch of the hepatic vein. Free hepatic venous pressure (FHVP) then is measured.

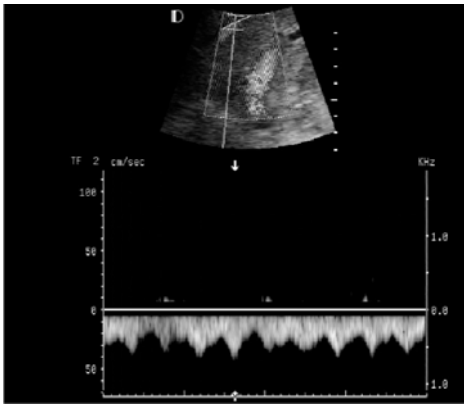


The balloon is inflated until it is wedged inside the hepatic vein, occluding it completely, thus equalizing the pressure throughout the static column of blood. The occluded hepatic venous pressure (ie, wedged hepatic venous pressure) minus the unoccluded, or free, portal venous pressure (ie, FHVP) is the HVPG.

Duplex-Doppler Ultrasonography :

Ultrasound (US) is a safe, economical, and effective method for screening for portal hypertension. It also can demonstrate portal flow and helps in diagnosing cavernous transformation of the portal vein, portal vein thrombosis, or splenic vein thrombosis.



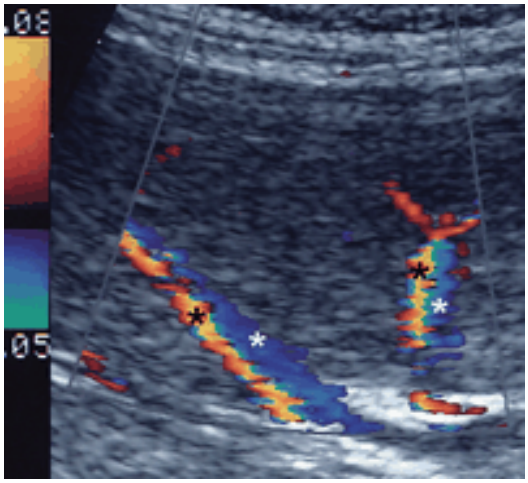


Features suggestive of hepatic cirrhosis with portal hypertension include the following :

- Nodular liver surface is suggestive. However, this finding is not specific for cirrhosis and can be observed with congenital hepatic fibrosis and nodular regenerative hyperplasia.

- Splenomegaly is a suggestive finding.

- Patients may demonstrate the presence of collateral circulation.



Limitations of US include the following :

- Reproducibility of data is problematic.

- Many variables, such as circadian rhythm, meals, medications, and the sympathetic nervous system, affect portal hemodynamics.

- Significant interobserver and intraobserver variation exist in quantitative ultrasonographic measurement

Patient Preparation & Positioning

- The abdominal Doppler examination is explained to the patient and any questions are answered.

- A history is obtained from the patient focusing on risk factors, signs, and symptoms of hepatocellular disease. Previous medical history relating to hepatocellular disease should be noted.

- Any recent surgical intervention of shunt placement within the portal venous system is documented in the patient history work sheet.

- The patient is placed initially in the supine position; the patient may be rolled into a slight left lateral decubitus position to obtain a better intercostal window. The images and Doppler evaluation may be obtained in the longitudinal, coronal, oblique, or transverse planes.

- Breath holding is very important in obtaining good Doppler color and spectral waveforms. Initially scan the patient in shallow respiration to set up your controls and depth. Then instruct the patient to stop breathing when you obtain the Doppler images.

Techniques

General Technical Points

- Place ultrasound gel on the abdomen to ensure good transducer-to-skin contact during the abdominal Doppler imaging examination.

- The transducer's orientation marker should be pointing toward the patient's right side during the examination when a transverse scan is performed; the orientation marker is directed toward the patient's head when a longitudinal scan is performed.

