DISSERTATION ON

COLOUR DOPPLER EVALUATION OF COMMON ADULT HEPATIC TUMORS MORE THAN 2 CM WITH HPE AND CECT CORRELATION

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CERTIFICATE

Certified that this dissertation titled "COLOUR DOPPLER EVALUATION OF COMMON ADULT HEPATIC TUMORS MORE THAN 2 CM WITH HPE AND CECT CORRELATION" is a bonafide work done by Dr.P. SENTHILKUMAR M.D.(RADIODIAGNOSIS), Post graduate student of Barnard Institute of Radiology, Madras Medical College, Chennai, under the guidance and supervision of PROF. T.S.SWAMINATHAN, MD., DMRD., FICR., during the academic year 2003 – 2006.

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DECLARATION

I declare that this dissertation titled " COLOUR DOPPLER EVALUATION OF COMMON ADULT HEPATIC TUMORS MORE THAN 2 CM WITH HPE AND CECT CORRELATION " has been conducted by me under the guidance and supervision of Prof. T.S. SWAMINATHAN, M.B., MD., DMRD., FICR, Director, Barnard Institute of Radiology, MMC. It is submitted in part of fulfillment of the requirement for the award of the M.D., Radiodiagnosis, September 2006 examination to be held under Dr.M.G.R. Medical University, Chennai. This has not been submitted previously by me for the award of any degree or diploma from any other University.

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CONTENTS

INTRODUCITON

Liver is a large, homogenous organ and therefore is well suited for evaluation by many imaging techniques. Liver tumors in the adults are one of the common lesions in day today practice. Common adult hepatic tumors include hepatocellular carcinoma, metastases and hemangiomas. [45]

Hepatocellular carcinoma (HCC) represents 5% of all cancers and is the dominant cause of death in compensated cirrhosis. HCC incidence is increasing worldwide because of increasing HBV and HCV infection. HCC accounts for 85% of primary liver cancer. Most patients die within one year after diagnosis. Survival is dependent on tumor size and associated disease at the time of diagnosis. So, early detection of HCC is very important to prolong the survival. HCC is more common in` males in the age group 30 to 60 years.[7]

Liver provides fertile soil in which metastases can establish, not only because of rich, dual blood supply but also because of humoral factors that promote cell growth. (The blood supply of liver is exceeded only by that of the lung, in terms of blood flow per minute). Liver is the most commonly involved organ by metastatic disease, after the lymphnodes. The liver may be the site of metastases for virtually any primary neoplasm. So, patients with any malignant neoplasm especially with primary tumors of colon, stomach, pancreas, breast, lung and eye should be intensely followed up with ultrasound and if any lesion is detected, colour doppler can be utilized for early diagnosis and treatment.[22]

Hemangiomas are the most common benign liver tumors. Reported incidence of hepatic hemangiomas is 2%. The prevalence at necropsy is as high as 7.4%. Most hepatic hemangiomas are diagnosed at 30 to 50 years with females more affected than males.[45]

The study of liver tumor is particularly challenging. In many cases, a preoperative diagnosis may be achieved with appropriate combination of imaging techniques in a purely noninvasive fashion. This is important because many adults have benign nonsurgical hepatic lesions such as hemangiomas.[45]

There are several imaging modalities to evaluate focal liver lesions starting from plain radiograph, USG and doppler, CT, MRI, angiography and nuclear medicine techniques. Ultrasound and doppler is the initial, noninvasive, easily available modality to characterize focal liver lesions followed by CECT or MRI. Scintigraphy done for selected cases. Angiogram is done prior to embolization.[33]

AIM

1)To characterize the colour doppler USG features of common adult hepatic tumors hepatocellular carcinoma, metastases and hemangiomas more than 2 cm in size with HPE and CECT correlation

2) To asses the sensitivity, specificity and accuracy of colour doppler ultrasound in differentiating HCCs, metastases and hemangiomas.

REVIEW OF LITERATURE

Normal anatomy

The liver is the largest abdominal organ, weighing 1400 to 1600 g. It occupies most of the right upper quadrant in the normal adult. It is bordered medially by the stomach, duodenum and transverse colon; inferiorly by the hepatic flexure of the colon; posteriorly by the right adrenal gland and kidney; and superiorly, ventrally, and laterally by the diaphragm. It is covered by peritoneum except in the region of the gallbladder fossa, the fossa for the inferior vena cava, and the bare area. In the bare area, the liver is in direct contact with the diaphragm without intervening peritoneum. This region is demarcated by the right lobe supporting structures: the superior and inferior coronary ligaments. These ligaments fuse laterally to become triangular ligament. The left lobe is supported from the diaphragm by the left coronary ligament, which is contiguous with the falciform ligament. The falciform ligament is a thin fibrous sheet containing the ligamentum teres, which extends from the umbilicus to the superior surface of the liver.[45]

On the right, the coronary ligament separates the Morison pouch (right posterior subhepatic space) from the right subphrenic space. The left coronary ligament divides the left subphrenic space into an anterior and a posterior compartment. The falciform ligament separates the right subphrenic space from the left subhepatic space.

The gastrohepatic ligament (lesser omentum) connects the liver and stomach. The free edge of lesser omentum (hepatoduodenal ligament) contains the common bile duct, hepatic artery, portal vein, nerves and lymphatics.

Vascular Anatomy

The liver receives 15 to 20% of the cardiac output and constitutes a significant reservoir for blood. The liver has a dual blood supply: the hepatic artery, which provides systemic arterial circulation, and the portal vein which returns blood from the spleen and gut. These two vascular inflows have different pressures, flow rates and compositions. Arterial flow is primarily nutritive and provides about 20% of the blood supply; the remainder is supplied by the mesenteric portal drainage, which is a consequence of gastrointestinal functional activity. The relative contribution of blood flow to the liver by the arterial and portal systems depends on a number of factors: hormones, neural stimulation (sympathetic, vagal), nutritional state (including fasting or postprandial), and the presence of hepatic parenchymal disease.[33]

Hepatic Artery

The celiac artery typically gives rise to the common hepatic, splenic and left gastric arteries at the level of T12-L1. The common hepatic artery courses along the upper border of the pancreatic head, anteriorly and to the right, behind the posterior layer of peritoneum of the lesser sac. It gives off the gastroduodenal artery and at upper margin of the duodenum the proper hepatic artery enters the subperitoneal space of the hepatoduodenal ligament. It ascends to the liver anterior to the portal vein and medial to the common bile

duct. After entering the porta hepatis, the proper hepatic artery divides into a right, a left and occasionally a middle hepatic artery. The right lobe is supplied by the right hepatic artery, the medial segment of the left lobe is supplied by the middle hepatic artery augmented by the branches of the left hepatic artery and the lateral segment of left lobe receives blood from left hepatic artery. Branches of the right hepatic artery nourish the caudate lobe, but in some cases the left or even middle hepatic artery contributes. The right hepatic artery also gives off the cystic artery which supplies the gallbladder.[45]

The vascular schema just described is present in only 55% of patients. Normal variants include (1)the right hepatic artery partially(18%) or completely (14%) replaced by superior mesenteric artery; (2)the entire hepatic artery arising from the superior mesenteric artery (2 to 4%); (3)the left hepatic artery having a partially or totally replaced origin from the left gastric artery (18% to 25%); and (4)the left hepatic artery giving rise to the middle hepatic artery in 45% of patients.

<u>Portal Vein</u>

The main portal vein arises behind the pancreatic neck at the junction of the splenic and superior mesenteric veins. The main portal vein courses to the right and superiorly in the hepatoduodenal ligament, along with the hepatic artery and common bile duct, anterior to the foramen of Winslow. At the porta hepatis, the portal vein divides into right and left branches. The right portal vein courses horizontally before bifurcating into anterior and posterior branches. The left portal vein is shorter as it ascends anterior to caudate lobe

before it courses ventrally to the left intersegmental fissure, where it divides into branches supplying the medial and lateral segments of the left hepatic lobe. The ligamentum teres (umbilical vein remnant) inserts into the anterior margin of the left portal vein. In embryonic life, blood in the umbilical vein empties into the left portal vein and much of it is shunted to the inferior vena cava and systemic circulation through the ductus venosus.[33]

Hepatic Veins

The hepatic veins reside between the hepatic segments and lobes. The right hepatic vein is usually the largest and courses obliquely between the anterior and posterior segments of the right lobe. The middle hepatic vein is in between superior aspect of the right and left lobes. The left hepatic vein courses between the medial and lateral segments of the left lobe. All these veins drain obliquely and superiorly into the inferior vena cava, near its entrance into the right atrium. The right hepatic vein usually enters the inferior vena cava separately from the middle and left hepatic veins. The last two veins typically form a common trunk as they enter the vena cava.[45]

Lobar and Segmental Anatomy

The segmental anatomy of the liver is eloquently depicted on cross-sectional imaging. Delineation of this anatomy is essential for the localization of focal hepatic pathology before surgical, angiographic or percutaneous intervention. Hepatic segmental topography is best appreciated radiographically by identification of the vascular and fissural anatomy. The portal venous, hepatic arterial and biliary systems travel together within hepatic segments and lobes (intrasegmental). The main hepatic veins course between segments and lobes (intersegmental).[45]

The right hepatic vein separates the posterior and anterior segments of the right lobe. The middle hepatic vein superiorly and the interlobar fissure inferiorly separate the right and left lobes of the liver. The medial and lateral segments of the left hepatic lobe are divided by three readily discernible structures: the ligamentum teres (inferiorly), the ascending portion of the left portal vein and the left hepatic vein (superiorly).

Advances in surgical techniques and percutaneous intervention have popularized the use of the subsegmental anatomic classification of Couinaud, with the modification of Bismuth and colleagues, to define hepatic location more precisely. In this system, the liver is divided into one segment and eight subsegments. Segment 1 is the caudate lobe. The well-known vertical divisions along the planes of hepatic veins are maintained, but each segment is further divided into superior and inferior subsegments by a transverse fissure (a plane through the right and left portal veins). The subsegments are numbered in a clockwise fashion when viewing the liver in the frontal projection except for segment 4a.

The caudate lobe is central hepatic lobe that has certain unique features. The anterior border of the caudate lobe is separated from the lateral segment of the left lobe by the fissure for the ligamentum venosum. The pars transversa of the left portal vein resides at the apex of this fissure. Fat in this fissure often communicates with fat in the fissure for ligamentum teres. Posteriorly caudate lobe is bordered by the inferior vena cava. Inferiorly caudate lobe forms the superior margin of foramen of Winslow.[45]

RADIOLOGIC TECHNIQUES

Plain Films

The plain abdominal radiograph usually reveals little detail of hepatic structure because of the homogenous, soft tissue density of the liver. The superior margin of the liver is clearly depicted by the diaphragm and lung. The other borders are less well defined. The presence of hepatic calcification should be carefully sought when evaluating plain abdominal radiograph.[33]

Ultrasound

The liver is ideally located in the right upper quadrant for sonographic evaluation. It has a broad area of contact with the abdominal wall, so that bowel gas and intraperitoneal fat are not limiting factors. Sonography is a fast, inexpensive and safe means of evaluating the liver noninvasively, particularly in thin patients. It can be done portably and fast and is inexpensive, safe and requires little preparation or cooperation of the patient.[5]

The highest frequency transducer possible should be employed. If sufficient penetration to the posterior aspect of the liver cannot be obtained with a high frequency transducer, a lower frequency transducer should be used. The near and far gain settings should be adjusted to give a uniform representation of the hepatic parenchyma.

With real time scanning, the ideal imaging plane can be selected rapidly to display normal and pathologic anatomy to allow uncooperative patients and children to be studied more easily and to assess motion to assist identification of

bowel. The major disadvantage of real time scanning is a restricted field of view, which can be problematic when measuring an enlarged liver. Focal lesions are easily identified on the real time study and may be less well appreciated on the hard copy films.[33]

Examination Techniques

Hepatic sonography requires meticulous study with active participation of the physician. The examination is begun with the patient in the supine position, but frequently it is necessary to rotate the patient onto the left side to promote descent of the liver below the rib cage. Asking the patient to take in and hold a breath or to push out the anterior abdomen also caudally displaces the liver, affording better visualization of the hepatic dome. A small footprint transducer is helpful in visualizing livers that lie in a subcostal location.[5]

The right lobe is examined by scanning lateral to medial in the parasagittal plane. The echogenicity of the liver should be compared with that of the right kidney and fluid in the Morison pouch should be sought. The right portal vein is followed medially until the common hepatic duct is found. The inferior vena cava is also seen at this point. More medially, the confluence of the right and left portal veins is seen and subsequently the ascending portion of the left portal vein. In the transverse plane, from a right subcostal or intercostals location with cephalad angulation, the confluence of the hepatic veins into the inferior vena cava can be seen. The transducer is then angulated sequentially caudally, showing the bifurcation of the portal veins.

Sonography is an excellent means of following the course of hepatic and portal veins. The portal vein divides at the porta hepatis into right and left main branches. The portal veins are anechoic structures with echogenic walls. The bile ducts run with the portal veins and are too small to be seen except at the hilum, unless they are dilated. The hepatic arteries also run with these structures but are usually too small to be seen except with the aid of colour flow imaging.[5]

The hepatic veins course posteriorly and superiorly through the liver to the inferior vena cava. They are intersegmental, whereas portal veins are intrasegmental with the exception of the ascending segment of the left portal vein. The walls of hepatic veins are usually less echogenic than those of the portal veins.

<u>Normal Size, Shape and Architecture</u>

Because of the variable size and shape of the liver, the sonographic assessment of hepatic size is ultimately subjective; no single method accurately reflects true hepatic mass. One method that has been found to be 87% accurate in determining the presence or absence of hepatomegaly is to measure the liver in two planes. In the midclavicular line, the normal liver measures 10.5 +_1.5 cm in longitudinal diameter and 8.1+_1.9 cm in the anterior-posterior projection, with 12.6 cm and 11.3 cm being the 95th percentile.[45] **The reflectivity of hepatic parenchyma should be evaluated carefully in each patient. The parenchymal echoes of the liver should be relatively even in brightness and texture and should be interrupted only by hepatic veins, the portal triads and**

fissures. The parenchyma echoes appear as moderately short dots or lines. Normal parenchyma should be isoechoic in youth, slightly brighter in 30 to 60 years of age and markedly more echogenic in older patients. In ultrasound we have to see for,[33]

1)Lesion Size

2)Shape

3)Margins

4)Number

5)Location (right or left lobe, segments)

6)Echogenicity

7)Calcification

8)Adjacent vessel involvement(portal vein thrombus)

9)Bile duct dilatation

10)Liver echoes and architecture (cirrhotic liver)

11)Regional lymphadenopathy

12)Ascites

IntraOperative UltraSound (IOUS) and Laparoscopic US

IOUS is an important diagnostic tool in patients undergoing hepatic resection for colorectal metastases. IOUS allows careful evaluation of the normal liver segments to exclude occult metastases in the segments that will be left in situ. The high accuracy of IOUS is due to the contact scanning possible with a high-frequency transducer and color flow Doppler imaging; with this technique, the complete organ can be covered without artifact. IOUS depicts 25-35% more lesions than does preoperative US. Most significantly, 40% of the lesions

detected by means of IOUS are neither visible nor palpable, and would presumably have been missed with other means. IOUS has also been shown to be a sensitive means of detecting HCC, particularly if US contrast agents are used to improve Doppler images.[46]

Laparoscopic US is also valuable. It has an advantage over abdominal US in that the probe can be used to palpate the surface of the liver. This ability aids in the diagnosis of hemangiomas, which can be compressed, unlike solid tumors, which cannot.

Synchronous liver metastases are frequently encountered at surgery for GI malignancy; of these, as many as 40% may not have been palpable. IOUS enables the detection of 93% of liver metastases, compared with the 51% detection rate with preoperative CT and US; 66% are palpable at surgery.

<u>Doppler Imaging</u>

Duplex and colour flow Doppler imaging substantially enhance the diagnostic capabilities of ultrasound in evaluating the complex circulatory dynamics of the liver.[56,42] **The use of colour doppler in the diagnosis of tumors is based on the principle of neovascularity that occur in tumors. The original description of arteriographic neovascularity or tumor vascularity is credited to Strickland, who reviewed the findings in a series of 33 bone tumors. He described a tumor vessel as one that was deployed seemingly without purpose, keeps to no set course and shows progressive diminution in caliber. The presence of tumor vascularity is often, but not always, associated with an increased number of vessels within a tumor, or hypervascularity. Neovascularity may be further**

characterized as fine or coarse. Histopathologically, these vessels are primitive, vascular channels, lacking smooth muscle and often consisting of an endothelial layer and connective tissue alone.[53]

Two different signal types were identified from malignant tumor. Most common tumor signal is high velocity shift, ranging from over 3 KHz to as high as 10 KHz (70 to 700 cm/s), with or without enhanced diastolic flow. This type of signal is due to presence of arteriovenous shunt in tumors. Doppler ultrasound is more sensitive than angiography in the detection of arteriovenous shunting. Second type tumor signal consisted of an almost continuous high velocity doppler shift, with little or no systolic diastolic variation (low systolic / diastolic index); this signal pattern would be expected to originate from a high velocity jet into vessels with little or no vascular impedance. Histologic examination in these patients will demonstrate the presence of large, thin walled, sinusoidal spaces that lacked muscular support. Spectral broadening will be seen in tumor signals, in contrast to laminar plug flow seen in normal large vessels in which all red blood cells move at the same velocity. Flow velocity of 40 cm/s is the optimal threshold value with which benign and malignant tumors can be differentiated. This simple, economic doppler technique has great potential for noninvasive characterization of tumors.[53]

In general, HCCs and metastatic tumors are supplied directly by the hepatic artery branches. In these tumors, the small branches supplying the tumors are larger than the normal artery, and the branches do not taper normally as they approach the lesions and appear to break up into irregular

tumor vessels. Arterial branches supplying HCCs tend to show an irregularly tortuous extension, and the tumor vessels have widened, sclerosed lumina. Stenoses increase the peak systolic velocity, assessed with duplex doppler sonography, in large vessels. In normal hepatic arterial branches, peak systolic velocities seen in the proximal side generally exceed velocities seen in the distal side. If HCCs have irregularly tortuous vessels with widening or narrowing of the lumina, elevation of peak systolic velocities attributed to stenotic changes in the lumina may be seen in arteries feeding the tumor.[37]

Hepatic Artery

Vessels can be differentiated from bile ducts and from one another by their flow characteristics. Thrombosis, reverse flow, aneurysms and fistulas are well demonstrated with duplex and colour flow Doppler sonography. The hepatic artery has a Doppler tracing that reflects low impedance characterized by high diastolic flow that is seen in normal parenchymal organs. Spectral broadening is commonly seen in vessels of this size. Colour flow images may be needed to localize the hepatic artery. Doppler sonography is most often used to differentiate the hepatic artery from a bile duct in the porta hepatis. The intrahepatic branches of the hepatic artery are normally too small to be visualized on gray scale sonography. They may undergo compensatory dilatation in cirrhosis or become ectatic, simulating the parallel channel sign and incorrectly suggesting biliary obstruction. Doppler sonography is useful in differentiating the two. Most of the malignant tumors are supplied by the hepatic artery, so flow changes in the hepatic artery and its branches are seen

in HCCs and metastases. Evaluation of hepatic arterial flow is also important for patients who are candidates for or have had liver transplantation.[33]

We have to see in Doppler,[37]

1)Intralesional flow pattern (pulsatile flow, continuous flow, basket pattern or spot pattern, central or peripheral flow)

2)Intralesional peak systolic velocity

3)Common hepatic artery peak systolic velocity

4)Tumor index (intralesional PSV/common hepatic artery PSV)

5)Portal vein involvement

<u>Ultrasound Contrast Agents and Harmonic Imaging</u>

In the liver, the goal of these agents is to increase visualization of slow-flow vessels, thereby increasing lesion conspicuity and improving lesion characterization. Contrast agents must increase the strength of the echo from blood, improving the signal to noise ratio, which determines the detectability of vessels. Agents are injected intravenously, and imaging proceeds immediately thereafter. One major drawback of these agents has been the narrow window available for scanning after contrast administration. There are two major types of ultrasound contrast agents: blood pool agents and agents that act by selective uptake into tissues.[1]

Blood pool agent uses stabilized microbubbles, which are adsorbed to galactose particles and palmitic acid (Levovist). Levovist enhances small vessels and improves Doppler signal in the portal vein and has been found to improve

the visualization of tumor vessels in hepatocellular carcinoma. Levovist is also useful to differentiate between benign hyperechoic lesions and hepatocellular carcinoma. The imaging window of levovist is less than 7 minutes. More recently developed agents employ low-solubility gases to last longer in the bloodstream and increase the returning echo.[1]

Harmonic imaging involves modifying the scanner to receive echoes at twice the transmitted transducer frequency. This modification detects microbubbles as they resonate at their characteristic frequencies.

