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Comparison of CT Portography and Color Doppler Ultrasound for Detection of Varices in Cirrhotic Patients

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Abstract
Background: *Cirrhosis is the end result of all chronic liver disease. Most common cause of death in cirrhosis patient is upper gastrointestinal tract bleeding due to development of esophageal varices. Diagnosis of portosystemic collaterals by non-invasive techniques will help to avoid potential complications during interventional procedures and surgery.*
Aim of the Study: *To compare diagnostic efficacy of CT Portography and Color Doppler Ultrasound for detection of varices in cirrhotic patients.*
Materials and Methods: *A cross sectional study including 45 patients who presented at medical gastroenterology department with liver cirrhosis based on symptoms and laboratory values from March 2018 to February 2019. Firstly Color Doppler US was performed using GE-Logic S7 and selection of transducer and gain settings varied in each case for optimum demonstration of portal venous anatomy, pathology and venous collaterals. CT was performed with a Toshiba Aquilion Lightning MDCT and Portography images were obtained using the Work Station. All the patients were subjected to Endoscopy and findings were compared with USG and CT using Pearson's Coefficient test.*
Statistical Analysis Used: *Statistical analysis for comparing collateral detection was performed using McNemars tests and measurement of agreement was done using Kappa Coefficient.*
Results: *Of the 45 patients 13, 7, 19 & 6 patients had no varices and Grade I/ II & III oesophageal varices respectively. USG was able to detect 4/6 Grade III varices and Grade I / II varices were not detected in USG. CT detected all 19 cases of grade II varices and 6 cases of Grade III varices. There was strong agreement (Kappa values >0.7) between USG and CT for diagnosis of paraesophageal, splenorenal, anterior abdominal wall, peri-umbilical and peri-cholecystic collaterals. There was no agreement for detection of esophageal , gastric mucosal, perigastric and retroperitoneal collaterals between USG and CT.*
Conclusion: *USG detects Grade III varices and CT detects Grade II and III varices. CT is better for delineation of all portosystemic collaterals compared to USG. USG is inferior to MDCT portal venous phase in delineating complex collateral pathways. Multislice CT can detect potentially problematic varices by detailing the course of tortuous vessels which is important in liver transplantation surgeries for detection of unexpected varices that can result in significant bleeding.*
Keywords: *CT Portography, Color Doppler USG, Varices, Liver cirrhosis*
Keymessage: *MDCT portography can detect problematic varices by detailing the tortuous vessels which is essential in liver transplantation surgeries for detection of unexpected varices that can result in torrential bleeding. CT Portography images can replace the endoscope in the detection of problematic varices.*

Introduction

Chronic liver disease and portal hypertension are common clinical encounters. Liver disease continues to account for substantial proportion of health care utilization in India and particularly Tamil Nadu and is an important cause of morbidity. Cirrhosis related death is estimated to increase and expected to be the 12th leading cause of death in 2020[(1)]. Cause of cirrhosis varies in different parts of the World with Hepatitis C virus infection and alcoholism predominating in Western countries and Hepatitis B in Asia and Africa. In India , alcoholism is the most common cause of cirrhosis while Hepatitis B is the cause of chronic liver disease in general and non-cirrhotic chronic liver disease[(2)]. It is important to identify the patients with high risk of complications of chronic liver disease. Portal hypertension is a common end result of chronic liver disease. Elevated hydrostatic pressure within the portal vein or its tributaries manifesting as increase in pressure gradient between portal vein and hepatic vein or inferior vena cava is termed as portal hypertension[(3)]. Development of portal hypertension and hyperdynamic circulation is the ultimate end result in cirrhotic patients leading to significant morbidity and mortality[(4)]. Lifetime incidence of esophageal varices in cirrhotic patients is 80–90% and about one third of patients with esophageal varices develop variceal bleeding, leading to high morbidity and mortality. This demands understanding of the natural course of chronic liver disease, pathophysiology of development of portosystemic collaterals (Figure 1), imaging modalities and laboratory investigations for diagnosis of portal hypertension. Such clinical knowledge would permit early interventions and may alter the course of patients with portal hypertension towards a favorable outcome. Hence, there is a need to develop a non-invasive reliable imaging technique for diagnosis and assessment of portal hypertension.

The accurate incidence and prevalence of liver cirrhosis is difficult to ascertain because liver cirrhosis is a dynamic process that is clinically silent. Most common cause of death in cirrhosis patient is upper gastrointestinal tract bleeding due to development of esophageal varices. We must be aware of the normal sonographic and CT anatomy of the portal and systemic circulation to understand the various collateral pathways (Figure 1). Understanding the anatomy of portosystemic collaterals will help to avoid potential complications during interventional procedures and surgery. The normal sites of portosystemic anastomoses are tabulated as follows (Table 1).

This study is aimed to compare USG and CT Portography for detection of varices in cirrhotic patients.

Materials and Methods

This is a cross sectional study and institutional ethical committee approval obtained. The study subjects were patients who presented at the medical gastroenterology department of Government Kilpauk Medical College Hospital with liver cirrhosis based on clinical symptoms and laboratory values. Subjects were selected consecutively from March 2018 to February 2019 and 45 patients have been included. All eligible patients were briefed on the study procedure.

Inclusion criteria

- Patients with decompensated liver cirrhosis due to any etiology.