- The examination is performed with both gray scale and Doppler evaluation of the portal venous system, the hepatic veins, and hepatic arteries.

- Remember, the transducer must be PARALLEL to the vessel; the Doppler angle should be less than sixty degrees to obtain the maximum peak systolic velocity. At the end of the examination, the ultrasound gel should be removed from the patient and any excess gel should be removed from the transducer. The transducer should be cleaned using a disinfectant.

Doppler

- The evaluation of the portal venous system, hepatic veins, and hepatic artery is performed during the Doppler imaging examination.

- Doppler signals or color Doppler imaging should be obtained from the imaging plane that allows the beam to be as parallel to the vessel as possible.

- A liver Doppler should also evaluate flow in the extra-hepatic portal venous system, and IVC. These images should be obtained prior to the PW evaluation.

- Also document the size of the CBD, liver, kidneys, and spleen.

- Look in the pelvic cavity and lower quadrants for the presence of free fluid.

Doppler Technique

- The pulse repetition frequency (PRF) allows one to record lower velocities as the PRF is lowered; as the PRF is increased, the lower velocities are filtered out to record only the higher velocity signal.

- The PRF may be changed with the scale control on the Doppler panel (look at the color bar on the left side of the monitor, the PRF will change as the "scale" on the Doppler control is changed.

- The PRF increases as imaging depth increases and decreases as depth decreases. Flow within the normal hepatic venous system is low; therefore a lower PRF is necessary to record the flow pattern. As the flow increases beyond 40 cm/sec, the PRF should be increased to prevent aliasing. (Aliasing may also be reduced by scanning at a lower frequency).

- The Doppler sample volume should be smaller than the diameter of the lumen. If you have difficulty finding the vessel, increase the width of the sample volume to locate the flow, and then reduce the volume width to clean up the spectral waveform.

- The Doppler angle correction should be less than 60 degrees to display the peak spectral velocity.

- Wall filters help to eliminate "noise" or low level Doppler shifts seen within the vessel.

Doppler Observations

Hepatic Artery

- Low resistance waveform; forward flow in diastole above baseline
- Vessel is tortuous; flow may appear to move toward and away from the transducer.
- Systolic window with narrow bandwidth with parabolic flow profile
- Spectral fill-in of systolic window due to small vessel diameter
- High resistance waveforms may indicate veno-occlusive disease

Portal Venous System

- Continuous low velocity phasic signal; phasic means that the velocity increases and decreases with respirations giving the signal a smooth wavelike appearance
- Normal flow is termed hepatopedal (toward the liver)

- Reversed flow is hepatofugal.

- Portal venous thrombosis or post op anastomosis from a liver transplant can cause an abnormal portal vein signal: results from decreased vessel lumen size which reduces the pressure, and consequently increases the velocity of flow through the narrowed region - "choppy" appearance as result of increased velocities.

NOTE: The hepatic artery and portal vein flow should be in the same direction as the hepatic artery runs parallel with the portal vein.

Hepatic Venous System

- Multi-phasic pulsatile flow pattern secondary to proximity of the right atrium with flow above and below the baseline due to close proximity to the right atrium which results in hemodynamic changes

- Right sided heart failure may cause the hepatic veins to become pulsatile and dilated.

- Increased intrahepatic pressure or venous obstruction demonstrates a more continuous or monophasic signal

Inferior Vena Cava

- Continuous waveform with respiratory variations; become more pulsatile as it empties into the right atrium.

- Best imaged with a slight cranial-caudal sweep in the longitudinal plane with the patient in deep inspiration

- Anastomosis from surgical transplantation may alter the normal flow into the IVC

- Thrombosis can cause the IVC waveform to appear monophasic with high velocities ("choppy" appearance). Evaluate for thrombus in the renal veins as well.

- If a surgical shunt is present, be sure to check the patient's history to find out the specific type of shunt (portal/cava or mesenteric/cava) is in place.