Computed Tomography

The widespread availability of helical CT has significantly changed the way the liver is imaged. Helical CT provides several important advantages over conventional CT. The most important is its ability to image the entire liver rapidly to exploit contrast dynamics and thus improve lesion detectability.[45]

Noncontrast Scans

Noncontrast CT scans of liver are inferior to contrast enhanced studies for lesion detection and thus are not routinely performed except in certain specific situations. The liver parenchyma is usually homogenous with attenuation values ranging between 40 and 70 HU. The attenuation of the liver is variable from person to person and may be different from time to time in the same individual. The density of the liver parenchyma is greater than that of the blood vessels and other intra-abdominal organs. It is usually 7 to 8 HU greater than that of the spleen on noncontrast scans.[33]

Contrast Scans

The goal of contrast enhancement is to improve lesion visibility by increasing the relative attenuation difference between the lesion and normal hepatic parenchyma. This difference is a fundamental factor in lesion conspicuity and characterization. Hepatic enhancement is most dependant on the phase of the contrast delivery during which scanning occurs. These phases can be divided into vascular(arterial), redistribution(portal venous), equilibrium(delayed) phases. Arterial phase taken 20 to 30 seconds after intravenous contrast bolus and portal venous phase taken 60 to 90 seconds after intravenous contrast bolus.[45]

Helical Portal-Venous Phase Scan (Single-Phase Scan)

This is preferred CT technique for routine hepatic evaluation. With helical CT, entire liver can be scanned during peak contrast enhancement, further improving diagnostic accuracy. This is accomplished by imaging the liver beginning at about 55 to 70 seconds after the start of contrast bolus, depending on injection rate. Only 20 seconds are required to image the entire liver. Most centers use 150ml of 60% iodinated contrast material injected at a rate of 3 ml/s or more.[33]

Biphasic Helical Scan

The liver is imaged at two different times after contrast administration. Arterial phase is accomplished by scanning 20 to 30 seconds after the initiation of contrast administration. A second acquisition is then obtained during the portal venous phase of contrast delivery (55 to 65 seconds after contrast

initiation). Contrast material is delivered at a faster rate than in portal venous scanning (4 to 5 ml/s) and thus the portal venous phase is initiated earlier. Biphasic helical scanning has been found especially helpful in hepatocellular carcinoma, in which the addition arterial phase scan improves lesion detection when compared to portal phase scans alone or CT arterial portography.[3]

Computed Tomographic Angiography and Portography

In this technique, an arterial catheter is placed selectively in the hepatic artery, splenic artery or superior mesenteric artery at angiography and the patient is transferred for CT imaging. Because of its invasiveness, CTAP is generally reserved for patients in whom hepatic resection is contemplated. Hepatic arterial injection (computed tomographic hepatic arteriography) produces dense enhancement of most lesions because hepatic tumors are predominantly supplied by the hepatic artery. Liver metastases that receive primarily arterial rather than portal blood appear as low attenuation defects. Because of its high sensitivity in detecting focal liver lesions, CTAP has been considered the best imaging test for the detection of liver metastases.[20]

MR Imaging

MR imaging is increasingly being used to image the liver. Its role is either as a compliment to CT (to characterize a focal lesion or possibly improve sensitivity to metastatic disease) or as a first-line study (such as in patients with possible metastases or allergy to iodinated contrast material). Many different pulse sequences have been used in MR imaging. In general, T1-weighted and T2-weighted sequences are performed. Contrast agents may be added in certain situations.[45]

T1-Weighted Sequences

On T1-weighted images, the signal intensity of normal liver is greater than that of spleen, muscle and kidney and less than that of surrounding fat. Most hepatic tumors have a long T1 and thus appear as hypointense lesions on T1-weighted images.

T2-Weighted Sequences

Spin-echo, segmented spin-echo (such as fast or turbo spin-echo) and short tau inversion recovery (STIR) sequences can be used to obtain T2-like information. Fast spin-echo techniques have shown consistently sharper anatomic detail with less respiratory and cardiac motion artifact than conventional spin-echo sequences. Half Fourier acquisition single shot turbo spin echo (HASTE) is modification of turbo spin echo allowing for a further reduction in scan time.[33]

MRI contrasts

The contrast agents available for use in liver imaging can be classified into 4 groups according to their biologic distribution: (1) gadolinium chelates, which have an extra cellular distribution; (2) macrophage-monocytic agents targeted to the phagocytic system; (3) hepatobiliary agents; and (4) blood pool agents. This classification is not strictly accurate because these agents are distributed successively or simultaneously to more than one site. Dynamic gadolinium-enhanced MRI not only improves the detection of focal liver masses but also permits the differentiation of benign and malignant lesions.[45]

PET

Pet is a quantitative physiologic imaging modality using positron emitters, such as fluorine-18. The most commonly used radiotracer is 2-fluoro-2-deoxy-D-glucose (FDG). FDG-PET proved to be highly sensitive in detecting metastases from different primaries. Delbeke and coworkers studied the diagnostic value of FDG-PET in hepatic metastases measuring 1 cm or larger, and detected all 66 metastatic lesions originating from various primaries, such as the colon, pancreas, esophagus, sarcoma and parotid. In cases of known solitary hepatic metastasis diagnosed by CT, several groups reported discovery of additional hepatic metastases by FDG-PET. This is of particular importance in preoperative evaluation of solitary hepatic metastasis because detection of additional lesions often changes the management.[46]

CLASSIFICATION OF LIVER TUMORS:[45]

Benign liver tumors and tumor like conditions

Hepatocellular Origin

Hepatocellular adenoma

Hepatocellular hyperplasia

Focal nodular hyperplasia

Nodular regenerative hyperplasia

Macroregenerative nodule(adenomatous hyperplasia)

Cholangiocellular Origin

Hepatic cysts

Simple hepatic cysts

Congenital hepatic fibrosis or polycystic liver disease

Benign cystadenoma

Bile duct adenoma

Mesenchymal Origin

Mesenchymal hemartoma

Hemangioma

Infantile hemangioendothelioma

Lymphangioma

Lipoma, angiolipoma, myelolipoma

Leiomyoma

Fibroma

MALIGNANT TUMORS OF THE LIVER

PRIMARY

SECONDARY

Lymphoma

Metastases

Primary malignant liver tumors:

Hepatocellular origin

Hepatocellular carcinoma

Clear cell carcinoma

Giant cell carcinoma

Childhood HCC

Carcinosarcoma

Fibrolamellar carcinoma

Hepatoblastoma

Sclerosing hepatic carcinoma

Cholangiocellular origin

Cholangiocarcinoma

Cystadenocarcinoma

Mesenchymal origin

Angiosarcoma

Epetheloid hemangioendothelioma

Leiomyosarcoma

Fibrosarcoma

Malignant fibrous histiocytoma

Primary lymphoma

Primary hepatic osteosarcoma

Commonest malignant liver tumors encountered in day today practice are hepatocellular carcinoma and metastases and the commonest benign tumor is hemangioma.

Hepatocellular Carcinoma

Hepatocellular carcinoma (HCC) represents more than 5% of all cancers and is the dominant cause of death in patients with compensated cirrhosis. Its incidence is increasing worldwide. HCC accounts for up to 85% of primary cancers. The tumor is linked to environmental, dietary and lifestyle factors, so that its incidence and distribution vary widely among ethnic groups, geographic regions and the two sexes.[7]

Incidence and Geographic Distribution

Internationally: HCC is more common in Asia and Africa than in the United States. Internationally, the highest incidence of HCC is in Japan (4-5%). Other high-incidence regions include sub-Saharan Africa. In terms of relative frequency, HCC ranks as the fifth most common cancer in the world and the second most common cancer of the digestive tract, after cancer of the stomach.[33]

Risk factors[45]

Alcohol: As many as 50% of alcoholics may have subclinical HCC at autopsy. The risk of HCC is greater once the patient stops drinking alcohol because heavy drinkers do not survive long enough to develop cancer.

Hepatitis B virus: Global incidence of HBV infection is estimated to be 400 million persons. Chronic infection in the setting of cirrhosis increases the risk of HCC 1000-fold. This is the most common cause worldwide and may be related to integration of the viral genome into the host DNA.

Hepatitis C virus: HCV is a global pandemic affecting 170 million persons. HCV infection results in a higher rate of chronic infection compared to HBV infection (approximately 80% of infected subjects). It has become the most common cause of HCC in Japan and Europe, and it also is responsible for increased incidence in the United States.

Hemochromatosis, aflatoxin, primary biliary cirrhosis, androgenic steroids, thorotrast, oral contraceptives, and porphyria cutanea tarda.

Mortality/Morbidity: Most patients with HCC die within 1 year after diagnosis. Survival is dependent on tumor size and associated diseases at the time of diagnosis. Patients with cirrhosis have a shorter survival. Surgical cure is possible in less than 5% of patients. The causes of death include bleeding (variceal, intraperitoneal) and cachexia.

Race: A high incidence is seen in Japan and Africa.

Sex: In high-incidence regions of the world (ie, Asia, Africa), the male-to-female ratio is approximately 8:1.

Age: In high-incidence regions of the world (ie, Asia, Africa), patients present at age 30-50 years

Clinical Details

Clinical presentation varies among high-incidence and low-incidence regions. In high-incidence regions (ie, Asia, Africa), clinical presentation of HCC tends to be aggressive and includes bleeding, hepatic rupture, and hemoperitoneum. In low-incidence regions (ie, Western Hemisphere), clinical presentation of HCC tends to be less aggressive and includes symptoms such as fever of unknown origin, abdominal pain, malaise, weight loss, and hepatomegaly. Jaundice is rare. Liver function tests can be normal. AFP levels may be elevated since this protein commonly is produced by HCC.[7]

Pathology

Based on gross anatomic features, HCC is classified as solitary, multifocal, diffuse

Solitary mass - Often large

Multifocal or nodular pattern - Multiple nodules

Diffuse - Multiple, small foci scattered diffusely throughout the liver

Based on growth patterns, HCC is classified as infiltrative, expanding, multinodular or mixed.[11]

Lab Studies

Expect total bilirubin, aspartate aminotransferase (AST), alkaline phosphatase, albumin, and prothrombin time to show results consistent with cirrhosis. Alpha-fetoprotein (AFP) is elevated in 75% of cases. The level of elevation correlates inversely with prognosis. An elevation of greater than 400 ng/mL predicts for HCC with specificity greater than 95%. In the setting of a growing mass, cirrhosis, and the absence of acute hepatitis, many centers use a level greater than 1000 ng/mL as presumptive evidence of HCC (without biopsy).[12]

Imaging

Plain Radiograph: Plain films are nonspecific but may show a mass in the upper abdomen if the HCC is large. Rarely calcifications can be detected in HCC.

Ultrasound and Doppler

The sonographic appearance of HCC is varied. These lesions are frequently hyperechoic, particularly if there is fatty change or marked sinusoidal dilatation. Ultrasonography can detect extremely small tumors and when combined with serum alpha-fetoprotein assays, serves as an excellent screening method for high risk patients with long standing cirrhosis. Sonography, in conjunction with colour and duplex Doppler, is an excellent means of diagnosing tumor thrombus in the portal and hepatic veins as well as the inferior vena cava.[5]

Colour Doppler ultrasound has been used to asses the vascularity of HCC because HCC tumor nodules are supplied by hepatic artery. Lesions show both intratumoral and peritumoral flow. A basket pattern (a fine blood flow network surrounding the tumor nodule) was observed in HCC. In lesions less than 2 cm it is difficult to detect the flow pattern. Intralesional pulsatile flow with peak systolic velocity (PSV) more than 40 cm/s with relatively normal hepatic artery flow is strongly suggestive of HCC.[37]

Nuclear Medicine: Nuclear medicine provides relatively nonspecific findings. The HCC may present as a "cold" defect on a sulfur-colloid study or may demonstrate uptake of radiopharmaceutical if the mass produces bile. Gallium uptake is seen in 90% of HCCs.

Computed Tomography

Cross-sectional imaging with CT and MRI is used most commonly to detect HCC. Sensitivity of good quality dual- or triple-phase CT for the detection of

patients with tumors is 60-70%. CT appearance of HCC varies depending on tumor size and the imaging phase. The most common attenuation pattern is iso-hyper-isoattenuation on pre-, arterial, and venous phases, respectively. However, this pattern is shared by other hepatocellular nodules, including regenerative and dysplastic nodules. Unenhanced CT typically reveals an iso-hypodense mass.[33]

MRI

HCC appearance varies on MRI depending on multiple factors, such as hemorrhage, degree of fibrosis, histologic pattern, degree of necrosis, and the amount of fatty change. HCC on T1-weighted images may be isointense, hypointense, or hyperintense relative to the liver. On T2-weighted images, HCC usually is hyperintense. Pre- and postcontrast MRI has a 70-85% chance of detecting a solitary mass of HCC. MRI can help differentiate cirrhotic nodules from HCC. Gadolinium-enhanced MRI typically demonstrates that HCCs densely enhance, usually in the arterial phase and particularly if they are small.[45]

PET

Positron emission tomography with fluorodeoxyglucose (FDG PET) is primarily useful in assessing the degree of differentiation and in staging moderately and poorly differentiated tumors than in primary lesion detection. Sensitivities of FDG PET for the detection of HCC range from 50-70%. This limited sensitivity is due to the low level of FDG uptake in well-differentiated

tumors. However, FDG PET may be superior to CT in detecting extrahepatic spread.

Angiography

Angiography for diagnosis of HCC has been replaced largely by cross-sectional imaging. Normal vasculature typically is displaced by a large mass. HCC is characteristically hypervascular with bizarre neovascularity and arteriovenous shunting. An enlarged hepatic artery may be present. Look for vascular invasion (portal veins, hepatic veins).[45]

Treatment options

Available treatment options depend on the size, number, and location of tumors; presence or absence of cirrhosis; operative risk based on extent of cirrhosis and comorbid diseases; overall performance status; patency of portal vein; and presence of metastatic disease. Surgical resection and liver transplantation are the only chances of cure but have limited applicability. The main prognostic factors for resectability are tumor size and liver function. Other local therapies are chemoembolization, ethanol ablation, radiofrequency ablation, cryoablation, and radiotherapy. Systemic treatment with chemotherapy may be employed.

METASTASES

Background: The liver provides a fertile soil in which metastases can establish, not only because of its rich, dual blood supply but also because of humoral factors that promote cell growth. (The blood supply of the liver is exceeded only

by that of the lung, in terms of blood flow per minute.) The fenestrations in the sinusoidal endothelium allow a foothold into the space of Disse for tumor emboli arriving via the blood stream.[33]

The liver is the second most commonly involved organ by metastatic disease, after the lymph nodes. In Europe and the United States, a focal liver lesion is more likely to represent a metastatic deposit than a primary malignancy. The liver may be the site of metastases from virtually any primary malignant neoplasm, but the most common primary sites are the colon, stomach, pancreas, breast, and lung. Most liver metastases are multiple, involving both lobes in 77% patients, and only 10% are solitary.

<u>Pathologic-anatomic characteristics of metastases</u>

The pathologic anatomy of metastases resembles that of the primary tumor. Metastases often show the same degree of vascularity as that of the primary tumor. Most metastases are hypovascular, but some primaries characteristically have hypervascular metastases. These include metastases from carcinoids; leiomyosarcomas; neuroendocrine tumors; renal carcinomas; thyroid carcinomas; choriocarcinomas.[33]

Blood flow is said to increase relative to the normal parenchyma in all metastases, even in hypovascular tumors. Large metastases tend to displace the surrounding vessels, and they may compress or occlude the portal venous branches. However, neovascularity, vascular encasement, and arteriovenous shunting are rare. Large metastases often outgrow their blood supply, causing hypoxia and necrosis at the center of the lesion. The patterns of blood supply of

liver metastases are of considerable clinical importance because of a number of diagnostic and therapeutic approaches depend on the degree of neovascularity, source and type of blood supply.

Incidence and Distribution: Depending on the site of the primary tumor 30-70% of patients dying of cancer have liver metastases.

Mortality/Morbidity: A large number of local or regional treatments are now available. These include hepatic resection and several minimally invasive techniques. These treatments have been successful, particularly in the treatment of colorectal cancers for which hepatic resection can offer the potential for cure.[45] Studies have shown a 20-40% 5-year survival rate after hepatic resection in selected patients. In patients with more-extensive disease, chemotherapy is now a feasible option; it may produce a response in 20% of patients. Hepatic involvement of metastatic tumor and the duration of survival appear to be inversely related. Most patients with liver metastases die with metastases rather than from metastases.

Race: Liver metastases have no known racial predilection.

Sex: The male-to-female ratio is 3:2 for colon carcinoma. The male-to-female ratio is 1:1 for pancreatic cancer, gastric cancer, and lung cancer.

Age: Metastases from primary sites in the eye, colon, stomach, pancreas, breast, or lung affect adults, usually those in the 50- to 70-year age group.

Clinical Presentation: Approximately 50% of patients who die with metastatic carcinoma of the liver have some hepatic signs or symptoms. Hepatomegaly (31%) is the most common finding, followed by ascites (18%), jaundice (14.5%), and varices (1%). Liver function tests are notoriously unreliable for detecting metastases; they are normal in 25 to 50% of patients with metastases and can be abnormal in any number of conditions, such as parenchymal tumor replacement, tumor obstructing the intrapheatic or extrahepatic bile ducts, or chemotherapy hepatotoxicity.

Imaging techniques:

Plain radiograph

A plain abdominal radiograph has a limited role in the investigation of liver metastases and the serial follow-up of liver metastases. Calcification is a more specific sign, seen in 2-3% of lesions, but it is insensitive. Common calcified metastases are from mucinous adenocarcinoma from stomach, pancreas, colon and rectum, ovarian serous lesions, leiomyosarcoma, carcinoid and medullary carcinoma of thyroid.

Ultrasound and Doppler

Ultrasound has a diagnostic sensitivity of greater than 90% in the detection of metastases. In the absence of complications, such as hemorrhage, infection or necrosis, focal metastatic liver disease presents with six basic sonographic patterns: hyperechoic, bulls-eye or target, hypoechoic, cystic, calcified and diffuse. In Doppler most of the lesions are hypovascular, some lesions may show intralesional flow which may be pulsatile or continuous flow with intralesional

peak systolic velocity less than 40 cm/s. The common hepatic artery flow has increased because metastases are supplied by hepatic artery.[5]

Computed Tomography

Metastases may appear in a multitude of ways on CT scans. The majority of liver metastases are hypovascular (hypoattenuating) compared with surrounding parenchyma; therefore, on nonenhanced CT scans, most lesions appear either hypoattenuating or isoattenuating relative to the surrounding parenchyma. Hypovascular lesions are routinely detected by using contrast-enhanced techniques. The accuracy of the technique depends on the timing of the acquisition relative to the administration of contrast material. The optimal scanning time is in the portal venous phase (approximately 60 s). When vascular metastases are suspected, a nonenhanced scan is recommended. The most sensitive technique for detecting liver metastases is CT arteriography (CTA) and CT arterioportography (CTAP).

MRI

As with CT and US, liver metastases have a variety of appearances on MRI. Most liver tumors benign or malignant appear as hypointense lesions on T1-weighted images and hyperintense lesions on T2-weighted images. Morphologic characteristics on T2-weighted images that suggest metastatic liver disease include the following: heterogeneous signal intensity with irregular and indistinct outer margins, and a smooth or irregular central area of high signal intensity with a surrounding ring of signal intensity lower than that of the

central focus but higher than that of the adjacent normal liver. Intravenous contrast agents improve the detection of liver mass lesions.

Nuclear Medicine

Metastases typically present as focal defects on both sulfur colloied and hepatobiliary scintiscans. They are the most common cause of focal cold liver lesions. PET using F-18 fluorodeoxy glucose (18-FDG) is a sensitive tool for the detection of liver metastases from colorectal primaries.

Angiography

Angiography is no longer used to diagnose liver metastases but is performed to provide a vascular road map for the surgeon and to guide intra-arterial therapy.

HEMANGIOMA

Hemangioma is the most common benign tumor affecting the liver. Hepatic hemangiomas are mesenchymal in origin and usually are solitary. Some authorities consider them to be benign congenital hamartomas. Hemangiomas are composed of masses of blood vessels that are atypical or irregular in arrangement and size. Etiology remains unknown.[33]

Pathophysiology

Although no definite familial or genetic mode of inheritance has been described, Moser et al reported a large family of Italian origin in which 3 female patients in 3 successive generations had large symptomatic hepatic hemangiomas. The authors postulated that restriction of the disease to the

female sex could be explained by sex-dependent differences in penetrance, the expression of a presumed liver-hemangioma gene, or the production of proliferative factors, such as female sex hormones.[33]

Frequency: The reported incidence rate of hepatic hemangiomas is approximately 2%. The prevalence rate at necropsy is as high as 7.4%. The widespread use of noninvasive abdominal imaging modalities has led to increased detection of asymptomatic lesions in vivo.[45]

Sex: Women, especially with a history of multiparity, are affected more often than men. The female-to-male ratio is 4-6:1.

Age: Hepatic hemangiomas can occur at all ages. Most hepatic hemangiomas are diagnosed in individuals aged 30-50 years. Female patients often present at a younger age and with larger tumors.

Clinical Features

Cavernous hemangiomas of the liver usually are small and asymptomatic. They most often are discovered when the liver is imaged for another reason or when the liver is examined at laparotomy or autopsy. Hemangiomas are usually solitary. Sizes range from 2mm to more than 20 cm. Larger and multiple lesions may produce symptoms. Right upper quadrant pain or fullness is the most common complaint. The only findings upon physical examination are, infrequently, an enlarged liver or the presence of an arterial bruit over the right upper quadrant.

Imaging Techniques

Ultrasound

This is the most commonly employed initial diagnostic tool. It is widely available and inexpensive. Hepatic hemangiomas usually are echogenic, but their sonographic appearance is variable and nonspecific. Addition of color Doppler to routine US provides qualitative and quantitative data and increases the sensitivity and specificity of the test. In Doppler hemangiomas will show minimal continuous or no flow with common hepatic artery showing normal flow. The intralesional peak systolic velocity will be less than 40cm/s.[37] Serial US examinations can be used to monitor any increase in size of the hemangioma over time. Recent work has studied the use of microbubble-enhanced US. Lesions show peripheral puddles and pools of enhancement that expand in a centripetal pattern during the portal venous phase of enhancement. With delayed imaging, the lesion may completely "fill in." However, complete enhancement might not occur in large lesions where central thrombosis or scarring may be present. In one recent study, the addition of a contrast agent to routine US improved sensitivity from 78% to 100% and specificity from 23% to 92%. In general, the US finding of a suspected hemangioma should be diagnostically integrated with CT scan or MRI to assure a correct diagnosis.[34]

Computed Tomography

Dynamic contrast-enhanced CT scanning is preferred to routine CT scanning. When requesting a CT scan to investigate a liver mass, the physician should inform the radiologist about the need for nonenhanced, arterial, portal venous and delayed imaging (the so-called triple phase CT with delayed imaging).