Exclusion criteria

- Severe hematemesis.
- Previous history of allergy to contrast agents.
- Renal failure patients / Hepato-renal syndrome.
- Refusal to participate in the study

Study design

Color Doppler Ultra Sound was performed using GE-Logic S7 machine using a curvilinear transducer probe. Scans were obtained along sagittal and transverse axis and in supine and right lateral decubitus positions. Selection of transducer and gain settings varied in each case for optimum

demonstration of portal venous anatomy and pathology.

CT was performed with a multidetector Toshiba Aquilion Lightningin the Government Kilpauk Medical College Hospital.

Patient Preparation

(1) Patients in fasting 6 hours before scan.
(2) No oral contrast was used.
(3) GFR had to be at least 90 ml/min.
(4) The patients were adequately hydrated with water up to 2 litres.
(5) An intravenous cannula was introduced through accessible vein in upper limb.

Patient Position

(1) In supine position, using the scout image scanning was done from base of lungs to pubic symphysis in all phases.
(2) Pre-contrast images was taken at 5 mm thickness, at a slice pitch of 1.5, a gantry rotation period of 0.9s, and a table speed of 15 mm/ rotation. The X-ray tube voltage was 120 kV, and current was 150 mA.
(3) Images using a MDCT scanner were taken in the arterial, portovenous, and delayed phases for all patients. All patients received 100 ml of low osmolar nonionic iodinated material (Omnipaque 350) introduced at an infusion rate of 3-5 ml/s intravenous using a single power injector.
(4) Arterial phase images were acquired at 18 s, portal phase images were acquired at 60 s and delayed-phase images were also taken of the entire liver at 200 s

All the data acquired were reconstructed and post processed on the workstation equipped with software for generation of 3D images. The Portography and portal venous phase images were analyzed for the presence of collaterals and their sites were recorded.

Dilated veins within and outside the wall of distal esophagus are called as Esophageal (Figure 2)and ParaesophagealVarices respectively. Esophageal varices are evidenced by nodularity and protrusion into the esophageal lumen. Dilated veins present in the submucosal layer of the stomach are Gastric Mucosal Varices (Figure 3). Dilated veins surrounding the stomach are Perigastric Collaterals (Figure 4). Enhancing tortuous vessels around the gall bladder (Figure 5).Veins along the spleen and left kidney were termed as Splenorenal Collaterals (Figure 6). Recanalizedparaumbilical vein is seed dilated at ligamentumteres and falciform ligament level. Dilated veins along the anterior abdominal wall and around the umbilicus were called as Anterior Abdominal and Periumbilical Collaterals respectively.

All patients included in the study were subjected to endoscopy and the varices were graded by modified Paquet classification[4] as follows.

Grade I – Varices extending just above the mucosal level.

Grade II – Varices projecting by one third of the luminal diameter that cannot be compressed with air insufflations.

Grade III – Varices projecting upto 50 % of the luminal diameter and in contact with each other.

Statistical Analysis and Results

Data were collected, recorded, coded and processed using SPSS software and statistical tests were applied. Results were collected, tabulated, and statistically analyzed. McNemar test used to determine the difference between USG and CT Portography for detection of varices in cirrhotic patients. Cohens Kappa is used to estimate the level of agreement between USG and CT Portography. The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and diagnostic accuracy were calculated between USG and CT for each type of collaterals. Non parametric chi square test was used to determine the relation between USG and different endoscopic grading and CT and different endoscopic grading.

Out of 45 patients, 33 patients had esophageal varices of different grades in endoscopy. Endoscopy detected seven grade I varices, nineteen grade II varices and six grade III varices

in a study population of forty five patients. USG was able to detect 4/6 Grade III varices and Grade I / II varices were not detected in USG. CT detected all 19 cases of grade II and 6 cases of grade III varices (Table 2). Grade I / II varices were not detected in USG. One case without varices in endoscopy was found to have varices in CT. This is attributed to better visualisation of mucosal nodularity and contrast enhancement in CT portography.USG detects Grade III varices and CT detects Grade II and III varices.Bar diagram, illustrates that out of four grade III varices detected in endoscopy, ultrasonogram diagnosed only one case (Table 3). Grade I and Grade II varices were not detected on ultrasonogram.

The following table (Table 4) depicts the number of collaterals detected in Color Doppler USG and CT portography and the level of agreement between the two imaging modalities. USG detected only 4 cases of varices and CT detected 28 varices. There was no agreement between USG and CT Portography with a Kappa value of 0.112. USG has very low sensitivity (14.29%) for detection of esophageal varices compared to CT Portography. Out of 28 cases detected in CT portography, only 4 cases were diagnosed in ultrasound Color Doppler.

18 out of 45 patients had para-esophageal collaterals. USG detected 13/18 cases (72.22%) and CT detected 18/18 cases (100%). There was a good agreement between USG and CT detection for detection of para esophageal varices with a Kappa value of 0.757. Comparing USG to CT portography had a sensitivity and specificity of 72.2% and 100% respectively.

10 out of 45 patients had gastric mucosal varices. USG detected 3/10 cases (30%) and CT detected 18/18 cases (100%). There was no strong agreement between USG and CT detection for detection of gastric mucosal varices with a Kappa value of 0.4.