Duplex Imaging Technique

Terminology:

- Left hepatic vein - LHV

- Left hepatic artery - LHA
- Left portal vein - LPV
- Right hepatic vein - RHV
- Right hepatic artery - RHA
- Right portal vein - RPV
- Common (main) hepatic artery - CHA
- Main portal vein - MPV
- Middle hepatic vein - MHV

The hepatic vessels should be imaged at four anatomical locations:

- Midline, beneath the xyphoid for the LHV, LHA, and LPV;
- Mid-clavicular and intercostal at the portal hepatis for the MHA and MPV;
- Lateral and intercostal at the right lobe for the RHA and RPV;
- Subcostal and midclavicular for the RHV and MHV.

Primary Prophylaxis :

Primary prophylaxis is administered to patients at high risk of bleeding. These patients have large varices, red wale markings on the varices, and severe liver failure.

Beta-Blockers :

Beta-blockers include propranolol and nadolol. They are used most commonly. Beta-blockers are noncardioselective and reduce portal and collateral blood flow. Reduction in cardiac output (blockade of beta1-adrenoreceptors) occurs. Splanchnic vasoconstriction (blockade of vasodilatory adrenoreceptors of the splanchnic circulation) also occurs.

A recent meta-analysis of 11 trials evaluating nonselective beta-blockers in the prevention of first variceal bleeding shows that the bleeding rate in controls (25%) is significantly reduced (to 15%) in patients treated with beta-blockers after a median follow-up of 24 months. The mortality rate also is lower in the beta-blocker group; however, the difference does not achieve statistical significance. The effect of beta-blockers as a function of variceal size also is analyzed. The risk of first variceal bleeding in patients with medium-to-large varices is 30% in controls, which is significantly reduced to 14% in

patients treated with beta-blockers. In patients with small varices, a tendency exists for reduction in the first bleeding episode; however, the number of patients and the rate of first bleeding are too low to achieve statistical significance.

Propranolol is administered at a dose of 20 mg every 12 h, which is increased or decreased every 3-4 days until a 25% reduction in the resting heart rate occurs or the heart rate is down to 55 beats per minute (bpm). The average dose of propranolol usually is 40 mg bid. Administering more than 320 mg/d is not recommended. Nadolol dosing is half the daily dose of propranolol, administered once a day.

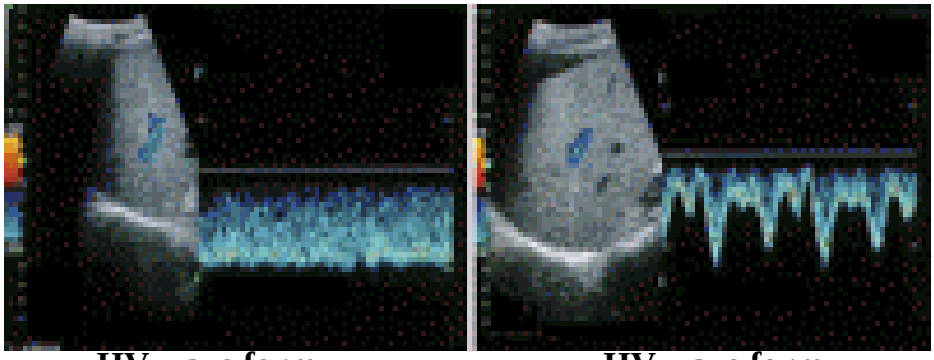
Response to treatment is monitored by a reduction of the portal pressure gradient by more than 20% of the baseline value or less than 12 mm Hg. Checking the HVPG response in primary prophylaxis is not mandatory because 60% of patients who do not achieve these targets do not bleed at 2-year follow-up evaluations.

Propranolol is contraindicated in patients with asthma, chronic obstructive pulmonary disease (COPD), atrioventricular (AV) block, intermittent claudication, and psychosis. The most frequent adverse effects are light-headedness, fatigue, dyspnea upon exertion,

bronchospasm, insomnia, impotence, and apathy. Reducing the dose of propranolol frequently controls these adverse effects.