First, the liver is imaged by CT before the administration of intravenous contrast. The next series of images is obtained about 30 seconds after the injection of contrast, at the time that contrast is entering the liver via the hepatic artery. Portal venous imaging occurs 60 seconds later, as contrast is returning to the liver from the mesenteric veins via the portal vein. Finally, delayed images are obtained several minutes later. Hepatic hemangiomas are typically hypodense on precontrast imaging. In arterial phase, there may be enhancement of the peripheral portions of the lesion. There may be ring enhancement or globular enhancement. The center of the lesion typically remains hypodense. In portal venous phase and in delayed images, contrast enhancement progresses centripetally. The center of the lesion may only become hyperdense in delayed images.[33]

Magnetic resonance imaging

MRI is highly sensitive and specific in the diagnosis of hepatic hemangioma. Typically, hemangiomas have low signal intensity on T1-weighted images and high signal intensity on T2-weighted images. When gadolinium is employed as an intravenous contrast agent, hemangiomas enhance in a fashion similar to that seen on dynamic CT.[45]

Nuclear medicine

Tc-^{99}m pertechnetate-labeled RBC pool studies have been used for many years to help diagnose hepatic hemangiomas. For lesions that are greater than 2 cm in diameter, the sensitivity of the test has been reported at 82%. The specificity is up to 100%. SPECT with ^{99}mTc-labeled RBCs improves the sensitivity of the test for detecting small hemangiomas.[33]

Following are various studies to differentiate HCC, metastases and hemangioma more than 2 cm using colour Doppler sonography.

Numata K, Tanaka K, Kiba T, Morimoto M et al[37] evaluated hepatic tumor index on colour Doppler sonography for differentiating large hepatic tumors. 80 patients with 108 hepatic lesions more than 2 cm are evaluated. A peak systoloic velocity of 40 cm/s or greater suggested a malignant hepatic tumor rather than a hemangioma, with a sensitivity of 67%, a specificity of 91% and an accuracy of 71%. A hepatic tumor index equal to or greater than 1 was associated with 76% sensitivity, 92% specificity and 82% accuracy in distinguishing hepatocellular carcinomas and metastases. In lesions with a tumoral peak systolic velocity of 40 cm/s or greater, a hepatic tumor index equal to greater than 1 was associated with 91% sensitivity, 83% specificity and 89% accuracy in distinguishing hepatocellular carcinomas from hepatic metastases.

Tanaka S, Kitamura T, Fujitha M et al[51] made a study on differential diagnosis of liver tumors on the basis of the pattern of blood flow within and around tumors on colour Doppler flow images. 35 patients with liver mass lesions are analysed: 20 patients had hepatocellular carcinoma, six had hemangiomas four had metastatic lesions, one had cholangiocellular carcinoma, one had focal fatty liver and three had liver cysts. A basket pattern (a fine blood-flow network surrounding the tumor nodule) was observed in 15 (75%) of the 20 HCCs. In patients with multiple hepatic metastases a detour pattern (a dilated portal vein meandering around the tumor nodules) was observed. In

three of six hemangiomas, a spot pattern (colour stained dots or patches in the central region of the tumor). Their experience suggests that hepatocellular carcinomas have a characteristic appearance on colour Doppler flow images.

Gonzalez M, Cervera J, Garcia JH et al[15] evaluated the usefulness of colour Doppler and duplex sonography in the characterization of 106 solid liver lesions. With colour Doppler, the aspect and distribution of tumoral vessels and the pulsed Doppler parameters are considered only for those showing the highest systolic peak velocity values. Intra tumoral colour and pulsed Doppler signals were obtained in 81% of malignant tumors ($p<0.0001$) but only in 18% of benign tumors. Ninety percent of the lesions with arterial intratumoral and peritumoral signals were malignant, whereas 4% were benign ($p<0.0001$). Only 11% of malignant lesions had intratumoral venous signal vis-à-vis 70% benign. The type of signal (arterial or venous) and its distribution detected by colour and pulsed Doppler is more helpful than the assessment of the spectral quantitative parameters obtained by pulsed Doppler. The presence of intratumoral venous flow remarkably suggests benignancy. The presence of both intra and peritumoral arterial flow in the same lesion strongly suggests malignancy.

Lin ZY, Wang LY, Wang JH, Lu SN et al[31] assessed the clinical utility of colour Doppler sonography in the differentiation of hepatocellular carcinoma from metastases and hemangioma. They investigated 72 hepatocellular carcinomas (80 lesions), 30 metastases (82 lesions) and 39 hemangiomas (54 lesions). Overlaps of colour pattern were found among

hepatocellular carcinoma, metastases and hemangioma. Pulsatile waves from lesions with the basket vessels within the tumor or spot patterns or lesions less than 3 cm with detectable signals did not favour the diagnosis of hemangioma. Colour Doppler sonography can aid in the differentiation of HCCs from hemangioma but may be unreliable in the differentiation of HCCs from hypervascular metastases.

Yasuhara K, Kimura K, Ohto M, Matsutani S et al[59] studied blood flow detection using Doppler ultrasound in primary HCCs as well as in metastatic liver cancer and hemangioma. The pulsatile wave which was detected from HCC (35 out of 48 lesions) and metastatic liver lesions (in all seven with positive signals) and the continuous wave, which was seen from HCC (41 out of 48) and hemangioma (in all four with signals). In six patients who underwent transarterial embolization, the pulsatile wave detected before therapy disappeared immediately thereafter and it is possible that this type of wave originates from tumor vessels. Small hypoechoic mass lesions appearing in liver cirrhosis such signals were demonstrated, even in 8 of 10 small hepatocellular carcinoma less than 2 cm in diameter, whilst they are not detected from nine regenerative nodules related to cirrhotic change. Doppler ultrasound method may be a useful in detecting blood flow within liver tumors and may offer the possibility of differential diagnosis of small tumors.

Oguma M, Kawano M, Monma T et al[40] evaluated the diagnostic significance of blood flow pattern and velocity in hepatic tumors detected by colour Doppler ultrasonography. 57 patients with HCC and 12 patients with

hemangioma were studied. The detection rate of blood flow in HCC was significantly higher than in hemangioma . Pulsatile flow was detected in 43 of 57 patients with HCC. Average maximum velocity of pulsatile flow was over 40 cm/s. Analysis of blood flow after treatment provided useful on the effect of treatment. Analysis of blood flow in hepatic tumors on US with colour Doppler system may provide useful information on differential diagnosis between HCC and hemangioma, the assessment of the therapeutic effect of TAE or PEI, whether additional treatment is required or not, and when it should be done if required.

Wang WP, Xu ZZ, Shen SC et al[54] studied colour Doppler and pulsed Doppler in 56 patients with 71 solid hepatic lesions smaller than 3 cm in diameter. The detecting rates of arterial signals in small hepatocellular carcinomas group, hemangiomas group and otheres group were 86.9%, 37% and 33% respectively. Whereas, the average value of resistance index (RI) in small HCC group was very higher than (more than 0.5) that in other groups. The specificity of 96% and accuracy of 90% for the diagnosis of HCC and is superior to conventional USG.

Tang J et al[52] examined 40 cases of primary liver cancer with colour Doppler flow imaging and duplex Doppler. In 20 cases, there was arterial flow in the tumor. In 17 cases, there was arterial and portal venous flow in the tumor. In 22 cases, there was arterial flow entering the tumor from its surroundings. In 28 cases, the right or left hepatic artery was dilated. They compared the results of DSA with the Doppler ultrasound in 28 cases and

found the difference was not significant (p>0.05). They concluded that Doppler ultrasonography is the method of choice in the diagnosis of primary liver cancer.

Shrivastava DN, Mahajan A, Berry M, Sharma MP et al[49] evaluated 54 focal liver lesions with colour Doppler flow imaging (CDFI) to differentiate various types of lesions based on the flow pattern in terms of peritumoral and intratumoral blood flow. Marked intratumoral flow on CDFI was seen in 12.5% of primary hepatic malignancies and in infantile hemangioendothelioma, while a moderate flow pattern was seen in 56.2% of HCC and 18.7% of metastases; and 16.7% of hemangiomas. No intratumoral flow was seen in 100% of inflammatory lesions; 83.3% hemangiomas; 62.5% of metastases; and only one HCC (5.6%). Finally they concluded that CDFI when used along with other morphological imaging features, can assist in diagnosis or in narrowing the list of different diagnoses in a particular clinical situation.

Gaiani S, Casali A, Serra C, Piscaglia F et al[14] aimed to investigate the value and limitation of the different Doppler ultrasound modalities (spectral analysis, colour and power Doppler imaging) in the differential diagnosis of small liver tumors to identify the optimal diagnostic approach with the presently available Doppler technology. Presence and distribution of colour and power Doppler signals, Doppler peak frequency, resistive index and systolic accelereation time were examined in 133 liver nodules (< or = 4 cm). By discriminant analysis, peak frequency (cut-off 1320 Hz) differentiates small hepatocellular carcinoma (< or =2 cm) from macroregenerative nodules and

hemangiomas (accuracy 92.6%); resistive index (cut-off 0.65) differentiates malignancies from benign lesions (accuracy 83.8%); and systolic acceleration time (cut-off 105 ms) differentiates hepatocellular carcinoma from metastases (accuracy 80.9%).

Morimoto Y, Kubo S, Shuto T, Tanaka et al[35] studied the hemodynamics of intrahepatic tumors using power Doppler sonography. They used conventional B-mode ultrasonography, power Doppler ultrasonography and dynamic computed tomography to examine 71 hepatocellular carcinomas (</= 3 cm) before liver resection. Nodules with afferent pulsatile waves was higher in moderately or poorly differentiated hepatocellular carcinomas. Afferent continuous waves were detectable only in well-differentiated HCC. They concluded that Power Doppler can usually distinguish moderately or poorly differentiated from well-differentiated HCCs, which is useful in planning treatment and predicting outcome.

Kamalov IR, Sandrikov VA, Gautier SV, Tsirulnikova OM, Skipenko OG et al[19] developed a standard protocol of colour velocity and spectral Doppler ultrasound of liver tumor vascularization and to estimate the value of this method in differentiation of liver tumors. 68 patients with 128 primary and secondary liver tumors were observed. Qualitative features (vessel presence, vessel location and waveform of tumor vessel blood flow) and quantitative features (vessel quantity per $cm^{2,}$ vessel diameter, maximum velocity (Vmax), and resistance index (RI) of tumor artery and Vmax of tumor vein) are assessed. They concluded that tumor vascularization was found more

frequently in hepatocellular carcinoma than cavernous hemangioma or metastatic liver lesion ($p<0.01$).

Ignee A, Weiper D, Schuessler G, Teuber G, Faust D et al[17] investigated 100 consecutive patients with histologically proven hepatocellular carcinoma in order to evaluate sonographic characteristics in unselected patients and compared native and contrast enhanced techniques. The ultrasound appearance with conventional B-mode of hepatocellular carcinoma was hypoechoic in 48% of the cases, isoechoic in 9% cases, hyperechoic in 19% and in 25% a mixture between hyper and hypoechoic appearance was found compared to surrounding liver tissue. Contrast enhanced power Doppler techniques with SHU 508A changed the pattern of tumor vascularity in 27% of patients into hypervascular, mainly in small lesions. They concluded that the use of ultrasound contrast media should be considered to achieve characterization of liver nodules in cirrhotic livers because they can improve the evaluation of tumor vascularity. Hypovascular HCC are found in about 10% even after the administration of contrast agent.

Strunk H, Stuckmann G, Frohlich E et al[50] evaluated the characterization of liver lesions using power Doppler sonography before and after intravenous injection of the ultrasound contrast Levovist. They studied 39 patients with 41 liver lesions (10 hemangiomas, 2 focal nodular hyperplasias, 2 focal fatty infiltrations, 1 echinococcal lesion, 11 HCCs, 14 metastases and one cholangiocarcinoma). Power Doppler images before and after intravenous injection of the ultrasound contrast agent Levovist were analysed. Distribution

of flow (peripheral, central and diffuse) and amount (none, minimal, moderate and strong) of flow pattern in each sonographic examination. Histological verification was obtained in all liver lesions, except in hemangiomas, where MR imaging and in one FNH where scintigraphy was regarded as sufficient proof. On the whole, power Doppler sonography ws superior to unenhanced power Doppler sonography in 20 liver lesions and equal in 7. They concluded that intratumoral signal favour a malignant tumor. The absence of flow signals is a frequent finding in benign lesions but does not rule out malignancy.

Imamura M, Shiratori Y, Shiina S, Sato S et al[18] done this study to characterize the factors contributing to the power Doppler signals of HCC. Correlation of Doppler signals of HCC in 114 patients with 178 HCC nodules was analyzed in relation to the findings of CT and angiography, tumor characteristics (size, echo pattern and histological differentiation of tumor), viral markers and severity of liver disease. The sensitivity of power Doppler US was superior to that of CT and angiography (each p<0.05). The detection rate of power doppler signal was significantly higher in tumors with diameter > or =2 cm (vs <2 cm in diameter), and with low/mixed echo pattern (vs high echo appearance), and with moderately / poorly differentiated HCC (vs well differentiated HCC). They concluded that tumor characteristics play an important role in power Doppler signals an that these could be assessed by the presence or absence of power Doppler signals.

Numata K, Tanaka K, Mitsui K, Inoue S et al[39] studied benign and malignant hepatic tumors with colour Doppler sonography and arteriography

in order to correlate colour Doppler flow characteristics with tumor hemodynamics (vascularity, arteriovenous shunting, and portal vein involvement) shown by arteriography. They also evaluated the usefulness of colour Doppler flow characteristics in discriminating between tumor types. Colour Doppler sonography and arteriography was performed in 58 patients with 72 hepatic lesions larger than 2.0 cm in diameter. Differences in pulsatile flow (peritumoral or intratumoral) and the highest systolic peak flow velocities reached were evaluated on colour Doppler sonograms and compared with arteriography. The mean peak systolic flow velocity seen in hepatocellular carcinomas (0.52 cm/s) significantly exceeded the velocity seen in hemangiomas (0.16 m/s), but not the velocity in other malignant hepatic tumors (0.51 m/s). Finally they concluded that colour Doppler sonography was useful for evaluating hepatic tumor hemodynamics as seen at arteriography, and peak systolic velocity may be useful in differentiating malignant hepatic tumors from hemangiomas.

Wang YF, Zhang QP et al[55] used duplex Doppler ultrasound and colour Doppler flow imaging to study the characteristics of blood supply in neoplasms in 51 cases of 60 liver tumors, and compared with results of surgery, pathological examination and hepatic arterial angiography. The result showed that: 1)Doppler flow signals could be detected in all hepatic carcinomas, and in 10 cases of 18 hemangiomas, significant difference was observed ($p<0.001$); 2) Doppler blood flow spectra showed pulsatile pattern in 41 of 42 hepatic arcinomas, and in 6 of 10 hemangiomas ($p<0.01$); and 3) the peak systolic flow velocity was obviously lower in hemangioma group than in hepatic carcinoma

group (20.34 +/- 23.93 vs 64.74 +/- 30.18 cm, p<0.001). They concluded that colour flow characteristics of hemangiomas and HCCs are different and the blood supply of hepatic carcinomas mainly comes from hepatic arterial system, and is of value in duplex Doppler ultrasound and CDFI.

Kudo M, Tochio H, Zhou P et al[24] evaluated Doppler spectral analysis using colour Doppler sonography in a total of 133 patients with 135 hepatic lesions, including 88 HCCs, 30 metastatic hepatic cancers, 15 hemangiomas and 2 focal nodular hyperplasias. Maximum velocity (Vmax) of HCCs was significantly higher than hemangiomas. HCC showed wide spectrum in terms of Vmax and PI. Specificity of Vmax more than 60 cm/s and PI more than 2.0 for the diagnosis of HCC were 92 and 94% respectively. 87% of hemangiomas showed relatively lower Vmax (<30 cm/s) and low PI (<1.0 cm/s). When taking account of both parameters, Vmax and PI, diagnostic efficacy for hemangioma and HCC are greatly improved (sensitivity, specificity, accuracy, positive predictive value and negative predictive value of 80, 86, 85, 41 and 97% respectively, in hemangioma, and 38, 85, 54, 83 and 58%, respectively, in HCC). They concluded that in addition to the information obtained by Vmax, simultaneous measurement of PI adds valuable information useful in the noninvasive differentiation among hepatic tumors by Doppler spectral analysis at colour Doppler US.

Lee MG, Auh YH, Cho KS, Chung YH et al[28] evaluated the role of colour Doppler in differentiating HCCs from metastases and hemangiomas by the amount of tumoral colour signals. Intratumoral and peritumoral colour

signals were analyzed by a three-step grading system (grade 1 to 3) in 51 patients (32 HCCs, seven metastases, and 12 hemangiomas). Correlation of grading scores for intratumoral and peritumoral colour signals was evaluated with the size of the tumors as well. HCCs demonstrated a higher grade of intratumoral colour signals than did metastases or hemangiomas in all ($p<0.05$) and biopsy proved lesions ($p=0.0084$). There was no significant difference in the degree of peritumoral colour signals in all ($p>0.05$) or 17 biopsy-proved HCCs ($p=0.2078$) from the other tumor groups. Grade of both intratumoral and peritumoral colour signals was not related with the tumor size in all groups ($p>0.05$). They concluded that colour Doppler imaging provided a valuable role in the diagnosis of HCCs based on the qualitative analysis of the intratumoral colour signals.

Liang P, Cao B, Wang Y, Yu X, Yu D et al[30] conducted a study to evaluate the effectiveness of sonography, especially colour Doppler sonography, in the differential diagnosis of cystic hepatic lesions. 92 pathologically proven hepatic cystic lesions (20 cystic malignancies, 24 abscesses and 48 simple cysts) were evaluated with gray-scale and colour Doppler sonography. On gray scale sonography, the simple cysts were easily distinguished from cystic malignancies and abscesses. While no significant differences were found between hepatic cystic malignancies and hepatic abscesses on gray scale US. The sensitivity and specificity of colour Doppler sonography in differentiating cystic malignancies from abscesses and simple cysts were 85% and 96%, respectively. They concluded that presence of colour signals in the solid portion of the cystic

lesions carries a high diagnostic value in differentiating hepatic cystic malignancies from abscesses and simple cysts.

Kumada T, Nakno S, Toyoda H, Hayashi K, Kiriyama S, Sone Y et al[25] evaluated the usefulness of Doppler ultrasonography (DUS) for the analysis of tumor hemodynamics in small HCC. They compared DUS findings with CTAP and CTA in the evaluation of the intratumoral hemodynamics and with pathologic findings in 45 small HCC nodules (< or =3.0 cm in diameter) of 43 patients. DUS flow pattern of each nodule categorized into three types: afferent continuous flow (Type 1), afferent pulsatile flow with afferent continuous flow (Type 2) and afferent pulsatile flow without afferent continuous flow (Type 3). Intratumoral blood supply was determined by Angio-CT, and pathologic findings were evaluated on resected or biopsied specimen. DUS findings well represented blood supply of HCC evaluated by Angio-CT. In addition, all Type 1 and 2 nodules were well-differentiated HCC, and all Type 3 nodules were moderately or poorly differentiated HCC. They concluded that DUS is a non-invasive imaging method and can be used for the evaluation of the stage of malignancy of small HCC.

Shirato K, Numata K, Mitsui K, Kitamura T, Morita K et al[48] evaluated 86 patients with 92 HCCs (2.0 cm or greater in diameter) who underwent colour Doppler sonography before and after transcatheter arterial embolization and after subsequent percutaneous ethanol injection for 1) identification of pulsatile flow in the reisudal tumor area after TAE, 2) evaluation of therapeutic effectiveness of combined TAE and PEI, and 3)

detection of recurrence during follow-up evaluation. Before and 2 weeks after TAE, colour Doppler sonography revealed pulsatile flow in 76 and 43 lesions, respectively. During follow-up study colour Doppler sonography revealed pulsatile flow in 76.3% (local) and 63.2% (new). They concluded that colour Doppler sonography was useful for complying with our three objectives, especially for detecting local recurrence during follow-up evaluation.

Numata K, Tanaka K, Kiba T, Saito S, Kirikoshi H et al[38] assessed a possible correlation between the hepatic tumor index (as the ratio of the tumoral PSV to the PSV of the right or left hepatic artery) and grade of tumor vessel in large HCCs. Colour Doppler findings were evaluated and compared with selective hepatic arteriographic findings in 78 patients with 93 HCCs larger than 2.0 cm diameter. Pulsatile colour flow images were obtained in 78 of 93 lesions. The hepatic tumor index was equal to or greater than 1.0 in 57 of 78 lesions. These lesions were revealed arteriographically to have distinct tumor vessels and or arteriovenous shunting. When this index was 1.0 or greater, they calculated 90% accuracy in distinguishing HCCs with distinct tumor vessels from those without distinct tumor vessels. They concluded that hepatic tumor index correlated with the grade of tumor vessels and the presence of arteriovenous shunting.

Arai K et al[2] assessed the value of colour duplex Doppler sonography in evaluating tumor vascularity in 82 hepatic tumors (61 HCCs, 11 metastatic cancers, 8 adenomatous hyperplasia, one focal nodular hyperplasia and one cholangiocellular carcinoma). 28 (74%) of 38 tumors with signals within them

had definite tumor vessels on angiography and continuous blood flow within the tumors showed as association with dilated tumor vessels. 31% of tumors less than or equal to 3 cm showed signals within them in contrast to 78% of tumors greater than 3 cm. They concluded that Doppler sonography is somewhat useful in evaluating tumor vascularity, but less so in small tumors.

Shimamoto K, Sakuma S, Ishigaki T, Ishiguchi T et al[47] evaluated 15 patients of HCC with colour Doppler ultrasound, magnetic resonance imaging, dynamic computed tomography and angiography. Doppler signals ranging from 0.22 to 3.48 KHz could be obtained from within the tumor in 14 of 15 patients. The resistive index was 0.38-0.77. Colour Doppler signals were visualized in 9 of 15 patients with a Doppler shift greater than 0.7 KHz. The Doppler signals and the RI of tumor vessels became lower as the vessels progressed into the center of the lesion. The appearance of tumor vessels recognized on MR images obtained with gradient-recalled acquisition in the steady state (GRASS) in 11 of 15 lesions was compared with that on CT scans and angiograms. Tumors that were hyperintense on GRASS images obtained with flip angle of 15 degrees transmitted Doppler signals of considerably higher amplitude compared with the isointense lesions. They concluded both colour Doppler US and MR imaging provided useful information for characterizing intratumoral blood flow.