24 out of 45 patients had perigastric collaterals in CT. USG detected 9/24 cases (37.5%). There was a poor agreement between USG and CT detection for detection of perigastric collaterals with a Kappa value of 0.359. The diagnostic accuracy comparing USG to CT is only 66.6%. Sensitivity and specificity is 37.5 and 100% respectively.

Out of 30 cases of splenorenal collaterals detected in CT, USG was to detect 29 cases and has a strong agreement with CT with a Kappa value of 0.9.

Out of 45 patients, 10 patients had retroperitoneal collaterals in CT. USG could not detect any retroperitoneal collaterals due to poor penetration of sound waves.

Out of 34 cases of periumbilical collaterals detected in CT, USG was able to detect 32 cases and has a strong agreement with CT with a Kappa value of 0.887.

Out of 36 cases of anterior abdominal wall collaterals detected in CT, USG was able to detect 34 cases and has a strong agreement with CT with a Kappa value of 0.872.

Out of 18 cases of pericholecystic collaterals detected in CT, USG was to detect 13 cases and has a strong agreement with CT with a Kappa value of 0.757.

The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and diagnostic accuracy of USG compared to CT is depicted in Table 5.

SITE	PORTAL COMPONENT	SYSTEMIC COMPONENT
Lower esophagus	Left gastric vein	Esophageal vein
Rectum and Anal Canal	Superior rectal vein	Middle and Inferior rectal Vein
Umbilicus	Para Umbilical Vein	Superior and Inferior epigastric vein
Bare area of liver	Portal venous branches	Inferior phrenic and right internal thoracic vein
Retroperitoneum	Tributaries of splenic and pancreatic and colic veins	Renal, suprarenal, para vertebral and gonadal vein
Patent ductus venosus (rare)	Left branch of portal vein	Inferior vena cava (IVC)

Table 1: Normal sites of portosystemic anastomoses

OESOPHAGEAL VARICES – CT & USG VS ENDOSCOPY					
CT & USG VS ENDOSCOPY			CT & USG		
			NEGATIVE	POSITIVE	TOTAL
ENDOSCOPY	NO VARICES	COUNT (CT)	12 (26.7)	1(2.2)	13 (28.9)
		COUNT (USG)	13 (28.9)	0	13(28.9)
	GRADE I	COUNT (CT)	5 (11.1)	2 (4.4)	7 (15.6)
		COUNT (USG)	7 (15.6)	0	7 (15.6)
	GRADE II	COUNT (CT)	0	19 (42.2)	19 (42.2)
		COUNT (USG)	19 (42.2)	0	19 (42.2)
	GRADE III	COUNT (CT)	0	6 (13.3)	6 (13.3)
		COUNT (USG)	2 (4.4)	4 (8.9)	6 (13.3)
	TOTAL	COUNT (CT)	17 (37.8)	28 (62.2)	45 (100)
		COUNT (USG)	41 (91.1)	4 (8.9)	45 (100)

Table 2: Comparison of different grades of Oesophageal varices classified on endoscopy, detected in CD USG and CT Portography.

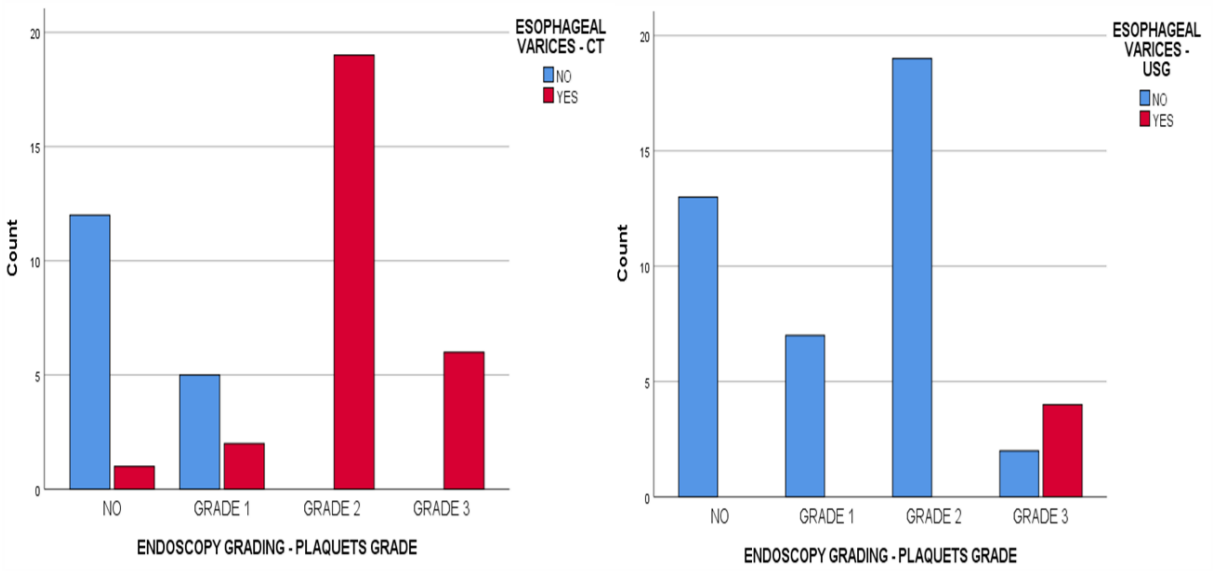

Table 3: Bar diagram showing the grading of oesophageal varices in endoscopy (Paquet grade) and those detected in CT and CD USG.