Beta-blockers are best continued for the patient's lifetime because the risk of variceal hemorrhage returns to that of the untreated population once beta-blockers are withdrawn.

Soon Koo Baik et al.[9] prospectively evaluated both the correlation between abnormal Doppler ultrasonography (US) hepatic vein waveforms and the hepatic venous pressure gradient (HVPG) and the response to drug treatment in patients with cirrhosis. And he concluded that Doppler US hepatic vein waveform assessment is useful in the noninvasive evaluation of the severity of portal hypertension and the response to vasoactive drugs (Terlipressin)in patients with portal hypertension and variceal bleeding.



HV wave form before terlipressin

HV wave form after terlipressin

Matreials And Methods

A prospective study of 60 patients with portal hypertension and Variceal bleeding was done in the Barnard Institute of Radiology.

INCLUSION CRITERIA :

All the patients with portal hypertension and recent variceal bleeding.

EXCLUSION CRITERIA :

All the patients with

1. Hepato cellular carcinoma

2. Hepatic encephalopathy

3. Thrombosis in IVC, hepatic vein or portal vein

4. Congestive heart failure.

Patients with portal hypertension and variceal bleeding were included in this study. There were no limitations to the study with respective age and sex. All the patients were started with oral

propranolol after the initial Doppler ultrasonography. The treatment response was studied with hepatic venous waveform. The patients were evaluated using Doppler ultrasound with a 3.5MHz curvilinear transducer.(ALOKA-3500). The study was done by a single observer and thus inter observer variation was eliminated.

Doppler traces were obtained in the right or middle hepatic vein at a distance of 3 to 6cms from the junction of the hepatic vein and inferior vena cava. The 3.5MHz curvilinear probe was placed right lateral intercostals approach. Hepatic vein Doppler wave forms were recorded for atleast 5 seconds with end expiration breath holding.

In colour Doppler flow mapping, a blue hepatic vein waveform indicates flow away from the probe. Where as a red portal vein waveform indicates flow towards the probe. The hepatic vein waveforms are classified as triphasic (reversed flow in atleast one phase), biphasic (no reversed flow) or monophasic (flat and with or without fluttering).

Waveform classification depended on the prescence or absence of phasic oscillation. Monophasic waveform is defined as complete loss of normal phasic oscillation.

RESULTS AND OBSERVATIONS

No. of Patients	-	60
Male Patients	-	39
Female Patients	-	21

Male Prepondrance is due to Alcoholic Liver Disease. The baseline examination shows Triphasic Hepatic Venous waveforms in 18 patients, Biphasic waveforms in 30 patients and Monophasic waveforms in 12 patients.

All the patients were given Propranolol (PPNL). And followup Hepatic venous waveform taken every 15 days. No patients showed improvement in 15 days. Most of the patients showed improvement in 1 Month.

Thirty Nine Out of Forty Two Patients showed improvement in the Hepatic venous waveform. And this correlates with the clinical improvement. ie 92.8% patients showed improvement after PPNL both clinically and Dopplerwise.

Patients Distribution - Sexwise

Sexwise Diagnosis	No. of Patients	Percentage
Male	39	65 %
Female	21	35 %
Total	60	

Patients Distribution - Agewise

Age Distribution	No. of Patients
Below 20 Yrs	-
21 - 30 Yrs	7
31 - 40 Yrs	22
41 - 50 Yrs	16
51 - 60 Yrs	12
Above 60 Yrs	3
Total	60

Patients Distribution – Age & Sexwise

Age & Sex wise Distribution	No. of Patients		
	Female	Male	Total
Below 20 Yrs	-	-	-
21-30 Yrs	3	4	7
31-40 Yrs	10	12	22
41-50 Yrs	4	12	16
51-60 Yrs	4	8	12
Above 60 Yrs	0	3	3
Total	21	39	60