Dock W, Grabenwoger F, Metz V, Eibenberger K et al[10] examined 123 patients with benign and malignant neoplasms (breast cancer, n=44; liver neoplasms, n=43; and tumors affecting other organs, n=36) to establish general

criteria for evaluation of neoplastic lesions by means of duplex sonography. The frequency shifts determined by means of different Doppler requencies (2.31 or 3.75 MHZ) were converted in flow velocities. Only the highest systolic peak flow velocity obtained from a lesion was used for statistical evaluation. Receiver operating characteristic curves showed that a flow velocity of 40 cm/s is the optimal threshold value with which benign from malignant tumors can be differentiated. The data indicated that only positive findings are potentially reliable. They concluded that negative results of sonography should not be used to diagnose the presence of a benign lesion.

MATERIALS AND METHODS

A prospective study of 63 patients with 88 liver lesions detected on gray scale ultrasound referred from the Departments of Gastroenterology and Surgery was done in Barnard Institute of Radiology, Madras Medical College between February 2004 to December 2005. They were subjected to ultrasound, colour Doppler USG and CECT. The histopathological diagnosis was taken as the gold standard for confirmation of Hepatocellular carcinoma and metastases and triphasic CECT was taken as the gold standard for confirmation of hemangioma. Only adult patients are included in the study. There were no limitations to study with respect to sex.

CASES:

INCLUSION CRITERIA:

All adult patients with liver tumor on gray scale ultrasound more than 2 cm in diameter

EXCLUSION CRITERIA:

1) **History of surgery**
2) **History of chemotherapy**
3) **History of FNAC / biopsy of liver lesion**
4) **Very obese patients (nonvisualization or poor colour flow visualization of hepatic artery due to deep location)**
5) **Lesions less than 2 cm in diameter (the colour flow signals of such small lesions are not sufficiently distinct)**

EQUIPMENT AND TECHNIQUE

Gray scale and colour Doppler sonography were performed using Aloka 3500 SSD series unit. Gray scale sonography was performed at 3.5 MHz curved array transducer.

In the USG following parameters have taken for consideration.

1)Lesion Size

2)Shape

3)Margins

4)Number

5)Location (right or left lobe, segments)

6)Echogenicity

7)Calcification

8)Adjacent vessel involvement(portal vein thrombus)

9)Bile duct dilatation

10)Liver echoes and architecture (cirrhotic liver)

11)Regional lymphadenopathy

12)Ascites

In all examinations, colour assignment was chosen so that flow toward the trasnsducer was red and the flow away from the transducer was blue. Threshold levels were set to optimize the sensitivity without having excessive noise, examinations were performed at various flow settings, depending on the flow velocities. Examinations included real time colour images of the lesion, followed by point spectral analysis. Velocity was calculated from multiple

peritumoral and intratumoral arteries visualized in the two dimensional images. Velocity measurements were obtained at peak systole and end diastole after correction for the angle of insonation. A Doppler angle of 0 to 60 degrees was used when possible to reduce errors in velocity calculations. Of the five to 20 measurements obtained from each tumor, only the highest systolic peak flow velocity obtained from a tumor was used for statistical evaluation. Common hepatic artery flow and angle corrected PSV measurements are taken at the level of porta hepatis. The hepatic tumor index was calculated (defined as the ratio of the peak systolic velocity in the tumor to the peak systolic velocity in the hepatic artery).

In Doppler, we see the following

1)Intralesional flow pattern (pulsatile flow, continuous flow, basket pattern or spot pattern, central or peripheral flow)

2)Intralesional peak systolic velocity

3)Common hepatic artery peak systolic velocity

4)Tumor index (intralesional PSV / common hepatic artery PSV)

5)Portal vein involvement

Lesions are examined with USG, Doppler confirmed by FNAC, biopsy and CECT.

This study confines to ethics and was done with the consent and full cooperation of the patients.