S.NO	VARICES	Color Doppler	CT PORTOGRAPHY	CT vs CD			KAPPA VALUE	DEGREE OF AGREEMENT
		Postive	Positive	Positive in both	CD only	CT only		
1	Oesophageal varices	4 (8.9)	28(62.2)	28(62.2)	0	24(53.3)	0.112	Poor
2	Para Oesophageal Collaterals	13 (28.9)	18 (40)	18 (40)	0	5 (11.1)	0.757	Substantial
3	Gastric Mucosal Varices	3 (6.7)	10 (22.2)	10 (22.2)	0	7 (15.6)	0.54	Moderate
4	Perigastric collaterals	9 (20)	24 (53.3)	24 (53.3)	0	15 (33.3)	0.359	Fair
5	Splenorenal collaterals	29 (64.3)	30 (66.5)	30 (66.5)	0	1 (2.2)	0.903	Perfect
6	Pericholecystic collaterals	13 (28.9)	18 (40)	18 (10)	0	5 (11.1)	0.757	Substantial
7	Retroperitoneal Collaterals	0	10 (22.2)	0	0	10 (22.2)	-	-
8	Periumbilical Collaterals	32 (71.1)	34 (75.6)	34 (75.6)	0	2 (4.4)	0.887	Perfect
9	Anterior Abdominal Wall Collaterals	34 (75.6)	36 (80)	36 (80)	0	2 (4.4)	0.872	Perfect
Kappa interpretation: <0-No agreement, 0.0 to 0.2 - Slight agreement, 0.21 to 0.40 - Fair agreement, 0.41 to 0.60 - Moderate agreement, 0.61 to 0.80 - Substantial agreement, 0.81 to 1.0 - Perfect agreement								
Values in the brackets indicate the percentage of total								

Table 4: Degree of agreement between Color Doppler USG (CD) vs CT Portography (CT) for different portosystemic collaterals

S.No	Varices	Sensitivity	Specificity	PPV	NPV	Diagnostic accuracy
1	Oesophageal varices	14.29	100	100	41.46	46.67
2	Para Oesophageal Collaterals	72.22	100	100	84.38	88.89
3	Gastric Mucosal Varices	30	100	100	83.33	84.44
4	Perigastric collaterals	37.5	100	100	58.33	66.67
5	Splenorenal collaterals	65.12	50	96.5	6.25	64.44
6	Pericholecystic collaterals	32.5	100	100	15.63	40
7	Retroperitoneal Collaterals	-	-	-	-	-
8	Periumbilical Collaterals	94.12	100	100	84.62	95.56
9	Anterior Abdominal Wall Collaterals	79.07	100	100	18.18	80

Table 5: Sensitivity, specificity, PPV, NPV and diagnostic accuracy of USG vs CT for different portosystemic collaterals