Clinical Diagnosis Distribution

Clinical Diagnosis	No. of Patients	Percentage
Alcoholic Liver Diseas	21	35 %
DCLD	6	10 %
EHPVO	5	8 %
Portal Hypertension	15	25 %
Viral Hepatits	13	22 %
Total	60	

Clinical Diagnosis Distribution - Sexwise

Sex / Diagnosis	Alcoholic Liver Disease	DCLD	EHPVO	Portal Hyper tension	Viral Hepatits	Total
Female	-	4	2	9	6	21
Male	21	2	3	6	7	39
Total	21	6	5	15	13	60

Clinical Diagnosis Distribution - Agewise

Age / Diagnosis	Alcoholic Liver Disease	DCLD	EHPVO	Portal Hyper tension	Viral Hepatits	Total
Below 20 Yrs	-	-	-	-	-	-
21 - 30 Yrs	1	-	3	1	2	7
31 - 40 Yrs	7	2	2	7	4	22
41 - 50 Yrs	7	-	-	5	4	16
51 - 60 Yrs	5	2	0	2	3	12
Above 60 Yrs	1	2	-	-	-	3
Total	21	6	5	15	13	60

Hepaticvein Waveform – Before PPNL

Hepaticvein Waveform Before PPNL	No. of Patients	Percentage
Triphasic	18	30 %
Biphasic	30	50 %
Monophasic	12	20 %
Total	60	

Hepaticvein Waveform – After PPNL

Hepaticvein Waveform (After PPNL)	No. of Patients	Percentage
Triphasic	50	83 %
Biphasic	7	12 %
Monophasic	3	5 %
Total	60	

Hepaticvein Waveform – Before & After PPNL

Hepaticvein Waveform		No. of Patients	Percentage
Before PPNL	After PPNL		
Monophasic	Monophasic	3	5 %
Monophasic	Biphasic	7	12 %
Monophasic	Triphasic	2	3 %
Biphasic	Triphasic	30	50 %
Triphasic	Triphasic	18	30 %
Total		60	

Response to PPNL

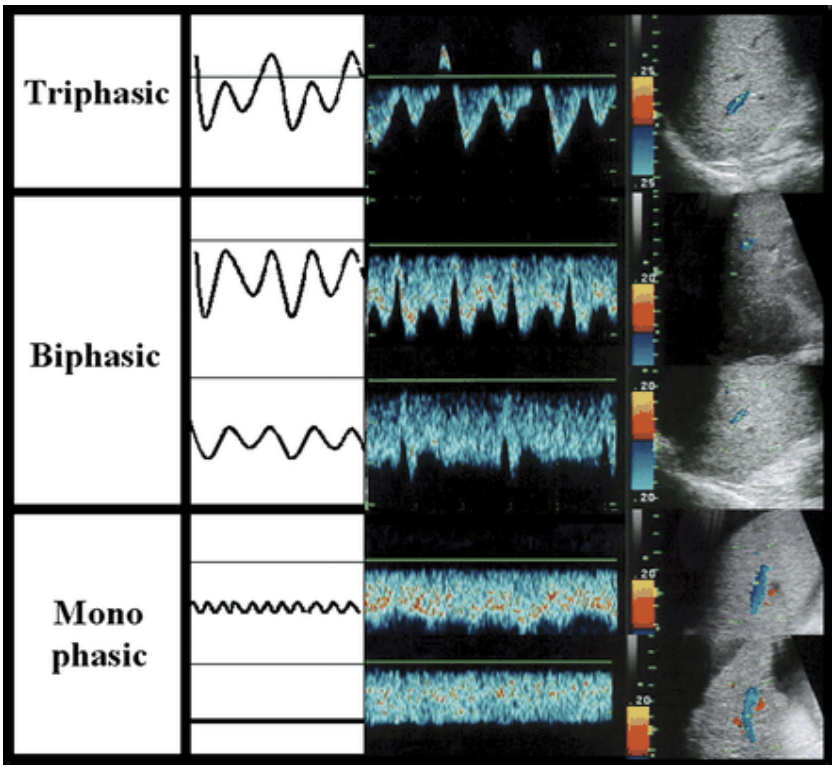
Response to PPNL	No. of Patients	Percentage
Yes (+)	42	93%
No (-)	3	7%
Total	45	