FIG 1.NORMAL LIVER GREY SCALE AND COLOUR

DOPPLER

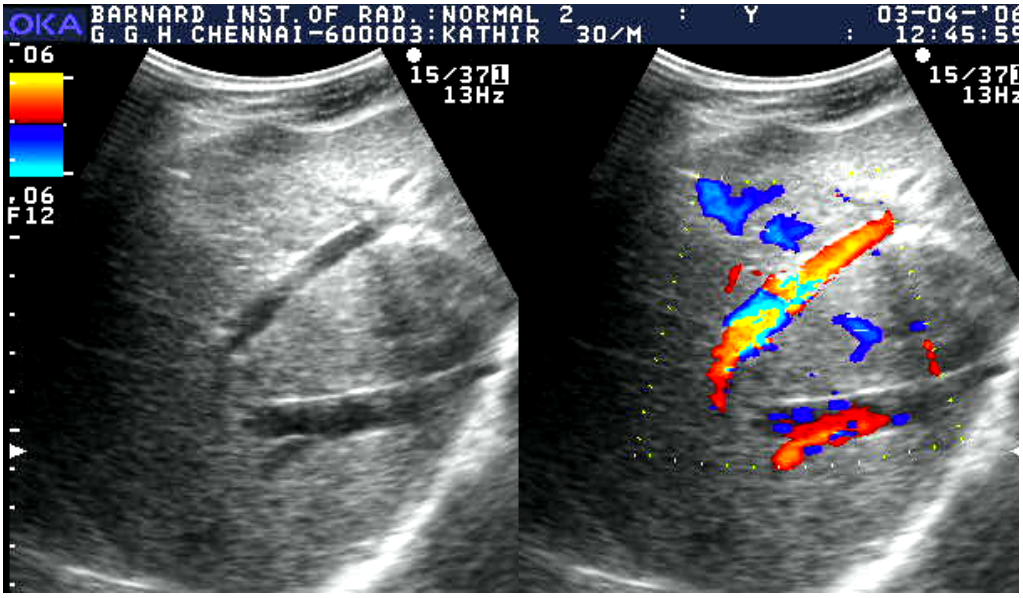


FIG 2. COMMON HEPATIC ARTERY ORIGIN

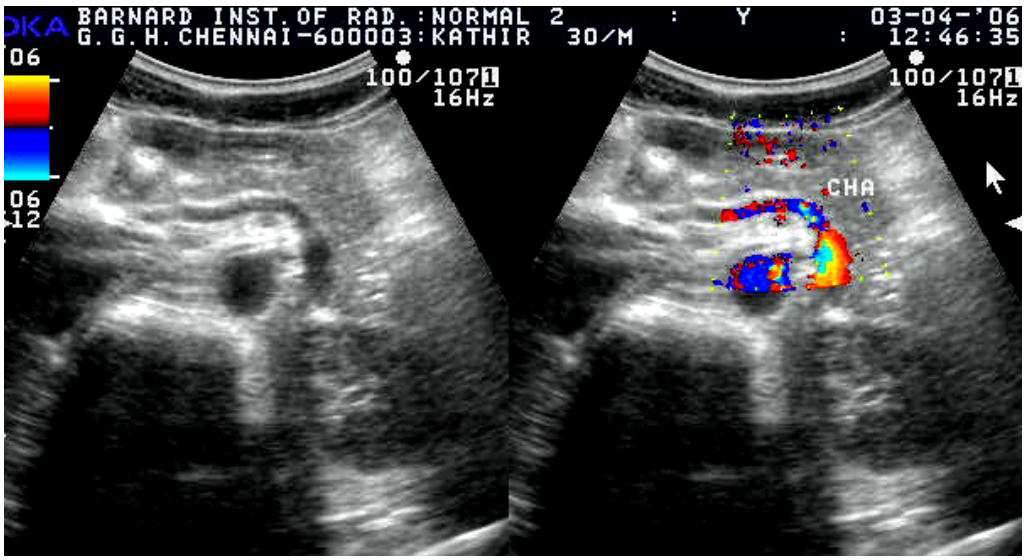


FIG 3. HEPATOCELLULAR CARCINOMA

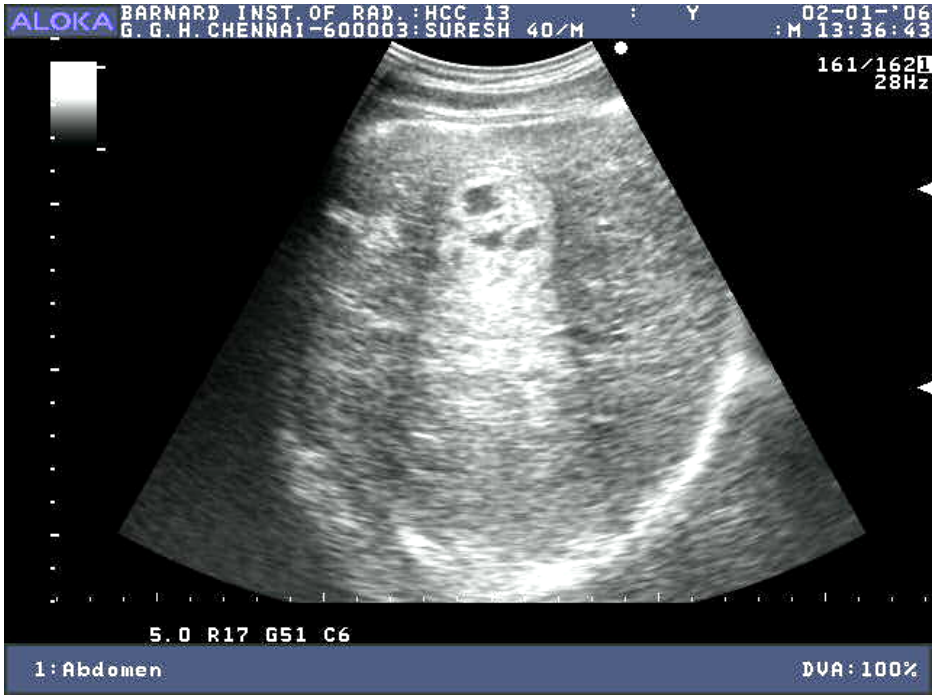


FIG 4. PULSATILE, HIGH VELOCITY ILFLOW>40 CM/S

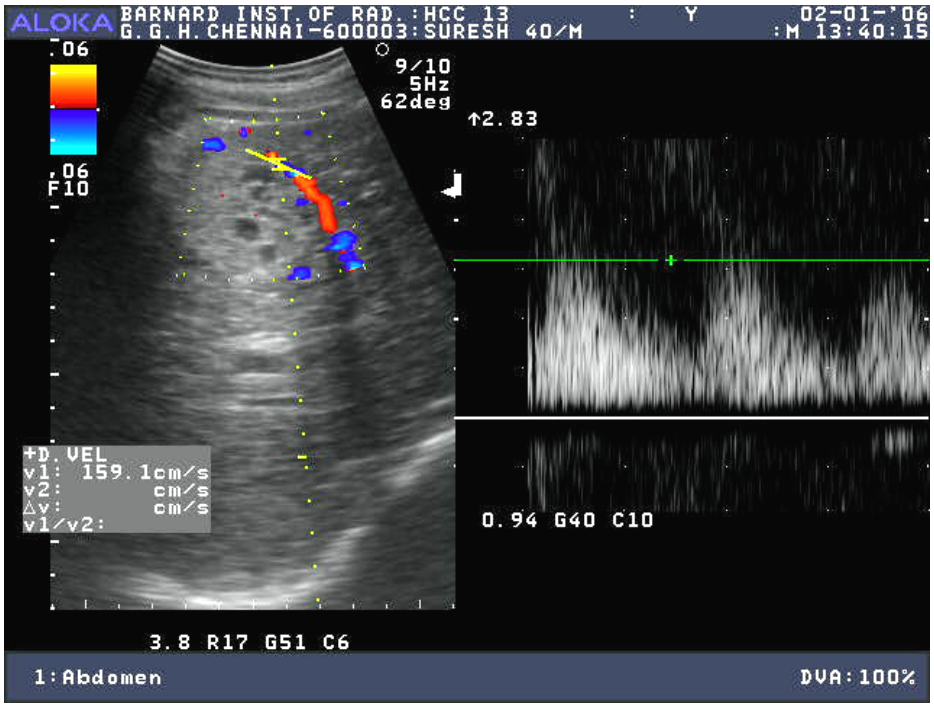


FIG 5. HCC INTRA LESIONAL AV SHUNTING

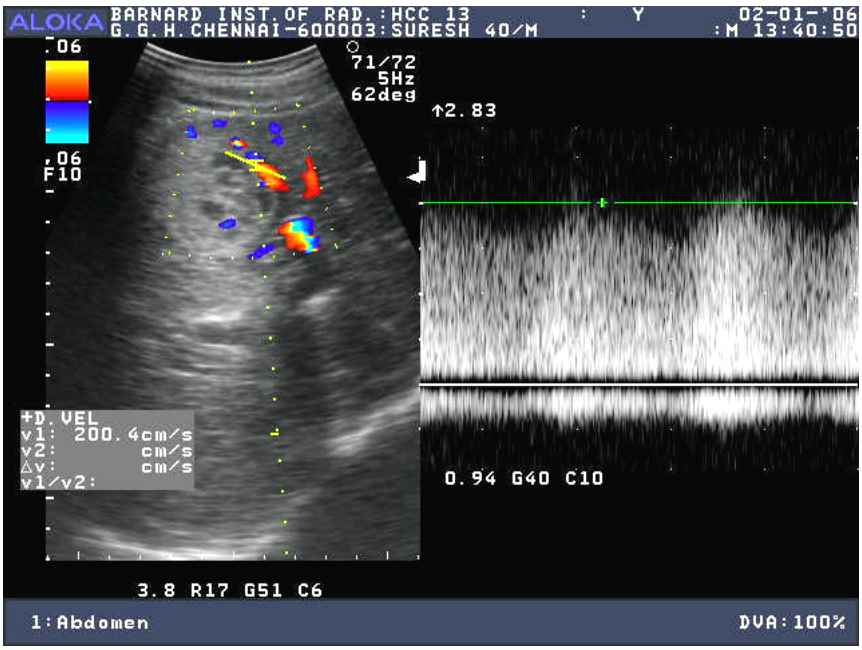


FIG 6. NORMAL COMMON HEPATIC ARTERY FLOW

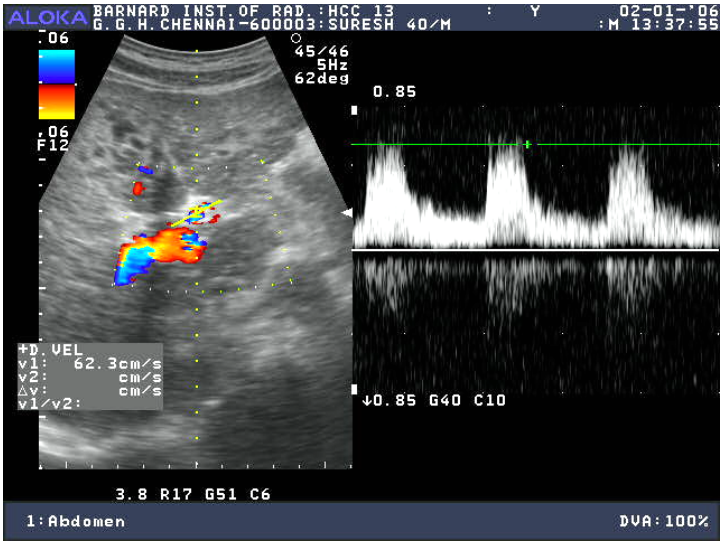


FIG 7. HCC WITH INCREASED COLOUR FLOW

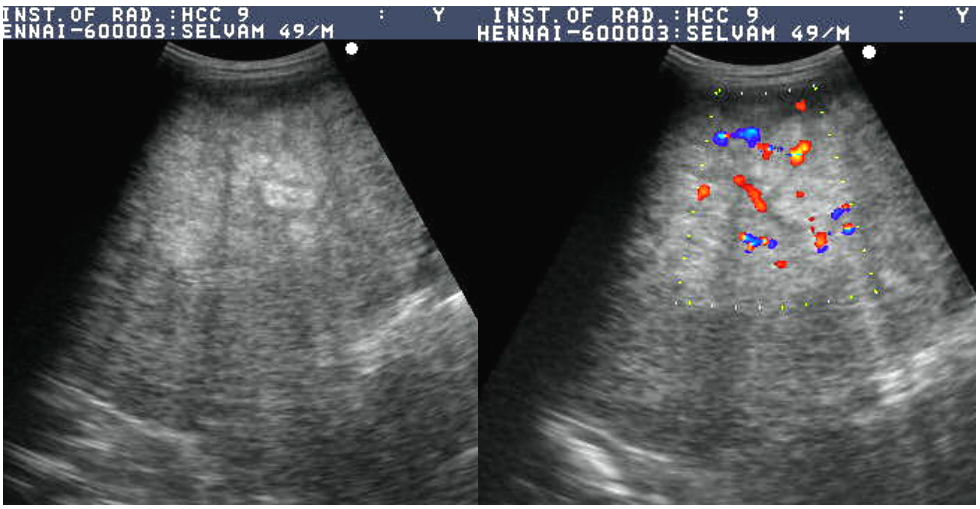


FIG 8. PULSATILE HIGH VELOCITY ILFLOW

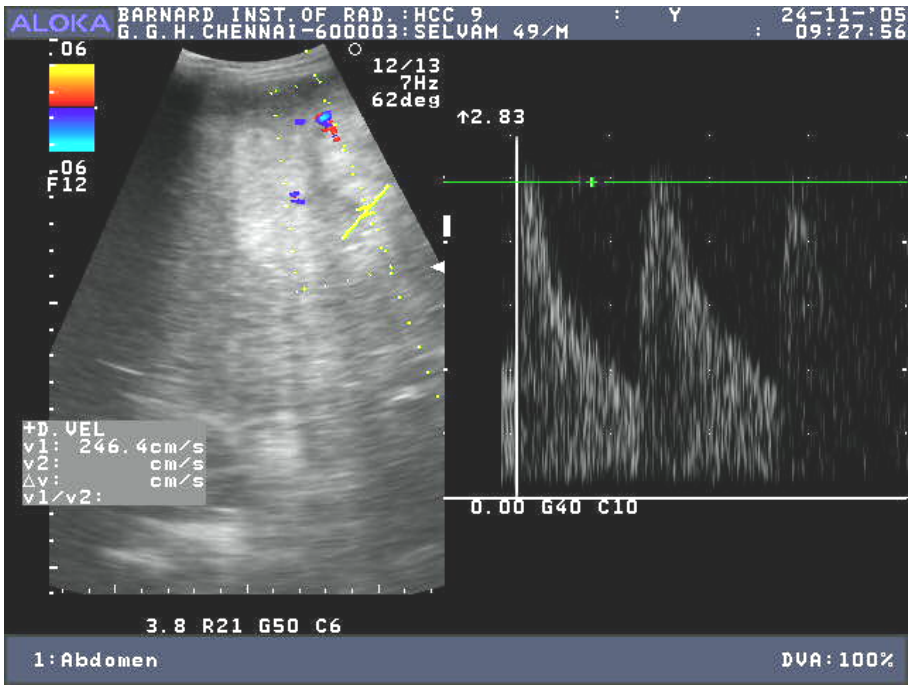


FIG 9. INCREASED FLOW IN CHA BUT PSV<ILPSV

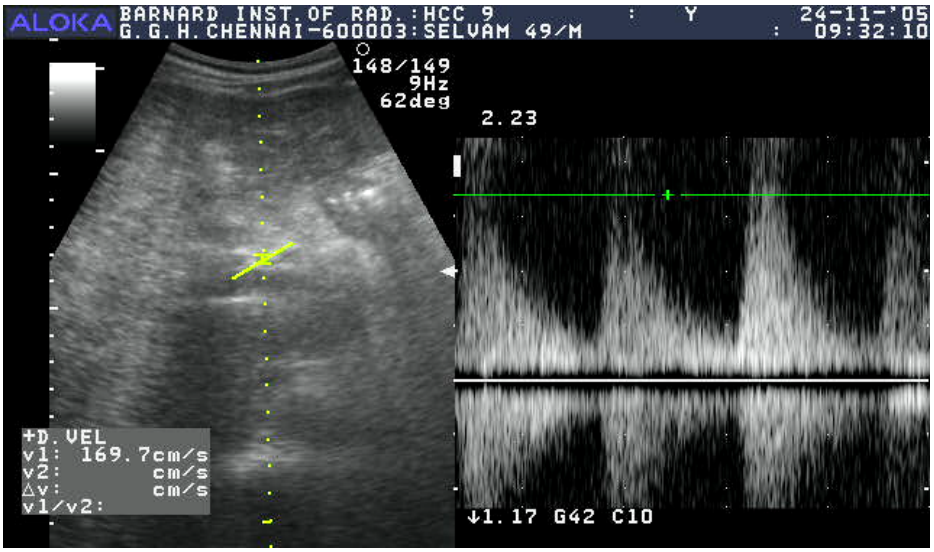


FIG 10. LARGE HCC WITH INCREASED ILFLOW

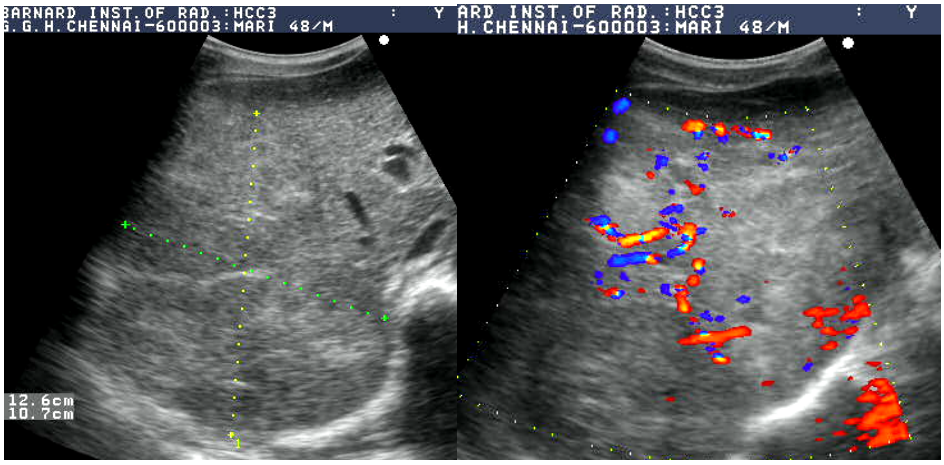


FIG 11. PULSATILE ILFLOW WITH ILPSV>40 CM/S

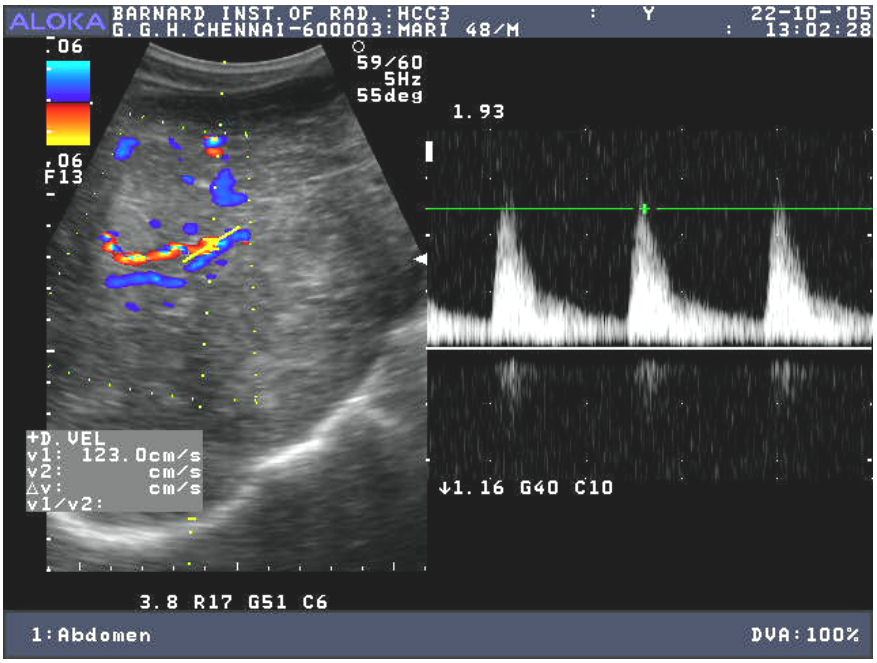


FIG 12. CHA PSV < INTRALESIONAL PSV

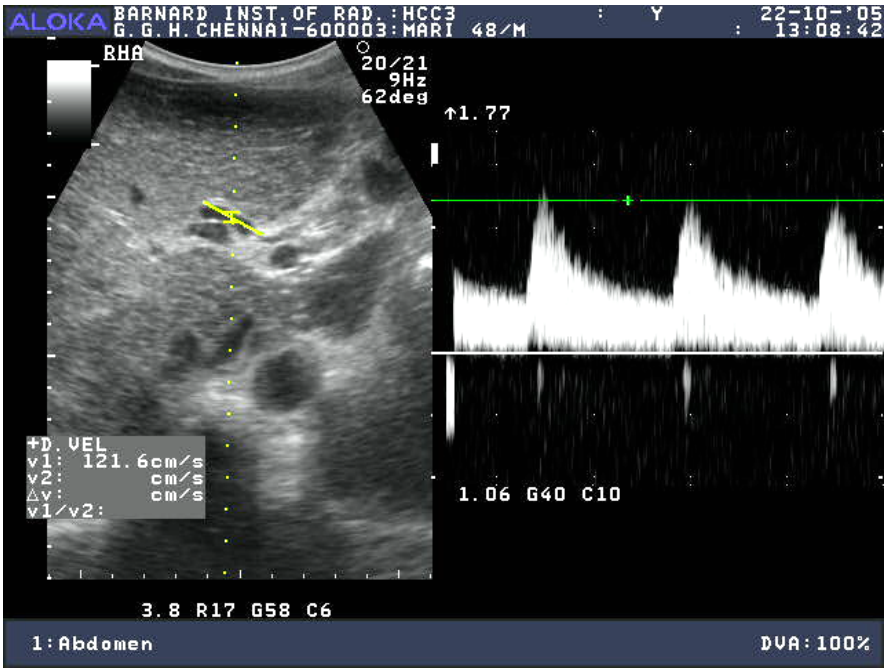


FIG 13. NO INTRA LESIONAL FLOW IN METASTASES

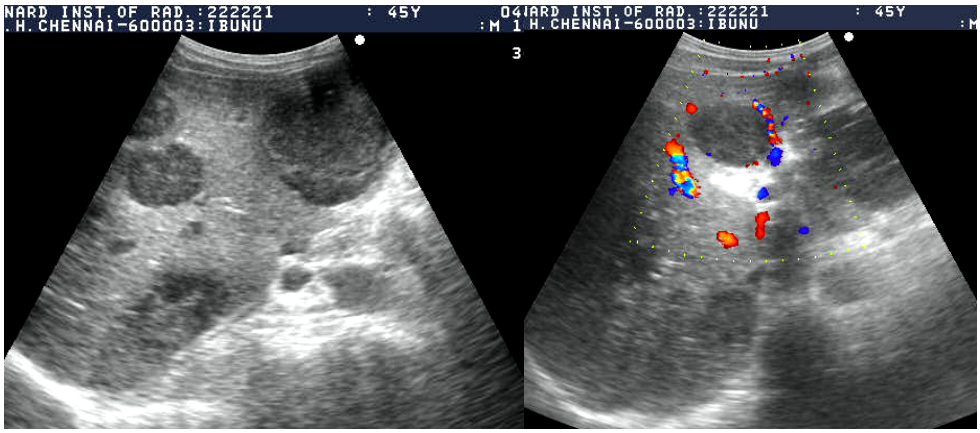


FIG 14. MINIMAL INTRALESIONAL FLOW IN METASTASES

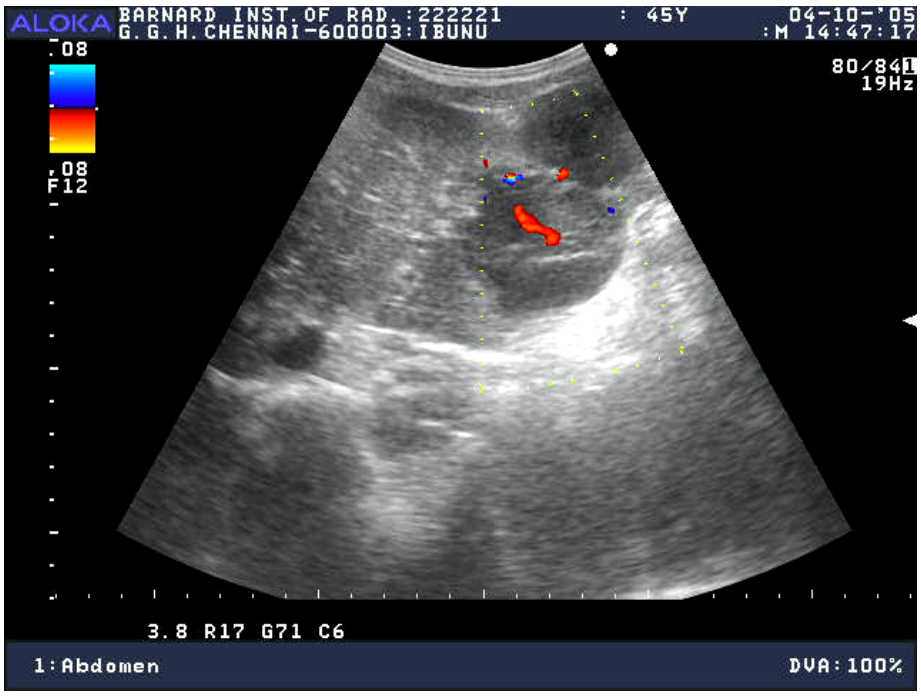


FIG 15. MINIMAL CONTINUOUS FLOW INTRALESIONAL FLOW WITH PSV<40 CM/S, WITH HIGHLY ELEVATED CHA FLOW

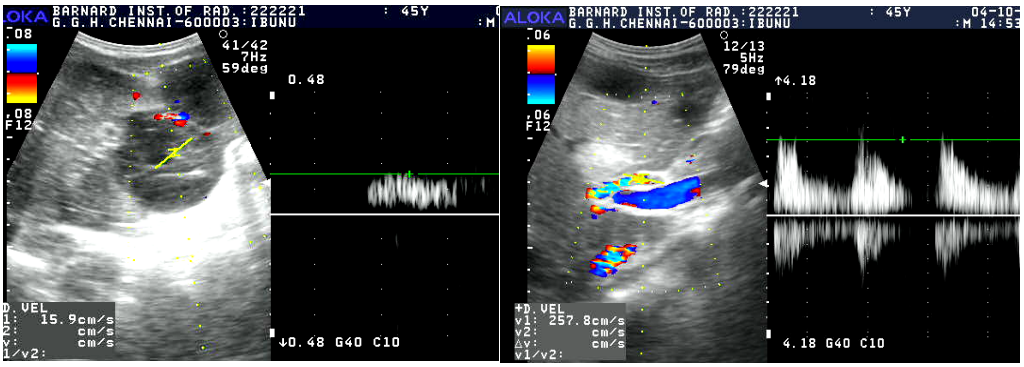


FIG 16. METASTASES WITH CONTINUOUS INTRA LESIONAL FLOW

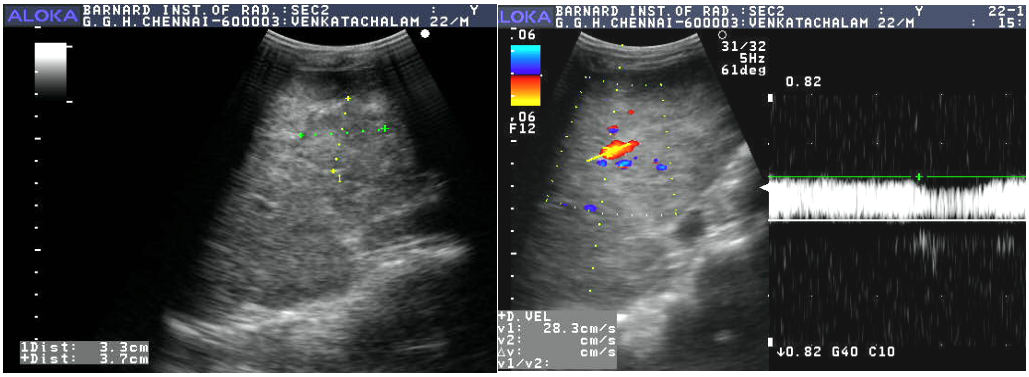


FIG 17. COMMON HEPATIC ARTERY FLOW IN METASTASES

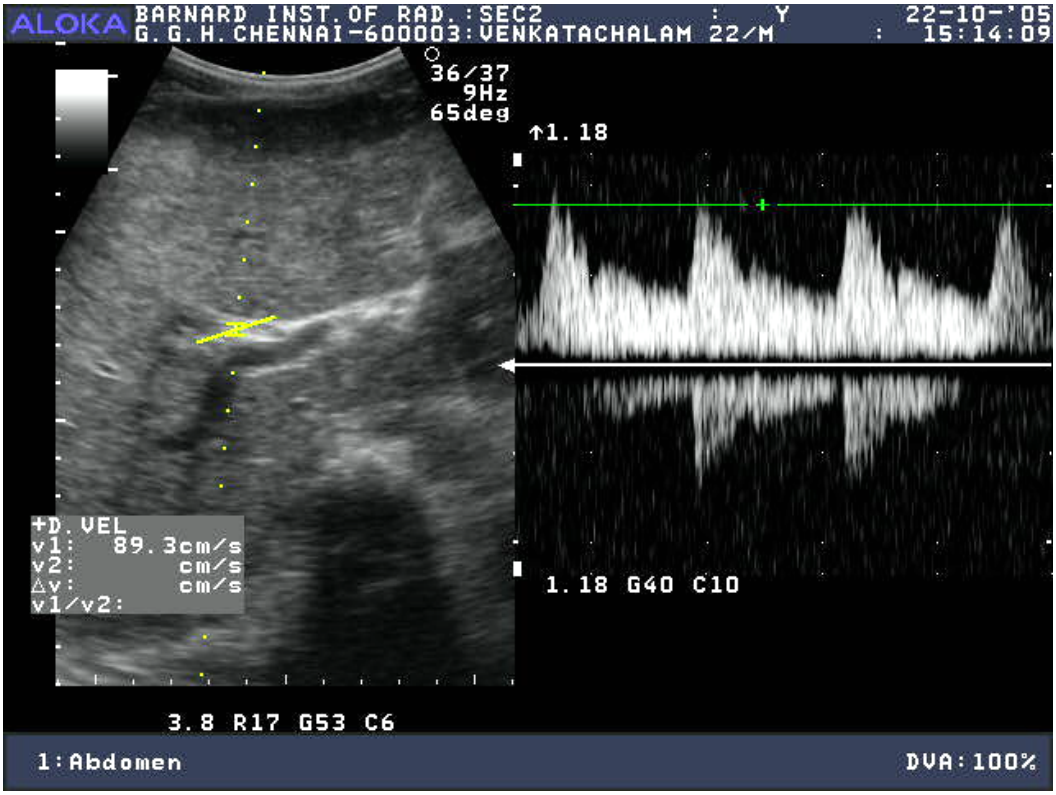


FIG 18. MULTIPLE HYPERECHOIC METASTASES WITH NO FLOW

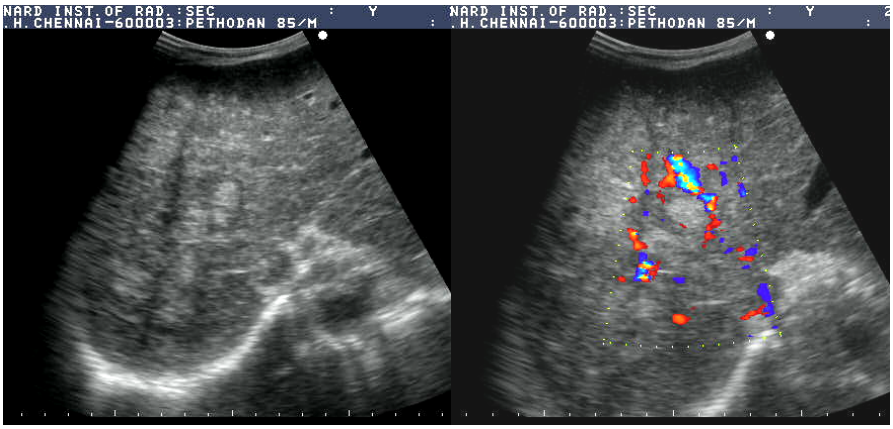


FIG 19. HIGHLY ELEVATED CHA FLOW IN METASTASES

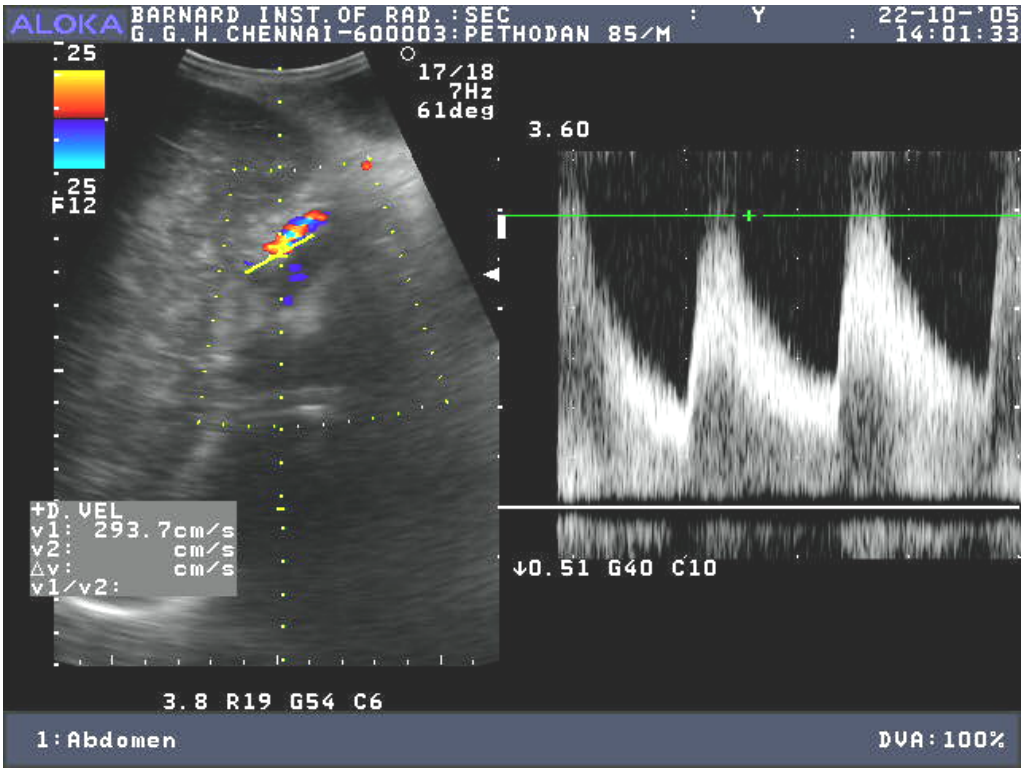


FIG 20. HEMANGIOMA WITH SPOT PATTERN OF MINIMAL CONTINUOUS INTRA LESIONAL FLOW WITH ILPSV<40 CM/S

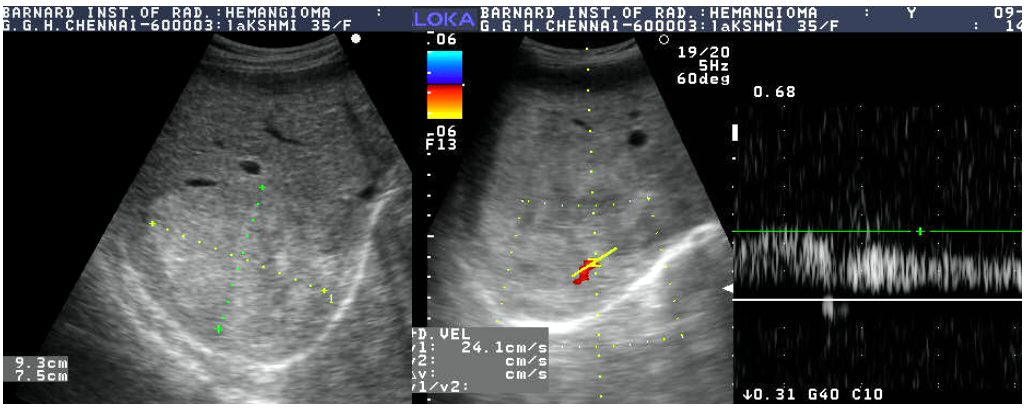


FIG 21. NORMAL FLOW PATTERN IN HEMANGIOMA IN CHA

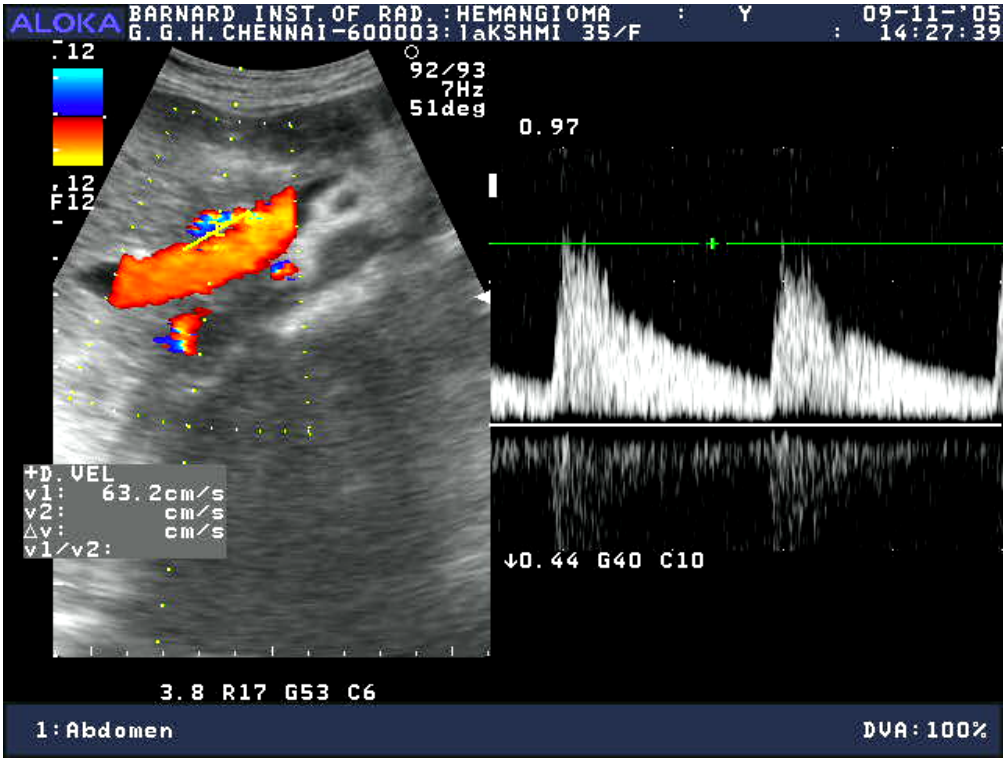


FIG 22. MULTIPLE HEMANGIOMAS WITH NO IL FLOW

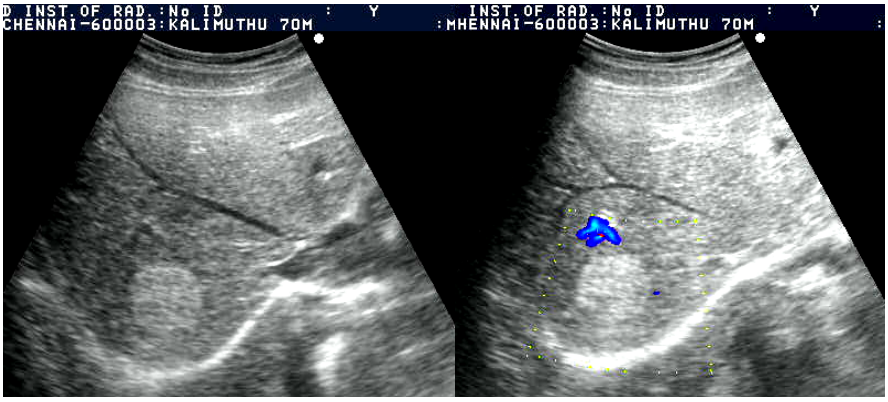


FIG 23. HEMANGIOMA WITH NO COLOUR FLOW

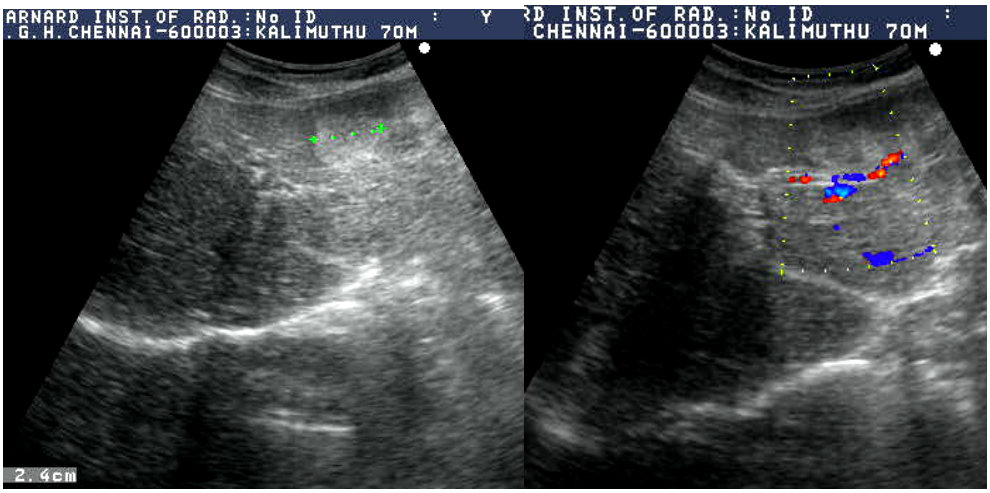
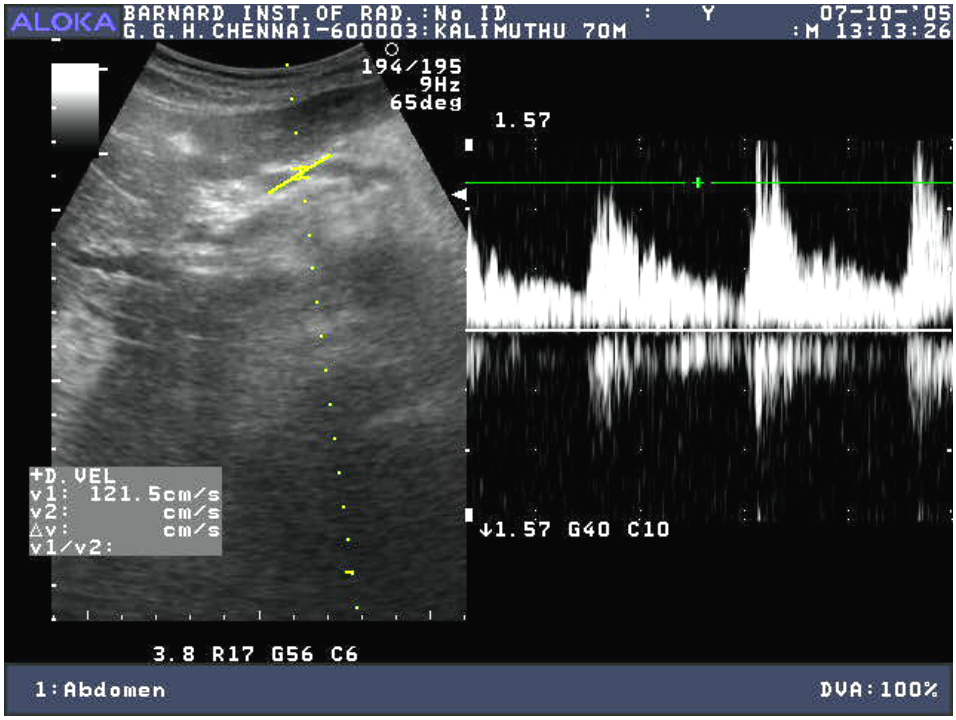


FIG 24. COMMON HEPATIC ARTERY FLOW IN HEMANGIOMA



RESULTS AND ANALYSIS

The ability of colour Doppler ultrasound to characterize HCCs, metastases and hemangiomas and are compared with HPE for HCCs and metastases and with CECT for hemangiomas. The final HP findings after FNAC / Biopsy were accepted as reference standards for HCCs and metastases and CECT was accepted as reference standard for hemangioma against which colour Doppler ultrasound results were compared.

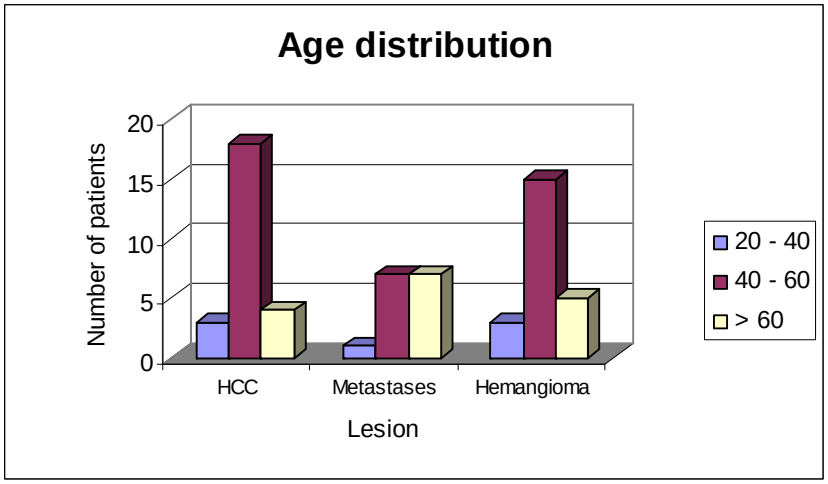
Sensitivity, specificity, correct classification, misclassification, positive predictive value, negative predictive value, false positive rate, false negative rate were calculated for colour Doppler ultrasound in differentiating HCCs, metastases and hemangiomas from each other.