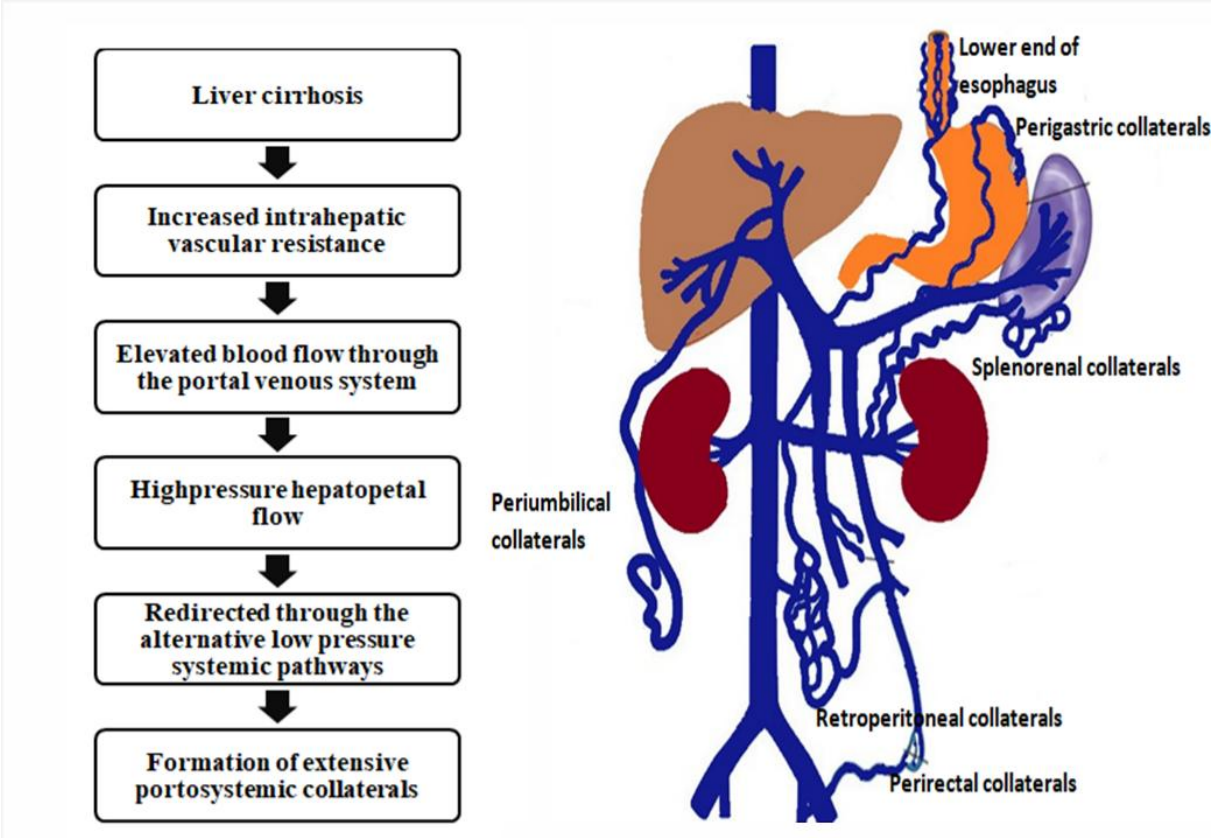

Figure 1: Pathophysiology of development of collaterals in portal hypertension and different sites of portosystemic collaterals.

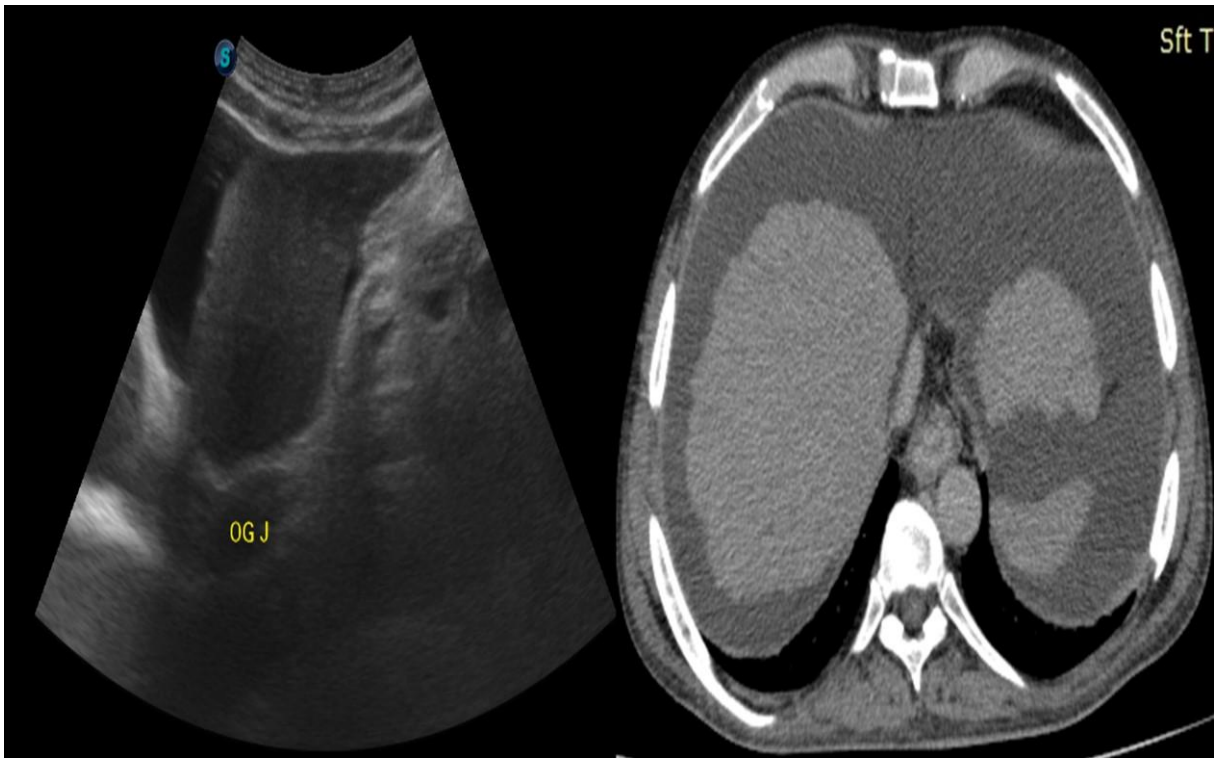

Figure 2: 47 years old male presenting with hematemesis and abdominal distension. Longitudinal USG showing normal OG junction. Axial CT image shows shrunken liver with nodular surface and gross ascites. Multiple nodular enhancing protrusions noted in oesophageal wall consistent with Grade I varices on endoscopy – OESOPHAGEAL VARICES.