DISCUSSION

The hepatic vein Doppler waveform in healthy humans is triphasic because of central venous pressure variations that are due to the cardiac cycle. In patients with cirrhosis, other studies have incontrovertibly demonstrated the presence of abnormal biphasic or monophasic hepatic vein waveforms. In addition, a previous study showed that the monophasic waveform was correlated with higher Child-Pugh scores and a decreased survival rate.

However, little is known about the relationship between hepatic vein Doppler waveform abnormalities and portal hypertension. In one study, a correlation was found between abnormalities in the hepatic vein waveform and the HVPG (ie, as HVPG increased, the hepatic vein waveform tended to flatten). Furthermore, the monophasic waveform was associated with severe portal hypertension with relatively high sensitivity and specificity in that study population. Hence, flattening of the hepatic vein waveform in patients with cirrhosis indicates a high likelihood of severe portal hypertension.

Some investigators have suggested classifying the hepatic vein waveform into six subtypes. In our experience, however, we have found that the availability of this many subtypes leads to greater complexity and larger inter- and intraobserver variability when assigning a subtype to a particular hepatic vein waveform. We believe that the disadvantages associated with the availability of more subtypes outweigh the advantage of a slight improvement in discriminatory ability. Thus, we used a simpler system that we believed was more clinically useful and that had only three subtypes.



Sixty patients clinically diagnosed as Portal Hypertension, Alcoholic Liver Disease, EHPVO, DCLD and Viral Hepatitis referred for portal Doppler.

In those patients 21 were Female (35%) and 39 were Male (65%) There was no age limit. Baseline Doppler Ultra sonography was done and the Hepatic venous waveform was recorded. All the patients were given Propranolol (PPNL). And followup studies were done fortnightly. The response to PPNL was recorded.

The baseline examination shows Triphasic Hepatic Venous waveforms in 18 patients, Biphasic waveforms in 30 patients and Monophasic waveforms in 12 patients.

Kemal Arda et al. studied 30 patients who had been diagnosed with chronic liver disease (Child-Pugh class A) and 30 healthy subjects. The diagnosis was confirmed with histopathologic examinations of biopsy specimens in 17 patients. He concluded that there was a significant difference ($p < 0.05$) between the control group and the patient group with respect to the presence of abnormal (type I + type II) Doppler waveform. The diagnostic accuracy in the patients who had biopsy was 76.47% and that in the patients who did not was 69.23%.

So, the Monophasic waveform implies the severity of the disease when compared to Biphasic waveform.

In those 60 Patients 35% were Clinically Diagonised as Alcoholic Liver Disease, 10% were DCLD, 8% were EHPVO, 25% were Portal Hypertension and 22% were Viral Hepatits.

All the patients were given Propranolol (PPNL). And followup Hepatic venous waveform taken every 15 days. No patients showed improvement in 15 days. Most of the patients showed improvement in 1 Month.

Thirty Nine Out of Forty Two Patients showed improvement in the Hepatic venous waveform. And this correlates with the clinical improvement. ie 92.8% patients showed improvement after PPNL both clinically and Dopplerwise.

Soon Koo Baik et al. prospectively evaluated both the correlation between abnormal Doppler ultrasonography (US) hepatic vein waveforms and the hepatic venous pressure gradient (HVPG) and the response to drug treatment in patients with cirrhosis. And he concluded that Doppler US hepatic vein waveform assessment is useful in the noninvasive evaluation of the severity of portal hypertension and the

response to vasoactive drugs (terlipressin) in patients with portal hypertension and variceal bleeding.