A test is said to be sensitive when the percentage of false negative is low. A test is said to be specific when the percentage of false negative is low. Positive and negative predictive value estimates probability of presence or absence of a particular lesion. False positive means disease is present in a test when in fact it is not. False negative means failure of a test to detect a disease when it is present.

For diagnostic tests that produce results on continuous scale of measurement, the performance of a test can be represented graphically by a receiver operating characteristic curve (ROC). The area under the ROC curve serves as an overall measure of test performance, with an area of 1 indicating a perfect test and an area of 0.5 indicating a test that is unable to distinguish persons with and without the disease of interest. The respective areas under the ROC curves for 2 diagnostic tests for a particular disease can be used to identify the test that will provide the greater diagnostic value.

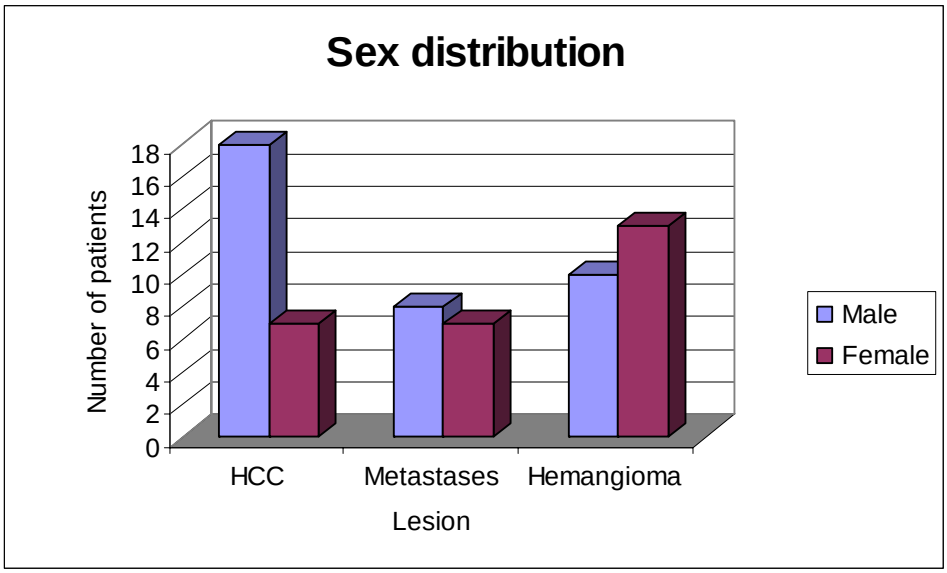
AGE DISTRIBUTION

Age	TYPE						Total	
	HCC		Metastases		Hemangioma			
	Count	%	Count	%	Count	%	Count	%
20 - 40	3	12	1	6.7	3	13.0	7	11.1
40 - 60	18	72	7	46.7	15	65.2	40	63.5
> 60	4	16	7	46.7	5	21.7	16	25.4
Total	25	100	15	100.0	23	100.0	63	100.0



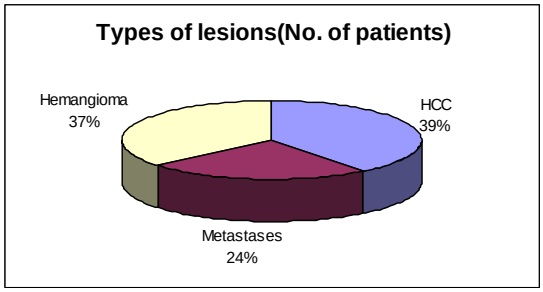
SEX DISTRIBUTION

SEX	TYPE						Total	
	HCC		Metastases		Hemangioma			
	Count	%	Count	%	Count	%	Count	%
Male	18	72	8	53.3	10	43.5	36	57.1
Female	7	28	7	46.7	13	56.5	27	42.9
Total	25	100	15	100.0	23	100.0	63	100.0



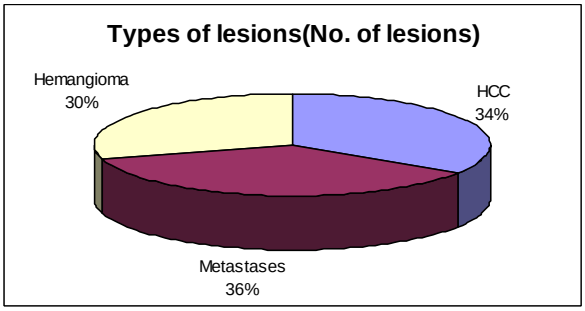
TYPES OF LESIONS ACCORDING TO NO. PATIENTS

Type	No. of patients
HCC	25
Metastases	15
Hemangioma	23
Total	63



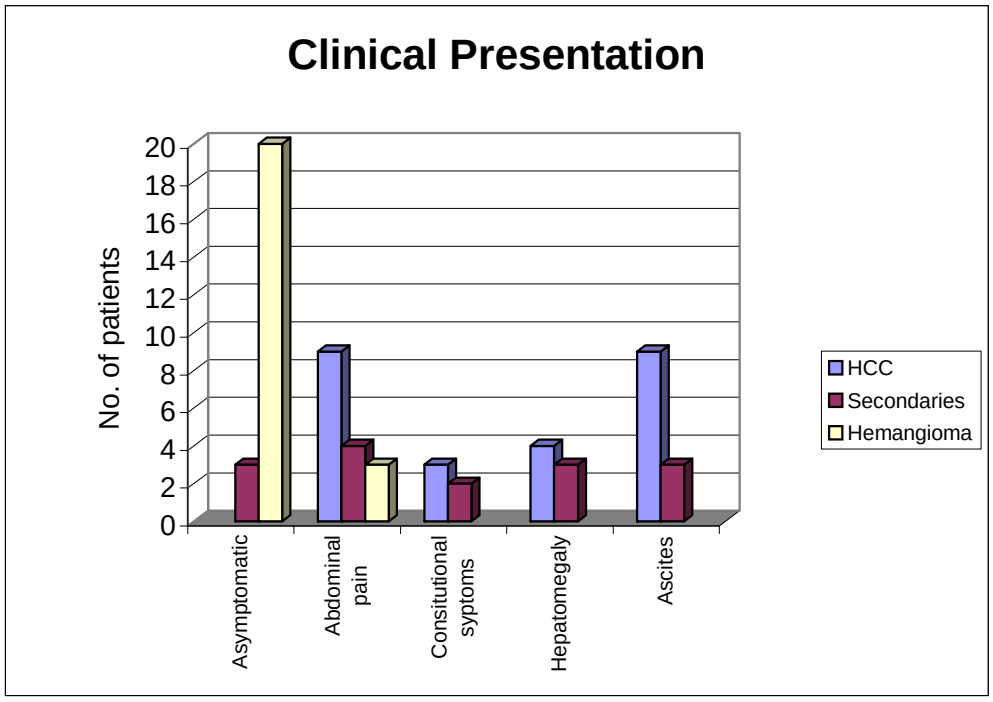
ACCORDING TO NO. OF LESIONS

Type	Frequency
HCC	30
Metastases	32
Hemangioma	26
Total	88



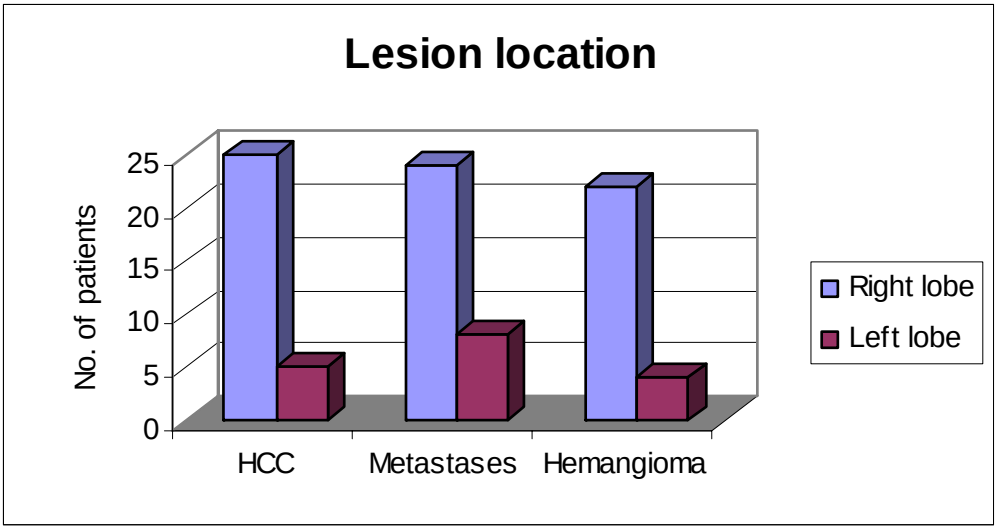
CLINICAL PRESENTATION

Clinical presentation	TYPE			Total
	HCC	Metastases	Hemangioma	
Asymptomatic		3	20	23
Abdominal pain	9	4	3	16
Constitutional symptoms	3	2		5
Hepatomegaly	4	3		7
Ascites	9	3		12
Total	25	15	23	63



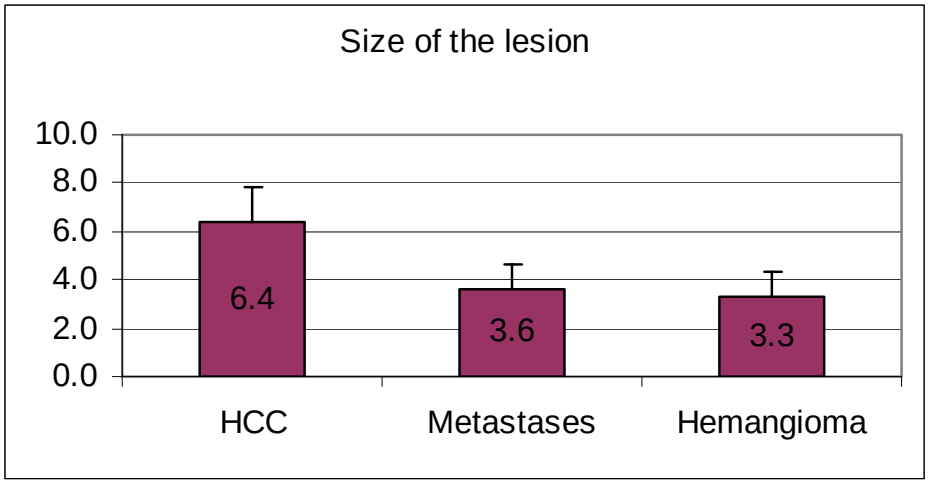
LESION LOCATION

Location	HCC	Metastases	Hemangioma	Total
Right lobe	25	24	22	71
Left lobe	5	8	4	17
Total	30	32	26	88



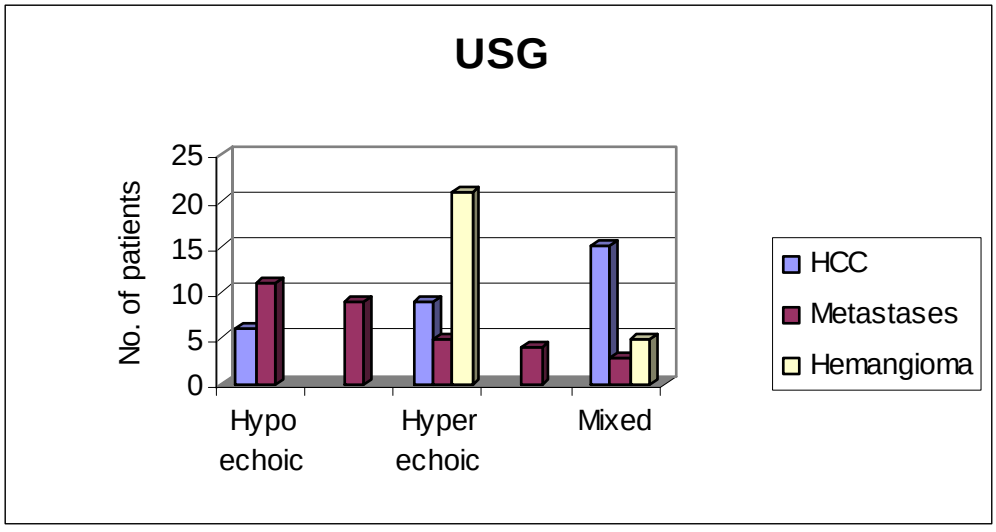
SIZE OF LESIONS

Type	NO	Mean	Median	Minimum	Maximum	Std. Deviation
HCC	30	6.4	6.25	3.7	10.2	1.51
Metastases	32	3.6	3.7	2.1	6.3	1.05
Hemangioma	26	3.3	3.1	2.2	6.4	1.01
Total	88	4.5	4.2	2.1	10.2	1.83



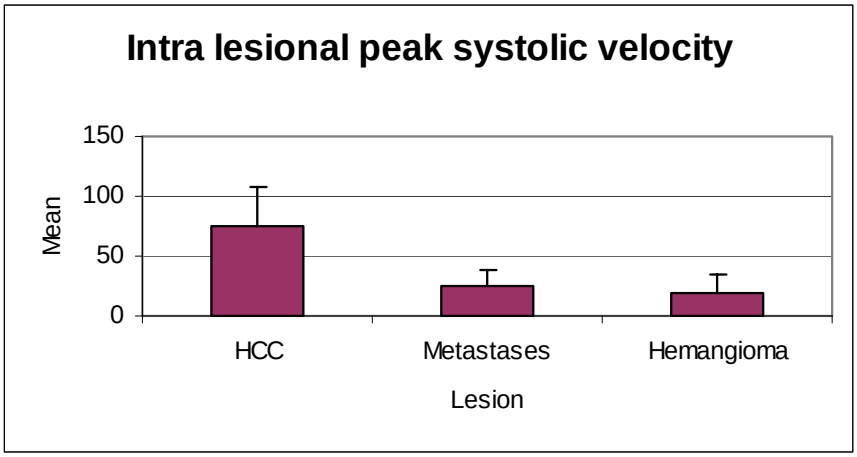
GRAY SCALE APPEARANCE OF LESIONS

Echogenicity	HCC	Metastases	Hemangioma	Total
Hypo echoic	6	11		17
Iso echoic		9		9
Hyper echoic	9	5	21	35
Calcified		4		4
Mixed	15	3	5	23
Total	30	32	26	88