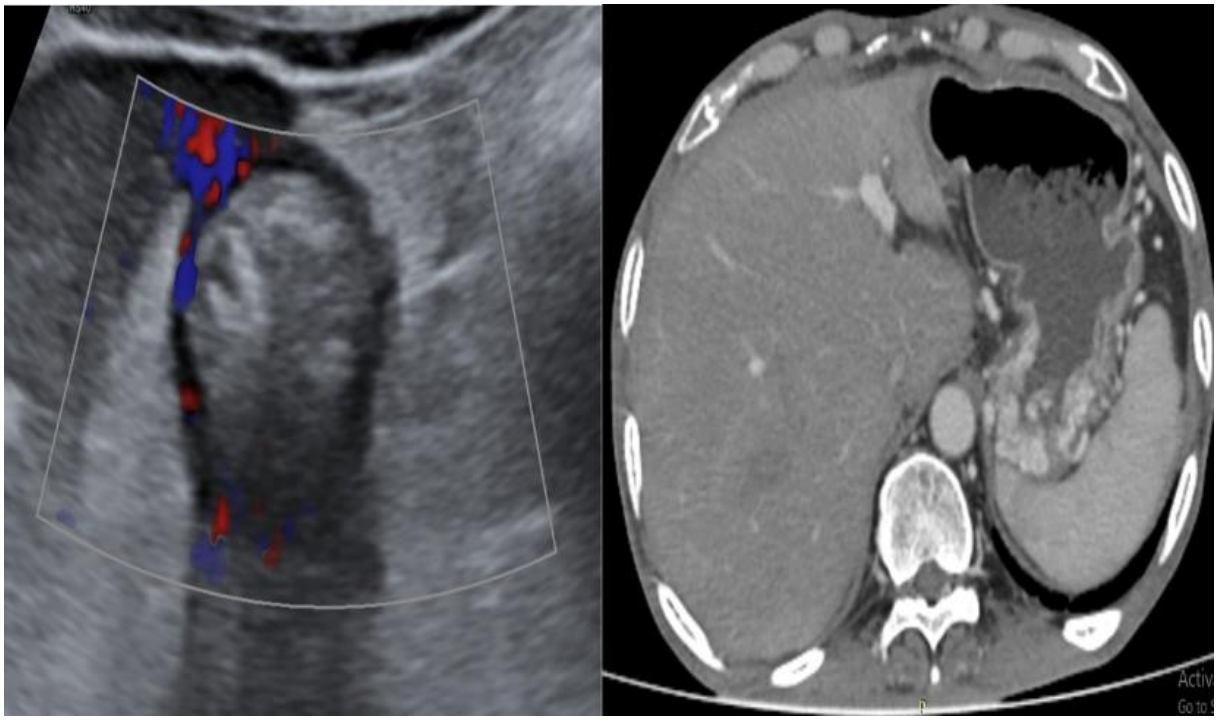

Figure 3: 56 years old male patient, chronic alcoholic presented with two episodes of hematemesis. Axial Doppler flow study showing the presence of large caliber, tortuous vessels in stomach wall. Axial CT portal venography images shows serpiginous collaterals in gastric wall- GASTRIC MUCOSAL VARICES.

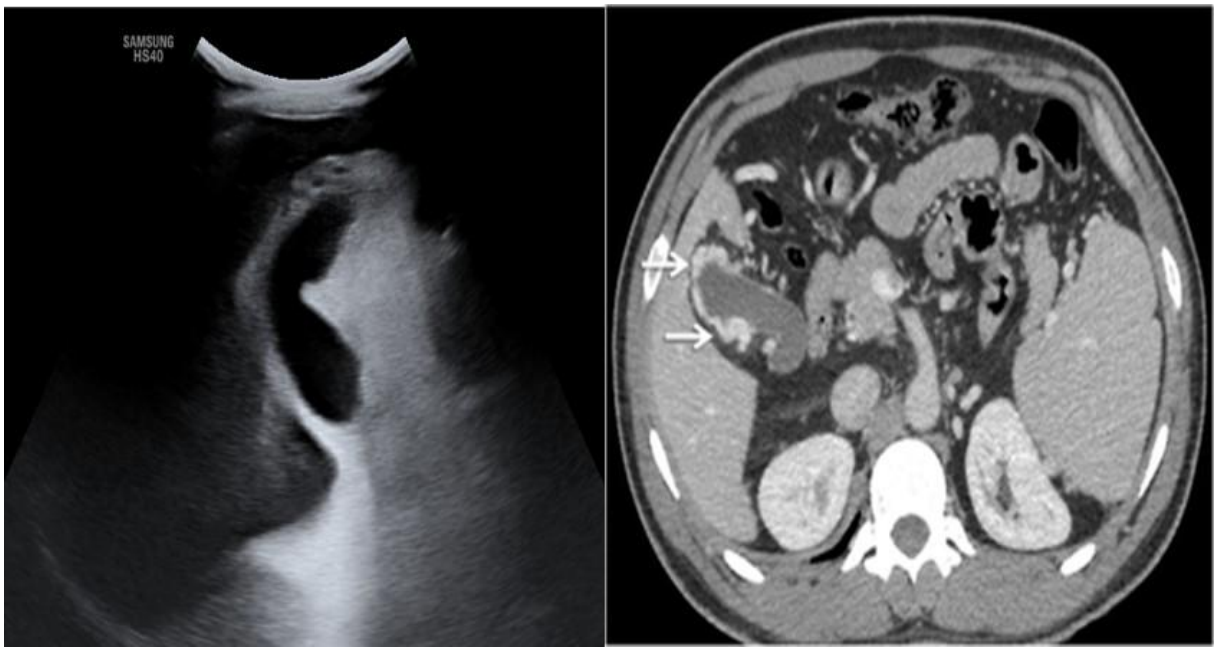

Figure 4: 55 years old male chronic alcoholic patient presenting with vague abdominal discomfort, breathlessness and loss of weight. Longitudinal Doppler flow study showing the presence of tortuous vessels in the pericholecystic region. Axial CT image shows mildly enlarged spleen with multiple serpiginous pericholecystic collaterals. – PERICHOLECYSIC COLLATERALS