A change in hepatic vein waveform seems to be closely associated with a change in HVPG. Hence, these results indicate that the evaluation of hepatic vein Doppler waveform could be a valuable supplemental tool when assessing the therapeutic response to vasoactive drugs used to treat portal hypertension when HVPG measurement is unfeasible or unavailable. For instance, if a monophasic waveform transformed into a biphasic or triphasic waveform after administration of ß-blockers, one might presume that the ß-blockers reduced the portal pressure.

The exact cause of changes in the hepatic vein Doppler waveform remains unclear. Some investigators have suggested that the hepatic vein wall is thin and surrounded by liver parenchyma so that its compliance can be easily reduced by parenchymal fibrosis and fat infiltration. However, the terlipressin-induced improvement in the waveforms suggests that a hemodynamic effect of high portal pressure rather than a fixed structural abnormality is the pathogenic mechanism responsible for the abnormal waveforms. We believe that high portal pressure probably contributes to the flattening of the normal triphasic hepatic vein waveform by hemodynamically blunting the effect of variations in central venous pressure during the cardiac cycle.

In our study Hepatic venous forms were not correlated with Hepatic venous pressure gradient (HVPG) which is an invasive procedure. So many studies concluded that there was a strong correlation between the severity of portal hypertension and dampening of hepatic venous waveform in Doppler ultra sound.

Our study showed 70% of abnormal HV waveforms in clinically diagnosed portal hypertension patients.

In those abnormal waveform patients 71% showed Biphasic. 39% showed Monophasic (Baseline observations). After PPNL all those Biphasic patients showed triphasic waveforms. In those Monophasic waveform patients 75% showed improvement either to Biphasic or Triphasic. 25% of Baseline Monophasic patients showed no improvement even after two months followup.

Our study had some limitations. This is a single observer study. And the findings were not correlated with HVPG. There was a preponderance of men in our study. This was unavoidable, and it reflects the fact that cirrhosis due to alcohol, viral hepatitis, or both, is more prevalent in Indian men.

SUMMARY

A prospective study of 60 patients with clinical diagnosis of portal hypertension referred from in and out patient department of Surgery and Gastroenterology was done in the Barnard Institute of Radiology, Madras Medical College. Male to Female ratio was 2 : 1. The patients belonged to age group ranging from 22 to 62 years. Patients were then evaluated using Duplex-Doppler Ultrasound with the 3.5 MHz curvilinear transducer.

This study takes into account a single variable (Hepatic Venous waveform Pattern) to detect the response to vasoactive drug (PPNL) in patients with clinical diagnosis of portal hypertension. It is not correlated with HPVG.

Our study showed a strong correlation between the severity of the disease and dampening of hepatic venous waveform in spectral Doppler. 92.8% of patients showed improvement of baseline waveform and this correlates with the clinical improvement.

So, Doppler ultra sound evaluation of hepatic venous waveform pattern (Qualitative) can be used to assess the severity of portal

hypertension and to monitor the response to vasoactive drug (PPNL). It can be a useful non invasive tool in portal hypertension evaluation and is an alternative to HPVG.

CONCLUSION

Classification of the hepatic vein Doppler waveform seems to be superior to any quantitative Doppler indices in terms of reproducibility, technical ease of use, and accuracy. Indeed, the method used for qualitative evaluation of hepatic vein Doppler waveforms is simple enough to potentially allow widespread clinical use.

In our study thirty nine out of forty two Patients showed improvement in the Hepatic venous waveform after PPNL. And this correlates with the clinical improvement. i.e. 92.8% patients showed improvement after PPNL both clinically and Doppler wise.

In conclusion, assessment of the hepatic vein waveform with Doppler US could be considered a useful adjunctive method in the noninvasive assessment of the severity of portal hypertension and the response to vasoactive drugs in patients with portal hypertension and variceal bleeding.

BIBLIOGRAPHY

- 1. Ohta M, Tomikawa M, Ueno K, Tanoue K, Sugimachi K. Analysis of hepatic vein waveform by Doppler ultrasonography in 100 patients with portal hypertension. PMID: 8304297.