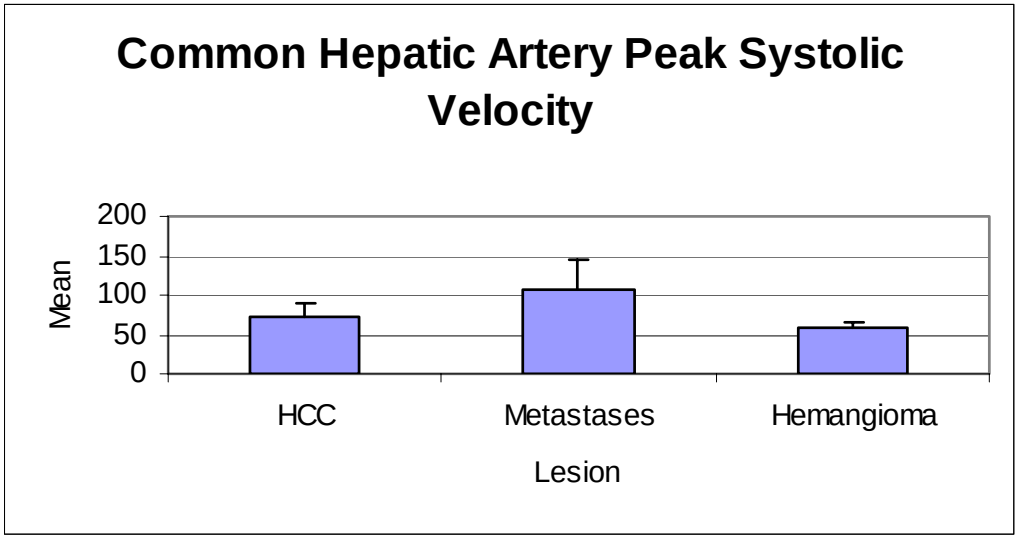
INTRALESIONAL PSV

Type	No	Mean	Std. Deviation
HCC	30	75.1	33.11
Metastases	32	24.1	15.04
Hemangioma	26	19.0	16.46
Total	88	39.9	34.25



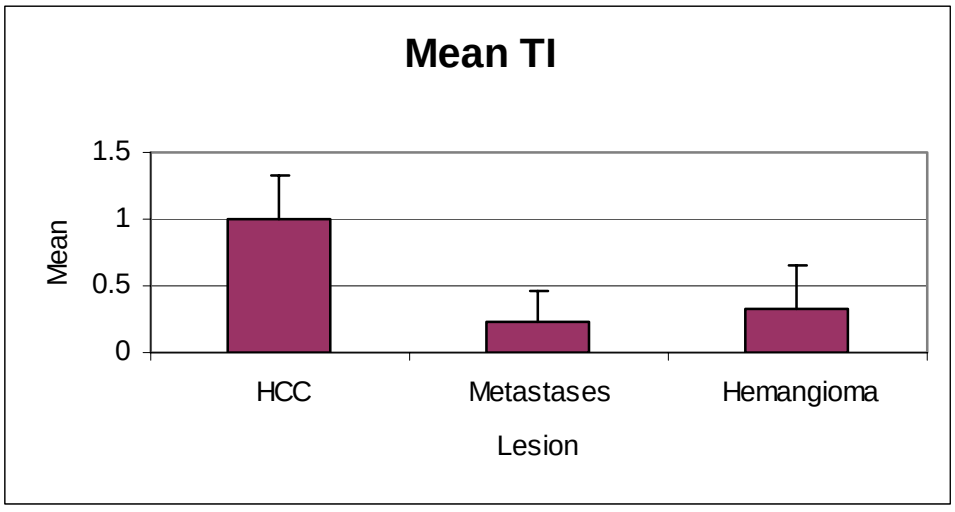
COMMON HEPATIC ARTERY PSV

Type	No	Mean	Std. Deviation
HCC	30	72.9	17.06
Metastases	32	108.4	34.90
Hemangioma	26	58.1	8.35
Total	88	81.4	31.72



HEPATIC TUMOR INDEX

Type	No lesions	Mean	Std. Deviation
HCC	30	0.99	0.33
Metastases	32	0.23	0.22
Hemangioma	26	0.33	0.32
Total	88	0.52	0.45



DIFFERENTIATION OF HCC BY COMBINING ILF, ILPSV, CHAPSV AND TI

HCC	HPE		Total
	+	-	
Doppler +	**25**	**3**	**28**
Doppler -	**5**	**55**	**60**
Total	**30**	**58**	**88**

$p<0.001$

PARAMETERS	%	CONFIDENCE LIMIT
Sensitivity	**83.3**	**65-94%**
Specificity	**94.8**	**86-99%**
Concordance	**90.9**	**79-97%**
Discordance	**9.1**	**3-21%**
Positive predictive value	**89.3**	**72-98%**
Negative predictive value	**91.7**	**82-98%**
False positive rate	**5.2**	**1-14%**
False negative rate	**16.7**	**6-35%**

DIFFERENTIATION OF METASTASES BY COMBINING ILF, ILPSV, CHAPSV AND TI

Metastases	HPE		Total
	+	-	
Doppler +	**28**	**1**	**29**
Doppler -	**4**	**55**	**59**
Total	**32**	**56**	**88**

$p<0.001$

PARAMETERS	%	CONFIDENCE LIMIT
Sensitivity	**87.5**	**71-97%**
Specificity	**98.2**	**91-100%**
Concordance	**94.3**	**85-99%**
Discordance	**5.7**	**1-15%**
Positive predictive value	**96.5**	**82-100%**
Negative predictive value	**93.2**	**84-98%**
False positive rate	**1.8**	**0-9%**
False negative rate	**12.5**	**3-29%**

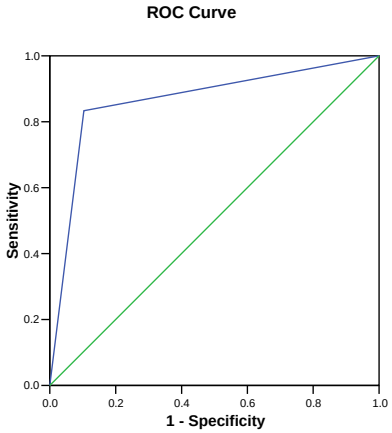
DIFFERENTIATION OF HEMANGIOMA BY COMBINING ILF, ILPSV, CHAPSV AND TI

Hemangioma	CECT		Total
	+	-	
Doppler +	**23**	**8**	**31**
Doppler -	**3**	**54**	**57**
Total	**26**	**62**	**88**

PARAMETERS	%	CONFIDENCE LIMIT
Sensitivity	**88.5**	**70-98%**
Specificity	**87.1**	**76-94%**
Concordance	**87.5**	**76-93%**
Discordance	**12.5**	**7-24%**
Positive predictive value	**74.2**	**55-88%**
Negative predictive value	**94.7**	**85-99%**
False positive rate	**12.9**	**6-24%**
False negative rate	**11.5**	**2-30%**

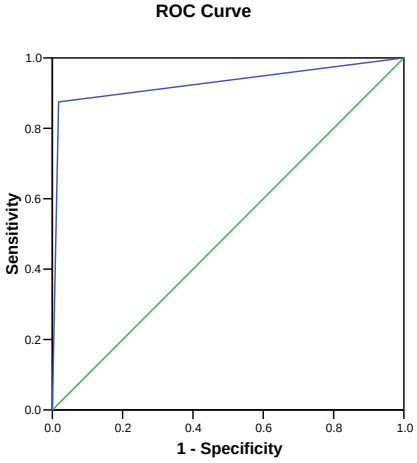
$p<0.001$

HCC (Area under curve = .891)



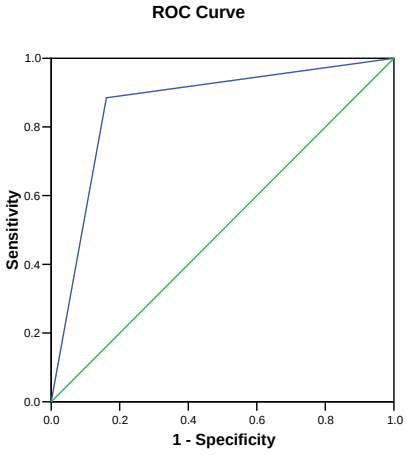
Diagonal segments are produced by ties.

Metastases (Area under the curve = 0.929)



Diagonal segments are produced by ties.

Hemangioma (Area under the curve = 0.862)



Diagonal segments are produced by ties.

DISCUSSION

Gray scale ultrasound and CDS were performed on 63 patients with 88 lesions in the liver referred by Departments of Gasteroenterology and Surgery.

Out of 63 patients, 25 patients had HCCs, 15 patients had metastases and 23 patients had hemangiomas. Out of 25 HCC patients, 72% (18) were male patients, 28% (7) female patients. Out of 15 patients with metastases, 53.3% (8) were male patients, 46.7% (7) were female patients. Out of 23 patients with hemangiomas 43.5% (10) patients were male, 56.5% (13) patients were female. In total 36 male patients and 27 female patients. Male to female ratio is 1.3:1.

HCC patients were in the age group ranging from 22 years to 75 years. Metastases patients were in the age group ranging from 28 to 85 years. Hemangioma patients were in the age group ranging from 30 to 70 years. Out of 63 patients, 7 patients were in the age group of 20 to 40 years, 40 patients were in the age group of 40 to 60 years, 16 patients were in the age group of above 60 years.

In HCC, out of 25 patients, 9 patients presented with abdominal pain, 9 patients with ascites, 4 patients with hepatomegaly and 3 patients with constitutional symptoms. In metastases, out of 15 patients, 4 patients presented with abdominal pain, 3 with hepatomegaly, 3 with ascites, 3 patients presented with no symptoms and 2 patients with constitutional symptoms. In hemangioma, out of 23 patients, 20 patients had no symptoms and 3 patients presented with abdominal pain.

Out of 88 lesions in total, 71 lesions were located in the right lobe and 17 lesions were located in the left lobe. Out of 15 metastatic patients 4 patients had metastases from carcinoma stomach, 3 had colorectal carcinoma, 3 had breast and lung carcinoma respectively, and 2 patients had carcinoma ovary.

Out of 30 lesions of HCC, 15 lesions were mixed appearance in gray scale ultrasound, 9 lesions are hyperechoic and 6 lesions are hypoechoic. In metastases, out of 32 lesions, 11 lesions were hypoechoic, 9 lesions were isoechoic, 5 were hyperechoic, 4 calcified and 3 mixed appearance. Out 26 hemangiomas, 21 lesions appear hyperechoic and 5 lesions were mixed echogenic in appearance.

Out of 88 lesions, 41 lesions were less than 5 cm and 47 lesions were more than or equal to 5 cm. The mean size of HCCs (6.4cm) is significantly higher than that of metastases (3.6 cm) and hemangiomas (3.3 cm) ($p<0.001$)

In 25 patients of HCCs, 22 had solitary lesions, 2 patients had 3 lesions and one patient had 2 lesions. In 15 patients with metastases, 5 patients had single lesion, 3 patients had two lesions, 7 patients had 3 lesions. In 23 patients with hemangiomas, 20 patients had single lesion, 3 patients had 2 lesions.

Colour Doppler sonogram findings in favour of HCC include pulsatile intralesional flow, intralesional PSV more than 40 cm/s, normal or minimally increased common hepatic artery flow and hepatic tumor index more than or equal to one. CDS findings in favour of metastases include pulsatile or continuous flow within the lesion with intralesional PSV less than 40 cm/s,

elevated common hepatic artery flow and Tumour Index(TI) less than one. CDS findings suggestive of hemangiomas include minimal continuous flow with intralesional PSV less than 40 cm/s, normal common hepatic artery PSV and TI less than one.

On CDS, out 30 HCCs, 27 lesions showed pulsatile flow, 2 lesions showed continuous flow and one lesion showed no flow. In metastases, out of 32 lesions, 15 lesions showed pulsatile flow, 14 continuous flow and 3 lesions showed no flow. In hemangiomas, 15 continuous flow, 6 no flow and 5 lesions showed pulsatile flow. The detection rate of pulsatile flow was significantly higher ($p<0.01$) in HCCs than in metastases and hemangiomas.

Out of 88 lesions, 31 lesions showed intralesional peak systolic velocity (ILPSV) of 40 cm/s and above. In which, 25 were HCCs, 3 were metastases and 3 were hemangiomas. Mean peak systolic velocity of HCC is 75.1 cm/s which is higher than that of metastases (24.1 cm/s) and hemangioma (19 cm/s) which is statistically significant ($p<0.01$).

Mean peak systolic velocity obtained form common hepatic artery (CHAPSV) of metastases (108.4 cm/s) significantly exceeded that of HCCs (72.9 cm/s) and hemangiomas (58.1 cm/s) ($p<0.01$).

The hepatic tumor index (TI) calculated by dividing the intralesional PSV by common hepatic artery PSV. Hepatic tumor index was equal to or greater than one in 22 of 30 HCCs, one of 32 metastases and two of 26 hemangiomas. The mean hepatic tumor index for HCC was significantly greater than those of metastases and hemangiomas ($p<0.01$ in both cases).

Combining intralesional pulsatile flow with PSV more than 40 cm/s with normal common hepatic artery flow velocity for detection of HCC, there is 83.3% sensitivity, 89.7% specificity and 87.5% accuracy. Combining continuous or pulsatile flow with PSV<40 cm/s, with increased PSV of common hepatic artery for detection of metastases, there is 87.5% sensitivity, 94.6% specificity and 92.0% accuracy. Combining minimal continuous flow or no flow with intralesional PSV<40 cm/s, normal common hepatic artery PSV, there is 84.6% sensitivity, 93.5% specificity and 90.9% accuracy for the detection of hemangiomas.

When intralesional flow, ILPSV, common hepatic artery PSV and hepatic TI there is 83.3% sensitivity, 94.8% specificity and 90.9% accuracy for HCCs, 87.5% sensitivity, 98.2% specificity and 94.3% accuracy for the detection of metastases and for the detection of hemangioma there is 88.5% sensitivity, 87.1% specificity and 87.5% accuracy.

The hepatic tumor index was more than or equal to one in 25 lesions (22 HCCs, 1 metastases and 2 hemangiomas) and less than one in 63 lesions (8 HCCs, 31 metastases and 24 hemangiomas) resulting in sensitivity of 88.0%, specificity of 87.3% and accuracy of 87.5%.

On comparing to the Numata K, Tanaka K, Kiba T, Morimoto M et al[37] **study in which a PSV of 40 cm/s or greater, with a hepatic tumor index equal to or greater than 1.0 was associated with a sensitivity of 91%, specificity of 83% and an accuracy of 89% in distinguishing HCCs from hepatic metastases, our study had 83.3% sensitivity, 94.8% specificity and 90.9% accuracy.**

Wang WF, Zhang QP et al[55] studied the use of CDFI in characterization of liver tumors. Their results showed Doppler flow signals could be detected in all hepatic carcinomas and 10 of 18 hemangiomas, with pulsatile flow in 41 of 42 lesions and in 6 of 10 hemangiomas, with mean PSV obviously lower in hemangiomas (20.34 +/- 23.93) than HCCs (64.74 +/- 30.18). Our studied showed colour Doppler flow signals in 29 of 30 HCCs and 20 of 26 hemangiomas. Out of which, pulsatile flow detected in 27 of 30 HCCs and 5 of 26 hemangiomas. The mean PSV of HCCs 75.1 +/- 33.1 which is higher than that of hemangiomas 19.0 +/- 16.4.

Kudo M, Tochio H, Zhou P et al[24] study showed mean +/- SD of maximum velocity in hemangiomas (15.0 +/- 16.0 cm/s) was significantly lower than in HCCs (34.0 +/- 26.7 cm/s) and in metastases (37.9 +/- 17.4 cm/s). In our study the mean velocity of hemangiomas (19.0 +/- 16.4), HCCs (75.1 +/- 33.1) and metastases (24.1 +/- 15).

On comparing to Nino-Murcia M, Ralls PW, Jeffrey RB Jr, Johnson M et al[36] in which 76% HCCs showed internal vascularity, 67% metastases and 75% of benign lesions showed no internal vascularity, our study showed 96.7% HCCs showed flow and 9.4% of metastases and 11.4% of hemangiomas showed no flow.

Yashura K, Kimura K, Ohto M, Matsutani S et al[59] study showed presence of pulsatile flow in 35 of 55 HCCs, 7 of 25 metastases and continuous flow detected in 4 of 30 hemangiomas. On comparing to their study, our study showed pulsatile flow in 27 of 30 HCCs, 15 of 32 metastases and 5 of 26 hemangiomas and continuous flow in 2 HCCs, 14 metastases and 15 hemangiomas.

SUMMARY

63 patients with 88 liver lesions referred by the Gastroenterology and Surgery Departments to our department for ultrasound and colour doppler sonography.

Out of 63 patients, 36 patients were males 27 patients were females. Among 63 patients, 7 patients were between 20 to 40 years, 40 patients between 40 to 60 years and 16 patients were above 60 years. 25 patients had HCCs, 15 patients had metastases and 23 patients had hemangiomas. Out of 30 HCCs, 25 were correctly identified by colour doppler ultrasound, 5 lesions were missed and 3 lesions were falsely identified as HCCs which turned out to be 2 hemangiomas and one metastases on CECT, HPE. Out of 32 metastases, 28 were correctly shown by doppler and 4 lesions were missed and one lesion was falsely diagnosed as metastases which on follow up turned out to be HCC. Out of 26 hemangiomas, 23 were correctly shown by doppler, 3 lesions were missed and 8 lesions were mistakenly diagnosed as hemangiomas which on further follow up turned out to be 5 HCCs and 3 metastases.

Sensitivity for colour doppler to differentiate HCC, metastases and hemangioma is 83.3%, 87.5% and 88.5%. Specificity to exclude the above lesions are 94.8%, 98.2% and 87.1%. So as to summarise, hepatocellular carcinoma, metastases and hemangiomas more than 2 cm are better characterized and reasonably differentiated with colour doppler ultrasound with good sensitivity and specificity.

CONCLUSION

Colour doppler ultrasound is highly sensitive in evaluating common adult hepatic tumors more than 2 cm including hepatocellular carcinoma, metastases and hemangiomas.

Pulsatile intralesional flow with peak systolic velocity more than 40 cm/s with hepatic tumor index more than or equal to one is diagnostic of HCCs. Intralesional pulsatile or continuous flow with intralesional PSV less than 40 cm/s, increased common hepatic artery PSV with hepatic tumor index less than one is diagnostic of metastases. With intralesional continuous flow or no flow, intralesional PSV less than 40 cm/s, normal common hepatic artery PSV, hepatic tumor index less than one hemangiomas can be diagnosed with a reasonable degree of confidence.

Finally we conclude that colour doppler sonography is readily available, relatively inexpensive, well tolerated, noninvasive tool with high diagnostic capability in differentiating common adult hepatic tumors (HCCs, metastases and hemangiomas) more than 2 cm.

BIBLIOGRAPHY

1. **Albrecht T, Hoffmann CW, Schmitz SA: Phase inversion sonography during the liver specific late phase contrast enhancement:improved detection of liver metastases. AJR Am J Roentgenol 2001 May;176(5):1191-8**

2. **Arai K, Doppler sonography in the diagnosis of liver tumors, Nippon Igaku Hoshasen Gakkai Zasshi. 1992 Mar25;52(3):320-37**

3. **Baron RL, Oliver JH 3rd, Dodd GD 3rd: Hepatocellular carcinoma: evaluation with biphasic, contrast-enhanced, helical CT. Radiology 1996 May; 199(2): 505-11**

4. **Bender H, Bangard N, Metten N: Possible role of FDG-PET in the early prediction of therapy outcome in liver metastases of colorectal cancer. Hybridoma 1999 Feb; 18(1): 87-91**

5. **Carol M. Rumack, Stephanie R. Wilson, William Cahrboneau, Diagnostic ultrasound 3rd edition, Vol 1 77-145**

6. **De Franco A, Monteforte MG, Maresca G, Integrated diagnosis of liver angioma: comparison of Doppler color ultrasonography, computerized tomography, and magnetic resonance, Radiol Med (Torino) 1997 Jan-Feb; 93(1-2): 87-94**

7. **Di Bisceglie AM, Rustgi VK, Hoofnagle JH: NIH conference. Hepatocellular carcinoma. Ann Intern Med 1988; 108: 390-401**

8. **Di Giulio G, Lupto L, Tirelli A, Vinci R, Rotondo A, Angelelli G, Blood flow assessment with Doppler colour Ultrasonography in primary and secondary tumors of the liver. Radiol Med(Torino).1997 Mar;93(3):225-9**

9. **Dishi H, Hirai T, Yamada R, Hirohashi S, Three dimensional power Doppler sonography of tumor vascularity, J Ultrasound Med. 1998 Oct;17(10):619-22**

10. **Dock W, Grabenwoger F, Metz V, Eibenberger K, Farres MT, Tumor vascularization: assessment with duplex sonography. Radiology.1991 Oct;181(1):241-4**

11. **Edmondson HA, Peters RL: Tumors of the liver: pathologic features. Semin Roentgenol 1983 Apr; 18(2): 75-83**

12. **Fong Y, Sun RL, Jarnagin W: An analysis of 412 cases of hepatocellular carcinoma at a Western center. Ann Surg 1999; 229: 790-9**

13. **Furuse J, Iwaski M, Yoshino M, Konishi M, Kawano N, Kinoshita T, Ryu M, Evaluation of blood flow signal in small hepatic nodules by colour Doppler sonography. Jpn J Clin Oncol.1996 Oct;26(5):335-40**

14. **Gaini S, Casali A, Serra C, Piscaglia F, Gramantieri L, Volpe L, Siringo S, Bolondi L, Assesment of vascular patterns of small liver mass lesions: value and limitation of the different Doppler ultrasound modalities**

15. **Gonzalez-Anen M, Cervera-Deval J, Garcia-Vila JH, Bordon-Ferre F, Characterization of solid liver lesions with colour pulsed Doppler imaging. Abdom Imaging.1999 Mar-Apr;24(2):137-43**

16. **Hosten N, Puls R, Bechstein WO, Felix R, Focal liver lesions:Doppler ultrasound. Eur Radiol.1999;9(3):428-35**

17. **Ignee A, Weiper D, Schuessler G, Teuber G, Faust D, Dietrich CF, Sonographic characterization of hepatocellular carcinoma at time of diagnosis. Gasteroentero 2005 Mar;43(3):289-94**

18. **Imamura M, Shirotori Y, Shiina S, Sato S, Obi S, Power doppler sonography for hepatocellular carcinoma. Liver 1998 Dec;18(6):427-33**

19. **Kamalov IR, Sandrikov VA, Gautier SV, Tsirulnikova OM, Skipenko OG, The significance of colour velocity and spectral Doppler ultrasound in the differentiation of liver tumors. Eur J Ultrasound. 1998 Apr;7(2):101-8**