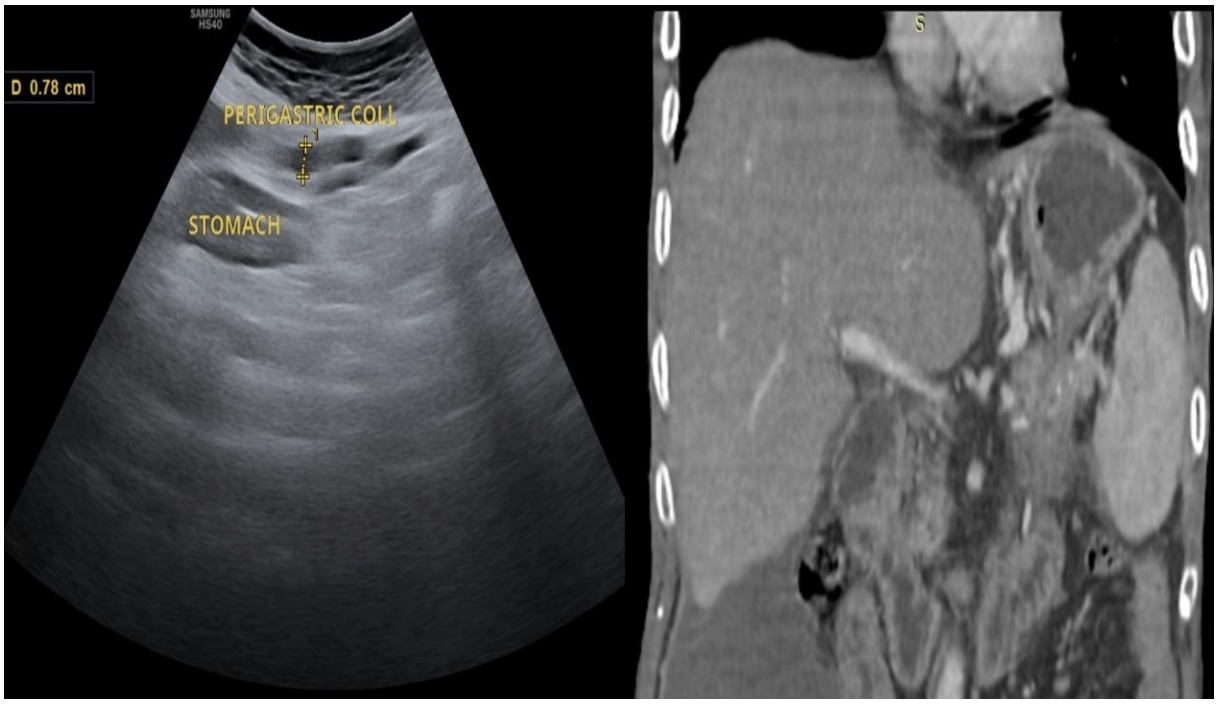

Figure 5: 58 years old chronic alcoholic male patient presented with abdominal distension and one bout of hematemesis. Axial grey scale ultrasound using low frequency probe shows dilated perigastric collaterals. CT Portal Venography in the same patients the perigastric collaterals in addition to ascites and enlarged nodular liver – PERI GASTRIC COLLATERALS.