- 2. Hepatic vein Doppler waveform changes in early stage (Child-Pugh A) chronic parenchymal liver disease Journal of Clinical Ultrasound Volume 25, Issue 1, Pages 15 – 19.

- 3. Doppler waveform of the hepatic veins in an obese population European Radiology, Volume 14, Number 12 / December, 2004, Pages 2268-2272.

- 4. Hepatic vein Doppler waveform in patients with diffuse fatty infiltration of the liver doi:10.1016/j.ejrad.2004.05.011.

- 5. S. Jequier, J. C. Jequier, S. Hanquinet, J. Gong, C. Le Coultre and D. C. Belli Doppler Waveform of Hepatic Veins in Healthy Children, AJR 2000; 175:85-90.

- 6. Hashizume M. Prognostic significance of hepatic vein waveform by Doppler ultrasonography in cirrhotic patients with portal hypertension. Am. j. gastroenterol. ISSN 0002-9270. 1995, vol. 90, no10, pp. 1853-1857 (24 ref.)

- 7. W Gorka, A al Mulla, M al Sebayel, I Altraif and TS Gorka Qualitative hepatic venous Doppler sonography versus portal flowmetry in predicting the severity of esophageal varices in hepatitis C cirrhosis American Journal of Roentgenology, Vol 169, 511-515

- 8. H. Sugimoto ,M. Hirota, S. Kure, N. Kanazumi, S. Nomoto, S. Inoue, S. Takedaa, T. Kiuchia and A. Nakaoa Normal Hepatic Hemodynamics During Early Postoperative Period in Recipients With Adult Live Donor Liver Transplantation Proceedings Volume 39, Issue 1, January-February 2007, Pages 160-165

- 9. Soon Koo Baik. Recent Variceal Bleeding: Doppler US Hepatic Vein Waveform in Assessment of Severity of Portal Hypertension and Vasoactive Drug Response. (RSNA)Radiology 2006;240:574-580

- 10. Moon Young Kim. Damping index of Doppler hepatic vein waveform to assess the severity of portal hypertension and response to propranolol in liver cirrhosis: a prospective nonrandomized study. Liver International Volume 27 Issue 8 Page 1103-1110, October 2007

- 11. J F PEDERSEN, Abnormal hepatic vein Doppler waveform in patients without liver disease. The British Journal of Radiology, March 2005

- 12. KC Sudhamshu, Doppler study of hepatic vein in cirrhotic patients: Correlation with liver dysfunction and hepatic hemodynamics. World J Gastroenterol 2006 September 28; 12(36): 5853-5858, World Journal of Gastroenterology ISSN 1007-9327

PROFORMA

Hepatic Venous Waveform Pattern In Cirrhosis Before And After Propanolol

1. Name :

2. Age/Sex :

3. Address :

4. Present Complaint :

5. Relevant H/O :

   Jaundice

   - Hematemesis
   - Malena
   - Abdominal Distension

6. Clinical Examination :

- Anaemia,
- Pulse Rate
- Blood Pressure
- Jaundice
- Flapping Tremor

7. Investigations :
   - Hb%
   - Sr.Bilirubin
   - Sr.Hb S Ag
   - Usg Abdomen

8. Treatment H/O :

9. Portal Doppler (Before PPNL) :
   - Portal Vein - Size, PSV, Direction Of Flow, Phasic Variation
   - Hepatic Vein - Wave Form
   - Splenic Vein - Size, PSV, Direction Of Flow

10. Follow Up HV Waveform :

11. Response To PPNL :

ABBREVIATIONS

DCLD	-	decompensted liver disease
EHPVO	-	extra hepatic portal vein obstruction
F	-	female
HV	-	hepatic vein
HVPG	-	hepatic venous pressure gradient
M	-	male
PPNL	-	propranolol
PV	-	portal vein
US	-	ultrasonography