20. **Kim HC, Kim TK, Sung KB: CT during Hepatic Arteriography and Portography: An Illustrative Review. Radiographics 2002 Sep-Oct; 22(5): 1041-51**

21. **Kim KW, Kim TK, Han JK, Kim AY, Lee HJ, Hepatic hemangiomas: spectrum of US appearances of grey scale, power Doppler, and contrast enhanced US. Korean journal of radiology, 2000 Oct-Dec;1(4):191-7**

22. **Kinkel K, Lu Y, Both M: Detection of hepatic metastases from cancers of the gastrointestinal tract by using noninvasive imaging methods (US, CT, MR imaging, PET): a meta-analysis. Radiology 2002 Sep; 224(3): 748-56**

23. **Kubota K, Hissa N, Fujiwara Y, Fukumoto M, Yoshida D, Yoshida S, Evaluation of the intratumoral vasculature of hepatocellular carcinoma by power Doppler sonography: advantages and disadvantages versus conventional colour Doppler sonography. Abdom Imaging. 2000 Mar-Apr;25(2):172-8**

24. **Kudo M, Tochio H, Zhou P, Differentiation of hepatic tumors by colour Doppler imaging: role of the maximum velocity and pulsatility index of the intratumoral blood flow signal. Intervirology 2004;47(3-5):154-61**

25. **Kumuda T, Nakano S, Toyoda H, Hayashi K, Kiriyama S, Sone Y, Tanikawa M, Assessment of tumor hemodynamics in small hepatocellular carcinoma: comparison of Doppler Ultrasonography, angiography-assisted computed tomography and pathological findings. Liver Int.2004 Oct;24(5):425-31**

26. **Kunishima S, Taniguchi H, Yamaguchi A, Koh T, Yamagishi H, Changes in hepatic parenchymal blood flow with colorectal metastases: increase in arterial and decrease in portal blood flow. Hepatogastroenterology.2003 Sep-Oct;50(53):1457-62**

27. **Kurohiji T, Yamshita Y, Hiraki M, Horiuchi, Intraoperative real time observation of tumor blood flow in hepatocellular carcinoma by using colour Doppler imaging. Nippon Shokakibyo Gakki Zasshi.1993 Dec;90(12):3028-31**

28. **Lee MG, Auh YH, Cho KS, Chung YH, Lee IC, Kang EM, Colour Doppler flow imaging of hepatocellular carcinomas. Comparison with metastatic tumors and hemangiomas by three step grading for colour hues. Clin Imaging.1996 Jul-Sep;20(3):199-203**

29. **Leen E, Goldberg JA, Robertson J, Sutherland GR, Hemingway DM, Cooke TG, McArdle CS. Detection of hepatic metastases using duplex/colour doppper sonography. Ann Surg. 1991 Nov;214(5):599-604**

30. **Liang P, Cao B, Wang Y, Yu X, Yu D, Dong B, Differential diagnosis of hepatic cystic lesions with gray-scale and colour Doppler sonography. J Clin Ultrasound. 2005 Mar-Apr;33(3):100-5**

31. **Lin ZY, Wang LY, Wang JH, Lu SN, Chen SC, Chuang WL, Heish MY, Tsai JF, Chang WY. Clinical utility of colour Doppler sonography in the differentiation of hepatocellular carcinoma, metastases and hemangioma. J Ultrasound Med.1997 Jan;16(1):51-8**

32. **Lopez Cano A, Munoz Benvenuty A, Herrera MD, Analysis of doppler signal (colour and pulsed) in hepatocarcinoma. Gastroenterology Hepatology, 1997 Oct;20(8):387-90**

33. **Margulis and Burhenne's, Alimentary tract radiology , 5th edition, Vol 2,1440-1732**

34. **McArdle CR: Ultrasonic appearances of a hepatic hemangioma. J Clin Ultrasound 1978 Apr; 6(2): 124**

35. **Morimoto Y, Kubo S, Shuto T, Tanaka H, Power Doppler ultrasonographic diagnosis of small hepatocellular caracinomas. Dig surg, 2002;19(5):379-87;**

36. **Nino-Murcia M, Ralls PW, Jeffrey RB Jr, Johnson M, Colour flow Doppler characterization of focal hepatic lesions. AJR Am J Roentgenol. 1992 Dec;159(6):1195-7**

37. **Numuta K, Tanaka K, Kiba T, Morimoto M, Arata S, Kondo M, Sekihara H, Use of hepatic tumor index on colour Doppler sonography for differentiating large hepatic tumors. AJR Am J Roentgenol.1997 Apr;168(4):991-95**

38. **Numuta K, Tanaka K, Kiba T, Saito S, Kirikoshi H, Morita K, Shimamura T, Sekihara H, Correlation between hepatic tumor index on colour Doppler sonography and tumor vessels on arteriography in large hepatocellular carcinomas. Cancer Detect Prev.1999;23(6):496-505.**

39. **Numuta K, Tanaka K, Mitsui K, Morimoto M, Inoue S, Yonezawa H, Flow characteristics of hepatic tumors at colour Doppler sonography: Correlation with arteriographic findings. AJR Am J Roentgenol.1993 Mar;160(3):515-21**

40. **Oguma M, Kawano M, Monma T, Analysis of blood flow in hepatic tumors byt colour Doppler Ultrasonography. Nippon Shokakibyo Gakki Zasshi. 1994 Mar;91(3):279-86**

41. **Ohnishi K, Nomura F, Ultrasonic Doppler studies of hepatocellular carcinoma and comparison with other hepatic focal lesions. Gasterenterology.1989 Dec;97(6):1489-97**

42. **Paul L. Allan, Paul A. Dubbins, Myron A. Pozniak, Norman Mcdicken, Clinical doppler ultrasound, 123-160**

43. Rafaelsen SR, Solvig J, Ultrasound imaging of flow patterns in liver meatstases from colorectal cancer. Scand J Gasteroenterol. 2004 Aug;39(8):761-5

44. Ralls PW, Johnson MB, Lee KP, Radin DR, Halls J, Colour Doppler sonography in hepatocellular carcinoma. Am J Physiology Imaging.1991;6(2):57-61

45. Richard M. Gore, Marc S. Levine, Text book of gastrointestinal radiology, 2nd edition, Vol 2,1416-1568

46. Rydzewski B, Dehdashti F, Gordon BA: Usefulness of intraoperative sonography for revealing hepatic metastases from colorectal cancer in patients selected for surgery after undergoing FDG PET. AJR Am J Roentgenol 2002 Feb; 178(2): 353-8

47. Shimamoto K, Sakuma S, Ishigaki T, Ishiguchi T, Itoh S, Fukatsu H, Hepatocellular carcinoma: evaluation with colour Doppler US and MR imaging. Radiology.1992 Jan;182(1):149-53

48. Shirato K, Numata K, Mitsui K, Kitamura T, Morita K, Saito S, Morimoto M, Kiba T, Okazaki H, Tanaka K, Sekihara H, Colour Doppler sonography for evaluating response to transcatheter arterial embolization and percutaneous ethanol injection therapy and for detecting recurrence of hepatocellular carcinoma. J Ultrasound Med.2000 Dec;19(12):807-14

49. Srivastava DN, Mahajan A, Berry M, Sharma MP, Colour Doppler flow imaging of focal hepatic lesions. Australas Radio.2000 Aug;44(3):285-9

50. Strunk H, Stuckmann G, Frolich E, Textor J, Wilhelm K, Hortling N, Remig J, Native and signal-enhanced power Doppler sonography for characterization of liver lesions. Rofo.1998 Apr;168(4):344-51

51. Tanaka S, Kitamura T, Fujitha M, Nakanishi K, Okuda S, Colour doppler flow imaging of liver tumors. AJR Am J Roentgenol.1990 Mar;154(3):509-14

52. Tang J, Colour doppler flow imaging and duplex doppler in the examination of primary liver cancer. Zhonghua Zhong Liu Za Zhi 1992 Mar;14(2):138-40

53. Taylor KJ, Ramos I, Carter D, Morse SS, Correlation of doppler US tumor signals with neovascular morphologic features. Radiology 1998 Jan;166,57-62

54. Wang WP, Xu ZZ, Shen SC, Combined colour Doppler and pulsed Doppler in the diagnosis of small hepatocellular carcinomas, Zhounghua Wai Ke Za Zhi. 1994 Aug;32(8):474-6

55. Wang YF, Zhang QP, A study of blood supply of liver tumors using duplex Doppler ultrasound and colour Doppler flow imaging. J Tongji Med Univ.1993;13(1):18-22.

56. **William J Zwiebel, Introduction to vascular ultrasonography, 5th edition, 513-528.**

57. **Xu J, Wu Y, She Z, Wang H, Feng X, Song H. Use of power Doppler sonography for differential diagnosis of small hepatocellular carcinoma and adenomatous hyperplastic nodule. Chin Med J 2003 Feb;116(2):212-4**

58. **Yashura K, Kimura K, Nakamura H, Uchibori T, Hirama M, New colour Doppler technique for detecting turbulent tumor blood flow: a possible aid to hepatocellular carcinoma diagnosis. Journal of clinical ultrasound 1997 May; 25(4):183-8.**

59. **Yashura K, Kimura K, Ohto M, Matsutani S, Ebara M, Tsuchiya Y, Saisho, Pulsed Doppler in the diagnosis of small liver tumors. Br J Radiol.1998 Oct61(730):898-902**

60. **Zhonghua zhoung Liu Za Zhi, Color doppler flow imaging and duplex doppler in the examination of primary cancer. 1992 Mar;14(2):138-40**

ABBREVIATIONS

CD	**-**	**Colour doppler**
CDFI	**-**	**Colour doppler flow imaging**
CDS	**-**	**Colour doppler sonogram**
CECT	**-**	**Contrast enhanced computed tomography**
CHAPSV	**-**	**Common hepatic artery peak systolic velocity**
CT	**-**	**Computed tomography**
CTA	**-**	**Computed Tomographic angiography**
CTAP	**-**	**Computed Tomographic arterio portography**
DUS	**-**	**Doppler ultrasound**
FNAC	**-**	**Fine needle aspiration cytology**
HCC	**-**	**Hepatocellular carcinoma**
HPE	**-**	**Histopathological examination**
ILF	**-**	**Intralesional flow**
ILPSV	**-**	**Intralesional peak systolic velocity**
MRI	**-**	**Magnetic resonance imaging**
PET	**-**	**Positron emission tomography**
PSV	**-**	**Peak systolic velocity**
TACE	**-**	**Transarterial chemoembolization**
TAE	**-**	**Transarterial embolization**
TI	**-**	**Tumor index**
US	**-**	**Ultrasound**
USG	**-**	**Ultrasonogram**

DOPPLER EVALUATION OF COMMON ADULT HEPATIC TUMORS MORE THAN 2 CM IN COMPARISON WITH HPE AND CECT

PROFORMA

Name **IP/OP NO:**

Age **Date**

Sex

Occupation

Address

Presenting Complaints

Abdominal pain

Lump

Loss of appetite, loss of weight

Fever

Ascites

Jaundice

Past History

Cirrhosis

HBV

HCV

H/O Primary

Surgery

Blood transfusion

Personal History

Smoker

Alcoholic

Vaccination against HBV

General Examination

Anaemia

Jaundice

Lymphadenopathy

Systemic Examination

Hepatomegaly

Splenomegaly

Ascites

Clinical Diagnosis

Investigation

AFP

Gray scale ultrasound

1)Lesion Size

2)Shape

3)Margins

4)Number

5)Location (right or left lobe, segments)

6)Echogenicity

7)Calcification

8)Adjacent vessel involvement(portal vein thrombus)

9)Bile duct dilatation

10)Liver echoes and architecture (cirrhotic liver)

11)Regional lymphadenopathy

12)Ascites

Colour doppler ultrasound

1)Intralesional flow pattern (pulsatile flow, continuous flow, basket pattern or spot pattern, central or peripheral flow)

2)Intralesional peak systolic velocity

3)Common hepatic artery peak systolic velocity

4)Tumor index (intralesional PSV/common hepatic artery PSV)

5)Portal vein involvement

HPE and CECT

Final conclusion

MASTER CHART

S.NO.	PATIENT NAME	AGE	SEX	CLINICAL PRESENTATION
	HCC			
1	MR.ELLAPPAN	75	1	2
2	MR.YACOB	65	1	5
3	MR.SUBBARAYAN	55	1	2
4	MR.MANOHARAN	35	1	5
5	MR.RAMASAMY	72	1	2
6	MR.MARI	48	1	5
7	MRS.SARASA	35	2	2
8	MRS.CHANDRA	50	2	5
9	MR.VENKATESAN	22	1	4
10	MR.VARADHAN	55	1	3
11	MR.SELVAM	49	1	5
12	MR.RANGARAJAN	60	1	4
13	MR.RAMASAMY	60	1	5
14	MRS.KALIYAMMAL	55	2	2
15	MRS.KUPPAMMAL	52	2	3
16	MR.MURUGAN	49	1	2
17	MRS.PENCILLAMMAL	52	2	5
18	MRS.RATHINAM	60	2	4
19	MR.KUPPUSAMY	52	1	5
20	MR.MEYYIAPPAN	48	1	2
21	MR.MUTHU	70	1	3
22	MR.KARUPPAN	44	1	5
23	MRS.CHINNAMMAL	48	2	4
24	MR.ANTHONY	52	1	2
25	MR.GOPAL	49	1	2

S.NO.	PATIENT NAME	AGE	SEX	CLINICAL PRESENTATION
	METASTASES			
26.	MR.PERUMAL	65	1	1
27.	MR.IBUNU	45	1	5
28.	MR.PETHODAN	85	1	4
29.	MRS.MARIAMMAL	55	2	1
30.	MRS.CHINNAPILLAI	62	2	2
31.	MR.SUBRAMANI	45	1	4
32.	MR.MUNIRATHINAM	28	1	3
33.	MRS.MURUGAMMAL	49	2	5
34.	MRS.KONDAMMAL	62	2	2
35.	MRS.KUMARIAMMAL	65	2	1
36.	MRS.ANGELMARY	50	2	2
37.	MR.MUNUSAMUY	65	1	4
38.	MR.RANGASAMY	71	1	3
39.	MRS.RATHINAMMAL	58	2	5
40.	MR.MANI	50	1	2
	HEMANGIOMA			
41.	MR.KALIMUTHU	70	1	1
42.	MRS.KUPPAMMAL	60	2	1
43.	MR.MURUGESAN	42	1	1
44.	MR.SURIYANARAYANAN	40	1	1
45.	MR.AYYAVU	52	1	1
46.	MRS.SUBBAMMMAL	45	2	1
47.	MRS.RAJI	42	2	1
48.	MRS.VEDAVALLI	30	2	1
49.	MR.KALIAPPAN	52	1	1
50.	MRS.KANDAMMAAL	49	2	1
51.	MR.MOORTHY	52	1	2

S.NO.	PATIENT NAME	AGE	SEX	CLINICAL PRESENTATION
52.	MR.MU8NUSAMY	72	1	2
53.	MRS.LAKSHMIAMMAL	59	2	1
54.	MRS.CHINNATHAYI	52	2	1
55.	MRS.LAKSHMI	35	2	1
56.	MRS.THANGAMANI	49	2	1
57.	MR.MARIAPPAN	60	1	1
58.	MRS.GOVINDAMMAL	62	2	2
59.	MR.KANDASAMY	62	1	1
60.	MRS.MURUGAMMAL	52	2	1
61.	MRS.KRISHNAVENI	68	2	1
62.	MR.CHELLAPPAN	60	1	1
63.	MRS.KANNIAMMAL	55	2	1

S.NO.	SIZE(cm)	LOCATION	USG	ILF	ILPSV(cm/s)	CHA PSV(cm/s)	TI	D+E	DEFG	HPE/CECT
HCC										
1.	5.2	1	5	3	80	68	2	1	1	1
2.	6.3	1	5	3	70	65	2	1	1	1
3.	4	1	3	3	95	73	2	1	1	1
4.	5.4	1	5	3	65	55	2	1	1	1
5.	7.2	1	1	3	110	84	2	1	1	1
6.	7.8	1	5	3	85	75	2	1	1	1
7.	6.4	2	5	3	98	85	2	1	1	1
8.	3.7	1	3	3	129	94	2	1	1	1
9.	6.3	1	1	3	55	62	1	1	1	1
10.	6.2	2	5	3	60	60	2	1	1	1
11.	4.8	1	5	3	73	65	2	1	1	1
12.	6.7	1	5	3	34	52	1	2	3	1
13.	8.3	2	3	3	120	95	2	1	1	1
14.	5.6	1	3	3	113	120	1	1	1	1
15.	5.4	1	1	3	30	64	1	2	3	1
16.	4.6	1	5	1	0	55	1	3	3	1
17.	9.1	1	1	3	120	100	2	1	1	1
18.	8.2	1	5	3	76	65	2	1	1	1
19.	5	1	3	3	68	62	2	1	1	1
20.	7.9	2	5	2	12	68	1	3	3	1
21.	5.8	1	1	3	49	65	1	1	1	1
22.	4.9	1	5	3	76	65	2	1	1	1
23.	6.1	1	3	3	84	77	2	1	1	1
24.	7.3	1	5	2	18	45	1	3	3	1
25.	7.8	1	1	3	110	96	2	1	1	1
26.	10.2	2	5	3	114	102	2	1	1	1
27.	6.4	1	3	3	89	75	2	1	1	1
28.	7.1	1	3	3	79	65	2	1	1	1
29.	4.9	1	3	3	69	63	2	1	1	1
30.	6	1	5	3	72	68	2	1	1	1

S.NO.	SIZE(cm)	LOCATION	USG	ILF	ILPSV(cm/s)	CHA PSV(cm/s)	TI	D+E	DEFG	HPE/CECT
METASTASES										
31.	3.1	1	1	1	0	85	1	2	2	2
32.	4.2	1	2	2	28	90	1	2	2	2
33.	2.1	2	1	3	34	86	1	2	2	2
34.	3.3	1	3	1	0	51	1	2	3	2
35.	3.2	1	1	2	28	104	1	2	2	2
36.	4.3	2	2	3	52	120	1	1	2	2
37.	2.2	1	3	3	15	94	1	2	2	2
38.	5.2	2	1	2	44	105	1	2	2	2
39.	2.6	1	3	2	12	88	1	2	2	2
40.	4.1	1	4	2	26	75	1	2	2	2
41.	2.2	1	5	2	16	90	1	2	2	2
42.	5.1	1	1	3	22	105	1	2	2	2
43.	4.4	1	2	3	35	120	1	2	2	2
44.	4.5	2	4	3	28	140	1	2	2	2
45.	2.8	1	1	2	15	65	1	2	3	2
46.	4	1	2	2	22	114	1	2	2	2
47.	4.2	1	1	2	11	95	1	2	2	2
48.	2.3	1	1	2	24	130	1	2	2	2
49.	4.6	2	2	3	56	175	1	1	2	2
50.	6.3	1	3	3	37	144	1	2	2	2
51.	3	1	1	1	0	45	1	3	3	2
52.	4.4	1	1	3	62	48	2	1	1	2
53.	5.3	2	1	2	14	114	1	2	2	2
54.	3.1	1	2	2	8	96	1	2	2	2
55.	2.1	1	5	3	22	124	1	2	2	2
56.	3.7	2	2	3	18	145	1	2	2	2
57.	3.9	1	4	3	32	128	1	2	2	2
58.	3.2	1	3	2	19	96	1	2	2	2
59.	3.8	1	2	3	24	133	1	2	2	2
60.	3.7	2	2	3	32	195	1	2	2	2
61.	2.5	1	4	3	22	166	1	2	2	2

S.NO.	SIZE(cm)	LOCATION	USG	ILF	ILPSV(cm/s)	CHA PSV(cm/s)	TI	D+E	DEFG	HPE/CECT
62.	2.9	1	5	2	14	103	1	2	2	2
HEMANGIOMA										
63.	2.2	1	3	2	8	55	1	3	3	3
64.	3.1	1	5	2	12	86	1	2	3	3
65.	3.2	1	3	1	0	52	1	3	3	3
66.	2.8	1	3	2	9	62	1	3	3	3
67.	2.2	1	3	3	45	65	1	1	2	3
68.	4.6	1	3	1	0	60	1	3	3	3
69.	3.1	1	3	2	18	55	1	3	3	3
70.	2.8	1	3	3	58	52	2	1	1	3
71.	3.2	1	3	2	22	59	1	3	3	3
72.	4.1	2	3	2	14	62	1	3	3	3
73.	2.3	1	3	1	0	56	1	3	3	3
74.	3.1	1	5	2	22	64	1	3	3	3
75.	4.2	1	3	2	28	61	1	3	3	3
76.	6.4	1	3	3	59	45	2	1	1	3
77.	2.7	2	5	2	28	62	1	3	3	3
78.	4.3	1	3	2	11	55	1	3	3	3
79.	2.8	1	5	1	0	45	1	3	3	3
80.	2.5	2	3	2	17	52	1	3	3	3
81.	5.2	1	3	2	22	51	1	3	3	3
82.	2.6	1	3	1	0	49	1	3	3	3
83.	2.9	1	3	1	0	62	1	3	3	3
84.	3.1	1	3	3	28	65	1	3	3	3
85.	2.4	2	5	3	32	69	1	3	3	3
86.	3.1	1	3	2	21	54	1	3	3	3
87.	2.4	1	3	2	18	56	1	3	3	3
88.	4.2	1	3	2	22	57	1	3	3	3

KEY TO MASTER CHART

1) Location

Right lobe - 1

Left lobe - 2

2) USG

Hypoechoic - 1

Isoechoic - 2

Hyperechoic - 3

Calcified - 4

Mixed - 5

3) ILF (Intra lesional flow)

No flow - 1

Continuous flow - 2

Pulsatile flow - 3

4) TI (Tumor index)

Less than one - 1

Greater than or equal to one - 2

5) HPE/CECT

HCC - 1

Metastases - 2

6) Sex

Male - 1

Female - 2

7)Clinical Presentation

Asymptomatic - 1

Abdominal pain - 2

Constitutional symptoms - 3

Lump - 4

Ascites