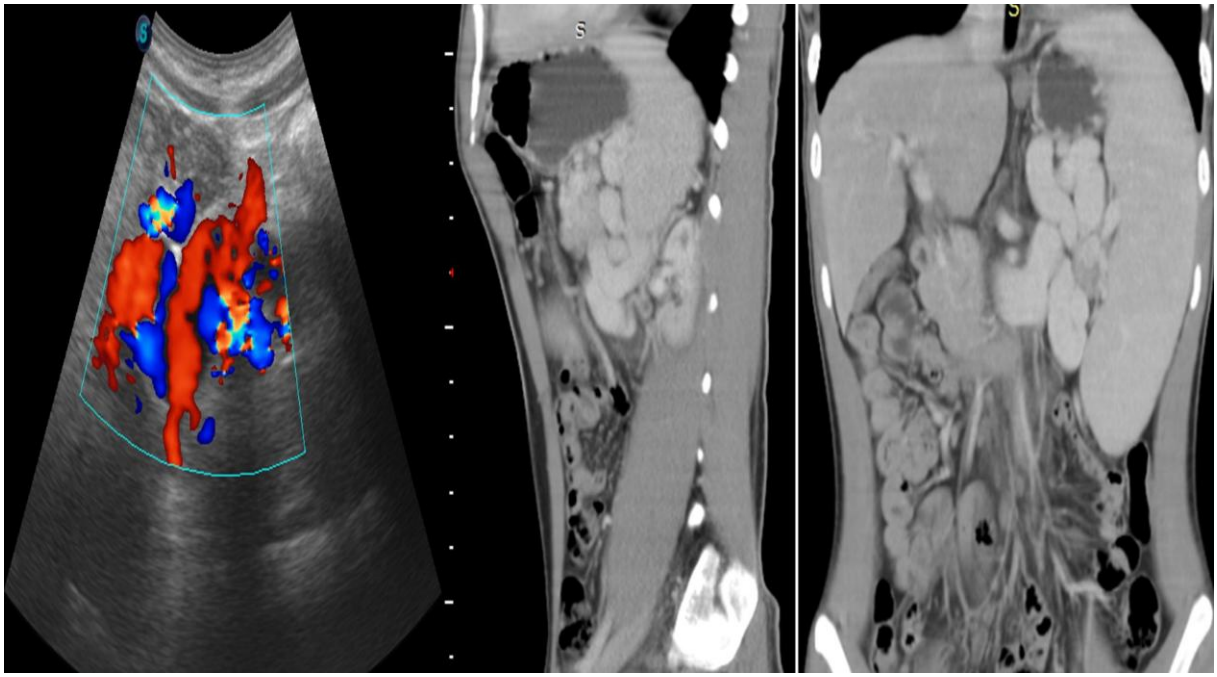

Figure 6: 38 years old male patient presented with abdominal pain and shortness of breath. Longitudinal Doppler flow study showing the presence of large caliber, tortuous vessels between the left kidney and spleen. Coronal and Sagittal CT images shows enlarged spleen with multiple serpiginous collaterals between spleen and left kidney – SPLENO RENAL COLLATERALS.

Discussion

In our study, most of the patients included were between 40 to 60 years (53.3%) of age. The cause of cirrhosis in most cases was either chronic alcoholism or chronic hepatitis infection. Other causes include non alcoholic fatty liver disease,

Wilson's disease and extra hepatic portal venous obstruction. 2 out of 45 patients had no identifiable cause and were included in cryptogenic cirrhosis category.

The following sites were evaluated for presence of varices in USG and CT. Distal esophagus, paraesophageal, perigastric, gastric mucosal, splenorenal, anterior abdominal wall, periumbilical, retroperitoneal and pericholecystic regions were studied.

FengHua Li et al[5] stated that duplex Doppler has no value in identification of cirrhosis patients with potential for variceal bleeding. In his study, PV and LGV haemodynamic only were evaluation in both study an control groups. He concluded that endoscopy is the best modality followed by PV haemodynamics. This was in contrary to our study in which Color Doppler Ultrasound was able to detect higher grade esophageal varices and hence can serve as an initial modality for evaluation in cirrhosis patients.

Zhang et al[6] in his study in 286 patients stated that trans abdominal USG can be used as a routine non invasive method for prediction of esophageal varices. He simply correlated the diameter of the spleen and PV haemodynamics with endoscopic findings and gave USG grading of the varices.

In most of the studies for evaluation of esophageal varices, direct assessment of varices in the esophageal wall was not done. Most of the researchers preferred to use parameters like PV velocity, diameter, spleen diameter, spleno portal index, splenic vein diameter, LGV hemodynamic, thickness of distal esophagus and platelet count. In our study attempt was made to directly visualize the varices in esophageal wall and it was found that USG was able to detect 4/6 Grade III esophageal varices correctly in a study population of 45 patients. Hence USG can be used a modality for detection of higher grade varices in decompensated cirrhosis patients. USG color Doppler also had strong agreement with CT portal venography for detection of splenorenal, anterior abdominal wall, periumbilical. Paraesophageal and pericholecystic collaterals.

In agreement with our study, **Young Jun Kim et al**[4] showed in his study of 67 patients with liver cirrhosis that MDCT has sensitivity, specificity and accuracy for identifying large from small or no esophageal varices were 92%, 84% and 85% respectively. However the overall sensitivity for detection of varicieswere less than 70% due to poor detection of small varices.

Our study is in agreement with **Cho et al**[7] demonstration of varices in CT may be more accurate than with angiography, ultrasound, or endoscopy. Only exception is for esophageal varices, for which CT is relatively insensitive according to Cho et al. In our study CT is effective for Grade II and Grade III esophageal varices.

A study by **Perri et al**[8] showed that CT is 90% sensitive for detection of larger endoscopic varices and 87% sensitive for gastric varices detection. This is in concordance with our study stating that abdominal CT may be the initial investigation for varices detection and could be cost effective compared to endoscopy.

Nam C Yu et al[9] in a study with 109 cirrhotic patients proved that standard MDCT is sensitive for detection of higher grade varices and it can be used as a potential effective screening tool for evaluation of CLD patients.

Conclusion

Liver cirrhosis complicated by portal hypertension is a commonly encountered clinical syndrome in current day practice. USG is a first line, non expensive, radiation free and easily available investigation for evaluation in liver cirrhosis. However USG is inferior to MDCT portal venous phase in delineating complex collateral pathways. It is of prime importance to report these esophageal varices and other collaterals to avoid potential accidental vascular injury during intervention.

MDCT Portography has better agreement for detection of esophageal varices identified by

endoscopy. CT is able to detect all higher grade II and III esophageal varices and other portosystemic collaterals with higher accuracy compared to USG. CT Portography can be used for evaluation of collaterals in cirrhotic patients in addition to its role in detecting the early HCC and follow up of malignant transformation of nodules.

MDCT portography can detect problematic varices by detailing the tortuous vessels which is essential in liver transplantation surgeries for detection of unexpected varices that can result in torrential bleeding. CT Portography images can replace the endoscope in the detection of problematic varices

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